—Original—

Changes in Treatment Conditions for Patients Receiving Hemodialysis at Nippon Medical School Hospital during the COVID-19 Pandemic

Naoko Shimoda[1], Yukinao Sakai[1], Takuya Nishino[2,3], Sayuri Kawasaki[1], Akio Hirama[1], Tetsuya Kashiwagi[1] and Masato Iwabu[1]

[1]Department of Endocrinology, Metabolism and Nephrology, Graduate School of Medicine, Nippon Medical School, Tokyo, Japan
[2]Department of Health Care Administration, Graduate School of Medicine, Nippon Medical School, Tokyo, Japan
[3]Department of Medical Affairs, Nippon Medical School Hospital, Tokyo, Japan

Background: The COVID-19 pandemic has had an enormous impact on hemodialysis patients. This study investigated changes in hemodialysis treatment at our hospital after the start of the pandemic.
Methods: We analyzed data from the Diagnosis Procedure Combination (DPC) system. Data for inpatients receiving dialysis during collection periods A (before the COVID-19 pandemic) and B (after the start of the COVID-19 pandemic) were extracted and compared. The numbers of inpatients and new patients, the number of patients admitted (by department), duration of stay, mortality, place of residence, surgical procedures, and DPC classification were compared.
Results: There were no significant differences between periods in patient age, duration of hospital stay, number of new patients, number of ambulance transports, number of deaths, body mass index, comorbidities, laboratory variables before the first dialysis after hospitalization, or patient area of residence. Although differences were observed among the departments, the numbers of emergency dialysis inpatients and maintenance dialysis inpatients increased. The number of surgeries also increased overall, particularly for maintenance dialysis patients ($p = 0.0273$). The percentage of DPC III patients was significantly higher in period B ($p = 0.0368$).
Conclusions: The number of surgeries performed on maintenance dialysis patients and the overall DPC III rate significantly increased after the start of the COVID-19 pandemic at our hospital, suggesting that COVID-19 worsened the condition of maintenance dialysis patients and prolonged hospital stays.
(J Nippon Med Sch 2024; 91: 172–179)

Key words: SARS coronavirus-2, COVID-19 pandemic, hemodialysis

Introduction

To date, four types of coronaviruses that infect humans have been reported. Coronaviruses are a cause of the common cold and account for 10-15% of such cases. However, coronaviruses can also cause pneumonia: severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome were first reported in 2002 and 2012, respectively[1].

SARS coronavirus 2, which was first reported in December 2019 in Wuhan, Hubei Province, China, causes symptoms that were previously rarely reported in the coronavirus family, such as disorders of taste and smell, upper respiratory symptoms, and severe pneumonia. As of October 30, 2022, 627 million confirmed cases and 6.5 million deaths were reported worldwide[2]. The first case of coronavirus infection in Japan was reported on January 16, 2020, and more than 22.5 million cases and over 46,000 deaths were reported as of November 5, 2022. In Japan, the first wave of coronavirus infection started in April 2020 and progressed to a seventh wave despite development of vaccines and neutralizing antibodies. Coronavirus disease 2019 (COVID-19) has greatly affected the

Correspondence to Yukinao Sakai, Department of Endocrinology, Metabolism and Nephrology, Graduate School of Medicine, Nippon Medical School, 1–1–5 Sendagi, Bunkyo-ku, Tokyo 113–8603, Japan
E-mail: y-sakai@nms.ac.jp
https://doi.org/10.1272/jnms.JNMS.2024_91-207
Journal Website (https://www.nms.ac.jp/sh/jnms/)

lives of people in Japan.

The increase in the number of patients with COVID-19 changed the situation of patients visiting medical centers. Some medical facilities initially refused to accept patients with COVID-19, and facilities varied in their policies regarding admission of inpatients and outpatient treatment. In addition, patients were wary of infection during hospital visits and while using public transportation for hospital visits and thus often cancelled regular medical checkups[3]. This may have led to worsening of some medical conditions, as suggested by increases in the numbers of ambulance transports and emergency visits after the start of the COVID-19 pandemic.

A total of 11,226 patients receiving dialysis had received a COVID-19 diagnosis as of September 8, 2022. Morbidity and mortality rates are high for dialysis patients with COVID-19, underscoring the importance of preventive measures[4]. The COVID-19 vaccine was shown to be effective for dialysis patients, thus highlighting the need for vaccination in dialysis facilities[5]. The hospitalization rate for dialysis patients infected with COVID-19 to the total number of dialysis patients was reported to be relatively low[6].

We therefore examined changes after the start of the COVID-19 pandemic in patient characteristics and treatments, and in the number of ambulance transports, for patients receiving hemodialysis in our hospital.

Methods

Data from the Diagnosis Procedure Combination (DPC) system were classified in relation to the start of the pandemic as those obtained before the pandemic (period A) and those collected after the start of the pandemic (period B). The date when the first infected person was confirmed in Japan was defined as the cutoff. We compared data on the number, characteristics, and treatment of inpatients at our hospital during the periods 1 year before and 1 year after the cutoff.

Data for inpatients receiving dialysis were extracted and compared for periods A (February 2019 through January 2020) and B (February 2020 through January 2021). Patients requiring acute dialysis were defined as those needing emergency dialysis rather than maintenance dialysis and those whose data were extracted by using the keywords "emergency hospitalization/artificial kidney (others)/no introductory period addition." Patients requiring maintenance dialysis were defined as those whose data were extracted by using the keywords "artificial dialysis (maintenance dialysis)/artificial kidney (others)" or "no introductory period addition/no artificial kidney (others)."

New patients were defined as those who visited our hospital for the first time and—to exclude regular patients after annual medical checkups—those for whom the last visit was more than 540 days previously. For patients requiring emergency or maintenance dialysis, we compared periods A and B for the number of inpatients in the hospital, the number of new patients, the duration of stay, mortality, place of residence (city and ward), the number of admitted patients (by clinical department), the number of operations, and DPC classification.

All data obtained were expressed as real numbers. Laboratory values and average number of patients were presented as means ± standard deviations. Continuous variables were compared with the unpaired t-test. Fisher's exact test was used to compare proportions between groups. Emergency dialysis patients and maintenance dialysis patients before and after the pandemic were classified by clinical department, and the means were compared using the paired t-test. The number of surgeries was similarly classified by clinical department, and the averages were compared before and after the pandemic using the paired t-test. The test for trend using the chi-square test was used to compare DPC classification. P values < 0.05 were considered to indicate statistical significance. All the statistical analyses were performed using Prism software version 9 (GraphPad Software, La Jolla, CA, USA).

The study protocol was designed in accordance with the principles of the Declaration of Helsinki and approved by the Ethics Committee of Nippon Medical School Hospital (B-2021-366).

Results

Patient Characteristics

Table 1 shows the number and characteristics of inpatients who required emergency and maintenance dialysis in periods A and B. No significant difference was observed between periods A and B in patient age, duration of hospital stay, number of new patients, number of ambulance transports, number of deaths, body mass index, comorbidities, or laboratory results (ie, estimated glomerular filtration rate, serum albumin, and C-reactive protein) before the first dialysis after hospitalization.

Total Number of Inpatients

The numbers of emergency and maintenance dialysis patients were 82 and 297, respectively, in Period A and 95 and 341, respectively, in Period B. Both the total num-

Table 1

total, n	Patients Before COVID-19 n = 379	Patients After COVID-19 n = 436	*P* Value
Female, n (%)	110 (29.0)	127 (29.1)	>0.9999
Age (years)	69.79 ± 13.30	61.99 ± 15.25	0.868
BMI (kg/m^2)	23.31 ± 4.83	23.06 ± 4.47	0.476
Diabetes mellitus, n (%)	85 (22.4)	94 (21.6)	0.799
Hypertension, n (%)	300 (79.2)	337 (77.3)	0.552
eGFR at HD initiation (mL/min/1.73 m^2)	7.84 ± 9.69	8.26 ± 8.65	0.553
Serum Alb at HD initiation (g/dL)	2.96 ± 0.75	2.98 ± 0.75	0.731
CRP at HD initiation (mg/dL)	5.47 ± 8.12	4.42 ± 6.59	0.065
Emergency HD initiation, n (%)	82 (21.6)	127 (21.8)	>0.9999
Hospital Days (Days)	24.16 ± 25.13	26.67 ± 21.95	0.240
Initial Patients, n (%)	73 (19.3)	88 (20.2)	0.792
Deaths, n (%)	29 (7.7)	29 (6.7)	0.588
Patients receiving emergency HD, n (%)	16 (19.5)	14 (14.7)	0.399
Patients receiving maintenance HD, n (%)	13 (4.4)	15 (4.4)	0.989

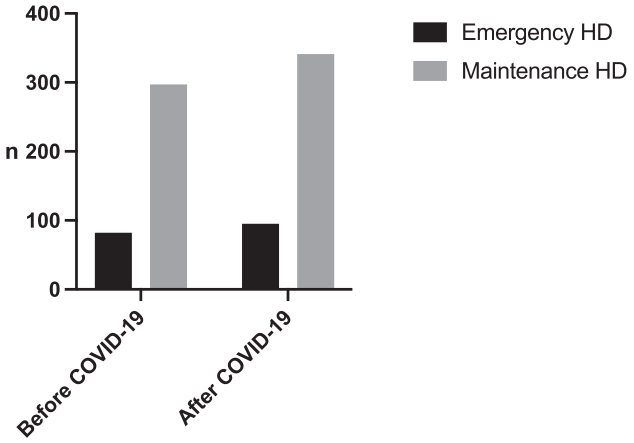

Fig. 1 Number of inpatients, by hemodialysis (HD) status, before and after the start of the COVID-19 pandemic

ber of emergency dialysis patients and maintenance dialysis patients increased (**Fig. 1**).

Place of Residence of Inpatients

Table 2 shows the number of patients by place of residence of the main patients referred to our hospital. During period B, there were more patients from Adachi, Arakawa, Bunkyo, Kita, Taito, and Toshima Wards.

Number of Admitted Patients, by Clinical Department

Table 3 shows the number of patients admitted, by clinical department. The number of patients admitted to the Department of Nephrology, Emergency and Critical Care Medicine, Gastroenterology, and Urology increased. Counted by clinical department and compared before and after the pandemic, there was no significant change in admissions of emergency or maintenance dialysis patients (emergency HD: p = 0.3894; maintenance HD: p = 0.1837).

Numbers of Surgeries for Patients Requiring Emergency and Maintenance Dialysis

The numbers of surgeries performed by each clinical department on emergency and maintenance dialysis patients were counted and compared between periods A and B (**Table 4**). Surgeries for maintenance dialysis patients increased significantly after the start of the pandemic (p = 0.0273; **Table 4**). However, there was no significant difference in the number of surgeries performed on emergency dialysis patients before and after the start of the pandemic (p = 0.3975).

After the start of the pandemic, the number of cancer-related surgeries increased by 14.3% for patients requiring emergency dialysis and by 73.3% for those requiring maintenance dialysis.

Change in DPC Classification

Figure 2 shows DPC classifications for periods A and B. The proportion of DPC III cases was significantly higher in period B (Period A: 34.6%; Period B: 45.9%; p = 0.0368).

Discussion

Although COVID-19 can cause serious outcomes even in healthy individuals, the risks of infection and severe disease in patients with kidney disease (including patients with end-stage renal failure, such as those requiring hemodialysis) may be higher than in healthy individuals because, in addition to the age of patients with kidney disease, the primary causes of kidney disease—hypertension and diabetes mellitus—are also risks for COVID-19

Table 2

	Before COVID-19		After COVID-19	
	Number of Emergency HD	Number of Maintenance HD	Number of Emergency HD	Number of Maintenance HD
Adachi	18	62	30	91
Arakawa	10	60	13	55
Bunkyo	10	37	9	42
Kita	7	17	4	32
Katsushika	6	15	5	12
Taito	5	32	4	27
Edogawa	3	3	3	9
Toshima	3	12	2	17
Sumida	2	9	1	11
Koutou	2	9	2	7
Kawaguchi	3	4	2	4
Other Regions	13	37	20	34

Table 3

	Before COVID-19		After COVID-19	
	Number of Emergency HD	Number of Maintenance HD	Number of Emergency HD	Number of Maintenance HD
Nephrology	15	92	15	108
Cardiovascular Medicine	2	49	4	45
CCM	12	30	22	39
CCU	6	19	4	16
Gastroenterology	1	22	6	46
Gastro S	8	11	11	9
SCU	0	14	0	15
Cardio S	3	9	3	7
Dermatology	3	7	1	4
Ortho S	4	6	1	8
General Medicine	1	7	2	1
Hematology	2	5	8	2
Urology	3	4	4	7
Ophthalmology	3	2	3	5
Reconst S	1	3	2	7
Radiology	0	4	0	1
Endocrinology	0	4	2	3
Neurology	1	3	0	5
Otolaryngology	1	2	1	1
Endo S	3	0	1	1
Thoracic S	3	0	1	1
Gynecology	3	0	1	2
SICU	2	1	0	0
Breast S	2	0	1	0
Neurol S	1	1	1	2
Pulmonary Medicine	0	2	1	3
Rheumatology	1	0	0	3
Pediatrics	1	0	0	0
Mean ± SD	2.93 ± 3.51	10.61 ± 19.34	3.39 ± 5.07	12.19 ± 22.82

infection and severe disease[7]. In addition, patients with kidney disease (especially hemodialysis patients) are severely immunosuppressed[8], and biological changes associated with kidney disease may increase the risks of in-

Table 4

	Before COVID-19		After COVID-19	
	Number of Emergency HD	Number of Maintenance HD	Number of Emergency HD	Number of Maintenance HD
Nephrology	7	74	7	80
Cardiovascular Medicine	2	29	2	41
CCM	17	28	41	21
CCU	2	10	5	6
Gastroenterology	1	39	10	54
Gastro S	13	22	19	26
SCU	0	0	0	0
Cardio S	13	33	11	33
Dermatology	6	8	0	2
Ortho S	4	10	2	22
General Medicine	0	0	0	0
Hematology	0	0	0	0
Urology	10	8	8	18
Ophthalmology	4	4	4	10
Reconst S	1	15	3	28
Radiology	0	0	0	0
Endocrinology	0	0	0	0
Neurology	0	0	0	0
Otolaryngology	1	3	1	5
Endo S	3	1	3	1
Thoracic S	3	0	1	2
Gynecology	3	1	1	2
SICU	0	0	0	0
Breast S	2	0	1	0
Neurol S	4	0	1	2
Pulmonary Medicine	0	0	0	0
Rheumatology	0	0	0	0
Pediatrics	0	0	0	0
Mean ± SD	3.43 ± 4.61	10.18 ± 17.08	4.29 ± 8.46	12.61 ± 19.74

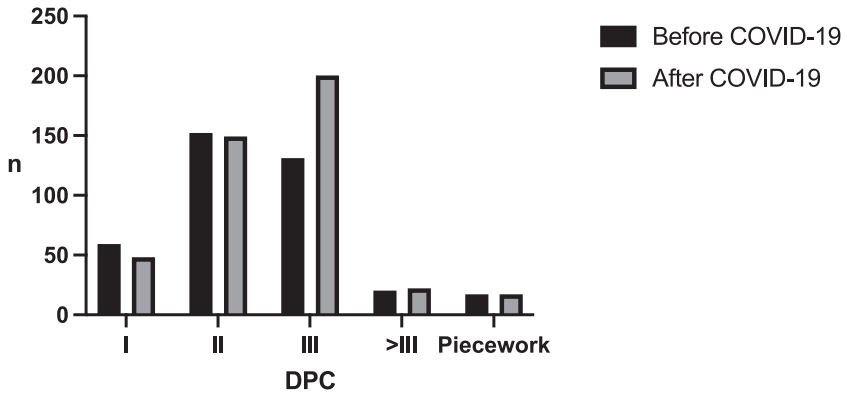

Fig. 2 Number of inpatients, by Diagnosis Procedure Combination (DPC) system classification

fection and severe disease. However, because of the role of cytokine storms to COVID-19 severity, it is possible that immunosuppression in renal disease patients might limit cytokine storms. In addition, regular use of anticoagulants in hemodialysis may reduce COVID-19 hypercoagulability[9], and some believe that dialysis patients are not necessarily severely ill. However, most studies of the risks of infection and severe disease and related factors

in patients with kidney disease were conducted outside Japan; thus, we believe it is important to collect and analyze the unique data from our hospital.

Patient Characteristics

There was no significant difference in the characteristics of patients admitted to our hospital after the start of the pandemic. The Japanese Society for Dialysis Therapy has reported that, after excluding unknown underlying diseases, the most common underlying disease for initiating dialysis for patients with COVID-19 was diabetic nephropathy, followed by chronic glomerulonephritis and nephrosclerosis. After 2018, the order of prevalence changed to diabetic nephropathy, followed by nephrosclerosis and chronic glomerulonephritis[10]. Notably, the present results were mostly consistent with previously reported prevalences of underlying conditions necessitating initiation of dialysis. In addition, there was no significant change in the number of new patients, and although we assumed that the numbers of patients from areas not normally served by our hospital would increase because of hospital bed shortages at other hospitals, no significant increase occurred.

Number of Inpatients

At our hospital, the number of hospital admissions to the emergency department was higher in period B, and the percentage increase was greater than that for the total number of admissions, but these differences were not significant. The number of inpatients in Period B was lower for some clinical departments, which is consistent with increases in the numbers of inpatients at centers nationwide. Moreover, comparison with the Transitions in the Medical Industry Activity Index revealed no significant difference. Some general ward beds in our hospital were later used as part of a ward for patients admitted with COVID-19, but not during the observation period of this survey, and there was no drastic change in the numbers of hospital beds.

No department showed a significant increase in the number of maintenance dialysis patients or emergency dialysis patients during Period B. However, there was a nonsignificant increase in the number of emergency dialysis inductions at the emergency center, suggesting that patients with severe conditions involving multiple organ failure were transported there. In period B, patients infected with COVID-19 were accepted only at the emergency center, and it is possible that the increase was due to acceptance of patients with severe COVID-19 infection.

Place of Residence of Inpatients

Analysis of inpatients' ward of residence showed no significant increase for any ward. Adachi Ward was the most frequently recorded place of residence for inpatients in our hospital. Data collected after March 3, 2020, are published on the website for Adachi Ward, and the number of infected patients from that date until January 2021 was 4,914. In addition, data on the number of disease clusters at medical centers indicate that clusters occurred at 10 hospitals and clinics, and at 13 health and rehabilitation centers for elderly adults, during the period from July 11, 2020, through January 31, 2021, in period B. Therefore, patients with severe medical conditions could not be treated in Adachi Ward and were transferred to Bunkyo Ward. The number of clusters is not shown on the website of the Bunkyo Ward, but the website does disclose data on the number of transfers (health centers transporting COVID-19-positive patients from their home to a hospital for hospitalization). Because the number of infected cases increased during the present observation period and the number of patients who visited our hospital and resided in Bunkyo Ward did not decrease, it is likely that our hospital was accepting patients from Adachi Ward while accepting patients from Bunkyo Ward after the start of the COVID-19 outbreak.

Number of Surgeries

The number of surgeries increased significantly for patients receiving maintenance dialysis but not for those receiving emergency dialysis. Although the type of surgery was not mentioned, the departments with increases in the number of surgeries performed on maintenance dialysis patients at the hospital were Gastrointestinal and Hepato-Biliary-Pancreatic Surgery, Orthopedic Surgery, Reconstructive and Aesthetic Surgery, and Urology. The number of surgeries performed by the Nephrology Department was similar for periods A and B. The surgeries performed by the Nephrology Department were peritoneal dialysis catheter insertion and blood access surgery, indicating that the number of dialysis inductions at our hospital remained unchanged after the COVID-19 pandemic.

Certain medical conditions may have increased the need for surgery—initially, because of the impact of COVID-19 infection itself and, later, because of postponement of regular medical checkups and examinations during the COVID-19 pandemic. According to a Survey of the Japan Society of Health Evaluation and Promotion and the National Federation of Industrial Health Organization, 19,357,000 people underwent medical examinations in 2020, a decrease of 2.12 million (9.9%) from 21,478,000 in 2019. Data from a 2017 survey on screening

in Japan for lung, stomach, colon, breast, and cervical cancers showed that 1.53-6.84% of patients required detailed examination and that the incidence of cancer was 1.50-4.15%[11]. The rate of medical checkups decreased in April and May 2020 and recovered thereafter. Thus, we also examined the number of surgeries for cancer, which increased among patients receiving maintenance dialysis after the start of the COVID-19 outbreak, but not by a significant margin. However, this survey was conducted within 1 year of the decrease in medical screening and, given the rate of cancer progression, long-term tracking of data on surgeries may be warranted.

Changes in DPCs

The DPC system is a medical fee system based on diagnosis and treatment combinations introduced in the Japanese medical care system. Under the conventional reimbursement system, reimbursement is paid mainly for individual medical procedures and treatments. Under the DPC system, however, diagnosis and treatment of specific diseases and surgeries are comprehensively evaluated, and reimbursement is made accordingly. DPC is based on the number of hospitalization days—I: up to the 25th percentile, II: up to the average length of stay, and III: up to the average length of stay + 2 SD. If the length of stay exceeds III, the cost of care is calculated.

The number of patients requiring Period III duration of hospitalization increased significantly after the start of the COVID-19 outbreak. Although there was no difference between groups in duration of hospital stay, the proportion of DPC III patients was higher in period B, perhaps because of the many cases in which the expected duration of hospital stay was extended, either because of the severity of the patient's condition or the difficulty of transferring the patient.

Conclusion

The COVID-19 pandemic was associated with an increase in the number of hospitalized patients receiving hemodialysis at our hospital, with particularly important changes in the emergency and critical care departments. In addition, there were significant increases in the number of surgeries performed on maintenance dialysis patients and the proportion of DPC III cases, suggesting that COVID-19 worsened the health status of this patient group.

Data availability: All data generated or analyzed during this study are available from the corresponding author on request.

Authors' Contributions: NS wrote the first draft of the manuscript. TN collected the data. SK, AH, TK, and MI helped design the study. YS coordinated the data analysis and helped revise the manuscript. All authors participated in discussions of the manuscript and read and approved the final manuscript.

Acknowledgments: The authors are grateful to the staff of Nippon Medical School Hospital.

Funding: None.

Conflict of Interest: None declared.

References

1. Graham RL, Donaldson EF, Baric RS. A decade after SARS: strategies for controlling emerging coronaviruses. Nat Rev Microbiol [Internet]. 2013 Dec;11(12):836–48. Available from: https://www.ncbi.nlm.nih.gov/pubmed/24217413
2. World Health Organization. Weekly epidemiological update on COVID-19 - 2 November 2022 [Internet]. Geneva: World Health Organization; 2022 Nov 2. Available from: https://www.who.int/publications/m/item/weekly-epidemiological-update-on-covid-19---2-november-2022
3. Di Bidino R, Cicchetti A. Impact of SARS-CoV-2 on provided healthcare. Evidence from the emergency phase in Italy. Front Public Health [Internet]. 2020 Nov 23;8:583583. Available from: https://www.ncbi.nlm.nih.gov/pubmed/33330324
4. Li P, Guan Y, Zhou S, et al. Mortality and risk factors for COVID-19 in hemodialysis patients: a systematic review and meta-analysis. Sci Prog [Internet]. 2022 Jul-Sep;105(3):368504221110858. Available from: https://www.ncbi.nlm.nih.gov/pubmed/35775141
5. Oliver MJ, Blake PG. Clinical utility of COVID-19 vaccination in patients undergoing hemodialysis. Clin J Am Soc Nephrol [Internet]. 2022 Jun;17(6):779–81. Available from: https://www.ncbi.nlm.nih.gov/pubmed/35649720
6. Bell S, Campbell J, McDonald J, et al. COVID-19 in patients undergoing chronic kidney replacement therapy and kidney transplant recipients in Scotland: findings and experience from the Scottish renal registry. BMC Nephrol [Internet]. 2020 Oct 1;21(1):419. Available from: https://www.ncbi.nlm.nih.gov/pubmed/33004002
7. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet. 2020 Mar 28;395(10229):1054–62.
8. Betjes MG. Immune cell dysfunction and inflammation in end-stage renal disease. Nat Rev Nephrol. 2013 May;9(5):255–65.
9. Asakura H, Ogawa H. Potential of heparin and nafamostat combination therapy for COVID-19. J Thromb Haemost. 2020 Jun;18(6):1521–2.
10. Hyodo T, Yamashita AC, Hirawa N, Isaka Y, Nakamoto H, Shigematsu T. Present status of renal replacement therapy in lower-middle-income Asian countries: Cambodia, Myanmar, Laos, Vietnam, Mongolia, and Bhutan as of June 2019 (before COVID-19), from the interviews of leading doctors in every country: (duplicated English

publication from "the special Japanese edition of educational lectures in the 64th annual meeting of the Japanese Society for Dialysis Therapy"). Ren Replace Ther [Internet]. 2022;8(1):54. Available from: https://www.ncbi.nlm.nih.gov/pubmed/36277446
11. Foundation for Promotion of Cancer Research. Cancer statistics in Japan - 2022 [Internet]. Tokyo: National Cancer Center Japan; 2022 Apr [cited 2022 Dec 4]. Available from: https://ganjoho.jp/public/qa_links/report/statistics/index.html. Japanese, English.

(Received, December 11, 2022)
(Accepted, October 25, 2023)
(J-STAGE Advance Publication, March 2, 2024)