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## Mortality and morbidity after hepatic resection in patients undergoing hemodialysis: analysis of a national inpatient database in Japan

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### ARTICLE INFO

#### Article history:

Accepted 30 December 2017

### ABSTRACT

**Background.** Whether patients undergoing hemodialysis have greater risks of mortality and morbidity after hepatic resection remains unclear.

**Methods.** We used the Diagnosis Procedure Combination database, a national inpatient database in Japan, to identify patients who underwent hepatic resection from July 2010 to March 2014. Propensity score-matching analysis was performed to compare morbidity and mortality between patients with and without hemodialysis.

**Results.** Of 53,651 eligible patients, 498 (0.93%) underwent hemodialysis. Propensity score-matching analysis indicated greater in-hospital mortality in patients with than without hemodialysis (8.6% vs 2.0%;  $P < .001$ ). Patients undergoing hemodialysis had more postoperative major complications than did patients not undergoing hemodialysis (18.1% vs 7.4%;  $P < .001$ ). In the subgroup analyses for in-hospital mortality, the odds ratio of hemodialysis was 2.36 (95% confidence interval, 0.78–6.59;  $P = .067$ ) in limited resection, 4.61 (95% confidence interval, 1.90–11.2;  $P < .001$ ) in segmentectomy or sectoriectomy, and 5.58 (95% confidence interval, 3.40–14.9;  $P < .001$ ) in bisectoriectomy or trisectoriectomy. In the age subgroup analyses, the odds ratio of hemodialysis was 4.38 (95% confidence interval, 2.66–7.21;  $P < .001$ ) in patients aged <80 years and 7.20 (95% confidence interval, 1.55–36.7;  $P = .0011$ ) in those aged ≥80 years.

**Conclusion.** Patients undergoing hemodialysis had a substantially increased risk of mortality and morbidity after hepatic resection. Surgical indications for major hepatectomy in patients undergoing hemodialysis who are ≥80 years of age may be limited and require careful scrutiny.

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Although hepatic resection is a curative treatment for hepatobiliary neoplasms, it is associated with complications related to potentially large volumes of blood loss and loss of functional liver tissue. With the improvements in diagnostic modalities, operative techniques, and perioperative management,<sup>1,2</sup> the mortality rate after hepatic resection has decreased from 10% to 2%–4% during the last 2 decades<sup>3,4</sup>; however, several patient-related characteristics are associated with increased morbidity and mortality after hepatic resection, including cardiovascular disease, cerebrovascular disease, and older age.<sup>5–7</sup>

This work was supported by grants for Research on Policy Planning and Evaluation from the Ministry of Health, Labour and Welfare, Japan (grant numbers: H28-Policy-Designated-009 and H27-Policy-Strategy-011).

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<https://doi.org/10.1016/j.surg.2017.12.033>

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Hemodialysis (HD) is a maintenance therapy for end-stage renal disease. The number of patients undergoing HD has continued to grow and is now more than 1 million worldwide.<sup>8</sup> A previous study reported that terminal kidney failure requiring HD was associated with an unfavorable health condition and poor prognosis with a more than 4-fold greater mortality rate than in the general population.<sup>9</sup> Also, patients undergoing HD have greater mortality than those not undergoing HD after cardiovascular surgery,<sup>10</sup> colorectal surgery,<sup>11</sup> total hip or knee arthroplasty,<sup>12</sup> and spinal surgery.<sup>13</sup> Only a few studies, however, have investigated the mortality and morbidity rates among patients undergoing concurrent HD and hepatic resection.<sup>14–17</sup> Although these studies reported increased morbidity rates in patients with HD, no statistically significant difference in the mortality rate after hepatic resection was confirmed.

In the present study, we compared mortality and postoperative complications after hepatic resection between patients with and without HD using a large national inpatient database in Japan.

## Methods

### Data source

The Diagnosis Procedure Combination (DPC) database is a national, inpatient database in Japan.<sup>7</sup> All 82 academic hospitals are obliged to participate in the database, but participation by community hospitals is voluntary. The database includes administrative claims data and discharge abstract data, including patient age and sex; diagnoses, comorbidities at admission, and complications after admission recorded with text data in Japanese and the *International Classification of Diseases*, 10th revision (ICD-10) codes; operative procedures and HD coded with Japanese original codes; and in-hospital deaths. To optimize the accuracy of the diagnoses, physicians in charge are required to record diagnoses with reference to the medical charts. Because of the anonymous nature of the data, informed consent was not required for the present study. The study was approved by the Institutional Review Board at the University of Tokyo and conducted in accordance with the principles invoked in the Helsinki Declaration.

### Patients

We identified patients aged  $\geq 20$  years who underwent hepatic resection from July 2010 to March 2014. Patients were divided into those who were and were not on chronic HD. Patients were also divided into the following 3 groups according to the type of hepatic resection performed: (1) limited resection, (2) segmentectomy or sectoriectomy, and (3) bisectoriectomy or trisectoriectomy with or without vascular reconstruction. Patient background factors included age, sex, primary diagnosis, and preoperative comorbidities. Age was stratified into 4 categories: 20 to 59, 60 to 69, 70 to 79, and  $\geq 80$  years. The primary diagnoses were divided into primary liver malignant neoplasms (ICD-10 code C22) and other diseases. Preoperative comorbidities included diabetes mellitus (E10–E14), history of ischemic heart disease (I20–I25), history of cerebrovascular disease (I60–I69), and chronic lung disease (J40–J47).

### Outcomes

The outcome variables included in-hospital death and postoperative major complications. Postoperative major complications included acute coronary events (I20–I24), stroke (I60–I64), pneumonia (J12–J18), peritonitis (K65), and sepsis (A40, A41) or disseminated intravascular coagulation syndrome (D65).

### Statistical analysis

We compared demographic data between patients with and without HD in unmatched and propensity score-matched cohorts using the standardized difference. An absolute standardized difference of  $>0.1$  was considered to indicate significant imbalance.<sup>18</sup> We performed propensity score matching to adjust for measured confounding factors.<sup>19</sup> Variables entered in the propensity model were age, sex, diabetes mellitus, hypertension, chronic lung disease, ischemic heart disease, cerebrovascular disease, hospital volume, and types of hepatic resection. We calculated propensity scores using a logistic regression model applied with these variables. The C-statistic was calculated to evaluate the goodness of fit. We conducted 1-to-4 propensity score matching with replacement using the nearest available matching, setting the caliper as 0.2. We used Fisher exact test to compare postoperative major complications, 30-day mortality, 90-day mortality, and in-hospital mortality between patients with and without HD in the propensity

score-matched cohort. The time to in-hospital death and postoperative hospital stay were compared using Student *t* test. We also performed subgroup analyses in the cohort who were propensity score matched. We compared the odds ratios (ORs) for in-hospital mortality between patients with and without HD stratified by the type of hepatic resection or age category ( $<80$  or  $\geq 80$  years). All statistical analyses were conducted using Stata software Version 14.1 (StataCorp LP, College Station, TX).

## Results

We identified 53,651 eligible patients who underwent hepatic resection from 1,040 hospitals during the study period. Of these patients, 498 (0.93%) underwent HD. The propensity score-matched cohort comprised 2,490 patients, including 498 patients with HD and 1,992 patients without HD. The C-statistic was 0.69. The background characteristics of the patients with and without HD in the unmatched and propensity score-matched cohorts are shown in [Table 1](#). In the unmatched cohort, the age distribution and proportions of male sex, primary liver cancer, ischemic heart disease, cerebrovascular disease, and diabetes mellitus were substantially greater in patients with than without HD. After propensity score matching, the background patient characteristics were well-balanced between the 2 groups.

[Table 2](#) shows the proportions of postoperative outcomes in patients with and without HD in the propensity score-matched cohort. Several postoperative complications were observed more often in patients with than without HD, including peritonitis (2.6% vs 0.8%,  $P = .001$ ), sepsis or disseminated intravascular coagulation syndrome (8.2% vs 4.0%,  $P < .001$ ), and acute coronary events (5.6% vs 1.0%,  $P < .001$ ). The proportion of patients with at least 1 postoperative complication was greater in patients with HD (18.1% vs 7.4%,  $P < .001$ ). The mean duration of postoperative hospital stay was greater in patients with HD ( $38.3 \pm 40.1$  vs  $25.1 \pm 21.3$  days,  $P < .001$ ). The 30-day and 90-day mortality rates were also greater in patients with HD (2.0% vs 0.4%,  $P < .001$  and 5.0% vs 1.4%,  $P < .001$ , respectively). The in-hospital mortality rate was 8.6% and 2.0% in patients with and without HD, respectively ( $P < .001$ ). The time to in-hospital death was comparable between patients with and without HD ( $76.0 \pm 73.6$  vs  $69.8 \pm 61.4$  days,  $P = .68$ ).

For postoperative complications and in-hospital mortality in the propensity score-matched cohort, patients with HD had a greater risk of postoperative complications (OR, 2.75; 95% confidence interval [CI], 2.07–3.65;  $P < .001$ ) and in-hospital mortality (OR, 4.61; 95% CI, 2.96–7.18;  $P < .001$ ).

In the subgroup analyses for in-hospital mortality, the OR for patients with HD was 2.36 (95% CI, 0.78–6.59;  $P = .067$ ) in limited resection, 4.61 (95% CI, 1.90–11.2;  $P < .001$ ) in segmentectomy or sectoriectomy, and 7.06 (95% CI, 3.40–14.9;  $P < .001$ ) in bisectoriectomy or trisectoriectomy. In the age subgroup analyses, the OR of patients with HD was 4.38 (95% CI, 2.66–7.21;  $P < .001$ ) in patients aged  $<80$  years and 7.20 (95% CI, 1.55–36.7;  $P = .0011$ ) in patients aged  $\geq 80$  years ([Table 3](#)).

## Discussion

The present study showed that patients undergoing HD had an approximately 2-fold greater risk of postoperative complications and a more than 4-fold greater risk of in-hospital mortality after hepatic resection compared with patients not undergoing HD. Both the 30-day and 90-day mortality rates were greater in patients with HD. In the subgroup analyses, the OR for in-hospital mortality of patients undergoing HD tended to be increased in segmentectomy or sectoriectomy and bisectoriectomy or trisectoriectomy. Furthermore,

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