

Supplemental Appendix

AKI Treated with Renal Replacement Therapy in Critically Ill Patients with COVID-19



Study of the Treatment and Outcomes in critically ill
Patients with COVID-19

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SUPPLEMENTAL METHODS

Data Collection and Validation

Data were collected by both medical doctors and research coordinators and were entered into a secure, HIPAA-compliant, web-based application (REDCap). Wherever possible, data were captured using checkboxes rather than manual entry to minimize keystroke errors. For data that required keystroke entry (e.g., laboratory values), we implemented validation ranges to flag potential errors in real-time. We also implemented automated data validation rules to flag errors in dates (e.g., if the date of death was entered as being before the date of ICU admission). Finally, all data were manually reviewed, and values that appeared incongruent or out of range were manually validated by confirming the accuracy of the data with the collaborator who entered it.

Definition of an ICU Patient

Patients were considered to have been admitted to an ICU if they were either admitted to a regular ICU room or if they were in a non-ICU room that was functioning as an ICU room for surge capacity. Non-ICU rooms were considered to be functioning as an ICU room under any of the following conditions: 1) the patient was being treated by an ICU team; 2) the patient was receiving invasive mechanical ventilation or extracorporeal membrane oxygenation; 3) the patient was receiving continuous renal replacement therapy; or 4) the patient was receiving vasopressors/inotropes or mechanical cardiac support (e.g., ventricular assist device) in a room where this would traditionally not be permitted. Of the 3099 patients, 21 (0.7%) were admitted to a non-ICU bed for surge capacity.

Sensitivity Analysis of 28-day mortality in patients discharged from the hospital prior to 28 days

In a subset of 50 patients who had been admitted to one of six hospitals in Boston, MA, and who had been discharged prior to 28 days, we manually reviewed their charts or called them to ascertain their 28-day survival status. Among 50 patients reviewed, all 50 remained alive at 28 days.

Multivariable Modeling of AKI-RRT

We performed multivariable logistic regression modeling to estimate the association between patient- and hospital-level covariates and the primary outcome of acute kidney injury treated with renal replacement therapy (AKI-RRT) within 14 days following ICU admission. We prespecified the variables below for inclusion in the multivariable model based on clinical knowledge, biologic plausibility, and completeness of data. For laboratory and physiologic data, we selected the worst value on ICU day 1 or 2 to minimize the degree of missingness.

1. Age (years): 18-39; 40-49; 50-59; 60-69; 70-79; ≥ 80
2. Sex: male vs. female
3. Race: White vs. Non-White
4. Hypertension
5. Diabetes mellitus
6. Body mass index (kg/m^2): <25 ; 25-29; 30-34; 35-39.9; ≥ 40
7. Chronic kidney disease (CKD): no CKD (estimated glomerular filtration rate [eGFR] ≥ 60 $\text{ml}/\text{min}/1.73\text{m}^2$); CKD stage III (eGFR 30-59 $\text{ml}/\text{min}/1.73\text{m}^2$); CKD stages IV and V (eGFR <30 $\text{ml}/\text{min}/1.73\text{m}^2$)
8. Coronary artery disease
9. Congestive heart failure
10. Active malignancy
11. Days from hospital to ICU admission: ≤ 3 vs. >3
12. Lymphocyte count (per mm^3) (lowest value on ICU day 1 or 2): <1000 vs. ≥ 1000 per mm^3
13. Liver and Coagulation components of the Sequential Organ Failure Assessment (SOFA) score:

	Categories		
	0	1	2-4*
SOFA Liver (Bilirubin, mg/dl)	<1.2	1.2-1.9	≥ 2
SOFA Coagulation (Platelets, K/mm^3)	≥ 150	100-149	≤ 99

*Categories 2, 3, and 4 of the liver and coagulation components of the SOFA score were binned due to low frequency of events in categories "3" and "4".

14. PaO₂:FiO₂ ratio (lowest value on ICU day 1 or day 2): not mechanically ventilated; mechanically ventilated and PaO₂:FiO₂ ratio ≥200; mechanically ventilated and PaO₂:FiO₂ ratio 100-199; mechanically ventilated and PaO₂:FiO₂ ratio <100
15. Secondary infection on ICU day 1: confirmed or suspected infection(s) on ICU Day 1 other than COVID-19, including bacterial pneumonia (must have a positive blood or sputum culture, or a positive urine antigen for pneumococcus or legionella, or a new infiltrate on chest imaging suspected to be separate from COVID-related pneumonia), viral respiratory infection (e.g., influenza, parainfluenza, and RSV), biliary sepsis, cellulitis, bacteremia or endocarditis (only if confirmed by blood cultures and/or cardiac imaging), or other
16. Altered mental status on ICU day 1 (for patients who are intubated/sedated, the most recent exam prior to intubation/sedation was used)
17. Shock, defined as the requirement for ≥2 vasopressors
18. D-dimer (ng/ml) (highest value on ICU day 1 or 2): <1000; 1000-2500; >2500
19. Hospital size (number of ICU beds, not including surge capacity): ≥100, 50-99, <50
20. Regional density of COVID-19, assessed by categorizing hospitals into quartiles according to the regional (county) density of COVID-19 positive cases present on the median date of ICU admission for each site. Specifically, we calculated the number of COVID-19 cases per 100,000 population in the county in which each of the participating hospitals is located. We then categorized hospitals according to quartiles of the density of COVID-19 cases.

Multivariable modeling was performed using logistic regression for the binary outcome of AKI-RRT within 14 days of ICU admission. Odds ratios and confidence intervals are reported. Missing data were not imputed. Rather, we created a separate missing category for each covariate that had missing data, since data may not have been missing at random. Further, the missingness of a variable could have clinical relevance (e.g., a healthier patient may not have certain physiologic or laboratory values assessed as frequently), which could affect treatment decisions.

Multivariable Modeling of 28-Day Mortality among Patients with AKI-RRT

We also examined independent predictors of 28-day mortality among patients with AKI-RRT using the following covariates, selected based on clinical knowledge and previously published data.¹ For physiologic and acute severity-of-illness covariates, unless otherwise specified we used the value on the day of RRT initiation. If unavailable, we used the value from the day prior.

1. Age (years): 18-39; 40-49; 50-59; 60-69; 70-79; ≥80
2. Sex: male vs. female
3. Race: White vs. Non-White
4. Hypertension
5. Diabetes mellitus
6. Body mass index (kg/m²): <25; 25-29; 30-34; 35-39.9; ≥40
7. Chronic kidney disease (CKD): no CKD (estimated glomerular filtration rate [eGFR] ≥60 ml/min/1.73m²); CKD stage III (eGFR 30-59 ml/min/1.73m²); CKD stages IV and V (eGFR <30 ml/min/1.73m²)
8. Coronary artery disease
9. Congestive heart failure
10. Active malignancy
11. Days from hospital admission to ICU admission: ≤3 vs. >3 days
12. PaO₂:FiO₂ ratio: not mechanically ventilated; mechanically ventilated and PaO₂:FiO₂ ratio ≥200; mechanically ventilated and PaO₂:FiO₂ ratio 100-199; mechanically ventilated and PaO₂:FiO₂ ratio <100
13. Vasopressors: 0, 1, ≥2
14. Urine output (ml/day): >500; 100-500; <100
15. Lymphocyte count (per mm³): <1000 vs. ≥1000
16. Liver and Coagulation components of the Sequential Organ Failure Assessment (SOFA) score:

	Categories		
	0	1	2-4*
SOFA Liver (Bilirubin, mg/dl)	<1.2	1.2-1.9	≥2
SOFA Coagulation (Platelets, K/mm ³)	≥150	100-149	≤99

*Categories 2, 3, and 4 of the liver and coagulation components of the SOFA score were binned due to low frequency of events in categories “3” and “4”.

17. Secondary infection on ICU day 1: confirmed or suspected infection(s) on ICU Day 1 other than COVID-19, including bacterial pneumonia (must have a positive blood or sputum culture, or a positive urine antigen for

- pneumococcus or legionella, or a new infiltrate on chest imaging suspected to be separate from COVID-related pneumonia), viral respiratory infection (e.g., influenza, parainfluenza, and RSV), biliary sepsis, cellulitis, bacteremia or endocarditis (only if confirmed by blood cultures and/or cardiac imaging), or other
18. Altered mental status on ICU day 1 (for patients who are intubated/sedated, the most recent exam prior to intubation/sedation was used)
 19. Initial RRT modality: intermittent hemodialysis versus continuous renal replacement therapy for 12-24 hours/day
 20. Hospital size (# ICU beds, not including surge capacity): ≥ 100 , 50-99, < 50
 21. Regional density of COVID-19, quartiles

Interhospital Variation in AKI-RRT:

To estimate hospital-specific rates of AKI-RRT, we used multilevel logistic regression modeling with patients nested in hospitals. This approach addresses the poor reliability of estimates stemming from hospitals submitting few cases. Three models were performed: unadjusted, adjusted for patient-level characteristics, and adjusted for both patient- and hospital level characteristics. The patient-level covariates included were the same as those described above in the multivariable model of AKI-RRT. We also included stage 3 AKI (defined as a three-fold or greater increase in serum creatinine [SCr] from baseline) as a covariate to account for varying degrees of AKI severity across hospitals. Hospital-level characteristics included number of ICU beds and regional density of COVID-19, defined above.

Assessment of AKI not treated with RRT:

We categorized AKI severity as stages 1, 2, or 3 according to modified SCr-based definitions established by the Kidney Disease: Improving Global Outcomes criteria² (**Supplemental Table 2**). To assess AKI and its severity on hospital admission, we compared the initial SCr value on admission to the pre-hospital baseline value. Accordingly, AKI on hospital admission was only assessed in the subset of patients with a pre-hospital baseline SCr available (44.1% of the cohort). To assess AKI and its severity occurring within 14 days following ICU admission, we compared the highest SCr value achieved within 14 days following ICU admission to the pre-hospital baseline SCr value. If a pre-hospital baseline SCr was not available, we used the SCr value on hospital admission as the baseline.

References:

- ¹Demirjian S, Chertow GM, Zhang JH, et al. Model to predict mortality in critically ill adults with acute kidney injury. *Clin J Am Soc Nephrol* Sep;6(9):2114-20, 2011.
- ²Kidney Disease; Improving Global Outcomes (KDIGO) Acute Kidney Injury Work Group. KDIGO clinical practice guideline for acute kidney injury. *Kidney Int Suppl* 2, 2012: 1-138.

Supplemental Table 1. List of Participating Sites

Northeast
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Hackensack Mountainside Hospital
Johns Hopkins Hospital
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Lowell General Hospital
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New York-Presbyterian Queens Hospital
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New York University Langone Hospital
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Rutgers/Robert Wood Johnson Medical School
Temple University Hospital
Thomas Jefferson University Hospital
Tufts Medical Center
United Health Services Hospitals
University of Pennsylvania Health System
University of Pittsburgh Medical Center
Westchester Medical Center
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Duke University Medical Center
Mayo Clinic, Florida
Memphis VA Medical Center
Methodist University Hospital
Ochsner Medical Center
Tulane Medical Center
University of Alabama-Birmingham Hospital
University of Florida Health-Gainesville
University of Florida Health-Jacksonville
University of Miami Health System
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University of Illinois Hospital and Health Sciences System
University of Kentucky Hospital
University of Michigan Hospital
University of Oklahoma Health Sciences Center
West
Loma Linda University Medical Center
Mayo Clinic, Arizona
Oregon Health and Science University Hospital
Renown Health
Stanford Healthcare
University of California-Davis Medical Center
University of California-Los Angeles Medical Center
University of California-San Diego Medical Center
University of California-San Francisco Medical Center
UCHealth University of Colorado
University Medical Center of Southern Nevada
University of Washington Medical Center

Supplemental Table 2. Definitions of Baseline Characteristics, Comorbidities, Treatments, and Outcomes

Baseline Characteristics	
Baseline serum creatinine	Lowest value (mg/dl) within 365 to 7 days prior to hospital admission. If not available, serum creatinine on hospital admission
Home medications	Medications that the patient was taking at home within 1 week prior to admission. Does not include those started at an outside hospital if the patient was transferred.
Anticoagulation	Therapeutic anticoagulants, not including anti-platelet agents such as aspirin or clopidogrel
Immunosuppressive medication	Chemotherapy (in the 30 days prior to admission), corticosteroids >10 mg prednisone/day (or equivalent), calcineurin inhibitors (systemic, not topical), mycophenolate mofetil, azathioprine, rituximab, other
Coexisting Conditions	
Asthma	Per chart review
Chronic kidney disease	Classified into stages using baseline serum creatinine and the CKD-EPI equation (eGFR ≥90, 60-89, 45-59, 30-44, 15-29, <15 ml/min)
Chronic liver disease	Cirrhosis, alcohol-related liver disease, nonalcoholic fatty liver disease, autoimmune hepatitis, hepatitis B or hepatitis C, primary biliary cirrhosis, or other
Chronic obstructive pulmonary disease	Per chart review
Congestive heart failure	Per chart review; heart failure with preserved versus reduced ejection fraction
Coronary artery disease	Per chart review; any history of angina, myocardial infarction, or coronary artery bypass graft surgery
Diabetes mellitus	Per chart review; insulin versus non-insulin dependent
End stage kidney disease	Per chart review; on hemodialysis or peritoneal dialysis
History of alcohol abuse	Per chart review
HIV/AIDS	Per chart review
Homelessness	Per chart review
Hypertension	Per chart review
Malignancy	Per chart review; active malignancy (other than non-melanoma skin cancer) treated in the past year. Defined as cancer of the lung, breast, colorectal, prostate, gastric, pancreatic, melanoma, ovarian, brain, or other
Renal transplant	Per chart review
Smoking	Per chart review; does not include vaping or smoking of non-tobacco products. Non-smoker, former smoker, current smoker
Longitudinal Treatments^a	
Mechanical ventilation	Invasive mechanical ventilation
Renal replacement therapy	CRRT, intermittent hemodialysis, peritoneal dialysis, other
PaO ₂ ^b	Lowest PaO ₂ available during each 24 hour day (midnight to midnight)
FiO ₂ ^b	FiO ₂ corresponding to the lowest PaO ₂
PEEP ^b	Highest PEEP available during each 24 hour day (midnight to midnight)
Vasopressors	Maximum number of vasopressors required each day
Outcomes^a	
AKI	Determined by comparing the maximum baseline serum creatinine over the first 14 days following ICU admission to baseline serum creatinine. Baseline serum creatinine was defined as the lowest value from within 365 to 7 days prior to hospital admission. If unavailable, the hospital admission value was used as the baseline.
Stage 1 AKI	A 1.5-1.9 fold increase in serum creatinine from baseline, corresponding with stage 1 of the Kidney Disease: Improving Global Outcomes criteria ¹
Stage 2 AKI	A 2-2.9-fold increase in serum creatinine from baseline, corresponding with stage 2 of the Kidney Disease: Improving Global Outcomes criteria ¹
Stage 3 AKI	A three-fold or greater increase in serum creatinine from baseline, corresponding with stage 3 of the Kidney Disease: Improving Global Outcomes criteria. ¹ Patients with AKI treated with RRT were not included, as AKI-RRT was analyzed as a separate category.
AKI-RRT	AKI treated with RRT at any time in the first 14 days following ICU admission
RRT/death	AKI-RRT or death at any time in the first 14 days following ICU admission
28-Day mortality	Death at any time in the 28 days following ICU admission
Secondary Infection on ICU Day 1	A confirmed or suspected infection(s) on ICU Day 1 other than COVID-19, including bacterial pneumonia (must have a positive blood or sputum culture, or a positive urine antigen for pneumococcus or legionella, or a new infiltrate on chest imaging suspected to be separate from COVID-related pneumonia), viral respiratory infection (e.g., influenza, parainfluenza, and RSV), biliary sepsis, cellulitis, bacteremia or endocarditis (only if confirmed by blood cultures and/or cardiac imaging), or other
Shock	Requirement for 2 or more vasopressors

Abbreviations: AKI, acute kidney injury; CKD-EPI, Chronic Kidney Disease-Epidemiology Collaboration equation; CRRT, continuous renal replacement therapy, eGFR, estimated glomerular filtration rate; FiO₂, fraction of inspired oxygen; PaO₂, partial pressure of oxygen; PEEP, positive end-expiratory pressure; RSV, respiratory syncytial virus.

^aLongitudinal treatments and outcomes were recorded daily for the first 14 days following admission to the ICU.

^bIf multiple values were present, the lowest PaO₂ available, along with the corresponding FiO₂, was recorded, while the highest PEEP on each day was recorded.

References:

¹Kidney Disease; Improving Global Outcomes (KDIGO) Acute Kidney Injury Work Group. KDIGO clinical practice guideline for acute kidney injury. *Kidney Int Suppl* 2, 2012: 1-138.

Supplemental Table 3. Complete List of Patient Characteristics According to AKI Stage. AKI and its stages in this table refer to AKI occurring in the first 14 days following ICU admission.

Characteristic	All Patients (N=3099)	No AKI (N=1414)	Stage 1 AKI (N=355)	Stage 2 AKI (N=338)	Stage 3 AKI* (N=355)	AKI-RRT (N=637)
Demographics						
Age (yr)						
Median (IQR)	62 (51-71)	60 (49-70)	64 (52-74)	66 (57-75)	65 (55-73)	62 (52-69)
Distribution – no. (%)						
18–39	271 (8.7)	159 (11.2)	31 (8.7)	18 (5.3)	22 (6.2)	41 (6.4)
40–49	394 (12.7)	211 (14.9)	39 (11.0)	31 (9.2)	36 (10.1)	77 (12.1)
50–59	661 (21.3)	315 (22.3)	71 (20.0)	58 (17.2)	61 (17.2)	156 (24.5)
60–69	869 (28.0)	353 (25.0)	88 (24.8)	95 (28.1)	119 (33.5)	214 (33.6)
70–79	618 (19.9)	252 (17.8)	83 (23.4)	86 (25.4)	73 (20.6)	124 (19.5)
≥80	286 (9.2)	124 (8.8)	43 (12.1)	50 (14.8)	44 (12.4)	25 (3.9)
Male sex – no. (%)	2003 (64.6)	864 (61.1)	235 (66.2)	212 (62.7)	235 (66.2)	457 (71.7)
Race – no. (%)						
White	1154 (37.2)	581 (41.1)	155 (43.7)	135 (39.9)	110 (31.0)	173 (27.2)
Black	952 (30.7)	364 (25.7)	99 (27.9)	108 (32.0)	101 (28.5)	280 (44.0)
Asian	190 (6.1)	106 (7.5)	17 (4.8)	18 (5.3)	22 (6.2)	27 (4.2)
Other	803 (25.9)	363 (25.7)	84 (23.7)	77 (22.8)	122 (34.4)	157 (24.7)
Hispanic – no. (%)	1045 (33.7)	485 (34.3)	113 (31.8)	111 (32.8)	144 (40.6)	192 (30.1)
BMI – median (IQR)	30.4 (26.6-36.1)	29.4 (25.9-34.6)	31.5 (26.8-36.2)	30.5 (26.6-34.7)	29.8 (26.1-35.7)	32.6 (28.1-39.3)
Pregnant – no. (%)	20 (0.6)	14 (1.0)	3 (0.8)	1 (0.3)	2 (0.6)	0 (0)
Homeless – no. (%)	21 (0.7)	12 (0.9)	3 (0.8)	1 (0.3)	3 (0.9)	2 (0.3)
Source of admission to ICU – no. (%)						
Emergency department	1727 (55.7)	757 (53.5)	226 (63.7)	191 (56.5)	225 (63.4)	328 (51.5)
Hospital ward	966 (31.2)	458 (32.4)	91 (25.6)	114 (33.7)	106 (30.0)	197 (30.9)
Transfer from another hospital	391 (12.6)	193 (13.7)	35 (9.9)	30 (8.9)	23 (6.5)	110 (17.3)
Other	15 (0.5)	6 (0.4)	3 (0.9)	3 (0.9)	1 (0.3)	2 (0.3)
Days from symptom onset to ICU admission – median (IQR)	7 (4-10)	7 (4-11)	7 (4-9)	7 (4-10)	7 (4-10)	7 (5-10)
Coexisting conditions – no. (%)^a						
IDDM	419 (13.5)	129 (9.1)	56 (15.8)	65 (19.2)	54 (15.2)	115 (18.1)
NIIDDM	811 (26.2)	318 (22.5)	84 (23.7)	88 (26.0)	98 (27.6)	223 (35.0)
Hypertension	1869 (60.3)	718 (50.8)	232 (65.4)	240 (71.0)	222 (62.5)	457 (71.7)
COPD	258 (8.3)	91 (6.4)	41 (11.6)	37 (11.0)	34 (9.6)	55 (8.6)
Asthma	337 (10.9)	161 (11.4)	49 (13.8)	30 (8.9)	44 (12.4)	53 (8.3)
Other pulmonary disease	224 (7.2)	78 (5.5)	41 (11.6)	31 (9.2)	31 (8.7)	43 (6.8)
Current or former smoker	917 (29.6)	385 (27.2)	117 (33.0)	114 (33.7)	120 (33.8)	181 (28.4)
Alcohol abuse disorder	169 (5.5)	76 (5.4)	21 (5.9)	26 (7.7)	24 (6.8)	22 (3.5)
Coronary artery disease	390 (12.6)	127 (9.0)	57 (16.1)	60 (17.8)	61 (17.2)	85 (13.3)
Congestive heart failure	270 (8.7)	77 (5.5)	45 (12.7)	44 (13.0)	34 (9.6)	70 (11.0)
Chronic liver disease	104 (3.4)	26 (1.8)	16 (4.5)	17 (5.0)	18 (5.1)	27 (4.2)
Chronic kidney disease ^b						
eGFR ≥90 ml/min/1.73m ²	1033 (33.3)	523 (37.0)	130 (36.6)	99 (29.3)	135 (38.0)	146 (22.9)
eGFR 60-89 ml/min/1.73m ²	1164 (37.6)	542 (38.3)	127 (35.8)	134 (39.6)	145 (40.9)	219 (34.4)
eGFR 45-59 ml/min/1.73m ²	419 (13.5)	170 (12.0)	53 (14.9)	59 (17.5)	41 (11.6)	96 (15.1)
eGFR 30-44 ml/min/1.73m ²	255 (8.2)	102 (7.2)	30 (8.5)	30 (8.9)	27 (7.6)	66 (10.4)
eGFR 15-29 ml/min/1.73m ²	159 (5.2)	60 (4.2)	13 (3.7)	16 (4.7)	7 (2.0)	64 (10.1)
eGFR <15 ml/min/1.73m ²	64 (2.1)	17 (1.2)	2 (0.6)	0 (0)	0 (0)	46 (7.2)
Active malignancy	58 (1.9)	19 (1.3)	7 (2.0)	9 (2.7)	2 (0.6)	21 (3.3)
Immunodeficiency	158 (5.1)	55 (3.9)	23 (6.5)	25 (7.4)	23 (6.5)	32 (5.0)
HIV/AIDS	40 (1.3)	16 (1.3)	40 (2.0)	2 (0.6)	3 (0.9)	12 (1.9)
Home medications – no. (%)						
Immunosuppressants	312 (10.7)	120 (8.5)	40 (11.3)	54 (16.0)	32 (9.0)	66 (10.4)
ACE-I	566 (18.3)	220 (15.6)	68 (19.2)	67 (19.8)	76 (21.4)	135 (21.2)
ARB	513 (16.6)	178 (12.6)	56 (15.8)	70 (20.7)	55 (15.5)	154 (24.2)
Mineralocorticoid antagonist	81 (2.6)	19 (1.3)	14 (3.9)	14 (4.1)	15 (4.2)	19 (3.0)
Beta-blocker	788 (25.4)	281 (19.9)	108 (30.4)	101 (29.9)	100 (28.2)	198 (31.1)
Other antihypertensive	892 (28.8)	312 (22.1)	106 (30.0)	126 (37.3)	113 (31.8)	235 (36.9)
Statin	1156 (37.3)	453 (32.0)	142 (40.0)	146 (43.2)	144 (40.6)	271 (42.5)
NSAID	260 (8.4)	120 (8.5)	25 (7.0)	37 (11.0)	17 (4.8)	61 (9.6)
Aspirin	664 (21.4)	236 (16.7)	90 (25.4)	87 (25.7)	97 (27.3)	154 (24.2)
Anticoagulant	272 (8.8)	99 (7.0)	48 (13.5)	45 (13.3)	38 (10.7)	42 (6.6)
Vitamin C	77 (2.5)	34 (2.4)	13 (3.7)	8 (2.4)	9 (2.5)	13 (2.0)
Vitamin D	317 (10.2)	123 (8.7)	47 (13.2)	41 (12.1)	38 (10.7)	68 (10.7)
Vital signs on the day of ICU admission – median (IQR)						
Temperature – °C	38.1 (37.3-38.9)	38.0 (37.3-38.8)	38.1 (37.2-38.9)	38.1 (37.3-38.9)	37.9 (37.2-38.9)	38.2 (37.4-39.0)
SBP – mm Hg	97 (86-111)	98 (88-112)	98 (85-114)	95 (84-107)	94 (82-108)	95 (84-111)
Heart rate – beats per min	104 (90-120)	102 (88-115)	108 (93-122)	104 (92-120)	109 (93-127)	108 (93-122)
Respiratory rate – per min	31 (26-38)	32 (26-39)	32 (25-36)	30 (26-38)	30 (26-39)	32 (27-38)
Urine output – ml/day	725 (350-1250)	855 (500-1375)	760 (350-1268)	749 (442-1128)	675 (300-1250)	500 (200-930)

Characteristic	All Patients (N=3099)	No AKI (N=1414)	Stage 1 AKI (N=355)	Stage 2 AKI (N=338)	Stage 3 AKI* (N=355)	AKI-RRT (N=637)
Laboratory findings on the day of ICU admission – median (IQR)						
White-cell count – per mm ³	8.2 (5.9-11.5)	7.6 (5.7-10.6)	8.0 (5.7-11.5)	8.5 (4.7-11.7)	9.3 (6.3-13.1)	8.9 (6.5-12.2)
Lymphocyte count – per mm ³	824 (561-1152)	854 (603-1158)	765 (504-1100)	787 (508-1121)	815 (528-1201)	796 (541-1148)
Hemoglobin – g/dl	12.7 (11.2-14.1)	12.8 (11.5-14.2)	12.6 (11.2-14.0)	12.6 (11.1-14.1)	12.8 (10.9-14.2)	12.6 (10.9-14.0)
Platelet count – K/mm ³	214 (164-272)	217 (166-276)	208 (155-268)	215 (166-277)	213 (168-277)	207 (164-260)
Creatinine – mg/dl	1.04 (0.80-1.55)	0.91 (0.72-1.18)	1.07 (0.81-1.48)	1.16 (0.90-1.91)	1.20 (0.82-1.81)	1.47 (1.0-2.85)
Albumin – g/dl	3.2 (2.8-3.6)	3.3 (2.9-3.6)	3.3 (2.8-3.6)	3.2 (2.8-3.6)	3.1 (2.7-3.4)	3.1 (2.7-3.5)
AST – U/L	55 (36-85)	52 (35-80)	47 (33-72)	53 (36-83)	65 (42-112)	63 (41-96)
ALT – U/L	37 (23-60)	36 (23-59)	32 (21-51)	34 (21-56)	43 (26-71)	39 (24-62)
Total bilirubin – mg/dl	0.6 (0.4-0.8)	0.6 (0.4-0.8)	0.6 (0.4-0.8)	0.6 (0.4-0.9)	0.6 (0.4-0.9)	0.6 (0.4-0.8)
Lactate – mmol/L	1.5 (1.1-2.3)	1.4 (1.1-2.1)	1.5 (1.1-2.2)	1.6 (1.2-2.5)	1.9 (1.2-2.5)	1.5 (1.1-2.3)
Arterial pH	7.37 (7.30-7.43)	7.40 (7.34-7.45)	7.37 (7.31-7.42)	7.37 (7.31-7.42)	7.34 (7.26-7.40)	7.33 (7.26-7.40)
D-dimer – ng/mL	1310 (700-3263)	1040 (610-2119)	1320 (680-2630)	1509 (785-3565)	1980 (820-6110)	2000 (869-6998)
C-reactive protein – mg/L	157 (90-237)	145 (80-221)	157 (82-235)	167 (105-249)	158 (100-252)	175 (104-269)
Interleukin-6 – pg/mL	56 (19-154)	46 (17-115)	54 (10-180)	55 (28-119)	50 (18-160)	100 (29-251)
Procalcitonin – ng/ml	0.4 (0.2-1.3)	0.3 (0.1-0.7)	0.4 (0.1-1.0)	0.5 (0.2-1.4)	0.6 (0.2-2.0)	0.8 (0.3-3.4)
Ferritin – ng/ml	1005 (499-1977)	978 (467-1655)	827 (414-1737)	919 (511-1996)	1275 (477-2729)	1206 (643-2262)
CPK – U/L	212 (98-565)	178 (92-459)	166 (75-377)	183 (78-431)	233 (110-689)	361 (159-1074)
Sodium – mEq/l	137 (134-40)	137 (134-140)	137 (134-140)	137 (134-140)	137 (134-141)	136 (133-139)
Severity-of-illness on the day of ICU admission						
Invasive MV – no. (%)	2044 (66.0)	785 (55.5)	241 (67.9)	237 (70.1)	277 (78.0)	504 (79.1)
FiO ₂ – median (IQR)	0.8 (0.6-1.0)	0.7 (0.5-1.0)	0.8 (0.5-1.0)	0.9 (0.6-1.0)	1.0 (0.6-1.0)	0.9 (0.6-1.0)
PEEP, cm H ₂ O – median (IQR)	12 (10-15)	12 (10-15)	12 (10-15)	12 (10-15)	14 (10-15)	14 (10-16)
PaO ₂ :FiO ₂ , mm Hg – median (IQR) ^c	126 (85-194)	146 (103-217)	134 (88-216)	114 (79-181)	117 (84-183)	104 (74-104)
Non-invasive MV – no. (%)	54 (1.7)	20 (1.4)	7 (2.0)	12 (3.6)	7 (2.0)	8 (1.3)
HFNC or NRB – no. (%)	619 (20.0)	381 (26.9)	58 (16.3)	57 (16.9)	44 (12.4)	79 (12.4)
Vasopressors – no. (%)	1305 (42.1)	388 (27.4)	156 (43.9)	162 (47.9)	175 (49.3)	324 (50.9)
Altered mental status – no. (%)	681 (22.0)	255 (18.0)	90 (25.4)	94 (27.8)	113 (31.8)	129 (20.3)

The stages of AKI are defined according to modified serum creatinine (SCr)-based definitions established by the Kidney Disease: Improving Global Outcomes Criteria. *AKI stage 3 is exclusive of AKI treated with RRT (AKI-RRT), as AKI-RRT is presented separately. Thus, each of the categories above are mutually exclusive. The lowest SCr between 365 and 7 days prior to hospital admission was used as the baseline value. If unavailable, the hospital admission SCr was used as the baseline value.

Abbreviations: ACE-I, Angiotensin converting enzyme inhibitor; ALT, alanine aminotransferase; ARB, Angiotensin II receptor blocker; AST, aspartate aminotransferase; BMI, body mass index; COPD, chronic obstructive pulmonary disease; CPK, creatinine phosphokinase; eGFR, estimated glomerular filtration rate, HFNC, high flow nasal cannula; IDDM, insulin dependent diabetes mellitus; MV, mechanical ventilation; NIDDM, non-insulin dependent diabetes mellitus; NRB, nonrebreather; NSAID, non-steroidal anti-inflammatory drug; PaO₂:FiO₂, the ratio of the partial pressure of arterial oxygen (PaO₂) over the fraction of inspired oxygen (FiO₂); PEEP, positive end-expiratory pressure; SBP, systolic blood pressure.

^aThe definitions of the coexisting disorders are provided in the supplemental material.

^bBaseline eGFR was calculated using the CKD-EPI equation, using the lowest SCr between 365 and 7 days prior to hospital admission as the baseline value. If unavailable, the hospital admission SCr was used as the baseline value.

^cPaO₂:FiO₂ refers to the ratio of the partial pressure of arterial oxygen (PaO₂) over the fraction of inspired oxygen (FiO₂), and was only assessed in patients receiving invasive mechanical ventilation.

Data regarding BMI were missing for 215 patients (6.9%)
 Data regarding homelessness were missing in 3 patients (0.1%)
 Data regarding alcohol abuse were missing in 1 patient (0.03%)
 Data regarding systolic blood pressure were missing in 2 patients (0.1%)
 Data regarding heart rate were missing in 1 patient (0.03%)
 Data regarding respiratory rate were missing in 1 patient (0.03%)
 Data regarding white blood cell count were missing in 142 patients (4.5%)
 Data regarding lymphocyte count were missing in 537 patients (17.3%)
 Data regarding hemoglobin were missing in 149 patients (4.8%)
 Data regarding platelets were missing in 159 patients (5.1%)
 Data regarding creatinine were missing in 108 patients (3.4%)
 Data regarding albumin were missing in 566 patients (18.3%)
 Data regarding AST were missing in 557 patients (18%)
 Data regarding ALT were missing in 536 patients (17.3%)
 Data regarding bilirubin were missing in 543 patients (17.5%)
 Data regarding lactate were missing in 1147 patients (37%)
 Data regarding pH were missing in 934 patients (30.1%)
 Data regarding D-dimer were missing in 1520 patients (49%)
 Data regarding C-reactive protein were missing in 1204 patients (38.9%)
 Data regarding interleukin-6 were missing in 2472 patients (79.8%)
 Data regarding pro-calcitonin were missing in 1145 patients (37%)
 Data regarding ferritin were missing in 1337 patients (43%)
 Data regarding creatine phosphokinase were missing in 1612 patients (52%)
 Data regarding sodium were missing in 12 patients (0.4%)
 Data regarding FiO₂ were missing in 225 out of 2044 patients who received invasive mechanical ventilation (11.0%)
 Data regarding PEEP were missing in 255 out of 2044 patients who received invasive mechanical ventilation (11.0%)
 Data regarding PaO₂:FiO₂ were missing in 357 out of 2044 patients who received invasive mechanical ventilation (17.5%)

Supplemental Table 4. Characteristics of Patients with AKI-RRT on Days 1 and 2 Versus Days 3 Through 14.

Characteristic	RRT Initiation on Days 1-2 (n=166)	RRT Initiation on Days 3-14 (n=471)
Demographics		
Age (yrs) – median (IQR)	57 (49-67)	63 (54-70)
Male sex – no. (%)	119 (71.7)	338 (71.8)
White Race – no. (%)	38 (22.9)	135 (28.7)
Hispanic – no. (%)	46 (27.7)	146 (31.0)
Body mass index (kg/m ²) – median (IQR)	33.9 (29.6-42.0)	32.4 (27.5-38.6)
Comorbidities		
Diabetes mellitus	89 (53.6)	248 (52.7)
Hypertension	122 (73.5)	335 (71.1)
Coronary artery disease	15 (9.0)	70 (14.9)
Congestive heart failure	18 (10.8)	52 (11.0)
Active malignancy	9 (5.4)	23 (4.9)
Chronic kidney disease		
eGFR ≥90 ml/min/1.73m ²	35 (21.1)	111 (23.6)
eGFR 60-89 ml/min/1.73m ²	36 (21.7)	183 (38.9)
eGFR 45-59 ml/min/1.73m ²	21 (12.7)	75 (15.9)
eGFR 30-44 ml/min/1.73m ²	14 (8.4)	52 (11.0)
eGFR 15-29 ml/min/1.73m ²	28 (16.9)	36 (7.6)
eGFR <15 ml/min/1.73m ²	32 (19.3)	14 (3.0)
Vital Signs on ICU Day 1		
Temperature – °C	38.0 (37.2-38.9)	38.3 (37.4-39.0)
Systolic blood pressure – mm Hg	95 (85-111)	95 (84-110)
Heart rate – beats per min	107 (93-121)	108 (94-122)
Urine output – ml/day	250 (100-600)	600 (280-1020)
Labs on ICU Day 1		
White-cell count – per mm ³	9.8 (7.7-13.1)	8.5 (6.1-11.8)
Lymphocyte count – per mm ³	772 (517-1134)	814 (547-1154)
Platelet count – K/mm ³	208 (162-254)	207 (165-266)
Total bilirubin – mg/dl	0.6 (0.4-0.9)	0.6 (0.4-0.8)
D-dimer – ng/mL	3793 (1390-9958)	1608 (822-4971)
C-reactive protein – mg/L	192 (119-314)	165 (102-261)
Severity of Illness on ICU Day 1		
Invasive mechanical ventilation – no. (%)	152 (91.6)	352 (74.7)
FiO ₂ - median (IQR)	90 (60-100)	90 (60-100)
PEEP, cm of water – median (IQR)	15 (12-18)	14 (10-16)
PaO ₂ :FiO ₂ , mm Hg – median (IQR)	101 (74-150)	108 (74-167)
Non-invasive mechanical ventilation – no. (%)	1 (0.6)	7 (1.5)
High-flow nasal cannula or NRB – no. (%)	8 (4.8)	71 (15.1)
Altered mental status – no. (%)	106 (63.9)	218 (46.3)
Vasopressors – no. (%)	38 (22.9)	91 (19.3)
Hospital Characteristics		
Regional Density of COVID-19 – median (IQR)	3 (2-4)	3 (2-4)
Number of ICU beds – median (IQR)	100 (48-130)	73 (47-111)

Abbreviations: COVID-19, coronavirus disease 2019; eGFR, estimated glomerular filtration rate; ICU, intensive care unit; IQR, interquartile range; PaO₂:FiO₂, the ratio of the partial pressure of arterial oxygen over the fraction of inspired oxygen; PEEP, positive end-expiratory pressure

Supplemental Table 5. Multivariable Model for AKI-RRT, Accounting for Clustering. Additional details provided in the Methods.

Variable	Odds Ratio (95% CI) for AKI-RRT
Age (yrs)	
18-39 (REF)	1.00
40-49	1.14 (0.84-1.55)
50-59	1.53 (1.11-2.10)
60-69	1.59 (1.16-2.18)
70-79	1.24 (0.87-1.76)
≥80	0.48 (0.27-0.88)
Male Sex	1.88 (1.58-2.23)
Non-White Race	1.75 (1.48-2.06)
Hypertension	1.25 (0.99-1.58)
Diabetes Mellitus	1.59 (1.33-1.91)
Body Mass Index (kg/m ²)	
<25 (REF)	1.00
25-29.9	1.79 (1.30-2.46)
30-34.9	2.14 (1.56-2.93)
35-39.9	2.38 (1.69-3.37)
≥40	3.21 (2.31-4.47)
Chronic Kidney Disease	
No CKD (eGFR >60 ml/min/1.73m ²) (REF)	1.00
CKD stage 3 (eGFR 30-60 ml/min/1.73m ²)	1.62 (1.30-2.01)
CKD stages 4 or 5 (eGFR <30 ml/min/1.73m ²)	5.34 (4.24-6.72)
Coronary Artery Disease	0.90 (0.71-1.15)
Congestive Heart Failure	1.29 (1.02-1.64)
Active Malignancy	1.17 (0.85-1.61)
≤3 days from Hospital Admission to ICU Admission	0.79 (0.66-0.93)
Lymphocyte Count <1,000 per mm ³ on ICU Day 1	1.11 (0.89-1.38)
Hypoxemia, ICU Day 1	
Not Receiving Mechanical Ventilation (REF)	1.00
Mechanically ventilated and PaO ₂ :FiO ₂ ≥200	1.22 (0.88-1.70)
Mechanically ventilated and PaO ₂ :FiO ₂ 100–199	1.23 (0.93-1.61)
Mechanically ventilated and PaO ₂ :FiO ₂ <100	3.00 (2.33-3.86)
Shock on ICU Day 1	1.01 (0.76-1.33)
Altered Mental Status, ICU Day 1	0.72 (0.59-0.86)
Secondary Infection, ICU Day 1	1.11 (0.92-1.35)
Coagulation Component of SOFA Score	
0 (REF)	1.00
1	1.17 (0.92-1.48)
2-4	1.23 (0.85-1.78)
Liver Component of SOFA Score	
0 (REF)	1.00
1	1.08 (0.75-1.55)
2-4	1.24 (0.85-1.78)
D-dimer (ng/ml) on ICU Day 1	
<1000 (REF)	1.00
1000-2500	1.14 (0.90-1.45)
>2500	1.85 (1.47-2.34)
Hospital Size (no. of ICU beds)	
Large (≥100 ICU beds) (REF)	1.00
Medium (50–99 ICU beds)	0.90 (0.64-1.27)
Small (<50 ICU beds)	1.03 (0.76-1.38)
Regional Density of COVID-19	
1 (REF)	1.00
2	0.93 (0.52-1.66)
3	0.72 (0.44-1.17)
4	0.77 (0.48-1.24)

Abbreviations: CKD, chronic kidney disease; COVID-19, coronavirus disease 2019; eGFR, estimated glomerular filtration rate; ICU, intensive care unit; PaO₂:FiO₂, the ratio of the partial pressure of arterial oxygen over the fraction of inspired oxygen; SOFA, Sequential Organ Failure Assessment.

Supplemental Table 6. Multivariable Model for AKI-RRT among Patients with a Pre-Hospital Baseline Serum Creatinine Available.

Variable	Odds Ratio (95% CI) for AKI-RRT
Age (yrs)	
18-39 (REF)	1.00
40-49	1.09 (0.49-2.41)
50-59	1.24 (0.60-2.57)
60-69	1.36 (0.67-2.74)
70-79	0.98 (0.47-2.05)
≥80	0.42 (0.16-1.08)
Male Sex	1.78 (1.28-2.47)
Non-White Race	2.34 (1.67-3.28)
Hypertension	1.43 (0.96-2.13)
Diabetes Mellitus	1.45 (1.06-1.90)
Body Mass Index (kg/m ²)	
<25 (REF)	1.00
25-29.9	1.50 (0.87-2.59)
30-34.9	1.70 (0.98-2.95)
35-39.9	2.63 (1.42-4.87)
≥40	2.22 (1.22-4.07)
Chronic Kidney Disease	
No CKD (eGFR >60 ml/min/1.73m ²) (REF)	1.00
CKD stage 3 (eGFR 30-60 ml/min/1.73m ²)	1.61 (1.11-2.35)
CKD stages 4 or 5 (eGFR <30 ml/min/1.73m ²)	8.92 (4.86-16.36)
Coronary Artery Disease	1.10 (0.68-1.50)
Congestive Heart Failure	1.18 (0.77-1.83)
Active Malignancy	1.42 (0.82-2.44)
≤3 days from Hospital Admission to ICU Admission	0.73 (0.52-1.03)
Lymphocyte Count <1,000 per mm ³ on ICU Day 1	1.17 (0.82-1.68)
Hypoxemia, ICU Day 1	
Not Receiving Mechanical Ventilation (REF)	1.00
Mechanically ventilated and PaO ₂ :FiO ₂ ≥200	1.45 (0.80-2.65)
Mechanically ventilated and PaO ₂ :FiO ₂ 100–199	3.22 (2.13-4.88)
Mechanically ventilated and PaO ₂ :FiO ₂ <100	3.90 (2.57-5.92)
Shock on ICU Day 1	0.93 (0.58-1.51)
Altered Mental Status, ICU Day 1	0.71 (0.49-1.04)
Secondary Infection, ICU Day 1	1.06 (0.75-1.51)
Coagulation Component of SOFA Score	
0 (REF)	1.00
1	1.16 (0.77-1.73)
2-4	1.34 (0.73-2.43)
Liver Component of SOFA Score	
0 (REF)	1.00
1	1.15 (0.52-2.51)
2-4	1.20 (0.72-2.01)
D-dimer (ng/ml) on ICU Day 1	
<1000 (REF)	1.00
1000-2500	1.42 (0.86-2.35)
>2500	1.60 (0.99-2.60)
Hospital Size (no. of ICU beds)	
Large (≥100 ICU beds) (REF)	1.00
Medium (50–99 ICU beds)	0.88 (0.59-1.33)
Small (<50 ICU beds)	1.25 (0.85-1.84)
Regional Density of COVID-19	
1 (REF)	1.00
2	1.24 (0.72-2.11)
3	0.73 (0.45-1.19)
4	0.52 (0.32-0.88)

Abbreviations: CKD, chronic kidney disease; COVID-19, coronavirus disease 2019; eGFR, estimated glomerular filtration rate; ICU, intensive care unit; PaO₂:FiO₂, the ratio of the partial pressure of arterial oxygen over the fraction of inspired oxygen; SOFA, Sequential Organ Failure Assessment.

Supplemental Table 7. Multivariable Model for AKI-RRT Excluding Patients Transferred from an Outside Hospital. N=391 excluded; n=2708 included in the analysis.

Variable	Odds Ratio (95% CI) for AKI-RRT
Age (yrs)	
18-39 (REF)	1.00
40-49	0.98 (0.59-1.64)
50-59	1.45 (0.91-2.31)
60-69	1.39 (0.87-1.20)
70-79	1.12 (0.68-1.85)
≥80	0.36 (0.18-0.71)
Male Sex	1.87 (1.47-2.37)
Non-White Race	1.70 (1.35-2.15)
Hypertension	1.33 (1.04-1.71)
Diabetes Mellitus	1.61 (1.29-2.01)
Body Mass Index (kg/m ²)	
<25 (REF)	1.00
25-29.9	1.64 (1.12-2.42)
30-34.9	1.85 (1.24-2.76)
35-39.9	2.23 (1.43-3.48)
≥40	2.83 (1.84-4.36)
Chronic Kidney Disease	
No CKD (eGFR >60 ml/min/1.73m ²) (REF)	1.00
CKD stage 3 (eGFR 30-60 ml/min/1.73m ²)	1.71 (1.32-2.21)
CKD stages 4 or 5 (eGFR <30 ml/min/1.73m ²)	5.98 (4.13-8.67)
Coronary Artery Disease	0.84 (0.60-1.18)
Congestive Heart Failure	1.17 (0.81-1.70)
Active Malignancy	1.10 (0.69-1.77)
≤3 days from Hospital Admission to ICU Admission	0.79 (0.62-1.01)
Lymphocyte Count <1,000 per mm ³ on ICU Day 1	1.07 (0.83-1.38)
Hypoxemia, ICU Day 1	
Not Receiving Mechanical Ventilation (REF)	1.00
Mechanically ventilated and PaO ₂ :FiO ₂ ≥200	1.18 (0.78-1.79)
Mechanically ventilated and PaO ₂ :FiO ₂ 100-199	1.94 (1.45-2.60)
Mechanically ventilated and PaO ₂ :FiO ₂ <100	3.13 (2.34-4.18)
Shock on ICU Day 1	1.01 (0.72-1.42)
Altered Mental Status, ICU Day 1	0.66 (0.50-0.87)
Secondary Infection, ICU Day 1	1.10 (0.85-1.42)
Coagulation Component of SOFA Score	
0 (REF)	1.00
1	1.05 (0.79-1.41)
2-4	1.33 (0.85-2.06)
Liver Component of SOFA Score	
0 (REF)	1.00
1	0.96 (0.55-1.69)
2-4	1.22 (0.85-1.74)
D-dimer (ng/ml) on ICU Day 1	
<1000 (REF)	1.00
1000-2500	0.99 (0.69-1.41)
>2500	1.54 (1.10-2.16)
Hospital Size (no. of ICU beds)	
Large (≥100 ICU beds) (REF)	1.00
Medium (50-99 ICU beds)	0.88 (0.66-1.18)
Small (<50 ICU beds)	1.22 (0.92-1.62)
Regional Density of COVID-19	
1 (REF)	1.00
2	1.15 (0.76-1.73)
3	0.73 (0.50-1.07)
4	0.73 (0.50-1.05)

Abbreviations: CKD, chronic kidney disease; COVID-19, coronavirus disease 2019; eGFR, estimated glomerular filtration rate; ICU, intensive care unit; PaO₂:FiO₂, the ratio of the partial pressure of arterial oxygen over the fraction of inspired oxygen; SOFA, Sequential Organ Failure Assessment.

Supplemental Table 8: Multivariable Model for AKI-RRT Among Patients who Survived 14 Days.
N=2307. No. events=413.

Variable	Odds Ratio (95% CI) for AKI-RRT
Age (yrs)	
18-39 (REF)	1.00
40-49	1.23 (0.71-2.13)
50-59	1.64 (0.98-2.74)
60-69	1.97 (1.18-3.30)
70-79	1.46 (0.83-2.58)
≥80	0.69 (0.29-1.62)
Male Sex	2.44 (1.83-3.25)
Non-White Race	1.77 (1.36-2.31)
Hypertension	1.21 (0.91-1.61)
Diabetes Mellitus	1.68 (1.30-2.17)
Body Mass Index (kg/m ²)	
<25 (REF)	1.00
25-29.9	1.70 (1.08-2.66)
30-34.9	1.91 (1.21-3.03)
35-39.9	2.83 (1.70-4.71)
≥40	3.50 (2.11-5.82)
Chronic Kidney Disease	
No CKD (eGFR >60 ml/min/1.73m ²) (REF)	1.00
CKD stage 3 (eGFR 30-60 ml/min/1.73m ²)	1.92 (1.41-2.58)
CKD stages 4 or 5 (eGFR <30 ml/min/1.73m ²)	9.04 (5.83-14.02)
Coronary Artery Disease	1.03 (0.70-1.53)
Congestive Heart Failure	1.30 (0.84-2.03)
Active Malignancy	1.02 (0.55-1.87)
≤3 days from Hospital Admission to ICU Admission	0.79 (0.60-1.04)
Lymphocyte Count <1,000 per mm ³ on ICU Day 1	0.93 (0.70-1.24)
Hypoxemia, ICU Day 1	
Not Receiving Mechanical Ventilation (REF)	1.00
Mechanically ventilated and PaO ₂ :FiO ₂ ≥200	1.17 (0.73-1.88)
Mechanically ventilated and PaO ₂ :FiO ₂ 100–199	1.88 (1.35-2.62)
Mechanically ventilated and PaO ₂ :FiO ₂ <100	3.69 (2.63-5.16)
Shock on ICU Day 1	1.16 (0.78-1.71)
Altered Mental Status, ICU Day 1	0.67 (0.47-0.95)
Secondary Infection, ICU Day 1	1.11 (0.82-1.49)
Coagulation Component of SOFA Score	
0 (REF)	1.00
1	1.29 (0.92-1.79)
2-4	1.71 (0.99-2.95)
Liver Component of SOFA Score	
0 (REF)	1.00
1	0.90 (0.45-1.82)
2-4	0.96 (0.63-1.45)
D-dimer (ng/ml) on ICU Day 1	
<1000 (REF)	1.00
1000-2500	1.00 (0.67-1.50)
>2500	1.86 (1.28-2.70)
Hospital Size (no. of ICU beds)	
Large (≥100 ICU beds) (REF)	1.00
Medium (50–99 ICU beds)	0.71 (0.52-0.97)
Small (<50 ICU beds)	1.00 (0.73-1.38)
Regional Density of COVID-19	
1 (REF)	1.00
2	1.00 (0.65-1.54)
3	0.67 (0.44-1.01)
4	0.76 (0.51-1.15)

Abbreviations: CKD, chronic kidney disease; COVID-19, coronavirus disease 2019; eGFR, estimated glomerular filtration rate; ICU, intensive care unit; PaO₂:FiO₂, the ratio of the partial pressure of arterial oxygen over the fraction of inspired oxygen; SOFA, Sequential Organ Failure Assessment.

Supplemental Table 9. Multivariable Model for 28-Day Mortality from the Day of RRT Initiation.

Variable	Odds Ratio (95% CI) for 28-Day Mortality
Age (yrs)	
18-39 (REF)	1.00
40-49	1.25 (0.51-3.10)
50-59	1.33 (0.57-3.07)
60-69	2.45 (1.05-5.76)
70-79	3.44 (1.36-8.67)
≥80	6.56 (1.61-26.70)
Male Sex	1.31 (0.84-2.04)
Non-White Race	1.08 (0.69-1.69)
Hypertension	0.89 (0.55-1.42)
Diabetes Mellitus	1.09 (0.72-1.64)
Body Mass Index (kg/m ²)	
<25 (REF)	1.00
25-29.9	0.95 (0.44-2.03)
30-34.9	1.17 (0.53-2.56)
35-39.9	0.79 (0.34-1.85)
≥40	1.34 (0.60-3.01)
Chronic Kidney Disease	
No CKD (eGFR >60 ml/min/1.73m ²) (REF)	1.00
CKD stage 3 (eGFR 30-60 ml/min/1.73m ²)	0.85 (0.53-1.36)
CKD stages 4 or 5 (eGFR <30 ml/min/1.73m ²)	0.53 (0.31-0.90)
Coronary Artery Disease	1.43 (0.78-2.63)
Congestive Heart Failure	1.39 (0.73-2.63)
Active Malignancy	3.67 (1.25-10.76)
≤3 days from Hospital Admission to ICU Admission	0.92 (0.60-1.40)
Lymphocyte Count <1,000 per mm ³	0.85 (0.52-1.38)
PaO ₂ :FiO ₂	
Not Receiving Mechanical Ventilation (REF)	1.00
Mechanically ventilated and PaO ₂ :FiO ₂ ≥200	0.68 (0.36-1.29)
Mechanically ventilated and PaO ₂ :FiO ₂ 100-199	0.79 (0.45-1.37)
Mechanically ventilated and PaO ₂ :FiO ₂ <100	1.57 (0.83-2.99)
Vasopressors	
0 (REF)	1.00
1	1.42 (0.88-2.30)
≥2	2.35 (1.33-4.15)
Altered Mental Status on ICU Day 1	1.51 (0.91-2.49)
Secondary Infection on ICU Day 1	0.82 (0.52-1.30)
Coagulation Component of SOFA Score	
0 (REF)	1.00
1	1.30 (0.68-2.45)
2-4	2.04 (0.77-5.41)
Liver Component of SOFA Score	
0 (REF)	1.00
1	0.98 (0.52-1.85)
2-4	1.20 (0.59-2.45)
Urine Output (ml/day)	
>500 (REF)	1.00
100-500	1.22 (0.75-1.98)
<100	2.13 (1.25-3.61)
Initial RRT Modality	
Intermittent Hemodialysis (REF)	1.00
CRRT for 12-24 hours/day	1.28 (0.77-2.11)
Hospital Size (no. of ICU beds)	
Large (≥100 ICU beds) (REF)	1.00
Medium (50-99 ICU beds)	3.59 (2.15-6.01)
Small (<50 ICU beds)	7.48 (4.37-12.83)
Regional Density of COVID-19	
1 (REF)	1.00
2	1.66 (0.81-3.43)
3	1.06 (0.53-2.11)
4	1.83 (0.89-3.73)

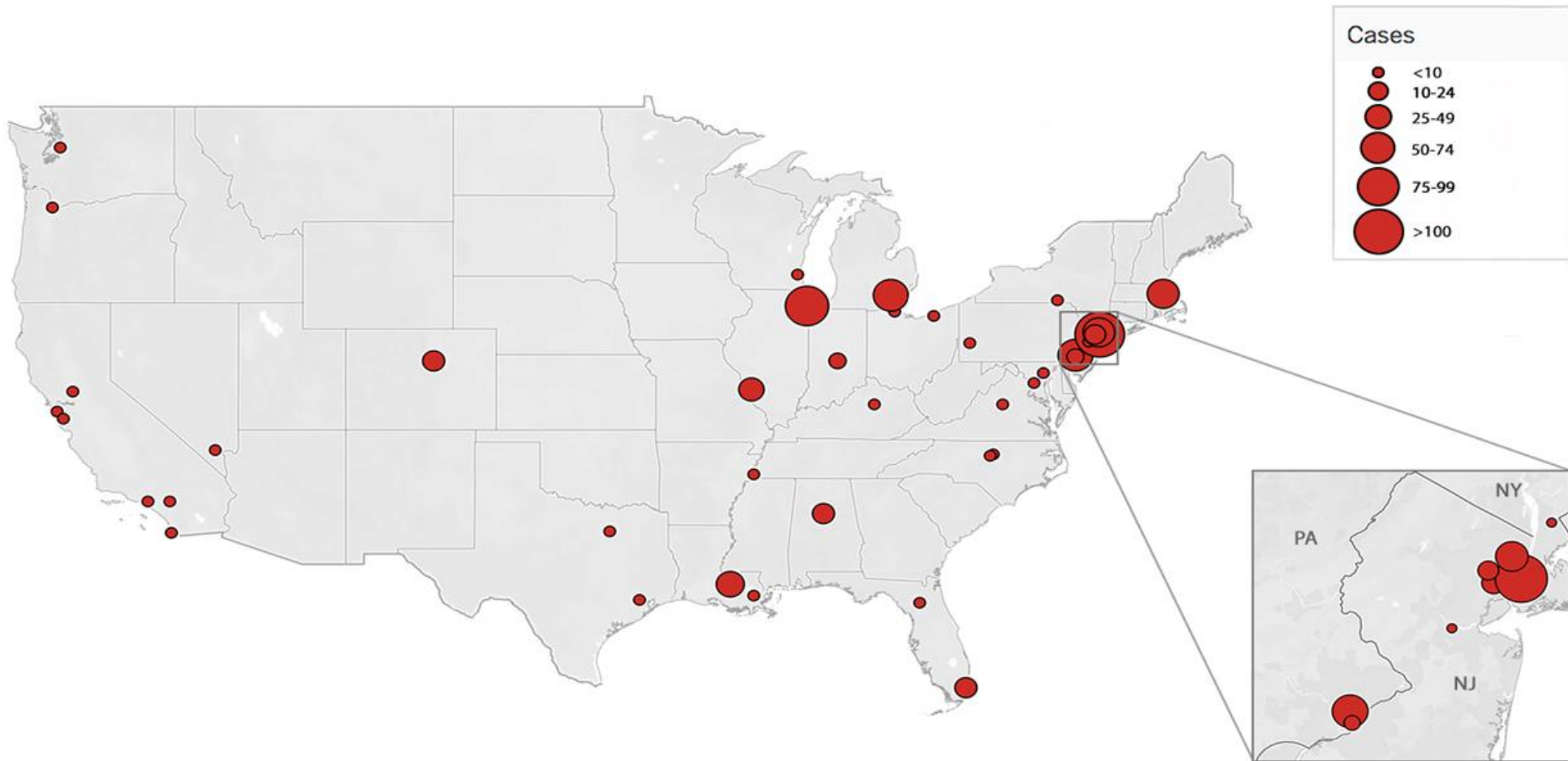
Abbreviations: CKD, chronic kidney disease; COVID-19, coronavirus disease 2019; CRRT, continuous renal replacement therapy; eGFR, estimated glomerular filtration rate; ICU, intensive care unit; PaO₂:FiO₂, the ratio of the partial pressure of arterial oxygen over the fraction of inspired oxygen; RRT, renal replacement therapy; SOFA, Sequential Organ Failure Assessment. Of n=637 patients initiated on RRT, 365 had died (57.3%), 91 had been discharged (14.3%), and 181 remained hospitalized (28.4%) 28 days following the day of RRT initiation.

Supplemental Table 10. AKI by Stage and 28-Day Mortality Among Patients with a Pre-Hospital Baseline SCr Available. n=1367

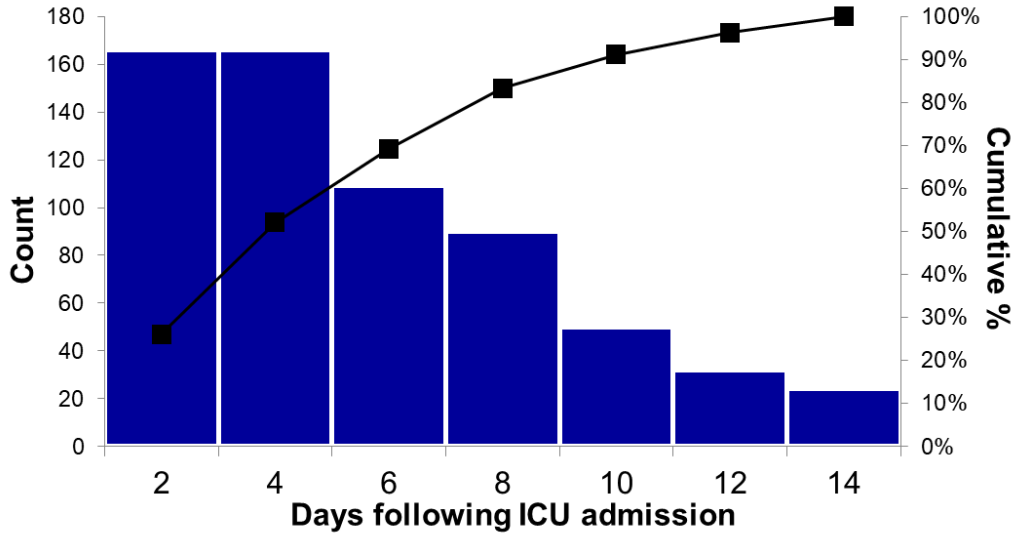
AKI Stage	N (%)	Death at 28 days, N (%)
No AKI	522 (38.2)	107 (20.5)
AKI Stage 1	183 (13.4)	61 (33.3)
AKI Stage 2	185 (13.5)	90 (48.7)
AKI Stage 3 (without RRT)	195 (14.3)	121 (62.1)
AKI-RRT	282 (20.6)	153 (54.3)

Abbreviations: AKI, acute kidney injury; RRT, renal replacement therapy.

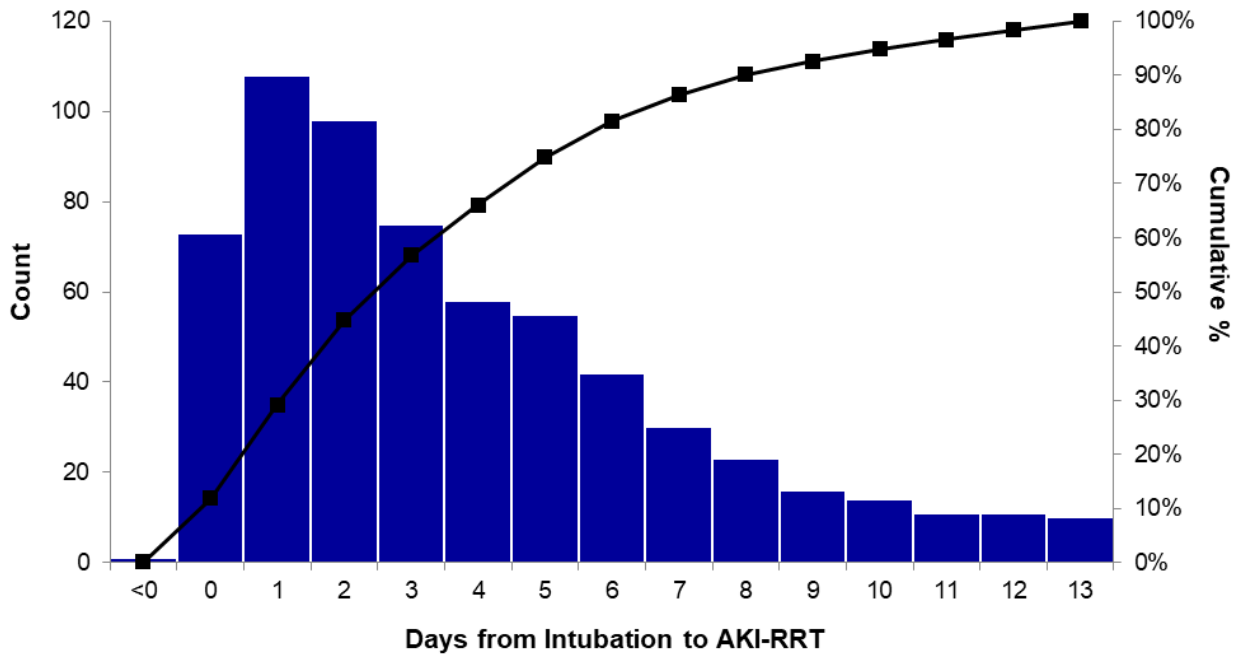
Supplemental Figure 1. Number of Patients with AKI-RRT by State among Contributing Sites. Red bubbles demonstrate the number of patients contributed by each site.



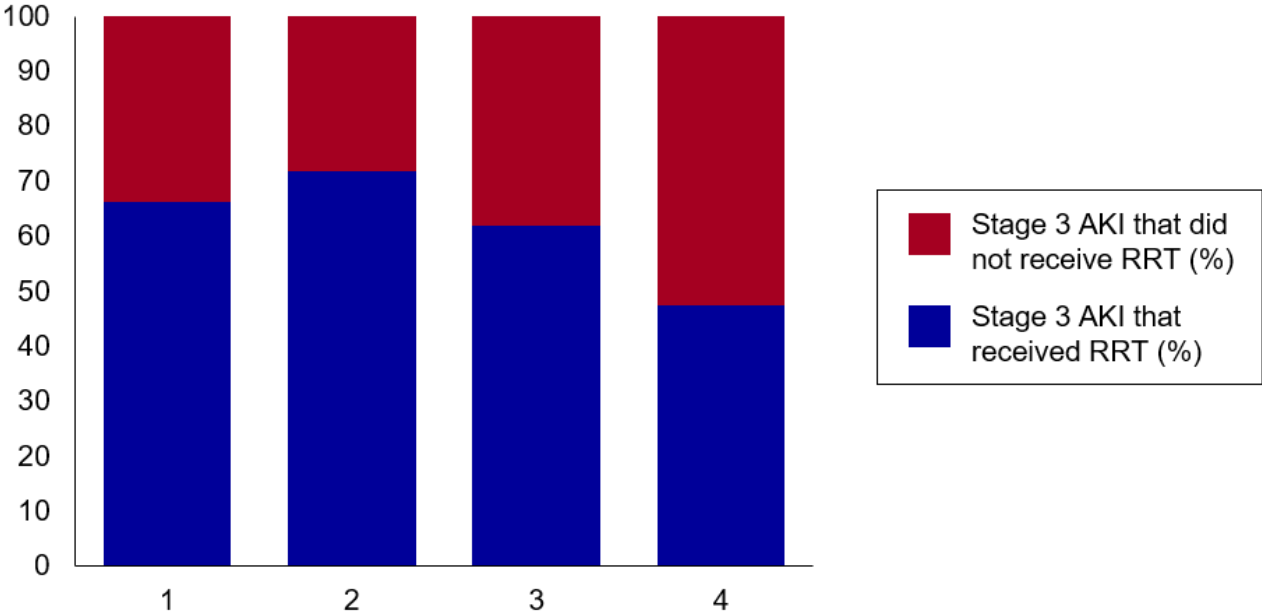
Supplemental Figure 2. Time to AKI-RRT. Total n=637. The median time from ICU admission to RRT initiation was 4 days (interquartile range, 2 to 7 days). Abbreviations: ICU, intensive care unit.



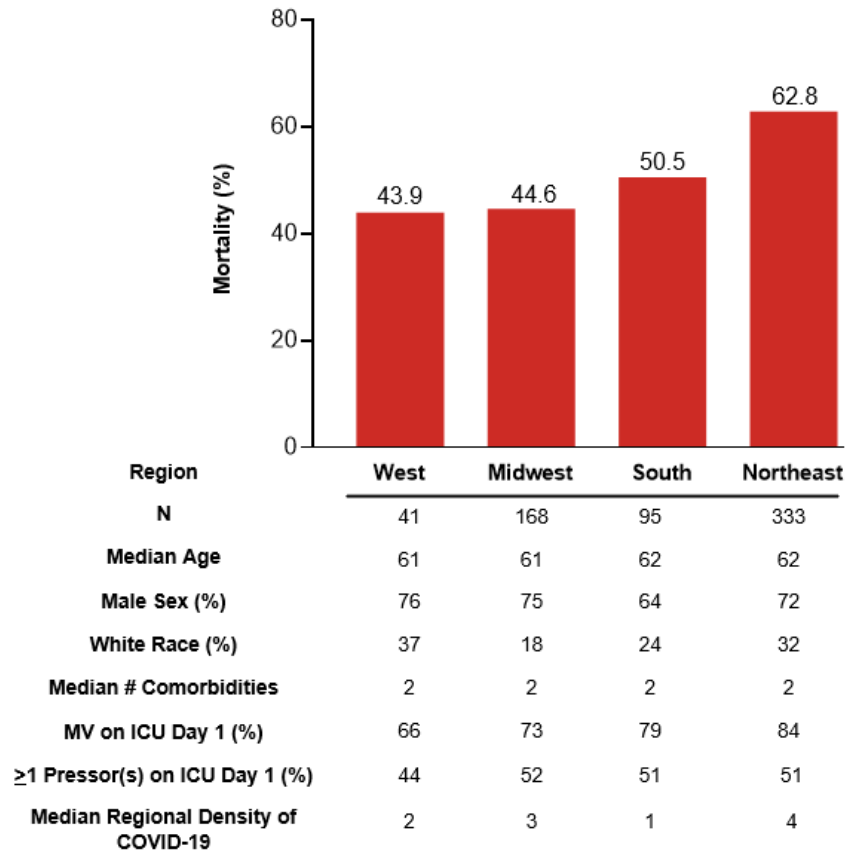
Supplemental Figure 3. Timing of AKI-RRT in Relation to Intubation. N=625 of 637 (98.1%) AKI-RRT patients received mechanical ventilation, of whom 3 (0.5%) had AKI-RRT prior to intubation.



Supplemental Figure 4. Proportion of Patients with AKI Stage 3 Treated with RRT by Quartile of Regional Density of COVID-19. Abbreviations: AKI, acute kidney injury; RRT, renal replacement therapy



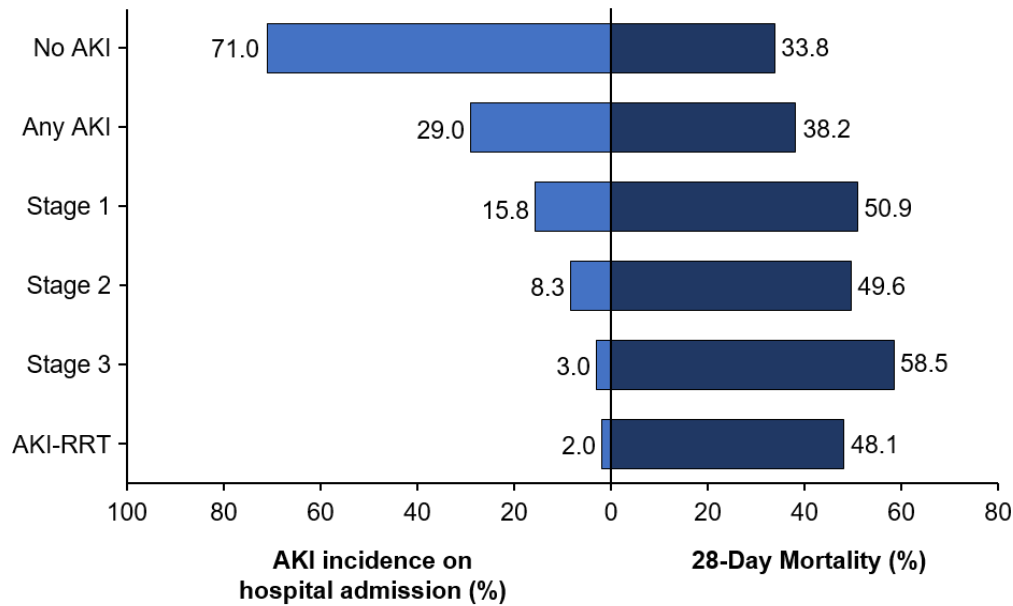
Supplemental Figure 5. 28-Day Mortality of Patients with AKI-RRT by Region. Comorbidities include diabetes mellitus, hypertension, coronary artery disease, congestive heart failure, atrial fibrillation or flutter, chronic obstructive pulmonary disease, asthma, other lung disease, chronic liver disease, HIV or AIDS, active malignancy, prior solid organ transplantation, prior bone marrow transplantation, and other immunodeficiency. Hospitals were categorized as having a regional density of COVID-19 category of 1, 2, 3, or 4, with 4 constituting the highest regional density (see Supplemental Methods for further details). Abbreviations: ICU, intensive care unit; MV, mechanical ventilation.



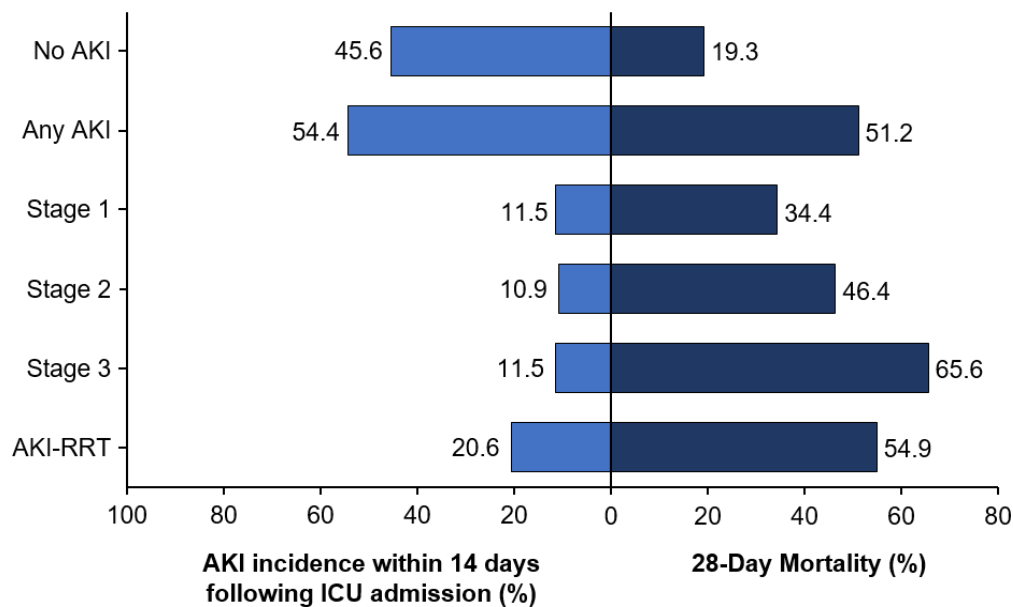
Supplemental Figure 6. AKI on Hospital Admission and within 14 Days following ICU Admission.

Panel A shows incidence and stage of AKI on hospital admission among those with a pre-hospital baseline serum creatinine available (n=1367), and the association with 28-day mortality. Panel B shows AKI incidence and stage in the 14 days following ICU admission (n=3099), and the association with 28-day mortality. Note that stage 3 AKI does not include RRT (stage 3 AKI and AKI-RRT are thus mutually exclusive categories). Abbreviations: AKI-RRT (renal replacement therapy-treated acute kidney injury)

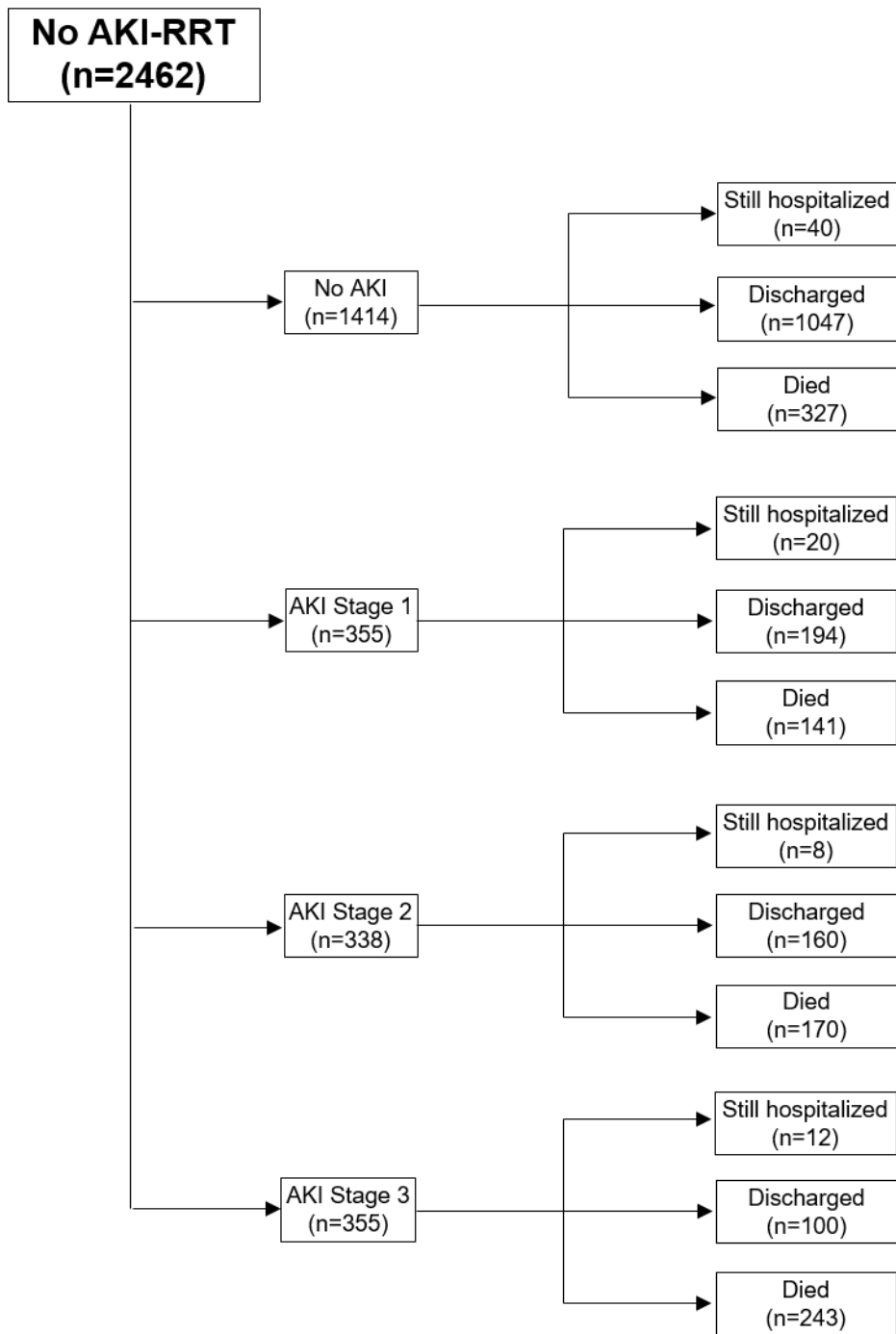
A. AKI on Hospital Admission



B. AKI within 14 days following ICU admission



Supplemental Figure 7: Flowchart of Outcomes of Patients without AKI-RRT. Abbreviations: AKI, acute kidney injury; RRT, renal replacement therapy.



ACKNOWLEDGEMENT OF PATIENT OVERLAP

Of the 3099 patients in this study, 153 were reported in a study of AKI among patients hospitalized with COVID-19 within the Mount Sinai Health System in New York City (Chan et al., *J Am Soc Nephrol*, in press), and 29 were reported in a single-center study of AKI in hospitalized patients in New Orleans (Mohamed et al., *Kidney360*, 2020). Additionally, 58 patients from the current study were reported in a single-center case series from New York City (Goyal et al., *N Engl J Med*, 2020) and 12 patients were reported in a case series of critically ill patients from the Seattle region (Bhatraju et al., *N Engl J Med*, 2020), neither of which was focused on AKI. Finally, 2215 patients from the current study were reported in the primary STOP-COVID publication: a multicenter cohort study that examined risk factors for death among critically ill patients with COVID-19 (Gupta et al., *JAMA Intern Med*, 2020).