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COVID-19 Infection in Patients with Glomerular Disease: Follow-up Results from the IRoc-GN International Registry

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Key Points:

*Mortality and incidence of acute kidney injury (AKI) do not differ between COVID-19 patients with or without glomerular diseases.

*The main predictor of AKI is pre-COVID-19 eGFR, independent of the presence of GN.

*Incomplete kidney function recovery after COVID-19-associated AKI is more common in GN patients than in controls.

Abstract:

Background: The acute and long-term effects of SARS-CoV2 infection in individuals with glomerular diseases (GN) are still unclear. To address this relevant issue, we created the International Registry of COVID-19 infection in glomerulonephritis (IRoc-GN). Methods: We collected serial information on kidney-related and kidney-unrelated outcomes from 125 GN patients (63 hospitalized and 62 outpatients) and 83 non-GN hospitalized patients with COVID-19 and a median follow-up period of 6.4 (IQR: 2.3 to 9.6) months after diagnosis. We used logistic regression for the analyses of clinical outcomes and linear mixed models for the longitudinal analyses of eGFR. All multiple-regression models were adjusted for age, gender, ethnicity, and RAASI use. Results: After adjustment for pre-COVID-19 eGFR and other confounders, mortality and AKI did not differ between GN patients and controls (adjusted odds ratio [aOR] for AKI: 1.28 [95% CI: 0.46 to 3.60]; P=0.64). The main predictor of AKI was pre-COVID-19 eGFR (aOR per 1SD unit decrease in eGFR: 3.04 [95% CI: 1.76 to 5.28]; P<0.001). GN patients developing AKI were less likely to recover pre-COVID-19 eGFR compared to controls (adjusted 6-month post-COVID-19 eGFR = 0.41 [95%CI: 0.25 to 0.56] times pre-COVID-19 eGFR). Shorter duration of GN diagnosis, higher pre-COVID-19 proteinuria, and diagnosis of focal segmental glomerulosclerosis or minimal change disease (FSGS/MCD) were associated with a lower post-COVID-19 eGFR. Conclusions: Pre-COVID-19 eGFR is the main risk factor for AKI regardless from GN diagnosis. However, GN patients are at higher risk of impaired eGFR recovery after COVID-19-associated AKI. These patients (especially those with high baseline proteinuria or FSGS/MCD diagnosis) should be closely monitored not only during the acute phases of COVID-19, but also after its resolution.

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COVID-19 in Patients with Glomerular Disease: Follow-up Results from the IRoc-GN International Registry

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KEY POINTS

- Mortality and incidence of acute kidney injury (AKI) do not differ between COVID-19 patients with or without glomerular diseases.
- The main predictor of AKI is pre-COVID-19 eGFR, independent of the presence of GN.
- Incomplete kidney function recovery after COVID-19-associated AKI is more common in GN patients than in controls.

ABSTRACT

Background: The acute and long-term effects of SARS-CoV2 infection in individuals with glomerular diseases (GN) are still unclear. To address this relevant issue, we created the International Registry of COVID-19 infection in glomerulonephritis (IRoc-GN).

Methods: We collected serial information on kidney-related and kidney-unrelated outcomes from 125 GN patients (63 hospitalized and 62 outpatients) and 83 non-GN hospitalized patients with COVID-19 and a median follow-up period of 6.4 (IQR: 2.3 to 9.6) months after diagnosis. We used logistic regression for the analyses of clinical outcomes and linear mixed models for the longitudinal analyses of eGFR. All multiple-regression models were adjusted for age, gender, ethnicity, and RAASi use.

Results: After adjustment for pre-COVID-19 eGFR and other confounders, mortality and AKI did not differ between GN patients and controls (adjusted odds ratio [aOR] for AKI: 1.28 [95% CI: 0.46 to 3.60]; P=0.64). The main predictor of AKI was pre-COVID-19 eGFR (aOR per 1SD unit decrease in eGFR: 3.04 [95% CI: 1.76 to 5.28]; P<0.001). GN patients developing AKI were less likely to recover pre-COVID-19 eGFR compared to controls (adjusted 6-month post-COVID-19 eGFR = 0.41 [95%CI: 0.25 to 0.56] times pre-COVID-19 eGFR). Shorter duration of GN diagnosis, higher pre-COVID-19 proteinuria, and diagnosis of focal segmental glomerulosclerosis or minimal change disease (FSGS/MCD) were associated with a lower post-COVID-19 eGFR.

Conclusions: Pre-COVID-19 eGFR is the main risk factor for AKI regardless of GN diagnosis. However, GN patients are at higher risk of impaired eGFR recovery after COVID-19-associated AKI. These patients (especially those with high baseline proteinuria or FSGS/MCD diagnosis) should be closely monitored not only during the acute phases of COVID-19, but also after its resolution.
INTRODUCTION

The International Registry of COVID-19 infection in glomerulonephritis (IRoc-GN) was created shortly after the spread of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection was declared a pandemic in March 2020 by the World Health Organization. The purpose of the registry was to examine the short and long term impact of Coronavirus Disease 2019 (COVID-19) in patients with underlying glomerulonephritis (GN) and identify risk factors for unfavorable outcomes.

Our initial report comparing 40 GN patients with COVID-19 and 80 SARS-CoV2 positive control cases showed that the GN cohort had higher overall mortality (15% vs. 5%, respectively) and acute kidney injury (AKI) (39% vs. 14% respectively) rates. Immunosuppressive therapy at presentation was not associated with greater mortality or AKI in the GN cohort, but more pronounced hypoalbuminemia at presentation and shorter duration of glomerular disease were associated with greater risk of AKI and need for kidney replacement therapy (KRT) in GN patients.

Enrollment of new patients in the IRoc-GN registry and collection of longitudinal data continued throughout the pandemic. Herein, we present the results of our follow-up study that was aimed to extend the findings of our initial report, describe the spectrum of COVID-19 in a larger GN cohort and explore the interactions of underlying GN, immunosuppressive medications and other determinants on susceptibility and outcomes of COVID-19 (AKI, need for KRT, death). In addition, we aimed to characterize the kidney recovery after COVID-19 associated AKI in GN patients as well as the longer-term consequences of COVID-19 on kidney prognosis.
METHODS

Study design and participants
Details of this registry have been previously described.¹ We used data collected from 20 April 2020 to 20 April 2021 via a secure public survey (https://redcapsurvey.niddk.nih.gov/surveys/?s=FPM87NK7T4) on REDCap (Research Electronic Data Capture).²

Briefly, we included patients with biopsy-proven GN diagnosed with COVID-19, managed as inpatients or outpatients, from centers participating in the IRoc-GN registry. For each GN patient entered in the registry, reporters were asked to enter at least 1 age- and sex-matched control patient who was positive for SARS-CoV2 but without GN and with estimated glomerular filtration rate (eGFR) >60 ml/min/1.73m². Controls were hospitalized within ± 2 weeks of the GN cases to account for changes in treatment strategies over time that may influence outcomes. Patients on maintenance hemodialysis before infection and kidney transplant recipients were excluded.

Data collection
The “Initial Survey” collected data on pre-COVID-19 renal parameters, glomerular disease diagnosis, immunosuppressive medications, COVID-19–related symptoms, COVID-directed therapies, management of immunosuppression during infection, outcomes, the maximum level of care, non-renal complications, AKI, need for KRT, disposition (i.e., recovery, death) and laboratory parameters. Links to “Follow-up Surveys” were automatically generated and sent by REDCap at pre-defined (eight weeks) intervals to collect longitudinal data on patient status and kidney outcomes after infection. With this combination of surveys, renal parameters were collected at various time points: (i) pre-COVID-19 (latest available before infection onset), (ii) at COVID-19 presentation, (iii) peak, (iv) post-COVID-19 as defined by the absence of, or marked improvement in, original COVID-19-related symptoms or signs.
and (v) during extended follow up after recovery from acute infection. All data were checked for quality by 3 physicians (MW, PC and UM).

Statistical Analysis

We compared baseline differences between groups in continuous variables using the Kruskal-Wallis test for three-group equality testing and Mann-Whitney for pairwise testing. We compared baseline differences between groups in categorical variables using Fisher's exact test. We used Wilcoxon matched-pairs signed-rank test to compare crude paired continuous measurements over follow-up.

We used logistic regression to examine the association between glomerular disease status (indicator variable for patients with history of glomerular disease) and the clinical outcomes of AKI, KRT, and death (primary endpoints). This analysis was limited to hospitalized patients (i.e., glomerular disease patients vs controls). We calculated crude odds ratios (OR), OR adjusted for pre-COVID-19 eGFR, and OR additionally adjusted for demographic characteristics (age, continuous variable; male gender, indicator variable for male; ethnicity, indicator variable for non-white ethnicity), and Renin-Angiotensin-Aldosterone System Inhibitors (RAASi) use (indicator variable for their use). We deemed that RAASi use is a potential confounder because it had different distribution between patients with glomerular disease and controls (and within glomerular disease patients, between patients with different disease severity), and may also be associated with increased risk of AKI and KRT. Models that additionally adjusted for diabetes, obesity, and hypertension provided similar results. However, to avoid having to report several regression models that included more variables than the data could support, we did not report them in the final results.

The analysis of recovery of kidney function was based on the multiple regression models examining the effect of each variable on post-COVID-19 eGFR analyzed as longitudinal (repeated measures)
continuous variable. Because the longitudinal eGFR measurements were unbalanced between patients, and because there was inconsistency among subjects in timing of the eGFR assessment, we examined longitudinal eGFR using random effects regression models estimated via restricted maximum likelihood (REML). These models estimated eGFR as a linear change over time which provided a good fit to the data points (Supplemental Figure 1-2).

We performed all the analyses using Stata release 17 (2021 StataCorp, 4905 Lakeway Drive, College Station, TX, USA). The Stata code for all the analyses is freely available at: https://github.com/UMaggiore/iROC-GN.

A two-sided P value of less than 0.05 was regarded as statistically significant. Unless otherwise stated, we reported nominal P values without adjustment for multiple testing.

Further details on statistical analyses are included in the Supplemental Methods.
RESULTS

Study population

The study population included 125 patients with a history of GN diagnosed with COVID-19 (63 requiring hospitalization and 62 managed as outpatients) and 83 patients without GN who developed COVID-19 requiring hospitalization (Ctrl-hospitalized). Baseline kidney function (pre-COVID-19 eGFR) was assessed at a median of 3.7 months (interquartile range: 1.8 to 6.2 months) prior to infection. After COVID-19, median follow-up of kidney function was 6.4 months (interquartile range: 2.3 to 9.6). The characteristics of the study population are reported in Table 1. Compared to Ctrl-hospitalized, GN hospitalized patients had lower eGFR, serum albumin and hemoglobin pre-COVID-19 and at time of admission (Table 1 and Supplemental Table 1). GN-hospitalized patients also had lower eGFR, lower serum albumin and higher proteinuria levels pre-COVID-19 and at COVID-19 diagnosis than GN-outpatients (Table 1).

GN-hospitalized and GN-outpatients had similar distributions in the type of glomerular disease (Table 2). However, compared to GN-outpatients, GN-hospitalized patients were more likely to have received rituximab prior to COVID-19 diagnosis, to be on calcineurin inhibitors at the time of COVID-19, and have shorter duration of GN disease (<6 months) (Table 2), while RAASI therapy was less common (Table 1). The percentage of patients with active GN disease at COVID-19 onset was similar between the two groups (Table 2). Tapering or withdrawal of immunosuppression during COVID-19 was uncommon and did not statistically differ between GN-outpatients and GN-hospitalized patients, with the exception of mycophenolate mofetil (MMF) which was more frequently reduced or discontinued in GN-hospitalized patients (Table 2).
At disease presentation, GN-outpatients had less severe inflammatory indexes compared to GN-hospitalized (C-reactive protein, serum ferritin, d-dimer levels), whereas the same characteristics were similar between GN-hospitalized and Ctrl-hospitalized (Table 1). The rates of in-hospital complications (i.e., need for intubation or inotropes/vasopressors, superimposed bacterial infections, thrombotic and cardiovascular complications) were similar between GN-hospitalized and Ctrl-hospitalized, but the duration of hospitalization was slightly longer in GN patients (mean 16.3 vs 14.4 days, respectively P=0.033) (Supplemental Table 1). As predicted based on the lower disease severity, fewer GN-outpatients received any COVID-19 treatment compared to GN-hospitalized and Ctrl-hospitalized (Supplemental Table 2). Within hospitalized patients, fewer GN-hospitalized received hydroxychloroquine and azithromycin than Ctrl-hospitalized (Supplemental Table 2).

**Clinical outcomes in patients with glomerular disease**

We assessed the effect of glomerular disease on COVID-19 outcomes by comparing GN-hospitalized with Ctrl-hospitalized, before and after adjusting for potential confounders (Table 3). Primary endpoints were incidence of AKI, initiation of KRT, and death. Incidence of AKI, KRT, and death were 46.0 vs. 19.3%, 12.7 vs. 9.6%, 19.1 vs. 9.6% in GN-hospitalized vs. Ctrl-hospitalized patients, respectively. In crude analyses, GN-hospitalized had increased odds of AKI (OR: 3.44 [95% Confidence Interval: 1.58 to 7.47; P=0.002), but not of KRT or death (Table 3). However, after adjusting for pre-COVID-19 eGFR and additional confounders (age, gender, non-white ethnicity, and RAASi use), the odds of AKI were similar between groups (OR: 1.28 [95% CI: 0.43 to 3.60; P=0.64, Table 3). The adjusted analyses confirmed that OR for KRT and death were similar between GN hospitalized and Ctrl-hospitalized (Table 3).
Pre-COVID-19 eGFR was the major determinant of clinical outcomes in adjusted analyses: for every 1 standard deviation unit decrease in eGFR (approximately 30 ml/min/1.73m\(^2\) decrease), the adjusted OR for AKI was 3.04 (95% CI: 1.76 to 5.28; P<0.001), for KRT 2.39 (95% CI: 1.20 to 4.78; P=0.014), and for death 1.76 (95% CI: 0.91 to 3.37; P=0.091) (Table 3).

The multivariable-adjusted relationship between pre-COVID-19 eGFR and the probability of AKI is reported in Figure 1: patients with pre-COVID-19 eGFR below 30 ml/min/1.73m\(^2\) had a probability of developing AKI during hospital stay greater than 50%. In the adjusted analyses, the rate of death increased with older age (OR per 1 SD unit increase, which is approximately 15 years: 2.33 [95% CI: 1.10 to 4.94]; P=0.028) and in patients with non-white ethnicity (OR 4.62 [95% CI: 1.30 to 16.44]; P=0.018) (Table 3).

**Determinants of clinical outcomes in patients with glomerular disease**

We assessed the effect of determinants of clinical outcomes (AKI, KRT, death) in patients with glomerular disease by performing analyses on GN-hospitalized and GN-outpatients pooled, after adjusting for potential confounders, including hospitalization status. Similar to the results above, pre-COVID-19 eGFR was the only significant determinant of AKI, KRT, and death (OR for death associated with 1 SD unit decrease in eGFR: 3.00 [95% CI: 1.15 to 7.85; P=0.025]), the latter being also associated with older age (OR for death associated with 1 SD increase in age: 3.97 [95% CI: 1.47 to 10.74; P=0.007]). In the crude analysis, only serum albumin was associated with AKI and the presence of SLE was associated with need for KRT (Supplemental Table 3). However, in the adjusted analyses, serum albumin, urinary protein excretion, immunosuppressive drugs (azathioprine, calcineurin inhibitors, mycophenolate, rituximab, steroids), were not significantly associated with the main clinical outcomes (Supplemental Table 3). In addition, the duration of glomerular disease diagnosis and type of
GN (including a comparison of systemic GN vs renal limited GN) were not significantly associated with the main clinical outcomes (Supplemental Table 3).

**Effect of presence of glomerular disease on recovery of kidney function post COVID-19**

We assessed the effect of presence of glomerular disease on post-COVID-19 kidney function by comparing GN-hospitalized with Ctrl-hospitalized, after adjusting for potential confounders. Kidney function recovery was assessed as a categorical outcome (i.e., any post-COVID-19 eGFR within -10% of pre-COVID-19 eGFR [baseline]). Overall, the rate of kidney function recovery was similar in GN-hospitalized and Ctrl-hospitalized (OR: 1.47 [95% CI: 0.57 to 3.77; P=0.425]) (Table 4). In adjusted models, the only borderline statistically significant determinant of kidney function recovery was pre-COVID-19 eGFR (OR of kidney function recovery per 1 SD unit eGFR decrease: 0.55 [95% CI: 0.33 to 0.90; P=0.018]) (Table 4).

We next analyzed data using kidney function as a continuous outcome (by comparing pre- and post-COVID-19 eGFR). Overall, there was no significant difference in the correlation between pre-COVID-19 and post-COVID-19 eGFR between GN-hospitalized and Ctrl-hospitalized patients. However, when we stratified patients based on development of AKI, the correlation between pre-COVID-19 and post-COVID-19 eGFR significantly differed between GN-hospitalized and Ctrl-hospitalized patients. In particular, we found that Ctrl-hospitalized patients who developed AKI had a full recovery of eGFR (to pre-COVID-19 levels) by 6 months after COVID-19. In contrast, kidney recovery was only partial in GN-hospitalized patients who developed AKI during hospitalization. This is demonstrated by the four-way interaction term between GN vs Ctrl, time, AKI, and pre-COVID-19 eGFR, which was statistically significant (P=0.025). To have a visual appraisal of the interaction term we estimated the adjusted coefficient of the relationship between pre-COVID-19 eGFR and 6-month post-COVID-19 eGFR.
according to the history of glomerular disease and AKI and plotted the results predicted by the multiple regression model (Supplemental Table 4 and Figure 2). For all the groups, except GN-hospitalized who had AKI, the coefficient between pre-COVID-19 and 6-month post-COVID-19 was close to one (Supplemental Table 4) and the line close to the line of identity (the line of identity between pre-COVID-19 and 6-month post-COVID-19 eGFR is the dotted line in Figure 2): Ctrl-hospitalized-no-AKI, 0.90 (95% CI: 0.75 to 1.04); GN-hospitalized-no-AKI: 0.87 (95% CI: 0.70 to 1.04); Ctrl-hospitalized-with-AKI: 0.98 (95% CI: 0.82 to 1.14); GN-hospitalized-with-AKI: 0.41 (95% CI: 0.25 to 0.56). The intercept was not statistically significantly different from zero in all four groups (data not shown). The visual representation of how the four-way interaction in terms of changes in eGFR over time is shown in Supplemental Figure 3.

In the multivariable regression models, determinants that were significantly associated with lower post-COVID-19 eGFR were older age (-3.5 ml/min/1.73m² per 1 SD unit increase) and non-white ethnicity (-5.4 ml/min/1.73m²).

**Determinants of kidney function recovery in patients with glomerular disease**

Among infected GN patients, pre-COVID-19 eGFR and serum albumin decreased only in those who were hospitalized (Supplemental Table 5). The only borderline significant determinant of kidney function recovery was pre-COVID-19 eGFR (OR of kidney function recovery per 1 SD unit decrease of eGFR: 0.62 (95% CI: 0.38 to 1.01; P=0.055) (Table 4). In the adjusted analyses, serum albumin, urinary protein, type of immunosuppressive drugs (azathioprine, mycophenolate, calcineurin inhibitors, rituximab, steroids), and duration and type of glomerular disease were not significantly associated with the rate of kidney function recovery (categorical variable; Supplemental Table 6). At variance, when we examined the effect of the same determinants of post-COVID-19 eGFR (continuous variable), we
found that higher baseline proteinuria (-2.1 ml/min/1.73m$^2$ per 1 SD unit increase) and, more importantly, pre-existing focal segmental glomerulosclerosis (FSGS) or minimal change disease (MCD) diagnosis (-7.7 ml/min/1.73m$^2$), were associated with significantly lower post-COVID-19 eGFR (Supplemental Table 7).

**DISCUSSION**

To our knowledge, this is the first analysis of both the short and long-term outcomes of COVID-19 infection among GN patients. Based on a meta-analysis from 2020, the pooled incidence of COVID-19 associated AKI among hospitalized patients was 28.6% (95% CI 19.8–39.5) in the United States and Europe, although the reported ranges are quite broad.\(^3\) In our study, nearly half of the hospitalized GN patients experienced AKI suggesting that the incidence of COVID-associated AKI in GN patients is at the higher range of estimates of AKI reported among hospitalized patients.\(^4\)–\(^8\) However, our data indicate that the presence of underlying GN does not confer an independent risk for COVID-19 associated AKI. In line with the well-established association between pre-existing CKD and risk of in-hospital AKI in general,\(^9\)–\(^11\) and in the setting of COVID-19,\(^4\) \(^12\)–\(^14\) we showed that pre-COVID-19 eGFR is the main determinant of AKI and of need for KRT.

There was no difference in mortality between GN and control patients. Both in-hospital AKI and presence of CKD have been consistently associated with higher COVID-19 associated mortality.\(^5\) \(^15\)–\(^20\) The similar adjusted rates of AKI between the GN and control cohorts may partly explain the observed lack of difference in mortality in this study. AKI as well as death were almost entirely confined to hospitalized patients. Although we do not have information on COVID-19 severity scores, these data suggest that milder cases of COVID-19 in GN patients, managed in the outpatient setting have a more benign outcome than hospitalized cases.
Importantly, our results indicate that, while controls with COVID-19-associated AKI tend to show recovery of kidney function by 6 months, GN patients with AKI have slower, incomplete kidney recovery and persistently lower eGFR at longer-term follow-up. Longitudinal outcome and recovery data on patients with COVID-19 associated AKI are still limited.\textsuperscript{4, 21, 22} One recent cohort study reported accelerated eGFR decline and lower rates of kidney recovery after hospitalization in patients with COVID-19-associated AKI compared with AKI for other reasons, independent of comorbidities or AKI severity.\textsuperscript{21} The etiology of the observed slower and incomplete kidney recovery in GN patients compared to control patients after COVID-19-associated AKI is likely multifactorial.\textsuperscript{20} It is noteworthy that shorter duration of GN diagnosis was associated both with a greater risk of AKI and slower kidney recovery. In addition, a higher degree of pre-COVID-19 proteinuria and a history of FSGS/MCD were associated with decreased kidney recovery and lower eGFR post-COVID-19 at follow-up. These interesting observations set the basis for future studies aimed to better define GN subgroups that are particularly vulnerable to CKD progression after COVID-19-associated AKI.

Several pathophysiological pathways are believed to be activated in the context of SARS-CoV-2 infection leading to kidney injury, and a spectrum of histologic changes in the glomerular, tubulointerstitial, and vascular compartments of the kidney have been described. The extent to which baseline patient characteristics (i.e., type, duration or immunologic activity of underlying GN, proteinuria, kidney gene expression profiles) contribute to the type of AKI or subsequent recovery warrants further study. The lack of kidney biopsies in the GN and control cohorts with COVID-19-associated AKI precludes comparisons. However, it is conceivable that GN patients with underlying immune dysregulation, kidney immune cell infiltration and prothrombotic tendencies are more prone to endothelial dysfunction, coagulopathy, complement activation or have greater sensitivity of podocytes and tubules to the effects of SARS-CoV2 which may impact renal prognosis compared to those without
GN. Superimposed on limited renal reserve, persistence of proteinuria, hematuria and maladaptive repair mechanisms in GN patients after AKI may also promote renal fibrosis leading to incomplete kidney recovery. Limited serial proteinuria values and relevant serological data in our study preclude meaningful conclusions regarding the contribution of changes in GN activity or GN relapses (possibly related to reduction of immunosuppression during infection or to the infection itself) in delayed kidney recovery.

Our data do not indicate an association between immunosuppressive treatment before COVID-19, level of pre-COVID-19 proteinuria or the type of GN (systemic vs kidney limited) on the primary outcomes of mortality and AKI. However, hospitalized GN patients had higher pre-COVID-19 proteinuria and lower serum albumin than those managed as outpatients. In addition, a greater proportion of hospitalized patients were on calcineurin inhibitors at the time of COVID-19 or received rituximab within 6 months preceding infection. The published data regarding the influence of longitudinal immunosuppression on COVID-19 susceptibility and outcomes has been changing and contradictory. While our data regarding calcineurin inhibitors and rituximab are too limited to draw firm conclusions, these observations deserve further study, particularly in light of the importance of B cell depleting therapy for GN. Some early reports suggested no effect of rituximab or a slightly increased risk of hospitalization from COVID-19. More recently studies have reported unfavorable prognosis particularly in those with shorter duration between last rituximab infusion and infection. These conflicting results may reflect heterogeneity in the diseases treated with rituximab, intensity of B cell depletion and IgG levels at infection onset and number of previous treatments. Similarly, the data regarding calcineurin inhibitors has been mixed. In a large Danish cohort study, treatment with cyclosporine or tacrolimus was associated with a significantly increased risk of hospitalization. In contrast, a retrospective study from Spain indicated beneficial effects of cyclosporine in COVID-19 (76% reduction in mortality). This preliminary evidence has
boosted interest in these drugs for treatment of COVID-19 and there are several ongoing clinical trials.\textsuperscript{36} Results of such trials may influence treatment decisions of underlying GN during the ongoing pandemic.\textsuperscript{37}

Among GN patients, those of non-white ethnicity had a higher adjusted mortality risk, a finding consistent with many published reports that have highlighted racial/ethnic related differences in COVID-19 rates and outcomes. Research to disentangle the various complex factors that contribute to ethnic variability is ongoing though socioeconomic and sociodemographic factors appear to play important roles.\textsuperscript{19, 33, 38–40}

Our study has many strengths. There is global representation with a diverse population. It focuses on a subpopulation of CKD patients with unique (and potentially dynamic) baseline clinical characteristics and treatment challenges for which little data is currently available. The study is reflective of the various presentations of COVID-19 in GN patients managed as inpatients and outpatients. We also analyzed longitudinal laboratory data extending from pre-COVID-19 through recovery. This is particularly relevant as the 25\textsuperscript{th} Consensus Conference of the Acute Disease Quality Initiative (ADQI) highlighted the natural history of kidney sequelae after COVID-associated AKI as major research recommendations.\textsuperscript{41, 42} Importantly, inclusion of a control group of non-GN patients strengthened the validity of the findings. However, there are some caveats that should be considered. The sample size remains relatively small despite our large network. There were missing data at various time points particularly for GN patients managed as outpatients. Serial laboratory tests (i.e., proteinuria) that would provide a better understanding of GN relapses or changes in disease activity post-COVID-19 were not consistently performed. Also, the control and GN groups were not perfectly matched, and we chose to include only hospitalized controls due to limitations in data collection in outpatients. Adjustments for
confounders allowed us to minimize the bias of the unbalanced control characteristics, but it is possible that differences between the two groups persist that cannot be fully accounted for.

In conclusion, in a diverse international cohort of patients with COVID-19, mortality and AKI did not differ between GN patients and controls. The main predictor of AKI was pre-COVID-19 eGFR. Incomplete kidney recovery after COVID-19 associated AKI was more common in GN patients compared to controls. Shorter duration of GN diagnosis, higher grade proteinuria and FSGS/MCD diagnosis were associated with impaired kidney recovery during longer term follow up. These findings remain highly relevant despite the availability of COVID-19 vaccines in light of the rising rates of COVID-19 spread of the delta variant and other variants of concern, impaired vaccine response among immunocompromised patients,\textsuperscript{43-47} breakthrough infections among vaccinated,\textsuperscript{48, 49} and waning vaccine immunity over time.

DISCLOSURES

P. Cravedi reports the following: Honoraria: Advisor for Chinook Therapeutics.; and Scientific Advisor or Membership: Associate Editor for Journal of Nephrology (JN) and American Journal of Transplantation (AJT). O. Bestard reports the following: Patents and Inventions: Oxford Immunotec; and Scientific Advisor or Membership: Associate Editor of Transplant International and Frontiers in Immunology journals. A. Bruchfeld reports the following: Consultancy Agreements: Merck, Chemocentryx, Astra-Zeneca, Fresenius; Research Funding: Astra-Zeneca research grant.; Honoraria: Merck, Chemocentryx, Vifor, Fresenius, Bayer; and Scientific Advisor or Membership: Member of ERA-EDTA scientific advisory board 2018-2024, Chair ERA EDTA Immunonephrology Working Group, Vice-chair of the Swedish Renal Fund. G. Comai reports the following: Honoraria: Alexion, Astellas, Novartis. G. Fernandez Juarez reports the following: Research Funding: Instituto Salud Calos III; and Honoraria: GSK., Alexion. E. Fiaccadori reports the following: Scientific Advisor or Membership: Editorial Board Journal of Nephrology, Editorial Board Blood Purification; and Other Interests/Relationships: Member Italian Society of Nephrology, Member European Society of Parenteral & Enteral Nutrition. O. Flossmann reports the following: Consultancy Agreements: Vifor Pharma; and Other Interests/Relationships: European Vasculitis Society, Renal Association (UK), UK Ireland Vasculitis Society, British Medical Association, Royal College of Physicians London. C. García-Carro reports the following: Consultancy Agreements: Astra-Zeneca, Esteve, NovoNordisk, BoehringerIngelheim Lilly, Astellas, Otsuka, Novartis and Baxter; Honoraria: Astra-Zeneca, Esteve, NovoNordisk, Boehringer-Ingelheim Lilly, Astellas, Otsuka, Novartis and Baxter; and Scientific Advisor or Membership: Astra-Zeneca, Boehringer-Ingelheim Lilly, Mundipharma and NovoNordisk. M. Griffith reports the following: Honoraria: Retrophin Advisory Board. A. Hamilton reports the following: Scientific Advisor or Membership: Journal of Kidney Care Editorial Board; and
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AUTHOR CONTRIBUTIONS
M. Waldman and P. Cravedi conceived and oversaw the project. M. J Soler, C. Garcia-Carro, L. Lightstone, T. Turner-Stokes, M. Griffith, J. Torras, L. Martinez Valenzuela, O. Bestard, C. Geddes, O. Flossman, K. L Budge,
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All the authors reviewed and approved the final version of the manuscript.

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Table 1. Baseline characteristics of the study population.

|                          | Ctrl – Hospitalized (n=83) | Study Group | GN – Hospitalized (n=63) | GN – Outpatients (n=62) | P value |
|--------------------------|-----------------------------|-------------|------------------------|------------------------|---------|
| **Age, years**           | 80                          | 60.0        | (14.4)                 | 60                     | (15.9)  | 60      | 45.4     | (12.9)     | <0.001<sup>b,c</sup> |
| **Female gender**        | 29                          | 34.9%       | 28                     | 44.4%                  | 36      | 58.1%   |          |            | 0.022<sup>a</sup> |
| **Race**                 |                             |             |                        |                        |         |         |          |            |                   |
| White                    | 59                          | 71.1%       | 38                     | 60.3%                  | 28      | 45.2%   |          |            | 0.049<sup>h</sup> |
| Black/AAm                | 5                           | 6.0%        | 3                      | 4.8%                   | 4       | 6.5%    |          |            |                    |
| Asian                    | 0                           | 0.0%        | 3                      | 4.8%                   | 3       | 4.8%    |          |            |                    |
| Other                    | 18                          | 21.7%       | 19                     | 30.2%                  | 27      | 43.5%   |          |            |                    |
| Unknown                  | 1                           | 1.2%        | 0                      | 0.0%                   | 0       | 0.0%    |          |            |                    |
| **Ethnicity**            |                             |             |                        |                        |         |         |          |            |                   |
| Hispanic/Latino          | 20                          | 24.1%       | 19                     | 30.6%                  | 26      | 41.9%   |          |            | 0.031<sup>b</sup> |
| **BMI, kg/m<sup>2</sup>**| 68                          | 30.2        | (7.4)                  | 50                     | 27.6    | (4.9)   | 53       | 27.2       | (5.6) 0.061     |
| **Comorbidities**        |                             |             |                        |                        |         |         |          |            |                   |
| Hypertension             | 45                          | 54.2%       | 43                     | 68.3%                  | 29      | 46.8%   |          |            | 0.048<sup>c</sup> |
| Diabetes                 | 23                          | 27.7%       | 14                     | 22.2%                  | 5       | 8.1%    |          |            | 0.009<sup>b,c</sup> |
| Cardiovascular disease   | 16                          | 19.3%       | 12                     | 19.0%                  | 4       | 6.5%    |          |            | 0.055     |
| Asthma                   | 6                           | 7.2%        | 3                      | 4.8%                   | 1       | 1.6%    |          |            | 0.336     |
| COPD                     | 4                           | 4.8%        | 7                      | 11.1%                  | 2       | 3.2%    |          |            | 0.233     |
| Liver disease            | 4                           | 4.8%        | 3                      | 4.8%                   | 1       | 1.6%    |          |            | 0.061     |
| Cancer*                  | 4                           | 4.8%        | 7                      | 11.1%                  | 0       | 0.0%    |          |            | 0.015<sup>c</sup> |
| HIV/AIDS                 | 0                           | 0.0%        | 0                      | 0.0%                   | 1       | 1.6%    |          |            | 0.298     |
| Rheumatoid Arthritis     | 0                           | 0.0%        | 3                      | 4.8%                   | 0       | 0.0%    |          |            | 0.052     |
| Smoking habit            | 5                           | 6.0%        | 1                      | 1.6%                   | 1       | 1.6%    |          |            | 0.303     |
| Use of RAASi             | 3                           | 3.6%        | 17                     | 27.0%                  | 22      | 35.5%   |          |            | <0.001<sup>a,b,c</sup> |
| **Clinical presentation**|                             |             |                        |                        |         |         |          |            |                   |
| Fever                    | 66                          | 79.5%       | 46                     | 73.0%                  | 31      | 50.0%   |          |            | 0.001<sup>b,c</sup> |
| Dyspnea                  | 53                          | 63.9%       | 34                     | 54.0%                  | 8       | 12.9%   |          |            | <0.001<sup>b,c</sup> |
| Cough                    | 27                          | 32.5%       | 32                     | 50.8%                  | 28      | 45.2%   |          |            | 0.069     |
| GI symptoms              | 26                          | 31.3%       | 13                     | 20.6%                  | 11      | 17.7%   |          |            | 0.138     |
| Anosmia                  | 15                          | 18.1%       | 4                      | 6.3%                   | 12      | 19.4%   |          |            | 0.059     |
| Fatigue                  | 8                           | 9.6%        | 19                     | 30.2%                  | 24      | 38.7%   |          |            | <0.001<sup>b</sup> |
| Myalgia                  | 8                           | 9.6%        | 14                     | 22.2%                  | 20      | 32.3%   |          |            | 0.003<sup>b</sup> |
| Anorexia                 | 4                           | 4.8%        | 12                     | 19.0%                  | 7       | 11.3%   |          |            | 0.022<sup>a</sup> |
| Chills                   | 4                           | 4.8%        | 9                      | 14.3%                  | 5       | 8.1%    |          |            | 0.124     |
| Sore throat              | 3                           | 3.6%        | 2                      | 3.2%                   | 8       | 12.9%   |          |            | 0.051     |
| Nasal congestion         | 2                           | 2.4%        | 3                      | 4.8%                   | 8       | 12.9%   |          |            | 0.044<sup>b</sup> |
| Neurologic symptoms      | 0                           | 0.0%        | 1                      | 1.6%                   | 0       | 0.0%    |          |            | 0.601     |
| **Pre-COVID-19 kidney parameters** |                     |             |                        |                        |         |         |          |            |                   |
| sCr, mg/dl               | 74                          | 1.1         | (0.9)                  | 62                     | 1.8     | (1.7)   | 62       | 1.5        | (1.6) <0.001<sup>a,c</sup> |
### Kidney parameters at presentation/admission

| Parameter                  | Ctrl | GN-hospitalized | GN-outpatients |
|----------------------------|------|-----------------|----------------|
| sCr, mg/dl                 | 80   | 1.5             | 2.7            |
| eGFR, ml/min/1.73m²        | 77   | 76.2            | 72.0           |
| Serum albumin, g/dl        | 64   | 3.5             | 3.0            |
| Proteinuria, g/day         | 5    | 0.1             | 5.1            |

### Lab parameters during COVID-19

| Parameter                  | Ctrl | GN-hospitalized | GN-outpatients |
|----------------------------|------|-----------------|----------------|
| White blood cells (n/μl)   | 43   | 8208.8          | 52             |
| Lymphocytes (n/μl)         | 65   | 1126.5          | 57             |
| Neutrophils (n/μl)         | 43   | 7105.1          | 51             |
| Hemoglobin (g/dl)          | 43   | 13.1            | 11.5           |
| Platelets (n/μl)           | 43   | 248720.9        | 52             |
| Ferritin (ng/ml)           | 64   | 1128.8          | 38             |
| CRP (mg/l)                 | 79   | 111.0           | 11             |
| D-Dimer (ng/ml)            | 70   | 1382.2          | 1721.2         |

Continuous data are reported as number of non-missing variables, mean (standard deviation); categorical data are reported as number of non-missing variables and percentages. Due to the distribution of serum creatinine which, unlike eGFR, is highly skewed on the right, and due to missing values in eGFR, mean serum creatinine and mean eGFR may erroneously appear inconsistent with each other. *None of the patients with cancer were on active chemotherapy treatment.

For continuous data, P values refer to Kruskal-Wallis test for any difference between the three groups, and Mann-Whitney for pairwise two-sample comparisons, for categorical data, to Fisher's exact test. The test for pairwise differences between the groups are indicated by superscripts as follows:

- a, if P<0.05 Ctrl-hospitalized vs GN-hospitalized
- b if P<0.05 Ctrl-hospitalized vs GN-outpatients
- c, if P<0.05 GN-hospitalized vs GN-outpatients

GN, history of glomerular disease; Ctrl, controls (i.e. no history of glomerular disease); AAm, African American; BMI, body mass index; sCr, serum creatinine; eGFR, estimated glomerular filtration rate (by CKD-EPI); SLE, systemic lupus erythematosus; RAASi, renin-angiotensin-aldosterone system inhibitors; GI, gastrointestinal; COVID-19, corona virus disease-2019); CRP, C-reactive protein.
Table 2. Baseline characteristics of GN patients: diagnosis, treatment, and disease duration.

| Admission Status | Outpatients | Hospitalized | P value |
|------------------|-------------|--------------|---------|
| **SLE GN or Vasculitis** (systemic GN) | 26 | 41.9% | 26 | 41.3% | 1.000 |
| Lupus Nephritis | 19 | 30.6% | 11 | 17.5% | 0.097 |
| Vasculitis | 7 | 11.3% | 15 | 23.8% | 0.099 |
| IgA nephropathy | 13 | 21.0% | 5 | 7.9% | 0.044 |
| FSGS or MCD | 11 | 17.7% | 9 | 14.3% | 0.633 |
| Membranous nephropathy | 8 | 12.9% | 5 | 7.9% | 0.396 |
| Amyloidosis/fibrillary glomerulonephritis | 2 | 3.2% | 2 | 3.2% | 1.000 |
| Thrombotic microangiopathy | 1 | 1.6% | 0 | 0.0% | 0.496 |
| Membranoproliferative glomerulonephritis | 0 | 0.0% | 4 | 6.3% | 0.119 |
| Post infectious glomerulonephritis | 0 | 0.0% | 2 | 3.2% | 0.496 |
| Not specified | 1 | 1.6% | 10 | 15.9% | 0.009 |

**Immunosuppression at time of COVID-19**

| Prednisone | 23 | 37.1% | 23 | 36.5% | 1.000 |
| Prednisone dose (mg/day) | 8.6 (7.4) | 15.7 (22.0) | 0.210 |
| MMF | 15 | 24.2% | 11 | 17.5% | 0.385 |
| AZA | 1 | 1.6% | 4 | 6.3% | 0.365 |
| RTX | 1 | 1.6% | 11 | 17.5% | 0.004 |
| CNI | 2 | 3.2% | 15 | 23.8% | 0.001 |

**Therapy reduction/withdrawal during COVID-19***

| Prednisone | 0 | 0.0% | 1 | 4.3% | 1.000 |
| MMF | 3 | 20.0% | 8 | 72.7% | 0.007 |
| AZA | 0 | 0.0% | 3 | 75.0% | 0.244 |
| CNI | 1 | 50.0% | 1 | 6.7% | 0.468 |

**Duration of GN disease**

| 1-6 months | 5 | 8.3% | 13 | 26.5% | 0.004 |
| 6-12 months | 0 | 0.0% | 6 | 12.2% | |
| 12-24 months | 9 | 15.0% | 5 | 10.2% | |
| 2-5 years | 17 | 28.3% | 6 | 12.2% | |
| >5 years | 29 | 48.3% | 19 | 38.8% | |

**Active GN disease at COVID-19 onset**

| 5 | 8.3% | 8 | 17.8% | 0.230 |

Continuous data are reported as number of non-missing variables, mean (standard deviation); categorical data are reported as number of non-missing variables and percentages. *Out of patients on immunosuppression at time of COVID-19. P values refer to Fisher's exact, and to Cochran-Armitage test for trend (with exact P values) for GN disease. GN, history of glomerular disease; FSGS, Focal segmental glomerulosclerosis; MCD, minimal change disease; SLE, systemic lupus erythematosus; MMF, mycophenolate mofetil; AZA, azathioprine; CNI, calcineurin inhibitor; RTX, rituximab. Active GN disease was defined based on reporter assessment of patient’s clinical and laboratory features.
Table 3. Association between presence of glomerular disease and clinical outcomes AKI, KRT, and death.

|                     | AKI       |                      | KRT       |                      | Death     |                      |
|---------------------|-----------|----------------------|-----------|----------------------|-----------|----------------------|
|                     | crude     | eGFR-adj             | fully-adj | crude                | eGFR-adj | fully-adj             | crude     | eGFR-adj | fully-adj |
| Pre-existing GN     | 3.44**    | 1.62                 | 1.28      | 1.43                 | 0.68      | 0.60                  | 1.80      | 0.90     | 0.80      |
|                     | [1.58,7.47] | [0.66,4.00]          | [0.46,3.60] | [0.49,4.22]          | [0.19,2.36] | [0.15,2.38]          | [0.67,4.83] | [0.29,2.79] | [0.23,2.81] |
|                     | 0.002     | 0.292                | 0.638     | 0.512                | 0.538     | 0.464                 | 0.240     | 0.853    | 0.732     |
| Prior eGFR          |           |                      |           |                      |           |                      |           |          |           |
| (per 1 SD unit      | 2.68**    | 3.04**               | 2.31*     | 2.39*                | 2.21**    | 1.76                  |           |          |           |
| decrease)           | [1.64,4.37] | [1.76,5.28]         | [1.21,4.44] | [1.20,4.78]          | [1.22,3.99] | [0.91,3.37]          |           |          |           |
|                     | <0.001    | <0.001               | 0.012     | 0.014                | 0.009     | 0.091                 |           |          |           |
| Age (per 1 SD       |           |                      |           |                      |           |                      |           |          |           |
| unit increase)      |           |                      |           |                      |           |                      |           |          |           |
|                     | 0.84      | 0.90                 | 2.33*     | 0.543                | 0.754     | 0.028                 |           |          |           |
|                     | [0.48,1.47] | [0.46,1.76]          | [1.10,4.94] | [0.25,2.35]          | [0.25,2.35] | [0.028,5.14]          |           |          |           |
| Gender              | 1.81      | 1.04                 | 0.77      | 0.234                | 0.948     | 0.648                 |           |          |           |
|                     | [0.68,4.79] | [0.31,3.50]          | [0.25,2.35] | [0.23,4.82]          | [0.23,4.82] | [0.028,5.14]          |           |          |           |
| Non-White Race      | 3.06*     | 1.50                 | 4.62*     | 0.029                | 0.543     | 0.018                 |           |          |           |
|                     | [1.12,8.34] | [0.41,5.57]          | [1.30,16.44] | [0.13,3.26]          | [0.13,3.26] | [0.018,5.04]          |           |          |           |
| RAASi use           | 1.55      | 1.08                 | 0.87      | 0.500                | 0.933     | 0.880                 |           |          |           |
|                     | [0.44,5.51] | [0.19,6.21]          | [0.15,4.99] | [0.05,2.14]          | [0.05,2.14] | [0.05,2.14]          |           |          |           |

The table reports Odds Ratios from logistic regression models examining the association between history of glomerular disease and the clinical outcomes AKI, KRT and death, comparing GN-Hospitalized vs Ctrl-Hospitalized. For each outcome three regression models are reported namely, “crude” model (no adjustment), “eGFR-adj” (adjusted for pre-COVID-19 eGFR), and “fully-adj” (additionally adjusted for age, gender, non-white ethnicity, and RAASi use). Odds ratios associated with eGFR are expressed per one standard deviation unit (approximately 30 ml/min/1.73m²) decrease. Therefore, an odds ratio for AKI associated with prior eGFR (i.e., pre-COVID-19 eGFR) of 3.04 means that the odds of AKI increases by 3.04 times every 30 ml/min/1.73m² decrease of pre-COVID-19 eGFR; the odds ratio for age is expressed per one standard deviation (approximately 15 years) increase in age.

Numbers in square brackets represent 95 percent confidence interval; the numbers below the square brackets are the associated P value. Stars are included to ease the readability of the table; they represent the level of significance of the P values as follows: "**" P <0.01; "*" P <0.05.

GN, glomerulonephritis; Ctrl, control; AKI, acute kidney injury; KRT, kidney replacement therapy; GN, glomerulonephritis; SD, standard deviation; RAASi, renin–angiotensin–aldosterone system inhibitors.
Table 4. Association between history of glomerular disease with kidney function recovery, and determinants of kidney function recovery in patients with history of glomerular disease.

|                        | GN-Hospitalized vs Ctrl-Hospitalized | GN-Hospitalized and GN – Outpatients pooled |
|------------------------|--------------------------------------|--------------------------------------------|
|                        | crude | eGFR-adj | fully-adj | eGFR | full model |
| Pre-existing GN        | 1.23  | 1.60     | 1.47      | [0.62,2.43] | [0.66,3.86] | [0.57,3.77] | 0.550 | 0.299 | 0.425 |
| Prior eGFR (per 1 SD unit decrease) | 0.57* | 0.55* | 0.55** | 0.59* | [0.36,0.90] | [0.33,0.90] | [0.35,0.86] | [0.36,0.95] | 0.015 | 0.018 | 0.009 | 0.030 |
| Age (per 1 SD unit increase) | 1.10  | 1.02     | [0.66,1.82] | [0.61,1.73] | 0.726 | 0.931 |
| Gender                 | 0.93  | 1.25     | [0.40,2.15] | [0.49,3.18] | 0.861 | 0.642 |
| Non-White Race         | 1.78  | 2.73*    | [0.69,4.60] | [1.03,7.28] | 0.235 | 0.044 |
| RAASi use              | 1.07  | 1.24     | [0.31,3.67] | [0.44,3.46] | 0.920 | 0.687 |

The table reports Odds Ratios from logistic regression models examining the association between history of glomerular disease and recovery of kidney disease (i.e., at least one eGFR values with -10% of pre-COVID-19 eGFR [baseline]), comparing GN-Hospitalized vs Ctrl-Hospitalized. For each outcome three regression models are reported namely, “crude” model (no adjustment), “eGFR-adj” (adjusted for pre-COVID-19 eGFR), and “fully-adj” (additionally adjusted for age, gender, non-white ethnicity, and RAASi use). On the right, the same logistic model is fitted in GN-Hospitalized and GN-Outpatients (pooled) for examining prior eGFR (i.e. pre-COVID). The model is fitted before (“eGFR” model), and after (“full model”) adjusting for the other covariates. Odds ratios associated with eGFR are expressed per one standard deviation unit (approximately 30 ml/min/1.73m²) decrease. Therefore, an odds ratio associated with prior eGFR of 0.55 means that the odds of recovery decreases by 0.55 times every 30 ml/min/1.73m² decrease of pre-COVID-19 eGFR; the odds ratio for age is expressed per one standard deviation (approximately 15 years) increase in age.

Numbers in square brackets represent 95 percent confidence interval, the numbers below the squares are the associated P value. Stars are included to ease the readability of the table; they represent the level of significance of P values as follows: “***” P <0.01; “**” P <0.05.

GN, glomerulonephritis; Ctrl, control; SD, standard deviation; RAASi, renin–angiotensin–aldosterone system inhibitors.
FIGURE LEGENDS

Figure 1. Probability of developing AKI as a function of eGFR before COVID-19. The probability is based on a regression model which is adjusted for age, gender, non-white ethnicity, and use of renin-angiotensin-aldosterone system inhibitors (RAASi). The model is estimated only in hospitalized patients with glomerular disease. The shadowed area represents 95 percent confidence interval. The adjusted odds ratio of AKI per one standard deviation unit decrease in eGFR (approximately 15 ml/min/1.73m$^2$) was 2.88 (95%CI: 1.38 to 6.02; P=0.005).

Figure 2. Visual representation of the results of the four-way interaction term from the longitudinal mixed model on eGFR between GN- vs Ctrl hospitalized, time, AKI, and pre-COVID-19 eGFR (P=0.024). The figure represents the predicted relationship between pre-COVID-19 and post-COVID-19 eGFR after stratification of hospitalized patients according to the absence (left panel) and presence (right panel) of history of glomerular disease (named Ctrl-hospitalized and GN-hospitalized, respectively throughout the text). Patients are additionally stratified based on those who not developed (blue) or developed (red) AKI during hospital stay. The dotted grey line represents the line of identity between pre-COVID-19 and post-COVID-19 eGFR (i.e. full recovery of kidney function). While Ctrl-hospitalized patients had a full recovery of eGFR at 6 months after COVID-19, the recovery was only partial in GN-hospitalized patients, who developed AKI during hospital stay. For all the groups, except GN-hospitalized who had AKI, the coefficient between pre-COVID-19 and 6-month post-COVID-19 was close to one and the line close to the line of identity: Ctrl-hospitalized-no-AKI, 0.90 (95% CI: 0.75 to 1.04); GN-hospitalized-no-AKI: 0.87 (95% CI: 0.70 to 1.04); Ctrl-hospitalized-with-AKI: 0.98 (95% CI: 0.82 to 1.14); GN-hospitalized-with-AKI: 0.41 (95% CI: 0.25 to 0.56) (see Supplemental Table 4). The visual representation of the four-way interaction term as eGFR change over time is reported in Supplemental Figure 3.
Figure 2

Pre-Existing Glomerular Disease

6-month post-COVID-19 eGFR (mL/min/1.73m²)

Pre-COVID-19 eGFR (mL/min/1.73m²)

- AKI = No
- AKI = Yes

Hospitalized patients, adjusted analysis
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SUPPLEMENTAL METHODS

Definitions and endpoints

Primary endpoints were incidence of AKI, initiation of kidney replacement therapy (KRT), and death. Acute kidney injury (AKI) is defined by Kidney Disease Improving Global Outcomes (KDIGO) criteria as follows: stage 1, increase in baseline serum creatinine by ≥0.3 mg/dl within 48 h or a 1.5 to 1.9 times increase in serum creatinine from baseline within 7 days; stage 2, 2 to 2.9 times increase in baseline serum creatinine within 7 days; stage 3, ≥3 times increase in serum creatinine within 7 days or increase to ≥4 mg/dl or the initiation of KRT. The eGFR was calculated using the Chronic Kidney Disease Epidemiology Collaboration creatinine equation.\(^1\)

To study longitudinal eGFR trajectory and changes in other renal parameters, we included patients who survived, with available “pre-COVID-19” renal parameters and at least one measure of serum creatinine after discharge from the hospital (if hospitalized) or after acute infection if managed as outpatients. We included patients who required initiation of KRT during hospitalization for COVID-19 and continued to require KRT after discharge.

Supplementary statistical analyses

To examine the association of clinical outcomes with pre-COVID-19 serum albumin, urinary protein (continuous variable), duration of glomerular disease (ordered categorical variable), immunosuppressive drugs (indicator variable for each drug), and type of glomerular disease (indicator variable), we fitted the same logistic regression models described in Methods in patients with glomerular disease (hospitalized or not).

Recovery of kidney function was arbitrarily defined by an indicator variable which took the value of 1 for every patient if at least one post-COVID-19 eGFR was within -10% of pre-COVID-19 eGFR (baseline), and a value of 0 otherwise. We additionally performed sensitivity
analyses by changing the cut-point to 15 and 5 (data not shown). We used logistic regression models to examine the association between glomerular disease status and recovery of pre-COVID-19 by calculating, in hospitalized patients (i.e., glomerular disease vs controls), crude ORs, pre-COVID-19 eGFR-adjusted ORs, and ORs additionally adjusted for age, gender, non-white ethnicity and RAASi use. Similarly, we used logistic regression models fitted in patients with glomerular disease (hospitalized or not) to examine the association between recovery of pre-COVID-19 and serum albumin, urinary protein, duration of glomerular disease, immunosuppressive drugs, and type of glomerular disease (before and after adjusting for pre-COVID-19 eGFR, age, gender, non-white ethnicity and RAASi use). The regression models of recovery of kidney function were based on a four-way interaction term between time (months from COVID-19 diagnosis), AKI, glomerular disease and pre-COVID-19 eGFR, and were additionally adjusted for age, gender, non-white ethnicity and RAASi use. The analyses on the effect of glomerular disease on eGFR were based on hospitalized patients (glomerular disease vs controls), whereas the analysis on the effect on albumin urinary protein, immunosuppressive drugs and type of glomerular disease was based on glomerular disease patients (hospitalized or not). We estimated the multiple regression-adjusted correlation between pre-COVID-19 and post-COVID-19 eGFR based on the predictions of the previously fitted model. We chose to estimate the correlation at 6 months because this was the approximate median study population follow-up time after COVID-19. We constructed plots of pre-COVID-19 eGFR vs 6-month eGFR, based on model predictions and estimated the corresponding regression coefficients. A regression coefficient of 1, with an intercept statistically not different from zero, implied full eGFR recovery of pre-COVID-19 eGFR (i.e., post-COVID-19 eGFR was proportional to pre-COVID-19 eGFR); a coefficient of less than 1 implied lack of eGFR recovery (i.e., the higher the loss of eGFR with respect to pre-COVID-19 eGFR, the closer the coefficient to 0).

Supplemental Reference

S1. Levey AS, Deo A, Jaber BL: Filtration markers in acute kidney injury. Am J Kidney Dis, 56: 619-622, 2010 10.1053/j.ajkd.2010.08.001
Supplemental Figures

Supplemental Figure 1. Analysis on the goodness of fit of the linear random-coefficient mixed model on eGFR.
A) Plots of residuals and of observed vs predicted eGFR, B) Plots of individual observed vs predicted eGFR trajectories.
**Supplemental Figure 2.** Data used for longitudinal analyses.

Number of hospitalized patients analyzed: 139; total eGFR measurements: 436 (average 3.1 (1-7) per pt)

Ctrl, controls; GN, patients with history of glomerulonephritis; KRT, kidney replacement therapy.
**Supplemental Figure 3.** Visual representation of the results of the four-way interaction term from the longitudinal mixed model on eGFR between GN vs Ctrl-hospitalized, time, AKI, and pre-COVID-19 eGFR (P=0.024). The figure represents the predicted linear eGFR over time after stratification of hospitalized patients according to the absence (left panel) or presence (right panel) of history of glomerular disease. Patients are additionally stratified based on those who not developed (blue) or developed (red) AKI during hospital stay. Panel A predicts the linear change for patients with pre-COVID-19 eGFR in Stage 4; panel B in Stage 3; panel C in Stage 2. GN patients developing AKI having best pre-COVID-19 eGFR (stage 2) had the largest absolute eGFR decline.
# Supplemental Table 1. Complications during hospital stay

|                                             | Pre-existing Glomerular Disease | P value |
|---------------------------------------------|--------------------------------|---------|
|                                             | No                             | Yes     |         |
| Length of hospital stay, days               | 79 (14.4)                      | 61 (16.3) | 0.033 |
| Death                                       | 8 (9.6%)                       | 12 (19.0%) | 0.144 |
| Intubated                                   | 7 (9.6%)                       | 7 (11.1%) | 0.789 |
| Use of inotropes/vasopressors               | 7 (8.4%)                       | 5 (7.9%)  | 1.000 |
| Developed AKI                               | 16 (19.3%)                     | 29 (46%)  | 0.001 |
| AKI stages                                  | 16                             | 28       |       |
| Stage 1                                     | 4 (25.0%)                      | 8 (28.6%) | 0.616 |
| Stage 2                                     | 3 (18.8%)                      | 9 (32.1%) |       |
| Stage 3                                     | 9 (56.3%)                      | 11 (39.3%)|       |
| KRT Requirement                             | 8 (9.6%)                       | 8 (12.7%) | 0.600 |
| Days of KRT                                 | 7 (34.4)                       | 7 (26.1) | 0.874 |
| Discharge on KRT                            | 2 (25.0%)                      | 3 (37.5%) | 1.000 |
| Admission serum creatinine, mg/dl           | 80 (1.5)                       | 56 (2.7) | 0.000 |
| Peak serum creatinine, mg/dl                | 49 (2.7)                       | 49 (3.6) | 0.006 |
| Admission serum albumin, g/dl               | 64 (3.5)                       | 47 (3.0) | 0.011 |
| Nadir serum albumin, g/dl                   | 9 (3.4)                        | 19 (2.7) | 0.038 |
| Peak proteinuria, g/day                     | 5 (0.1)                        | 14 (5.1) | 0.003 |
| Superimposed bacterial infection            | 9 (11.1%)                      | 12 (20.7%) | 0.151 |
| GI complications                            | 10 (12.3%)                     | 7 (12.3%) | 1.000 |
| Cardiac complications                       | 7 (8.8%)                       | 4 (7.1%)  | 1.000 |
| Arrhythmia                                  | 6 (7.2%)                       | 2 (3.2%)  | 0.466 |
| MI                                          | 0 (0.0%)                       | 2 (3.2%)  | 0.185 |
| Thrombotic complications                    | 3 (3.6%)                       | 2 (3.2%)  | 1.000 |
| DVT                                         | 0 (0.0%)                       | 1 (1.6%)  | 0.432 |
| CNS complications                           | 2 (2.5%)                       | 1 (1.8%)  | 1.000 |

Five GN patients suddenly deceased before intubation. Continuous data are reported as number of non-missing variates, mean (standard deviation); categorical data are reported as number of non-missing variates and percentages. For continuous data P values refer to Mann-Whitney test for two-sample comparisons, for categorical data, to Fisher’s exact test. GN, history of glomerular disease; AKI, acute kidney injury, KRT, kidney replacement therapy, MI, myocardial infarction; GI, gastrointestinal; CNS, central nervous system; PE, pulmonary emobolism; DVT, deep venous thrombosis.
Supplemental Table 2. Treatments for COVID-19

| Treatment                              | Ctrl-Hospitalized (n=83) | GN-Hospitalized (n=63) | GN-outpatients (n=62) | P value   |
|----------------------------------------|--------------------------|------------------------|-----------------------|-----------|
| Hydroxychloroquine                     | 55 (66.3)                | 26 (41.3)              | 5 (8.1)               | <0.001<sup>a,b,c</sup> |
| Azithromycin                           | 38 (45.8)                | 18 (28.6)              | 5 (8.1)               | <0.001<sup>a,b,c</sup> |
| Remdesivir                             | 1 (1.2)                  | 3 (4.8)                | 0 (0.0)               | 0.188     |
| Lopinavir                              | 12 (14.5)                | 6 (9.5)                | 0 (0.0)               | 0.003<sup>b,c</sup> |
| Darunavir                              | 3 (3.6)                  | 1 (1.6)                | 0 (0.0)               | 0.389     |
| Ritonavir                              | 12 (14.5)                | 4 (6.4)                | 0 (0.0)               | 0.002<sup>c</sup> |
| Other antivirals                       | 1 (1.2)                  | 3 (4.8)                | 0 (0.0)               | 0.188     |
| Cobicistat                             | 0 (0.0)                  | 1 (1.6)                | 0 (0.0)               | 0.6       |
| Anti-IL6 receptor monoclonal antibodies| 14 (16.9)                | 9 (14.3)               | 0 (0.0)               | 0.001<sup>b,c</sup> |
| Anakinra                               | 1 (1.2)                  | 0 (0.0)                | 0 (0.0)               | 1.00      |
| Convalescent serum                     | 1 (1.2)                  | 3 (4.8)                | 0 (0.0)               | 0.188     |
| IVIg                                   | 0 (0.0)                  | 1 (1.6)                | 0 (0.0)               | 0.6       |
| IV methylprednisolone                  | 22 (26.5)                | 8 (12.7)               | 0 (0.0)               | <0.001<sup>b,c</sup> |
| Oral steroids                          | 9 (10.8)                 | 8 (12.7)               | 1 (1.6)               | 0.039<sup>b,c</sup> |
| Vitamin C                              | 1 (1.2)                  | 0 (0.0)                | 0 (0.0)               | 1.00      |
| Complement inhibitors                  | 1 (1.2)                  | 0 (0.0)                | 0 (0.0)               | 1.00      |

Data are expressed as numbers (percentages). P values were obtained with Fisher’s exact test. Test for pairwise differences between the groups are indicated by superscripts as follows:

a, if P<0.05 Ctrl-hospitalized vs GN-hospitalized
b, if P<0.05 Ctrl-hospitalized vs GN-outpatients
c, if P<0.05 GN-hospitalized vs GN-outpatients

Ctrl, controls (i.e. no history of glomerular disease); GN, history of glomerular disease; IVIg, intravenous immunoglobulins.
Supplemental Table 3. Association of various determinants with clinical outcomes AKI, KRT, and Death in the overall cohort of GN patients (hospitalized + outpatients).

|                        | AKI crude | eGFR-adj | fully-adj | Death crude | eGFR-adj | fully-adj |
|------------------------|-----------|----------|-----------|-------------|----------|-----------|
| Serum albumin, g/dl (per 1 SD unit decrease) | 1.95* [1.02,3.74] | 1.14 [0.68,2.91] | 1.62 [0.73,3.62] | 2.17 [0.93,5.07] | 1.48 [0.59,3.71] | 1.75 [0.61,5.01] | 1.63 [0.85,3.12] | 1.26 [0.62,2.58] | 1.62 [0.68,3.85] |
| Urinary protein, g/day (per 1 SD unit increase) | 1.16 [0.71,1.89] | 1.08 [0.62,1.89] | 1.12 [0.58,2.16] | 1.26 [0.75,2.13] | 1.27 [0.69,2.36] | 1.48 [0.73,3.00] | 1.02 [0.58,1.79] | 0.83 [0.35,2.02] | 1.15 [0.44,3.02] |
| Azathioprine           | 0.40 [0.03,4.71] | 0.38 [0.03,4.91] | 0.26 [0.02,3.39] | 1.00 [0.02,3.39] | 1.00 [0.02,3.39] | 1.00 [0.02,3.39] | 1.00 [0.02,3.39] | 1.00 [0.02,3.39] | 1.00 [0.02,3.39] |
| Mycophenolate         | 1.02 [0.27,3.78] | 2.09 [0.47,9.39] | 2.93 [0.49,17.62] | 1.71 [0.19,15.51] | 3.12 [0.31,31.22] | 5.45 [0.36,82.17] | 1.50 [0.15,2.83] | 0.65 [0.05,2.41] | 0.97 [0.05,2.41] |
| Rituximab             | 2.24 [0.52,9.68] | 3.00 [0.62,14.41] | 3.90 [0.71,21.30] | 1.50 [0.16,13.75] | 1.58 [0.16,15.06] | 1.98 [0.18,21.46] | 0.26 [0.06,1.13] | 0.23 [0.05,1.14] | 0.22 [0.04,1.25] |
| Steroids              | 1.53 [0.53,4.38] | 0.87 [0.26,2.87] | 0.66 [0.18,2.43] | 0.48 [0.09,2.59] | 0.48 [0.05,1.68] | 0.28 [0.04,1.43] | 0.22 [0.03,4.13] | 1.16 [0.20,2.99] | 0.78 [0.02,3.58] |
| CNI                    | 0.84 [0.05,14.08] | 0.90 [0.02,36.75] | 0.72 [0.01,46.66] | 0.14 [0.01,2.50] | 0.14 [0.00,4.72] | 0.12 [0.00,6.55] | 1.00 [0.00,6.55] | 1.00 [0.00,6.55] | 1.00 [0.00,6.55] |
| Duration of GN (trend across categories) | 0.74 [0.52,1.05] | 0.67 [0.45,1.00] | 0.68 [0.45,1.03] | 0.64 [0.36,1.13] | 0.64 [0.34,1.09] | 0.61 [0.29,1.07] | 0.55 [0.55,1.20] | 0.81 [0.50,1.16] | 0.76 [0.46,1.16] |

* p < 0.05
The table reports odds ratios from logistic regression models examining the association between history of glomerular disease and the clinical outcomes AKI, KRT, and Death in patients with glomerular disease. For each outcome three regression models are reported namely, “crude” model (no adjustment), “eGFR-adj” (adjusted for pre-COVID-19 eGFR), and “fully-adj” (additionally adjusted for age, gender, non-white ethnicity, and RAASi use). Odds ratios associated with serum albumin are expressed per one standard deviation unit decrease (approximately 0.7g/dl), those associated with urinary protein are expressed per one standard deviation increase (approximately 3g/day). The odds ratio for duration of GN express a trend across the categories 1-6 months, 6-12 months, 12-24 month, 2-5 years, and >5 years: how the odds of the outcome increase for every step increase in the ordered category of GN duration.

Numbers in square brackets represent 95 percent confidence interval; the numbers below the squares are the associated P value. Stars are included to ease the readability of the table: "*" P <0.05. An odds ratio of 1.00 without associated 95 percent confidence intervals indicate that the regression model could not be estimated.

CNI, calcineurin inhibitors; GN, glomerulonephritis; SLE, systemic lupus erythematosus; AKI, acute kidney injury; FSGS, focal segmental glomerulosclerosis; MCD, minimal change disease.

| Glomerular Disease | Odds Ratio (95% CI) | Odds Ratio (95% CI) | Odds Ratio (95% CI) | Odds Ratio (95% CI) | Odds Ratio (95% CI) |
|-------------------|---------------------|---------------------|---------------------|---------------------|---------------------|
| SLE GN            | 1.54 (0.41,5.76)    | 0.98 (0.22,4.33)    | 0.62 (0.07,5.44)    | 6.29* (1.27,31.10)  | 4.74 (0.88,25.42)   |
|                   | 0.519               | 0.982               | 0.664               | 0.024               | 0.069               |
|                   |                     |                     |                     | 0.040               | 0.770               |
|                   |                     |                     |                     | 0.78                | 0.50                |
|                   |                     |                     |                     | 2.22               |                     |
| Vasculitis        | 1.25 (0.38,4.16)    | 0.98 (0.27,3.60)    | 1.09 (0.27,4.36)    | 1.00 (0.50,7.79)    | 1.00 (0.43,7.48)    |
|                   | 0.716               | 0.980               | 0.908               |                     |                     |
|                   |                     |                     |                     | 1.98                | 1.79                |
|                   |                     |                     |                     | 1.20                |                     |
| SLE GN or Vasculitis | 1.55 (0.55,4.38)   | 0.98 (0.30,3.15)    | 0.90 (0.24,3.37)    | 1.43 (0.32,6.36)    | 0.96 (0.20,4.67)    |
|                   | 0.411               | 0.968               | 0.877               | 0.640               | 0.963               |
|                   |                     |                     |                     | 0.684               | 0.555               |
|                   |                     |                     |                     | 0.949               | 0.599               |
|                   |                     |                     |                     | 1.51                |                     |
| IgA nephropathy   | 0.77 (0.12,5.00)    | 1.12 (0.14,8.94)    | 0.43 (0.05,4.09)    | 1.00 (0.24,7.03)    | 1.00 (0.41,18.66)   |
|                   | 0.787               | 0.914               | 0.466               |                     |                     |
|                   |                     |                     |                     | 6.15                |                     |
| FSGS or MCD       | 0.35 (0.06,1.88)    | 0.52 (0.09,3.17)    | 0.35 (0.04,3.04)    | 1.00 (0.24,7.03)    | 1.00 (0.41,18.66)   |
|                   | 0.220               | 0.478               | 0.342               |                     |                     |
| Membranous nephropathy | 5.39 (0.56,51.50) | 6.33 (0.44,90.22)  | 7.71 (0.58,103.15)  | 1.68 (0.16,17.26)   | 1.19 (0.10,13.98)   |
|                   | 0.143               | 0.173               | 0.123               | 0.663               | 0.891               |
|                   |                     |                     |                     | 0.724               | 0.312               |
|                   |                     |                     |                     | 0.312               | 0.420               |
|                   |                     |                     |                     | 1.24                |                     |
|                      | No AKI |                              | AKI   |
|----------------------|--------|------------------------------|-------|
|                      | Ctrl   | GN                           | Ctrl  |
| Coeff. pre- vs 6 months post-COVID-19 eGFR | 0.90   | 0.87                         | 0.98  |
| 95% CI               | [0.75, 1.04] | [0.70, 1.04]                | [0.82, 1.14] |
| p-value              | <0.001 | <0.001                       | <0.001 |

Coefficient of the predicted relationship between pre-COVID-19 and post-COVID-19 eGFR after stratification of hospitalized patients according to the absence (Ctrl) and presence (GN) of history of glomerular disease (throughout the text, named Ctrl-hospitalized and GN-hospitalized, respectively). Patients are additionally stratified based on those who did not develop (NO AKI) or developed (AKI) AKI during hospital stay. For all the groups, except GN-hospitalized who had AKI, the coefficient between pre-COVID-19 and 6-month post-COVID-19 was close to one and the line close to the line of identity (see Figure 2). The difference of the coefficient in the AKI GN patients is demonstrated by the four-way interaction term between GN vs Ctrl, time, AKI, and pre-COVID-19 eGFR, which was statistically significant (P= 0.024). After pairwise comparison, and Bonferroni adjustment for multiple testing, the coefficient of AKI GN was statistically significantly different from the other groups (not shown).
**Supplemental Table 5. Serial kidney parameters in patients with glomerular disease based on admission status.**

| Survey Time Points | Pre-COVID-19 | At admission | During COVID-19 | After COVID-19 | Most Recent |
|--------------------|--------------|--------------|------------------|----------------|-------------|
| **Admission status** |              |              |                  |                |             |
| Outpatients        |              |              |                  |                |             |
| Months since COVID-19 diagnosis |              |              |                  |                |             |
| n                  | 58           | 58           | 58               | 58             | 58          |
| eGFR, ml/min/1.73m² | 72.6 (31.2)  | (35.8)       | 65.6 (36.8)      | 77.1 (29.9)    | 68.1 (33.9) |
|                    | 58           | 0.0          | 0.3              | 2.2            | 7.1         |
|                    | [-13.1, -0.1]|[0.0, 0.0]    | [0.0, 1.2]       | [0.5, 6.5]     | [0.8, 12.4] |
| Serum creatinine, mg/dl | 1.5 (1.6)    | 1.5 (1.3)    | 1.8 (1.9)        | 1.2 (0.8)      | 1.7 (1.7)   |
|                    | 58           | 0.360        | 0.307            | 0.629          | 0.146       |
| Serum albumin, g/dl | 4.1 (0.7)    | 4.0 (0.6)    | 3.9 (0.4)        | 4.1 (0.6)      | 4.1 (0.6)   |
|                    | 58           | 0.773        | 0.060            | 0.918          | 0.019       |
| Urinary protein, g/day | 1.4 (2.3)    | 0.3 (0.4)    | -                | 0.9 (1.6)      | 0           |
|                    | 54           | 0.374        | -                | -              | -           |
| **Hospitalized**   |              |              |                  |                |             |
| Months since COVID-19 diagnosis |              |              |                  |                |             |
| n                  | 55           | 52           | 52               | 41             | 41          |
| eGFR, ml/min/1.73m² | 53.3 (28.7)  | 44.9 (31.5)  | 36.1 (31.7)      | 54.7 (33.0)    | 47.7 (30.1) |
|                    | 55           | <0.001       | <0.001           | 0.856          | 0.002       |
| Serum creatinine, mg/dl | 1.8 (1.8)    | 2.8 (2.9)    | 3.7 (3.4)        | 1.9 (1.6)      | 2.4 (2.2)   |
|                    | 55           | <0.001       | <0.001           | 0.368          | 0.002       |
| Serum albumin, g/dl | 3.7(0.6)     | 3.0 (0.9)    | 2.9 (0.9)        | 3.1 (0.9)      | 3.8 (0.7)   |
|                    | 48           | <0.001       | <0.001           | <0.001         | 0.531       |
| Urinary protein, g/day | 2.2 (2.8)    | 5.1 (6.3)    | -                | 3.1 (3.8)      | 0           |
|                    | 45           | 0.140        | -                | -              | -           |

Crude data on time points (before, during, and after COVID-19) of patients with glomerular disease. Only patients with pre-COVID-19 values and at least a subsequent serial value are included. Time points are reported as median [minimum, maximum]. The other variables are reported as number of non-missing data, mean (standard deviation). Due to the distribution of serum creatinine which, unlike eGFR, is highly skewed on the right, and due to missing values in eGFR, mean serum creatinine and mean eGFR may erroneously appear inconsistent with each other. The number below the mean represents P value of the difference vs pre-COVID-19 eGFR by Wilcoxon matched-pairs signed-rank test.
### Supplemental Table 6. Analysis on determinants of kidney function recovery (categorical variable) in GN patients.

|                                | Crude          | Adjusted         |
|--------------------------------|----------------|-----------------|
| Serum albumin, g/dl (per 1 SD unit decrease) | 0.79 [0.53,1.17] | 0.94 [0.57,1.56] |
|                                | 0.244          | 0.820           |
| Urinary protein, g/day (per 1 SD unit increase) | 0.88 [0.60,1.30] | 1.04 [0.64,1.70] |
|                                | 0.532          | 0.870           |
| Azathioprine                   | 4.13 [0.66,25.83] | 2.10 [0.25,17.44] |
|                                | 0.130          | 0.492           |
| Mycophenolate                  | 0.72 [0.26,1.99] | 0.84 [0.25,2.87] |
|                                | 0.531          | 0.784           |
| Rituximab                      | 2.90 [0.87,9.69] | 2.53 [0.64,10.02] |
|                                | 0.084          | 0.187           |
| Steroids                       | 0.70 [0.32,1.56] | 0.69 [0.28,1.73] |
|                                | 0.382          | 0.427           |
| CNI                            | 1.49 [0.50,4.38] | 0.3.27 [0.77,13.81] |
|                                | 0.473          | 0.108           |
| Duration of GN (trend across categories) | 1.20 [0.91,1.59] | 1.37 [0.98,1.91] |
|                                | 0.186          | 0.063           |
| Diagnosis                  | Crude Odds Ratio | Adjusted Odds Ratio |
|---------------------------|------------------|---------------------|
| SLE GN                    | 1.76 (0.65, 4.76) | 0.67 (0.17, 2.62)   |
| Vasculitis                | 0.49 (0.19, 1.27) | 0.70 (0.22, 2.22)   |
| SLE GN or Vasculitis      | 0.93 (0.42, 2.05) | 0.62 (0.23, 1.69)   |
| IgA nephropathy           | 2.13 (0.58, 7.88) | 4.73 (0.76, 29.59)  |
| FSGS or MCD               | 0.68 (0.24, 1.86) | 0.44 (0.13, 1.53)   |
| Membranous nephropathy    | 2.30 (0.48, 10.94)| 2.08 (0.38, 11.44)  |

The table reports odds ratios from logistic regression models examining the association of various determinants with recovery of kidney disease (i.e. at least one eGFR values with -10% of pre-COVID-19 eGFR) in GN-hospitalized and GN-outpatients pooled. For each determinant, it is reported the “crude” model (no adjustment), and the “adjusted” model (adjusted for age, gender, non-white ethnicity, and RAASi use and pre-COVID-19 eGFR). Odds ratios associated with serum albumin are expressed per one standard deviation unit (approximately 0.7g/dl) decrease; odds ratio associated with urinary protein are reported per one standard deviation unit (approximately 3g/day) increase. Numbers in square brackets represent 95 percent confidence interval; the number below the square brackets is the P value.

CNI, calcineurin inhibitors; GN, glomerulonephritis; SD, standard deviation; SLE, systemic lupus erythematosus; FSGS, focal segmental glomerulosclerosis; MCD, minimal change disease.
### Supplemental Table 7. Analysis on the determinants of post-COVID-19 eGFR (continuous variables).

|                                      | Base Model       | Fully Adjusted  |
|--------------------------------------|------------------|-----------------|
| Serum albumin, g/dl (per 1 SD unit decrease) | 1.1 [−1.5, 3.7]  | 0.1 [−2.5, 2.6] |
|                                      | 0.399            | 0.964           |
| Urinary protein, g/day (per 1 SD unit increase) | −1.5 [−3.4, 0.4] | −2.1* [−4.0, −0.2] |
|                                      | 0.114            | 0.029           |
| Azathioprine                         | −9.8 [−19.7, 0.1] | −8.5 [−18.2, 1.2] |
|                                      | 0.052            | 0.085           |
| Mycophenolate                        | −3.2 [−9.2, 2.8]  | −1.5 [−7.9, 5.0] |
|                                      | 0.285            | 0.654           |
| Rituximab                            | −0.4 [−6.4, 5.7]  | −2.5 [−8.4, 3.3] |
|                                      | 0.897            | 0.383           |
| Steroids                             | 4.1 [−0.6, 8.8]   | 3.2 [−1.6, 7.9]  |
|                                      | 0.083            | 0.187           |
| Duration of GN (trend across categories) | 0.0 [−1.8, 1.8]  | 0.4 [−1.4, 2.1]  |
|                                      | 0.965            | 0.670           |
| SLE GN                               | 0.5 [−5.5, 6.6]   | −0.2 [−7.8, 7.3] |
|                                      | 0.861            | 0.948           |
| Diagnosis                        | Crude Coefficient | Adjusted Coefficient | 95% CI                  | p Value  |
|---------------------------------|-------------------|----------------------|-------------------------|----------|
| Vasculitis                      | 3.3               |                      | [2.1; 8.7]              | 0.229    |
|                                 |                   |                      | [-0.7; 9.7]             | 0.091    |
| SLE GN or Vasculitis            | 2.8               |                      | [-1.9; 7.5]             | 0.239    |
|                                 |                   |                      | [-1.2; 8.2]             | 0.138    |
| IgA nephropathy                 | -0.5              |                      | [-8.4; 7.4]             | 0.905    |
|                                 |                   |                      | [-6.2; 10.3]            | 0.619    |
| FSGS or MCD                     | -3.5              |                      | [-10.3; 3.4]            | 0.316    |
|                                 |                   |                      | [-14.6; -0.9]           | 0.027    |
| Membranous nephropathy          | -4.5              |                      | [-12.6; 3.6]            | 0.270    |
|                                 |                   |                      | [-10.7; 5.0]            | 0.472    |

The table reports the coefficient of difference in average post-COVID-19 eGFR associated with each determinant in GN-hospitalized and GN-outpatients, pooled. For each determinant, it is reported the “crude” model (no adjustment), and the “adjusted” model (adjusted for age, gender, non-white ethnicity, and RAASi use and pre-COVID-19 eGFR). Coefficients associated with serum albumin are expressed per one standard deviation unit (approximately 0.7g/dl) decrease; coefficients associated with urinary protein are reported per one standard deviation unit (approximately 3g/day) increase. For instance, a coefficient of -2.1 associated with urinary protein means that per every 3g/day pre-COVID-19 urinary protein, average post-COVID-19 eGFR was 2.1ml/min/1.73m² lower. A coefficient of -7.6 means that patients with FSGS or MCD had on average -7.6ml/min/1.73m² lower eGFR compared to the other patients (pooled). Numbers in square brackets represent 95 percent confidence interval; the numbers below the square brackets are the associated P values. Stars are included to ease the readability of the table: **”** P <0.05.

GN, glomerulonephritis; SD, standard deviation; SLE, systemic lupus erythematosus; FSGS, focal segmental glomerulosclerosis; MCD, minimal change disease.