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Outcomes of COVID-19 in CKD Patients

A Multicenter Electronic Medical Record Cohort Study

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CKD and kidney failure are important comorbidities that are associated with unfavorable outcomes in patients with coronavirus disease 2019 (COVID-19) (1,2). Patients with CKD/kidney failure also have a disproportionate burden of other comorbidities (*e.g.*, coronary artery disease, hypertension, and diabetes mellitus), which are associated with more severe presentations of COVID-19 (2). We investigated the effect of CKD/kidney failure on COVID-19 using propensity matching to account for significant comorbidities.

In this cohort study, we included patients ≥18 years of age diagnosed with COVID-19 between January 20, 2020 and September 10, 2020 identified *via* real-time search and analysis of >49 million patients (inpatients and outpatients) from 33 health care organizations participating in a global health research network called TriNetX (Cambridge, MA). Patients with COVID-19 were confirmed using COVID-19–specific diagnostic criteria recommended by the World Health Organization and the Centers for Disease Control and Prevention.

Patients with COVID-19 were divided into cohorts (CKD or no CKD) on the basis of presence of CKD or kidney failure identified *via* validated International Classification of Diseases-10th modification codes prior to the date of COVID-19 diagnosis. Propensity matching was done for age, sex, race, and multiple comorbidities, including obesity, hypertension, diabetes, ischemic heart disease, heart failure, chronic lung disease, cerebrovascular disease, and nicotine and alcohol use, using a greedy neighbor-matching algorithm to balance the baseline characteristics between the study groups. Primary outcome tested was 30-day all-cause mortality post–COVID-19 diagnosis. Secondary outcomes tested were hospitalization and need for mechanical ventilation. Subgroup analyses were reported for different CKD stages: patients with stage 2 (mild), stages 3 and 4 (moderate), or stage 5/kidney failure (severe) and included need for KRT in the mild/moderate CKD group. All statistical analyses were performed using TriNetX with standard methodology previously reported (3).

A total of 152,463 patients with COVID-19 were identified (CKD: 8810 [inclusive of kidney failure]; non-CKD: 143,653). The CKD cohort was older (67±15 versus 46±18 years; $P<0.001$) and had higher proportions of men (52% versus 44%; $P<0.001$), people of Black race (35% versus 21%; $P<0.001$), and comorbid conditions. After propensity matching, two well-matched groups of 7901 patients were formed. Table 1 shows the outcomes before and after propensity matching. Higher mortality (10.0% versus 1.5%; $P<0.001$) and worse outcomes were found in the unmatched sample, with persistent differences after matching (mortality: 9.4% versus 5.8%; hospitalization: 41.5% versus 28.5%; ventilation: 7.1% versus 4.1%; $P<0.001$). Similar findings were seen in the severe CKD group (mortality: 9.8% versus 6.0%; $P<0.001$) and in the moderate CKD group (10.4% versus 7.5%; $P<0.001$), with a higher need for KRT (2.7% versus 0.8%; $P<0.001$) in the latter. Patients with mild CKD had similar mortality and need for ventilation/KRT, but they still had slightly higher hospitalization rates.

The effect of CKD on COVID-19 is poorly understood at this point. A meta-analysis of four studies indicated a three-fold higher likelihood of severe COVID-19 (1) without adjusting for other relevant comorbidities. Thus, it is important to know whether CKD has any effect on COVID-19 outcomes independent of these covariates. Our results from an all-comers sample of outpatients and inpatients suggest that the majority of higher risk of disease severity in patients with CKD and patients with kidney failure is due to the comorbidity burden as mortality risk decreases markedly after adjusting for relevant comorbidities. Nevertheless, a sizeable incremental risk remains for the CKD population in terms of mortality as well as need for hospitalization and ventilation. In a report from the large health analytics platform OpenSafely from the United Kingdom, similar estimates of mortality were reported for patients with CKD but were much higher for patients with severe CKD/kidney failure (2). CKD is known to cause a background of low-level inflammation and is postulated to cause baseline lymphopenia (4). These factors can thus be hypothesized to play a role in the greater disease severity of COVID-19 in patients with CKD, and thus, immunomodulation may have a role to play in controlling the disease process in this population. The finding of higher need for KRT in patients with moderate CKD is also important. This is likely secondary to the insult from hypoxemia and systemic organ failure that accompanies the cytokine storm seen in patients with severe COVID-19.

This electronic medical record database analysis is limited by possible errors secondary to coding/data

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Table 1. Outcomes of patients with coronavirus disease 2019 with and without CKD before and after propensity matching

Outcome			Risk Ratio (95% Confidence Interval)	*P* Value
	Before Propensity Matching			
	Coronavirus Disease 2019 with CKD, *n*=8810, % (*n*)	Coronavirus Disease 2019 without CKD, *n*=143,653, % (*n*)		
Mortality	10.0 (883)	1.5 (2136)	6.7 (6.2 to 7.3)	<0.001
Ventilation	7.2 (633)	2.0 (2800)	3.7 (3.4 to 4.0)	<0.001
Hospitalization	42.8 (3771)	15.0 (10,611)	2.9 (2.8 to 2.9)	<0.001
	After Propensity Matching			
	Coronavirus Disease 2019 with CKD, *n*=7901, % (*n*)	Coronavirus Disease 2019 without CKD, *n*=7901, % (*n*)		
Mortality	9.4 (744)	5.8 (462)	1.6 (1.4 to 1.8)	<0.001
Ventilation	7.1 (562)	4.1 (320)	1.8 (1.5 to 2.0)	<0.001
Hospitalization	41.5 (3275)	28.5 (2251)	1.5 (1.4 to 1.5)	<0.001
	Severity Subgroups After Propensity Matching			
	Coronavirus Disease 2019 with Severe CKD, *n*=2415, % (*n*)	Coronavirus Disease 2019 without Severe CKD, *n*=2415, % (*n*)		
Mortality	9.8 (237)	6.0 (145)	1.6 (1.3 to 2.0)	<0.001
Ventilation	9.2 (222)	6.1 (147)	1.5 (1.2 to 1.9)	<0.001
Hospitalization	52.2 (1261)	32.5 (784)	1.6 (1.3 to 1.9)	<0.001
	Coronavirus Disease 2019 with Moderate CKD, *n*=5432, % (*n*)	Coronavirus Disease 2019 without Moderate CKD, *n*=5432, % (*n*)		
Mortality	10.4 (564)	7.5 (407)	1.4 (1.2 to 1.6)	<0.001
Ventilation	6.9 (373)	5.1 (276)	1.4 (1.2 to 1.6)	<0.001
Hospitalization	43.4 (2358)	33.8 (1835)	1.3 (1.3 to 1.4)	<0.001
Need for KRT	2.7 (121)	0.8 (40)	3.5 (2.4 to 4.9)	<0.001
	Coronavirus Disease 2019 with Mild CKD, *n*=1536, % (*n*)	Coronavirus Disease 2019 without Mild CKD, *n*=1536, % (*n*)		
Mortality	8.2 (126)	7.1 (109)	1.2 (0.9 to 1.5)	0.25
Ventilation	7.0 (107)	6.1 (93)	1.2 (0.9 to 1.5)	0.31
Hospitalization	40.2 (618)	35.4 (543)	1.1 (1.0 to 1.3)	0.005
Need for KRT	1.9 (30)	1.2 (19)	1.5 (0.8 to 2.8)	0.17

entry, a bias toward sicker patients who got tested, inability to perform patient-level analysis, lack of patient-level data, and inability to track clinical course.

In conclusion, our findings from a large electronic medical record patient cohort establish CKD as an independent risk factor for more severe COVID-19 disease presentation and mortality after accounting for other coexistent comorbidities. Risk of requiring KRT is also higher in patients with moderate CKD compared with the non-CKD population. This stresses the need for better recognition of the CKD population as a high-risk subgroup in this COVID-19 pandemic.

Disclosures

All authors have nothing to disclose.

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