


Effectiveness of SARS-CoV-2 vaccines on hemodialysis patients in Japan: A nationwide cohort study

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Abstract

Introduction: This study compared the outcomes of dialysis patients who received SARS-CoV-2 vaccine with those who did not use data from the Japanese COVID-19 registry.

Methods: A total of 1260 dialysis patients with confirmed positive SARS-CoV-2 infection was included in this study. Patients were divided into two groups: patients who experienced breakthrough infection and those who were unvaccinated. The need of oxygen supplementation and mortality risks were compared using multivariate logistic regression analysis.

Results: The mortality rate was 24.2% in unvaccinated patients and 8.6% in breakthrough patients. The odds ratio of need of oxygen supplementation in the breakthrough patients relative to unvaccinated patients was 0.197. The hazard ratio of mortality in the breakthrough patients relative to unvaccinated patients was 0.464.

Conclusion: Our prospective observational study showed that SRAS-CoV-2 vaccination in hemodialysis patients is vital for reducing need of oxygen supplementation and mortality risk.

KEYWORDS

breakthrough infection, COVID-19, dialysis, SARS-CoV-2, SARS-CoV-2 vaccine

1 | INTRODUCTION

The new coronavirus disease (COVID-19) has rapidly spread around the world; a total of 318 648 834 COVID-19 cases and 5 518 343 deaths were reported worldwide as of January 15, 2022 [1]. In Japan, a total of 1 852 958 COVID-19 cases and 18 431 deaths were reported in the general population as of January 16, 2022 [2]. In dialysis patients, on the other hand, a total of 2693 COVID-19 cases and 426 deaths were reported [3]. After the first case of COVID-19 was reported in a dialysis patient, the Japanese Association of Dialysis Physicians, the Japanese Society for Dialysis Therapy, and the Japanese Society of Nephrology jointly established COVID-19 Task Force Committee [4, 5].

SARS-CoV-2 vaccination is thought to be vital to reduce SARS-CoV-2 infection, severe disease, and mortality risks. The effectiveness of the SARS-CoV-2 vaccination in the general population has been reported [6, 7]; in dialysis patients, antibody titers against SARS-CoV-2 receptor binding domain spike protein after vaccination are reported to be positive at a rate similar to that of the general population, but the titers are low [8, 9]. At this point, it is still unknown how the low antibody titer in dialysis patients is associated with increased severity or mortality in dialysis patients in clinical practice. Thus, we investigated the outcome of dialysis patients who received the SARS-CoV-2 vaccine and those who did not using the COVID-19 registry of the COVID-19 Task Force Committee, which has been collecting nationwide data in Japan.

2 | MATERIALS AND METHODS

2.1 | Patients

Surveillance of new cases of COVID-19 in dialysis facilities in Japan was initiated by the COVID-19 Task Force Committee of the Japanese Association of Dialysis Physicians, the Japanese Society for Dialysis Therapy, and the Japanese Society of Nephrology on April 8, 2020 [4]. Data of a total of 2621 dialysis patients with COVID-19 who were registered before October 11, 2021 (the end of 5th

wave in Japan) were extracted from this registry. Among those, data of 1361 patients (1164 patients whose outcome was unknown, 87 patients whose age, dialysis history, and gender were unknown, and 110 patients with missing data for factors required for analysis) were excluded; a total of 1260 patients were included in this analysis.

It should be noted that the treatment policy defined by the Ministry of Health, Labour, and Welfare in Japan for dialysis patients diagnosed with COVID-19 requires hospitalization [4].

2.2 | Outcomes and statistical methods

SARS-CoV-2 infection positive was diagnosed by antigen test or PCR test. Patients who reported SARS-CoV-2 infection positive 2 weeks or more after the second SARS-CoV-2 vaccination (BNT162b2 vaccine) were considered as breakthrough infections. Need of oxygen supplementation and mortality risks were compared between patients who received the vaccine and patients who did not. Patients who needed oxygen supplementation were defined as those who received oxygen supplementation, ventilator, or extracorporeal membrane oxygenation (ECMO) after diagnosis.

Multivariate logistic regression analysis was performed for SARS-CoV-2 vaccination and need of oxygen supplementation, with age, gender, dialysis history, remdesivir administration, and presence of diabetes as adjustment factors. In addition, conditional logistic regression analysis was performed to compare the patients with breakthrough infection and patients who were unvaccinated using propensity score for age, gender, and dialysis history, at the ratio of 1:3. Multivariate logistic regression analysis was also performed for SARS-CoV-2 vaccination and mortality, with age, gender, dialysis history, remdesivir administration, and presence of diabetes as adjustment factors. In addition, stratified log-rank test and stratified Cox regression analysis were performed to compare the patients with breakthrough infection and patients who were unvaccinated using propensity score for age, gender, and dialysis history, at the ratio of 1:3.

TABLE 1 The number of unvaccinated patients and breakthrough patients and their mortality rates

	Age group	<50	50s	60s	70s	≥80	Total
Unvaccinated	<i>n</i>	154	194	249	300	270	1167
	Deaths	8	21	43	92	118	282
	%	(5.2)	(10.8)	(17.3)	(30.7)	(43.7)	(24.2)
Breakthrough	<i>n</i>	3	15	15	37	23	93
	Deaths	0	0	0	4	4	8
	%	(0.0)	(0.0)	(0.0)	(10.8)	(17.4)	(8.6)

TABLE 2 Patients' background

		Unmatched			Matched		
		Unvaccinated	Breakthrough	<i>p</i> -Value	Unvaccinated	Breakthrough	<i>p</i> -Value
Gender	M/F	819/348	61/32	0.350	168/84	56/28	1.000
Age	<60	348	18	0.019	51	17	1.000
	60	249	15		45	15	
	≥70	570	60		156	52	
Dialysis history	<1 year	144	4	0.220	12	4	1.000
	1–5 years	438	42		117	39	
	5–10 years	283	23		63	21	
	10–15 years	149	11		30	10	
	≥15 years	153	13		30	10	
Primary disease	Chronic glomerulonephritis	197	14	0.941	35	11	0.970
	Diabetes mellitus	553	48		135	46	
	Nephrosclerosis	159	14		31	12	
	Others	169	14		36	13	
Hypertension	No/yes	572/558	16/75	<0.001	129/117	15/68	<0.001
Diabetes mellitus	No/yes	550/617	41/52	0.591	101/151	34/50	1.000
Ischemic heart disease	No/yes	772/334	62/27	1	168/73	57/25	1.000
Cerebrovascular disease	No/yes	895/202	73/18	0.779	194/44	69/14	0.869
Chronic respiratory disease	No/yes	1013/101	77/14	0.061	222/21	71/13	0.096
Peripheral arterial disease	No/yes	917/176	69/20	0.137	195/42	63/19	0.328
Malignant tumor	No/yes	940/168	73/18	0.231	195/46	68/16	1.000
Number of complications	0	167	4	0.006	29	2	0.060
	1	339	26		74	25	
	>2	661	63		149	57	
Clinical laboratory values	Alb (g/dl)	3.2 ± 0.6	3.3 ± 0.6	0.065	3.1 ± 0.5	3.3 ± 0.6	0.001
	UN (mg/dl)	56.7 ± 22.2	50.8 ± 19.8	0.078	55.0 ± 21.0	50.7 ± 20.2	0.425
	Cr (mg/dl)	10.4 ± 8.3	9.2 ± 3.3	0.381	8.9 ± 3.5	9.3 ± 3.4	0.332
	CRP (mg/dl)	5.56 ± 6.81	5.46 ± 6.77	0.587	5.55 ± 6.93	5.59 ± 6.90	0.582
	WBC (/μl)	5732 ± 3693	5992 ± 3167	0.266	5611 ± 2907	5998 ± 3242	0.458
	Hb (g/dl)	11.1 ± 1.8	11.6 ± 1.6	0.031	11.4 ± 1.6	11.7 ± 1.6	0.575
Height and weight	Height (cm)	162 ± 10	161 ± 10	0.149	161 ± 11	161 ± 10	0.737
	Dry weight (kg)	61 ± 18	60 ± 15	0.717	59 ± 17	61 ± 15	0.311

Abbreviations: Alb, albumin; Cr, creatinine; CRP, C-reactive protein; Hb, hemoglobin; UN, urea nitrogen; WBC, white blood cell count.

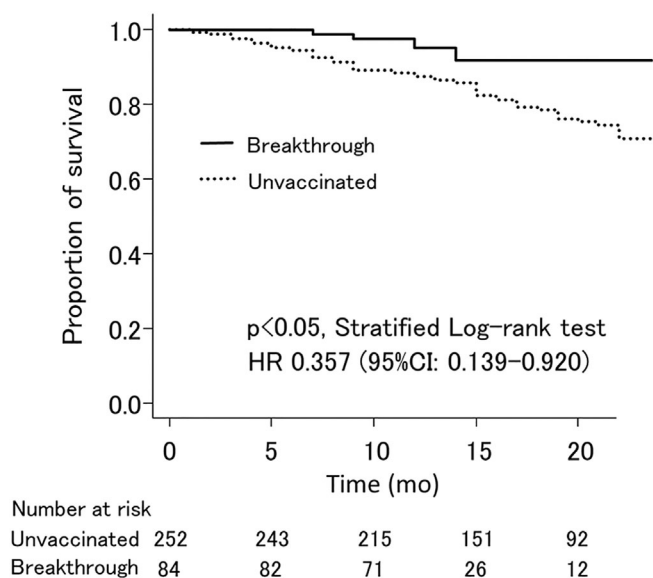


FIGURE 1 Survival of breakthrough patients and unvaccinated patients

All analyses were performed using SPSS Statistics Ver.21 (IBM SPSS Statistics for Windows, IBM, Armonk, NY), and $p < 0.05$ was considered statistically significant.

3 | RESULTS

3.1 | Age and mortality

The number of unvaccinated and breakthrough patients and their mortality rates are shown in Table 1; the patients' backgrounds are shown in Table 2. A total of 1167 infection and 282 death cases were reported in unvaccinated patients; the mortality rate was 24.2%. On the other hand, in breakthrough patients, 93 infection and 8 death cases were reported; the mortality rate was 8.6%, which was significantly less than that in unvaccinated patients ($p < 0.05$). In terms of mortality by age group, breakthrough patients had a 0% mortality rate under the age of 70, and those over 70 had a lower mortality rate compared to unvaccinated patients.

3.2 | SARS-CoV-2 vaccination and oxygen supplementation

The odds ratio of need of oxygen supplementation in the breakthrough patients relative to unvaccinated patients was 0.197 (95% CI: 0.120–0.322, $p < 0.001$). Among matched patients (84 breakthrough patients and 252 unvaccinated patients), the odds ratio of need of oxygen supplementation in the breakthrough patients relative to unvaccinated

patients was 0.243 (95% CI: 0.142–0.416, $p < 0.001$). In both matched and unmatched cohorts, breakthrough patients had significantly less need of oxygen supplementation.

3.3 | SARS-CoV-2 vaccination and mortality

The hazard ratio of mortality in the breakthrough patients relative to unvaccinated patients was 0.464 (95% CI: 0.228–0.945, $p < 0.05$) (Figure 1). Among matched patients (84 breakthrough patients and 252 unvaccinated patients), the hazard ratio of mortality in the breakthrough patients relative to unvaccinated patients was 0.357 (95% CI: 0.139–0.920, $p < 0.05$). In both matched and unmatched cohorts, breakthrough patients had significantly less mortality risk.

4 | DISCUSSION

Since the low antibody titer in dialysis patients after SARS-CoV-2 vaccination has not known to affect the outcome, we conducted a cohort study using real-world data. In our analysis, patients with breakthrough infection had significantly less need of oxygen supplementation and mortality risk compared to patients who were unvaccinated.

Breakthrough infection in dialysis patients at U.S. Renal Care has been reported [10]. Antibody titers in dialysis patients were found to drop to almost the same levels in about 6 months, albeit with variations depending on age, whether the patient has a previous infection with SARS-CoV-2, and the type of vaccine they received. In addition, the peak IgG index in the 60 days after vaccination and the IgG index value in the period immediately preceding infection are important factors for the occurrence of breakthrough infections. Thus, to prevent SRAS-CoV-2 infection, high antibody titer is important.

A large-scale, retrospective, observational study examining the efficacy of two mRNA SARS-CoV-2 vaccines, BNT162b2 and mRNA-1273, in hemodialysis patients in the United States has been reported [11]. The results showed that vaccination with BNT162b2 or mRNA-1273 was associated with a lower risk of COVID-19 diagnosis and lower risk of hospitalization or death in hemodialysis patients. In this prospective observational study using the Japanese registry, multivariate analysis showed a decreased need of oxygen supplementation by 80.3% (95% CI: 67.8–88.0) and improved survival outcomes by 53.6% (95% CI: 5.5–77.2). Furthermore, propensity score matching analysis also showed similarly a decrease in the need of oxygen supplementation by 75.7% (95% CI: 58.4–

85.8) and improved survival outcomes by 64.3% (95% CI: 8.0–86.1). Taken together, SRAS-CoV-2 vaccination in hemodialysis patients is vital for reducing disease severity and improving survival outcome. There are some limitations: not all facilities measure antibody titers since this is a nationwide survey, and we selected only five adjustment factors (i.e., age, gender, dialysis history, remdesivir administration, and presence of diabetes) for the logistic regression model.

5 | CONCLUSION

Our prospective observational study showed that SRAS-CoV-2 vaccination in hemodialysis patients is vital for reducing the need of oxygen supplementation and mortality risk.

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CONFLICT OF INTEREST

The authors have no conflicts of interest directly relevant to the content of this article.

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