

# Dialysis Case Volume Associated With In-Hospital Mortality in Maintenance Dialysis Patients



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**Introduction**: Accumulating evidence suggests that a large hospital volume (HV) is associated with favorable outcomes in various diseases or surgical procedures. The aim of this study is to clarify the correlation of HV and dialysis case volume (DCV) with in-hospital death in patients on maintenance dialysis.

**Methods**: The study cohort was derived from the Diagnosis Procedure Combination database, a national inpatient database in Japan, from 2012 to 2014. We included 382,689 admissions of maintenance dialysis patients over the age of 20 years in the analysis. HV was defined as the mean number of daily hospitalized patients, and DCV was defined as the mean number of annually hospitalized patients on maintenance dialysis. The primary outcome was in-hospital all-cause mortality, evaluated using multivariable logistic regression models across the respective quartiles of HV and DCV.

**Results:** The mean age of participants was  $69 \pm 12$  years; 94% were receiving hemodialysis, and 21,182 patients (5.5%) died after hospitalization. In unadjusted models, larger HV and DCV were both associated with lower in-hospital mortality. However, this association remained significant only for DCV after adjustment for potential confounders, with multivariable-adjusted odds ratios of 0.82 (95% confidence interval [CI], 0.79–0.85), 0.76 (95% CI, 0.73–0.80), and 0.68 (95% CI, 0.65–0.72) for DCV 249 to 432, 433 to 713, and  $\geq$ 714 (vs.  $\leq$  248) admissions per year, respectively. Multivariable subgroup analyses determined that this association was independent of age, sex, dialysis modality, Charlson Comorbidity Index, and emergency admission.

Conclusion: Selective admission to hospitals with a large DCV may improve outcomes of dialysis patients.

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**E** nd-stage kidney disease (ESKD) is highly associated with morbidity and mortality, accounting for a substantial proportion of the social and economic burden worldwide.<sup>1-3</sup> Despite much advancement in dialysis care and techniques over the past several decades, mortality risk remains considerably high in patients on maintenance dialysis at approximately 10% to 15% per year, which is 7- to 8-fold higher than in the general population.<sup>2-5</sup> The hospitalization rate of

dialysis patients also remains high, with 1.5 to 2.0 admissions per person-year; this rate is nearly 3- to 4-fold that of the general population when age adjusted.<sup>3,6</sup> Therefore, the much greater risk of in-hospital mortality of dialysis patients would explain the greater overall risk of mortality.

Recent attempts to clarify the association between hospital volume (HV) and in-hospital mortality showed that a larger HV is associated with increased survival in various diseases such as sepsis, breast cancer, chronic obstructive pulmonary disease, acute myeloid leukemia, peripheral arterial disease, and deep vein thrombosis,<sup>7–13</sup> as well as after surgical procedures.<sup>14,15</sup> HV is usually defined as the number of hospitalization cases<sup>7–11</sup> or specific procedures<sup>12–15</sup> at each hospital. Thus, a larger HV is associated with a greater number of case

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experiences, doctors with expertise in treating the disease, hospital infrastructure, and resources. These factors ultimately result in higher-quality patient care, leading to improved outcomes. Thus, these results suggest that selective admission or referrals to large HV hospitals could potentially improve outcomes, particularly when the disease is severe and requires more expertise for treatment. However, it has not been elucidated whether HV is associated with outcomes in maintenance dialysis patients. Moreover, dialysis case volume (DCV), when defined as the number of hospitalized patients on maintenance dialysis at each hospital, would be a previously unrecognized hospital volume factor specifically related to dialysis patients, indicating dialysis care quality of the hospital. Thus, we hypothesized that DCV also has an impact on clinical outcomes in this population. The aim of the present study was to investigate whether HV and DCV are associated with in-hospital mortality in patients undergoing maintenance dialysis, using a Japanese nationwide database.

# METHODS

#### Data Source

The study cohort was derived from the Diagnosis Procedure Combination (DPC) database, a nationwide inpatient database in Japan, as well as a case-mix classification system linked with a payment system. Additional details of the database have been described elsewhere.<sup>16</sup> Briefly, more than 1000 hospitals in Japan, including all 82 teaching hospitals, participate in the database. The annual number of admissions added to the database is approximately 7 million, accounting for about 50% of all admissions in Japan. The database contains administrative claims and discharge abstract data, including the following: a unique hospital identifier; patient age and sex; diagnoses and comorbidities at the time of admission, coded according to the International Classification of Diseases and Related Health Problems, 10th Revision (ICD-10)<sup>17</sup>; Charlson Comorbidity Index (CCI)<sup>18</sup> updated for use in ESKD patients<sup>19</sup> at the time of admission; and discharge status. Although the updated CCI in ESKD<sup>19</sup> divided the original CCI category "any malignancy, including leukemia and lymphoma" into neoplasia, leukemia, and lymphoma, data for each of these subsets were unavailable in our datasets. Thus, for the category "any malignancy, including leukemia and lymphoma," we applied the score from the original CCI score.<sup>18</sup> The database also includes information on patient care processes, including drug administration, surgical procedures, or devices used.

This study was approved by the ethics committee of Tokyo Medical and Dental University, and the research

# Patient Selection and Data

Among the 22,433,171 admissions of patients who were hospitalized from 2012 to 2014, we retrieved records for all patients  $\geq 20$  years of age who had received maintenance dialysis sessions during hospitalization (Figure 1). Each maintenance hemodialysis or peritoneal dialysis session was identified based on the code of patient care procedures: chronic maintenance hemodialysis with <4 hours per session,  $\geq$ 4 hours and <5 hours per session,  $\geq 5$  hours per session, chronic maintenance hemodiafiltration, or continuous peritoneal dialysis. Incident dialysis patients who were admitted for initiation of dialysis are not included in this data extraction. Patients were excluded if their hospital length of stay was <24 hours, and therefore patients for day stay procedures and dialysis sessions are not included. Patients were also excluded if they lacked body mass index (BMI) data or admission type (elective or emergency admission). Overall, 382,689 admissions were included in the analysis (Figure 1).

Patient-level data included age, sex, BMI, dialysis modality (hemodialysis, peritoneal dialysis, or both), CCI score on admission, admission type, fiscal year of admission, length of stay, and in-hospital death. The hospital-level characteristics included HV, DCV, and hospital type (advanced treatment hospital approved by the Minister of Health, Labor and Welfare in Japan or not). HV was defined as the mean daily number of hospitalized patients with and without ESKD. DCV was defined as the mean annual number of hospitalized patients receiving maintenance dialysis.



Figure 1. Flowchart of patient selection.

The primary outcome was the occurrence of overall in-hospital death. Diagnostic causes of admission were stratified into 7 categories based on the previously described Healthcare Cost and Utilization Project mapping of ICD-10 codes,<sup>20,21</sup> including the following: vascular access (n = 54,358); chest pain (n = 153); overload (n = 14,265); falls/fracture/trauma (n = 14,202); sepsis (n = 25,114); vascular event (n = 89,189); and other (n = 185,408).

#### **Data Analysis**

Continuous or categorical variables were expressed as medians and interquartiles or as numbers and percentages. Comparisons between the 2 groups were evaluated by t test for continuous variables and  $\chi^2$  test for categorical variables. A logistic regression analysis was used to assess patient and hospital factors associated with in-hospital mortality in dialysis patients. This logistic regression model was adjusted for age, sex, BMI, dialysis modality, CCI, admission type, advanced treatment hospital, HV, and DCV. HV (mean number of admissions per day) was categorized into quartile 1:  $\leq 242$ , n = 95,031; quartile 2: 243 to 376, n = 95,165; quartile 3: 377 to 574, n = 96,789; and quartile 4:  $\geq$ 575, n = 95,704. DCV (mean number of dialysis case admissions per year) was categorized into quartile 1:  $\leq 248$ , n = 95,442; quartile 2: 249 to 432, n = 95,760; quartile 3: 433 to 713, n = 95,401; and quartile 4:  $\geq$ 714, n = 96,086. To further assess the respective effects of HV and DCV on in-hospital mortality in dialysis patients, the study subjects were stratified into 4 groups based on the status of their admitted hospitals: small HV (less than a median value, 377 per day) and small DCV (less than a median value, 433 per year), n = 127,811; large HV ( $\geq 377$ ) and small DCV (<433), n = 63,723; small HV (<377) and large DCV ( $\geq$ 433); n = 63,694; and large HV ( $\geq$ 377) and large DCV ( $\geq$ 433), n = 127,461.

In addition, we performed subgroup analysis using a multivariable logistic regression model and examined the odds ratio of in-hospital death in dialysis patients admitted to hospitals with the largest DCV (quartile 4) versus those with the smallest DCV (quartile 1). For the logistic regression models, a robust sandwich estimator was used to account for clustering at the facility level.<sup>22</sup> All statistical analyses were performed using JMP software (version 11 pro; SAS Institute, Cary, NC) and Stata (version 15.0; Stata Corp., College Station, TX). *P* values <0.05 were considered statistically significant.

## RESULTS

#### **Characteristics of Study Subjects**

A total of 382,689 admissions from 205,572 patients, who were hospitalized and receiving maintenance

dialysis between 2012 and 2014 in a national inpatient database, were enrolled in the analysis (Figure 1). Patient and hospital characteristics are shown in Table 1. Among the study participants, 21,182 (5.5%) patients died during hospitalization, whereas 361,507 survived to discharge. Nonsurvivors were older and included a lower proportion of female patients, lower BMI, higher CCI scores, and higher proportions of hemodialysis treatment and emergency admissions. Survivors were more likely to be admitted to advanced treatment hospitals and hospitals with larger HV or DCV quartiles (Table 1).

# Outcomes

Overall, 21,182 dialysis patients (5.5%) died after hospitalization. In univariate and multivariable analyses (Table 2), older age, male sex, lower BMI, and hemodialysis treatment were associated with increased mortality in dialysis patients. Higher CCI scores, indicating more severe comorbidities and emergency admission also markedly increased mortality risk. Admission to an advanced treatment hospital was associated with lower mortality in both univariate and multivariable analyses. In a crude model, increasing HV and DCV quartiles were predictive of lower risk for in-hospital death. However, multivariable analysis showed that patients hospitalized at large HV hospitals had a risk of in-hospital death similar to that of patients hospitalized at small HV hospitals; however, there was a strong association between larger DCV quartiles and lower mortality (Table 2). Funnel plots of the observed and expected range of mortality rate based on the Poisson distribution<sup>23</sup> for HV and DCV are shown in Figure 2.

Instead of DCV, we also examined the effect of the actual patient number of annually hospitalized dialysis patients (DP) on outcome, given that DP may more appropriately reflect the dialysis case experience. The result showed very similar effect of DP quartiles on inhospital mortality, with multivariable-adjusted odds ratios of 0.83 (95% confidence interval [CI], 0.79–0.87), 0.76 (95% CI, 0.73–0.80), and 0.70 (95% CI, 0.67–0.73) for DP 160 to 279, 280 to 442, and  $\geq$ 443 (vs.  $\leq$ 159) patients per year, respectively.

To further verify the predominant effect of DCV over HV on the outcomes of dialysis patients, odds of in-hospital death were assessed across the 4 groups consisting of the following: small HV/small DCV, large HV/small DCV, small HV/large DCV, and large HV/ large DCV hospitals, with the median values being the respective thresholds, using a logistic regression analysis. As shown in Table 3, admissions to large HV/small DCV, small HV/large DCV, and large HV/small DCV, small HV/large DCV, and large HV/large DCV hospitals were associated with lower mortality than the 
 Table 1. Clinical and hospital characteristics in patients receiving maintenance dialysis from the Japanese national inpatient database from 2012 to 2014

Patient and hospital characteristics	Whole group (n $=$ 382,689)	Survivors (n = $361,507$ )	Nonsurvivors (n = $21,182$ )	P value
Age (yr)	70 (62–77)	68 (62–77)	76 (68–82)	< 0.001
Female sex	131,564 (34.4)	124,592 (34.5)	6,972 (32.9)	< 0.001
BMI (kg/m <sup>2</sup> )	22 (19–24)	22 (19–24)	20 (18–23)	< 0.001
Dialysis modality				
HD	358,204 (93.6)	337,797 (93.4)	20,407 (96.3)	< 0.001
PD	19,171 (5.0)	18,609 (5.2)	562 (2.7)	
HD + PD	5,314 (1.4)	5,101 (1.4)	213 (1.0)	
Charlson comorbidity				
Myocardial infarction	10,774 (2.8)	9,996 (2.8)	778 (3.7)	< 0.001
Congestive heart failure	49,386 (12.9)	45,289 (12.5)	4,097 (19.3)	< 0.001
Peripheral vascular disease	24,963 (6.5)	23,225 (6.4)	1,738 (8.2)	< 0.001
Cerebrovascular disease	28,332 (7.4)	26,183 (7.2)	2,149 (10.1)	< 0.001
Dementia	9,096 (2.4)	8,110 (2.2)	986 (4.7)	< 0.001
Chronic pulmonary disease	6,847 (1.8)	6,319 (1.7)	528 (2.5)	< 0.001
Rheumatologic disease	4,173 (1.1)	3,837 (1.1)	336 (1.6)	< 0.001
Peptic ulcer disease	12,362 (3.2)	11,814 (3.3)	548 (2.6)	< 0.001
Mild liver disease	12,150 (3.2)	11,153 (3.1)	997 (4.7)	< 0.001
Diabetes without chronic complications	45,296 (11.8)	42,972 (11.9)	2,324 (11.0)	< 0.001
Diabetes with chronic complications	87,101 (22.8)	82,849 (22.9)	4,252 (20.1)	< 0.001
Hemiplegia or paraplegia	2,097 (0.5)	1,930 (0.5)	167 (0.8)	< 0.001
Renal disease	284,364 (74.3)	269,227 (74.5)	15,137 (71.5)	< 0.001
Any malignancy, including leukemia and lymphoma	19,255 (5.0)	16,997 (4.7)	2,258 (10.7)	< 0.001
Moderate or severe liver disease	1,349 (0.4)	1,085 (0.3)	264 (1.2)	< 0.001
Metastatic solid tumor	4,155 (1.1)	3,021 (0.8)	1,134 (5.4)	< 0.001
AIDS/HIV	100 (0.03)	91 (0.03)	9 (0.04)	0.16
Charlson Comorbidity Index				
0–1	236,590 (61.8)	226,762 (62.7)	9,828 (46.4)	< 0.001
2–3	118,236 (30.9)	110,161 (30.5)	8,075 (38.1)	
≥4	27,863 (7.3)	24,584 (6.8)	3,279 (15.5)	
Emergency admission	104,585 (27.3)	94,219 (26.1)	10,366 (48.9)	< 0.001
Advanced treatment hospital	61,898 (16.2)	59,381 (16.4)	2,517 (11.9)	< 0.001
Hospital volume (mean admissions per day)				
≤242	95,031 (24.8)	88,698 (24.5)	6,333 (29.9)	< 0.001
243–376	95,165 (24.9)	89,977 (24.9)	5,188 (24.5)	
377–574	96,789 (25.3)	91,562 (25.3)	5,227 (24.7)	
≥575	95,704 (25.0)	91,270 (25.3)	4,434 (20.9)	
Annual dialysis case volume (mean dialysis admissions per year)				
≤248	95,442 (24.9)	88,547 (24.5)	6,895 (32.6)	< 0.001
249–432	95,760 (25.0)	90,395 (25.0)	5,365 (25.3)	
433–713	95,401 (25.0)	90,626 (25.1)	4,775 (22.5)	
≥714	96,086 (25.1)	91,939 (25.4)	4,147 (19.6)	

BMI, body mass index; HD, hemodialysis; PD, peritoneal dialysis.

Data are numbers (percentiles) or medians (interquartile ranges).

small HV/small DCV hospitals in a univariate model. After adjustment for confounders, the large HV/small DCV group showed slightly lower odds of death compared with the small HV/small DCV group. In contrast, admission to large DCV hospitals, regardless of HV size, provided a profound decrease in in-hospital mortality, even after adjustment. These findings confirmed the superior impact of large DCV compared with HV on the outcome for dialysis patients.

#### Subgroup Analysis

As shown in Figure 3, the lower odds of in-hospital death in the largest DCV (quartile 4) compared with

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the smallest DCV (quartile 1) were statistically significant for most causes of admission, with the exception of "overload." Analysis in the "chest pain" subgroup was not available because of a limited number of cases. In addition, this statistically significant relationship was independent of various subgroups, including age, sex, BMI, dialysis modality, CCI score, admission type, year of admission, and length of stay ( $\leq 30$  or  $\geq 31$ days) (Figure 4). Even when we excluded elective admissions due to "vascular access" (44,064 admissions), which are potentially associated with low mortality risk in dialysis patients, the benefit of large DCV remained significant, with an adjusted odds ratio of

#### Table 2. Factors associated with in-hospital mortality in maintenance dialysis patients

Patient and hospital characteristics	Unadjusted OR (95% CI)	P value	Multivariable-adjusted OR (95% CI) <sup>a</sup>	P value
Age (yr)				
≤50	Reference		Reference	
51–60	1.531 (1.382–1.695)	< 0.001	1.386 (1.251–1.536)	< 0.001
61–70	2.314 (2.112-2.536)	<0.001	1.907 (1.739–2.091)	< 0.001
71–80	3.872 (3.540-4.234)	< 0.001	2.925 (2.671-3.202)	< 0.001
≥81	6.445 (5.887-7.056)	< 0.001	4.341 (3.958-4.760)	< 0.001
Female	0.933 (0.906-0.961)	< 0.001	0.832 (0.806–0.858)	< 0.001
BMI (kg/m <sup>2</sup> )				
≤18.4	2.125 (2.060-2.192)	< 0.001	1.964 (1.901–2.029)	< 0.001
18.5–24.9	Reference		Reference	
≥25.0	0.652 (0.625-0.681)	< 0.001	0.787 (0.754–0.822)	< 0.001
Dialysis modality				
HD	Reference		Reference	
PD	0.500 (0.459-0.544)	< 0.001	0.724 (0.664–0.789)	< 0.001
HD + PD	0.691 (0.602-0.793)	< 0.001	1.017 (0.883–1.171)	0.82
Charlson Comorbidity Index				
0–1, n (%)	Reference		Reference	
2–3, n (%)	1.691 (1.641–1.743)	< 0.001	1.526 (1.479–1.574)	< 0.001
≥ 4, n (%)	3.077 (2.952-3.208)	< 0.001	2.683 (2.568-2.803)	< 0.001
Emergency admission	2.719 (2.644–2.796)	< 0.001	2.329 (2.262–2.397)	< 0.001
Hospital				
Advanced treatment hospital	0.686 (0.658-0.716)	< 0.001	0.928 (0.880-0.979)	0.006
Hospital volume (mean admissions per day)				
≤242	Reference		Reference	
243–376	0.808 (0.776-0.839)	< 0.001	0.893 (0.858-0.929)	< 0.001
377–574	0.800 (0.770-0.830)	< 0.001	0.908 (0.872-0.946)	< 0.001
≥575	0.680 (0.654-0.708)	< 0.001	1.018 (0.966–1.072)	0.508
Annual dialysis case volume (mean dialysis admissions per year)				
≤248	Reference		Reference	
249–432	0.762 (0.735-0.791)	< 0.001	0.818 (0.786–0.850)	< 0.001
433–713	0.677 (0.651-0.703)	<0.001	0.762 (0.731–0.795)	< 0.001
≥714	0.579 (0.557–0.603)	< 0.001	0.684 (0.654–0.716)	< 0.001

BMI, body mass index; CI, confidence interval; HD, hemodialysis; OR, odds ratio; PD, peritoneal dialysis.

<sup>a</sup>Models were adjusted for age, sex, body mass index, dialysis modality, Charlson Comorbidity Index, admission type, advanced treatment hospital, hospital volume, and annual dialysis case volume. Analyses accounted for facility clustering effects.

0.72 (95% CI, 0.69-0.76) for DCV quartile 4 versus quartile 1. The lower risk of death in the largest DCV was also independent of HV quartiles, except for the largest HV quartile.

#### DISCUSSION

This study identified a novel hospital factor, DCV, specifically related to dialysis care. The principal finding was that a larger DCV was associated with lower in-hospital mortality in patients receiving maintenance dialysis. This study also showed that DCV, rather than HV, predominantly affects clinical outcome of this population. To the best of our knowledge, this is the first study to determine the prognostic impact of DCV in dialysis patients. Selective hospitalization or referral to hospitals with a large DCV, not necessarily those with a large HV, may improve the unfavorable mortality.

Dialysis-dependent patients are at markedly greater risk for death than those without  $\mathrm{ESKD.}^{2-5}$  One of the

primary reasons for this is greater mortality after hospitalization. The mean in-hospital mortality rate was 5.5% in this study. We evaluated multivariate predictors for in-hospital mortality with a specific focus on HV and DCV, including conventionally recognized risk factors.<sup>24,25</sup> Neither HV nor DCV was recognized as or included in the variables in the previous studies. This study is the first to clarify the relationship between HV, DCV, and clinical outcomes in patients on maintenance dialysis, with the strength of our study being the considerably large and generalizable dataset, accounting for approximately one-half of all hospitalization cases in Japan.

Numerous prior studies have shown the beneficial effect of a large HV on clinical outcomes in a wide variety of diseases or in patients needing operations or procedures.<sup>7–15</sup> A larger HV is associated with larger caseloads and increased experience, and greater numbers of surgeons or physicians, both of which potentially lead to favorable outcomes for patients.<sup>7–15</sup> Admissions to larger HV and DCV hospitals both were



Figure 2. Funnel plots for hospital volume or dialysis case volume and in-hospital mortality. Each hospital is represented by a point on the funnel plots for (a) hospital volume and (b) dialysis case volume, showing the mortality rate among the total admissions in each hospital. The control limits represent an expected range of mortality rate based on the Poisson distribution.

associated with lower in-hospital mortality, as expected, in a univariate analysis. Interestingly, admissions to a large DCV was the predominant factor improving survival of the patients after adjustments for potential cofounders. In addition, this association was regardless of the subgroups of participants. These findings may be helpful for more effective and equitable policies about admission or referral of dialysis patients, leading to improvement of outcomes.

Cause of admission	Multivariable-adjus	ted OR (95% CI)	P value
Vascular event	0.738 (0.664–0.821)		<0.001
Overload	0.937 (0.775–1.133)		0.50
Sepsis	0.862 (0.760-0.978)		0.021
Vascular access	0.684 (0.552-0.849)		0.001
Falls/fracture/trauma	0.638 (0.492-0.827)	_ <b>-</b>	0.001
Other	0.718 (0.675–0.763)	-	<0.001
	0.25	0.5	2

Large DCV better Small DCV better

**Figure 3.** Odds ratios for in-hospital mortality according to diagnostic cause of admission in dialysis patients admitted to hospitals with the largest (quartile 4) versus the smallest (quartile 1) dialysis case volume (DCV). Models were adjusted for age, sex, body mass index, dialysis modality, Charlson Comorbidity Index, admission type, advanced treatment hospital, and hospital volume. Analyses accounted for facility clustering effects. Each box represents a point estimate of odds ratio (OR), and the solid lines represent the corresponding 95% confidence interval (CI).

A larger DCV is presumably associated with a greater number of dialysis-related clinical staff, including nephrologists, as well as greater experience for each staff. This would result in higher quality of ordinary dialysis care and better treatment of dialysisrelated complications, including cardiovascular events, during a hemodialysis session or in the case of infection of a vascular access. Therefore, the findings in this study suggest that expertise in managing the patient's daily hemodynamics and treating dialysisrelated complications may provide a greater impact on the outcomes of dialysis patients than that in treating the specific cause of admission. This speculation is supported by the finding that the beneficial effects of large DCV were not significant in diseases related to simple volume overload, which do not require particularly high expertise in dialysis care (Figure 3). However, further investigations focusing on specific diseases or procedures (i.e., dialysis patients with acute coronary syndrome requiring revascularization) are warranted.

This study has several limitations. First, long-term outcomes after discharge were not available in this study because of the nature of the inpatient database. Thus, the study findings are limited to the short-term outcomes. Second, the primary cause of death was

Table 3. Effect of admission to hospitals with a small/large hospital volume and dialysis case volume on in-hospital mortality in maintenance dialysis patients

Hospital characteristics	Death/n (%)	Unadjusted OR (95% CI)	P value	Multivariable-adjusted OR (95% CI) $^{a}$	P value
Small HV and small DCV	8,709/127,811 (6.8)	Reference		Reference	
Large HV and small DCV	3,562/63,723 (5.6)	0.810 (0.779–0.843)	< 0.001	0.877 (0.840-0.915)	< 0.001
Small HV and large DCV	2,899/63,694 (4.6)	0.652 (0.625-0.681)	< 0.001	0.732 (0.700-0.765)	< 0.001
Large HV and large DCV	6,012/127,461 (4.7)	0.677 (0.654–0.700)	< 0.001	0.787 (0.759–0.817)	< 0.001

CI, confidence interval; DCV, dialysis case volume; HV, hospital volume; OR, odds ratio.

<sup>a</sup>Models were adjusted for age, sex, body mass index, dialysis modality, Charlson Comorbidity Index, admission type, and advanced treatment hospital. Analyses accounted for facility clustering effects.

Subgroups	Multivariable-adjusted OR (95% CI)	P value
Age (yr)		
≤50	0.463 (0.338–0.634)	<0.001
51–60	0.757 (0.627–0.914)	0.004
61–70	0.708 (0.639–0.784) -	< 0.001
71–80	0.727 (0.672–0.787) -	<0.001
≥81	0.639 (0.582–0.701) -	<0.001
Sex		
Female	0.679 (0.624–0.740) -	<0.001
Male	0.692 (0.651–0.735) -	<0.001
BMI (kg/)		
≤18.4	0.734 (0.673–0.801) -	<0.001
18.5–24.9	0.665 (0.623–0.711) -	<0.001
≥25.0	0.675 (0.589–0.773)	<0.001
Dialysis modality		
HD	0.686 (0.653–0.721) -	<0.001
PD	0.703 (0.507–0.975)	0.034
HD + PD	0.802 (0.473–1.358)	0.41
Charlson Comorbidity Inde	X	
0–1	0.645 (0.600–0.693) -	<0.001
2–3	0.739 (0.682–0.800) -	<0.001
≥4	0.725 (0.636–0.827)	<0.001
Emergency admission		
Yes	0.746 (0.693–0.802) -	<0.001
No	0.661 (0.618–0.707) -	<0.001
Hospital volume (mean ad	mission/per day)	
≤242	0.684 (0.623–0.750) -	<0.001
243–376	0.563 (0.508–0.625) -	<0.001
377–574	0.739 (0.662–0.824)	<0.001
≥575	0.918 (0.771–1.095)	0.34
Hospital length of stay (day	/S)	
≤30	0.698 (0.651–0.749) -	<0.001
>30	0.703 (0.656–0.752) -	<0.001
Year of admission		
2012	0.675 (0.625–0.730) -	<0.001
2013	0.650 (0.594–0.712) -	<0.001
2014	0.701 (0.632–0.778)	<0.001
	0.25 0.5 1 •	2

Large DCV better Small DCV better

Figure 4. Subgroup analysis of in-hospital mortality in maintenance dialysis patients admitted to hospitals with the largest (quartile 4) versus the smallest (quartile 1) dialysis case volume (DCV). Models were adjusted for age, sex, body mass index (BMI), dialysis modality, Charlson Co-morbidity Index, admission type, advanced treatment hospital, hospital volume, hospital length of stay, and year of admission. Analyses accounted for facility clustering effects. Each box represents a point estimate of odds ratio (OR), and the solid lines represent the corresponding 95% confidence interval (CI).

not available in our datasets. Thus, the most relevant complications or plausible mechanisms that contribute to mortality in hospitals with small DCV cannot be elucidated. Third, this study lacked dialysis vintage in both hemodialysis and peritoneal dialysis patients, which is 1 of the major confounding factors related to survival for dialysis patients. Finally, the study cohort was based on a single race or ethnicity, although the DPC database covers approximately one-half of Japanese admission cases and the study population represents the Japanese dialysis population.<sup>16</sup>

In summary, DCV, rather than HV, has a much greater impact on clinical outcomes in maintenance dialysis patients, and the admission to larger DCV hospitals was associated with an improved survival rate in patients on maintenance dialysis. Admission to hospitals with a large DCV may improve outcomes of dialysis patients, particularly those with severe disease.

# DISCLOSURE

All the authors declared no competing interests.

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#### REFERENCES

- Schieppati A, Remuzzi G. Chronic renal diseases as a public health problem: epidemiology, social, and economic implications. *Kidney Int Suppl.* 2005;98:S7–S10.
- Goodkin DA, Young EW, Kurokawa K, et al. Mortality among hemodialysis patients in Europe, Japan, and the United States: case-mix effects. *Am J Kidney Dis.* 2004;44:16–21.
- 3. Saran R, Robinson B, Abbott KC, et al. US Renal Data System 2016 annual data report: epidemiology of kidney disease in the United States. *Am J Kidney Dis.* 2017;69:A7–A8.
- Masakane I, Nakai S, Ogata S, et al. An overview of regular dialysis treatment in Japan (as of 31 December 2013). *Ther Apher Dial*. 2015;19:540–574.
- Longenecker JC, Coresh J, Powe NR, et al. Traditional cardiovascular disease risk factors in dialysis patients compared with the general population: the CHOICE Study. J Am Soc Nephrol. 2002;13:1918–1927.
- Dalrymple LS, Johansen KL, Romano PS, et al. Comparison of hospitalization rates among for-profit and nonprofit dialysis facilities. *Clin J Am Soc Nephrol.* 2014;9:73–81.
- Gaieski DF, Edwards JM, Kallan MJ, et al. The relationship between hospital volume and mortality in severe sepsis. *Am J Respir Crit Care Med.* 2014;190:665–674.
- Greenup RA, Obeng-Gyasi S, Thomas S, et al. The effect of hospital volume on breast cancer mortality. Ann Surg. https:// doi.org/10.1097/SLA.0000000002095.
- Stefan MS, Pekow PS, Shieh MS, et al. Hospital volume and outcomes of noninvasive ventilation in patients hospitalized with an acute exacerbation of chronic obstructive pulmonary disease. *Crit Care Med.* 2017;45:20–27.
- Diamant MJ, Coward S, Buie WD, et al. Hospital volume and other risk factors for in-hospital mortality among diverticulitis patients: a nationwide analysis. *Can J Gastroenterol Hepatol.* 2015;29:193–197.
- 11. Thompson MP, Waters TM, Kaplan EK, et al. Hospital volume and acute myeloid leukemia mortality in Medicare beneficiaries aged 65 years and older. *Blood.* 2016;128:872–874.
- Arora S, Panaich SS, Patel N, et al. Impact of hospital volume on outcomes of lower extremity endovascular interventions

(insights from the Nationwide Inpatient Sample [2006 to 2011]). *Am J Cardiol.* 2015;116:791–800.

- Jarrett H, Zack CJ, Aggarwal V, et al. Impact of institutional volume on outcomes of catheter directed thrombolysis in the treatment of acute proximal deep vein thrombosis: a 6year US experience (2005-2010). *Circulation*. 2015;132:1127– 1135.
- 14. Park HS, Detterbeck FC, Boffa DJ, et al. Impact of hospital volume of thoracoscopic lobectomy on primary lung cancer outcomes. *Ann Thorac Surg.* 2012;93:372–379.
- Tchouta LN, Park HS, Boffa DJ, et al. Hospital volume and outcomes of robot-assisted lobectomies. *Chest.* 2017;151: 329–339.
- Isogai T, Yasunaga H, Matsui H, et al. Effectiveness of inferior vena cava filters on mortality as an adjuvant to antithrombotic therapy. *Am J Med.* 2015;128:312.e23– 312.e31.
- 17. Brämer GR. International statistical classification of diseases and related health problems. Tenth revision. *World Health Stat.* 1988;41:32–36.
- Charlson ME, Pompei P, Ales KL, et al. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chron Dis.* 1987;40:373– 383.
- Hemmelgarn BR, Manns BJ, Quan H, et al. Adapting the Charlson Comorbidity Index for use in patients with ESRD. *Am J Kidney Dis.* 2003;42:125–132.
- 20. Healthcare Cost and Utilization Project (HCUP). Beta Classifications Software (CCS) for Mortality Reporting. Available at: www.hcup-us.ahrq.gov/toolssoftware/icd\_10/ccs\_icd\_10.jsp. Accessed August 28, 2017.
- 21. Fotheringham J, Fogarty DG, El Nahas M, et al. The mortality and hospitalization rates associated with the long interdialytic gap in thrice-weekly hemodialysis patients. *Kidney Int.* 2015;88:569–575.
- Klein J, Moeschberger M. Survival Analysis Techniques for Censored and Truncated Data. New York, NY: Springer; 1997: 416–418 pp.
- 23. Spiegelhalter DJ. Funnel plots for comparing institutional performance. *Stat Med.* 2005;24:1185–1202.
- Iseki K, Shinzato T, Nagura Y, et al. Factors influencing longterm survival in patients on chronic dialysis. *Clin Exp Nephrol.* 2004;8:89–97.
- Li T, Liu J, An S, et al. Body mass index and mortality in patients on maintenance hemodialysis: a meta-analysis. *Int Urol Nephrol.* 2014;46:623–631.