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# Early Report on Published Outcomes in Kidney Transplant Recipients Compared to Nontransplant Patients Infected With Coronavirus Disease 2019

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## ABSTRACT

**Background.** Kidney transplant recipients (KTR) present unique characteristics, including disease vintage, immunosuppression, and single functioning kidneys. We conducted preliminary analyses to assess the impact of coronavirus disease 2019 (COVID-19) on outcomes in KTR compared to nontransplant patients.

**Methods.** We evaluated published information in peer-reviewed journals between January 1, 2020, and April 24, 2020, with available data on acute kidney injury (AKI), renal replacement therapy (RRT), intensive care unit (ICU) stay, and death and compared clinical outcomes in KTR vs nontransplant recipients with COVID-19.

**Results.** A total of 19 published articles were identified, including a total of 88 KTR and 5342 nontransplant patients. The sample size varied between 2 and 2634. Mean age was 58.6 years vs 58.9 years in KTR vs nontransplant patients. Patient-level incidence of AKI (27.5% vs 13.3%,  $P < .001$ ), RRT (15.4% vs 3.3%,  $P < .001$ ), ICU stay (34.1% vs 15.1%,  $P < .001$ ), and death (22.7% vs 16.2%,  $P = .10$ ) was higher in KTR, representing relative risks of 2.06 (1.44, 2.96), 4.72 (2.62, 8.51), 2.25 (1.67, 3.03), and 1.41 (0.95, 2.08), respectively.

**Conclusion.** Early results suggest that the KTR are at significantly higher risk of AKI, RRT, and ICU stay from SARS-CoV-19 infection compared to the general population. The risk of death may not be significantly different.

**C**ORONAVIRUS disease 2019 (COVID-19) from severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) emerged as a life-threatening infection that has affected more than 2.7 million people and caused the deaths of close to 200,000 patients worldwide over the last few months. Original studies from Wuhan, China, where the novel virus emerged, showed that 5% to 29% of patients with SARS-CoV-19 infection experienced acute kidney injury (AKI) [1,2]. With the evolving pandemic, kidney transplant recipients (KTR) with chronically suppressed immune systems and baseline chronic kidney disease might be theoretically at significant risk of this potentially fatal infection. The clinical manifestations, treatment, and prognosis of SARS-CoV-19 infection in KTR are limited to only

a few case reports and case series. We reviewed the literature to compare the outcome of SARS-CoV-19 infection in KTR to those in nontransplant patients.

## METHODS

We reviewed the incidence of AKI, intensive care unit (ICU) stay, renal replacement therapy (RRT) requirement, and death in published articles of SARS-CoV-19 infection published in journals with

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an impact factor > 2.5 between January 1, 2020, and April 24, 2020. Single case reports were not included. We compared these clinical outcomes in patients with and without kidney transplantation using patient-level analyses. Studies of autopsies were excluded from mortality analyses.

## RESULTS

We identified 19 case series [1–19], 6 of which included only KTR (Table 1) [12–15,17,19]. A total of 5342 patients with SARS-CoV-19 infection were included in the studies of nontransplant patients, and a total of 88 were included in the studies of KTR. The sample size varied between 2 and 2634 patients (Table 1). The mean age was 58.6 years vs 58.9 years in KTR vs nontransplant patients. Patient-level incidence of AKI (27.5% vs 13.3%,  $P < .001$ ), RRT (15.4% vs 3.3%,  $P < .001$ ), ICU stay (34.1% vs 15.1%,  $P < .001$ ), and death (22.7% vs 16.2%,  $P = .10$ ) was higher in KTR (Table 2, Fig 1), representing relative risks of 2.06 (1.44, 2.96), 4.72 (2.62, 8.51), 2.25 (1.67, 3.03), and 1.41 (0.95, 2.08), respectively (Table 2). Mean age was not statistically associated with the prevalence of death, ICU admission, or need for renal replacement therapy ( $P$  value = .1) in analyses weighted by the relative size of each study.

## DISCUSSION

With the sudden and unexpected spread of COVID-19 throughout the world, there is significant uncertainty about the management of patients with the virus. This uncertainty becomes further complicated when KTR, a particularly vulnerable group, are infected with SARS-CoV-19. We analyzed the recent literature and compared outcomes between KTR and the general population. Our analysis indicated that AKI, RRT, ICU stay, and death were more common in KTR with COVID-19. Although the

**Table 2. Patient-Level Outcomes in Kidney Transplant Recipients and Nontransplant Patients With Coronavirus Disease 2019**

AKI	Native	Transplant	<i>P</i>
Patient-level	n/N (%) 712/5342 (13.3) RR = 2.06 (1.44, 2.96)	n/N (%) 22/80 (27.5)	< .001
RRT	Native	Transplant	<i>P</i>
Patient-level	n/N (%) 174/5342 (3.3) RR = 4.72 (2.62, 8.51)	n/N (%) 10/65 (15.4)	< .001
ICU Stay	Native	Transplant	<i>P</i>
Patient-level	n/N (%) 805/5316 (15.1) RR = 2.25 (1.67, 3.03)	n/N (%) 30/88 (34.1)	< .001
Death	Native	Transplant	<i>P</i>
Patient-level	n/N (%) 841/5203 (16.2) RR = 1.41 (0.95, 2.08)	n/N (%) 20/88 (22.7)	.10

Abbreviations: AKI, acute kidney injury; ICU, intensive care unit; RRT, renal replacement therapy.

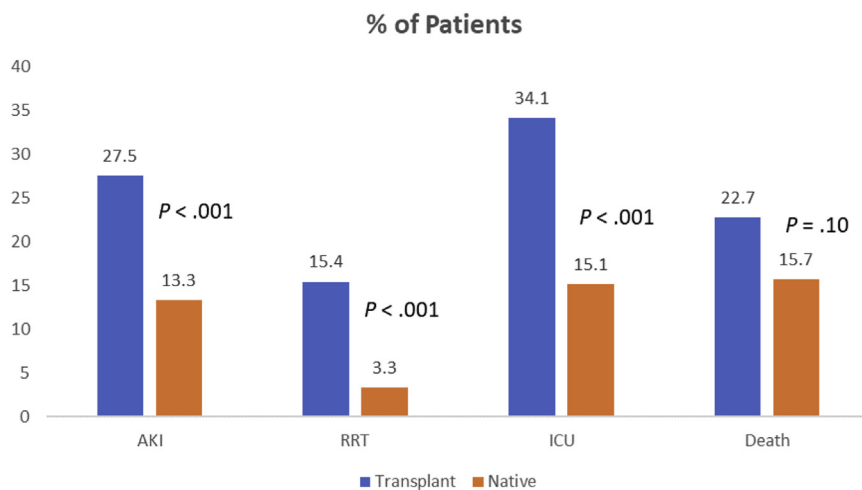
difference in mortality did not reach statistical difference, the other outcomes were significantly worse in KTR.

Not all published data reported poor outcomes in KTR. In a recent case series from Columbia University in New York, KTR with SARS-CoV-19 infection were found to have a similar presentation and favorable outcomes compared to the general population [17]. On the other hand, Akalin et al [19] observed high rates of AKI, need for RRT, and death in KTR, which is intriguing because both studies reported data from NYC. However, similar to the Akalin study, others have found rapid disease progression

**Table 1. Summary of Studies and Clinical Outcomes**

First Author	Journal	Transplant	N	Age	AKI	RRT	ICU	Death	Reference
Yang	Lancet Respir Med	-	52	59.7	29.0%	17.0%	100.0%	61.5%	1
Zhou	Lancet	-	191	56	5.0%	15.0%	26.0%	28.0%	2
Chen	BMJ	-	113	68	25.0%	2.6%	82.0%	100.0%	3
Chen	Lancet	-	99	55.5	9.0%	9.0%	4.0%	11.0%	4
Huang	Lancet	-	41	49	7.0%	7.0%	31.0%	15.0%	5
Grein	N Engl J Med	-	53	64	6.0%	0.0%	64.0%	13.0%	6
Cheng	Kidney Int	-	701	63	5.1%	2.0%	10.4%	16.1%	7
Cao	N Engl J Med	-	199	58	4.5%	4.5%	22.0%	22.0%	8
Guan	N Engl J Med	-	1099	47	0.5%	0.8%	5.0%	1.4%	9
Young	JAMA	-	18	47	0.0%	0.0%	11.0%	0.0%	10
Wang	Am J Nephrol	-	116	54	0.0%	0.0%	9.4%	6.0%	11
Richardson	JAMA	-	2634	63	22.2%	3.2%	14.2%	21.0%	18
Su	Kidney Int	-	26	69	35.0%	19.0%	NA	100.0%	16
Banerjee	Kidney Int	+	7	54	42.0%	42.0%	60.0%	14.0%	14
Alberici	Kidney Int	+	20	59	30.0%	5.0%	20.0%	25.0%	15
Akalin	N Engl J Med	+	36	60	16.0%	16.0%	27.0%	28.0%	19
Gandolfini	Am J Transplant	+	2	63	50.0%	0.0%	100.0%	50.0%	12
Fernandez-Ruiz	Am J Transplant	+	8	69	NA	NA	75.0%	25.0%	13
Columbia Univ.	JASN	+	15	51	40.0%	NA	27.0%	7.0%	17

Abbreviations: AKI, acute kidney injury; ICU, intensive care unit; RRT, renal replacement therapy.



**Fig 1.** Percentage of patients for each outcome based on kidney transplant status. AKI, acute kidney injury; ICU, intensive care unit; RRT, renal replacement therapy.

and poor outcomes in KTR [12–15]. While environmental and social-economic factors might, in part, explain the differences in these observations, KTRs have unique characteristics including immunosuppression, single functioning kidneys, and potentially long disease vintage that place them at a higher risk of progression and death with COVID-19.

It is not clear how immunosuppression should be managed after the diagnosis of SARS-CoV-19 infection in KTR. Current recommendations are based on expert opinions only. Most centers prefer reducing the immunosuppression in KTR when diagnosed with COVID-19; however, the specifics remain unknown. While it seems logical to avoid T-cell depletion for induction therapy in pandemic areas, it is unclear how immunosuppression management can prevent or mitigate the cytokine storm, known to be associated with poor outcomes in patients with COVID-19. Furthermore, despite the favorable outcomes of high-dose dexamethasone treatment for acute respiratory distress syndrome [20], the role of intravenous steroids in KTR with COVID-19 remains unknown.

We recognize several limitations to our study, including the lack of detailed characteristics of patients from each study, missing data from some studies, potential selection bias, and relatively few transplant recipients. Due to a lack of patient-level information, meta-analysis cannot be performed. Despite its limitations, our study highlights the importance of close follow-up in transplant recipients with SARS-CoV-19 infection. In conclusion, based on current evidence, KTRs may be at higher risk of poor outcomes than nontransplant patients with SARS-CoV-19 infection. Preventive strategies, close monitoring, and a low threshold for hospitalization may be indicated.

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