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Mortality and morbidity after pancreatoduodenectomy in patients undergoing hemodialysis: Analysis using a national inpatient database

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ABSTRACT

Background: Whether patients undergoing hemodialysis have greater risks of mortality and morbidity after pancreatoduodenectomy remains unknown.
Methods: We used the Diagnosis Procedure Combination database, a national Japanese inpatient database, to identify patients who underwent pancreatoduodenectomy from July 2010 to March 2015. We conducted propensity-score-matching analyses to compare the outcomes, including postoperative complications and 30- and 90-day mortality after pancreatoduodenectomy between patients with and without hemodialysis.
Results: Of 30,495 eligible patients, 307 (1.0%) received hemodialysis. In the unmatched cohort, the proportions of male sex, younger age, pancreatic cancer, ischemic heart disease, diabetes mellitus, and hypertension were greater in patients with hemodialysis than those without hemodialysis. A 1-to-4 propensity score matching created a total of 1,535 patients, including 307 with hemodialysis and 1,228 without hemodialysis. Patients undergoing hemodialysis had greater proportions of postoperative complications, including peritonitis (8.8% vs 4.8%, $P = .012$), sepsis or disseminated intravascular coagulation (3.6% vs 0.7%, $P = .001$), intra-abdominal bleeding (4.9% vs 0.7%, $P < .001$), and acute coronary event (4.2% vs 1.7%, $P = .015$). Propensity score matching showed that patients undergoing hemodialysis had an increased risk of postoperative complications (OR, 1.62; 95% CI, 1.23–2.14; $P = .001$), 30-day mortality (OR, 7.45; 95% CI, 3.26–17.0; $P < .001$), and 90-day mortality (OR, 10.9; 95% CI, 6.58–18.2; $P < .001$) than those not undergoing hemodialysis.
Conclusion: Patients undergoing hemodialysis had a significantly increased risk of postoperative complications and death after pancreatoduodenectomy. In particular, surgeons should consider the increased risk of intra-abdominal bleeding, peritonitis, sepsis or disseminated intravascular coagulation, and acute coronary event in patients with hemodialysis.

Introduction

More than 1,000,000 patients with end-stage renal disease undergo hemodialysis (HD) every year worldwide. This number of patients has been increasing at an average annual global rate of 7%.[1] Patients with end-stage renal disease have a high burden of comorbidities, such as diabetes mellitus and cardiovascular disease, which may influence their survival outcomes.[2] The reported crude mortality rate of patients undergoing HD is about 10% every year. In 1 study, the standardized mortality ratio for all-cause mortality was 4.6-fold greater in patients undergoing HD than in the general population.[3] Previous studies have also shown that among patients undergoing several types of operations, the mortality rate is greater in patients with HD than in those without HD.[4–6]

Pancreatoduodenectomy (PD) is performed to resect periampullary tumors and pancreatic neoplasms.[7,8] The number of patients undergoing PD has been increasing worldwide.[8,9] This operation is 1 of the most complex procedures in the field of general gastrointestinal surgery. Although operative techniques and

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modalities have improved in recent years, population-based studies have shown that the morbidity and mortality rates of PD range from 20% to 40%[9,10] and 2.8% to 8.1%,[8,11,12] respectively. Previous studies have also revealed several preoperative risk factors for postoperative complications and in-hospital death after PD, including age, sex, ischemic heart disease, and the extent of the operative procedure.[8,12,13] The PD-associated risk of mortality in patients receiving HD, however, has not been investigated. Given the growing number of patients undergoing HD, it is necessary to clarify the PD-associated risks of morbidity and mortality in patients undergoing HD.

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

Methods

Data source

The Diagnosis Procedure Combination database is a national inpatient database in Japan.[14–16] All 82 academic hospitals are required to participate in the database, but participation by community hospitals is voluntary. The database includes the following information: patient age, sex, diagnoses, comorbidities at admission, and complications after admission recorded using the International Classification of Diseases 10th revision (ICD-10) codes, operative procedures, HD coded with Japanese original codes, and in-hospital death. To optimize the accuracy of the diagnoses, physicians in charge are required to record diagnoses with reference to medical charts. Because of the anonymous nature of the data used in this study, informed consent was waived. The current study was approved by the Institutional Review Board at the University of Tokyo.

Patients

We identified patients aged ≥20 years who underwent PD from July 2010 to March 2015. The patients were divided into those with and without HD. The following patient data were examined: age, sex, primary diagnosis, preoperative comorbidities, hospital volume, and type of PD. Age was stratified into 5 categories: 20–49, 50–59, 60–69, 70–79, and ≥80 years. The primary diagnoses were divided into pancreatic cancer (International Classification of Diseases 10th revision codes C250, C251, C252, C253, C257, C258, and C259) and other diseases. Preoperative comorbidities included diabetes mellitus (E10–E14), hypertension (I10–I15), history of ischemic heart disease (I20–I25), history of cerebrovascular disease (I60–I69), and chronic lung disease (J40–J47). Hospital volume was defined as the average annual number of PDs performed at each hospital. Hospital volume was stratified into 4 categories: <8, 8–14, 15–28, and ≥29 PDs per year. The types of PD included standard PD, PD with lymph node dissection, PD with vascular reconstruction, and PD with resection of other organs.

Outcomes

The outcome variables were in-hospital death within 30 and 90 days and postoperative major complications. Postoperative major complications included acute coronary events (I20–I24), stroke (I60–I64), pneumonia (J12–J18), peritonitis (K65), bile leakage (K83.3), pancreatic leakage (K86.8), intra-abdominal bleeding (K66.1), and sepsis (A40, A41) or disseminated intravascular coagulation syndrome (DIC; D65).

Statistical analysis

We compared the backgrounds of patients with and without HD in unmatched and cohorts who were propensity score matched using the standardized difference. The absolute value of a standardized difference of >0.1 was considered indicative of substantial imbalance.[17]

We performed propensity score matching (PSM) to adjust for measured confounding factors.[18] We calculated propensity scores using a logistic regression model for the receipt of HD as a function of patient background variables, including age, sex, diabetes mellitus, hypertension, chronic lung disease, ischemic heart disease, cerebrovascular disease, hospital volume of PDs, and type of PD. C-statistics were calculated to evaluate the goodness of fit. One-to-four PSM was performed with replacement and a caliper width ranging <0.25 of the pooled standard deviation of the estimated propensity scores. We performed Fisher exact test to compare the proportion of postoperative major complications, 30-day mortality, and 90-day mortality between patients with and without HD in the propensity-score-matched cohort. Logistic regression analyses for the propensity-score-matched cohort were performed to estimate the odds ratio (OR) and 95% confidence interval (CI) of patients undergoing HD with reference to those not undergoing HD for postoperative complications, 30-day mortality, and 90-day mortality. The threshold for statistical significance was $P < .05$. All statistical analyses were conducted using Stata software version 14.1 (StataCorp LLC, College Station, Texas).

Results

We identified 30,495 eligible patients who underwent PD from 996 hospitals during the survey period. Among these patients, 307 (1.0%) were receiving HD. The propensity-score-matched cohort comprised 1,535 patients, including 307 with HD and 1,228 without HD. The C-statistic was 0.66. The backgrounds 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 proportions of males, age 20–49, pancreatic cancer, ischemic heart disease, diabetes mellitus, and hypertension were greater in patients with HD than without HD. After PSM, the distributions of the patients' background variables were balanced closely between the patients with and without HD.

Table 2 shows the proportions of postoperative major complications and 30- and 90-day mortality in patients with HD and without HD in the unmatched and propensity-score-matched cohort. Several postoperative complications were observed more frequently in patients with HD than without HD, including peritonitis (8.8% vs 4.8%, $P = .012$), sepsis or DIC (3.6% vs 0.7%, $P = .001$), intra-abdominal bleeding (4.9% vs 0.7%, $P < .001$), and acute coronary event (4.2% vs 1.7%, $P = .015$) in the propensity-score-matched cohort.

Logistic regression analyses for postoperative complications and 30- and 90-day mortality in the propensity-score-matched cohort were calculated. Patients undergoing HD were more likely to have postoperative complications (OR, 1.62; 95% CI, 1.23–2.14; $P = .001$), 30-day mortality (OR, 7.45; 95% CI, 3.26–17.0; $P < .001$), and 90-day mortality (OR, 10.9; 95% CI, 6.58–18.2; $P < .001$).

Discussion

The current study revealed that patients undergoing HD had significantly increased risks of postoperative complications and 30- and 90-day mortality using PSM. Patients undergoing HD showed a 1.6-fold greater risk of postoperative complications, an approximately 7.4-fold greater risk of 30-day mortality, and a 10.9-fold greater risk of 90-day mortality after PD. Peritonitis, sepsis or DIC,

Table 1
Characteristics of patients with and without HD in the unmatched and propensity-score-matched cohorts.

	Unmatched cohort			Propensity-score-matched cohort		
Variables	Patients without HD(n = 30,188) (%)	Patients with HD(n = 307) (%)	Standardized difference	Patients without HD(n = 1,228) (%)	Patients with HD(n = 307) (%)	Standardized difference
Sex (male), *n* (%)	18,351 (61)	236 (77)	0.352	945 (77)	236 (77)	−0.002
Age (years)						
20–49	1,335 (4.4)	4 (1.3)	−0.188	14 (1.1)	4 (1.3)	0.015
50–59	3,217 (10.6)	33 (10.8)	0.003	122 (9.9)	33 (10.7)	0.027
60–69	10,105 (33.5)	106 (34.5)	0.022	433 (35.3)	106 (34.5)	−0.017
70–79	12,304 (40.8)	131 (42.7)	0.039	530 (43.2)	131 (42.7)	−0.012
≥80	3,227 (10.7)	33 (10.7)	0.002	126 (10.3)	33 (10.7)	0.013
Diagnosis, *n* (%)						
Pancreatic cancer	13,580(45.0)	104(33.9)	−0.23	405 (33)	104 (33.9)	0.024
Hospital volume (no. of PDs/year)						
<8	7,463 (24.7)	82 (26.7)	0.046	336 (27.4)	82 (26.7)	−0.016
8–14	7,608 (25.2)	74 (24.1)	−0.025	297 (24.2)	74 (24.1)	−0.002
15–28	7,540 (25.0)	79 (25.7)	0.017	312 (25.4)	79 (25.7)	0.007
≥29	7,577 (25.1)	72 (23.5)	−0.038	282 (23)	72 (23.5)	0.012
Procedure type of PD, *n* (%)						
Standard PD	5,172 (17.1)	54 (17.6)	0.012	217 (17.7)	54 (17.6)	−0.002
with lymph node dissection	17,576 (58.2)	184 (59.9)	0.035	720 (58.6)	184 (59.9)	0.028
with vascular reconstruction	2,552 (8.5)	24 (7.8)	−0.023	106 (8.6)	24 (7.8)	−0.030
with resection of other organ	4,888 (16.2)	45 (14.7)	−0.042	185 (15.1)	45 (14.7)	−0.014
IHD, *n* (%)	2,074 (6.9)	38 (12.4)	0.187	135 (11)	38 (12.4)	0.051
CRD, *n* (%)	981 (3.3)	9 (2.9)	−0.018	24 (2.0)	9 (2.9)	0.075
CVD, *n* (%)	971 (3.2)	16 (5.2)	0.099	74 (6.0)	16 (5.2)	−0.025
DM, *n* (%)	10,023 (33.2)	137 (44.6)	0.236	540 (44)	137 (44.6)	0.016
HT *n* (%)	7,455 (24.7)	106 (34.5)	0.216	418 (34)	106 (34.5)	0.005

IHD = ischemic heart disease; CRD = chronic respiratory disease; CVD = cerebrovascular disease; DM = diabetes mellitus; HT = hypertension.

Table 2
Postoperative complications in patients with and without HD in the unmatched and propensity-score-matched cohorts.

	Unmatched cohort			Propensity-score-matched cohort		
	Patients without HD(n = 30,188) (%)	Patients with HD(n = 307) (%)	*P*	Patients without HD(n = 1,228) (%)	Patients with HD(n = 307) (%)	*P*
Pneumonia	322 (1.1)	7 (2.3)	.05	17 (1.4)	7 (2.3)	.30
Peritonitis	1,183 (3.9)	27 (8.8)	<.001	59 (4.8)	27 (8.8)	.012
Sepsis or DIC	330 (1.1)	11 (3.6)	.001	9 (0.7)	11 (3.6)	.001
Stroke	110 (0.4)	2 (0.7)	.31	5 (0.4)	2 (0.7)	.63
Acute coronary event	488 (1.6)	13 (4.2)	.002	21 (1.7)	13 (4.2)	.015
Abdominal bleeding	297 (1.0)	15 (4.9)	<.001	9 (0.7)	15 (4.9)	<.001
Bile leakage	115 (0.4)	1 (0.3)	>.99	0 (0)	1 (0.33)	.20
Pancreatic fistula	3,253 (10.8)	33 (10.8)	>.99	169 (13.8)	33 (10.8)	.19
At least 1 complication	5,547 (18.4)	94 (30.6)	<.001	263 (21.4)	94 (30.6)	.001
30-day mortality	245 (0.8)	16 (5.2)	<.001	9 (0.7)	16 (5.2)	<.001
90-day mortality	668 (2.2)	53 (17.3)	<.001	23 (1.9)	53 (17.3)	<.001

intra-abdominal bleeding, and acute coronary event were significantly greater in patients undergoing HD.

A previous report indicated that patients with HD undergoing a general surgery operation had significantly increased risks of postoperative complications and death.[19] Among patients undergoing PD, Kimura et al[8] identified significantly greater mortality in those with renal dysfunction. Meanwhile, Squires et al[13] demonstrated no significant mortality risk in patients with renal dysfunction. This discrepancy may be due to the review of patients with various stages of renal dysfunction and the small sample sizes. The current study used a large, nationwide database from about 1,000 hospitals in Japan and focused on patients with end-stage renal disease undergoing HD. Furthermore, we confirmed the statistically increased risk of postoperative complications and mortality after PD by PSM.

Patients undergoing HD are known to have or develop ischemic heart disease and diabetes mellitus frequently[6,20]; moreover, these patients tend to develop cardiovascular events related to atherosclerosis.[21,22] The current study also showed that patients undergoing HD more frequently had a history of previous ischemic heart disease, diabetes mellitus, and hypertension. In the propensity-score-matched cohort, acute coronary events after PD were observed more frequently in patients with HD. HD was also associated with an increased risk of abdominal bleeding, peritonitis, and sepsis or DIC. A previous report indicated that impaired platelet function might be associated with chronic renal failure.[23] Patients undergoing HD have also been considered to be more susceptible to postoperative infection.[24,25] In the Diagnosis Procedure Combination database, the information associated with cause of death was not registered; however, postoperative major complications, including arterial hemorrhage, systemic sepsis, and cardiac events, can be causes of death as well as sentinel events leading to death after PD.[26,27] Therefore, it is necessary to manage abdominal bleeding, infectious complications, and cardiocirculatory dynamics aggressively in patients with HD undergoing PD.

The current study revealed that patients undergoing HD had significantly increased risks of both 30- and 90-day mortality after PD. Although the 30-day mortality rate has been used to evaluate the quality of operative procedures,[28] surgery-related death may occur later than 30 days after PD.[29,30] Several studies have indicated that 90-day mortality may be a more legitimate measure of surgery-related deaths in patients undergoing pancreatectomy.[29,30]

The current results showed that patients undergoing HD had an approximately 10.9-fold greater risk of 90-day mortality after PD.

Operative resection is currently the only curative treatment for periampullary malignancies. To prolong patients' life expectancy and prognosis, the performance of PD for malignant neoplasms is often unavoidable even in patients undergoing HD. A previous report showed that hospital volume was associated with the risk of mortality in patients undergoing PD.[12] Institutional limitations may be required for patients with HD.

The current study has several limitations inherent to studies involving administrative databases. First, the database we used did not include important clinical data, such as laboratory data and oncologic findings. Bias could be present because we could not adjust for several possible risk factors for morbidity and mortality. Second, we identified the patients undergoing chronic HD based on the code used to define HD. Because of a lack of prehospital clinical information, patients who had not received HD before operation may have been included in the HD cohort, but because we excluded patients who underwent creation of HD access after PD, the number of patients who initiated chronic HD after PD might be little or none in the current study. Third, mortality after PD might have been underestimated in the database. Several previous studies revealed a strong inverse association between greater hospital volumes and lesser mortality after PD.[12,31] The database might not be representative of all hospitals in Japan because participation of community hospitals in the database is voluntary.

Conclusion

Using a large national inpatient database in Japan, we found that patients undergoing chronic HD for end-stage renal disease had a significantly increased risk of postoperative complications and death after PD. In particular, surgeons should consider and watch closely for the increased risk of intra-abdominal bleeding, peritonitis, sepsis or DIC, and acute coronary events in these cases. These findings can help surgeons make adequate clinical decisions for patients undergoing HD.

Conflicts of interest

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). The authors have indicated that they have no other conflicts of interest regarding the content of this article.

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