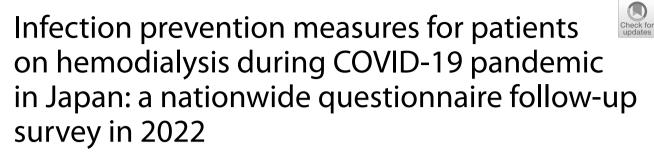
## RESEARCH

Renal Replacement Therapy

**Open Access** 



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## Abstract

**Background** Coronavirus disease (COVID-19) continues to be prevalent in 2023, and infection control measures against it remain important in medical practice. In 2020, we conducted a questionnaire survey mainly on the implementation of infection prevention measures for patients on hemodialysis under COVID-19 pandemic in Japan. Since then, vaccination for COVID-19 has been initiated and the outbreak of new variants had occurred. Infection prevention measures at dialysis facilities have possibly changed; therefore, we conducted a follow-up survey.

**Methods** Between October 11 and November 14, 2022, we distributed a questionnaire survey to 4,198 dialysis facilities in Japan. The survey investigated (i) the characteristics of the facilities, (ii) infection prevention measures in routine dialysis practice, (iii) experience in treating COVID-19-positive/suspected dialysis patients, (iv) feasibility of various isolation measures, (v) nosocomial transmission, (vi) COVID-19 vaccination status, and (vii) impact on medical practice and economic aspects. We then compared the answers from the previous survey conducted in 2020 with those of the current survey.

**Results** Responses were obtained from 1956 facilities (response rate: 46.6%). Overall, 83.5% of the facilities have examined and treated patients with COVID-19. While the compliance rate improved since the previous survey, it remained low for some factors such as linen exchange. More than 60% of the facilities reported that they were coping with a lack of manpower and space for isolation. Most patients at the surveyed facilities were vaccinated for COVID-19; only 2.8% were unvaccinated. Compared with unvaccinated patients, vaccinated patients had a lower infection rate (vaccinated 9.2% vs. unvaccinated 41.2%; crude risk ratio [RR] 0.22; 95% confidence interval [CI] 0.22–0.23; p < 0.001) and mortality rates (vaccinated 0.3% vs. unvaccinated 6.6%; crude RR 0.05; 95% CI 0.04–0.06; p < 0.001).

**Conclusion** The implementation rates of most of the infection prevention measures improved compared to those in the previous survey. However, labor shortages, lack of space, and problems coordinating with other medical facilities remain a challenge. COVID-19 vaccination was significantly associated with reduced infection and mortality in Japanese patients on hemodialysis, which should be confirmed by further studies with confounding adjustment.

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**Keywords** COVID-19, Hemodialysis, Infection prevention measures, Isolation, Nosocomial transmission, Personal protective equipment, Vaccine

## Background

As of January 2023, more than three years have passed since the outbreak of the coronavirus disease (COVID-19), caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), in China at the end of 2019. However, the disease remains a pandemic and continues to have a significant impact on the care of patients on dialysis [1-3]. Patients on hemodialysis are in the clinic three times a week, and contact a large number of people, leading to a higher risk for infection and death than the general population [4-10]. Thus, coping with and preventing the spread of COVID-19 during dialysis treatment is clinically and socially important.

Previously, we conducted a nationwide questionnaire survey on COVID-19 prevention and treatment systems in hemodialysis and nephrology facilities between October 20 and November 16, 2020 (between the second and third waves in Japan) and reported on the infection prevention measures and medical practice of 2227 out of 4198 Japanese dialysis facilities (response rate: 53%) [11, 12]. In the survey, we reported the low compliance rate of some components related to infection prevention measures, feasibilities regarding isolation protocols, and number of nosocomial transmissions.

After the previous survey, vaccination, a new measure against COVID-19 infection, was adopted [13, 14]. Simultaneously, there was a marked increase in the number of COVID-19 cases worldwide due to the emergence of various variants, especially the highly infectious Omicron variant during the sixth wave in Japan [15, 16], and it also affected patients under hemodialysis [17]. Considering that these changes occurred after the previous survey, it seems likely that infection prevention measures and medical care at dialysis facilities have changed. However, no nationwide surveys on infection prevention measures among dialysis facilities have been reported since our last survey.

Recently, a follow-up survey was conducted between October 11 and November 14, 2022 (between the seventh and eighth waves in Japan) at dialysis facilities belonging to the Japanese Association of Dialysis Physicians (JADP) and the Japanese Society for Dialysis Therapy (JSDT). Our study goal was to identify current issues in infection prevention by re-examining items on infection prevention measures in the previous survey and to determine the feasibility of various isolation protocols. Additionally, we explored vaccination status of Japanese hemodialysis patients and the impact of COVID-19 on medical and economic aspects at each facility.

## Methods

## **Surveyed facilities**

This survey was conducted in cooperation with the COVID-19 task force committee established by JADP, JSDT, and the Japanese Society of Nephrology, and several authors of this report are members of the committee [6, 11]. As in the previous survey, the current survey was conducted among dialysis facilities in Japan (n=4198) belonging to the JADP and/or JSDT, which are the preeminent societies representing dialysis therapy in Japan [11].

### Development of the questionnaire

The questionnaire used in this study is shown in Additional file 2 and Additional file 3 (Japanese version and English translation). The questionnaire consists of seven parts as follows: (i) the characteristics of the facilities (four questions, no. 1, no. 2, no. 4, and no. 5); (ii) infection prevention measures in routine dialysis practice (11 questions, nos. 6–16); (iii) experience in treating COVID-19 positive/suspected dialysis patients (four questions, nos. 17–20); (iv) feasibility of various isolation measures (seven questions, nos. 21-27); (v) nosocomial transmission in dialysis units (three questions, nos. 28–30); (vi) COVID-19 vaccination status (13 questions, nos. 31–43); and (vii) impact on medical care and economic aspects (four questions, no. 3 and nos. 44–46). Questions (i)–(v) were similar to those in the previous survey. The questions on infection prevention measures were prepared using the infection prevention checklist of the JADP "Guidelines for standard dialysis operations and infection prevention in dialysis facilities" (5th edition) [18]. Meanwhile, questions (i) no. 2, (ii) no. 15 and no. 16, (iii) no. 19 and no. 20, (vi), and (vii) are new items for this survey, not mentioned in the guideline. They are included because the recommendation and implementation of these items started during the Omicron strain's pandemic (the sixth wave) in Japan [19].

In addition, we made minor changes, as follows. Question (i) no. 5 previously asked each facility about the number of patients undergoing dialysis per day; in the current survey, the question was revised to ask for the number of patients undergoing dialysis per week. In question (ii) no. 13, "Linens are changed for each patient" was changed to "Linens are changed for each patient, or non-permeable bed mats are used, and the dialysis environment is disinfected between each patient".

We used the criteria proposed by the Japanese Ministry of Health, Labour and Welfare for the duration of treatment of patients with COVID-19 and for the termination of isolation: "Day 0 is the day of onset of COVID-19 (the day on which symptoms associated with infection appeared), 10 days have passed since Day 1, and 72 h have passed after symptoms abated" [20]. Additionally, since the definition of nosocomial transmission of COVID-19 has not been established [21], we defined it as horizontal transmission of COVID-19 among staff members and patients at a facility.

## Data collection

The questionnaires were mailed to the eligible facilities, and e-mails requesting responses were sent from the two related academic societies (JADP and JSDT). One person from each facility (physician, nurse, medical technician, medical office worker, etc.) was asked to respond to the questionnaire as the representative of the facility. This questionnaire could be answered either anonymously or non-anonymously. Non-anonymous responses were checked for duplicates; if duplicates were found, only the most recent response was considered valid. The response period was between October 11 and November 14, 2022 (between the seventh and eighth waves in Japan). The questionnaire could be answered either by sending a fax or by filling out an online form.

## Data analysis

Continuous values were expressed as mean±standard deviation or median (interquartile range), while binary values were expressed as proportion (%). Data obtained in the previous survey and in this survey were compared in the main analysis regarding the implementation status of infection prevention measures. In the previous survey, we examined the implementation status of infection prevention measures before the outbreak of COVID-19 and in 2020 (after the outbreak) [11], which would be partly re-shown in the result section of the current paper. The current study used chi-squared test to compare the results between the 2020 and 2022 surveys. If the same or similar question was asked in the previous survey, sensitivity analysis using McNemar's test was conducted on facilities that responded to both previous and current surveys. The sub-group analyses using chi-squared test were also conducted by clinics and hospitals, separately.

The number of COVID-19 vaccine recipients was calculated by subtracting the number of unvaccinated patients ([vi] no. 38) from the number of dialysis patients

treated per week ([i] no. 5) in the facilities that responded to the questionnaire. Each institution was requested to provide the number of infections and deaths in vaccinated and unvaccinated groups. We then investigated the COVID-19 infection and death rates in both groups (data on individual cases was not collected). Additionally, the chi-squared test was used to compare the COVID-19 infection and death rates between vaccinated and unvaccinated individuals.

A small number of unreasonable or inconsistent answers (e.g., the number of dialysis patients receiving vaccines were larger than the total number of dialysis patients in a facility) were excluded from each question. All statistical analyses were performed using JMP Pro 16.2.0 (SAS Institute Inc., Cary, North Carolina, USA) software.

## Results

## Characteristics of the facilities

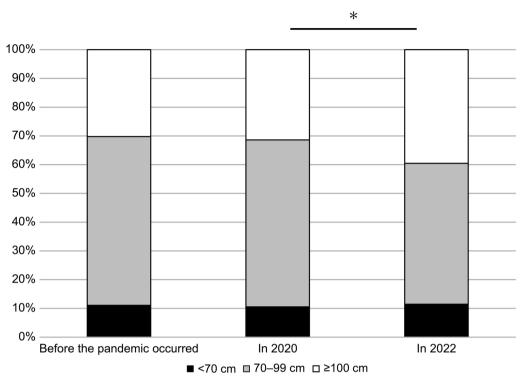
Responses were obtained from 2046 out of 4198 facilities, of which 264 facilities responded anonymously. Excluding 90 responses that were either duplicates or exclusions (not a member facility of either JADP or JSDT), responses from 1956 facilities (response rate: 46.6%) were included in the analysis. Overall, 1060 facilities (54.2%) responded to both current and previous surveys. The response rate (40–58%) was not very different by region: Hokkaido, 39.4%; Tohoku, 47.6%; Kanto (other than Tokyo), 51.7%; Tokyo, 58.2%; Chubu, 45.6%; Kinki, 39.7%; Chugoku, 46.7%; Shikoku, 45.9%; Kyushu, 41.7%; and Okinawa, 43.1%.

Of the responding facilities, 51.7% were clinics (<20 inpatient beds), 47.6% were hospitals ( $\geq$ 20 inpatient beds), and the remaining 0.6% were neither. This ratio was approximately similar to JSDT's 2021 data [22].

# Infection prevention measures in routine hemodialysis practice

Survey results on bed spacing at each facility are summarized in Fig. 1. A comparison between the 2020 and 2022 surveys showed an increase from 31.4 to 39.5% in facilities with a bed spacing of  $\geq 1$  m and a corresponding decrease from 58.1 to 49.0% in facilities with spacing of 70–99 cm (p < 0.001). However, the proportion of facilities with beds spaced < 70 cm apart did not significantly change before the outbreak, in 2020, and in 2022. Similar findings were also obtained in the sensitivity analysis restricted to institutions contributing to both surveys (Additional file 1: Table S1). In the sub-group analyses, both hospitals and clinics showed similar changes between 2020 and 2022 (Additional file 1: Table S2).

The results on the implementation of infection prevention measures are listed in Table 1 (note that in Table 1,



**Fig. 1** Differences in bed spacing during periods of outbreak at each dialysis facility. Each facility is placed into one of the three bed-spacing categories, and the ratio of each is shown at three time points: before the pandemic occurred, in 2020 (previous survey), and in 2022 (current survey). The results in 2020 and 2022 were compared by chi-squared test. \*p < 0.05

**Table 1** Implementation status of infection prevention measures at each dialysis facility before the outbreak of COVID-19, in 2020 (previous survey), and in 2022 (current survey)

Q	Questions	Implementatio	p value		
		Before the outbreak of COVID-19 N = 2227 (%)	ln 2020 (Previous survey) N = 2227 (%)	In 2022 (Current survey) N = 1956 (%)	
1	Staff members with symptoms of infection such as fever and diarrhea are examined by a doctor whether they can work or not before entering the dialysis room	1559 (70.0)	2092 (93.9)	1831 (93.6)	0.661
2	Staffs who perform initiating and terminating operation are wearing masks	1937 (87.0)	2186 (98.2)	1952 (99.8)	< 0.001
3	Staffs who perform initiating and terminating operation are wearing disposable, non-permeable gowns or plastic aprons	1291 (58.0)	1472 (66.1)	1496 (76.5)	< 0.001
4	Staffs who perform initiating and terminating operation are wearing goggles or face shields	1145 (51.4)	1648 (74.0)	1674 (85.6)	< 0.001
5	Patients are checked for their temperature and symptoms to confirm that they do not have a suspected infection, before entering the dialysis room	1199 (53.8)	2095 (94.1)	1864 (95.3)	0.079
6	Patients with suspected infection are observed before entering the room, and infection measures are modified according to their condition	1601 (71.9)	2141 (96.1)	1910 (97.6)	0.005
7	Linens are changed for each patient, or non-permeable bed mats are used and the dialysis environment is disinfected between each patient	653 (29.3)	765 (34.4)	1004 (51.3)	< 0.001
8	Items that are frequently touched by patient's and staff's hands (e.g., doorknobs) are wiped or disinfected several times a day	1165 (52.3)	2007 (90.1)	1757 (89.8)	0.751

Values in boldface type are significant (p < 0.05). Abbreviation: Q: question number, COVID-19, coronavirus disease. Note: the sentence about non-permeable bed mats was added to Q. 7 for this survey; hence, facilities using them may have also been added to those changing linen after each patient

(ii) nos. 7–14 from Additional file 2 and Additional file 3 have been changed to Q. 1-8). Because these items are all included in the JADP guidelines, the target implementation rate of 100% is desirable [18]. There were no items for which the implementation rate was significantly lower in this survey as compared to the previous survey. Significantly more facilities as compared to the previous survey complied with the following statements: "use of personal protective equipment (PPE)" (masks: Q. 2; 98.2% previous, 99.8% current, p < 0.001), disposable gowns or plastic aprons (Q. 3; 66.1% previous, 76.5% current, p < 0.001), goggles or face shields (Q. 4; 74.0% previous, 85.6% current, p < 0.001); "Patients with suspected infection are observed before entering the room, and infection measures are modified according to their condition" (Q. 6; 96.1% previous, 97.6% current, p = 0.005); and "Linens are changed for each patient, or non-permeable bed mats are used, and the dialysis environment is disinfected between each patient" (Q. 7; 34.4% previous, 51.3% current, p < 0.001). Sensitivity analysis showed significant differences between the previous and current surveys on all main questions except for Q. 6 (Additional file 1: Table S3). In the sub-group analyses, the trends were similar among hospitals and clinics (Additional file 1: Table S4). Meanwhile, clinics significantly improved the implementation rates for Q.3 "Staffs who perform initiating and terminating operation are wearing disposable, non-permeable gowns or plastic aprons." (50.5% previous, 64.8% current, p < 0.001) and Q.4 "Staffs who perform initiating and terminating operation are wearing goggles or face shields." (65.9% previous, 79.0% current, p < 0.001), although they were still lower than those of hospitals in 2022 (89.0% and 92.7%, respectively).

As for the new items in this survey, 97.0% and 99.0% of the facilities responded positively to no. 15 ("Staff members are instructed to refrain from talking when unmasked in the dining area") and no. 16 ("Patients are actively instructed to wear masks during dialysis"), respectively. It suggested that most dialysis facilities are implementing these measures, although these are not mentioned in the guideline.

## Experience in treating COVID-19-positive/suspected dialysis patients

The number of dialysis facilities with experience of examining and treating patients with suspected COVID-19 increased from 58.2% in 2020 to 97.1% in 2022. Furthermore, 83.5% of facilities had experience in treating COVID-19-positive dialysis patients with a significant increase from 12.6% in the previous survey. The number of facilities with experience treating patients with COVID-19 increased significantly from a median of 1 (interquartile range: 1–2; whole range, 1-20 patients) in the previous study to a median of 8 (interquartile: 4-14; whole range, 1-269 patients) in the current study.

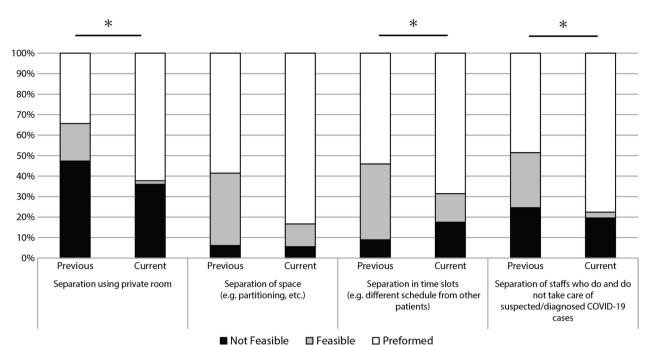
Of the 18,459 patients diagnosed with COVID-19 at 1713 facilities that provided valid responses, more than half (n = 12,700, 68.8%) completed dialysis treatment exclusively at the responding facility during their isolation period, while 5165 (28.0%) were transferred to other facilities to complete treatment. There were also some patients who, after being diagnosed at their own facilities, were treated at other hospitals, then returned to their own facilities during the isolation period and spent the remainder of their time receiving dialysis under isolation (n = 594; 3.2%). Comparing hospitals and clinics, hospitals were significantly more likely to complete dialysis treatment exclusively at their facilities than clinics (p < 0.001) (Additional file 1: Table S5).

## Feasibility of various isolation measures

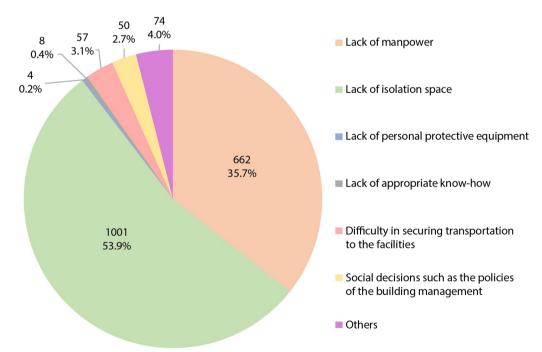
Figure 2 shows comparisons between the previous and current surveys on the feasibility of various isolation measures. There were significant increases in the number of facilities that were able to perform isolated dialysis using private rooms (52.6% previous, 64.0% current, p < 0.001) and those that can separate staff who do and do not cater to COVID-19 cases (75.4% previous, 80.4% current, p < 0.001). However, the number of facilities that could separate patients to be in different time slots (91.1% previous, 82.5% current, p < 0.001) decreased. There was no change in the ratio of facilities that were able to implement separation of space between the previous (93.9%) and current (94.4%) surveys. Sensitivity analysis also showed no significant differences between the results of the two surveys (Additional file 1: Table S6). In the sub-group analysis, the trends were generally similar among hospitals and clinics (Additional file 1: Table S7).

Despite a decrease in the number of responding facilities, the number of available private rooms increased by 478, from 2036 (2227 facilities) in the previous survey to 2514 (1956 facilities) in this survey. On sensitivity analysis, of the 1060 facilities, the number of private rooms increased by 325, from 1009 in the previous survey to 1334 in this survey.

In the previous survey, 73.3% of facilities responded that they were at capacity and could not accept any COVID-19-positive patients, which significantly decreased to 14.9% in this survey. In the question to select the strongest reason as preventing them from accepting more patients with COVID-19, 53.9% of the facilities selected "lack of isolation space", and 35.7% selected "lack of manpower" (Fig. 3).



**Fig. 2** Distribution of feasibility of various isolation measures for suspected/diagnosed cases of COVID-19. In addition to showing the distribution of the feasibilities of four isolation measures in dialysis facilities, a comparison of the ratio of facilities responding with "feasible and/or performed" or "not feasible" between the previous survey (in 2020) and the current survey (in 2022) was conducted by chi-squared test. The black bar is the percentage of facilities where preventive measures cannot be implemented. \*p < 0.05. Abbreviations: COVID-19, coronavirus disease



**Fig. 3** The strongest reason for preventing each facility from accepting any more patients with COVID-19. This figure shows the number and percentage of responding facilities that reported the strongest reason as preventing them from accepting any more patients with COVID-19 (single answer question). Abbreviations: COVID-19, coronavirus disease

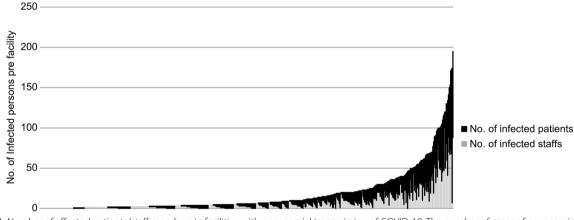
#### Nosocomial transmission in dialysis rooms

In the current survey, 626 facilities (32.0%) reported experiencing nosocomial transmission, a marked increase from the previous survey (4.0%). There were 10,059 COVID-19 infected cases by nosocomial transmission among the 557 facilities that provided information on the number of staff members and patients, with 4404 (43.8%) infections among staff members and 5655 (56.2%) among patients. Figure 4 shows the number of staff members and patients among the total number of nosocomial transmissions at each facility. There were significant decreases in the percentage of staff members among COVID-19-infected persons by nosocomial transmission (51.9% previous, 43.8% current, p < 0.001). Additionally, the average number of nosocomial transmissions significantly increased from  $7.8 \pm 1.2$  individuals in the previous survey to  $18.1 \pm 1.2$  individuals in this survey (*p* < 0.001).

## **COVID-19 vaccination status**

Overall, 83.7% of the facilities answered that they were able to ascertain their vaccination status and record it where it can be easily retrieved. Of the 164,095 patients undergoing dialysis in 1,620 responding facilities, 159,555 (97.2%) were vaccinated for COVID-19, while only 4,540 (2.8%) were unvaccinated. When asked whether they recommended vaccination to patients, 95.0% of facilities responded positively. However, most facilities (91.0%) cited "Patient does not want to get vaccinated" as the reason given by unvaccinated patients.

The results of a comparison of deaths due to COVID-19 between unvaccinated and vaccinated patients are summarized in Table 2. Compared with unvaccinated patients, vaccinated patients had a lower infection rate (vaccinated 9.2% vs. unvaccinated 41.2%; crude risk ratio [RR] 0.22; 95% confidence interval [CI] 0.22–0.23; p < 0.001) and mortality rates (vaccinated 0.3% vs. unvaccinated 6.6%; crude RR 0.05; 95% CI 0.04–0.06; p < 0.001). The mortality rate of infected patients of COVID-19 in the present study (3.5% for vaccinated and 16.1% for unvaccinated) was similar to that in another Japanese study that collected data on individual patients (2.1% for vaccinated and 14.3% for unvaccinated) [17].



**Fig. 4** Number of affected patients/staff members in facilities with nosocomial transmission of COVID-19. The number of cases of nosocomial transmission of COVID-19 in the 557 facilities that responded with details on the number of infections is indicated by color: black (patients) and white (staff members). Each facility is represented on the horizontal axis, with a total of 557 bar graphs shown. Abbreviations: COVID-19, coronavirus disease

Table 2 Comparison of COVID-19 infection	s, COVID-19-related deaths, and deaths among	y vaccinated and unvaccinated patients
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	Total number of patients N = 164,095	COVID-19 vaccine		Risk ratio (95% CI)	P value
		Vaccinated N = 159,555	Unvaccinated N=4540		
Number of COVID-19 infections, n (%)	16,628 (10.1)	14,758 (9.2)	1,870 (41.2)	0.22 (0.22-0.23)	< 0.001
Number of COVID-19-related deaths, n (%)	820 (0.5)	519 (0.3)	301 (6.6)	0.05 (0.04–0.06)	< 0.001
Deaths/Infections, %	4.9	3.5	16.1	0.22 (0.19–0.25)	< 0.001

Values in boldface type are significant (p < 0.05). Abbreviation: COVID-19, coronavirus disease, CI; confidence interval

## Impact on medical practice and economic aspects

Regarding the impact of COVID-19 on medical practice and economic aspects of each dialysis facility, when each facility was questioned about the problems caused by COVID-19 (multiple responses allowed), the majority responded "Staff members shortage" (69.0%) and "No space for isolation" (66.0%), while 37.6% answered "Collaborating with other hospitals to treat complications, etc., is more difficult than before." Other responses included "Hospital/clinic management has worsened" (18.2%); "Increased problems between patients and staff members, and between patients, etc." (10.4%); and "Lack of PPE" (8.2%). Meanwhile, 8.5% of facilities responded that "There are no problems."

Regarding the cost of implementing COVID-19 measures, the cost of facility renovation and large equipment installation was ¥1,000,000 per facility (quartile: ¥320,000-3,000,000). Specific costs included constructing additional private rooms (negative pressure rooms), installation of ventilation equipment, circulators, polymerase chain reaction testing machines, and body temperature sensors. Furthermore, responses showed that the median monthly maintenance cost for COVID-19 measures was ¥100,000 (quartile: ¥50,000-250,000) per facility; this includes the cost of purchasing PPE and disinfectants as well as additional labor costs. While supplementary funding for providing COVID-19 medical examination and treatment can be obtained by an application to the government (Additional Funds for Infection Prevention Measures, Additional Funds for Outpatient Infection Prevention Measures) [23], 44.6% of facilities did not apply for additional medical fee.

## Discussion

We conducted a follow-up survey on the current implementation status of infection prevention measures in dialysis facilities across Japan and obtained data that may be representative of Japan's dialysis care. Compared to that at two years ago, the number of facilities that examined and treated COVID-19-positive dialysis patients and/or experienced nosocomial transmissions increased as did the number of facilities that implemented thorough infection prevention measures and added isolation spaces. However, the survey also highlighted current challenges in implementing infection prevention measures, namely a lack of isolation space and personnel. Furthermore, while most patients on dialysis had been vaccinated against COVID-19, the significantly higher COVID-19 infection and mortality rates among unvaccinated patients underscores the importance of vaccination.

Following the outbreak of the highly infectious Omicron strain, the results of this survey showed that the number of patients with suspected and confirmed COVID-19 who underwent medical care at each facility markedly increased since the previous survey. More than half of the facilities completed dialysis treatment exclusively at the responding facility during their isolation period, which was more common in hospitals than in clinics. Possible reasons for this include the fact that it has been approximately three years since the emergence of COVID-19; hence, facilities may have adapted their treatment practices. Additionally, they may have been forced to respond to the COVID-19 outbreak because they could not find a place to transfer their patients.

The Omicron strain (dominant in the sixth wave in Japan), which has become prevalent since the last survey, was reported to be more infectious with increased cases of nosocomial transmissions, especially among healthcare workers [24], though it has lower mortality rate than the Delta strain [8, 25]. In the current survey, the number of nosocomial transmissions in each facility increased, but the proportion of transmission of COVID-19 to staff members significantly decreased. This may suggest that staff members are implementing infection prevention measures more effectively than that earlier. However, nosocomial transmissions still occur, emphasizing the difficulty of controlling the spread of COVID-19 in medical facilities. The nosocomial transmission of COVID-19, in addition to directly impacting affected patients, decreases the level of medical care available for other patients by reducing the number of available staff members. Therefore, facilities must remain vigilant in preventing future outbreaks of nosocomial transmission.

In the items of the infection prevention measures and various isolation measures, we found that compliance rates and the feasibility of each item improved as supported by the evidence in the increase in the number of private rooms, allotment of isolation environments, and implementation of other measures. These may be due to the increase in the number of facilities that need to complete treatment in-house because of the increasing number of patients with COVID-19 as well as the increased awareness of infection prevention measures, resulting in their implementation. Despite being recommended by the JADP guidelines, Q. 7 ("Linens are changed for each patient") was only implemented by 34.4% of facilities as of 2020 [18]. One possible reason for the low implementation rate is the non-trivial amount of time and effort it requires to change linens for each patient. Recently, some facilities have used non-permeable bed mats with environmental disinfection using sodium hypochlorite. These bed mats have the advantage of being easily

applicable to all patients without the need to change linens for each patient; accordingly, an item related to this was added to this survey. As a result, the implementation rate increased to 51.3%.

More than half of the facilities had problems with lack of sufficient isolation space and personnel as a result of the COVID-19 outbreak. The ratio of facilities with bed spacing of < 70 cm remained unchanged from that in the previous survey. Furthermore, the number of facilities that reported difficulties in separating patients to different time slots significantly increased by approximately 10% from the previous survey. Regarding the lack of space, Japan has a high population density, and comparatively few facilities are built on large sites; consequently, as the number of COVID-19 cases increased, many facilities struggled to provide private isolation spaces. Since fewer clinics can implement separation using private rooms compared to hospitals, separation using space was implemented instead. To compensate for the lack of space, it is necessary to implement other measures, such as temporal isolation, separation of staff members, or transfer to facilities with adequate isolation space. However, this presents other challenges, such as increased costs and the need to coordinate with other facilities, which may be difficult for a single facility to handle.

As for costs, the current survey revealed that facilities incurred high capital investment costs and that they continue to incur running costs. Although additional medical fee is available for providing COVID-19 medical examination and treatment [23], many facilities do not apply for these, which may not be sufficient compensation for the cost burden. Approximately half of the facilities did not apply for the additional medical fee for two possible reasons: they did not know they could apply, and they did not meet the application requirements. To better cope with the COVID-19 outbreak and other infectious diseases in the future, it is necessary for each facility to devise an appropriate isolation policy that is both clinically and economically sustainable. Moreover, a framework for sharing such measures would likely be a valuable addition as well.

This study showed that more patients on dialysis in Japan had received the COVID-19 vaccine compared to the general population in Japan (overall, 80.9% and elderly, 92.8%), and vaccination was significantly associated with a lower risk for infection and mortality [26]. In another survey of the general population in Japan conducted in December 2022, the overall infection rate of COVID-19 was 25.9%, with 17.3% among those aged 60–70 years, corresponding to the mean age of dialysis patients (69.7 years) [22, 27], which was higher compared to our study. It should be noted, however, that in the study in the general population, asymptomatic infection

(N-antibodies positive) was also treated as having a history of COVID-19 infection. Although some studies found that patients on dialysis have a reduced response to vaccines as compared to patients not on dialysis [8, 28, 29], COVID-19 vaccination is still recommended as it reduces infection and mortality rates in patients on dialysis [30–33]. These results including ours suggest that unvaccinated patients should be followed up more carefully. However, because this study did not collect data on patient-specific background factors, we cannot rule out the possibility of other confounding factors between vaccinated and unvaccinated patients; further research is needed to examine causal relationship between vaccination and outcomes of COVID-19 in dialysis patients.

Regarding the questionnaire respondents, while the response rate of this study was lower than that in the previous survey, responses were still obtained from close to half of the facilities, and the percentage of responding regions (previous: 48.9–66.2% in all prefectures nation-wide) as well as the ratio of hospitals to clinics (previous: 48.7% hospitals, 50.8% clinics) in this survey were similar to those of the previous survey. It suggested that the responding population was similar in both surveys. Furthermore, in this survey, we confirmed real-world changes over the past two years by conducting a sensitivity analysis using the paired test for the facilities that responded to both surveys.

We acknowledge several limitations of this study. Although the response rates did not differ significantly by region, the survey response rate was modest at 46.6%, and the representativeness of the facilities participating in the survey is unknown. It is possible that the facilities that responded to the questionnaire are generally better equipped and prepared for COVID-19 infections in addition to being more proactive about infection prevention measures than other facilities. Additionally, because it was a questionnaire survey, it is possible that recall bias and erroneous answers may have been included in the results.

## Conclusion

The results of this nationwide survey showed that the awareness of infection prevention measures against COVID-19 improved at each facility, and it seems that efforts are being made to create isolation spaces. However, there were still facilities where sufficient infection prevention measures could not be implemented because of a lack of available space and labor shortages. We also showed that COVID-19 vaccination was significantly associated with reduced infection and mortality in Japanese patients on dialysis, though potential confounders were unadjusted. The results of this study will help improve dialysis treatment as well as infection prevention

measures in the case of future pandemics of COVID-19, as well as new infectious diseases.

#### Abbreviations

COVID-19	Coronavirus disease
JADP	Japanese association of dialysis physicians
JSDT	Japanese society of nephrology
SARS-CoV-2	Severe acute respiratory syndrome coronavirus 2
PPE	Personal protective equipment

## Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s41100-023-00509-9.

Additional file 1: Results of sensitivity and subgroup analysis (Tables S1-S7).

Additional file 2: Questionnaire Original (Japanese).

Additional file 3: Questionnaire English Translation.

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#### Consortia

On behalf of 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.

## Author contributions

TH, YS, MI, KK, and MN planned the study and analyzed and interpreted the data. TH, YS, and MI wrote the manuscript. KK coordinated with the JADP. MR coordinated with the JSDT. TY, MR, KK, and MN coordinated with 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. TK and all other authors provided critical intellectual contributions in the development of the manuscript. All authors read and approved the final manuscript.

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#### Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

## Declarations

#### Ethics approval and consent to participate

This study was conducted in compliance with the 2013 Declaration of Helsinki, which details ethical principles for medical research involving human subjects and was approved by the Ethics Committee of the Graduate School of Medicine, the University of Tokyo (approval number: 2022175Nle). Informed consent was not required for this study as it was a facility-based questionnaire survey and did not include individual patient information. This study was therefore waived from the requirement to obtain written informed consent.

#### **Consent for publication**

Not applicable.

#### **Competing interests**

All the authors declared no competing interests.

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#### References

- Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, et al. A novel coronavirus from patients with pneumonia in China, 2019. N Engl J Med. 2020;382:727–33.
- 2. Burgner A, Ikizler TA, Dwyer JP. COVID-19 and the inpatient dialysis unit: managing resources during contingency planning pre-crisis. Clin J Am Soc Nephrol. 2020;15:720–2.
- Corbett RW, Blakey S, Nitsch D, Loucaidou M, McLean A, Duncan N, et al. Epidemiology of COVID-19 in an urban dialysis center. J Am Soc Nephrol. 2020;31:1815–23.
- Kikuchi K, Nangaku M, Ryuzaki M, Yamakawa T, Yoshihiro O, Hanafusa N, et al. Survival and predictive factors in dialysis patients with COVID-19 in Japan: a nationwide cohort study. Ren Replace Ther. 2021;7:59.
- Chen CY, Shao SC, Chen YT, Hsu CK, Hsu HJ, Lee CC, et al. Incidence and clinical impacts of COVID-19 infection in patients with hemodialysis: systematic review and meta-analysis of 396,062 hemodialysis patients. Healthcare. 2021;9.
- Kikuchi K, Nangaku M, Ryuzaki M, Yamakawa T, Hanafusa N, Sakai K, et al. COVID-19 of dialysis patients in Japan: current status and guidance on preventive measures. Ther Apher Dial. 2020;24:361–5.
- 7. El Karoui K, De Vriese AS. COVID-19 in dialysis: clinical impact, immune response, prevention, and treatment. Kidney Int. 2022;101:883–94.
- Mahalingasivam V, Su G, Iwagami M, Davids MR, Wetmore JB, Nitsch D. COVID-19 and kidney disease: insights from epidemiology to inform clinical practice. Nat Rev Nephrol. 2022;18:485–98.
- Chung EYM, Palmer SC, Natale P, Krishnan A, Cooper TE, Saglimbene VM, et al. Incidence and outcomes of COVID-19 in people with CKD: a systematic review and meta-analysis. Am J Kidney Dis. 2021;78:804–15.
- Hsu CM, Weiner DE, Aweh G, Miskulin DC, Manley HJ, Stewart C, et al. COVID-19 among US dialysis patients: risk factors and outcomes from a national dialysis provider. Am J Kidney Dis. 2021;77(748–56): e741.
- Sugawara Y, Iwagami M, Kikuchi K, Yoshida Y, Ando R, Shinoda T, et al. Infection prevention measures for patients undergoing hemodialysis during the COVID-19 pandemic in Japan: a nationwide questionnaire survey. Ren Replace Ther. 2021;7:27.
- Sugawara Y, Iwagami M, Yoshida Y, Kikuchi K, Ando R, Shinoda T, et al. Nationwide survey of the coronavirus disease 2019 prevention and treatment systems for kidney disease patients: a study of Japanese society of nephrology-certified educational facilities. Clin Exp Nephrol. 2021;25:996–1002.
- Dagan N, Barda N, Kepten E, Miron O, Perchik S, Katz MA, et al. BNT162b2 mRNA Covid-19 Vaccine in a nationwide mass vaccination setting. N Engl J Med. 2021;384:1412–23.
- Barda N, Dagan N, Cohen C, Hernan MA, Lipsitch M, Kohane IS, et al. Effectiveness of a third dose of the BNT162b2 mRNA COVID-19 vaccine for preventing severe outcomes in Israel: an observational study. Lancet. 2021;398:2093–100.
- Suzuki R, Yamasoba D, Kimura I, Wang L, Kishimoto M, Ito J, et al. Attenuated fusogenicity and pathogenicity of SARS-CoV-2 Omicron variant. Nature. 2022;603:700–5.
- Guo Y, Han J, Zhang Y, He J, Yu W, Zhang X, et al. SARS-CoV-2 Omicron variant: epidemiological features, biological characteristics, and clinical significance. Front Immunol. 2022;13: 877101.

- Kikuchi K, Nangaku M, Ryuzaki M, Yamakawa T. COVID-19 task force committee of the Japanese association of dialysis physicians; the Japanese society for dialysis therapy; the Japanese society of nephrology cumulative number of COVID-19 in dialysis patients. Available from: https://jsn.or. jp/medic/data/COVID-19number-of-infected\_20230113.pdf.
- Guidelines for Standard Hemodialysis Procedure and Prevention of Infection in Maintenance Hemodialysis Facilities (5<sup>th</sup> edition, 2020) [Akiba T, et al. 30. Apr. 2020]. The Japanese Association of Dialysis Physicians. Available from: http://www.touseki-ikai.or.jp/htm/07\_manual/doc/20200 430\_infection%20control\_guideline.pdf].
- Kikuchi K, Nangaku M, Ryuzaki M, Yamakawa T. COVID-19 task force committee of the Japanese association of dialysis physicians; the Japanese society for dialysis therapy; Request for measures at dialysis facilities to cope with the increase in the number of new coronavirus patients and to ensure dialysis care for dialysis patients. https://www.jsdt.or.jp/info/3480. html. Accessed 8 Aug 2023.
- Guideline for the treatment of new coronavirus infection (COVID-19). Edition 8.1. [Kato Y, et al. 5. Oct.2022 Internet]. Ministry of health, labour and welfare in Japan. Available from: [https://www.mhlw.go.jp/content/00093 6655.pdf].
- 21. Abbas M, Robalo Nunes T, Martischang R, Zingg W, Iten A, Pittet D, et al. Nosocomial transmission and outbreaks of coronavirus disease 2019: the need to protect both patients and healthcare workers. Antimicrob Resist Infect Control. 2021;10:7.
- Hanafusa N, Abe M, Joki N, Hoshino J, Wada A, Kikuchi K, et al. Annual dialysis data report, JSDT renal data registry. J Jpn Soc Dial Ther. 2022;55:665–723.
- Medical fee revision (in Japanese) [Internet]. Ministry of health, labour and welfare in Japan. [Accessed 2023 Jan 27]. Available from: [https:// www.mhlw.go.jp/stf/seisakunitsuite/bunya/kenkou\_iryou/iryouhoken/ newpage\_21053.html].
- Klompas M, Pandolfi MC, Nisar AB, Baker MA, Rhee C. Association of Omicron vs wild-type SARS-CoV-2 variants with hospital-onset SARS-CoV-2 infections in a US regional hospital system. JAMA. 2022;328:296–8.
- Nyberg T, Ferguson NM, Nash SG, Webster HH, Flaxman S, Andrews N, et al. Comparative analysis of the risks of hospitalisation and death associated with SARS-CoV-2 omicron (B.1.1.529) and delta (B.1.617.2) variants in England: a cohort study. Lancet. 2022;399:1303–12.
- COVID-19 Vaccines (in Japanese). Prime Minister's Office of Japan. https:// japan.kantei.go.jp/ongoingtopics/vaccine.html. Accessed 8 Aug 2023.
- Report on Seroepidemiological Surveillance for New Coronavirus Infections in 2022 (in Japanese). National Institute of Infectious Diseases, and Prime Minister's Office of Japan https://www.niid.go.jp/niid/images/epi/ corona/85/covid19-85b.pdf. Accessed 15 Aug 2023.
- Yoshifuji A, Toda M, Ryuzaki M, Kikuchi K, Kawai T, Sakai K, et al. Investigation for the efficacy of COVID-19 vaccine in Japanese CKD patients treated with hemodialysis. Ren Replace Ther. 2022;8:39.
- Beppu H, Fukuda T, Kawanishi T, Yasui F, Toda M, Kimura H, et al. Hemodialysis patients with coronavirus disease 2019: reduced antibody response. Clin Exp Nephrol. 2022;26:170–7.
- Alkadi MM, Hamad A, Ghazouani H, Elshirbeny M, Ali MY, Ghonimi T, et al. Effectiveness of messenger RNA vaccines against SARS-CoV-2 infection in hemodialysis patients: a case-control study. Vaccines. 2022;11
- Francis A, Baigent C, Ikizler TA, Cockwell P, Jha V. The urgent need to vaccinate dialysis patients against severe acute respiratory syndrome coronavirus 2: a call to action. Kidney Int. 2021;99:791–3.
- Sibbel S, McKeon K, Luo J, Wendt K, Walker AG, Kelley T, et al. Real-world effectiveness and immunogenicity of BNT162b2 and mRNA-1273 SARS-CoV-2 vaccines in patients on hemodialysis. J Am Soc Nephrol. 2022;33:49–57.
- Kikuchi K, Nangaku M, Ryuzaki M, Yamakawa T, Yoshihiro O, Hanafusa N, et al. Effectiveness of SARS-CoV-2 vaccines on hemodialysis patients in Japan: a nationwide cohort study. Ther Apher Dial. 2023;27:19–23.

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