



COVID-19 infection in patients with end-stage kidney disease undergoing renal replacement therapies in Korea

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Background: The global coronavirus disease 2019 (COVID-19) pandemic has placed patients with end-stage kidney disease (ESKD) at heightened risk owing to their vulnerability to infections. Our study focused on patients with ESKD, examining COVID-19 incidence, hospitalization, and mortality in relation to their renal replacement therapy (RRT) type and identifying factors influencing COVID-19 hospitalization.

Methods: We conducted a retrospective cohort study using health insurance claims data from the Health Insurance Review and Assessment Service for patients with ESKD between July 2017 and June 2022. COVID-19 data for the general population were sourced from the Korea Disease Control and Prevention Agency.

Results: Patients undergoing hemodialysis (HD) constituted 90.7% of the cohort, followed by kidney transplantation (KT) recipients and peritoneal dialysis (PD). After adjusting for every 10,000 individuals, KT recipients exhibited the highest COVID-19 incidence, followed by those undergoing HD and PD, whereas the general population showed a higher infection rate of 43.64. Patients undergoing HD had the highest hospitalization rates, followed by KT recipients and those undergoing PD. The mortality rate per 10,000 individuals was highest in HD, followed by PD, the general population, and KT. Multivariate analysis indicated that age, RRT duration, residence in a nursing hospital, and comorbidities were associated with COVID-19 hospitalization.

Conclusion: Among RRT modalities, KT recipients displayed the highest COVID-19 incidence, whereas those undergoing HD exhibited the highest hospitalization and mortality rates. This study contributes to our understanding of infectious diseases in patients on RRT and aids in preparedness for future infectious disease outbreaks.

Keywords: COVID-19, Dialysis, Kidney transplantation, Renal replacement therapy

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Introduction

Coronavirus disease 2019 (COVID-19), caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is a global pandemic that has caused numerous infections and deaths since 2019. South Korea was also affected by the pandemic, and as of August 2023, 34,571,873 people had been infected with SARS-CoV-2 [1]. During the pandemic, chronic kidney disease was a risk factor for severe COVID-19 and mortality [2–4]. Particularly, patients undergoing dialysis show a higher incidence of COVID-19 than those with chronic kidney disease who do not require renal replacement therapy (RRT) [5].

End-stage kidney disease (ESKD) has been associated with a considerably increased rate of infections due to uremia and associated immune dysfunction [6]. In addition, patients who undergo kidney transplantation (KT) are vulnerable to infection because they are administered immunosuppressive agents. In addition to these background medical conditions, patients who require RRT, especially those who undergo hemodialysis (HD) and visit dialysis units three times a week, are at an increased risk of contracting COVID-19 because they must visit medical institutions regularly. Therefore, guidelines to prevent COVID-19 transmission and protect patients have been implemented in dialysis units and hospitals in South Korea [7].

Over the past 4 years since the outbreak began, many studies have been conducted on COVID-19. However, Korean data comparing the incidence and outcomes of COVID-19 based on RRT modality in patients with kidney failure are lacking [8,9]. Here, we aimed to analyze COVID-19 incidence and COVID-19-related hospitalization and mortality rate based on RRT modality in patients with ESKD. Furthermore, we aimed to analyze the factors affecting COVID-19 hospitalization in these patients. This analysis may be helpful in preparing for future pandemics.

Methods

Ethics consideration

This retrospective cohort study, based on nationwide health insurance claims data, explored COVID-19 in patients with ESKD undergoing RRT. We analyzed variations based on RRT type and identified the risk factors and out-

comes for COVID-19 hospitalization cases using univariate and multivariate regression analyses. This study was approved by the Institutional Review Board of Ajou University Hospital (No. AJOUIRB-EX-2022-565). All research methods were conducted in accordance with the Declaration of Helsinki, as revised in 2013.

Data source

The data for patients with ESKD originated from health insurance claims data provided by the Health Insurance Review and Assessment Service (HIRA). However, COVID-19 data for the general population were sourced from the Korea Disease Control and Prevention Agency (KDCA). Data between July 2017 and June 2022 were used in this study. The HIRA claims dataset represents one of the primary sources of real-world data in Korea, encompassing medical utilization records, cost data, and other information such as hospital visits for various diagnoses and received medical procedures and covering 98% of the entire population. The national notifiable disease surveillance system from the KDCA manages and tracks confirmed patients with COVID-19 infection and their epidemiological characteristics.

Study population

The study population comprised patients with ESKD receiving RRT between July 2017 and June 2022 who were selected based on diagnostic information from the International Classification of Diseases, the 10th revision (ICD-10) codes and procedure codes in the claims data. Individuals who died before 2020, before the COVID-19 outbreak began, were excluded. During the study period, the study population was classified into three groups: HD, peritoneal dialysis (PD), and KT. Patients with ESKD who underwent two or more types of RRT were categorized based on the following criteria. 1) Patients were defined based on the RRT type they were undergoing at the time of COVID-19 infection. 2) Patients were defined based on the RRT they received during the COVID-19 pandemic. For example, patients who underwent HD before 2020 and those who underwent PD after 2020 were classified as patients who underwent PD. 3) KT recipients were categorized as patients who underwent KT regardless of whether they had

previously undergone HD or PD. Patients who underwent HD or PD after KT were classified as undergoing HD or PD, respectively. 4) Patients who underwent HD and PD after the pandemic were excluded from the analysis because their RRT types could not be determined (Fig. 1).

Case ascertainment of end-stage kidney disease and renal replacement therapy

Patients with ESKD were defined as individuals who had

one or more outpatient visits with ICD-10 code 'N18.' Patients with ESKD on RRT were identified based on specific procedure codes, including O7020, O7021, and O9991 for HD, O7076 and O7077 for PD, and R3280 for KT. For HD and PD, patients were ascertained if they had both the relevant ICD-10 code and corresponding procedure codes for 3 months or more. KT recipients were defined as patients who underwent KT if they had an ICD-10 code and at least one recorded procedure code.

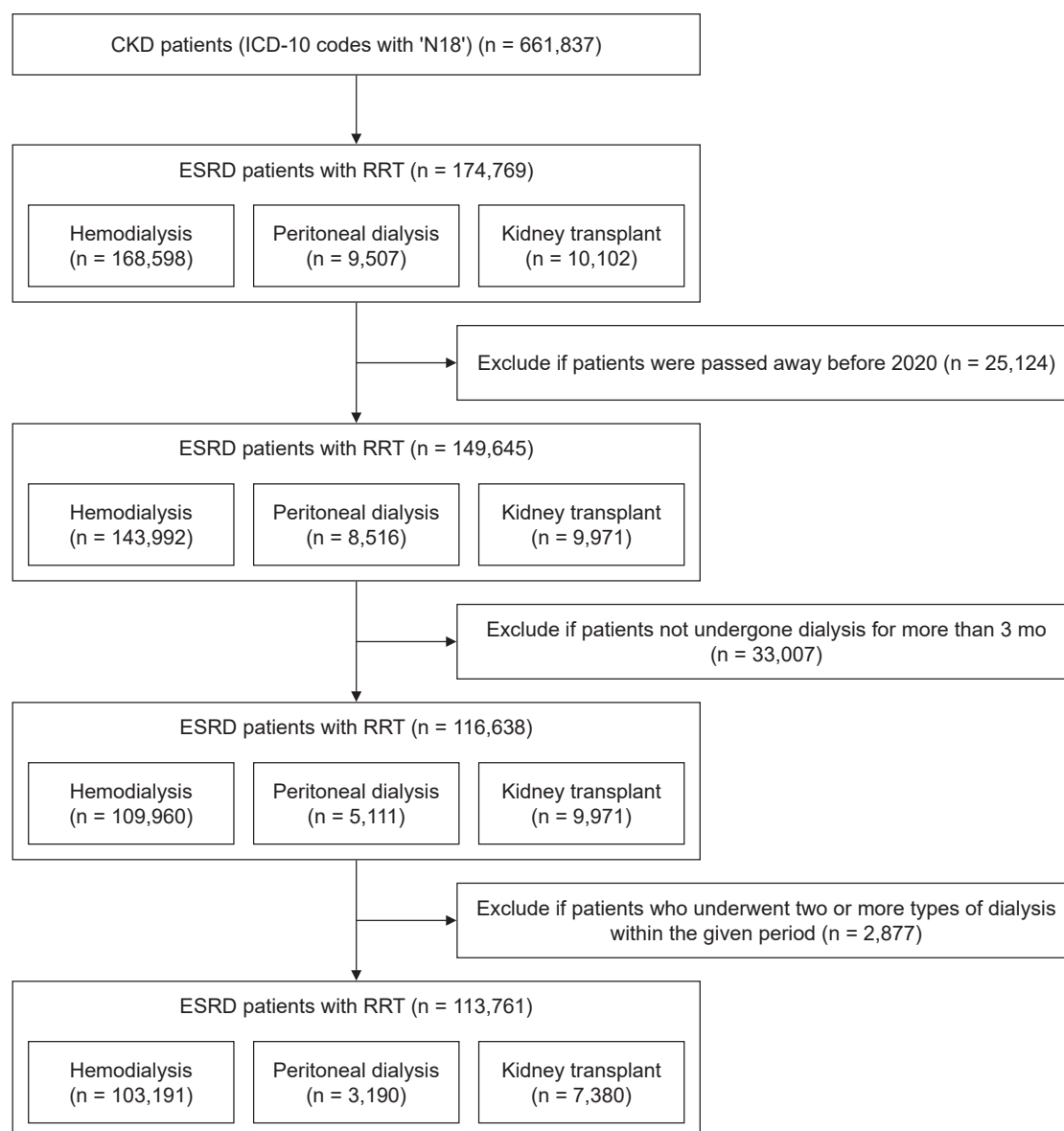


Figure 1. Flowchart of the study population.

CKD, chronic kidney disease; ESRD, end-stage renal disease; ICD-10, the International Classification of Diseases, the 10th revision; RRT, renal replacement therapy.

Definition of variables

To calculate the COVID-19 infection per population using the RRT modality, we divided the number of patients infected with COVID-19 by the total number of patients observed for each RRT type over the study period. COVID-19 infection is defined as patients who visited the hospital as outpatients or inpatients with the ICD-10 codes 'B342,' 'B972,' 'U071,' or 'U072' as the primary diagnosis or the first listed condition. Regarding the general population, the COVID-19 infection rate per population was determined by dividing the reported number of COVID-19 cases from KDCA by the population data provided by Statistics Korea. COVID-19 hospitalization and death rates were computed using the same method as the COVID-19-related mortality data for the general population derived from Statistics Korea's cause-of-death statistics. COVID-19 hospitalized patients are defined as those who, among the COVID-19-infected individuals, had one or more admissions specifically due to COVID-19. COVID-19 death refers to patients within healthcare facilities whose treatment outcomes for COVID-19 are recorded as 'death' in the claims data, indicating fatalities specifically due to COVID-19.

When identifying the risk factors for COVID-19 hospitalization, the following variable definitions were applied: age, sex, insurance type, and diabetes mellitus (DM) status were the most recent diagnoses. The Charlson comorbidity index (CCI) score, used to denote baseline health status, was analyzed from 1 year before RRT commencement to the initiation date [10] ([Supplementary Table 1](#), available online). Comorbidities were ascertained through the main diagnosis or subdiagnosis in the claims data, with dementia and human immunodeficiency virus infection remaining unconfirmed within the CCI score owing to data privacy concerns.

Statistical analysis

The characteristics of patients with ESKD and those hospitalized for COVID-19 are described using summary statistics. Differences among the RRT types were analyzed using the chi-square test and analysis of variance (ANOVA). For patients who underwent HD, the chi-square and t tests were performed based on whether they were in a nursing hospital. For both comparisons, continuous variables were

analyzed using the ANOVA and t tests, whereas categorical variables were analyzed using the chi-square analysis. Univariate and multivariate logistic regression models were used to investigate risk factors associated with COVID-19 hospitalization. The initial step involved conducting univariate logistic analysis for individual covariates, utilizing odds ratios with 95% confidence intervals to assess the association between COVID-19 hospitalization and each covariate. Covariates that exhibited significant associations in the univariate analysis were incorporated into the final multivariate model, and multivariate analysis was conducted. Statistical significance was set at $p < 0.05$. All statistical tests were performed using SAS version 9.4 (SAS Institute).

Results

This retrospective cohort study utilized nationwide data between July 2017 and June 2022 to examine the disparities in COVID-19 among renal replacement modalities throughout the pandemic period. During the COVID-19 pandemic, 113,761 patients survived and underwent RRT. Patients who underwent HD constituted the majority at 90.7% (103,191), followed by KT at 6.5% (7,380) and PD at 2.8% (3,190). Substantial differences were observed among the three groups in terms of sex, insurance type, COVID-19 infection status, RRT duration, and comorbidities. The proportion of males among those undergoing RRT ranged from 57% to 61%, with the average age being highest in the HD group, followed by the PD and KT groups. Regarding insurance type, the proportion of medical aid recipients was higher, ranging from 9.6% to 18.1%, which is considerably greater than the 3% medical aid rate in the general population [11]. Among patients with DM, the HD group had the highest prevalence (70.6%), and the CCI score, reflecting baseline health status, was also highest in the HD group, at 5.5 points, compared with 4.7 points in the PD and KT groups ([Table 1](#)).

The characteristics of the patients receiving HD at nursing and general hospitals differed. Patients in nursing hospitals were 8 years older, with an average age of 71.0 years. Additionally, the proportion of females was higher among nursing hospital patients. The CCI score was also higher, and the prevalence of cerebrovascular disease and paraplegia were higher among nursing hospital patients ($p < 0.001$) ([Supplementary Table 2](#), available online).

COVID-19 infection by renal replacement therapy modality

During the COVID-19 pandemic, 1.3% ($n = 1,391$) of patients who underwent HD, 0.9% ($n = 30$) of those who underwent PD, and 2.1% ($n = 153$) of those who underwent KT were infected with SARS-CoV-2. The proportion of infected patients who underwent HD residing in nursing hospitals was approximately three times higher than that of other patients. COVID-19-infected individuals across all RRT types tended to have a higher average age, with no sig-

nificant sex differences observed. In the HD and KT groups, the prevalence of DM and CCI scores were higher among COVID-19-infected patients. Individuals with COVID-19 infection in the PD group had lower CCI scores ([Table 2](#); [Supplementary Table 3](#), available online).

Among patients with COVID-19, those who were hospitalized for COVID-19 were older than those who were not hospitalized for COVID-19. No meaningful differences were observed in RRT duration between the two groups, but the CCI scores and DM prevalence of those who were

Table 1. Patients' characteristics of prevalent cases by renal replacement modality between July 2017 and June 2022

Characteristic	HD	PD	KT	p-value
Prevalence	103,191	3,190	7,380	<0.001
Age (yr)	64.0 $\pm$ 13.5	53.9 $\pm$ 14.3	49.7 $\pm$ 12.4	<0.001
Sex				
Male	61,556 (59.7)	1,804 (56.6)	4,481 (60.7)	<0.001
Female	41,635 (40.3)	1,386 (43.4)	2,899 (39.3)	<0.001
Insurance				
NHIS	84,212 (81.6)	2,732 (85.6)	6,667 (90.3)	<0.001
Medical aid	18,725 (18.1)	452 (14.2)	711 (9.6)	<0.001
Veterans	254 (0.2)	6 (0.2)	2 (0.0)	<0.001
DM	72,859 (70.6)	1,709 (53.6)	4,061 (55.0)	<0.001
Duration of RRT (yr)				
<1	19,526 (18.9)	509 (16.0)	542 (7.3)	<0.001
1 to <2	14,371 (13.9)	580 (18.2)	1,203 (16.3)	<0.001
2 to <3	13,903 (13.5)	654 (20.5)	2,021 (27.4)	<0.001
3 to <4	13,036 (12.6)	637 (20.0)	1,844 (25.0)	<0.001
>4	42,355 (41.0)	810 (25.4)	1,770 (24.0)	<0.001
COVID infection	1,391 (1.3)	30 (0.9)	153 (2.1)	<0.001
CCI score	5.5 $\pm$ 2.3	4.7 $\pm$ 2.1	4.7 $\pm$ 2.0	<0.001
Myocardial infarction	6,824 (6.6)	160 (5.0)	227 (3.1)	<0.001
Congestive heart failure	28,596 (27.7)	799 (25.0)	1,508 (20.4)	<0.001
Peripheral vascular disease	22,404 (21.7)	366 (11.5)	1,095 (14.8)	<0.001
Cerebrovascular disease	24,641 (23.9)	485 (15.2)	839 (11.4)	<0.001
Chronic pulmonary disease	41,548 (40.3)	1,106 (34.7)	2,590 (35.1)	<0.001
Rheumatic disease	3,943 (3.8)	119 (3.7)	358 (4.9)	<0.001
Peptic ulcer	30,171 (29.2)	837 (26.2)	2,669 (36.2)	<0.001
Liver disease	8,276 (8.0)	218 (6.8)	446 (6.0)	<0.001
DM	55,078 (53.4)	1,379 (43.2)	3,710 (50.3)	<0.001
DM complication	54,244 (52.6)	1,155 (36.2)	2,687 (36.4)	<0.001
Paraplegia	3,245 (3.1)	52 (1.6)	30 (0.4)	<0.001
Cancer	11,456 (11.1)	220 (6.9)	537 (7.3)	<0.001
Metastatic tumor	1,045 (1.0)	15 (0.5)	17 (0.2)	<0.001
Severe liver disease	1,421 (1.4)	47 (1.5)	42 (0.6)	<0.001

Data are expressed as number only, mean $\pm$ standard deviation, or number (%).

CCI, Charlson Comorbidity Index; DM, diabetes mellitus; HD, hemodialysis; KT, kidney transplantation; NHIS, National Health Insurance Service; PD, peritoneal dialysis; RRT, renal replacement therapy.

hospitalized for COVID-19 were higher than those who did not require hospitalization. COVID-19-related hospitalizations were all single occurrences across the three groups, and the average length of hospital stay was highest among patients who underwent PD at 16.8 days, followed by those who underwent HD and KT. However, the differences were

insignificant (Table 2).

Fig. 2 illustrates the number of COVID-19 cases, COVID-19-related hospitalizations, and COVID-19-related deaths per 10,000 individuals during the study period. Week 1 marked the initial observation of COVID-19 in patients with ESKD undergoing RRT on December 6, 2020.

Table 2. Characteristics of COVID-19 patients and patients hospitalized with COVID-19 by renal replacement modality

Characteristic	HD	PD	KT	p-value
Prevalence	103,191	3,190	7,380	
COVID-19 infected ESKD patients	1,319	30	153	
Age (yr)	66.7 ± 12.9	60.3 ± 13.6	52.7 ± 10.7	<0.001
Sex				0.06
Male	791 (56.9)	14 (46.7)	100 (65.4)	
Female	600 (43.1)	16 (53.3)	53 (34.6)	
Insurance				0.15
NHIS	1,139 (81.9)	26 (86.7)	135 (88.2)	
Medical aid	250 (18.0)	4 (13.3)	17 (11.1)	
Veterans	2 (0.1)	0 (0.0)	1 (0.7)	
DM	1,075 (77.3)	14 (46.7)	98 (64.1)	<0.001
RRT follow-up duration (yr)				<0.001
<1	271 (19.5)	5 (16.7)	21 (13.7)	
1 to <2	199 (14.3)	5 (16.7)	43 (28.1)	
2 to <3	187 (13.4)	8 (26.7)	36 (23.5)	
3 to <4	141 (10.1)	4 (13.3)	22 (14.4)	
>4	593 (42.6)	8 (26.7)	31 (20.3)	
CCI score	5.8 ± 2.2	4.7 ± 2.3	5.0 ± 2.1	<0.001
COVID-19 hospitalized ESKD patients	958	13	46	
Age (yr)	69.2 ± 11.8	63.5 ± 12.4	54.3 ± 12.4	<0.001
Sex				0.28
Male	532 (55.5)	7 (53.8)	31 (67.4)	
Female	426 (44.5)	6 (46.2)	15 (32.6)	
Insurance				0.18
NHIS	780 (81.4)	10 (76.1)	38 (82.6)	
Medical aid	176 (18.4)	3 (23.1)	7 (15.2)	
Veterans	0 (0)	0 (0)	1 (2.2)	
DM	748 (78.1)	6 (46.2)	31 (67.4)	0.007
RRT follow-up duration (yr)				0.006
<1	200 (20.9)	3 (23.1)	9 (19.6)	
1 to <2	145 (15.1)	5 (38.5)	15 (32.6)	
2 to <3	126 (13.2)	2 (15.4)	8 (17.4)	
3 to <4	100 (10.4)	2 (15.4)	5 (10.9)	
>4	387 (40.4)	1 (7.7)	9 (19.6)	
CCI score	6.0 ± 2.2	5.2 ± 2.2	4.9 ± 2.0	0.002
No. of hospitalizations	1.0 ± 0.0	1.0 ± 0.0	1.0 ± 0.0	
Length of stay (day)	11.5 ± 10.9	16.8 ± 13.4	10.1 ± 9.2	0.14

Data are expressed as number only, number (%), or mean ± standard deviation.

CCI, Charlson comorbidity index; COVID-19, coronavirus disease 2019; DM, diabetes mellitus; ESKD, end-stage kidney disease; HD, hemodialysis; KT, kidney transplantation; NHIS, National Health Insurance Service; PD, peritoneal dialysis; RRT, renal replacement therapy.

Throughout the study, the absolute number of COVID-19 cases was highest in patients who underwent HD. However, when adjusted per 10,000 people, the order was KT, HD, and PD, with a weekly average infection rate of 2.43 for KT, 1.64 for HD, and 1.45 for PD. In contrast, the general

population exhibited a significantly higher infection rate (43.64%), which was more than 20 times higher.

When considering COVID-19-related hospitalizations per 10,000 people, HD had the highest average at 1.13 patients, followed by KT and PD. For COVID-19-related deaths per

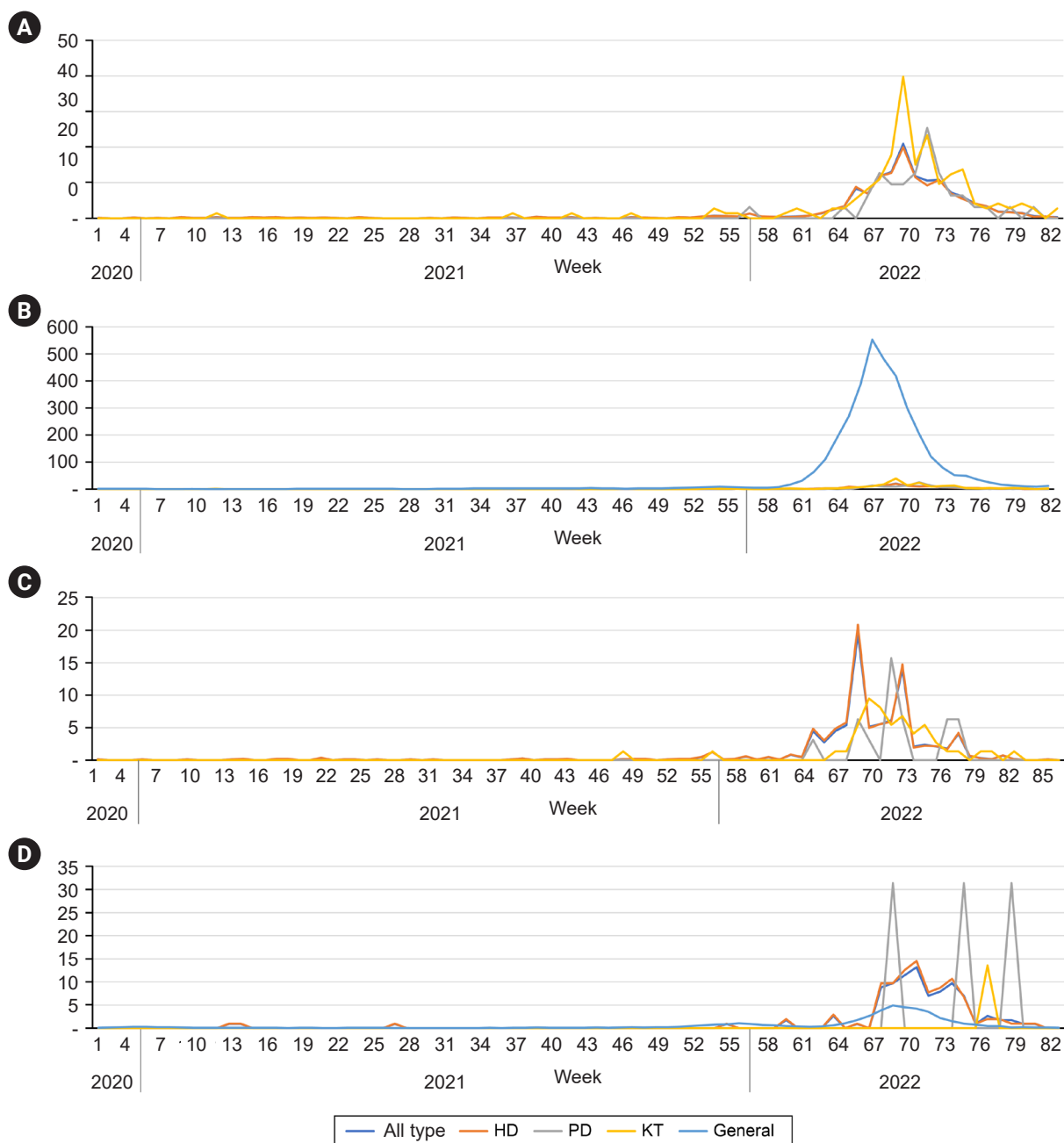


Figure 2. Incidence and numbers of COVID-19 outcomes. (A) Incidence of COVID-19 infections per 10,000 patients undergoing renal replacement therapy (RRT). (B) The number of COVID-19 cases per 10,000 population. (C) The number of hospitalizations due to COVID-19 per 10,000 patients undergoing RRT. (D) The number of COVID-19 deaths per 10,000 population. COVID-19, coronavirus disease 2019; HD, hemodialysis; KT, kidney transplantation; PD, peritoneal dialysis.

10,000 people, HD had the highest rate of 1.2 deaths, followed by PD (1.1 deaths), KT (0.2 deaths), and the general population (0.6 deaths). The rate of COVID-19 occurrence in patients undergoing RRT was relatively low; however, COVID-19-related deaths were higher than in the general population. Additionally, among patients on RRT, KT recipients had a higher incidence of COVID-19 but lower COVID-19-related hospitalization and death rates (Fig. 2; [Supplementary Table 4](#), available online).

Risk factors associated with COVID-19 hospitalization

An analysis was conducted to identify risk factors associated with COVID-19 hospitalization. Univariate analysis revealed that the following variables had a one-to-one association with COVID-19 hospitalization: RRT modality, age, sex, type of hospital, RRT duration, and comorbidities, including myocardial infarction, congestive heart failure, cerebrovascular disease, DM, DM complications, and paraplegia ([Table 3](#)).

Multivariate analysis was conducted to identify the risk factors influencing COVID-19 hospitalization when considering various variables together. When various variables were considered, compared with patients who underwent HD, KT recipients had a 1.22 times increased risk of COVID-19 hospitalization, although this increase was insignificant. Age exhibited an incremental risk of 1.018 for each 1-year increase, whereas RRT duration showed an increment of 1.127 for every 1-year increase. Being in a nursing hospital was associated with a 3.373 times higher risk. Additionally, individuals with comorbidities such as cerebrovascular disease, DM complications, and paraplegia had an increased risk of 1.237, 1.280, and 1.545, respectively. However, significant variables in the univariate analysis, including sex and comorbidities, such as myocardial infarction, congestive heart failure, and DM, were insignificant when considered alongside other variables in the multivariate analysis.

Discussion

In this study, we analyzed the incidence, hospitalization rate, and mortality rate of COVID-19 based on the RRT modality using data provided by the HIRA and investigated the factors that affect COVID-19 hospitalization. Based on our

analysis, among patients undergoing RRT in South Korea, KT recipients had the highest incidence of COVID-19, followed by those undergoing HD and PD; however, all had a lower incidence than the general population. Hospitalization rates were highest among patients who underwent HD, followed by those who underwent KT and PD. Similarly, the mortality rate was the highest among patients who underwent HD, followed by those who underwent PD and KT. The KT recipients exhibited a lower mortality rate than the general population. In the multivariate analysis of risk factors for hospitalization for COVID-19, age, residence in a nursing hospital, RRT duration, history of cerebrovascular disease, DM complications, and paraplegia were shown to be related to COVID-19 hospitalization in patients with ESKD.

In our analysis, among patients receiving RRT, those undergoing HD accounted for the majority (approximately 90.7%), followed by KT (6.5%) and PD (2.8%), which is generally consistent with the statistics of the prevalence of RRT modality reported by the Korean Renal Data System [12]. In this report, HD accounted for approximately 79.4% of RRT in South Korea, with KT (16.5%), followed by PD (4.1%). Although the ratios slightly differed, these data reflect the RRT situation in South Korea.

Among the RRT modalities, KT had the highest incidence of COVID-19, followed by HD and PD. This finding deviated from what was initially anticipated. As patients who underwent HD visit the dialysis center multiple times a week, they might have the highest risk considering the contagious nature of COVID-19. Previous studies conducted in other countries reported that patients on in-center HD showed the highest incidence of COVID-19 among RRT modalities [13,14]. However, in our analysis, patients who underwent HD had a lower incidence of COVID-19 than those who underwent KT. In South Korea, the rapid spread of COVID-19 has led to government regulations enforcing social distancing, which Koreans, including patients, have strictly followed. Moreover, the Korean Society of Nephrology presented practical guidelines for dialysis centers to respond to infectious diseases [7]. These efforts may have contributed to reducing the incidence of COVID-19 in patients undergoing HD.

The incidence of COVID-19 in patients undergoing RRT was considerably lower than that in the general population. Many other studies [15] have reported a higher inci-

Table 3. Risk factors associated with COVID-19 hospitalization

Factor	Univariable		Multivariable	
	OR (95% CI)	p-value	OR (95% CI)	p-value
Type				
Hemodialysis	-	-	-	-
Peritoneal dialysis	0.44 (0.25–0.76)	0.03	0.77 (0.44–1.34)	0.21
Kidney transplantation	0.67 (0.50–0.90)	0.095	1.22 (0.89–1.67)	0.11
Age	1.03 (1.03–1.04)	<0.001	1.02 (1.01–1.02)	<0.001
Sex				
Male	-	-	-	-
Female	1.16 (1.02–1.31)	0.02	1.04 (0.92–1.18)	0.53
Insurance				
NHIS	-	-	-	-
Medical aid	1.06 (0.90–1.24)	0.80	-	-
Veterans	1.30 (0.42–4.06)	0.69	-	-
Type of hospital				
General hospital	-	-	-	-
Nursing hospital	4.45 (3.91–5.07)	<0.001	3.37 (2.93–3.88)	<0.001
RRT duration	1.19 (1.14–1.23)	<0.001	1.13 (1.09–1.17)	<0.001
Comorbidity				
Myocardial infarction	1.34 (1.07–1.67)	0.01	1.10 (0.87–1.38)	0.44
Congestive heart failure	1.19 (1.04–1.36)	0.01	0.93 (0.81–1.07)	0.33
Peripheral vascular disease	1.12 (0.97–1.30)	0.13	-	-
Cerebrovascular disease	1.81 (1.59–2.06)	<0.001	1.24 (1.07–1.43)	0.004
Chronic pulmonary disease	1.10 (0.97–1.24)	0.15	-	-
Rheumatic disease	0.83 (0.59–1.17)	0.29	-	-
Peptic ulcer	1.04 (0.91–1.19)	0.58	-	-
Liver disease	0.93 (0.74–1.18)	0.57	-	-
DM	1.28 (1.13–1.45)	<0.001	1.00 (0.87–1.15)	0.99
DM complication	1.33 (1.17–1.51)	<0.001	1.28 (1.12–1.46)	0.003
Paraplegia	2.84 (2.25–3.58)	<0.001	1.55 (1.12–1.99)	0.008
Cancer	0.89 (0.72–1.09)	0.26	-	-
Metastatic tumor	0.72 (0.34–1.53)	0.40	-	-
Severe liver disease	1.11 (0.67–1.86)	0.68	-	-

CI, confidence interval; COVID-19, coronavirus disease 2019; DM, diabetes mellitus; NHIS, National Health Insurance Service; OR, odds ratio; RRT, renal replacement therapy.

dence of COVID-19 in patients on RRT than in the general population; however, some of these studies explained that because patients on RRT frequently visit medical centers and are perceived to be a high-risk group, COVID-19 tests are more readily available to them than to the general population [16,17]. In South Korea, the costs of COVID-19 testing and treatment after diagnosis were covered by the government, and indications for COVID-19 testing were strictly regulated. Several COVID-19 testing stations have been established to make testing accessible. The COVID-19 response system of Korea has been regarded as excellent

in other countries [18,19]. With this social background, not only high-risk patients on RRT but also the general population could easily undergo COVID-19 tests, which might have contributed to a significantly higher incidence of COVID-19 in the general population. In addition, making a direct comparison is challenging because the characteristics of the pandemic differed by country and region. However, it can be considered that South Korea effectively maintained a robust system for preventing COVID-19 in high-risk patients.

Among the RRT modalities, hospitalization and mortality

rates were highest in HD patients. The age of patients who underwent HD was higher than those of patients who underwent PD and KT. In addition, comorbidities such as DM and DM complications were more prevalent, and the CCI scores were higher in patients who underwent HD. A greater number of patients in the HD group had a longer RRT duration. These factors may be related to higher COVID-19 hospitalization and mortality rates in patients on HD, and this result correlates with those of previous studies [13,14]. As relatively older patients with multiple comorbidities and those admitted to nursing hospitals tend to undergo HD rather than KT or PD, COVID-19 hospitalization and mortality rates are commonly highest in patients who underwent HD.

As KT recipients use immunosuppressive agents, infectious diseases such as COVID-19 can be fatal. The findings from our study present an interesting contrast to what might have been expected. Despite KT recipients exhibiting the highest incidence of COVID-19, the mortality rate was lower than that observed in those who underwent HD and PD and even lower than that in the general population. Previous studies have reported that mortality rates among KT recipients were higher than those in the general population [20–22]. However, in one study, when solid organ transplant recipients diagnosed with COVID-19 were matched with non-solid organ transplant patients diagnosed with COVID-19 based on age, race, and admission status, the odds of COVID-19-associated severe disease and intubation rates were similar between the two groups [23]. Another study reported that KT was not associated with a higher rate of severe disease when matched to control patients with similar chronic conditions or disease severity upon admission [24]. This means that the higher mortality reported in other studies may have been influenced by other characteristics, such as age and comorbidities, rather than the fact that they had undergone transplantation. One study that reported higher mortality in KT recipients indicates that comorbidities had a stronger prognostic effect than immunosuppression use *per se* [21]. Therefore, if immunosuppressive agents are well controlled based on infection severity, KT may not be a risk factor for COVID-19 hospitalization. Moreover, given the low mortality rate among KT recipients in our analysis, it appears that the efforts of patients and medical staff, such as quick diagnosis and monitoring when symptoms occurred, were

successful.

When we analyzed the risk factors associated with COVID-19 hospitalization, age, residence in a nursing hospital, RRT duration, history of cerebrovascular disease, DM complications, and paraplegia were found to be related to COVID-19 hospitalization. Age is a well-known risk factor for COVID-19-related mortality in patients undergoing dialysis and the general population [25,26]. Considering that patients in nursing hospitals tend to be older and frailer than those receiving HD in general hospitals, coupled with the fact that COVID-19 can spread rapidly within nursing facilities, residing in a nursing hospital can be a risk factor for COVID-19 hospitalization [27].

In the multivariate analysis of risk factors for COVID-19 hospitalization, although the RRT modality was related to hospitalization due to COVID-19 in the univariate analysis, it was unrelated to hospitalization when multiple variables were considered together. This result correlates with our previous discussion, suggesting that poor prognosis, such as the mortality of KT recipients, can be related to patients' underlying conditions, such as age or comorbidities, rather than the transplantation. Factors other than the RRT modality might have a greater effect on COVID-19 hospitalization.

To our knowledge, this study is the first Korean study to compare the incidence, hospitalization, and mortality of COVID-19 based on RRT modalities and analyze the risk factors for COVID-19 hospitalization using health insurance claims data provided by HIRA. However, this study has some limitations. First, patients who could not be traced in claims data owing to data privacy concerns were excluded from the study. Second, patients treated in hospitals with fewer than three COVID-19 cases during the study were excluded from the provided statistical data. Additionally, patients who were infected with COVID-19 between January and March 2020 were excluded from the research [28]. However, between January and March 2020, the early stages of the COVID-19 outbreak, the number of COVID-19 cases was extremely low. Although there may have been variations in patient numbers, the patients included in this study adequately represented the overall population of patients who underwent RRT. Third, information on the vaccination status of the patients was unavailable; therefore, whether the patients had been vaccinated and, if so, how many times were not considered. Fourth, we did not include propensity score matching on baseline charac-

teristics such as age and sex. Since COVID-19 data for the general population were sourced from KDCA, we could not access the specific information of general population to perform propensity score matching. However, this study aimed to compare the characteristics of COVID-19 infection according to the RRT modality and analyze risk factors of COVID-19 hospitalization. Fifth, in this study, we could not analyze risk factors for COVID-19 deaths due to the small number of deaths reported during the study period. Further study about COVID-19 death would be helpful. Finally, as isolation guidelines due to the COVID-19 outbreak changed over time, the characteristics of hospitalized patients may have changed accordingly. Hospitalization usually indicates a serious infection, but this may be slightly different in the early stages of COVID-19 pandemic as patients with ESKD sometimes needed hospitalization for the purpose of isolation even if they did not show serious symptoms of COVID-19 [29]. However, because the observation period was relatively short, it was not possible to split the data by period according to isolation guidelines.

In conclusion, among the RRT modalities, KT showed the highest incidence of COVID-19; however, hospitalization and mortality rates were the highest in HD. Several factors, such as age, residence at a nursing hospital, RRT duration, history of cerebrovascular disease, DM complications, and paraplegia, were identified as risk factors for COVID-19 hospitalization in patients receiving RRT. As COVID-19 has not been completely resolved and infectious diseases such as this may appear in the future, this analysis will help to understand the characteristics of infectious diseases in patients on RRT and prepare for other infectious diseases that may occur in the future.

Conflicts of interest

All authors have no conflicts of interest to declare.

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Data sharing statement

The data presented in this study are available from the cor-

responding author upon reasonable request.

Authors' contributions

Conceptualization: IP, MJL

Data curation, Formal analysis, Visualization: AYK

Funding acquisition: HL

Investigation, Validation: HC, AYK

Methodology: AYK, HL

Project administration, Resources, Supervision: HL, MJL

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