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# Article Type: Original Investigation

# Short and Long-term Recovery after Moderate/Severe Acute Kidney Injury in patients with and without COVID-19

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#### **Key Points:**

\*Respiratory disease was associated with non-recovery and renal recovery was associated with survival in AKI-2/3 patients with COVID-19.

\*ML algorithms can predict AKI and recovery from COVID-19-associated AKI-2/3 and identifies key predictors.

\*At 12-month follow-up in moderate/severe AKI survivors, no difference in CKD between COVID positive and negative patients was observed.

#### Abstract:

Introduction: Severe AKI is strongly associated with poor outcomes in COVID-19, but data on renal recovery is lacking. Methods: We retrospectively analyzed these associations in 3,299 hospitalized patients (1,338 with COVID-19 and 1,961 with acute respiratory illness but tested negative for COVID-19). Uni- and multi-variable analyses were used to study mortality and recovery after KDIGO Stage 2&3 AKI and Machine Learning (ML) for predicting AKI and recovery using admission data. Long-term renal function and other outcomes were studied in a sub-group of AKI-2/3 survivors. Results: Among the 172 COVID-19 negative patients with AKI-2/3, 74.4% had partial & 44.2% complete renal recovery, while 11.6% died. Among 255 COVID-19 positive patients with AKI-2/3, lower recovery and higher mortality were noted (50.6% partial, 24.7% complete renal recovery, 23.9% died). On multivariable analysis, ICU admission and ARDS were associated with non-recovery, and recovery was significantly associated with survival in COVID-19 positive patients. With ML, we were able to predict recovery from COVID-19-associated AKI-2/3 with an average precision of 0.62 and the strongest predictors of recovery were initial arterial paO2 & CO2, SCr, K, lymphocyte count, & CPK. At 12 months follow-up, among 52 survivors with AKI-2/3, 25.7% COVID-19 positive and 23.5% COVID-19 negative had incident or progressive CKD. Conclusions: Recovery from COVID-19-associated moderate/severe AKI, can be predicted using admission data and is associated with severity of respiratory disease and in-hospital death. The risk of CKD might be similar between COVID-19 positive and negative patients.

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# Short and Long-term Recovery after Moderate/Severe Acute Kidney Injury in patients with and without COVID-19

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# **KEY POINTS**

- Respiratory disease was associated with non-recovery and renal recovery was associated with survival in AKI-2/3 patients with COVID-19.
- ML algorithms can predict AKI and recovery from COVID-19-associated AKI-2/3 and identifies key predictors.
- At 12-month follow-up in moderate/severe AKI survivors, no difference in CKD between COVID positive and negative patients was observed.

# ABSTRACT

Introduction: Severe AKI is strongly associated with poor outcomes in COVID-19, but data on renal recovery is lacking.

<u>Methods:</u> We retrospectively analyzed these associations in 3,299 hospitalized patients (1,338 with COVID-19 and 1,961 with acute respiratory illness but tested negative for COVID-19). Uni- and multi-variable analyses were used to study mortality and recovery after KDIGO Stage 2&3 AKI and Machine Learning (ML) for predicting AKI and recovery using admission data. Long-term renal function and other outcomes were studied in a sub-group of AKI-2/3 survivors.

<u>Results:</u> Among the 172 COVID-19 negative patients with AKI-2/3, 74.4% had partial & 44.2% complete renal recovery, while 11.6% died. Among 255 COVID-19 positive patients with AKI-2/3, lower recovery and higher mortality were noted (50.6% partial, 24.7% complete renal recovery, 23.9% died). On multivariable analysis, ICU admission and ARDS were associated with non-recovery, and recovery was significantly associated with survival in COVID-19 positive patients. With ML, we were able to predict recovery from COVID-19-associated AKI-2/3 with an average precision of 0.62 and the strongest predictors of recovery were initial arterial paO2 & CO2, SCr, K, lymphocyte count, & CPK. At 12 months follow-up, among 52 survivors with AKI-2/3, 25.7% COVID-19 positive and 23.5% COVID-19 negative had incident or progressive CKD.

<u>Conclusions</u>: Recovery from COVID-19-associated moderate/severe AKI, can be predicted using admission data and is associated with severity of respiratory disease and in-hospital death. The risk of CKD might be similar between COVID-19 positive and negative patients.

#### INTRODUCTION

Patients hospitalized with Coronavirus Disease 2019 (COVID-19) often develop sepsis leading to a cytokine storm and subsequent organ dysfunction<sup>1</sup>. Acute kidney injury (AKI) is a hallmark of COVID-19 and a major risk factor associated with poor outcomes in hospitalized patients<sup>2-5</sup>. To our knowledge, no study has compared the factors and outcomes associated with short and long-term renal recovery after AKI in hospitalized patients with and without COVID-19.

Most outcome studies of recovery after AKI in the pre-COVID era show favorable outcomes with renal recovery<sup>6</sup> including lower risk of progression to kidney failure<sup>7</sup> or death<sup>8</sup>. Other data suggest that AKI even in the presence of renal recovery has been associated with long-term mortality<sup>7,9</sup>. Among patients with COVID-19, factors associated with recovery after AKI include remission of proteinuria<sup>10</sup>, baseline CKD<sup>11</sup>, right heart failure<sup>12</sup>, and oxygenation status<sup>12</sup>. We previously reported the lower mortality in those recovered after COVID-19-associated AKI compared to those without recovery<sup>13</sup>. However, this study was limited by a small sample size, lack of a COVID-negative group, and short follow-up<sup>13</sup>.

Early prediction of AKI and recovery in COVID-19 can allow better preventive management, hospital resource allocation, and patient prognostication in this pandemic where acute surges in hospitalizations are seen. Machine learning (ML) approaches of AKI prediction using electronic health records (EHR) data have been reported in multiple settings<sup>14-17</sup>, with greater accuracy for predicting more severe AKI and closer time points to AKI onset.<sup>18-21</sup>. To the best of our knowledge, the use of ML models to predict recovery from COVID-19 AKI has not been previously reported. AKI is a risk factor for the development of CKD<sup>22</sup> including those with complete recovery<sup>23</sup>, however, there are very few studies that have reported the incidence of post-AKI CKD in the setting of COVID-19.<sup>24,25</sup>

The severity of AKI has been associated with worse outcomes<sup>26,27</sup> including in patients with COVID-19<sup>26</sup>. In this study, we investigated the factors and outcomes associated with renal recovery in patients with Kidney Disease: Improving Global Outcomes (KDIGO) stages 2 and 3 AKI hospitalized in the setting of COVID-19. We compared patients who tested negative for COVID-19 using ~100 variables around the time of hospitalization. We also investigated if ML can be used to predict moderate/severe AKI and subsequent recovery in patients with and without COVID-19 using 57 data features at the time of hospitalization. Finally, in a sub-group of survivors with AKI-2/3, we investigated the presence of new-onset or progressive CKD using serum creatinine (SCr) and estimated glomerular filtration rate (eGFR) data more than 3 months after hospital discharge.

# MATERIALS AND METHODS

# Study design and participants:

We conducted a retrospective cohort study on patients hospitalized at Stony Brook University Medical Center (SBUMC) from March 7, 2020 to July 31, 2020. COVID-19 was diagnosed by at least one positive result for SARS-CoV-2 on PCR testing of nasopharyngeal samples. Patients who were hospitalized with suggestive symptoms of COVID-19 but subsequently reported negative PCR were placed in the control (COVID-19 negative) group. All patients were followed until a final disposition of discharge alive from the hospital or in-hospital death. A sub-group of survivors with AKI-2/3 was followed for 12 months post-discharge. We excluded patients who were  $\leq$  18 years of age, with pregnancy and end-stage kidney disease (ESKD) including chronic dialysis or kidney transplant. The study was approved by the SBU Institutional Review Board.

# Data collection and definition of variables:

Detailed in the Supplementary Methods section.

### Acute Kidney Injury (AKI), Recovery and Post-AKI CKD definitions:

AKI was defined as a rise in SCr  $\ge$  1.5 times the baseline to maximum in-hospital SCr, based on the KDIGO definition<sup>28</sup>. Over 80% of patients did not have a pre-hospitalization SCr available, therefore, we used the lowest SCr in the hospital as the 'baseline' as has been previously used in COVID-19 studies<sup>29</sup>. Further discussion on the rationale of using this baseline SCr criteria is in the Supplementary Methods section. Renal replacement therapy (RRT) was defined as the need for either hemodialysis (HD), continuous kidney replacement therapy (CKRT), or both. AKI classes for in-hospital AKI were assigned for each patient based on the KDIGO<sup>28</sup> criteria. Class 1 was assigned for an acute increase in SCr by 50%, Class 2 for an increase by 100%, and Class 3 assigned for an increase of 200% or if the patient required RRT during the hospitalization. In this study, we focused on AKI Stage 2 and 3 and the rationale is further detailed in the Supplementary Methods section.

Recovery from AKI was defined in two ways. For the main analysis, we used the definition of Recovery-1 based on the Acute Dialysis Quality Initiative (ADQI) criteria<sup>30</sup> (final SCr at discharge returned to  $\leq$  50% above baseline SCr). For sensitivity analysis, we used the Recovery-2 definition based on a more strict criterion defined by Bucaloiu et al<sup>31</sup> (final SCr at discharge returned to  $\leq$  10% above baseline SCr). For both analyses, if a patient died prior to recovery, then he/she was treated as not recovered. In addition, patients with RRT requiring AKI had to get off RRT at least 3 days prior to discharge, and for those without RRT requiring AKI, the final SCr should be < 50% of the maximum SCr. These two criteria were applied to both recovery definitions. The rationale of using these Recovery definitions is further detailed in the Supplementary Methods section. A subgroup analysis was done on AKI 2/3 survivors who were followed 12 months post-discharge. For each patient, the most recent post-discharge outpatient SCr and eGFR values were used and were collected >90 days post-discharge after index hospitalization. Post-AKI 'Chronic kidney disease (CKD) was diagnosed if the patient's latest outpatient SCr value remained >10% above baseline SCr plus a final eGFR<60 ml/min/1.73m<sup>2</sup>. CKD was further divided into "Incident CKD" if patients had no history of CKD prior to hospitalization and "Progressive CKD" if the patient had a history of CKD prior to hospitalization based on EHR documentation.

### Univariate (simple regression) and multivariable (multiple regression) Analysis:

All statistical analyses were performed using R 3.6.0. Univariate logistic regression was used to select potential explanatory variables for the outcomes. For multivariable analysis, variables with too many missing values (> 5%) were removed. Variables that were significant based on univariate analysis were placed in the order of clinical importance (demographics, co-morbid conditions, severity of illness, medications followed by other measures), and then backward stepwise logistic regression was used to select the best model based on Akaike information criterion (AIC)<sup>32</sup>. Variable categories of clinical importance (demographics, co-morbid conditions, severity of p < 0.05 was considered statistically significant.

## Machine Learning (ML) Analysis:

We considered the task of predicting if a patient will develop AKI and recovery from AKI during their hospital stay using data at the times of hospitalization (first 48hrs of the ED visit) in the cohort. Our ML models were based on XGBoost, a state-of-the-art algorithm that can handle both numerical and categorical attributes and has been previously used in ML-based predictive modeling studies in COVID-19<sup>33</sup>. We calculated the Precision-Recall (PR) curve and calculated the Average Precision (AP) which are standard metrics to measure the performance of predictors. SHAP (SHapley Additive exPlanations), an established method to explain individual predictions<sup>34</sup>, including kidney disease<sup>35</sup>, was used to identify predictors of AKI and recovery. Further details of ML methodology are described in the Supplementary Methods section.

# **RESULTS:**

## Comparison of patients with and without COVID-19:

Out of 1,338 patients with COVID-19, 43.1% were female, 41.7% non-White and 18.2% Hispanic; while among the 1,961 COVID-19 negative patients, 44.5% were female, 17% non-White and 4.3 % Hispanic. Among patients with COVID-19, 553 (41.3%) were diagnosed with AKI, 255 (19.1%) had moderate/severe AKI (Stage 2&3) and 118 (8.8%) had severe AKI (only Stage 3). Among the COVID-19 negative patients, 474 (24.2%) had AKI, 172 (8.8%) had AKI-2/3 and only 67 (3.4%) had AKI-3 (*Supplementary Figure 0*). In the AKI-3 group, among patients with COVID-19, thirty-five (2.6% of total cohort and 6.3% of all AKI patients) required RRT while only 9 patients (0.46% & % 1.9% respectively) required RRT among COVID-19 negative. Comparison of the characteristics of patients with and without COVID-19 is detailed in Supplementary Table 0.

### Comparison of patients with and without moderate & severe AKI:

Patients with AKI-2/3 (compared to those without) had greater severity of illness and death (*Table 1*). On multivariable analysis, in both patients groups (COVID-19 positive and negative), those with ICU admission, greater length of hospital stay and sepsis had significantly higher odds of having AKI-2/3, while those receiving AC had lower odds (*Figure 1A&B*). Older age, MV and higher initial BUN were specifically associated with COVID-19 associated AKI-2/3 (*Figure 1A*). Sensitivity analysis restricted to patients with AKI-3 showed mostly similar associations (*Supplementary Table 1*, *Supplementary Figure 1A&B*).

# Comparison of patients with and without Recovery after AKI-2/3:

Out of a total of 255 patients with COVID-19 who had AKI-2/3, 129 (50.6%) had at least 'partial' renal recovery (Recovery-1), while 126 (49.4%) did not. Among the 172 patients with AKI-2/3 who tested negative for COVID-19, 128 (74.4%) had renal recovery, while 44 (25.6%) did not (*Table 2* and *Supplementary Figure 0*). In our sensitivity analysis (Recovery -2), out of the total of 255 patients with AKI-2/3 in the setting of COVID-19, 63 (24.7%) had 'complete' renal recovery, while 192 (75.3%) did not (*Supplementary Table 2*). Among the 172 patients with AKI-2/3 who tested negative for COVID-19, 76 (44.2%) had renal recovery, while 96 (55.8%) did not (*Supplementary Table 2*).

Among COVID-19 positive patients, we compared those with Recovery-1 after AKI-2/3 to those without Recovery-1 (*Table 2*). On multivariable analysis (*Figure 2A*), only ICU admission remained significantly associated with lower odds of recovery-1 (OR = 0.35 [0.18-0.67]). Among COVID-19 negative patients (*Figure 2B*), no association was noted.

The associations with Recovery-2 were similar to Recovery-1 on univariate analysis (*Supplementary Table 2*). On multivariable analysis (*Supplementary Figure 2A*), among COVID-19 positive patients, ARDS was significantly associated with lower odds of recovery (OR = 0.28 [0.12-0.70]). DM was associated with borderline higher odds of recovery. (OR=2.05 [1.04-4.05]). Among COVID-19 negative patients (*Supplementary Figure 2B*), ICU admission with lower odds of recovery (OR = 0.52 [0.28-0.97]).

# Comparison of patients with and without Recovery after AKI-3:

In the sensitivity analysis restricted to patients with AKI-3, out of a total of 118 patients with COVID-19 who had AKI-3, 43 (36.6%) had 'partial' renal recovery, while 75 (63.4%) did not (Recovery-1, *Supplementary Table 3*). Among the 67 patients with AKI-3 who tested negative for COVID-19, 47 (70.1%) had renal recovery, while 20 (29.1%) did not (*Supplementary Table 3*). Among COVID-19 positive patients, 24 (20.3%) had 'complete' renal recovery (Recovery-2), while 94 (79.7%) did not (*Supplementary Table 4*). Among the COVID-19 negative patients, 31 (46.2%) had renal recovery, while 36 (53.8%) did not.

We compared those with and without Recovery-1 & 2 after AKI-3 to those without (*Supplementary Tables 3 & 4*) and the results of multivariable analysis are presented in *Supplementary Figure 3A/B & 4A/B*).

# Analysis of death in patients with and without Recovery after AKI-2/3:

Among patients with COVID-19, 148 (11.1%) of the 1,338, and among COVID-19 negative, 119 (6.1%) of 1961 patients died (*Supplementary Table 5*). Among AKI-2/3 patients with COVID-19, 61 (23.9%) of the 255, while among COVID-19 negative, 20 (11.6%) of 172 patients died (*Table 3*). In COVID-19 positive patients, both Recovery-1 and Recovery-2; while in COVID-19 negative patients, only Recovery-1 was significantly associated with survival (*Table 3*).

On multivariable analysis, in both AKI-2/3 groups (with COVID-19 (*Figure 3*) or without COVID-19 (*Figure 4*), those with MV had significantly higher odds of death. Among COVID-19 positive patients, higher initial BUN was specifically associated with death, while female gender and Recovery-1 (partial) with survival (*Figure 3A*). However, the association of Recovery-2 (complete) with survival in patients with COVID-19 was no longer statistically significant (*Figure 3B*). Among COVID-19 negative patients, higher initial respiratory rate was associated with death and the association of Recovery-1 & 2 with survival was not statistically significant (*Figure 4A/B*).

### Analysis of death in patients with and without Recovery after AKI-3:

Among AKI-3 patients with COVID-19, 32 (27.1%) of the 118, while among COVID-19 negative, 8 (11.9%) of 67 patients died (*Supplementary Table 6*). On multivariable analysis, the associations between Recovery-1&2 and death were similar to patients with AKI-2/3 (*Supplementary Figure 5 & 6*).

# Prediction of AKI-2/3 and recovery using machine learning (ML) algorithms:

In patients with and without COVID-19, we were able to predict AKI-2/3 with an AP of 0.36 and 0.23 respectively (*Supplementary Figure 7*) and predict AKI-3 with an AP of 0.47 and 0.40 respectively (*Supplementary Figure 8*). For recovery prediction, we focused on Recovery-1 (partial) since Recovery-2 (complete) was achieved in a small sample size. In patients with COVID-19-associated AKI-2/3 and AKI-3, we were able to predict Recovery-1 with an AP of 0.62 (*Figure 6*) and 0.61 (*Supplementary Figure 9*) respectively, while in COVID-19 negative patients, we were able to predict Recovery-1 with an AP of 0.88 (*Figure 5 & Supplementary Figure 9*).

Among patients with AKI-2/3, the key recovery predictors are shown in the SHAP plots in *Figure 6* and among patients with AKI-3, in *Supplementary Figure 10*. The measures that predicted recovery among both AKI-2/3 and AKI-3 patients with COVID-19 were initial respiratory measures (arterial paO2 & CO2) and initial labs (SCr, K, lymphocyte count, & CPK).

The performance metrics of each of the tasks In the ML-based prediction models are summarized in Supplementary Table 7.

# 12-month follow-up of a sub-group of survivors with AKI-2/3:

Among 227 AKI-2/3 survivors followed for 12 months after their index hospitalization, COVID-19 AKI survivors were more likely to be non-White, Hispanic, less baseline CKD, and greater severity of illness (MV, ARDS, vasopressor use, and length of hospital stay) during hospitalization compared to COVID-19 negative survivors (all  $p \le 0.01$ ). COVID-19 negative AKI survivors were more likely to have re-hospitalization (p <0.001), although no difference was noted in re-hospitalization with AKI among the 2 groups. 25 out of 161 (15.5%) of COVID-19 positive AKI survivors died after their discharge from COVID hospitalization as compared to only 1 out of 66 patients (1.5%) of the COVID-19 negative AKI survivors (p<0.001).

45 (28.0%) of COVID-19 positive and 22 (33.3%) of the COVID-19 negative patients had a SCr and eGFR measure > 90 days after discharge. The median number of days from discharge to follow up serum creatinine was 326.5 days for those with, and 300 days for those without COVID-19 at presentation. COVID-19

positive AKI survivors had no difference in the rate of incident or progressive CKD compared with COVID-19 negative AKI survivors 15.6% vs 18.2% respectively, p = 0.99).

# **DISCUSSION:**

To our knowledge, this is one of the first detailed comparisons of in-hospital recovery and of long-term outcomes after moderate/severe AKI in hospitalized patients with and without COVID-19. Our key findings are: 1) COVID-19 associated AKI-2/3 was associated with lower recovery and greater mortality compared to AKI-2/3 without COVID-19.2) ICU admission was associated with non-recovery in all AKI-2/3 patients, while ARDS was specific to those with COVID-19. 3) Among both COVID positive and COVID negative patients with AKI-2/3, renal recovery was significantly associated with survival but this association was further observed only in patients with COVID-19 after adjusting for other key variables. 4) Sensitivity analysis using a stricter criterion of renal recovery (Recovery-2, complete) and restricting patients to severe AKI (AKI-3) were mostly consistent with our main analysis. 5) Using ML algorithms, we were able to predict AKI and recovery from COVID-19-associated AKI-2/3 and identified key predictors. 6) At 10-month follow-up in moderate/severe AKI survivors, no difference in CKD between COVID positive and negative patients was observed.

Some initial studies from China at the start of the COVID-19 pandemic reported a variable AKI recovery rate (17.4-45.7%<sup>10,12</sup>), however, subsequent studies report a higher recovery rate from 64-87.2% in AKI survivors<sup>36,37</sup> and 41% overall<sup>38</sup>, although some of these studies were restricted to critically ill patients. The recovery rates noted in our study of COVID-19 associated AKI-2/3 were 50.6% (partial) and 24.7% (complete). Unlike previous studies, we compared recovery after AKI-2/3 in COVID-19 negative patients.

We found that ARDS was associated with non-recovery in AKI-2/3 patients with COVID-19 suggesting that severe lung disease in COVID-19 is associated with a lower chance of AKI recovery. This association was not noted in our non-COVID-19 group after adjusting for covariates but has been previously reported in critically ill patients without COVID-19<sup>39</sup>. We also observed that among patients with AKI-2/3, renal recovery was significantly associated with survival, however, this association was observed only in patients with COVID-19 after adjusting for covariates. This finding, if replicated in other studies, has potentially important prognostic

implications. Therapies directed at enhancing renal recovery can be tested in clinical trials with the goal of improving survival in patients with COVID-19.

Using state-of-the-art ML techniques, we asked the question if AKI and recovery can be predicted using data at the time of hospitalization. While AP in the models for AKI was low, their prediction performance is much higher than AKI incidence, e.g. AKI-2/3 incidence was 19.1% in COVID-19 positive patients vs. our AP of 0.36. We were able to predict more severe AKI (AKI-3) with greater accuracy as previously observed<sup>18-21</sup>. For recovery prediction, we used the cohort of patients who were diagnosed with AKI. The AP was only slightly higher than the incidence of recovery noted in our cohort. This means that it is relatively more difficult to predict recovery using only admission data, however, as can be seen from the PR curves (Figure 6), the precision values of our models at 20% recall are high, around 80%. This suggests that there is a small population of AKI patients where our recovery prediction models can identify recovery with a high level of accuracy. The key predictors for recovery in patients with COVID-19-associated AKI-2/3 were: CAD, BMI, BP, respiratory status, and labs (SCr, BNP, lymphocyte count, K, CPK, albumin, procalcitonin, Ca, INR, AST, and ALT). These findings if replicated in our cohorts, can be used for guiding preventive therapies and patient prognostication.

Approximately 10-30% of COVID-19 patients are known to develop the 'Long-COVID' syndrome that includes symptoms of Post-Acute Sequalae of SARS-Cov2 (PASC)<sup>41</sup> and organ injury including kidney disease<sup>42,43</sup>. While AKI is an established independent risk factor for CKD<sup>44</sup>, COVID-19 studies have mostly reported the persistence of renal dysfunction at discharge<sup>45,46</sup>. Two studies report a 3-6 follow-up after COVID-19-associated AKI. Hulstrom et al found that inpatient AKI severity was associated with higher CKD stages<sup>24</sup>, while Nugent et al, reported that patients with COVID-19–associated AKI had a greater rate of GFR decrease compared to non-COVID-19 patients with AKI<sup>25</sup>. At the time of this report, we report a longer, 12 month, follow-up data on SCr and GFR measures on AKI-2/3 survivors where the incidence of CKD was noted to be not statistically different between the COVID-19 negative and positive groups. While ours is one of the first studies reporting long-term renal outcomes associated with COVID-19 AKI, further multi-center studies with larger sample sizes and longer follow-up are required to further analyze this COVID-19 AKI/CKD relationship.

A strength of our study was the use of two different criteria of renal recovery; partial (Recovery 1)<sup>30</sup>. and complete (Recovery 2)<sup>31</sup>. Various definitions of renal recovery have been used in COVID-19 studies and multicenter studies will be required to compare the outcomes associated with different recovery definitions in COVID-19-associated AKI. Other major strengths include the inclusion of multiple covariates (~100) including data on medications, respiratory measures, vitals, and multiple laboratory values that are often not captured in larger multi-center studies using different EHR systems leading to issues with data harmonization. This granularity of clinical data, allowed us to conduct a robust multivariable analysis of the association of AKI and recovery with outcomes. We also report a control group of patients admitted during the first wave (when isolation measures were delayed due to delay in the report of SARS-Cov-2 PCR tests). We believe that this was a better control group for comparative analysis than using a retrospective cohort since the hospitalization period was the same as our patients with COVID-19, and the COVID-19 negative patients initially presented with symptoms suggestive of COVID-19.

Our study has several limitations. The use of the lowest SCr in the hospital as the baseline would not only capture incident AKI cases in the hospital, but also AKI at the time of hospitalization that subsequently recovered. However, our approach has its limitations since AKI cases at admission that did not recover were included in the 'no AKI' control group. The restriction of our study cohort to AKI Stages 2 and 3 removes mild rises in SCr misdiagnosed as AKI by the KDIGO criteria, however, the limitation of this approach is the inclusion of 'true' mild AKI cases in the 'no AKI' control group. In addition our AKI diagnosis relied on baseline and maximum SCr measures and did not follow the 48 hours of 7 day time frame criteria of KIDIGO Other limitations of this study include retrospective analysis in a single-center study and incomplete data for inflammatory biomarkers as well as for urinary data, hence it was not included in the multivariable analysis. We did not have urine output data available for accurate definition of AKI, which was limited to only SCr measures. We also did not have access to the daily SCr measures to apply the time variable in KDIGO definition of AKI. While our 12-month follow-up data, is one of the longest reported thus far, the analysis was limited to only a small sub-group of survivors with AKI-2/3 since patients often followed at non SBU clinics. Also we were not able to use urinalysis and renal imaging criteria to diagnose CKD-1 or 2 and relied solely on SCr and eGFR which might lead to under-diagnosis of 'true' post-AKI CKD. We used ICD-9/10 codes to define prevalent CKD on index admission which is another limitation in our study due to the possibility of misclassification bias, but it was the most objective way to define CKD present on index admission due to the lack of baseline GFR prehospitalization. Due to the limited frequency of ARDS in COVID negative patients in our cohort, we were underpowered to observe significant associations with recovery. We do not have information on the trajectory of AKI due to lack of daily SCr data. Our initial hospitalization period was from the first wave of the pandemic when there was no new reported variants of SARS-CoV-2 including the delta variant. Finally, in this study, if a patient died prior to recovery, then the person was treated as not recovered, meaning that the models are predicting survival and recovery at hospital discharge.

In conclusion, non-recovery after moderate/severe AKI is associated with ARDS and in-hospital death in patients with COVID-19. Moderate/severe AKI and recovery can be predicted using admission data with ML algorithms hence informing clinicians of patient prognosis. COVID-19 associated AKI-2/3 is associated with the risk of CKD. These findings need to be validated in large multi-center cohorts.

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# Supplemental Materials:

Supplementary Materials and Methods

Supplementary Table 0: Univariate analysis of patients in presence and absence of COVID-19.

Supplementary Table 1: Univariate analysis of patients with and without AKI-3 in presence and absence of COVID-19.

Supplementary Table 2: Univariate analysis of patients with and without Recovery -2 from AKI-2/3 in presence and absence of COVID-19.

Supplementary Table 3: Univariate analysis of patients with and without Recovery -1 from AKI-3 in presence and absence of COVID-19.

Supplementary Table 4: Univariate analysis of patients with and without Recovery -2 from AKI-3 in presence and absence of COVID-19.

Supplementary Table 5: Univariate analysis comparing death in all patients with and without COVID-19.

Supplementary Table 6: Univariate analysis comparing death in patients with and without AKI-3 in presence and absence of COVID-19.

Supplementary Table 7

Supplementary Methods Table X: list of all the variables used for ML algorithms and the % missingness in each variable

Supplementary Figure 0: Flow chart of the study cohort.

Supplementary Figure 1: A. Forest plot showing the multivariable analysis of COVID-19 positive patients with vs. without AKI-3. B. Forest plot showing the multivariable analysis of COVID-19 negative patients with vs. without AKI-3.

Supplementary Figure 2: A. Forest plot showing the multivariable analysis of COVID-19 positive patients with vs. without Recovery-2 after AKI-2/3. B. Forest plot showing the multivariable analysis of COVID-19 negative patients with vs. without Recovery-2 after AKI-2/3.

Supplementary Figure 3: A. Forest plot showing the multivariable analysis of COVID-19 positive patients with vs. without Recovery-1 after AKI-3. B. Forest plot showing the multivariable analysis of COVID-19 negative patients with vs. without Recovery-1 after AKI-3.

Supplementary Figure 4: A. Forest plot showing the multivariable analysis of COVID-19 positive patients with vs. without Recovery-2 after AKI-3. B. Forest plot showing the multivariable analysis of COVID-19 negative patients with vs. without Recovery-2 after AKI-3.

Supplementary Figure 5: A. Forest plot showing the multivariable analysis of death in COVID-19 positive patients analyzing the association of Recovery-1 after AKI-3. B. Forest plot showing the multivariable analysis of death in COVID-19 positive patients analyzing the association of Recovery-2 after AKI-3

Supplementary Figure 6: A. Forest plot showing the multivariable analysis of death in COVID-19 negative patients analyzing the association of Recovery-1 after AKI-3. B. Forest plot showing the multivariable analysis of death in COVID-19 negative patients analyzing the association of Recovery-2 after AKI-3.

Supplementary Figure 7: Precision Recall (PR) Curves for patients with AKI-2/3 with and without COVID-19 Supplementary Figure 8: Precision Recall (PR) Curves for patients with AKI-3 with and without COVID-19 Supplementary Figure 9: Precision Recall (PR) Curves for patients with Recovery from AKI-3 with and without COVID-19

Supplementary Figure 10: SHapley Additive exPlanations (SHAP) plots for patients with Recovery after AKI-3 with and without COVID-19

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# Table 1: Univariate analysis of patients with and without AKI-2/3 in presence and absence of COVID-19.

Variables	COVID-19 Negative (N=1961)			COVID-19 Positive (N=1338)		-
	No AKI-2/3	AKI-2/3	p- value	No AKI-2/3	AKI-2/3	p- value
	N=1789	N=172		N=1083	N=255	
Demographics						
Gender (N, %)						
Male	996 (55.67)	92 (53.49)		601 (55.49)	161 (63.14)	
Female	793 (44.33)	80 (46.51)	0.5819	482 (44.51)	94 (36.86)	0.0269
Race (N, %)						
White	1476 (82.5)	152 (88.37)		632 (58.36)	148 (58.04)	
Non-White	313 (17.5)	20 (11.63)	0.0522	451 (41.64)	107 (41.96)	0.9264
Ethnicity (N, %)						
Non-Hispanic	1708 (95.47)	169 (98.26)		875 (80.79)	219 (85.88)	
Hispanic	81 (4.53)	3 (1.74)	0.0976	208 (19.21)	36 (14.12)	0.0594
			0.0470			1.00E-
Age (Mean, SD)	63.25 (19.42)	66.92 (17.25)	0.0173	60.87 (18.26)	65.76 (15.48)	04
Co-morbid conditions (N, %)			0.04.11			-
DM	440 (24.59)	57 (33.14)	0.0144	292 (26.96)	112 (43.92)	0
HF	343 (19.17)	49 (28.49)	0.0038	150 (13.85)	51 (20)	0.014
CKD	256 (14.31)	38 (22.09)	0.0068	124 (11.45)	61 (23.92)	0
COPD	259 (14.48)	34 (19.77)	0.0644	112 (10.34)	38 (14.9)	0.0389
HTN	858 (47.96)	79 (45.93)	0.6109	448 (41.37)	123 (48.24)	0.0464
CAD	483 (27)	47 (27.33)	0.9265	191 (17.64)	57 (22.35)	0.0819
Cancer	294 (16.43)	32 (18.6)	0.4655	74 (6.83)	24 (9.41)	0.1568
Asthma	109 (6.09)	11 (6.4)	0.8744	81 (7.48)	16 (6.27)	0.505
BMI $[kg/m^2]$ (Mean, SD)	29.41 (9.82)	29.58 (16.1)	0.8382	29.68 (9.63)	29.57 (7.34)	0.8784
Severity of illness						
Length of hospital stay [days] (Mean, SD)	6.33 (5.16)	13.52 (10.17)	0	8.98 (6.61)	21.23 (15.48)	0
ICU admission (N, %)	275 (15.37)	72 (41.86)	0	129 (11.91)	163 (63.92)	0
Length of ICU stay [days] (Mean,		72 (41.00)	9.00E-	120 (11.01)	100 (00.02)	7.00E-
SD)	7.77 (14.43)	15.74 (21.66)	04	10.77 (15.91)	17.6 (15.68)	04
MV (N, %)	146 (8.16)	24 (13.95)	0.0109	87 (8.03)	72 (28.24)	0
MV days (Mean, SD)	4.03 (3.58)	13.32 (12.5)	0	8.58 (5.62)	17.94 (12.54)	0
ARD (N, %)	296 (16.55)	61 (35.47)	0	723 (66.76)	221 (86.67)	0
ARDS (N, %)	2 (0.11)	4 (2.33)	4.00E- 04	99 (9.14)	103 (40.39)	0
Vasopressor (N, %)	232 (12.97)	37 (21.51)	0.0021	23 (2.12)	18 (7.06)	1.00E- 04
Sepsis (N, %)	163 (9.11)	59 (34.3)	0	257 (23.73)	161 (63.14)	0
Medications (N, %)						
ACEI	285 (15.93)	42 (24.42)	0.0047	153 (14.13)	75 (29.41)	0
ARB	321 (17.94)	19 (11.05)	0.0241	177 (16.34)	52 (20.39)	0.1233
AC	1488 (83.17)	110 (63.95)	0	1018 (94)	171 (67.06)	0
NSAIDs	644 (36)	65 (37.79)	0.6402	260 (24.01)	91 (35.69)	2.00E- 04

Remdesivir	0 (0)	0 (0)	NA	12 (1.11)	8 (3.14)	0.0215
Hydroxychloroquine	56 (3.13)	9 (5.23)	0.1458	714 (65.93)	203 (79.61)	0
Tocilizumab	0 (0)	0 (0)	NA	84 (7.76)	58 (22.75)	0
Azithromycin	227 (12.69)	29 (16.86)	0.1224	502 (46.35)	150 (58.82)	4.00E- 04
Vitals (Mean, SD)						
SBP [mmHg]	132.77 (28.24)	135.05 (33.22)	0.3215	132.88 (27.65)	136.85 (30.56)	0.0439
Oral temperature [degree Celsius]	37.12 (0.73)	36.99 (0.59)	0.0324	37.14 (0.75)	37.11 (0.77)	0.518
Respiratory measures (Mean, SD)						
FIO2	57.91 (24.58)	64.65 (27.52)	0.0924	57.55 (26.5)	67.76 (26.45)	8.00E- 04
Renal labs (Mean, SD)						
BUN [mg/dL]	22.79 (20.02)	27.15 (20.48)	0.0074	20.94 (17.85)	24.21 (17.07)	0.0101
K [mmol/L]	4.19 (0.62)	4.27 (0.73)	0.1052	4.15 (0.58)	4.25 (0.65)	0.0181
HCO3 [mmol/L]	23.74 (4.15)	23.38 (4.46)	0.2822	24.03 (3.86)	23.28 (4.83)	0.0078
iCa [mg/dL]	4.54 (0.57)	4.4 (0.55)	0.1994	4.58 (0.47)	4.41 (0.48)	0.0259
Phos [mg/dL]	3.39 (1.12)	3.63 (1.46)	0.0132	3.28 (1.06)	3.56 (1.45)	0.0014
Inflammatory labs (Mean, SD)						
Ferritin [ng/mL]	775.34 (1194.39)	1211.87 (2730.12)	0.0089	783.02 (1183.33)	1067.04 (1650.39)	0.0148
Serum Albumin [g/dL]	3.85 (0.59)	3.79 (0.57)	0.1963	3.83 (0.59)	3.74 (0.65)	0.035
CRP [mg/dL]	8.56 (9.23)	6.84 (7.71)	0.0664	8.55 (9.08)	10.16 (10.41)	0.0406
Other labs (Mean, SD)						
Hb [g/dL]	12.96 (2.34)	12.39 (2.9)	0.0029	13.04 (2.28)	12.72 (2.67)	0.0557
Lactate [mmol/L]	2 (1.95)	2.39 (2.58)	0.0523	1.9 (1.69)	2.59 (3.3)	3.00E- 04
INR	1.31 (0.8)	1.26 (0.5)	0.3936	1.27 (0.62)	1.4 (1)	0.0204
LDH [IU/L]	328.4 (254.43)	468.22 (450.42)	0.0346	285.12 (138.86)	283.61 (116.62)	0.9487
Death (N, %)	99 (5.53)	20 (11.63)	0.0018	87 (8.03)	61 (23.92)	0

Categorical variables presented as a count with associated percentage, continuous variables presented as value with standard deviation (std). p-values <0.05 were considered significant and those variables have been highlighted in yellow. p-values <0.0001 are labelled as '0' in the Table. All variables until "Severity of illness" section were included, for the rest only significant variables were kept in the table for simplicity.

## Abbreviations:

DM (Diabetes Mellitus), HF (Heart Failure), CKD (Chronic kidney disease), COPD (chronic obstructive lung disease), HTN (Hypertension), CAD (Coronary Artery Disease), BMI (Body Mass Index), ICU (Intensive Care Unit), MV (Mechanical Ventilation), ARD (Acute Respiratory Disease), ARDS (Acute Respiratory Distress Syndrome), ACEI (Angiotensin Converting Enzyme Inhibitor), ARB (Angiotensin Receptor Blocker), AC (Anticoagulation), NSAIDs (Non-Steroidal Anti-Inflammatory Drugs), SBP (Systolic Blood Pressure), DBP (Diastolic Blood Pressure), MAP (Mean Arterial Pressure), O2 (Oxygen), CO2 (Carbon Dioxide), Ox (Oxygenation), paO2 (partial pressure of oxygen), FIO2 (Fraction of Inspired Oxygen), BUN (Blood Urea Nitrogen), Na (Sodium), K (Potassium), CI (Chloride), HCO3 (Bicarbonate), Ca (Calcium), iCa (ionized Calcium), Phos (Phosphorus), Mg (Magnesium), Osm (Osmolality), RBCs (Red Blood Cells), IL-6 (Interleukin-6), WBC (White Blood Cell count), ESR (Erythrocyte Sedimentation Rate), CRP (C-reactive Protein), Hb (Hemoglobin), BNP (Brain Natriuretic Peptide), INR (International Normalized Ratio), LDH (Lactate Dehydrogenase), AST (aspartate aminotransferase), ALT (alanine aminotransferase), CPK (Creatine Phosphokinase). Units: mmHg (millimeters of mercury), mmol/L (millimoles per liter), mg/dL (milligrams per deciliter), mOsm/L (milliosmoles per liter), g/dL (grams per deciliter), mm/hr (millimeters per hour], K/uL (thousand per microliter), IU/L (international units per liter), ng/mL (nanogram per millliter), pg/mL (picogram per millliter), HPF (high power field)

Table 2: Univariate analysis of patients with and without Recovery -1 from AKI-2/3 in presence and absence of COVID-19.

Variables	Covid-19 Ne	gative (N=172)	Covid-19 Positive (N=255)			
	No Recovery	Recovery-1	p- value	No Recovery	Recovery-1	p- value
	N1=44	N2=128		N1=126	N2=129	
Demographics						
Gender (N, %)						
Male	23 (52.27)	69 (53.91)		84 (66.67)	77 (59.69)	
Female	21 (47.73)	59 (46.09)	0.851 4	42 (33.33)	52 (40.31)	0.2488
Race (N, %)						
White	39 (88.64)	113 (88.28)		63 (50)	85 (65.89)	
Non-White	5 (11.36)	15 (11.72)	0.949 5	63 (50)	44 (34.11)	0.0105
Ethnicity (N, %)						
Non-Hispanic	44 (100)	125 (97.66)		102 (80.95)	117 (90.7)	
Hispanic	0 (0)	3 (2.34)	0.986 2	24 (19.05)	12 (9.3)	0.0283
	70.00 (45.50)		0.079	C4 04 (45 40)	66.55	0 4070
Age (Mean, SD)	70.89 (15.56)	65.55 (17.65)	4	64.94 (15.18)	(15.79)	0.4073
Co-morbid conditions (N, %)			0.339			
DM	12 (27.27)	45 (35.16)	3	48 (38.1)	64 (49.61)	0.0646
HF	18 (40.91)	31 (24.22)	0.036 5	24 (19.05)	27 (20.93)	0.7072
СКD	11 (25)	27 (21.09)	0.590 5	31 (24.6)	30 (23.26)	0.8009
COPD	13 (29.55)	21 (16.41)	0.062 5	15 (11.9)	23 (17.83)	0.1867
HTN	16 (36.36)	63 (49.22)	0.142	62 (49.21)	61 (47.29)	0.7591
CAD	15 (34.09)	32 (25)	0.245	31 (24.6)	26 (20.16)	0.3946
Cancer	10 (22.73)	22 (17.19)	0.416 8	9 (7.14)	15 (11.63)	0.2242
Asthma	2 (4.55)	9 (7.03)	0.564 1	9 (7.14)	7 (5.43)	0.5731
			0.568			
<b>BMI</b> $[kg/m^2]$ (Mean, SD)	28.31 (5.58)	30.03 (18.44)	9	28.99 (6.39)	30.1 (8.09)	0.2564
Severity of illness Length of hospital stay [days] (Mean, SD)	12.82 (8.79)	13.77 (10.62)	0.593	22.6 (16.2)	19.89 (14.69)	0.1636
ICU admission (N, %)	25 (56.82)	47 (36.72)	0.021	102 (80.95)	61 (47.29)	0.1030
Length of ICU stay [days] (Mean,			0.207		16.03	
SD)	11.12 (13.65)	18.19 (24.69)	8	18.54 (16.81)	(13.59)	0.3253
MV (N, %)	9 (20.45)	15 (11.72)	0.154 1	44 (34.92)	28 (21.71)	0.02
MV days (Mean, SD)	11 (11.11)	14.52 (13.21)	0.395	17.54 (13.08)	18.79 (11.4)	0.5739
ARD (N, %)	22 (50)	39 (30.47)	0.021	119 (94.44)	102 (79.07)	7.00E- 04
ARDS (N, %)	2 (4.55)	2 (1.56)	0.279 4	67 (53.17)	36 (27.91)	0

Other labs (Mean, SD)			0.032			
Ferritin [ng/mL]	(4431.31)	(1851.46)	1	(2075.43)	(923.63)	0.01
Inflammatory labs (Mean, SD)	1374.13	1155.52	0.731	1433.56	691.79	
Urine Na [mEq/L]	47.69 (34.68)	50.74 (38.89)	1	42.78 (33)	(37.83)	0.0321
	302.23 (13)	234 (20.72)	0.798	300.33 (23.33)	58.41	0.0100
Serum Osm [mOsm/kg]	302.25 (19)	294 (26.72)	0.552	306.59 (29.39)	285.48 (16.22)	0.0105
iCa [mg/dL]	4 (0.68)	4.56 (0.41)	7	4.32 (0.56)	4.53 (0.33)	0.0542
Renal labs (Mean, SD)			0.040			
Pulse Ox	94.77 (6.95)	95.88 (4.16)	0.218 5	94.04 (6.03)	95.9 (4.19)	0.0066
Respiratory measures (Mean, SD)			0.040			
Azithromycin	7 (15.91)	22 (17.19)	1	89 (70.63)	61 (47.29)	04
Tocilizumab	0 (0)	0 (0)	NA 0.845	41 (32.54)	17 (13.18)	04 2.00E-
Taoilizumah	0 (0)	0 (0)		41 (22 54)	17 (12 10)	3.00E-
Hydroxychloroquine	3 (6.82)	6 (4.69)	0.586 2	108 (85.71)	95 (73.64)	0.0182
Medications (N, %)						
Sepsis (N, %)	18 (40.91)	41 (32.03)	0.265	87 (69.05)	74 (57.36)	0.054
Vasopressor (N, %)	8 (18.18)	29 (22.66)	0.534	8 (6.35)	10 (7.75)	0.6624

Categorical variables presented as a count with associated percentage, continuous variables presented as value with standard deviation (std). p-values <0.05 were considered significant and those variables have been highlighted in yellow. p-values <0.0001 are labelled as '0' in the Table. All variables until (and include) "Severity of illness" section were included, for the rest only significant variables were kept in the table for simplicity.

## Abbreviations:

DM (Diabetes Mellitus), HF (Heart Failure), CKD (Chronic kidney disease), COPD (chronic obstructive lung disease), HTN (Hypertension), CAD (Coronary Artery Disease), BMI (Body Mass Index), ICU (Intensive Care Unit), MV (Mechanical Ventilation), ARD (Acute Respiratory Disease), ARDS (Acute Respiratory Distress Syndrome), ACEI (Angiotensin Converting Enzyme Inhibitor), ARB (Angiotensin Receptor Blocker), AC (Anticoagulation), NSAIDs (Non-Steroidal Anti-Inflammatory Drugs), SBP (Systolic Blood Pressure), DBP (Diastolic Blood Pressure), MAP (Mean Arterial Pressure), O2 (Oxygen), CO2 (Carbon Dioxide), Ox (Oxygenation), paO2 (partial pressure of oxygen), FIO2 (Fraction of Inspired Oxygen), BUN (Blood Urea Nitrogen), Na (Sodium), K (Potassium), CI (Chloride), HCO3 (Bicarbonate), Ca (Calcium), iCa (ionized Calcium), Phos (Phosphorus), Mg (Magnesium), Osm (Osmolality), RBCs (Red Blood Cells), IL-6 (Interleukin-6), WBC (White Blood Cell count), ESR (Erythrocyte Sedimentation Rate), CRP (C-reactive Protein), Hb (Hemoglobin), BNP (Brain Natriuretic Peptide), INR (International Normalized Ratio), LDH (Lactate Dehydrogenase), AST (aspartate aminotransferase), ALT (alanine aminotransferase), CPK (Creatine Phosphokinase). Units: mmHg (millimeters of mercury), mmol/L (millimoles per liter), mg/dL (milligrams per deciliter), mOsm/L (milliosmoles per liter), g/dL( grams per deciliter), mm/hr (millimeters per hour], K/uL (thousand per microliter), IU/L (international units per liter), ng/mL (nanogram per millliter), pg/mL (picogram per millliter), HPF (high power field)

Table 3: Univariate analysis comparing death in patients with and without AKI-2/3 in presence and absence of COVID-19.

Variables	Covid-19 Ne	gative (N=172)	Covid-19 Positive (N=255)			
	No Death	Death	p- value	No Death	Death	p- value
	N1=152	N2=20		N1=194	N2=61	
Demographics						
Gender (N, %)						
Male	79 (51.97)	13 (65)		114 (58.76)	47 (77.05)	
Female	73 (48.03)	7 (35)	0.2764	80 (41.24)	14 (22.95)	0.0111
Race (N, %)						
White	134 (88.16)	18 (90)		116 (59.79)	32 (52.46)	
Non-White	18 (11.84)	2 (10)	0.8093	78 (40.21)	29 (47.54)	0.3121
Ethnicity (N, %)						
Non-Hispanic	149 (98.03)	20 (100)		169 (87.11)	50 (81.97)	
Hispanic	3 (1.97)	0 (0)	0.9916	25 (12.89)	11 (18.03)	0.3162
Age (Mean, SD)	66.62 (16.85)	69.15 (20.42)	0.5379	67.08 (15.14)	61.56 (15.92)	0.0164
Co-morbid conditions (N, %)						
DM	49 (32.24)	8 (40)	0.4895	92 (47.42)	20 (32.79)	0.0462
HF	43 (28.29)	6 (30)	0.8734	46 (23.71)	5 (8.2)	0.012
СКD	30 (19.74)	8 (40)	0.046	51 (26.29)	10 (16.39)	0.1177
COPD	29 (19.08)	5 (25)	0.5335	29 (14.95)	9 (14.75)	0.9703
HTN	73 (48.03)	6 (30)	0.1352	95 (48.97)	28 (45.9)	0.6759
CAD	38 (25)	9 (45)	0.0652	43 (22.16)	14 (22.95)	0.8978
Cancer	28 (18.42)	4 (20)	0.8646	22 (11.34)	2 (3.28)	0.078
Asthma	11 (7.24)	0 (0)	0.9896	8 (4.12)	8 (13.11)	0.0165
BMI $[kg/m^2]$ (Mean, SD)	29.84 (16.8)	27.17 (6.26)	0.5366	29.4 (7.21)	30.15 (7.78)	0.5154
Severity of illness						
Length of hospital stay [days] (Mean, SD)	12.99 (9.63)	17.55 (13.18)	0.0689	20.22 (15.52)	24.44 (15.03)	0.0658
ICU admission (N, %)	57 (37.5)	15 (75)	0.003	115 (59.28)	48 (78.69)	0.007
Length of ICU stay [days] (Mean, SD)	16.65 (23.93)	12.27 (8.57)	0.4909	17.1 (16.21)	18.79 (14.43)	0.5312
MV (N, %)	9 (5.92)	15 (75)	0	21 (10.82)	51 (83.61)	0
MV days (Mean, SD)	13.41 (12.3)	13.08 (13.53)	0.9379	16.84 (11.89)	20.1 (13.59)	0.1367
ARD (N, %)	51 (33.55)	10 (50)	0.1538	163 (84.02)	58 (95.08)	0.0368
ARDS (N, %)	3 (1.97)	1 (5)	0.4155	68 (35.05)	35 (57.38)	0.0023
Vasopressor (N, %)	31 (20.39)	6 (30)	0.3297	14 (7.22)	4 (6.56)	0.8609
Sepsis (N, %)	50 (32.89)	9 (45)	0.2873	117 (60.31)	44 (72.13)	0.0971
Medications (N, %)						
ACEI	37 (24.34)	5 (25)	0.9487	70 (36.08)	5 (8.2)	2.00E- 04
AC	93 (61.18)	17 (85)	0.0483	119 (61.34)	52 (85.25)	9.00E- 04
NSAIDs	53 (34.87)	12 (60)	0.0344	68 (35.05)	23 (37.7)	0.706
Vitals (Mean, SD)		12 (00)	0.0074		20 (01.1)	0.700

SBP [mmHg]	135.89 (33.63)	128.6 (29.92)	0.3553	139.39 (30.83)	128.67 (28.39)	0.0186
DBP [mmHg]	76.7 (16.22)	70.55 (12.75)	0.1061	77.16 (14.26)	70.85 (12)	0.0027
MAP [mmHg]	97.07 (18.2)	91.85 (16.44)	0.2229	96.15 (18.26)	88.24 (13.59)	0.0028
Oral temperature [degree Celsius]	36.97 (0.58)	37.14 (0.75)	0.3068	37.02 (0.71)	37.45 (0.92)	8.00E- 04
Respiratory rate	19.36 (4.5)	25.2 (13.08)	0.0018	19.85 (4.81)	25.84 (13.12)	0
Respiratory measures (Mean, SD)	19.30 (4.3)	23.2 (13.06)	0.0018	19.03 (4.01)	25.04 (15.12)	0
Pulse Ox	96.24 (3.55)	90.7 (9.92)	7.00E- 04	96.06 (3.82)	91.56 (7.37)	0
Renal labs (Mean, SD)						
Na [mmol/L]	137.5 (5.1)	134.9 (5.82)	0.039	137.42 (4.75)	134.7 (5.79)	4.00E- 04
CI [mmol/L]	99.42 (6.27)	95.65 (6.17)	0.016	99.42 (5.71)	96.15 (6.81)	4.00E- 04
HCO3 [mmol/L]	23.69 (4.27)	21 (5.25)	0.0138	24.03 (4.27)	20.9 (5.69)	0
Phos [mg/dL]	3.53 (1.28)	4.41 (2.31)	0.0238	3.43 (1.25)	3.95 (1.88)	0.0258
Mg [mg/dL]	1.99 (0.35)	2.19 (0.41)	0.0282	1.98 (0.32)	2.14 (0.43)	0.0049
Urine Na [mEq/L]	57.08 (39.58)	26.33 (14.14)	0.0314	60.91 (37.82)	37.75 (29.69)	0.0019
Urine RBCs (per HPF)	7.99 (24.24)	40.39 (69.84)	0.0075	17.37 (42.05)	24.58 (43.65)	0.3015
Inflammatory labs (Mean, SD)						
Ferritin [ng/mL]	850.81 (1562.35)	3544.82 (5994.73)	0.0322	813.65 (1451.99)	1611.36 (1915.27)	0.0089
Lymphocyte count [K/uL]	1.32 (0.8)	0.87 (0.38)	0.0424	1.46 (1.08)	0.76 (0.46)	0
ESR [mm/hr]	47.97 (32.74)	72.25 (23.63)	0.0661	44.21 (32.51)	57.45 (30.15)	0.0432
CRP [mg/dL]	5.39 (5.79)	14.8 (11.6)	2.00E- 04	8.09 (9.38)	14.61 (11.18)	3.00E- 04
Other labs (Mean, SD)						
Lactate [mmol/L]	2.03 (1.94)	4.41 (4.35)	0.0072	2.05 (2)	3.76 (4.92)	0.0077
BNP [pg/mL]	1947.37 (3522.84)	4756.67 (9475.9)	0.0748	2959.07 (9177.11)	4193.52 (7608.25)	0.4189
LDH [IU/L]	344.24 (269.16)	819.5 (678.6)	0.0601	242.88 (72.48)	451.62 (116.71)	0.0052
AST [IU/L]	41.21 (48.23)	129.2 (172.14)	8.00E- 04	44.12 (61.18)	84.95 (124.55)	0.0126
ALT [IU/L]	32.05 (37.29)	98 (200.78)	0.034	37.07 (67.05)	43.82 (39.15)	0.4648
Recovery 1 (N, %)	117 (76.97)	11 (55)	0.0396	110 (56.7)	19 (31.15)	7.00E- 04
Recovery 2 (N, %)	71 (46.71)	5 (25)	0.0741	56 (28.87)	7 (11.48)	0.0082

Categorical variables presented as a count with associated percentage, continuous variables presented as value with standard deviation (std). p-values <0.05 were considered significant and those variables have been highlighted in yellow. p-values <0.0001 are labelled as '0' in the Table. All variables until (and include) "Severity of illness" section were included, for the rest only significant variables were kept in the table for simplicity.

## Abbreviations:

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(Angiotensin Receptor Blocker), AC (Anticoagulation), NSAIDs (Non-Steroidal Anti-Inflammatory Drugs), SBP (Systolic Blood Pressure), DBP (Diastolic Blood Pressure), MAP (Mean Arterial Pressure), O2 (Oxygen), CO2 (Carbon Dioxide), Ox (Oxygenation), paO2 (partial pressure of oxygen), FIO2 (Fraction of Inspired Oxygen), BUN (Blood Urea Nitrogen), Na (Sodium), K (Potassium), CI (Chloride), HCO3 (Bicarbonate), Ca (Calcium), iCa (ionized Calcium), Phos (Phosphorus), Mg (Magnesium), Osm (Osmolality), RBCs (Red Blood Cells), IL-6 (Interleukin-6), WBC (White Blood Cell count), ESR (Erythrocyte Sedimentation Rate), CRP (C-reactive Protein), Hb (Hemoglobin), BNP (Brain Natriuretic Peptide), INR (International Normalized Ratio), LDH (Lactate Dehydrogenase), AST (aspartate aminotransferase), ALT (alanine aminotransferase), CPK (Creatine Phosphokinase). Units: mmHg (millimeters of mercury), mmol/L (millimoles per liter), mg/dL (milligrams per deciliter), mOsm/L (milliosmoles per liter), g/dL( grams per deciliter), mm/hr (millimeters per hour], K/uL (thousand per microliter), IU/L (international units per liter), ng/mL (nanogram per millliter), pg/mL (picogram per millliter), HPF (high power field)

# Table 4: CKD outcomes in AKI-2/3 survivors at 12 months follow-up

CKD Outcomes	COVID-19 positive	COVID-19 negative	p-value
Total number of patients followed for 12 months	161	66	
# of Patients with >90 Day Post Discharge Creatinine Data	45 (28.0%)	22 (33.3%)	
History of CKD	5 (11.1%)	2 (9.1%)	0.99
CKD			
Incident/Progressive CKD	7 (15.6%)	4 (18.2%)	0.99
No Incident/Progressive CKD	38 (84.6%)	18 (81.8%)	

# Figure Legends:

**Figure 1**: **A**. Forest plot showing the multivariable analysis of COVID-19 positive patients with vs. without AKI-2/3. **B**. Forest plot showing the multivariable analysis of COVID-19 negative patients with vs. without AKI-2/3.

**Figure 2**: **A**. Forest plot showing the multivariable analysis of COVID-19 positive patients with vs. without Recovery-1 after AKI-2/3. **B**. Forest plot showing the multivariable analysis of COVID-19 negative patients with vs. without Recovery-1 after AKI-2/3.

**Figure 3**: **A**. Forest plot showing the multivariable analysis of death in COVID-19 positive patients analyzing the association of Recovery-1 after AKI-2/3. **B**. Forest plot showing the multivariable analysis of death in COVID-19 positive patients analyzing the association of Recovery-2 after AKI-2/3.

**Figure 4: A.** Forest plot showing the multivariable analysis of death in COVID-19 negative patients analyzing the association of Recovery-1 after AKI-2/3. **B.** Forest plot showing the multivariable analysis of death in COVID-19 negative patients analyzing the association of Recovery-2 after AKI-2/3.

Figure 5: Precision Recall (PR) Curves for Recovery after AKI-2/3 in patients with and without COVID-19

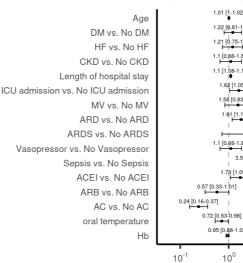
**Figure 6:** SHapley Additive exPlanations (SHAP) plots for Recovery after AKI-2/3 in patients with and without COVID-19

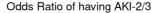
#### Figure 1A: Forest plot showing the multivariate analysis of COVID-19 positive patients with vs. without AKI-2/3

Female Gender vs. Male Gender Age		1.04 [0.7-1.53]						
DM vs. No DM		1.31 [0.87-1.96]						
HF vs. No HF		1.24 [0.73-2.12]						
CKD vs. No CKD		2.2 [1.3-3.72	]					
COPD vs. No COPD		0.84 [0.48-1.48]						
HTN vs. No HTN		1.19 [0.79-1.82]						
Length of hospital stay		1.07 [1.04-1.09]						
ICU admission vs. No ICU admission		4.04 [2.5	1-6.52]					
		2.29 [1.39-3.7	78]					
MV vs. No MV		1.14 [0.67-1.96]						
ARD vs. No ARD		1.12 [0.66-1.9]						
ARDS vs. No ARDS		1.18 [0.44-3.18]						
Vasopressor vs. No Vasopressor		1.97 [1.32-2.96	5]					
Sepsis vs. No Sepsis								
ACEI vs. No ACEI	0.11 [0.06-0.18]	i i i i i i i i i i i i i i i i i i i						
AC vs. No AC		 1.02 [0.66-1.59]						
NSAIDs vs. No NSAIDs		1.2 [0.29-4.98]						
remdesivir vs. No remdesivir	,		-					
hydroxychloroquine vs. No hydroxychloroquine		1.31 [0.79-2.16]						
tocilizumab vs. No tocilizumab		0.8 [0.44-1.48]						
azithromycin vs. No azithromycin		0.83 [0.54-1.26]						
SBP		1.01 [1-1.01]						
BUN		1.01 [1-1.02]						
	1 01	100	1	1.02				
	10 <sup>-1</sup>	10 <sup>0</sup>	10 <sup>1</sup>	10 <sup>2</sup>				
	Odds Ratio of having AKI-2/3							

DM=diabetes mellitus, HF=heart failure, CKD=chronic kidney disease, COPD=chronic obstructive pulmonary disease, HTN=hypertension, ICU=intensive care unit, MV=mechanical ventilation, ARD=acute respiratory disease, ARDS=acute respiratory distress syndrome, ACEI=angiotensin converting enzyme inhibitor, AC=anticoagulation, NSAIDs=nonsteroidal anti-inflammatory drugs, SBP=systolic blood pressure, BUN=blood urea nitrogen \*unit for SBP is mmHg (millimeters of mercury), unit for BUN is mg/dL (milligrams per deciliter)

Figure 1B: Forest plot showing the multivariate analysis of COVID-19 negative patients with vs. without AKI-2/3





1.01 [1-1.02]

1.22 [0.81-1.84]

1.21 [0.75-1.94]

1.1 [0.66-1.84]

1.1 [1.08-1.13]

1.1 [0.66-1.84]

0.95 [0.88-1.02]

10<sup>0</sup>

1.62 [1.05-2.51]

1.56 [0.83-2.92]

1.81 [1.18-2.79]

1.7β [1.09-2.76]

3.51 [2.27-5.45]

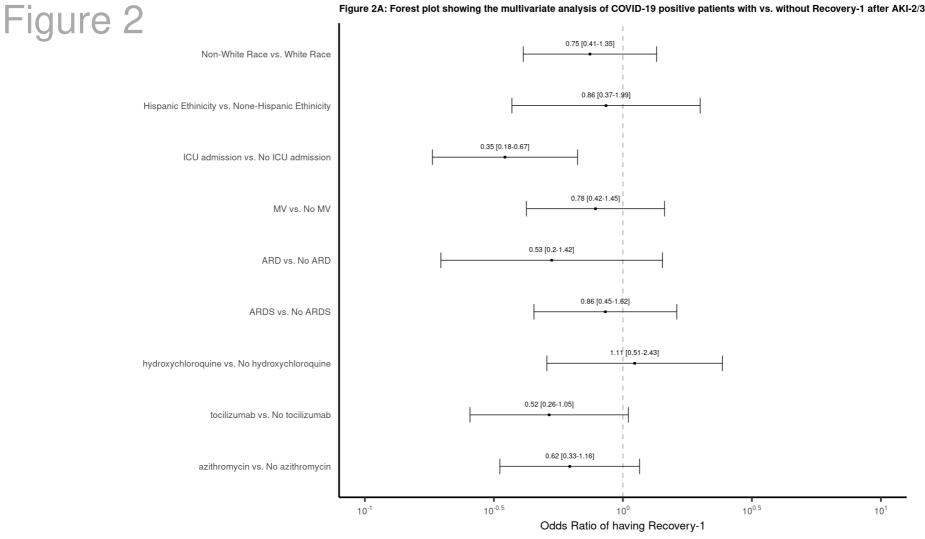
9.04 [0.72-113.02]

10<sup>1</sup>

10<sup>2</sup>

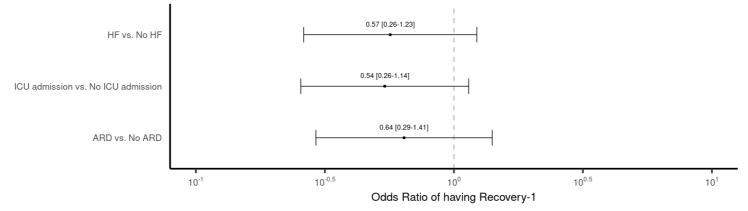
DM=diabetes mellitus, HF=heart failure, CKD=chronic kidney disease, ICU=intensive care unit, MV=mechanical ventilation, ARD=acute respiratory disease, ARDS=acute respiratory distress syndrome, ACEI=angiotensin converting enzyme inhibitor, ARB=angiotensin receptor blocker, AC=anticoagulation, Hb=hemoglobin \*unit for oral temperature is degree Celsius, unit for Hb is g/dL (grams per deciliter)

# Figure



ICU=intensive care unit, MV=mechanical ventilation, ARD=acute respiratory disease, ARDS=acute respiratory distress syndrome

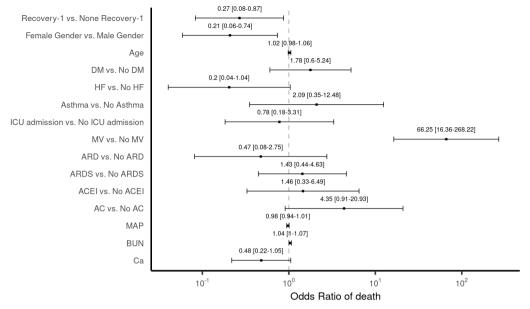
#### Figure 2B: Forest plot showing the multivariate analysis of COVID-19 negative patients with vs. without Recovery-1 after AKI-2/3



HF=heart failure, ICU=intensive care unit, ARD=acute respiratory disease

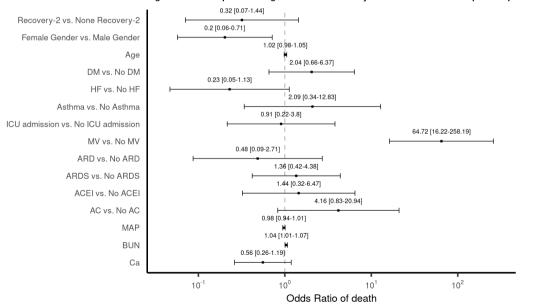
# Figure 3

#### Figure 3A: Forest plot showing the multivariate analysis of death in COVID-19 positive patients analyzing the association of Recovery-1 after AKI-2/3

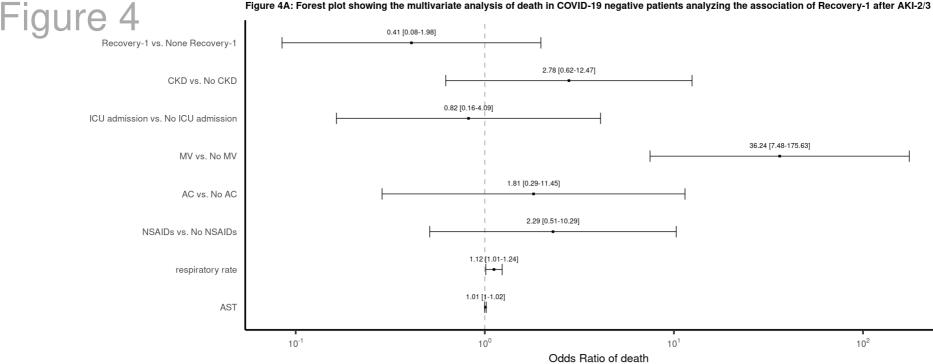


DM=diabetes mellitus, HF=heart failure, ICU=intensive care unit, MV=mechanical ventilation, ARD=acute respiratory disease, ARDS=acute respiratory distress syndrome, ACEI=angiotensin converting enzyme inhibitor, AC=anticoagulation, MAP=mean arterial pressure, BUN=blood urea nitrogen, Ca=serum calcium 'unit for MAP is mmHg (millimeters of mercury), unit for BUN is mg/dL (milligrams per deciliter), unit for Ca is mg/dL (milligrams per deciliter)

#### Figure 3B: Forest plot showing the multivariate analysis of death in COVID-19 positive patients analyzing the association of Recovery-2 after AKI-2/3



DM=diabetes mellitus, HF=heart failure, ICU=intensive care unit, MV=mechanical ventilation, ARD=acute respiratory disease, ARDS=acute respiratory distress syndrome, ACEI=angiotensin converting enzyme inhibitor, AC=anticoagulation, MAP=mean arterial pressure, BUN=blood urea nitrogen \*unit for MAP is mmHg (millimeters of mercury), unit for BUN is mg/dL (milligrams per deciliter), unit for Ca is mg/dL (milligrams per deciliter) Figure 4A: Forest plot showing the multivariate analysis of death in COVID-19 negative patients analyzing the association of Recovery-1 after AKI-2/3



CKD=chronic kidney disease, ICU=intensive care unit, MV=mechanical ventilation, AC=anticoagulation, NSAIDs=nonsteroidal anti-inflammatory drugs, AST=aspartate aminotransferase \*unit for AST is IU/L (international units per liter)

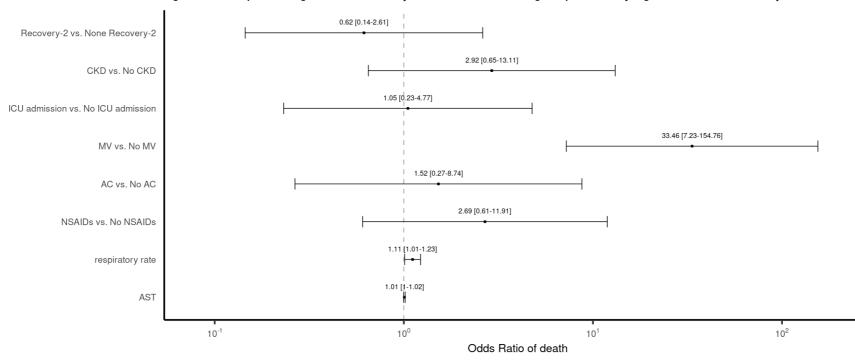


Figure 4B: Forest plot showing the multivariate analysis of death in COVID-19 negative patients analyzing the association of Recovery-2 after AKI-2/3

CKD=chronic kidney disease, ICU=intensive care unit, MV=mechanical ventilation, AC=anticoagulation, NSAIDs=nonsteroidal anti-inflammatory drugs, AST=aspartate aminotransferase \*unit for AST is IU/L (international units per liter)

# Figures 5 and 6

# Figure 5: Recovery PR Curves (patients with AKI-2/3)

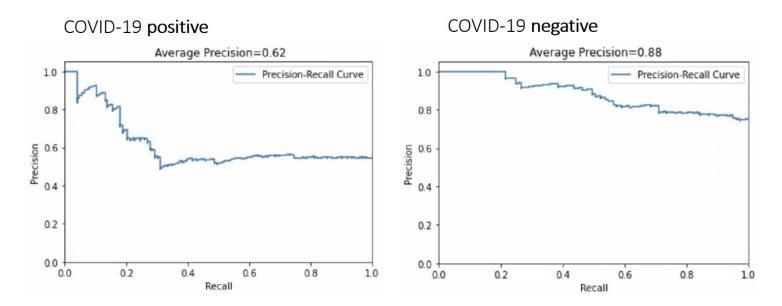
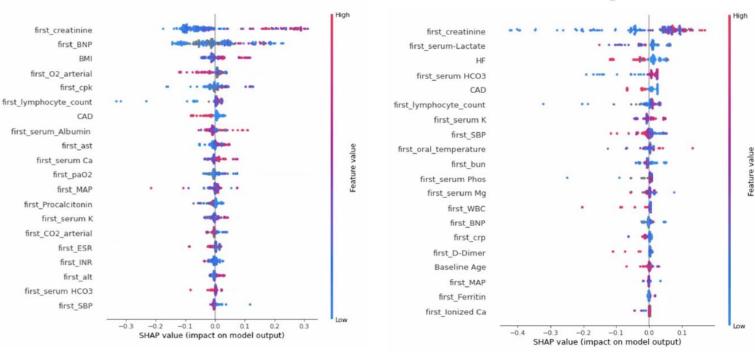


Figure 6: SHAP Plots- predictors of Recovery after AKI-2/3

COVID-19 positive

COVID-19 negative



# SUPPLEMENTARY MATERIALS AND METHODS

# Control group (COVID-19 negative) in the cohort:

The main cohort of hospitalized patients from March to July 2020 are from the first wave on the pandemic in NY when there was a delay in reporting of COVID-19 PCR. All patients in our cohort were admitted with symptoms suggestive of COVID-19 at presentation. The symptoms included systemic and respiratory illness suggestive of COVID-19 as was the existing knowledge of the disease in the first wave of the pandemic. All patients were initially kept in isolation and had a similar management until the COVID-19 PCR was reported. In our study, those whose PCR test results came back positive were retrospectively assigned to the COVID group while those who tested negative to the non-COVID (control) group.

# Data collection and definition of variables:

All data was collected using the SBUMC electronic health record (EHR) or intensive care unit (ICU) records. Data was automatically fed from the EHR into the "Data Commons COVID-19 registry" at SBU in a real-time computational method. We used the SBU Data Commons COVID-19 registry to extract data for analysis. Data was collected on race, ethnicity, age, and gender. Comorbid conditions like ESKD, diabetes mellitus (DM), heart failure (HF), chronic kidney disease (CKD), chronic obstructive pulmonary disease (COPD), hypertension (HTN), coronary artery disease (CAD), cancer, and asthma were diagnosed through Internal Classification of Diseases (ICD)-10 codes. Body Mass Index (BMI) was calculated through documented height and weight measures at the time of admission. The markers of 'severity of illness' (length of hospital stay, intensive care unit [ICU] admission, the number of ICU days, mechanical ventilation [MV], the number of MV days, acute respiratory disease [ARD], acute respiratory distress syndrome [ARDS], vasopressor use and sepsis) were determined through ICD-10 codes or documentation in the EHR. EHR was used to determine key medication use including angiotensin converting enzyme inhibitors (ACEIs), angiotensin receptor blockers (ARBs), non-steroidal anti-inflammatory drugs (NSAIDs), anticoagulants (AC), remdesivir, hydroxychloroquine, tocilizumab, azithromycin, and dexamethasone.

The first/admission (within 48 hours of Emergency Department [ED] visit) values of vital signs and respiratory parameters and labs were obtain from the EHR. The vital sign data included systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), oral temperature, respiratory rate] & pulse oxygenation (Pulse Ox). Arterial blood gas (ABG) data was

used to obtain partial pressures of arterial O2 and arterial CO2 and arterial pH. Fraction of inspired oxygen (FiO2) data was obtained from ICU records.

The renal laboratory measures were divided into 'renal function labs' that included serum creatinine (SCr), and blood urea nitrogen (BUN). 'Other renal labs' included serum sodium (Na), potassium (K), chloride (Cl), bicarbonate (HCO3), calcium (Ca), phosphate (phos), magnesium (Mg), osmolality (Osm) and blood ionized Ca. Urine labs included spot urine Na, osmolality, protein, blood & red blood cells (RBCs). Inflammatory labs included serum ferritin, D-Dimer, interleukin (IL)-6, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), white blood cell count (WBC), lymphocyte count, procalcitonin, and serum albumin. Other key laboratory measures included serum lactate, brain natriuretic peptide (BNP), troponin, international normalized ratio (INR), hemoglobin (Hb), lactate dehydrogenase (LDH), aspartate aminotransferase (AST), Alanine aminotransferase (ALT), and creatinine phosphokinase (CPK).

Finally, patient death was determined through documentation in the EHR.

# Rational for baseline Serum Creatinine (SCr):

One of the issues noted in outcome studies of hospitalized AKI patients (especially in those admitted with COVID-19) is the lack of recent laboratory data to estimate the baseline SCr and hence define AKI. The first inpatient SCr as a baseline<sup>1</sup> has been used in COVID-19 AKI studies<sup>2,3</sup>, but this would miss patients that present to the hospital with AKI. Others have proposed the use of the mean outpatient serum creatinine measured within a year of hospitalization<sup>4</sup>, however, we did not have enough outpatient SCr measures in our cohort to use this approach (< 20% patients with COVID-19 had an SCr value within 365 days prior to hospitalization). Another proposed approach is to estimate baseline SCr was to assume a baseline glomerular filtration rate (GFR) of 75 mL/min/1.73 m<sup>2</sup> using the four-variable Modification of Diet in Renal Disease (MDRD) equation<sup>5</sup> and employed for COVID-19 associated AKI<sup>6</sup>, but this method is fraught with misclassification issues<sup>1</sup>. Others analyzing COVID-19 –associated AKI<sup>7</sup> have used the United Kingdom National Health Service based AKI algorithm<sup>8</sup> to estimate baseline SCr. In this study, we used the lowest SCr in the hospital as the baseline as it has been previously proposed<sup>9</sup> and used in other COVID-19 AKI studies<sup>10</sup>. This approach would not only capture de novo AKI cases in the hospital, but also AKI at the time of hospitalization that subsequently recovered. However, our approach has its limitations since AKI cases at admission that did not recover were included in the 'no AKI' control group. Further studies using recent outpatient SCr as 'true' baseline will need to be conducted to address these issues.

# Rationale for the focus on AKI Stages 2 and 3 in this study:

An issue noted in AKI outcome studies is some minimum SCr values in the hospital would be below the true baseline (dilution due to volume), and the SCr based criteria to diagnose AKI has been associated with a high false-positive rate leading to over-diagnosis of AKI<sup>11</sup>. The SCr level can be influenced by poor Cr production during critical illness<sup>12</sup>. In this study, we tried to circumvent this issue by looking only at cases of moderate/severe AKI (KDIGO Stage 2 or 3)<sup>9</sup>. A > 2 fold rise in SCr from baseline is more likely to capture 'true' cases of AKI that are more reflective of renal injury. Moreover, moderate/severe AKI is associated with significantly increased health care utilization & costs and long-term patient outcomes including CKD<sup>13</sup> and death<sup>14</sup> If patients required acute dialysis during hospitalization, they were directly assigned to AKI-3 group and SCr was not used. The lowest and highest SCr were only used for patients who did not require dialysis for AKI during the hospitalization.

# Rational for the Recovery definitions used:

Various definitions of renal recovery have been used in COVID-19 studies including ADQI criteria<sup>15</sup>, acute RRT cessation<sup>16</sup>, improvement to baseline SCr<sup>17</sup>, 33% decline in SCr level<sup>18</sup>, recovery to KDIGO-stage 1<sup>19</sup>, within 25% of baseline SCr<sup>20</sup>, and difference in SCr (last compared to baseline)  $\leq 0.3$  and SCr change  $\leq 25\%^6$ . In this study, for the main analysis, we used a definition of recovery based on the ADQI criteria<sup>15</sup>. Among patients with COVID-19 who had AKI-2/3, around half the patients compared to almost 2/3<sup>rd</sup> of patients without COVID-19 had at least partial recovery. In a retrospective analysis<sup>21</sup>, the more strict Bucaloiu et al<sup>22</sup> criteria of AKI recovery was more closely associated with long-term outcomes compared to ADQI criteria. Hence, for sensitivity analysis, we used the Bucaloiu et al criteria where a significantly lower number of patients achieved renal recovery. However, the association of death was similar using either criteria.

# Machine Learning (ML) Analysis:

'Precision' is defined as the percentage of true positives among the positive class predictions. 'Recall' is defined as the percentage of true positives among the actual positive class examples. By default, the threshold of the binary classifier would be 0.5. Sometimes, especially if the data is imbalanced, the threshold would be adjusted to get more accuracy or to achieve more Precision over Recall (and vice versa). Lowering the threshold increases Recall but decreases Precision and vice versa. To determine the performance of a classifier, the threshold would be adjusted which would give varied Precision and Recall for each threshold. If Recall is plotted along the xaxis and Precision along the y-axis in the XY plane, a 'Precision-Recall curve (PR Curve)' would be achieved. Rather than comparing these curves, a single number can be compared that determines the performance of a classifier, called 'Average Precision (AP)', which is the 'Area Under the Precision-Recall Curve (AUC)'.

For recovery prediction, we focused on Recovery-1 (partial) since Recovery-2 (complete) was achieved in a smaller sample size We considered the task of predicting if a patient will develop AKI and recover from AKI during their hospital stay using data at the times of hospitalization (first 48hrs of the ED visit) in the cohort. We considered four prediction tasks. Task 1 was to predict whether a COVID-19 positive would develop AKI-2/3 and AKI-3. Task 2 was to predict whether a COVID-19 negative patient would develop AKI-2/3 and AKI-3. Task 3 was to predict if a COVID19 positive with AKI-2/3 or AKI-3 would recover from AKI. Task 4 was to predict if a patient with COVID-19 negative with AKI-2/3 or AKI-3 would recover from AKI. We considered the prediction tasks separately and trained separate ML models for each task. Our ML models were based on XGBoost, a state-of-the-art algorithm that can handle both numerical and categorical attributes and has been previously used in ML-based predictive modeling studies in COVID-19<sup>23</sup>. The input to our models was a vector of 57 features about the patient, including demographics, comorbid conditions, medications, and initial vitals, respiratory function & lab values. For each prediction task, we trained the prediction models and measured their performance based on five-fold cross validation. We split the applicable data into five different subsets. We used 5-fold cross-validation wherein we divided the data into 5 folds and ensured that each fold (containing 50 patients in that case) was used as testing set at some point\. We used four subsets to train a prediction model and the left-out subset for evaluation. We recorded the prediction scores and prediction labels for the test data in all experiment folds. Subsequently, we plotted the Precision-Recall (PR) curve and calculated the Average Precision (AP) which are standard metrics to measure the performance of predictors. For data with imbalanced classes, these performance metrics are better than other metrics such as the classification accuracy. The tunable hyperparameters of the XGBoost models were the depth of the decision trees, the learning rate, and the regularization parameter gamma. These hyperparameters were tuned to achieve the highest average precision over five-fold cross-validation.

All the 57 variables in the data at the time of hospitalization were used for AKI and Recovery prediction. The variables used are: Baseline Age, Gender, Race, Ethinicity, DM, HF, CKD, COPD, HTN, CAD, Cancer, Asthma, TIA, Cerebral ischemia, first\_creatinine, BMI, first\_SBP, first\_DBP, first\_MAP, first\_oral\_temperature, first\_serum Na, first\_serum K, first\_serum CI, first\_serum

HCO3, first\_serum Ca, first\_lonized Ca, first\_serum Phos, first\_serum Mg, first\_serum Osm, first\_pH\_arterial, first\_O2\_arterial, first\_CO2\_arterial, first\_Na\_urine, first\_osmolality\_urine, first\_protein\_urine\_strip, first\_pulse\_ox,first\_paO2, first\_FIO2, first\_respiratory\_rate, first\_Ferritin, first\_serum\_Albumin, first\_Hb, first\_lymphocyte\_count, first\_Procalcitonin, first\_D-Dimer, first\_serum\_Lactate, first\_BNP, first\_troponin, first\_INR, first\_IL-6, first\_WBC, first\_ESR, first\_Idh, first\_ast, first\_alt, first\_cpk, first\_crp, first\_bun, first\_rbc\_urine.

The missing values are handled by XGBoost itself. XGBoost is a gradient tree boosting-based machine learning algorithm that can handle both numerical and categorical attributes and it is superior to other models in handling missing data. XGboost decides at training time whether missing values go into the right or left node. It chooses which to minimize loss. If there are no missing values at training time, it defaults to sending any new missings to the right node.

The variables used for ML algorithms and the % 'missingness' in each variable are listed in Supplementary Methods Table X. The missing values of these features have no impact on the SHAP feature importance. The feature importance is calculated only from non-missing values of the features. We used the XGboost model which will automatically learn what is the best direction to go when a value is missing. Equivalently, this can be viewed as automatically "learning" what is the best imputation value for missing values based on reduction on training loss.

# Supplementary References:

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### Supplementary Table 0: Univariate analysis of patients in presence and absence of COVID-19.

Variables	COVID-19 S	tatus (N=3299)	
	COVID-19 Negative (N=1961)	COVID-19 Positive (N=1338)	p-value
Demographics			
Gender (N, %)			
Male	1088 (55.48)	762 (56.95)	
Female	873 (44.52)	576 (43.05)	0.4039
Race (N, %)			
White	1628 (83.02)	780 (58.3)	
Non-White	333 (16.98)	558 (41.7)	0
Ethnicity (N, %)			
Non-Hispanic	1877 (95.72)	1094 (81.76)	
Hispanic	84 (4.28)	244 (18.24)	0
Age (Mean, SD)	63.57 (19.27)	61.8 (17.86)	0.0079
Co-morbid conditions (N, %)			
DM	497 (25.34)	404 (30.19)	0.0022
HF	392 (19.99)	201 (15.02)	3.00E-04
СКD	294 (14.99)	185 (13.83)	0.3508
COPD	293 (14.94)	150 (11.21)	0.0021
HTN	937 (47.78)	571 (42.68)	0.0039
CAD	530 (27.03)	248 (18.54)	0
Cancer	326 (16.62)	98 (7.32)	0
Asthma	120 (6.12)	97 (7.25)	0.199
BMI $[kg/m^2]$ (Mean, SD)	29.42 (10.51)	29.66 (9.25)	0.5193
Severity of illness			
Length of hospital stay [days] (Mean, SD)	6.96 (6.12)	11.32 (10.2)	0
ICU admission (N, %)	347 (17.7)	292 (21.82)	0.0033
Length of ICU stay [days] (Mean, SD)	9.42 (16.48)	14.58 (16.12)	2.00E-04
MV (N, %)	170 (8.67)	159 (11.88)	0.0026
MV days (Mean, SD)	7.59 (9.35)	14.82 (11.6)	0
ARD (N, %)	357 (18.2)	944 (70.55)	0
ARDS (N, %)	6 (0.31)	202 (15.1)	0
Vasopressor (N, %)	269 (13.72)	41 (3.06)	0
Sepsis (N, %)	222 (11.32)	418 (31.24)	0

Medications (N, %)			
AC	1598 (81.49)	1189 (88.86)	0
NSAIDs	709 (36.16)	351 (26.23)	0
Hydroxychloroquine	65 (3.31)	917 (68.54)	0
Azithromycin	256 (13.05)	652 (48.73)	0
Dexamethasone	275 (14.02)	31 (2.32)	0
Vitals (Mean, SD)			
Respiratory rate	20.46 (7.21)	21.14 (8.73)	0.0179
Respiratory measures (Mean, SD)			
Arterial PH	7.38 (0.11)	7.36 (0.12)	0.0223
Renal labs (Mean, SD)			
BUN [mg/dL]	23.17 (20.1)	21.57 (17.75)	0.0191
Urine protein (dipstick)	93.36 (113.61)	112.53 (130.84)	0.0089
Urine RBCs (per HPF)	14.21 (38.38)	22.4 (50.41)	0
Other labs (Mean, SD)			
LDH [IU/L]	341.11 (279.57)	284.81 (134.23)	0.0143

Categorical variables presented as a count with associated percentage, continuous variables presented as value with standard deviation (std). p-values <0.05 were considered significant

and those variables have been highlighted in yellow. p-values <0.0001 are labelled as '0' in the Table. All variables until (and include) "Severity of illness" section were included, for the rest only significant variables were kept in the table for simplicity.

#### Abbreviations:

DM (Diabetes Mellitus), HF (Heart Failure), CKD (Chronic kidney disease), COPD (chronic obstructive lung disease), HTN (Hypertension), CAD (Coronary Artery Disease), BMI (Body Mass Index), ICU (Intensive Care Unit), MV (Mechanical Ventilation), ARD (Acute Respiratory Disease), ARDS (Acute Respiratory Distress Syndrome), ACEI (Angiotensin Converting Enzyme Inhibitor), ARB (Angiotensin Receptor Blocker), AC (Anticoagulation), NSAIDs (Non-Steroidal Anti-Inflammatory Drugs), SBP (Systolic Blood Pressure), DBP (Diastolic Blood Pressure), MAP (Mean Arterial Pressure), O2 (Oxygen), CO2 (Carbon Dioxide), Ox (Oxygenation), paO2 (partial pressure of oxygen), FIO2 (Fraction of Inspired Oxygen), BUN (Blood Urea Nitrogen), Na (Sodium), K (Potassium), CI (Chloride), HCO3 (Bicarbonate), Ca (Calcium), iCa (ionized Calcium), Phos (Phosphorus), Mg (Magnesium), Osm (Osmolality), RBCs (Red Blood Cells), IL-6 (Interleukin-6), WBC (White Blood Cell count), ESR (Erythrocyte Sedimentation Rate), CRP (C-reactive Protein), Hb (Hemoglobin), BNP (Brain Natriuretic Peptide), INR (International Normalized Ratio), LDH (Lactate Dehydrogenase), AST (aspartate aminotransferase), ALT (alanine aminotransferase), CPK (Creatine Phosphokinase). Units: mmHg (millimeters of mercury), mmol/L (millimotes per liter), mg/dL (milligrams per deciliter), mOsm/L (milliosmoles per liter), g/dL( grams per deciliter), mm/hr (millimeters per hour], K/uL (thousand per microliter), IU/L (international units per liter), ng/mL (nanogram per milliter), pg/mL (picogram per milliter), HPF (high power field)

#### Supplementary Table 1: Univariate analysis of patients with and without AKI-3 in presence and absence of COVID-19.

Variables	COVID-19 Neg	gative (N=1961)		COVID-19 Pos	sitive (N=1338)	
	No AKI-3	AKI-3	p-value	No AKI-3	AKI-3	p-value
	N1=1894	N2=67		N1=1220	N2=118	
Demographics						
Gender (N, %)						
Male	1050 (55.44)	38 (56.72)		682 (55.9)	80 (67.8)	

Female	844 (44.56)	29 (43.28)	0.8361	538 (44.1)	38 (32.2)	0.0135
Race (N, %)						
White	1568 (82.79)	60 (89.55)		719 (58.93)	61 (51.69)	
Non-White	326 (17.21)	7 (10.45)	0.1527	501 (41.07)	57 (48.31)	0.1288
Ethnicity (N, %)						
Non-Hispanic	1811 (95.62)	66 (98.51)		994 (81.48)	100 (84.75)	
Hispanic	83 (4.38)	1 (1.49)	0.2749	226 (18.52)	18 (15.25)	0.3806
Age (Mean, SD)	63.47 (19.29)	66.21 (18.6)	0.2542	61.52 (18.12)	64.75 (14.7)	0.0607
Co-morbid conditions (N, %)						
DM	479 (25.29)	18 (26.87)	0.7709	356 (29.18)	48 (40.68)	0.01
HF	373 (19.69)	19 (28.36)	0.0841	181 (14.84)	20 (16.95)	0.5399
СКD	278 (14.68)	16 (23.88)	0.0409	156 (12.79)	29 (24.58)	5.00E-04
COPD	284 (14.99)	9 (13.43)	0.7247	133 (10.9)	17 (14.41)	0.2509
HTN	905 (47.78)	32 (47.76)	0.9973	512 (41.97)	59 (50)	0.0931
CAD	514 (27.14)	16 (23.88)	0.5556	222 (18.2)	26 (22.03)	0.3067
Cancer	313 (16.53)	13 (19.4)	0.5348	88 (7.21)	10 (8.47)	0.6159
Asthma	115 (6.07)	5 (7.46)	0.6413	89 (7.3)	8 (6.78)	0.8367
BMI $[kg/m^2]$ (Mean, SD)	29.45 (10.65)	28.61 (5.08)	0.5379	29.71 (9.47)	29.11 (6.25)	0.5333
Severity of illness						
Length of hospital stay [days] (Mean, SD)	6.68 (5.61)	14.99 (11.89)	0	9.91 (7.83)	25.92 (17.75)	0
ICU admission (N, %)	309 (16.31)	38 (56.72)	0	200 (16.39)	92 (77.97)	0
Length of ICU stay [days] (Mean, SD)	8.52 (15.75)	16.76 (20.3)	0.0069	11.92 (14.82)	20.37 (17.35)	1.00E-04
MV (N, %)	159 (8.39)	11 (16.42)	0.025	118 (9.67)	41 (34.75)	0
MV days (Mean, SD)	6.05 (7.57)	14.3 (13.05)	0.003	10.89 (7.73)	20.81 (13.81)	0
ARD (N, %)	333 (17.58)	24 (35.82)	2.00E-04	836 (68.52)	108 (91.53)	0
ARDS (N, %)	4 (0.21)	2 (2.99)	0.0022	145 (11.89)	57 (48.31)	0
Vasopressor (N, %)	253 (13.36)	16 (23.88)	0.0158	29 (2.38)	12 (10.17)	0
Sepsis (N, %)	196 (10.35)	26 (38.81)	0	326 (26.72)	92 (77.97)	0
Medications (N, %)						
ACEI	304 (16.05)	23 (34.33)	1.00E-04	181 (14.84)	47 (39.83)	0
ARB	339 (17.9)	1 (1.49)	0.0082	217 (17.79)	12 (10.17)	0.0389
AC	1589 (83.9)	9 (13.43)	0	1154 (94.59)	35 (29.66)	0
NSAIDs	683 (36.06)	26 (38.81)	0.646	303 (24.84)	48 (40.68)	2.00E-04
Remdesivir	0 (0)	0 (0)	NA	15 (1.23)	5 (4.24)	0.0158
Hydroxychloroquine	62 (3.27)	3 (4.48)	0.5901	816 (66.89)	101 (85.59)	1.00E-04
Tocilizumab	0 (0)	0 (0)	NA	109 (8.93)	33 (27.97)	0

Azithromycin	249 (13.15)	7 (10.45)	0.5204	575 (47.13)	77 (65.25)	2.00E-04
Vitals (Mean, SD)						
DBP [mmHg]	76.21 (15.05)	74.7 (16.87)	0.4221	76.51 (14.29)	73.57 (14.78)	0.0333
Oral temperature [degree Celsius]	37.11 (0.73)	36.88 (0.48)	0.013	37.14 (0.74)	37.11 (0.86)	0.7377
Respiratory measures (Mean, SD)						
Arterial PH	7.38 (0.1)	7.32 (0.17)	0.0362	7.36 (0.11)	7.32 (0.17)	0.0303
FIO2	58.32 (24.9)	65.38 (25.04)	0.3173	59.15 (26.69)	69.26 (26.56)	0.0167
Renal labs (Mean, SD)						
BUN [mg/dL]	22.81 (19.82)	33.39 (24.91)	1.00E-04	21.32 (17.63)	24.15 (18.78)	0.1011
K [mmol/L]	4.19 (0.62)	4.46 (0.85)	7.00E-04	4.16 (0.59)	4.25 (0.59)	0.1127
HCO3 [mmol/L]	23.73 (4.12)	22.96 (5.57)	0.1327	23.98 (3.94)	22.97 (5.16)	0.0096
iCa [mg/dL]	4.54 (0.56)	4.21 (0.73)	0.0314	4.58 (0.43)	4.24 (0.55)	2.00E-04
Phos [mg/dL]	3.4 (1.12)	3.91 (2.02)	0.0017	3.29 (1.04)	3.83 (1.95)	1.00E-04
Urine Na [mEq/L]	54.91 (38.37)	49.56 (32.34)	0.5588	54.8 (40.67)	40.16 (32.8)	0.025
Inflammatory labs (Mean, SD)						
Ferritin [ng/mL]	804.97 (1366.74)	1091.47 (2239.02)	0.2808	780.9 (1167.61)	1486.82 (2169.75)	2.00E-04
Procalcitonin [ng/mL]	1.44 (13.4)	6.68 (28.87)	0.1349	1.82 (12.06)	5.25 (16.16)	0.0469
IL-6 [pg/mL]	108.6 (365.38)	983.5 (1666.17)	0.0252	114.36 (461.27)	449.73 (1321.12)	0.0387
CRP [mg/dL]	8.48 (9.16)	5.85 (7.09)	0.1213	8.61 (9.12)	11.82 (11.49)	0.0058
Other labs (Mean, SD)						
Hb [g/dL]	12.95 (2.35)	11.84 (3.23)	2.00E-04	13.03 (2.27)	12.4 (3.09)	0.0058
Lactate [mmol/L]	2.01 (1.96)	3 (3.34)	0.01	1.92 (1.65)	3.32 (4.69)	0
Troponin-T [ng/mL]	0.04 (0.14)	0.17 (0.98)	0.0291	0.05 (0.18)	0.03 (0.06)	0.51
Death (N, %)	111 (5.86)	8 (11.94)	0.0455	116 (9.51)	32 (27.12)	0

#### Abbreviations:

DM (Diabetes Mellitus), HF (Heart Failure), CKD (Chronic kidney disease), COPD (chronic obstructive lung disease), HTN (Hypertension), CAD (Coronary Artery Disease), BMI (Body Mass Index), ICU (Intensive Care Unit), MV (Mechanical Ventilation), ARD (Acute Respiratory Disease), ARDS (Acute Respiratory Distress Syndrome), ACEI (Angiotensin Converting Enzyme Inhibitor), ARB (Angiotensin Receptor Blocker), AC (Anticoagulation), NSAIDs (Non-Steroidal Anti-Inflammatory Drugs), SBP (Systolic Blood Pressure), DBP (Diastolic Blood Pressure), MAP (Mean Arterial Pressure), O2 (Oxygen), CO2 (Carbon Dioxide), Ox (Oxygenation), paO2 (partial pressure of oxygen), FIO2 (Fraction of Inspired Oxygen), BUN (Blood Urea Nitrogen), Na (Sodium), K (Potassium), CI (Chloride), HCO3 (Bicarbonate), Ca (Calcium), iCa (ionized Calcium), Phos (Phosphorus), Mg (Magnesium), Osm (Osmolality), RBCs (Red Blood Cells), IL-6 (Interleukin-6), WBC (White Blood Cell count), ESR (Erythrocyte Sedimentation Rate), CRP (C-reactive Protein), Hb (Hemoglobin), BNP (Brain Natriuretic Peptide), INR (International Normalized Ratio), LDH (Lactate Dehydrogenase), AST (aspartate aminotransferase), ALT (alanine aminotransferase), CPK (Creatine Phosphokinase). Units: mmHg (millimeters of mercury), mmol/L (millimoles per liter), mg/dL (milligrams per deciliter), mOsm/L (milliosmoles per liter), g/dL( grams per deciliter), mm/hr (millimeters per hour], K/uL (thousand per microliter), IU/L (international units per liter), ng/mL (nanogram per millliter), pg/mL (picogram per milliter), HPF (high power field)

## Supplementary Table 2: Univariate analysis of patients with and without Recovery -2 from AKI-2/3 in presence and absence of COVID-19.

Variables	COVID-19	legative (N=172)		COVID-19 F	Positive (N=255)	
	No Recovery	Recovery-2	p-value	No Recovery	Recovery-2	p-value
	N1=96	N2=76		N1=192	N2=63	
Demographics						
Gender (N, %)						
Male	47 (48.96)	45 (59.21)		120 (62.5)	41 (65.08)	
Female	49 (51.04)	31 (40.79)	0.1815	72 (37.5)	22 (34.92)	0.7128
Race (N, %)						
White	82 (85.42)	70 (92.11)		104 (54.17)	44 (69.84)	
Non-White	14 (14.58)	6 (7.89)	0.1804	88 (45.83)	19 (30.16)	0.0302
Ethnicity (N, %)						
Non-Hispanic	95 (98.96)	74 (97.37)		160 (83.33)	59 (93.65)	
Hispanic	1 (1.04)	2 (2.63)	0.445	32 (16.67)	4 (6.35)	0.0499
Age (Mean, SD)	66.94 (17.56)	66.89 (16.97)	0.9871	65.22 (14.95)	67.4 (17.02)	0.3326
Co-morbid conditions (N, %)						
DM	34 (35.42)	23 (30.26)	0.4762	77 (40.1)	35 (55.56)	0.0332
HF	33 (34.38)	16 (21.05)	0.0565	37 (19.27)	14 (22.22)	0.6116
СКD	20 (20.83)	18 (23.68)	0.6547	38 (19.79)	23 (36.51)	0.0079
COPD	21 (21.88)	13 (17.11)	0.4363	27 (14.06)	11 (17.46)	0.5119
HTN	43 (44.79)	36 (47.37)	0.7363	95 (49.48)	28 (44.44)	0.488
CAD	28 (29.17)	19 (25)	0.5429	41 (21.35)	16 (25.4)	0.5045
Cancer	23 (23.96)	9 (11.84)	0.0464	15 (7.81)	9 (14.29)	0.1323
Asthma	6 (6.25)	5 (6.58)	0.9302	12 (6.25)	4 (6.35)	0.9775
BMI $[kg/m^2]$ (Mean, SD)	28.09 (5.52)	31.44 (23.28)	0.2546	29.62 (7.06)	29.46 (8.14)	0.8859
Severity of illness						
Length of hospital stay [days] (Mean, SD)	14.51 (9.11)	12.28 (11.31)	0.1577	23.2 (15.89)	15.22 (12.46)	7.00E-04
ICU admission (N, %)	47 (48.96)	25 (32.89)	0.0349	136 (70.83)	27 (42.86)	1.00E-04
Length of ICU stay [days] (Mean, SD)	12.32 (17.14)	22.16 (27.57)	0.0852	18.84 (16.19)	11.37 (11.15)	0.0274
MV (N, %)	17 (17.71)	7 (9.21)	0.116	59 (30.73)	13 (20.63)	0.1252
MV days (Mean, SD)	11.44 (9.62)	16.93 (16.58)	0.1926	18.09 (12.86)	16.76 (9.97)	0.6809
ARD (N, %)	39 (40.62)	22 (28.95)	0.1132	174 (90.62)	47 (74.6)	0.0018
ARDS (N, %)	2 (2.08)	2 (2.63)	0.8131	94 (48.96)	9 (14.29)	0
Vasopressor (N, %)	21 (21.88)	16 (21.05)	0.8963	14 (7.29)	4 (6.35)	0.8001
Sepsis (N, %)	35 (36.46)	24 (31.58)	0.5035	121 (63.02)	40 (63.49)	0.9464

Medications (N, %)						
ACEI	25 (26.04)	17 (22.37)	0.5779	55 (28.65)	20 (31.75)	0.6395
Hydroxychloroquine	6 (6.25)	3 (3.95)	0.5042	159 (82.81)	44 (69.84)	0.0285
Tocilizumab	0 (0)	0 (0)	NA	51 (26.56)	7 (11.11)	0.0141
Azithromycin	19 (19.79)	10 (13.16)	0.2514	124 (64.58)	26 (41.27)	0.0013
Respiratory measures (Mean, SD)						
Pulse Ox	95.09 (5.71)	96.24 (3.93)	0.1497	94.55 (5.48)	96.29 (4.3)	0.0263
Renal labs (Mean, SD)						
Serum Osm [mOsm/kg]	300.8 (20.96)	290.11 (29.15)	0.352	302.05 (27.99)	282.36 (13.32)	0.0407
Other labs (Mean, SD)						
CPK [IU/L]	468.19 (1406.57)	516.45 (1081.84)	0.877	331.29 (556.65)	825.04 (1351.4)	0.0208

#### Abbreviations:

DM (Diabetes Mellitus), HF (Heart Failure), CKD (Chronic kidney disease), COPD (chronic obstructive lung disease), HTN (Hypertension), CAD (Coronary Artery Disease), BMI (Body Mass Index), ICU (Intensive Care Unit), MV (Mechanical Ventilation), ARD (Acute Respiratory Disease), ARDS (Acute Respiratory Distress Syndrome), ACEI (Angiotensin Converting Enzyme Inhibitor), ARB (Angiotensin Receptor Blocker), AC (Anticoagulation), NSAIDs (Non-Steroidal Anti-Inflammatory Drugs), SBP (Systolic Blood Pressure), DBP (Diastolic Blood Pressure), MAP (Mean Arterial Pressure), O2 (Oxygen), CO2 (Carbon Dioxide), Ox (Oxygenation), paO2 (partial pressure of oxygen), FIO2 (Fraction of Inspired Oxygen), BUN (Blood Urea Nitrogen), Na (Sodium), K (Potassium), CI (Chloride), HCO3 (Bicarbonate), Ca (Calcium), iCa (ionized Calcium), Phos (Phosphorus), Mg (Magnesium), Osm (Osmolality), RBCs (Red Blood Cells), IL-6 (Interleukin-6), WBC (White Blood Cell count), ESR (Erythrocyte Sedimentation Rate), CRP (C-reactive Protein), Hb (Hemoglobin), BNP (Brain Natriuretic Peptide), INR (International Normalized Ratio), LDH (Lactate Dehydrogenase), AST (aspartate aminotransferase), ALT (alanine aminotransferase), CPK (Creatine Phosphokinase). Units: mmHg (millimeters of mercury), mmol/L (millimoles per liter), mg/dL (milligrams per deciliter), mOsm/L (milliosmoles per liter), g/dL( grams per deciliter), mm/hr (millimeters per hour], K/uL (thousand per microliter), IU/L (international units per liter), ng/mL (nanogram per millliter), pg/mL (picogram per milliter), HPF (high power field)

Variables	COVID-19	Negative (N=67)		COVID-19	Positive (N=118)	
	No Recovery	Recovery-1	p-value	No Recovery	Recovery-1	p-value
	N1=20	N2=47		N1=75	N2=43	
Demographics						
Gender (N, %)						
Male	12 (60)	26 (55.32)		53 (70.67)	27 (62.79)	
Female	8 (40)	21 (44.68)	0.7236	22 (29.33)	16 (37.21)	0.3792
Race (N, %)						
White	18 (90)	42 (89.36)		34 (45.33)	27 (62.79)	
Non-White	2 (10)	5 (10.64)	0.9377	41 (54.67)	16 (37.21)	0.0696

### Supplementary Table 3: Univariate analysis of patients with and without Recovery -1 from AKI-3 in presence and absence of COVID-19.

Ethnicity (N, %)						
Non-Hispanic	20 (100)	46 (97.87)		60 (80)	40 (93.02)	
Hispanic	0 (0)	1 (2.13)	0.9919	15 (20)	3 (6.98)	0.07
Age (Mean, SD)	73.9 (10.43)	62.94 (20.37)	0.0326	64.45 (13.69)	65.28 (16.47)	0.7681
Co-morbid conditions (N, %)						
DM	5 (25)	13 (27.66)	0.8223	25 (33.33)	23 (53.49)	0.0335
HF	10 (50)	9 (19.15)	0.0132	10 (13.33)	10 (23.26)	0.1714
CKD	6 (30)	10 (21.28)	0.4455	16 (21.33)	13 (30.23)	0.2819
COPD	7 (35)	2 (4.26)	0.0038	10 (13.33)	7 (16.28)	0.6615
HTN	8 (40)	24 (51.06)	0.4082	41 (54.67)	18 (41.86)	0.1821
CAD	9 (45)	7 (14.89)	0.0112	15 (20)	11 (25.58)	0.4824
Cancer	6 (30)	7 (14.89)	0.1598	5 (6.67)	5 (11.63)	0.3574
Asthma	1 (5)	4 (8.51)	0.6209	6 (8)	2 (4.65)	0.4913
BMI $[kg/m^2]$ (Mean, SD)	29.29 (4.99)	28.33 (5.14)	0.5002	29.43 (5.6)	28.61 (7.2)	0.5208
Severity of illness						
Length of hospital stay [days] (Mean, SD)	13.65 (9.3)	15.55 (12.88)	0.5486	26.63 (17.51)	24.67 (18.3)	0.5643
ICU admission (N, %)	15 (75)	23 (48.94)	0.0544	67 (89.33)	25 (58.14)	2.00E-04
Length of ICU stay [days] (Mean, SD)	13.07 (16.42)	19.17 (22.5)	0.3698	21.22 (17.98)	18.08 (15.63)	0.4399
MV (N, %)	7 (35)	4 (8.51)	0.0124	34 (45.33)	7 (16.28)	0.0022
MV days (Mean, SD)	12.57 (13.05)	15.23 (13.48)	0.6581	20.54 (14.06)	21.67 (13.26)	0.7424
ARD (N, %)	10 (50)	14 (29.79)	0.1185	72 (96)	36 (83.72)	0.0323
ARDS (N, %)	1 (5)	1 (2.13)	0.5393	42 (56)	15 (34.88)	0.0287
Vasopressor (N, %)	4 (20)	12 (25.53)	0.6278	8 (10.67)	4 (9.3)	0.8136
Sepsis (N, %)	8 (40)	18 (38.3)	0.8959	62 (82.67)	30 (69.77)	0.1074
Medications (N, %)						
AC	5 (25)	4 (8.51)	0.0824	29 (38.67)	6 (13.95)	0.0066
Hydroxychloroquine	1 (5)	2 (4.26)	0.8928	68 (90.67)	33 (76.74)	0.0442
Tocilizumab	0 (0)	0 (0)	NA	28 (37.33)	5 (11.63)	0.0045
Azithromycin	3 (15)	4 (8.51)	0.4325	56 (74.67)	21 (48.84)	0.0053
Respiratory measures (Mean, SD)						
Pulse Ox	93.25 (9.55)	97.17 (3)	0.0553	93.11 (6.75)	97.49 (2.72)	6.00E-04
Renal labs (Mean, SD)						
Serum Osm [mOsm/kg]	303.33 (23.12)	291.33 (13.43)	0.4167	309.35 (29.74)	279.86 (9.7)	0.0377
Urine Na [mEq/L]	53.43 (41.47)	47.09 (27)	0.6776	34.06 (27.56)	58.45 (41.29)	0.0433

#### Abbreviations:

DM (Diabetes Mellitus), HF (Heart Failure), CKD (Chronic kidney disease), COPD (chronic obstructive lung disease), HTN (Hypertension), CAD (Coronary Artery Disease), BMI (Body Mass Index), ICU (Intensive Care Unit), MV (Mechanical Ventilation), ARD (Acute Respiratory Disease), ARDS (Acute Respiratory Distress Syndrome), ACEI (Angiotensin Converting Enzyme Inhibitor), ARB (Angiotensin Receptor Blocker), AC (Anticoagulation), NSAIDs (Non-Steroidal Anti-Inflammatory Drugs), SBP (Systolic Blood Pressure), DBP (Diastolic Blood Pressure), MAP (Mean Arterial Pressure), O2 (Oxygen), CO2 (Carbon Dioxide), Ox (Oxygenation), paO2 (partial pressure of oxygen), FIO2 (Fraction of Inspired Oxygen), BUN (Blood Urea Nitrogen), Na (Sodium), K (Potassium), CI (Chloride), HCO3 (Bicarbonate), Ca (Calcium), iCa (ionized Calcium), Phos (Phosphorus), Mg (Magnesium), Osm (Osmolality), RBCs (Red Blood Cells), IL-6 (Interleukin-6), WBC (White Blood Cell count), ESR (Erythrocyte Sedimentation Rate), CRP (C-reactive Protein), Hb (Hemoglobin), BNP (Brain Natriuretic Peptide), INR (International Normalized Ratio), LDH (Lactate Dehydrogenase), AST (aspartate aminotransferase), ALT (alanine aminotransferase), CPK (Creatine Phosphokinase). Units: mmHg (millimeters of mercury), mmol/L (millimoles per liter), mg/dL (milligrams per deciliter), mOsm/L (milliosmoles per liter), g/dL( grams per deciliter), mm/hr (millimeters per hour], K/uL (thousand per microliter), IU/L (international units per liter), ng/mL (nanogram per millliter), pg/mL (picogram per milliter), HPF (high power field)

### Supplementary Table 4: Univariate analysis of patients with and without Recovery -2 from AKI-3 in presence and absence of COVID-19.

Variables	COVID-19	Negative (N=67)		COVID-19	Positive (N=118)	
	No Recovery	Recovery-2	p-value	No Recovery	Recovery-2	p-value
	N1=36	N2=31		N1=94	N2=24	
Demographics						
Gender (N, %)						
Male	19 (52.78)	19 (61.29)		61 (64.89)	19 (79.17)	
Female	17 (47.22)	12 (38.71)	0.4838	33 (35.11)	5 (20.83)	0.1878
Race (N, %)						
White	30 (83.33)	30 (96.77)		46 (48.94)	15 (62.5)	
Non-White	6 (16.67)	1 (3.23)	0.1067	48 (51.06)	9 (37.5)	0.2384
Ethnicity (N, %)						
Non-Hispanic	36 (100)	30 (96.77)		76 (80.85)	24 (100)	
Hispanic	0 (0)	1 (3.23)	0.9914	18 (19.15)	0 (0)	0.991
Age (Mean, SD)	68.83 (17.76)	63.16 (19.38)	0.2148	65.03 (13.46)	63.67 (19.1)	0.6836
Co-morbid conditions (N, %)						
DM	9 (25)	9 (29.03)	0.7106	33 (35.11)	15 (62.5)	0.0176
HF	15 (41.67)	4 (12.9)	0.013	14 (14.89)	6 (25)	0.2442
СКD	9 (25)	7 (22.58)	0.8169	18 (19.15)	11 (45.83)	0.0088
COPD	7 (19.44)	2 (6.45)	0.1376	13 (13.83)	4 (16.67)	0.7243
HTN	17 (47.22)	15 (48.39)	0.9242	51 (54.26)	8 (33.33)	0.0719
CAD	10 (27.78)	6 (19.35)	0.4221	20 (21.28)	6 (25)	0.6948
Cancer	11 (30.56)	2 (6.45)	0.0231	7 (7.45)	3 (12.5)	0.4327
Asthma	4 (11.11)	1 (3.23)	0.249	6 (6.38)	2 (8.33)	0.7352
BMI $[kg/m^2]$ (Mean, SD)	28.31 (4.35)	28.97 (5.88)	0.6061	29.29 (6.03)	28.42 (7.11)	0.5689

Severity of illness						
Length of hospital stay [days] (Mean, SD)	15.06 (9.39)	14.9 (14.42)	0.958	27.95 (17.9)	17.96 (14.95)	0.0185
ICU admission (N, %)	23 (63.89)	15 (48.39)	0.2036	80 (85.11)	12 (50)	5.00E-04
Length of ICU stay [days] (Mean, SD)	12.43 (14.4)	23.4 (26.18)	0.1217	21.43 (17.59)	13.33 (14.31)	0.1393
MV (N, %)	7 (19.44)	4 (12.9)	0.4738	38 (40.43)	3 (12.5)	0.0169
MV days (Mean, SD)	11.55 (10.65)	17.67 (15.47)	0.3035	21.29 (13.95)	16 (12.06)	0.3065
ARD (N, %)	15 (41.67)	9 (29.03)	0.2842	88 (93.62)	20 (83.33)	0.1196
ARDS (N, %)	1 (2.78)	1 (3.23)	0.9145	52 (55.32)	5 (20.83)	0.0044
Vasopressor (N, %)	8 (22.22)	8 (25.81)	0.7317	11 (11.7)	1 (4.17)	0.2977
Sepsis (N, %)	13 (36.11)	13 (41.94)	0.6259	75 (79.79)	17 (70.83)	0.3478
Medications (N, %)						
Tocilizumab	0 (0)	0 (0)	NA	31 (32.98)	2 (8.33)	0.0284
Azithromycin	4 (11.11)	3 (9.68)	0.8484	66 (70.21)	11 (45.83)	0.0285
Respiratory measures (Mean, SD)						
Pulse Ox	94.92 (7.59)	97.26 (2.91)	0.1504	94.12 (6.39)	97 (3.26)	0.0433

#### Abbreviations:

DM (Diabetes Mellitus), HF (Heart Failure), CKD (Chronic kidney disease), COPD (chronic obstructive lung disease), HTN (Hypertension), CAD (Coronary Artery Disease), BMI (Body Mass Index), ICU (Intensive Care Unit), MV (Mechanical Ventilation), ARD (Acute Respiratory Disease), ARDS (Acute Respiratory Distress Syndrome), ACEI (Angiotensin Converting Enzyme Inhibitor), ARB (Angiotensin Receptor Blocker), AC (Anticoagulation), NSAIDs (Non-Steroidal Anti-Inflammatory Drugs), SBP (Systolic Blood Pressure), DBP (Diastolic Blood Pressure), MAP (Mean Arterial Pressure), O2 (Oxygen), CO2 (Carbon Dioxide), Ox (Oxygenation), paO2 (partial pressure of oxygen), FIO2 (Fraction of Inspired Oxygen), BUN (Blood Urea Nitrogen), Na (Sodium), K (Potassium), CI (Chloride), HCO3 (Bicarbonate), Ca (Calcium), iCa (ionized Calcium), Phos (Phosphorus), Mg (Magnesium), Osm (Osmolality), RBCs (Red Blood Cells), IL-6 (Interleukin-6), WBC (White Blood Cell count), ESR (Erythrocyte Sedimentation Rate), CRP (C-reactive Protein), Hb (Hemoglobin), BNP (Brain Natriuretic Peptide), INR (International Normalized Ratio), LDH (Lactate Dehydrogenase), AST (aspartate aminotransferase), ALT (alanine aminotransferase), CPK (Creatine Phosphokinase). Units: mmHg (millimeters of mercury), mmol/L (millimoles per liter), mg/dL (milligrams per deciliter), mOsm/L (milliosmoles per liter), g/dL( grams per deciliter), mm/hr (millimeters per hour], K/uL (thousand per microliter), IU/L (international units per liter), ng/mL (nanogram per millliter), pg/mL (picogram per milliter), HPF (high power field)

#### Supplementary Table 5: Univariate analysis comparing death in all patients with and without COVID-19.

Variables	COVID-19 Ne	gative (N=1961)		COVID-19 Pos	sitive (N=1338)	
	No Death	Death	p-	No Death	Death	р-
			value			value
	N1=1842	N2=119		N1=1190	N2=148	
Demographics						
Gender (N, %)						

Male	1020 (55.37)	68 (57.14)		670 (56.3)	92 (62.16)	
Female	822 (44.63)	51 (42.86)	0.7068	520 (43.7)	56 (37.84)	0.1753
Race (N, %)						
White	1525 (82.79)	103 (86.55)		695 (58.4)	85 (57.43)	
African American	113 (6.13)	3 (2.52)		86 (7.23)	9 (6.08)	
Asian	31 (1.68)	5 (4.2)		39 (3.28)	9 (6.08)	
Other	173 (9.39)	8 (6.72)	0.4442	370 (31.09)	45 (30.41)	0.8397
Ethinicity (N, %)						
Non-Hispanic	1763 (95.71)	114 (95.8)		971 (81.6)	123 (83.11)	
Hispanic	79 (4.29)	5 (4.2)	0.9637	219 (18.4)	25 (16.89)	0.6535
Age (Mean, SD)	63.84 (19.05)	59.4 (22.02)	0.0154	61.87 (17.77)	61.28 (18.67)	0.7037
Co-morbid conditions (N, %)						
DM	468 (25.41)	29 (24.37)	0.8009	355 (29.83)	49 (33.11)	0.4133
HF	366 (19.87)	26 (21.85)	0.601	179 (15.04)	22 (14.86)	0.9546
СКD	266 (14.44)	28 (23.53)	0.0079	161 (13.53)	24 (16.22)	0.3726
COPD	272 (14.77)	21 (17.65)	0.3938	128 (10.76)	22 (14.86)	0.1371
	899 (48.81)	38 (31.93)	4.00E-	508 (42.69)	63 (42.57)	0.9775
HTN			04			
CAD	508 (27.58)	22 (18.49)	0.0321	218 (18.32)	30 (20.27)	0.5648
Cancer	308 (16.72)	18 (15.13)	0.6508	91 (7.65)	7 (4.73)	0.2035
Asthma	117 (6.35)	3 (2.52)	0.1037	82 (6.89)	15 (10.14)	0.1539
<b>BMI</b> $[kg/m^2]$ (Mean, SD)	29.55 (10.69)	27.21 (6.13)	0.0146	29.67 (9.44)	29.56 (7.38)	0.8998
Severity of illness						
Length of hospital stay [days]	6.79 (5.81)	9.51 (9.39)	0	10.58 (9.49)	17.27 (13.34)	0
(Mean, SD)						
ICU admission (N, %)	302 (16.4)	45 (37.82)	0	209 (17.56)	83 (56.08)	0
Length of ICU stay [days] (Mean,	9.05 (16.73)	11.96 (14.58)	0.2752	14.14 (16.75)	15.69 (14.44)	0.4611
SD)						
MV (N, %)	125 (6.79)	45 (37.82)	0	68 (5.71)	91 (61.49)	0
MV days (Mean, SD)	7.51 (9.26)	7.77 (9.73)	0.8953	14.44 (11.26)	15.44 (12.19)	0.5337
ARD (N, %)	316 (17.16)	41 (34.45)	0	813 (68.32)	131 (88.51)	0

ARDS (N, %)	4 (0.22)	2 (1.68)	0.018	139 (11.68)	63 (42.57)	0
Vasopressor (N, %)	248 (13.46)	21 (17.65)	0.2003	33 (2.77)	8 (5.41)	0.0855
Sepsis (N, %)	203 (11.02)	19 (15.97)	0.1012	338 (28.4)	80 (54.05)	0
Medications (N, %)						
AC	1512 (82.08)	86 (72.27)	0.0082	1057 (88.82)	132 (89.19)	0.8939
NSAIDs	663 (35.99)	46 (38.66)	0.5582	302 (25.38)	49 (33.11)	0.0447
Remdesivir	0 (0)	0 (0)	NA	14 (1.18)	6 (4.05)	0.0106
Hydroxychloroquine	59 (3.2)	6 (5.04)	0.2818	804 (67.56)	113 (76.35)	0.0309
Tocilizumab	0 (0)	0 (0)	NA	112 (9.41)	30 (20.27)	1.00E- 04
Azithromycin	240 (13.03)	16 (13.45)	0.8961	558 (46.89)	94 (63.51)	2.00E- 04
Vitals (Mean, SD)						
SBP [mmHg]	133.51 (28.66)	124.69 (28.25)	0.0011	134.36 (28.16)	127.79 (28.46)	0.0079
DBP [mmHg]	76.5 (15.09)	70.87 (14.63)	1.00E- 04	76.97 (14.25)	70.42 (13.91)	0
MAP [mmHg]	94.37 (16.86)	89.64 (17.47)	0.0032	94.69 (17.09)	88.63 (16.1)	1.00E- 04
Respiratory rate	20.14 (6.92)	25.36 (9.43)	0	20.5 (8.23)	26.25 (10.74)	0
Respiratory measures (Mean, SD)						
Arterial PH	7.38 (0.1)	7.36 (0.12)	0.1217	7.38 (0.09)	7.32 (0.15)	0
Arterial O2 [mmHg]	92.88 (6.51)	91.58 (6.99)	0.1362	93.26 (4.56)	90.89 (7.52)	0.0017
Arterial CO2 [mmHg]	41.87 (13.91)	43.85 (15.67)	0.2767	41.67 (14.06)	46.04 (19.38)	0.0257
Pulse Ox	95.55 (5.36)	91.14 (8.54)	0	95.48 (4.64)	90.74 (8.7)	0
FIO2	56.68 (24.01)	66.27 (27.15)	0.0011	56.12 (25.52)	68.77 (27.51)	0
Renal labs (Mean, SD)						
BUN [mg/dL]	22.16 (18.96)	38.76 (28.91)	0	20.25 (15.42)	32.13 (28.57)	0
Na [mmol/L]	137.21 (5.16)	138.92 (8.4)	8.00E- 04	137.27 (4.93)	136.84 (6.65)	0.3338

	4.18 (0.62)	4.47 (0.79)	0	4.15 (0.57)	4.35 (0.75)	1.00E-
K [mmol/L]						04
CI [mmol/L]	99.1 (6)	99.51 (9.1)	0.4813	99.07 (5.72)	97.95 (7.54)	0.0299
HCO3 [mmol/L]	23.73 (4.04)	23.31 (5.99)	0.2828	24.15 (3.75)	21.78 (5.64)	0
	9.29 (0.71)	9.11 (0.93)	0.0064	9.29 (0.71)	9.03 (1.03)	1.00E-
Ca [mg/dL]						04
iCa [mg/dL]	4.55 (0.55)	4.44 (0.66)	0.2519	4.6 (0.37)	4.38 (0.58)	0.0028
Phos [mg/dL]	3.38 (1.13)	3.91 (1.5)	0	3.27 (0.97)	3.87 (1.98)	0
Serum Osm [mOsm/kg]	293.45 (30.51)	304.54 (27.02)	0.0925	291.23 (28.79)	306.5 (29.89)	0.0096
Urine Na [mEq/L]	57.26 (38.9)	35.33 (24.86)	0	56.04 (41.85)	43.57 (31.9)	0.0096
Urine Osm [mOsm/kg]	444.83 (172.37)	515.86 (216.72)	0.0757	439.71 (190.14)	429.64 (153.97)	0.7488
	13.09 (36.16)	29.89 (59.69)	1.00E-	20.62 (49.3)	32.21 (55.29)	0.0164
Urine RBCs (per HPF)			04			
Inflammatory labs (Mean, SD)						
	747.46	1519.28	1.00E-	770.14	1238.06	7.00E-
Ferritin [ng/mL]	(1131.46)	(2957.89)	04	(1245.94)	(1478.18)	04
Serum Albumin [g/dL]	3.88 (0.58)	3.36 (0.6)	0	3.87 (0.58)	3.43 (0.58)	0
Lymphocyte count [K/uL]	1.41 (0.88)	0.86 (0.55)	0	1.38 (0.84)	0.85 (0.51)	0
Procalcitonin [ng/mL]	1.42 (14.07)	3.02 (12.6)	0.3067	1.69 (10.52)	4.42 (20.3)	0.0357
	1547.31	2951.44	0.0196	1061.06	2413.36	0.0027
D-Dimer [ng/mL]	(5074.69)	(6875.29)		(3534.79)	(5050.29)	
WBC [K/uL]	9.97 (6.58)	9.61 (5.15)	0.5656	9.67 (5.92)	11.45 (10.61)	0.0051
CRP [mg/dL]	7.94 (8.82)	13.56 (10.66)	0	7.92 (8.55)	14.6 (11.79)	0
Other labs (Mean, SD)						
Hb [g/dL]	12.94 (2.39)	12.45 (2.48)	0.0296	13.04 (2.31)	12.44 (2.73)	0.0034
Lactate [mmol/L]	1.95 (1.86)	3.08 (3.15)	0	1.82 (1.45)	3.36 (4.09)	0
	2165.88	5175.74	0.0012	2139.6	6368.4	2.00E-
BNP [pg/mL]	(6475.5)	(9393.2)		(6544.28)	(16949.77)	04
Troponin-T [ng/mL]	0.04 (0.14)	0.11 (0.65)	0.0491	0.04 (0.16)	0.08 (0.24)	0.0106
	1.29 (0.71)	1.62 (1.47)	2.00E-	1.27 (0.63)	1.48 (1.12)	0.0022
INR			04			

	326.19 (260.07)	524.89 (424.44)	0.0087	270.03 (124.27)	407.9 (153.29)	1.00E-
LDH [IU/L]						04
AST [IU/L]	54.58 (147.38)	67.55 (83.81)	0.3672	50.35 (108.53)	99.34 (314.67)	0.0209
AKI-2 (N, %)	152 (8.25)	20 (16.81)	0.0018	194 (16.3)	61 (41.22)	0
AKI-3 (N, %)	59 (3.2)	8 (6.72)	0.0455	86 (7.23)	32 (21.62)	0

#### Abbreviations:

DM (Diabetes Mellitus), HF (Heart Failure), CKD (Chronic kidney disease), COPD (chronic obstructive lung disease), HTN (Hypertension), CAD (Coronary Artery Disease), BMI (Body Mass Index), ICU (Intensive Care Unit), MV (Mechanical Ventilation), ARD (Acute Respiratory Disease), ARDS (Acute Respiratory Distress Syndrome), ACEI (Angiotensin Converting Enzyme Inhibitor), ARB (Angiotensin Receptor Blocker), AC (Anticoagulation), NSAIDs (Non-Steroidal Anti-Inflammatory Drugs), SBP (Systolic Blood Pressure), DBP (Diastolic Blood Pressure), MAP (Mean Arterial Pressure), O2 (Oxygen), CO2 (Carbon Dioxide), Ox (Oxygenation), paO2 (partial pressure of oxygen), FIO2 (Fraction of Inspired Oxygen), BUN (Blood Urea Nitrogen), Na (Sodium), K (Potassium), CI (Chloride), HCO3 (Bicarbonate), Ca (Calcium), iCa (ionized Calcium), Phos (Phosphorus), Mg (Magnesium), Osm (Osmolality), RBCs (Red Blood Cells), IL-6 (Interleukin-6), WBC (White Blood Cell count), ESR (Erythrocyte Sedimentation Rate), CRP (C-reactive Protein), Hb (Hemoglobin), BNP (Brain Natriuretic Peptide), INR (International Normalized Ratio), LDH (Lactate Dehydrogenase), AST (aspartate aminotransferase), ALT (alanine aminotransferase), CPK (Creatine Phosphokinase). Units: mmHg (millimeters of mercury), mmol/L (millimoles per liter), mg/dL (milligrams per deciliter), mOsm/L (milliosmoles per liter), g/dL( grams per deciliter), mm/hr (millimeters per hour], K/uL (thousand per microliter), IU/L (international units per liter), ng/mL (nanogram per millliter), pg/mL (picogram per milliter), HPF (high power field)

Variables	COVID-19 Nega	ative (N=67)		COVID-19 Pos	itive (N= 118)	
	No Death	Death	p-value	No Death	Death	p-
						value
	N1= 59	N2= 8		N1= 86	N2= 32	
Demographics						
Gender (N, %)						
Male	33 (55.93)	5 (62.5)		54 (62.79)	26 (81.25)	
Female	26 (44.07)	3 (37.5)	0.7255	32 (37.21)	6 (18.75)	0.0618
Race (N, %)						
White	52 (88.14)	8 (100)		43 (50)	18 (56.25)	
NonWhite	7 (11.86)	0 (0)	0.9946	43 (50)	14 (43.75)	0.5463
Ethnicity (N, %)						
Non-Hispanice	58 (98.31)	8 (100)		73 (84.88)	27 (84.38)	
Hispanic	1 (1.69)	0 (0)	0.9952	13 (15.12)	5 (15.62)	0.9455
Age (Mean, SD)	64.54 (18.99)	78.5 (8.96)	0.0589	65.3 (14.32)	63.28 (15.8)	0.5058

### Supplementary Table 6: Univariate analysis comparing death in patients with and without AKI-3 in presence and absence of COVID-19.

Co-morbid conditions (N, %)						
DM	15 (25.42)	3 (37.5)	0.4737	43 (50)	5 (15.62)	0.0015
HF	16 (27.12)	3 (37.5)	0.5437	17 (19.77)	3 (9.38)	0.1914
CKD	13 (22.03)	3 (37.5)	0.3436	24 (27.91)	5 (15.62)	0.1745
COPD	7 (11.86)	2 (25)	0.3192	11 (12.79)	6 (18.75)	0.4151
HTN	29 (49.15)	3 (37.5)	0.5384	42 (48.84)	17 (53.12)	0.6789
CAD	12 (20.34)	4 (50)	0.0791	17 (19.77)	9 (28.12)	0.3325
Cancer	11 (18.64)	2 (25)	0.6711	8 (9.3)	2 (6.25)	0.599
Asthma	5 (8.47)	0 (0)	0.9929	3 (3.49)	5 (15.62)	0.0323
<b>BMI</b> $[kg/m^2]$ (Mean, SD)	28.46 (4.92)	30.05 (6.71)	0.4667	28.95 (6.44)	29.59 (5.71)	0.6574
Severity of illness						
Length of hospital stay [days]	15.53 (12.41)	11 (6.02)	0.3205	26.7 (18.39)	23.81 (15.99)	0.4321
(Mean, SD)						
ICU admission (N, %)	31 (52.54)	7 (87.5)	0.0938	62 (72.09)	30 (93.75)	0.0221
Length of ICU stay [days] (Mean,	19.03 (21.86)	6.71 (2.87)	0.2155	20.55 (18.3)	20 (15.49)	0.8864
SD)						
MV (N, %)	4 (6.78)	7 (87.5)	1.00E-04	10 (11.63)	31 (96.88)	0
MV days (Mean, SD)	16.87 (14.16)	6.6 (2.88)	0.1663	20.09 (12.98)	22.2 (15.42)	0.4947
ARD (N, %)	20 (33.9)	4 (50)	0.3787	77 (89.53)	31 (96.88)	0.2312
ARDS (N, %)	1 (1.69)	1 (12.5)	0.1502	37 (43.02)	20 (62.5)	0.0626
Vasopressor (N, %)	13 (22.03)	3 (37.5)	0.3436	10 (11.63)	2 (6.25)	0.3978
Sepsis (N, %)	22 (37.29)	4 (50)	0.492	62 (72.09)	30 (93.75)	0.0221
Medications (N, %)						
	20 (33.9)	3 (37.5)	0.8405	44 (51.16)	3 (9.38)	3.00E-
ACEI						04
AC	4 (6.78)	5 (62.5)	5.00E-04	11 (12.79)	24 (75)	0
Vitals (Mean, SD)						
DBP [mmHg]	74.63 (17.58)	75.25 (11.13)	0.9214	75.55 (15.61)	68.25 (10.76)	0.0192
MAP [mmHg]	93.56 (16.27)	95.5 (10.89)	0.7407	93.99 (15.15)	87.29 (12.55)	0.0333
Oral temperature [degree	36.86 (0.41)	37.12 (1.08)	0.2696	36.94 (0.73)	37.74 (1.01)	2.00E-
Celsius]						04

	18.83 (3.64)	25.62 (13.23)	0.0216	18.65 (3.48)	26.97 (16.27)	4.00E-
Respiratory rate						04
Respiratory measures (Mean,						
SD)						
Pulse Ox	96.83 (3.14)	89.88 (14.4)	0.0354	96.56 (3.44)	89.72 (8.24)	0
Renal labs (Mean, SD)						
BUN [mg/dL]	32.63 (25.02)	39 (24.97)	0.4984	20.64 (12.59)	33.59 (27.76)	0.0048
Na [mmol/L]	138.51 (5.02)	134.5 (5.18)	0.0571	137.21 (4.27)	135.19 (5.65)	0.0442
CI [mmol/L]	100.81 (6.66)	95.12 (5.46)	0.044	99.24 (5.4)	96.38 (7.7)	0.0304
	23.36 (5.15)	20 (7.84)	0.1156	24.1 (4.27)	19.91 (6.11)	4.00E-
HCO3 [mmol/L]						04
Ca [mg/dL]	9.18 (0.85)	9.35 (0.54)	0.5723	9.31 (0.79)	8.93 (1.03)	0.0354
Mg [mg/dL]	1.94 (0.36)	2.17 (0.38)	0.1315	2 (0.28)	2.18 (0.51)	0.0367
Inflammatory labs (Mean, SD)						
	1010.63	1819 (812.8)	0.5596	1005.92	2225.36	0.0355
Ferritin [ng/mL]	(2339.44)			(1924.21)	(2347.75)	
Serum Albumin [g/dL]	3.77 (0.61)	3.5 (0.7)	0.2551	3.9 (0.67)	3.46 (0.49)	0.0024
Lymphocyte count [K/uL]	1.48 (0.85)	1.05 (0.3)	0.2228	1.47 (0.93)	0.78 (0.51)	0.0013
CRP [mg/dL]	4.38 (5.05)	15.4 (11.51)	0.0323	8.91 (10.89)	15.9 (11.22)	0.0157
Lactate [mmol/L]	2.17 (1.61)	6.88 (6.13)	0.0311	2.4 (2.89)	4.79 (6.44)	0.0489
LDH [IU/L]	344.57 (242.08)	1013.5 (953.89)	0.18	244.22 (77.23)	421.6 (133.91)	0.0352
AST [IU/L]	39.85 (55.51)	97.25 (98.77)	0.0461	38.84 (48.75)	108.16 (167.57)	0.002
	46 (77.97)	1 (12.5)	0.004	40 (46.51)	3 (9.38)	9.00E-
Recovery 1 (N, %)						04
Recovery 2 (N, %)	30 (50.85)	1 (12.5)	0.072	23 (26.74)	1 (3.12)	0.0202

#### Abbreviations:

DM (Diabetes Mellitus), HF (Heart Failure), CKD (Chronic kidney disease), COPD (chronic obstructive lung disease), HTN (Hypertension), CAD (Coronary Artery Disease), BMI (Body Mass Index), ICU (Intensive Care Unit), MV (Mechanical Ventilation), ARD (Acute Respiratory Disease), ARDS (Acute Respiratory Distress Syndrome), ACEI (Angiotensin Converting Enzyme Inhibitor), ARB (Angiotensin Receptor Blocker), AC (Anticoagulation), NSAIDs (Non-Steroidal Anti-Inflammatory Drugs), SBP (Systolic Blood Pressure), DBP (Diastolic Blood Pressure), MAP (Mean Arterial Pressure), O2 (Oxygen), CO2 (Carbon Dioxide), Ox (Oxygenation), paO2 (partial pressure of oxygen), FIO2 (Fraction of Inspired Oxygen), BUN (Blood Urea Nitrogen), Na (Sodium), K (Potassium), CI (Chloride), HCO3 (Bicarbonate), Ca (Calcium), iCa (ionized Calcium), Phos (Phosphorus), Mg (Magnesium), Osm (Osmolality), RBCs (Red Blood Cells), IL-6 (Interleukin-6), WBC (White Blood Cell count), ESR (Erythrocyte Sedimentation Rate), CRP (C-reactive Protein), Hb (Hemoglobin), BNP (Brain Natriuretic Peptide), INR (International Normalized Ratio), LDH (Lactate Dehydrogenase), AST (aspartate aminotransferase), ALT (alanine aminotransferase), CPK (Creatine Phosphokinase).

Units: mmHg (millimeters of mercury), mmol/L (millimoles per liter), mg/dL (milligrams per deciliter), mOsm/L (milliosmoles per liter), g/dL( grams per deciliter), mm/hr (millimeters per hour], K/uL (thousand per microliter), IU/L (international units per liter), ng/mL (nanogram per milliter), pg/mL (picogram per milliter), HPF (high power field)

Task ID	Patient Population	Prediction target	Average Precision(AP)	Baseline AP
Task 1	COVID-19 positive	AKI-2/3	0.36	0.18
Task 2	COVID-19 negative	AKI-2/3	0.23	0.09
Task 3	COVID-19 positive	AKI-3	0.47	0.09
Task 4	COVID-19 negative	AKI-3	0.40	0.04
Task 5	COVID-19 positive & AKI-2/3 positive	Recovery	0.62	0.59
Task 6	COVID-19 negative & AKI-2/3 positive	Recovery	0.88	0.75
Task 7	COVID-19 positive & AKI-3 positive	Recovery	0.61	0.47
Task 8	COVID-19 negative & AKI-3 positive	Recovery	0.88	0.72

### Supplementary Methods Table X: list of all the variables used for ML algorithms and the % missingness in each variable

Variable Baseline Age	Missing Percentage 0.0
Gender	0.0
Race	0.0
Ethinicity	0.0
DM	0.0
HF	0.0
CKD	0.0
COPD	0.0
HTN	0.0
CAD	0.0
Cancer	0.0
Asthma	0.0
TIA	0.0
Cerebral ischemia	0.0
first creatinine	0.0
BMI	0.0
first_SBP	0.07
	0.23
first MAP	0.16
first_oral_temperature	1.02
first serum Na	0.07
first_serum K	0.13
first serum Cl	0.07
first_serum HCO3	0.07
first_serum Ca	0.07
first_lonized Ca	85.96
first_serum Phos	4.21
first_serum Mg	3.29
first_serum Osm	87.41
first_pH_arterial	78.59
first_02_arterial	78.66
first_CO2_arterial	78.59
first_Na_urine	70.04
first_osmolality_urine	87.14
first_protein_urine_strip first_pulse_ox	64.58 0.0
first_paO2	78.59
first FIO2	73.63
first_respiratory_rate	0.07
first Ferritin	38.18
first_serum_Albumin	5.03
first_Hb	0.1
first_lymphocyte_count	10.85
first Procalcitonin	34.46
first D-Dimer	39.53
first_serum-Lactate	23.78
first BNP	43.11
first troponin	22.59
first_INR	9.31
	81.29
	0.1
 first_ESR	66.39
 first_ldh	85.83
first_ast	5.03
first_alt	5.03
first_cpk	64.45
first_crp	32.56
first_bun	0.07
first rbc urine	30.45

Supplementary Figure Legends:

Supplementary Figure 0: Flow chart of the study cohort.

**Supplementary Figure 1**: **A**. Forest plot showing the multivariable analysis of COVID-19 positive patients with vs. without AKI-3. **B**. Forest plot showing the multivariable analysis of COVID-19 negative patients with vs. without AKI-3.

**Supplementary Figure 2**: **A**. Forest plot showing the multivariable analysis of COVID-19 positive patients with vs. without Recovery-2 after AKI-2/3. **B**. Forest plot showing the multivariable analysis of COVID-19 negative patients with vs. without Recovery-2 after AKI-2/3.

**Supplementary Figure 3: A.** Forest plot showing the multivariable analysis of COVID-19 positive patients with vs. without Recovery-1 after AKI-3. **B.** Forest plot showing the multivariable analysis of COVID-19 negative patients with vs. without Recovery-1 after AKI-3.

**Supplementary Figure 4: A.** Forest plot showing the multivariable analysis of COVID-19 positive patients with vs. without Recovery-2 after AKI-3. **B.** Forest plot showing the multivariable analysis of COVID-19 negative patients with vs. without Recovery-2 after AKI-3.

**Supplementary Figure 5**: **A**. Forest plot showing the multivariable analysis of death in COVID-19 positive patients analyzing the association of Recovery-1 after AKI-3. **B**. Forest plot showing the multivariable analysis of death in COVID-19 positive patients analyzing the association of Recovery-2 after AKI-3

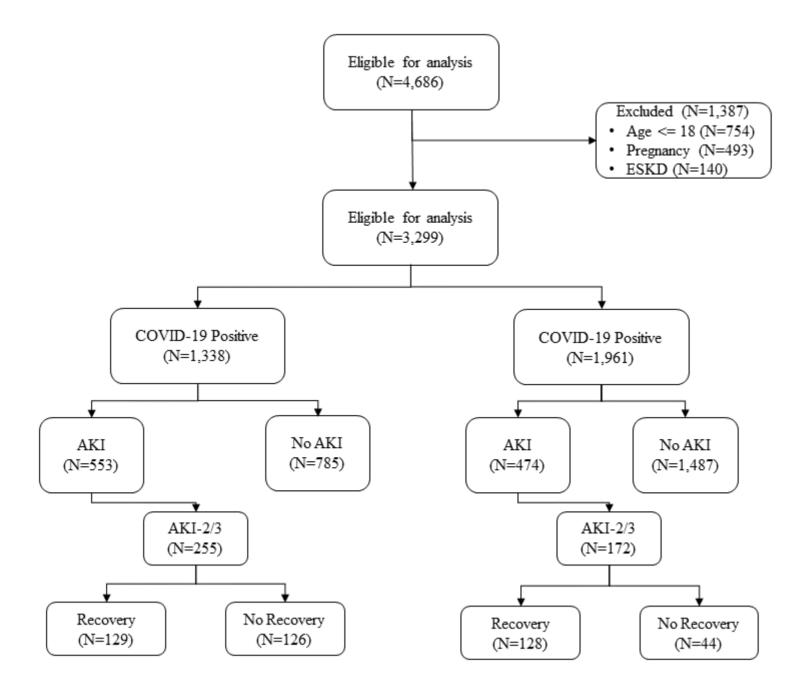
**Supplementary Figure 6**: **A.** Forest plot showing the multivariable analysis of death in COVID-19 negative patients analyzing the association of Recovery-1 after AKI-3. **B.** Forest plot showing the multivariable analysis of death in COVID-19 negative patients analyzing the association of Recovery-2 after AKI-3.

Supplementary Figure 7: Precision Recall (PR) Curves for patients with AKI-2/3 with and without COVID-19

Supplementary Figure 8: Precision Recall (PR) Curves for patients with AKI-3 with and without COVID-19

**Supplementary Figure 9**: Precision Recall (PR) Curves for patients with Recovery from AKI-3 with and without COVID-19

**Supplementary Figure 10**: SHapley Additive exPlanations (SHAP) plots for patients with Recovery after AKI-3 with and without COVID-19



Odds Ratio of having AKI-3

DM=diabetes mellitus, CKD=chronic kidney disease, ICU=intensive care unit, MV=mechanical ventilation, ARD=acute respiratory disease, ARDS=acute respiratory distress syndrome, ACEI=angiotensin converting enzyme inhibitor, ARB=angiotensin receptor blocker, AC=anticoagulation,

NSAIDs=nonsteroidal anti-inflammatory drugs, DBP=diastolic blood pressure,

 $10^{4}$ 

Phos=serum phosphorus, Hb=hemoglobin

2.57 [0.89-7.42]

5.06 [1.83-13.98]

3.52 [1.25-9.92]

2.06 [0.68-6.21]

8.96 [0.14-558.88]

6.87 [2.5-18.88]

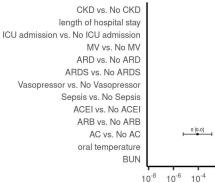
48.41 [11.47-204.25]

240.45 [24.73-2337.77]

1.1 [1.05-1.16]

\*unit for length of hospital stay is days, unit for DBP is mmHg (millimeters of mercury), unit for Phos is mg/dL (milligrams per deciliter), unit for Hb is g/dL (grams per deciliter)

Supplementary Figure 1B: Forest plot showing the multivariate analysis of COVID-19 negative patients with vs. without AKI-3

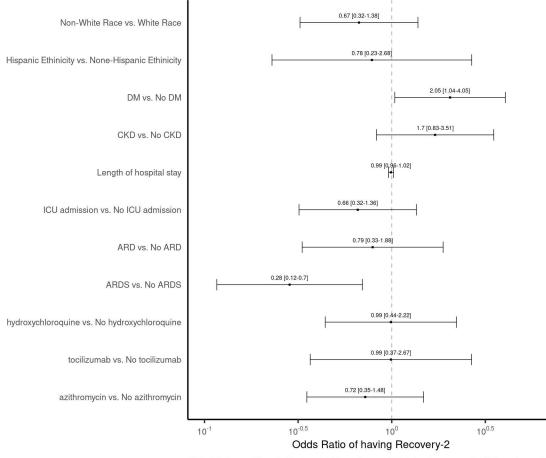


<sup>029</sup>(11.6.76) 1.01(1.1.03) <sup>8</sup> 10<sup>-6</sup> 10<sup>-4</sup> 10<sup>-2</sup> 10<sup>0</sup> 10<sup>2</sup> 10<sup>4</sup> Odds Ratio of having AKI-3

0.04 [0-0.39]

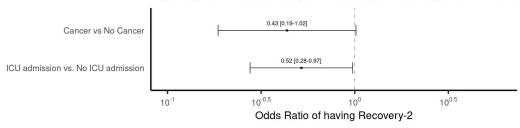
CKD=chronic kidney disease, ICU=intensive care unit, MV=mechanical ventilation, ARD=acute respiratory disease ARDS=acute respiratory distress syndrome, ACEI-angiotensin converting enzyme inhibitor, ARB=angiotensin receptor blocker, AC=anticoagulation, BUN=blood urea nitrogen \*unit for length of hospital stay is days, unit for oral temperature is degree Celsius, unit for BUN is mg/dL (milligrams per deciliter)





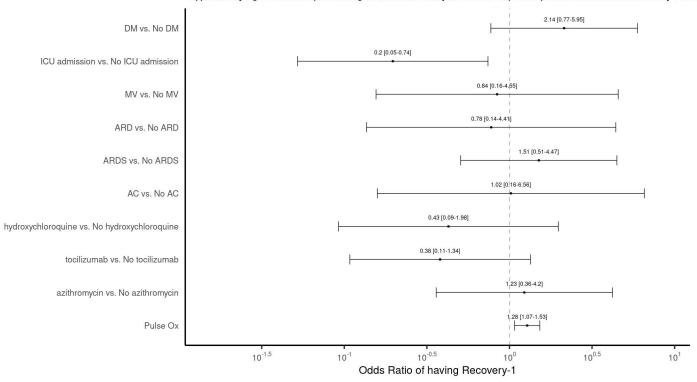
DM=diabetes mellitus, CKD=chronic kidney disease, ICU=intensive care unit, ARD=acute respiratory disease, ARDS=acute respiratory distress syndrome \*unit for length of hospital stay is days

Supplementary Figure 2B: Forest plot showing the multivariate analysis of COVID-19 negative patients with vs. without Recovery-2 after AKI-2/3



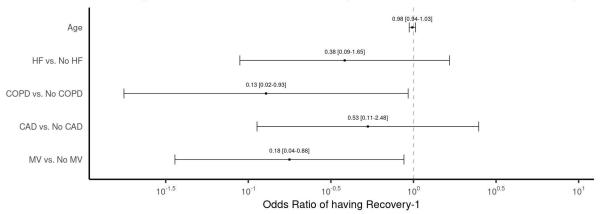
ICU=intensive care unit

Supplementary Figure 3A: Forest plot showing the multivariate analysis of COVID-19 positive patients with vs. without Recovery-1 after AKI-3

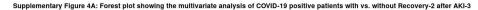


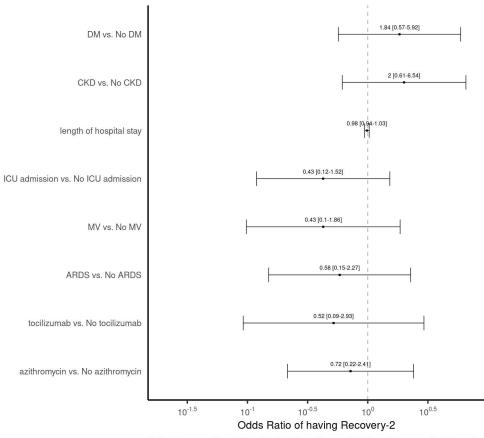
DM=diabetes mellitus, ICU=intensive care unit, MV=mechanical ventilation, ARD=acute respiratory disease, ARDS=acute respiratory distress syndrome, AC=anticoagulation

#### Supplementary Figure 3B: Forest plot showing the multivariate analysis of COVID-19 negative patients with vs. without Recovery-1 after AKI-3



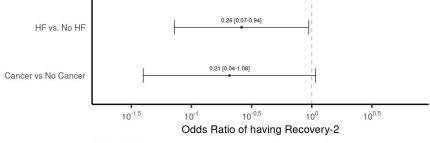
HF=heart failure, COPD=chronic obstructive pulmonary disease, CAD=coronary artery disease, MV=mechanical ventilation





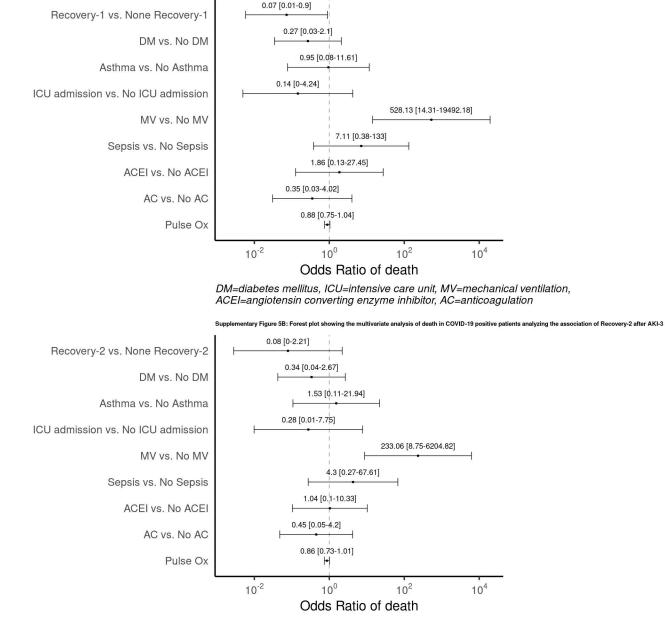
DM=diabetes mellitus, CKD=chronic kidney disease, ICU=intensive care unit, MV=mechanical ventilation, ARDS=acute respiratory distress syndrome \*unit for length of hospital stay is days

Supplementary Figure 4B: Forest plot showing the multivariate analysis of COVID-19 negative patients with vs. without Recovery-2 after AKI-3



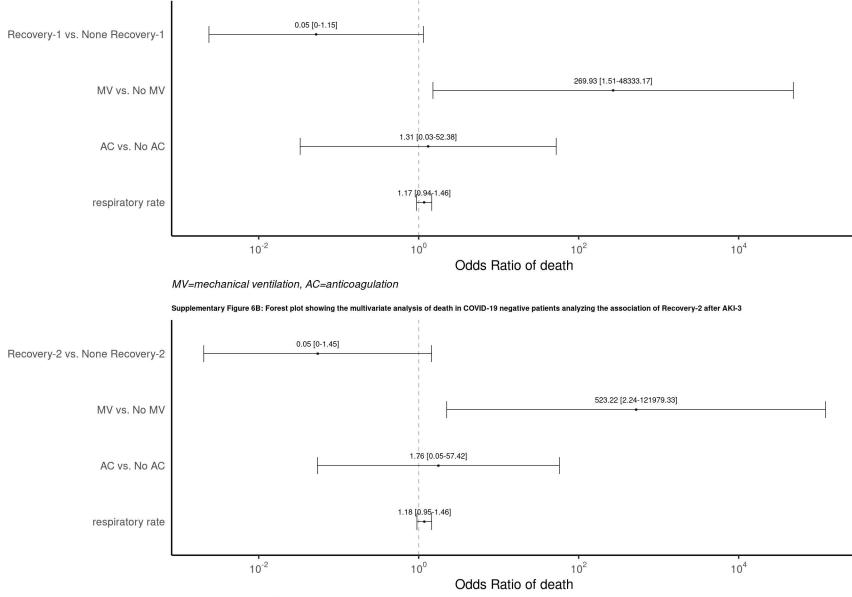


#### Supplementary Figure 5A: Forest plot showing the multivariate analysis of death in COVID-19 positive patients analyzing the association of Recovery-1 after AKI-3



DM=diabetes mellitus, ICU=intensive care unit, MV=mechanical ventilation, ACEI=angiotensin converting enzyme inhibitor, AC=anticoagulation

Supplementary Figure 6A: Forest plot showing the multivariate analysis of death in COVID-19 negative patients analyzing the association of Recovery-1 after AKI-3

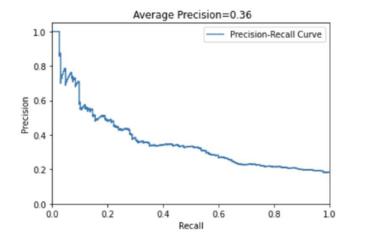


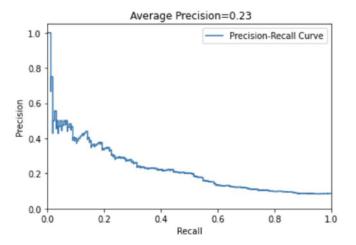
MV=mechanical ventilation, AC=anticoagulation

# Supplementary Figure 7: AKI-2/3 Precision-Recall Curves

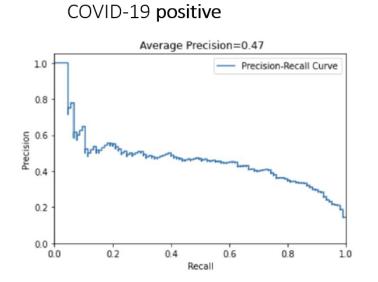
## COVID-19 positive

COVID-19 negative

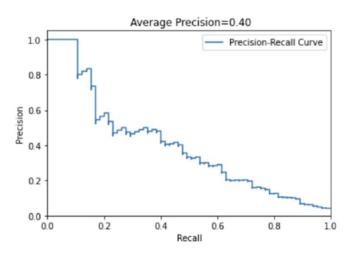




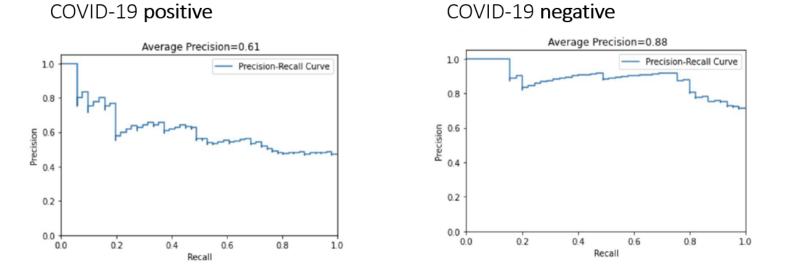
# Supplementary Figure 8: AKI-3 Precision-Recall Curves



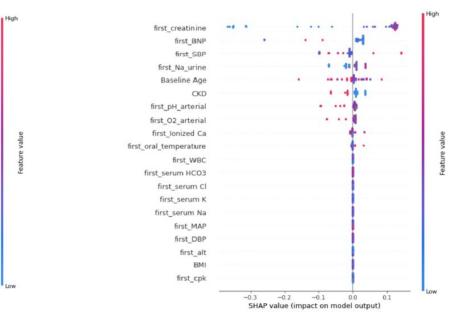
## COVID-19 negative



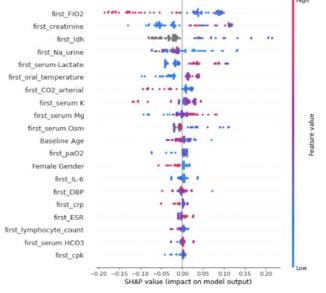
# Supplementary Figure 9: Recovery PR Curves (patients with AKI-3)



Supplementary Figure 10: SHAP Plots- predictors of Recovery after AKI-3



## COVID-19 positive



## COVID-19 negative