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Letter to the Editor

End-Stage renal disease and 30-day mortality for adults with and without COVID-19

Emerging evidence suggests that people with chronic kidney disease have a higher risk of severe infection with coronavirus disease 2019 (COVID-19) [1]. Furthermore, acute kidney injury is common amongst patients hospitalised with COVID-19 compared to historical controls (56.9% vs. 25.1%) [2]. An estimated 726,000 people in the United States (US) are affected by end-stage renal disease (ESRD), and one-year mortality for people with ESRD who receive dialysis is approximately 20–25% [3]. Reports from China, England, Italy and France have suggested between 9% and 27% of patients with ESRD who tested positive for COVID-19 died, compared to 4% globally as of July 2020 [4]. The extent to which COVID-19 may worsen outcomes for people with ESRD is unclear. Therefore, the objective of this study was to compare 30-day mortality for people with ESRD and COVID-19 (cases) to matched people with ESRD before the COVID-19 pandemic (historical controls).

The study data were provided by TriNetX, a global federated health research network with access to electronic medical records (EMRs) from participating healthcare organisations, including academic medical centres, speciality physician practices and community hospitals, predominately in the United States (US). The TriNetX network was searched on November 3, 2020. ESRD was defined using the International Classification of Disease (ICD)−10-Clinical Modification (CM) code N18.6. Cases were aged ≥18 years with COVID-19 and ESRD (ICD-10-CM code N18.6) recorded in EMRs between January 20, 2020 (date COVID-19 first confirmed in the US) [5] and October 3, 2020 (to allow for at least 30 days follow-up for all included patients). Historical controls were aged ≥18 years with ESRD (ICD-10-CM code N18.6) recorded in EMRs between January 20, 2019 and October 3, 2019. For both the case and control groups, only patients with first-recording of ESRD in EMRs during the specified time periods were included, therefore, patients were excluded if they had the ICD-10-CM code N18.6 included in EMRs prior to the specified dates. At the time of the search, 44 participating healthcare organisations had data available for patients meeting the study inclusion criteria. COVID-19 was identified using criteria provided by TriNetX based on Centres for Disease Control and Prevention (CDC) coding guidelines using ICD-10-CM codes, or specific laboratory Logical Observation Identifiers Names and Codes [6].

All statistical analyses were completed on the TriNetX platform. Baseline characteristics were compared with chi-squared tests or independent-sample t-tests. Cases and historical controls were 1:1 propensity score matched using logistic regression for age, sex, race, respiratory diseases, diseases of the nervous system, hypertension, heart failure, atrial fibrillation and flutter, other cardiac arrhythmias, ischaemic heart disease, cerebrovascular diseases, diabetes mellitus, neoplasms and mental, behavioural and neurodevelopmental disorders. Kaplan-Meier survival curves with log-rank tests and Risk Ratios with 95% Confidence Intervals (CIs) for 30-day mortality comparing cases and historical controls were produced. Statistical significance was set at $p<0.05$.

To gain access to the data in the TriNetX research network, a request can be made to TriNetX (https://live.trinetx.com), but costs may be incurred, a data sharing agreement would be necessary, and no patient identifiable information can be obtained.

Of the participating sites within the TriNetX network, 27,961 patients met the inclusion criteria for historical controls with ESRD and 865 patients met the inclusion criteria for cases with ESRD and COVID-19. Of the patients with ESRD and COVID-19, 73.2% ($n = 633$) were recorded as having a hospital inpatient visit two weeks before or after their COVID-19 diagnosis. Compared to cases, historical controls were younger, had a higher proportion of females, had a higher proportion of people identified as white and had a lower proportion of people with a history of the health conditions included in subsequent propensity score matching (Table 1). Table 1 also shows the characteristics of the cases and historical controls after 1:1 propensity score matching. After 1:1 propensity score matching, there were 863 patients in each cohort and the cohorts were well balanced (all differences on age, race, sex and included health conditions $p>0.05$).

Before propensity score matching, 30-day mortality was higher in cases than historical controls (Log Rank test $p<0.0001$). For cases, 30-day mortality was 12.7% ($n = 110$ of 865 patients), compared to 3.0% of historical controls ($n = 847$ of 27,961 patients). The Risk Ratio for 30-day mortality was 4.20 (95% CI: 3.48, 5.06) for cases compared to historical controls. After propensity score matching, 30-day mortality remained higher in cases than historical controls (12.7% of cases ($n = 110$ of 863 patients) compared to 3.4% of historical controls ($n = 29$ of 863 patients); Log Rank test $p<0.0001$, Fig. 1). The Risk Ratio for 30-day mortality was 3.80 (95% CI: 2.55, 5.65) for cases compared to historical controls after propensity score matching.

Sensitivity analyses were conducted excluding people with kidney transplant identified from ICD-10-CM or procedure codes, up to 30-days after ESRD was coded in EMRs, and showed no important difference in the results (data not shown).

The current study of over 1700 people with ESRD showed that COVID-19 was associated with significantly higher 30-day mortality when compared to propensity score matched patients without COVID-19.

In this study, 13% of people with ESRD died with COVID-19, compared to 3% of historical controls. Evidence from studies in China suggest people with chronic kidney disease are at a higher risk of severe infection with COVID-19 [1]. Recent studies from the United Kingdom (UK) and the US suggested chronic kidney disease associates with higher mortality for patients with COVID-19 [7, 8]. Furthermore, a study of patients hospitalised with COVID-19 in the US suggested higher in-hospital deaths in patients with ESRD [9]. However, patients with ESRD have substantially higher mortality than the general population so

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Table 1
Baseline characteristics of the patients with end stage renal disease with and without COVID-19, before and after propensity score matching.

	Before propensity score matching			After propensity score matching		
	ESRD and COVID-19 (*n* = 865)	ESRD, no COVID-19 (*n* = 27,961)	P-value	ESRD and COVID-19 (*n* = 863)	ESRD, no COVID-19 (*n* = 863)	P-value
Age (years), mean (SD)	61.2 (14.3)	60.0 (15.0)	0.02	61.2 (14.3)	61.3 (14.8)	0.90
Female	37.9 (328)	42.6 (11,907)	0.006	38.0 (328)	38.5 (332)	0.84
Race						
White	36.1 (312)	52.1 (14,554)	<0.001	36.2 (312)	36.8 (318)	0.76
Black or African American	37.9 (328)	26.6 (7426)	<0.001	37.8 (326)	36.3 (313)	0.52
Asian	3.6 (31)	3.6 (1011)	0.96	3.6 (31)	4.5 (39)	0.33
Native Hawaiian or other Pacific Islander	1.2 (10)	0.3 (75)	<0.001	1.2 (10)	1.2 (10)	1.00
American Indian or Alaska Native	1.2 (10)	0.8 (219)	0.22	1.2 (10)	1.2 (10)	1.00
Unknown	21.4 (185)	16.7 (4676)	<0.001	21.4 (185)	21.7 (187)	0.91
Hypertensive diseases	51.2 (443)	41.1 (11,492)	<0.001	51.3 (443)	54.5 (470)	0.19
Ischaemic heart diseases	22.2 (192)	17.2 (4815)	0.001	22.2 (192)	22.9 (198)	0.73
Heart Failure	22.3 (193)	16.3 (4570)	<0.001	22.4 (193)	21.7 (187)	0.73
Cerebrovascular diseases	14.3 (124)	8.6 (2401)	<0.001	14.1 (122)	14.6 (126)	0.78
Atrial fibrillation and flutter	11.3 (98)	8.2 (2300)	0.001	11.4 (98)	10.4 (90)	0.54
Other cardiac arrhythmias	12.5 (108)	8.4 (2358)	<0.001	12.5 (108)	12.3 (106)	0.88
Diabetes Mellitus	39.5 (342)	29.6 (8263)	<0.001	39.4 (340)	42.6 (368)	0.17
Neoplasms	16.9 (146)	14.8 (4147)	0.10	16.9 (146)	16.2 (140)	0.70
Diseases of the respiratory system	46.1 (399)	26.0 (7272)	<0.001	46.0 (397)	46.2 (399)	0.92
Diseases of the nervous system	36.2 (313)	25.0 (6992)	<0.001	36.0 (311)	39.7 (308)	0.88
Mental, behavioural and neurodevelopmental disorders	27.3 (236)	20.8 (5816)	<0.001	27.3 (236)	25.8 (223)	0.48

ESRD: end stage renal disease; SD: standard deviation.

this may be expected. By comparing people with ESRD and COVID-19 to historical matched controls with ESRD without COVID-19, the results of the current study suggest that COVID-19 further increases mortality nearly 4-fold in people with ESRD.

The study utilised a global federated research network with a large number of patients with ESRD and propensity score matched those with ESRD and COVID-19 to historical controls with ESRD without COVID-19, captured in the same time frame 12-months prior. The main limitation is that characterisation of ESRD and other health conditions is based on ICD codes from EMRs, and previous studies have suggested reporting of conditions with ICD codes may vary by patient characteristics and between different healthcare organisations [10]. Although patients were matched for many co-morbidities and demographic factors, residual confounding may still be possible.

In conclusion, this study suggests that mortality for people with ESRD and COVID-19 is significantly higher than for people with ESRD without COVID-19. Measures to prevent infection are particularly important for people with ESRD, as well as the targeting of early interventions such as increased monitoring post-infection and should be considered for people with ESRD.

Declaration of Competing Interest

Stephanie L Harrison and Benjamin JR Buckley: None declared.

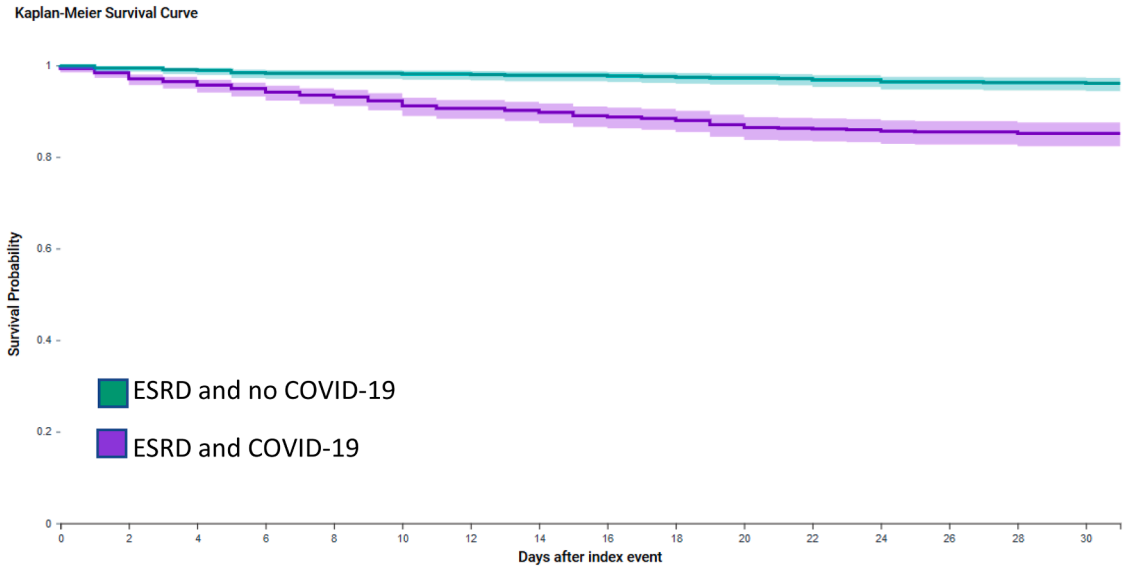

Fig. 1. Kaplan-Meier survival curve of 30-day mortality for cases (adults with end stage renal disease and COVID-19) compared to historical controls (adults with end stage renal disease without COVID-19).
ESRD: end stage renal disease. Propensity score matched for age, sex, race, respiratory diseases, diseases of the nervous system, hypertension, heart failure, atrial fibrillation and flutter, other cardiac arrhythmias, ischaemic heart disease, cerebrovascular diseases, diabetes mellitus, neoplasms, mental, behavioural and neurodevelopmental disorders. Purple line is cases (adults with end stage renal disease and COVID-19) and green line is historical controls (adults with end stage renal disease without COVID-19).

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Stephanie L. Harrison[a,*], Benjamin J.R. Buckley[a], Elnara Fazio-Eynullayeva[b], Paula Underhill[c], Deirdre A. Lane[a,d], Gregory Y.H. Lip[a,d]
[a] *Liverpool Centre for Cardiovascular Science, University of Liverpool and Liverpool Heart & Chest Hospital, Liverpool, United Kingdom*
[b] *TriNetX Inc., Cambridge, MA, United States*
[c] *TriNetX Inc., London, United Kingdom*
[d] *Aalborg Thrombosis Research Unit, Department of Clinical Medicine, Aalborg University, Aalborg, Denmark*

[*] Corresponding author: Dr Stephanie Harrison, Liverpool Centre for Cardiovascular Science, University of Liverpool, William Henry Duncan Building, Liverpool, L78TX United Kingdom.
E-mail address: stephanie.harrison@liverpool.ac.uk (S.L. Harrison).