Clinical, Functional, and Mental Health Outcomes in Kidney Transplant Recipients 3 Months After a Diagnosis of COVID-19

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Background. Kidney transplant patients are at high risk for coronavirus disease 2019 (COVID-19)–related mortality. However, limited data are available on longer-term clinical, functional, and mental health outcomes in patients who survive COVID-19. **Methods.** We analyzed data from adult kidney transplant patients in the European Renal Association COVID-19 Database who presented with COVID-19 between February 1, 2020, and January 31, 2021. **Results.** We included 912 patients with a mean age of 56.7 (±13.7) y. 26.4% were not hospitalized, 57.5% were hospitalized without need for intensive care unit (ICU) admission, and 16.1% were hospitalized and admitted to the ICU. At 3 mo follow-up survival was 82.3% overall, and 98.8%, 84.2%, and 49.0%, respectively, in each group. At 3 mo follow-up biopsy-proven acute rejection, need for renal replacement therapy, and graft failure occurred in the overall group in 0.8%, 2.6%, and 1.8% respectively, and in 2.1%, 10.6%, and 10.6% of ICU-admitted patients, respectively. Of the surviving patients, 83.3% and 94.4% reached their pre–COVID-19 physician-reported functional and mental health status, respectively, within 3 mo. Of patients who had not yet reached their prior functional and mental health status, their treating physicians expected that 79.6% and 80.0%, respectively, still would do so within the coming year. ICU admission was independently associated with a low likelihood to reach prior functional and mental health status. **Conclusions.** In kidney transplant recipients alive at 3-mo follow-up, clinical, physician-reported functional, and mental health recovery was good for both nonhospitalized and hospitalized patients. Recovery was, however, less favorable for patients who had been admitted to the ICU.

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INTRODUCTION

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has a major impact on global health.[1] Especially elderly and people with underlying conditions, such as diabetes, heart, lung, and kidney disease are at increased risk of developing life-threatening coronavirus disease 2019 (COVID-19).[2] In addition to mortality, there is concern about long-term consequences for those who survive COVID-19. Prolonged fatigue, muscle weakness, dyspnea, sleeping problems, anxiety, and depression have been reported by patients following their infection.[3,4]

Epidemiological studies indicated kidney transplant recipients to be particularly vulnerable for the development of severe COVID-19.[2] The OpenSAFELY study, which enrolled >17 million COVID-19 patients from the United Kingdom, reported a 6 times higher risk of mortality in organ transplant recipients when adjusted for age and gender and a 3.5 times higher risk when also accounting for comorbidities. In fact, organ transplantation was identified as one of the strongest risk factors for COVID-19–related death in this study.[2] In line with the OpenSAFELY results, many other observational studies from different geographical areas reported high mortality rates in kidney transplant patients with COVID-19.[2,5-10] We previously showed that mortality in these patients is higher than in patients on dialysis, when adjusted for differences in age and comorbidities between both groups.[5]

Although there are substantial data on COVID-19–related mortality in the kidney transplant population, only limited data are available on the clinical, functional, and mental health outcomes in patients who survive. We therefore studied these outcomes in a large cohort of kidney transplant recipients at 3 mo after their COVID-19 diagnosis.

MATERIALS AND METHODS

Study Design and Participants

For this study, we used data from the European Renal Association COVID-19 Database (ERACODA).[11] This database was established in March 2020 and currently involves the cooperation of approximately 220 physicians representing >130 centers in 33 countries, mostly in Europe. Data were collected on adult (>18 y) patients with kidney failure, either on dialysis or living with a functioning kidney allograft, who were diagnosed with COVID-19 based on a positive result on a real-time polymerase chain reaction assay or rapid antigen test of nasal or pharyngeal swab specimens, or compatible findings on computed tomography (CT) scan or chest x-ray of the lungs. Data are voluntarily reported from outpatients and hospitalized patients by physicians responsible for the care of these patients.

The ERACODA database is hosted at the University Medical Center Groningen, the Netherlands. Data are recorded using REDCap software (Research Electronic Data Capture, Vanderbilt University Medical Center, Nashville, TN) for data collection.[12] Each patient is assigned an identifier code. To protect privacy, no other data that are related to the identity of the patient are included in the database. The study was approved by the Institutional Review Board of the University Medical Center Groningen (the Netherlands). The clinical and research activities being reported are consistent with the Principles of the Declaration of Istanbul as outlined in the "Declaration of Istanbul on Organ Trafficking and Transplant Tourism."

Data Collection

Detailed information was collected on patient and COVID-19–related characteristics. Frailty was assessed using the Clinical Frailty Score developed by Rockwood et al.[13] Low scores (scores 1–3) indicate that patients are fit and managing well, middle scores (scores 4–6) indicate patients are vulnerable to moderately frail, and higher scores indicate patients are severely to very severely frail (scores 7 and 8) or terminally ill (score 9). Comorbidities were recorded from patient charts, and obesity was defined as a body mass index >30 kg/m^2. Graft function–related outcomes and functional and mental health outcome data were collected at 3 mo after first presentation with COVID-19. Physicians were asked to report the patient's functional and mental health status at 3 mo after presentation, using a standardized questionnaire (Appendix 1, **SDC**, http://links.lww.com/TP/C416). The data therefore represent physician-reported outcomes. Kidney transplant recipients who presented between February 1, 2020, and January 31, 2021, and had information on hospitalization, intensive care unit (ICU) admission, and 3-mo vital status (defined as being dead or alive) were included.

Statistical Analysis

Baseline characteristics are presented for the total population and hospitalization and ICU admission status. Continuous data are presented as mean ± standard deviation or as median and interquartile range (IQR) in case of a nonnormal distribution of data. Categorical data are presented as numbers (percentages). Characteristics were compared among groups using analysis of variance for continuous variables (Kruskal–Wallis test for nonnormally distributed data) and Pearson chi-square statistics for categorical variables. A Kaplan–Meier plot was made to show cumulative survival probability by hospitalization and ICU admission status. Predictors of 3-mo vital status were investigated using Cox proportional-hazards models. Variables with a P value of <0.1 in univariable models were included in multivariable models, and using a backward elimination procedure, variables with a P of <0.1 were selected as predictors. In addition, the use of immunosuppressive drugs was investigated as risk factor for 3-mo vital status in a multivariable Cox proportional-hazards model adjusted for age, sex, frailty, obesity, hypertension, diabetes, heart failure, chronic lung disease, estimated glomerular filtration rate (eGFR), and time after transplantation in a stepwise manner. Numbers and proportions of kidney graft–related outcomes and functional and mental health outcomes are presented for survivors at 3 mo by hospitalization and ICU admission status. Predictors of functional and mental health status among survivors at 3 mo were identified using univariable and multivariable logistic regression analyses. Because of smaller sample size, we used a stringent P value of <0.05 for identifying candidate predictors in a univariable model. In a multivariable model with a backward elimination procedure, a P value of <0.1 was used to identify main predictors. Missing data in multivariable models were handled using multiple imputation (10 imputed data sets created with 100

interactions).[14] Multiple imputation was performed with the chained equations method using all variables included in a multivariable model. All analyses were performed using Stata version 14.0 (College Station, TX). A 2-sided *P* value of <0.05 indicated statistical significance.

RESULTS

A total of 1035 adult kidney transplant patients who presented with COVID-19 between February 1, 2020, and January 31, 2021, were included in the ERACODA database. After excluding 123 patients for whom information was missing about vital status, hospitalization, or ICU admission (N = 111, N = 47, N = 2, respectively), 912 patients were eligible for our current analysis.

Patient Characteristics

Baseline characteristics are shown in Table 1. Mean (standard deviation) age was 56.7 (13.6) y, 61.5% were male, and 85.3% were White/Caucasian. Hospitalized patients were on average aged 7.8 y and had more comorbidities than nonhospitalized patients; particularly, obesity, hypertension, diabetes, coronary artery disease, and heart failure were more prevalent in hospitalized patients. Hospitalized patients also had a higher Clinical Frailty Score and were more often treated with a triple immunosuppressive regime than nonhospitalized patients. Regarding the presenting symptoms, patients who required hospitalization more often presented with shortness of breath, fever, nausea, and vomiting. Their respiration rate was higher and oxygen saturation lower at presentation.

TABLE 1.

Baseline demographic and clinical characteristics by hospitalization and ICU admission status

Variable	Total (N = 912)	Not hospitalized (n = 241)	Hospitalized, no ICU (n = 524)	Hospitalized, ICU (n = 147)	*P*
Patient characteristics					
Male sex, n (%)	561 (61.5)	149 (61.8)	321 (61.3)	91 (61.9)	0.98
Age, y	56.7 ± 13.6	51.0 ± 13.9	58.7 ± 13.6	58.9 ± 10.3	<0.001
BMI, kg/m^2	27.1 ± 5.0	26.3 ± 4.7	27.0 ± 5.0	28.2 ± 5.0	0.003
Race, n (%)					0.13
White or Caucasian	746 (85.3)	197 (85.3)	438 (86.7)	111 (79.9)	
Non-White	129 (14.7)	34 (14.7)	67 (13.3)	28 (20.1)	
Tobacco use, n (%)					0.41
Current	37 (4.1)	8 (3.4)	23 (4.4)	6 (4.1)	
Prior	201 (22.0)	42 (17.6)	125 (23.8)	34 (23.1)	
Never	456 (50.0)	133 (55.2)	248 (47.3)	75 (51.0)	
Unknown	218 (23.9)	58 (24.1)	128 (24.4)	32 (21.8)	
Clinical frailty scale, AU	2.9 ± 1.5	2.4 ± 1.3	3.1 ± 1.6	3.0 ± 1.4	<0.001
Comorbidities, n (%)					
Obesity	181 (24.1)	28 (16.7)	109 (24.1)	44 (33.6)	0.003
Hypertension	745 (81.7)	188 (78.0)	427 (81.5)	130 (88.4)	0.04
Diabetes	280 (30.7)	57 (23.6)	167 (31.9)	56 (38.1)	0.01
Coronary artery disease	152 (16.7)	22 (9.1)	105 (20.0)	25 (17.0)	0.001
Heart failure	79 (8.7)	10 (4.1)	46 (8.8)	23 (15.6)	<0.001
Chronic lung disease	69 (7.6)	10 (4.1)	40 (9.5)	9 (6.1)	0.02
Active malignancy	38 (4.2)	6 (2.5)	25 (4.8)	7 (4.8)	0.32
Autoimmune disease	49 (5.4)	14 (5.8)	26 (5.0)	9 (6.1)	0.81
No. of reported comorbidities	2 (1–2)	1 (1–2)	2 (1–3)	2 (1–3)	<0.001
Primary kidney disease, n (%)					
Primary glomerulonephritis	160 (17.9)	48 (20.3)	79 (15.5)	33 (22.6)	0.07
Pyelonephritis	26 (2.9)	5 (2.1)	19 (3.7)	2 (1.4)	0.23
Interstitial nephritis	32 (3.6)	7 (3.0)	21 (4.1)	4 (2.7)	0.62
Hereditary kidney disease	118 (13.2)	29 (12.3)	74 (14.5)	15 (10.3)	0.37
Congenital diseases	40 (4.5)	17 (7.2)	20 (3.9)	3 (2.0)	0.04
Vascular diseases	72 (8.1)	17 (7.2)	38 (7.4)	17 (11.6)	0.22
Sec. glomerular disease	40 (4.5)	8 (3.4)	21 (4.1)	11 (7.5)	0.13
Diabetic kidney disease	98 (11.0)	19 (8.0)	59 (11.5)	20 (13.7)	0.19
Other	184 (20.6)	59 (25.0)	100 (19.6)	25 (17.1)	0.12
Unknown	123 (13.8)	27 (11.4)	80 (15.7)	16 (11.0)	0.17
Time since transplantation, n (%)					0.04
<1 y	81 (9.0)	17 (7.1)	47 (9.1)	17 (11.6)	
1–5 y	346 (38.3)	106 (44.3)	174 (33.6)	66 (45.2)	
>5 y	476 (52.7)	116 (48.5)	297 (57.3)	63 (43.1)	

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TABLE 1. (Continued)

Variable	Total (N = 912)	Not hospitalized(n = 241)	Hospitalized, no ICU (n = 524)	Hospitalized, ICU (n = 147)	*P*
Medication use					
Use of RAAS inhibitors, n (%)	368 (40.6)	99 (41.8)	205 (39.3)	64 (43.5)	0.59
Use of immunosuppressive medication, n (%)					
Triple therapy	575 (64.0)	142 (59.9)	325 (62.9)	108 (74.5)	0.03
Tacrolimus + prednisone + mycophenolate	508 (88.3)	130 (91.6)	283 (87.1)	95 (88.0)	0.38
Others	67 (11.6)	12 (8.4)	42 (12.9)	13 (12.0)	
Dual therapy	302 (33.6)	91 (38.4)	177 (34.2)	34 (23.4)	
CNI + prednisone	125 (41.4)	36 (39.6)	75 (42.4)	14 (41.2)	0.30
CNI + antimetabolite	114 (37.7)	42 (46.1)	59 (33.3)	13 (38.2)	
Prednisone + antimetabolite	40 (13.2)	8 (8.8)	29 (16.4)	3 (8.8)	
Others, %	23 (7.6)	5 (5.5)	14 (7.9)	4 (11.8)	
Disease-related characteristics					
Presenting symptoms, n (%)					
Sore throat	147 (17.5)	35 (16.7)	86 (17.4)	26 (19.0)	0.86
Cough	543 (62.2)	128 (57.7)	312 (61.2)	103 (71.0)	0.03
Shortness of breath	353 (40.2)	31 (14.0)	228 (44.5)	94 (65.3)	<0.001
Fever	614 (69.5)	130 (57.8)	367 (71.1)	117 (82.4)	<0.001
Headache	171 (20.4)	51 (24.8)	90 (18.7)	30 (22.4)	0.17
Nausea or vomiting	133 (15.7)	12 (5.7)	91 (18.3)	30 (21.9)	<0.001
Diarrhea	233 (27.4)	41 (19.4)	150 (29.9)	42 (30.4)	0.01
Myalgia or arthralgia	266 (32.2)	77 (37.0)	146 (30.0)	43 (32.6)	0.19
Vital signs					
Temperature, °C	37.6 ± 1.1	37.5 ± 1.0	37.6 ± 1.1	37.6 ± 1.1	0.55
Respiration rate, /min	20.8 ± 6.9	16.5 ± 4.1	20.5 ± 6.1	24.9 ± 8.4	<0.001
O_2 saturation room air, %	94.0 ± 7.1	97.1 ± 2.0	94.0 ± 7.2	91.1 ± 8.5	<0.001
Systolic BP, mm Hg	132.6 ± 21.0	133.3 ± 15.7	132.7 ± 21.8	131.7 ± 21.9	0.84
Diastolic BP, mm Hg	78.1 ± 14.2	80.1 ± 11.7	78.0 ± 14.7	76.8 ± 14.0	0.23
Pulse rate, BPM	87.3 ± 17.0	83.3 ± 14.9	87.8 ± 16.3	88.8 ± 20.1	0.04
Intubated, n (%)				107 (72.3)	
Test results					
eGFR CKD-EPI, mL/min/1.73 m^2	37 (23–55)	52 (33–68)	36 (24–51)	30 (18–48)	<0.001
Creatinine increase (>25%), n (%)	230 (25.2)	11 (4.6)	154 (29.4)	65 (44.2)	<0.001
Lymphocytes, ×1000/μL	0.8 (0.5–1.4)	1.4 (0.9–2.2)	0.8 (0.5–1.3)	0.6 (0.4–1.0)	<0.001
CRP, mg/L	41 (9.9–94)	5 (3–30)	43 (12–95)	71 (24–124)	<0.001
SARS-CoV-2 PCR positive, n (%)	686 (94.6)	159 (97.5)	407 (93.8)	120 (93.7)	0.12
COVID-19 on x-ray, n (%)	375 (41.5)	16 (6.7)	261 (50.2)	375 (41.5)	<0.001
COVID-19 on CT scan, n (%)	242 (26.8)	9 (3.8)	174 (33.5)	59 (40.4)	<0.001

Continuous variables are reported as mean ± SD or median (IQR). Groups were compared using 1-way ANOVA, Kruskal–Wallis test, or chi-square test as appropriate. Obesity is defined as BMI >30 kg/m^2.

ANOVA, analysis of variance; BMI, body mass index; BP, blood pressure; BPM, beats per minute; CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration; CNI, calcineurin inhibitor; COVID-19, coronavirus disease 2019; CRP, C-reactive protein; CT, computed tomography; eGFR, estimated glomerular filtration rate; ICU, intensive care unit; IQR, interquartile range; PCR, polymerase chain reaction; RAAS, renin-angiotensin-aldosterone system; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

eGFR at presentation was lower, and a 25% increase in creatinine compared with the pre–COVID-19 baseline value was more frequently observed in patients who required hospital admission. Of ICU-admitted patients, 107 of 147 (72.5%) were intubated.

Survival at 3 Mo After Presenting With COVID-19

Three-month survival was 98.8% for nonhospitalized patients and 84.2% for hospitalized patients who were not admitted to the ICU (Figure 1). In these 2 groups, deaths occurred mostly within the first 14 d after presentation (Figure 2). In patients who were admitted to the ICU, 3-mo survival was much lower, at 49.0% (Figure 1), and the mortality plateaued later at around 50 d after presentation (Figure 2). Three months after initial presentation, the majority of patients were living at home, and only 4.5% of patients were still admitted to a hospital or a nursing home.

Baseline characteristics according to vital status are shown in **Table S1** (**SDC**, http://links.lww.com/TP/C365). Overall, patients who survived were younger, had a lower Clinical Frailty Score, and less comorbidities. Presenting symptoms and signs of disease were less severe, especially respiratory symptoms and markers of inflammation. In a multivariate analysis, age, frailty, heart failure, respiratory rate, and lymphocyte count were the most important predictors for survival at 3 mo (**Table S2**, **SDC**, http://links.lww.com/TP/C365). With respect to immunosuppressive medication, we found a hazard ratio pointing toward better survival for patients on dual therapy versus those on triple-drug therapy, although this did not reach formal

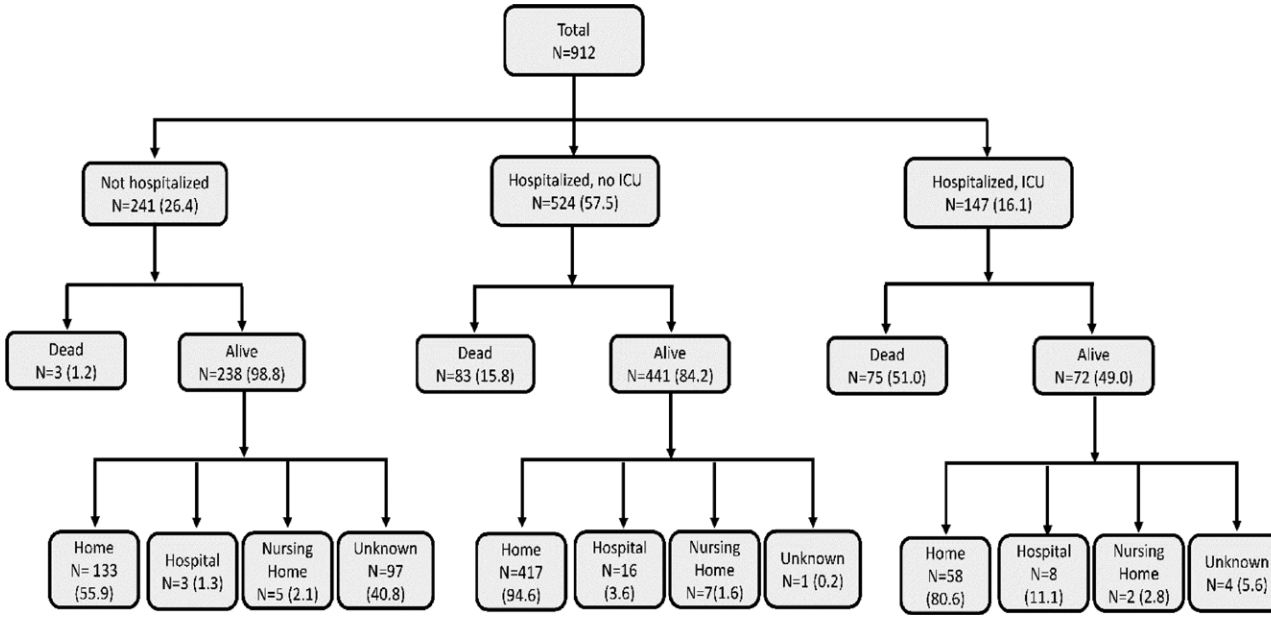

FIGURE 1. Flow diagram of hospitalization, ICU admission, and mortality within 3 mo after presenting with COVID-19. Status of alive patients is status at 3 mo or last known status. COVID-19, coronavirus disease 2019; ICU, intensive care unit.

statistical significance (**Table S3, SDC**, http://links.lww.com/TP/C365). There was no association between the type of immunosuppressive drug and survival (**Table S4, SDC**, http://links.lww.com/TP/C365).

Three-month Clinical, Functional, and Mental Health Outcomes in COVID-19 Survivors

In the subsequent analyses, we were specifically interested in the outcomes of kidney transplant patients who survived COVID-19. Of the 751 patients still alive at 3 mo, data of 487 patients were available for analysis of graft function–related outcomes and of 450 patients for physician-reported functional and mental health outcomes (Figure 3). Baseline characteristics were largely comparable between patients with complete and those with missing data, indicating that the missingness of data was likely random (**Tables S5** and **S6, SDC**, http://links.lww.com/TP/C365).

Graft Survival at 3 Mo After Presentation

In the 487 patients for whom data on graft function at 3 mo were available, the median eGFR at presentation was 40 (IQR, 26–59) mL/min/1.73 m^2. Baseline characteristics

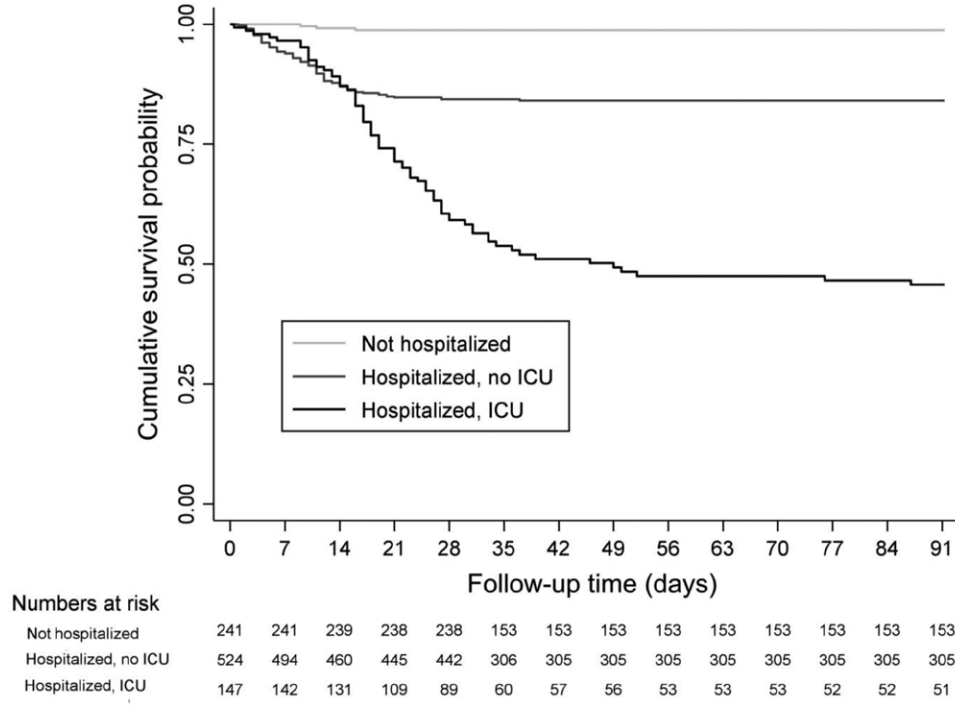

FIGURE 2. Kaplan–Meier curves showing cumulative survival probability by hospitalization and ICU admission status. ICU, intensive care unit.

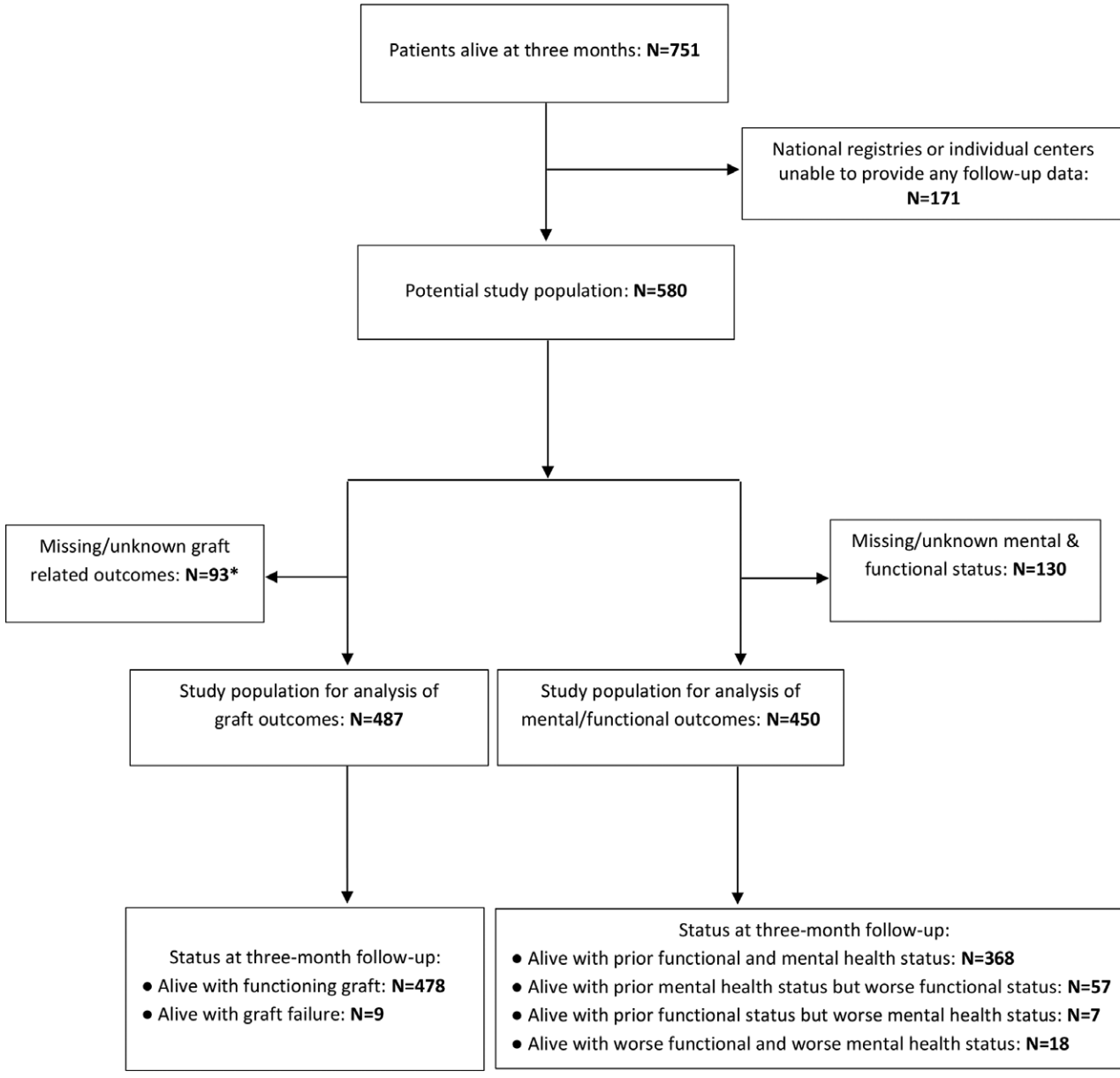

FIGURE 3. Flow diagram of patient inclusion and results for analysis of graft function–related outcomes and functional and mental health outcomes. Patients analyzed for kidney function status and patients analyzed for functional and mental health outcomes are not totally exclusive study populations. From a total of 450 patients analyzed for functional and mental status, 449 were also analyzed for kidney function status. Thirty-eight other patients had information on kidney function status but not on functional and mental status.

by hospitalization and ICU admission status are shown in **Table S7** (**SDC**, http://links.lww.com/TP/C365). At presentation, 21.8% of patients had an increase in creatinine of >25% compared with their pre–COVID-19 baseline creatinine level (**Table S5**, **SDC**, http://links.lww.com/TP/C365). Although calcineurin inhibitors and mycophenolate mofetil were tapered in many patients upon admission (stopping or decreasing the dose of mycophenolate mofetil in 62% and reduction in calcineurin inhibitor dose in 22%), biopsy-proven acute rejection was a rare event that occurred in only 4 (0.8%) patients who survived COVID-19 (Table 2). Two of 4 patients who experienced acute rejection developed temporary graft failure, but all 4 had a functioning graft at 3-mo follow-up. The need for hemodialysis or continuous renal replacement therapy within 3 mo after presentation was rare and occurred in only 2.6% of all surviving patients. In the subset of survivors who had been admitted to the ICU, the requirement of dialysis or CVVH was markedly higher at 10.6% (Table 2). Graft survival was good in patients surviving COVID-19, with 97.3% of patients having a functioning graft 3 mo after presentation (Table 2) with a median eGFR of 49 (IQR, 34–67) mL/min/1.73 m^2. Graft failure within 3 mo of follow-up occurred at a similar rate in nonhospitalized patients (0.7%) and hospitalized patients who were not admitted to the ICU (1.0%; Table 2). In patients who were admitted to the ICU, 5 of 47 (10.7%) experienced irreversible loss of graft function within 3 mo after

TABLE 2.

Kidney graft outcomes 3 mo after presenting with COVID-19

Outcomes within 3 mo since presentation	Total (N = 487)	Not hospitalized (n = 143)	Hospitalized, no ICU (n = 297)	Hospitalized, ICU (n = 47)	*P*
Acute rejection, n (%)					0.58
No	483 (99.2)	141 (98.6)	295 (99.3)	46 (97.9)	
No	4 (0.8)	21 (0.7)	2 (0.7)	1 (2.1)	
Required dialysis or CRRT, n (%)					0.002
No	474 (97.3)	140 (97.9)	292 (98.3)	42 (89.4)	
Yes	13 (2.6)	3 (2.1)	5 (1.7)	5 (10.6)	
Graft loss, n (%)					<0.001
No	478 (99.2)	142 (99.3)	294 (99.0)	42 (89.4)	
Yes	9 (1.8)	1 (0.7)	3 (1.0)	5 (10.6)	

[a]Four acute rejections were biopsy proven (1 in the group of not hospitalized, 2 in hospitalized no ICU, and 1 in hospitalized and ICU).
COVID-19, coronavirus disease 2019; CRRT, continuous renal replacement therapy; ICU, intensive care unit.

presentation, whereas 89.4% had a functioning graft 3 mo after presentation (Table 2). Of patients with a functioning graft at 3 mo, the median eGFR at presentation was 36 (IQR, 22–55) mL/min/1.73 m^2, whereas at 3-mo follow-up, this was markedly higher, namely 54 (IQR, 40–71) mL/min/1.73 m^2 (Table 1). This may be related to the fact that 40.4% of patients presented with an increase in creatinine of >25% compared with their pre–COVID-19 baseline creatinine level. Also, loss of muscle mass during ICU admission will have resulted in reduced serum creatinine and consequently increased eGFR.[15]

Physician-reported Functional and Mental Health Status at 3 Mo After Presentation

Among survivors at 3 mo, 450 patients had complete data on physician-reported functional and mental health status (Figure 3). 83.3% of patients reached their pre–COVID-19 functional status as reported by their physician. The percentage of patients who reached their prior functional status was similar in nonhospitalized patients and patients who were hospitalized but did not require ICU admission (87.9 and 87.0%; **Table S8, SDC**, http://links.lww.com/TP/C365). For patients who were admitted to the ICU, only 42.5% reached their prior functional status after 3 mo.

For patients who had not yet reached their prior functional status after 3 mo, tiredness, reduced muscle strength, and reduced mobility were recorded as limiting factors, together accounting for 56.0% of cases and impaired lung function in 22.7% of cases (**Table S8, SDC**, http://links.lww.com/TP/C365). Factors that limited the recovery of functional status were similar for nonhospitalized and hospitalized patients who did not require ICU admission. However, in patients who had been admitted to the ICU, tiredness, reduced muscle strength, and reduced mobility were indicated more often as limiting factors. In addition, disturbed mental health status was pointed out as a limiting factor in 21.7% of patients, whereas this was not noted in patients who had not been admitted to the ICU (**Table S8, SDC**, http://links.lww.com/TP/C365). Frailty and ICU admission were independently associated with a low likelihood to reach prior functional status (**Table S9, SDC**, http://links.lww.com/TP/C365). Of patients who had not yet reached their prior functional status, the treating physicians expected that 79.6% still would within the coming year (**Table S8, SDC**, http://links.lww.com/TP/C365; Figure 4A). This was also the case for patients who had been admitted to the ICU.

Regarding the physician-reported mental health status, 425 of 450 patients (94.4%) reached their pre–COVID-19 mental health status within 3 mo (**Table S10, SDC**, http://links.lww.com/TP/C365). This proportion was equally high for nonhospitalized and hospitalized patients who were not admitted to the ICU (95.7% and 96.3%). In ICU-admitted patients, it was, however, substantially lower, at 77.5% (**Table S10, SDC**, http://links.lww.com/TP/C365), and ICU admission was independently associated with a lower likelihood to reach prior mental health status (**Table S9, SDC**, http://links.lww.com/TP/C365). Among those who had not yet reached their prior mental health status, the most commonly noted limiting factors were depression, anxiety, grief, and posttraumatic stress disorder, together accounting for 32%. 83.3% of patients were expected to reach their prior mental health status within the coming year, which was similar in nonhospitalized, hospitalized, and ICU-admitted patients (**Table S10, SDC**, http://links.lww.com/TP/C365; Figure 4B).

DISCUSSION

Little information is available on how kidney transplant patients recover from COVID-19. Here we present the 3-mo clinical and physician-reported functional and mental health outcomes of kidney transplant patients from the ERACODA database. Our data show that >80% of kidney transplant patients are alive at 3 mo after presentation with COVID-19. Kidney graft outcomes were excellent, with acute rejection and graft failure being rare events (<5%). Physician-reported functional outcome was also favorable, with the vast majority of survivors living at home at 3 mo and >80% reaching their pre–COVID-19 functional status. Over 90% also reached their pre–COVID-19 physician-reported mental health status within 3 mo of presentation. Admission to the ICU was the most important factor associated with poor recovery after COVID-19, especially for the functional status.

The 3-mo survival rate of hospitalized patients in our current study is nearly identical to the survival rate of hospitalized patients in our previous report on 28-d survival in kidney transplant patients in the ERACODA database (76.5%. versus 76.4%).[5] Our data corroborate with

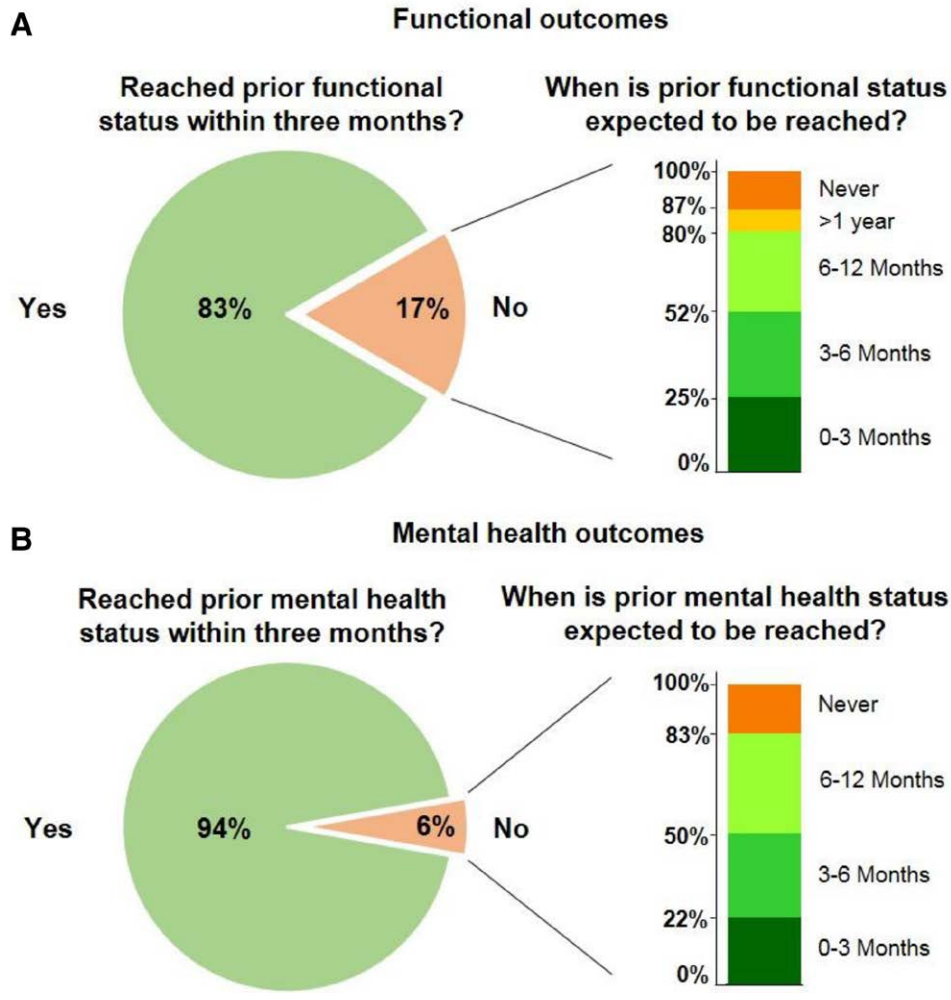

FIGURE 4. Functional and mental health outcomes among survivors 3 mo after presenting with COVID-19. COVID-19, coronavirus disease 2019.

previous studies that showed survival rates ranging from 72% to 84%.[6-10,16,17] These studies either documented survival of hospitalized patients or information on hospitalization was lacking. A study that mapped out the infection and survival rates of the entire kidney transplant population in Flanders region of Belgium for a period of 12 wk showed that 1.4% of the 3293 patients were diagnosed with SARS-CoV-2 infection, of which 82.6% were admitted to hospital and 86.0% survived.[18] In a similar study from Saudi Arabia that followed 3052 solid organ transplant patients, 2.2% were diagnosed with SARS-CoV-2 infection, of which 70% were admitted to hospital and 96% survived.[19] Our study shows comparable numbers (74% admitted and 82% survived), suggesting that our data are a fair representation of the kidney transplant population with COVID-19.

Acute rejection is a concern in kidney transplant recipients with COVID-19 because the infection induces systemic immune activation, and calcineurin inhibitors and mycophenolate mofetil are often reduced or discontinued upon admission. Little data are available in the literature on the risk of acute rejection in these circumstances. In a report on kidney biopsy findings in 17 patients with COVID-19, 4 kidney transplant patients were included. Three of these biopsies showed acute rejection.[20] Although more of such case reports and case series can be found in literature, they do not provide detailed insight into the frequency with which acute rejection occurs. Available data indicate that acute rejection rarely occurs. A prospective single-center study including 161 solid organ transplant recipients documented acute rejection in 3.4% of patients.[17] Another single-center prospective cohort study found only 1 acute rejection among the 491 included kidney transplant recipients.[18] In a series of 47 kidney transplant patients with COVID-19, none of them developed de novo donor-specific antibodies or an increase in panel reactive antibodies within 3 mo after discharge from hospital.[9,21] In line with these previous reports, we found acute rejection to be rare, occurring in 1% of patients who survived COVID-19.

In kidney transplant patients admitted for COVID-19, acute kidney injury frequently occurs, but long-term kidney outcome among survivors seems good. A systematic review of COVID-19 infections in kidney transplant patients included 63 articles published from January 1 to July 7, 2020, which included 420 kidney transplant patients with confirmed COVID-19. In this analysis, 23% of patients required kidney replacement therapy during hospital admission,[22] but later publications showed proportions <15%.[6,21,22] It is important to note that in one

of these studies, all of the surviving patients regained their baseline kidney function before being discharged from the hospital.[23] This is in line with our findings showing that 2.4% of surviving patients required dialysis or CVVH at some point after presentation and that the vast majority of patients have a functioning graft at 3-mo follow-up. Our data therefore provide a reassuring picture of maintained graft function among patients who survive COVID-19. It is important to note, however, that for patients who had been admitted to the ICU, graft-related outcomes were less favorable, with permanent loss of graft function in >10%.

We observed that physician-reported functional and mental health outcomes are reasonably well in kidney transplant patients who survived COVID-19. To our knowledge, data on functional and mental health outcomes after COVID-19 in kidney transplant patients have not been reported before. However, several studies on functional and mental health outcomes after COVID-19 in the general population can place our findings in perspective. In a French study performed after 4-mo follow-up in 834 COVID-19 patients, 51% of patients reported at least 1 symptom that did not exist before COVID-19.[3] In a Chinese study in 1733 COVID-19 patients, 76% reported at least 1 symptom after 6-mo follow-up.[4] Regarding functional outcome parameters, fatigue was reported by 31% of patients in the French study, whereas fatigue or muscle weakness was reported by 63% of patients in the Chinese study. In our data, tiredness, reduced muscle strength, and reduced mobility were reported for 56% of the patients. Regarding mental health outcomes, impaired memory was reported by 18% of patients in the general population,[3] whereas the reported prevalence was 12% in our study. For sleep disturbance, these proportions were 26%[4] and 12%, respectively. Although these studies cannot directly be compared because of differences in patient demographics, data acquisition, and data reporting, the overall picture is that functional and mental health outcome at 3 mo after COVID-19 do not seem much different in kidney transplant patients when compared with the general population.

Although clinical, functional, and mental health recovery was good for out-of-hospital and hospitalized patients 3 mo after being diagnosed with COVID-19, the prospects for patients admitted to the ICU were bleak. Nearly half did not survive, and of those who did survive, >10% had permanently lost their graft function, and 57.5% and 22.5% did not reach their pre–COVID-19 functional and mental health status, respectively, 3 mo after presentation. This indicates that these patients are indeed seriously ill and the majority of them only partially recover in the months following their infection. These patients should therefore be closely monitored after hospital discharge, and attention should be given to their functional and mental health well-being.

A strength of our study is that it is based on a complete and highly detailed data set retrieved from the largest European database that was specifically designed to obtain information on kidney replacement therapy patients with COVID-19. The ERACODA database is unique in the fact that it yields detailed information on demographics, disease characteristics, and outcomes. An additional strength is that follow-up data are obtained 3 mo after presentation, which enables us to investigate the clinical, functional, and mental health outcomes of kidney replacement therapy patients.

Our study also has limitations. First, the database may not include all kidney transplant patients with COVID-19 in the participating centers. A proportion of patients who presented with COVID-19 may not have been entered into the database, and some patients may not have contacted their medical center, especially if they had mild symptoms. Also, testing policies may have varied between centers, across countries, and over time. Consequently, patients with no or mild symptoms are expected to be underrepresented in our database, but this does not detract from the rather favorable outcome that we observed. Second, detailed information on in-hospital management of the patients was not available, which made it impossible to relate outcome to treatment strategies. Third, the follow-up of patients is 3 mo after the onset of the COVID-19 infection. A longer-term follow-up is important and is needed in the future. Fourth, White or Caucasian patients comprised 85.3% of the population. Although this may reflect the European population, our findings are not representative for populations with non-European ancestry. Finally, functional and mental health outcome parameters were physician-reported outcomes, based on clinical judgment. Ideally, both physician- and patient-reported outcomes would have been gathered because they both provide valuable information. Physicians might have missed deficiencies in physical or mental health functioning, and patients might not have reported them. Physician-reported outcomes are therefore less discriminative than patient-reported outcomes.[24] Furthermore, the fact that the identification of impairments in patient's functional and mental health status was left to the discretion of the physician may have resulted in heterogeneity in reporting by physicians.

In summary, our study shows that >80% of kidney transplant recipients are alive at 3 mo after presentation with COVID-19. In these survivors, acute rejection and graft failure within 3-mo follow-up were rare, and most patients reached their pre–COVID-19 physician-reported functional and mental health status. ICU admission was associated with poor recovery from COVID-19.

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Data Sharing Statement: Collaborators that entered data in ERACODA remain the owner of these data. The database can therefore not be disclosed to any third party

without the prior written consent of all data providers, but the database will be made available to the editorial offices of medical journals when requested. Research proposals can be submitted to the Working Group via COVID.19.KRT@umcg.nl. If deemed of interest and methodological sound by the Working Group and Advisory Board, the analyses needed for the proposal will be performed by the Management Team.

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