Digestive Surgery

Original Paper

The Outcome of Complex Hepato-Pancreato-Biliary Surgery for Elderly Patients: A Propensity Score Matching Analysis

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Abstract
Background/Aims: Postoperative mortality and morbidity rates after hepato-pancreato-biliary (HPB) surgery remain high, and the number of elderly patients requiring such surgery has been increasing. This study aimed to investigate postoperative outcomes of complex HPB surgery for elderly patients. ***Methods:*** We retrospectively reviewed perioperative data of 721 patients who underwent complex HPB surgery between 2010 and 2015. The patients were divided into 2 groups: elderly (≥75 years) and non-elderly (<75 years). Surgical outcomes of both groups were compared after propensity score-matching analysis. Subsequently, risk factors for serious postoperative morbidity were identified by multivariate analysis. ***Results:*** Before matching, the elderly group ($n = 170$) had more comorbidities, such as cardiovascular and renal disease, than the non-elderly group ($n = 551$). Matching yielded elderly ($n = 170$) and non-elderly groups ($n = 170$) with similar preoperative backgrounds. The mortality and morbidity rates did not differ significantly between the groups. In multivariate analyses, operative time (OR 1.79; $p = 0.005$) and blood loss (OR 1.66; $p = 0.03$) were identified as independent risk factors for serious postoperative morbidity, whereas older age did not have a predictive impact (OR 1.16; $p = 0.52$). ***Conclusions:*** Although elderly patients had more comorbidities and higher incidences of postoperative mortality and several complications before matching, their postoperative outcomes were equivalent to those of non-elderly patients after matching.

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Introduction

The complicated management of elderly patients with malignancy has become an important global issue. Increased life expectancy and the increasing number of elderly patients with cancer have resulted in expanded indications for hepato-pancreato-biliary (HPB) surgery [1]. However, the operative mortality and morbidity rates after

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Table 1. Number of complex hepato-pancreato-biliary surgeries between 2010 and 2015 at the Okayama University Hospital

Procedures	Patients ($n = 721$), n
Hepatobiliary surgery	
Right trisegmentectomy of the liver	9
Left trisegmentectomy of the liver	7
Right or extended right hepatectomy	64
Left or extended left hepatectomy	75
Central bisectionectomy of the liver	7
Hepatic sectionectomy (except lateral sectionectomy)	133
Hepatic segmentectomy (S1, S2, S3, S5, S6, S7, S8)	42
Hepatectomy (S4a + S5 or hemihepatectomy) with extrahepatic BDR	46
Extrahepatic BDR for congenital biliary dilatation	5
Hepatopancreatic surgery	
Hepatopancreatectomy	13
Pancreatic surgery	
Total pancreatectomy	8
Pancreatoduodenectomy	244
Distal pancreatectomy with lymph node dissection (for pancreatic cancer)	58
Middle segment pancreatectomy	9
Inferior pancreatic head resection	1

BDR, bile duct resection.

HPB surgery are still high. Although the 90-day mortality rate after complex HPB surgery has been decreasing, it was reported to be 1.7% in Japan [2]. Furthermore, nationwide surveys in Japan revealed that postoperative morbidity rates after major hepatectomy and pancreaticoduodenectomy are 25.7 and 41.6% respectively [3, 4]. When considering the surgical indications for HPB surgery for older patients, we should also consider age-related mortality and morbidity and cancer-related death. However, there is little evidence to support these approaches.

To date, a nationwide survey in the United States showed that age (>74 years) was associated with a nearly twofold increase in morbidity and mortality after HPB surgery [5]. Regarding hepatectomy, a previous literature review showed that surgical resection in elderly patients may be safe, and elderly patients had prognoses comparable to those of younger patients [6]. However, the result of a nationwide survey performed in Japan revealed that older age was closely associated with mortality following hepatectomy [7]. Regarding pancreatectomy, a previous literature review reported that although pancreatectomy can be performed safely in an elderly population (≥80 years), overall morbidity and mortality rates were 34.9 and 13.2% respectively [8].

Some studies have involved global perioperative outcomes after HPB surgery [5, 9]. However, the relationship between age and perioperative outcomes has not been investigated extensively for patients undergoing HPB surgery. Therefore, this study aimed to investigate the perioperative outcomes of complex HPB surgery by focusing on patient age and using a propensity score-matching (PSM) analysis and to subsequently examine risk factors for serious postoperative morbidity after HPB surgery.

Methods

Study Cohort

We retrospectively reviewed the medical records of 721 consecutive patients who underwent complex HPB surgery at the Okayama University Hospital (Okayama, Japan) between January 2010 and December 2015 (Table 1). Complex HPB surgery was defined according to the criteria of the Japanese Society of Hepato-Biliary-Pancreatic Surgery [2]. The present study included 3 categories of procedures: hepatobiliary surgery, hepatopancreatic surgery, pancreatic surgery. This study was approved by the Ethics Committee of the Okayama University Graduate School of Medicine, Dentistry, and Pharmaceutical Sciences and was conducted in accordance with the Declaration of Helsinki.

Clinical Data

For enrolled patients, the following patient characteristics were evaluated as preoperative factors: age, sex (male, female), body mass index (BMI; ≤25, >25), American Society of Anesthesiologists physical status (1–2, 3–4), laboratory values, liver function

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according to the Child-Pugh score (A or B), comorbidities (hypertension, diabetes, hyperlipidemia, cerebral disease, cardiac disease, chronic obstructive pulmonary disease), liver disease (hepatitis B virus and/or hepatitis C virus), chronic kidney disease, and etiology of the disease (hepatic disease, biliary disease, pancreatic disease, or miscellaneous). Patients were divided into 2 groups according to age, non-elderly (<75 years) and elderly (≥75 years) according to the proposal of the Joint Committee of Japan Gerontological Society and the Japan Geriatrics Society [10].

Surgical procedures (Table 1), operative time, intraoperative blood loss, and blood transfusion were recorded as intraoperative outcomes. Details of the surgical techniques of hepatectomy, pancreaticoduodenectomy, and hepatopancreatectomy have been reported previously [11–14]. At our center, age is not recognized as a contraindication. Patients, especially the elderly, meeting the following criteria were eligible for to undergo the following procedures: ability to perform self-care, independent mobility, no severe dementia, and adequate family support.

Postoperative outcomes, including postoperative 30- and 90-day mortality, morbidity (any of the following events: reoperation, wound infection, intra-abdominal abscess, bile leakage, intraabdominal bleeding, central nervous system complication, cardiac complication, pneumonia, delirium, ileus, cholangitis, or bacteremia), and postoperative hospital stay, were evaluated. Postoperative morbidity was assessed according to the American College of Surgeons National Surgical Quality Improvement Program criteria [15] and graded according to the Clavien-Dindo classification [16]. Morbidity was defined according to Clavien-Dindo classification ≥II, and serious morbidity was defined according to Clavien-Dindo classification ≥III.

Statistical Analysis

To avoid confounding differences due to baseline variability between the non-elderly and elderly groups, the PSM analysis was generated using a logistic regression model. Propensity scores were generated with preoperative variables with $p < 0.20$ (10 variables in total). This one-to-one matching was performed using a caliper width of 0.20 of the SD of the log of propensity score. We used the receiver-operating characteristic and area under the curve (AUC) to measure the balance of covariates. To investigate the impact of perioperative predictors associated with serious postoperative morbidity, we used a logistic regression model for univariate and multivariate analyses; ORs and 95% CIs were calculated. All preoperative and intraoperative variables with $p < 0.20$ in the univariate analysis were selected for the multivariate analysis. All analyses were performed with JMP version 11 software (SAS Institute, Cary, NC, USA). Student t test, Mann-Whitney's U test, Fisher's exact test, and the chi-square test were used appropriately. Two-sided $p < 0.05$ was considered significant.

Results

Patient Characteristics

Patient characteristics before and after PSM are shown in Table 2. Of the overall cohort ($n = 721$), 170 patients (23.6%) belonged to the elderly group. The elderly group had more hypertension ($p = 0.001$), cardiac disease

($p = 0.02$), chronic obstructive pulmonary disease ($p < 0.001$), and chronic kidney disease ($p < 0.001$). Malignant diseases were significantly more frequent in the elderly group than in the non-elderly group (94.1 vs. 82.0%; $p < 0.001$).

After PSM, a non-elderly group ($n = 170$) with preoperative characteristics similar to those of the elderly group was selected. Within this matched cohort, the AUC calculated from the receiver-operating characteristic curve was 0.724.

Perioperative Outcomes

Table 3 summarizes the intraoperative outcomes before and after PSM. In the PSM cohort, the operative time was significantly shorter for the elderly group ($p = 0.003$); however, other intraoperative factors did not differ significantly.

Concerning postoperative outcomes, the elderly group had higher rates of 90-day mortality ($p < 0.001$), wound infection ($p = 0.05$), pneumonia ($p = 0.02$), and delirium ($p < 0.001$) before PSM (Table 4). Regarding other factors, including serious morbidity and 30-day mortality, there was no significant difference between groups. After PSM, no significant differences between groups were found regarding the rates of postoperative 30-day mortality (0 vs. 0.6%; $p = 0.32$), 90-day mortality (3.5 vs. 0.6%; $p = 0.06$), serious morbidity (19.4 vs. 18.2%; $p = 0.78$), and any morbidity (61.8 vs. 59.4%; $p = 0.66$). Only the incidence of delirium was significantly higher for the elderly group ($p < 0.001$).

Predictive Factors for Postoperative Serious Morbidity

Table 5 shows the results of the univariate and multivariate analyses used to identify the perioperative predictors closely associated with serious postoperative morbidity after HPB surgery. In the multivariate analysis, operative time (OR 1.79; $p = 0.005$) and blood loss (OR 1.66; $p = 0.03$) were identified as independent risk factors associated with serious morbidity. However, age (≥75 years) was not an independent risk factor after complex HPB surgery (OR 1.16; $p = 0.52$).

Discussion

This retrospective study of 721 patients demonstrated that complex HPB surgery can be feasible, even for elderly patients. To the best of our knowledge, this study is the first to investigate the impact of age on global perioperative outcomes for patients following HPB surgery. Although the elderly group had more comorbidities, they

Table 2. Characteristics of patients undergoing complex hepato-pancreato-biliary surgery: overall and propensity score-matching cohort

Variables	Before PSM ($n = 721$)			After PSM ($n = 340$)		
	non-elderly group ($n = 551$)	elderly group ($n = 170$)	p value	non-elderly group ($n = 170$)	elderly group ($n = 170$)	p value
Gender, male/female	372/179	101/69	0.05	97/73	101/69	0.66
BMI (≤25, >25 kg/m^2)	421/130	142/28	0.05	134/36	142/28	0.27
ASA (1–2, 3–4)	477/74	141/29	0.24	133/37	141/29	0.27
Hemoglobin, g/dL	13.2 (1.7)	12.7 (1.5)	<0.001	12.7 (1.8)	12.7 (1.5)	0.96
Platelet count, ×10^4/μL	21.8 (8.1)	21.3 (7.6)	0.48	22.5 (8.5)	21.3 (7.6)	0.16
Total bilirubin, mg/dL	0.8 (0.6)	0.8 (0.5)	0.38	0.8 (0.8)	0.8 (0.5)	0.31
Albumin, g/dL	4.1 (0.5)	3.9 (0.4)	<0.001	4.0 (0.6)	3.9 (0.4)	0.67
Prothrombin time	106 (15.9)	105 (18.3)	0.25	105 (16.3)	105 (18.3)	0.87
Child-Pugh score (A or B)	533/18	164/6	0.87	158/12	164/6	0.15
Comorbidities						
Hypertension	234 (42.5)	96 (56.5)	0.001	105 (61.8)	96 (56.5)	0.32
Diabetes	174 (31.6)	61 (35.9)	0.30	63 (37.1)	61 (35.9)	0.82
Hyperlipidemia	181 (32.9)	65 (38.2)	0.20	74 (43.5)	65 (38.2)	0.32
Cerebral disease	30 (5.4)	10 (5.9)	0.83	12 (7.1)	10 (5.9)	0.66
Cardiac disease	52 (9.4)	27 (15.9)	0.02	24 (14.1)	27 (15.9)	0.65
COPD	84 (15.3)	54 (31.8)	<0.001	54 (31.8)	54 (31.8)	1.00
Liver disease (HBV ± HCV)	142 (25.8)	37 (21.8)	0.29	43 (25.3)	37 (21.8)	0.44
CKD	79 (14.3)	51 (30.0)	<0.001	49 (28.8)	51 (30.0)	0.81
Etiology of disease						
Hepatic disease	264 (47.9)	75 (44.1)	0.01	75 (44.1)	75 (44.1)	0.65
Hepatocellular carcinoma	158	51		46	51	
Metastatic hepatic cancer	54	11		17	11	
Intrahepatic cholangiocarcinoma	34	13		9	13	
Others	18	0		3	0	
Biliary disease	72 (13.1)	34 (20.0)		28 (16.5)	34 (20.0)	
Distal bile duct cancer	18	9		10	9	
Perihilar or proximal bile duct cancer	16	8		5	8	
Ampulla of vater cancer	14	8		6	8	
Gall bladder cancer	13	8		4	8	
Congenital bile duct dilatation	5	0		2	0	
Others	6	1		1	1	
Pancreatic disease	194 (35.2)	61 (35.9)		67 (39.4)	61 (35.9)	
Pancreatic cancer	125	52		39	52	
IPMN	35	7		16	7	
Others	34	2		12	2	
Miscellaneous	21 (3.8)	0 (0)		0 (0)	0 (0)	

Data are presented as mean (SD) or n (%).
PSM, propensity score matching; BMI, body mass index; ASA, American Society of Anesthesiologists; COPD, chronic obstructive pulmonary disease; HBV, hepatitis B virus; HCV, hepatitis C virus; CKD, chronic kidney disease; IPMN, intraductal papillary mucinous neoplasm.

had equivalent postoperative outcomes compared to non-elderly patients matched by propensity scores. In addition, age was not a risk factor for serious postoperative morbidity after HPB surgery.

Patient selection is important for minimizing postoperative morbidity or mortality after HPB surgery [5]. In our center, age is not recognized as a contraindication. We always considered the possibility of indications for procedures, even for the elderly, and patients underwent aggressive procedures regardless of age. However, the less extensive procedures for elderly patients were occasionally considered according to the patients' risks and tumor status. A more meticulous surgical approach would be necessary to shorten operative times and reduce blood loss as much as possible, especially for elderly patients. Accordingly, we suggested that individual assessment is most important for determining the strategy in accordance with perioperative factors.

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Table 3. Intraoperative outcomes

Variables	Before PSM (n = 721)			After PSM (n = 340)		
	non-elderly group (n = 551)	elderly group (n = 170)	p value	non-elderly group (n = 170)	elderly group (n = 170)	p value
Operative time, min	363 (112)	344 (107)	0.05	380 (111)	344 (107)	0.003
Blood loss, mL	737 (1383)	563 (638)	0.11	744 (1073)	563 (638)	0.06
Transfusion	85 (15.4)	29 (17.1)	0.61	36 (21.2)	29 (17.1)	0.33
Procedures						
Hepatobiliary surgery	298 (54.1)	90 (52.9)	0.96	86 (50.6)	90 (52.9)	0.91
Right trisegmentectomy	9	0		3	0	
Left trisegmentectomy	5	2		2	2	
Right or extended right hepatectomy	56	8		16	8	
Left or extended left hepatectomy	52	23		13	23	
Central bisectionectomy	4	3		3	3	
Hepatic sectionectomy (except lateral sectionectomy)	109	24		31	24	
Hepatic segmentectomy (S1, S2, S3, S5, S6, S7, S8)	30	12		7	12	
Hepatectomy (S4a+S5 resection or hemihepatectomy) with extrahepatic BDR	28	18		9	18	
Extrahepatic BDR for congenital biliary dilatation	5	0		2	0	
Hepatopancreatic surgery	10 (1.8)	3 (1.8)		3 (1.8)	3 (1.8)	
Pancreatic surgery	243 (44.1)	77 (45.3)		81 (47.6)	77 (45.3)	
Total pancreatectomy	7	1		1	1	
Pancreatoduodenectomy	190	54		68	54	
Distal pancreatectomy with LND (to treat pancreatic cancer)	38	20		10	20	
Others	8	2		2	2	
Vascular reconstruction	72 (13.1)	18 (10.6)	0.39	24 (14.1)	18 (10.6)	0.32

Data are presented as means (SD) or n (%).
PSM, propensity score matching; BDR; bile duct resection; LND, lymph node dissection.

Table 4. Postoperative outcomes

Variables	Before PSM (n = 721)			After PSM (n = 340)		
	non-elderly group (n = 551)	elderly group (n = 170)	p value	non-elderly group (n = 170)	elderly group (n = 170)	p value
30-day mortality	1 (0.2)	0 (0)	0.58	1 (0.6)	0 (0)	0.32
90-day mortality	2 (0.4)	6 (3.5)	<0.001	1 (0.6)	6 (3.5)	0.06
Serious morbidity (CDc ≥III)	102 (18.5)	33 (19.4)	0.79	31 (18.2)	33 (19.4)	0.78
Any morbidity (CDc ≥II)	311 (56.4)	105 (61.8)	0.22	101 (59.4)	105 (61.8)	0.66
Reoperation	18 (3.3)	10 (5.9)	0.12	4 (2.4)	10 (5.9)	0.10
Wound infection	68 (12.3)	31 (18.2)	0.05	23 (13.5)	31 (18.2)	0.24
Intraabdominal abscess	50 (9.1)	17 (10.0)	0.77	14 (8.2)	17 (10.0)	0.57
Bile leakage	54 (9.8)	22 (12.9)	0.24	18 (10.6)	22 (12.9)	0.50
Intraabdominal bleeding	8 (1.5)	4 (2.4)	0.42	2 (1.2)	4 (2.4)	0.41
CNS complication	4 (0.7)	2 (1.2)	0.57	2 (1.2)	2 (1.2)	1.00
Cardiac complication	11 (2.0)	3 (1.8)	0.85	6 (3.5)	3 (1.8)	0.31
Pneumoniae	9 (1.6)	8 (4.7)	0.02	4 (2.4)	8 (4.7)	0.24
Delirium	39 (7.1)	43 (25.3)	<0.001	17 (10.0)	43 (25.3)	<0.001
Ileus	15 (2.7)	2 (1.2)	0.25	1 (0.6)	2 (1.2)	0.56
Cholangitis	18 (3.3)	6 (3.5)	0.87	7 (4.1)	6 (3.5)	0.78
Bacteremia	17 (3.1)	10 (5.9)	0.09	6 (3.5)	10 (5.9)	0.31
Postoperative hospital stay	24 (17–32)	24 (18–33)	0.26	24 (18–36)	24 (18–33)	0.33

Data are presented as median (range) or n (%).
PSM, propensity score matching; CDc, Clavien-Dindo classification; CNS, central nervous system.

Table 5. Univariate and multivariate analyses of perioperative predictors associated with serious postoperative morbidity for patients undergoing complex hepato-pancreato-biliary surgeries

Variables	Patients	Events	Univariate analysis			Multivariate analysis		
			OR	95% CI	p value	OR	95% CI	p value
Age (≥75 years)	170	33	1.06	0.68–1.63	0.79	1.16	0.73–1.80	0.52
Gender, male	473	100	1.63	1.08–2.51	0.02	1.48	0.97–2.30	0.068
BMI (≥25 kg/m^2)	158	26	0.82	0.50–1.29	0.40			
ASA (3–4)	103	22	1.21	0.71–2.00	0.47			
Hemoglobin (<12 g/dL)	159	34	1.24	0.79–1.90	0.34			
Albumin (<3.5 g/dL)	67	12	0.94	0.47–1.75	0.86			
Child-Pugh score B	24	3	0.61	0.14–1.81	0.40			
Hypertension	330	63	1.05	0.72–1.52	0.82			
Diabetes	235	39	0.81	0.53–1.21	0.30			
Hyperlipidemia	246	43	0.88	0.59–1.31	0.54			
Cerebral disease	40	7	0.92	0.37–2.00	0.84			
Cardiac disease	79	18	1.32	0.74–2.28	0.34			
COPD	138	23	0.84	0.50–1.36	0.45			
Liver disease (HBV ± HCV)	179	28	0.75	0.47–1.17	0.22			
CKD	130	26	1.11	0.68–1.76	0.68			
Etiology of disease								
Hepatic disease	339	59	1					
Biliary disease	106	27	0.62	0.37–1.05	0.07			
Pancreatic disease	255	47	0.93	0.61–1.43	0.75			
Miscellaneous	21	2	2	0.56–12.8	0.32			
Operative time (>6 h)	323	80	2.05	1.41–3.02	<0.001	1.79	1.20–2.69	0.005
Blood loss (>1,000 mL)	131	37	1.98	1.27–3.04	0.003	1.66	1.05–2.60	0.031
Procedures								
Hepatobiliary surgery	338	73	1					
Hepatopancreatic surgery	13	3	0.77	0.23–3.01	0.71			
Pancreatic surgery	320	59	1.03	0.70–1.50	0.90			
Vascular reconstruction	90	24	1.7	1.01–2.80	0.05	1.31	0.75–2.23	0.33

BMI, body mass index; ASA, American Society of Anesthesiologists; COPD, chronic obstructive pulmonary disease; HBV, hepatitis B virus; HCV, hepatitis C virus; CKD, chronic kidney disease.

Regarding the comparisons of patient characteristics between groups, 8 out of 18 preoperative factors showed significant differences before PSM (Table 2). As expected, elderly patients tended to have lower BMI values, lower hemoglobin and albumin levels, and more comorbidities. Elderly patients had more age-related comorbidities, with an average of 2.4 complications. Therefore, the surgical risk for elderly patients would be higher than that for non-elderly patients. Furthermore, indications for surgery were significantly different. However, all differences in patient characteristics between groups disappeared after PSM. The covariate balance was considerably improved in the matched cohort.

Regarding the comparisons of intraoperative outcomes between groups, no significant differences were found before PSM (Table 3). This suggested that complex HPB surgery is being aggressively performed for elderly patients at our institution. After PSM, elderly patients tended to have shorter operative times and less blood loss. This might reflect our meticulous surgical approach. We made it a priority to shorten operative times and reduce blood loss during HPB surgery for elderly patients. Performing different procedures would also be a reason for the shorter operative times and reduced blood loss. For example, right trisegmentectomy, right or extended right hepatectomy, sectionectomy, and pancreatoduodenectomy were performed less often for the elderly group (not significant).

When we compared postoperative outcomes between groups, the 90-day mortality, pneumonia, and delirium rates were significantly higher for the elderly group before PSM. However, these differences, except for the incidence of delirium, disappeared after PSM. The main causes of 90-day mortality for the 2 groups ($n = 8$) were as follows: post-

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hepatectomy liver failure ($n = 2$) for the non-elderly group and post-hepatectomy liver failure ($n = 2$), gastrointestinal perforation ($n = 2$), pneumonia ($n = 1$), and postoperative bleeding ($n = 1$) for the elderly group. However, each patient finally experienced multiple organ failure.

Our multivariate analysis revealed that age (≥75 years) was not a risk factor for serious postoperative complications. Although many perioperative factors have been reported to have an impact on postoperative outcomes [5, 9], only intraoperative factors, including operative time and blood loss, were found to be risk factors for serious postoperative complications in the present study. These results supported previous findings that operative time and blood loss were independent predictors of adverse early outcomes following HPB surgery [9]. The reasons that serious postoperative morbidities only depended on intraoperative factors rather than preoperative factors might be explained by the more invasive nature of the surgery. Accordingly, decreasing operative time and blood loss may decrease the risk of postoperative morbidities after HPB surgery.

Perioperative strategies such as delirium management, nutrition, and mobilization may improve postoperative outcomes of patients undergoing HPB surgery. Postoperative delirium is a multifactorial and heterogeneous syndrome that is associated with increased morbidity and costs [17]. In the present study, elderly patients had a significantly higher incidence of postoperative delirium. At our institution, the Delirium Management and Assessment Center has participated in supporting perioperative delirium management [18], which would be effective for managing delirium. However, perioperative nutrition and mobilization are important components of perioperative care for pancreatic surgery and liver surgery and are recommended [19, 20]. Several literatures have shown the safety and efficiency of enhanced recovery after surgery for improving short-term outcomes after HPB surgery [21–25]. Among these literatures, some have involved elderly patients; however, others have excluded the elderly. Further studies examining the effects of perioperative care on the elderly are needed to reduce morbidity and mortality after HPB surgery.

Despite our important findings, this study had a few limitations. This was a retrospective, single-center study; therefore, there may have been selection bias for the patients who underwent HPB surgery. Therefore, PSM was used to reduce selection bias in this study. PSM is now a widely accepted statistical approach that enables robust comparisons [26]. Furthermore, the AUC of 0.724 suggested acceptable discrimination [27]. Another limitation of this study was that PSM could not correct biases that were not measured as cofounders. In addition, this study included different types of procedures. Intraoperative outcomes and postoperative morbidities would be expected to differ depending on the surgical procedure performed. However, the encouraging results of this study suggest that aging may not be a contraindication to complex HPB surgery. The present study did not examine patients who did not undergo procedures; therefore, it might comprise only healthy elderly patients. Future studies are required to investigate the elderly patients who did and did not undergo surgery. Finally, we did not investigate the long-term outcomes after HPB surgery because we investigated several etiologies of diseases, including benign diseases.

In conclusion, the present study demonstrated that age was not a risk factor for serious postoperative complications, even after complex HPB surgery. Although elderly patients had more comorbidities and higher incidences of postoperative mortality and several complications before PSM, they had outcomes similar to those of young patients after PSM. Careful patient selection and assessments of surgical risks should be considered individually.

Disclosure Statement

The authors of this manuscript declare that they have no conflicts of interest to disclose.

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References

1 Hankey BF, Ries LA, Kosary CL, Feuer EJ, Merrill RM, Clegg LX, Edwards BK: Partitioning linear trends in age-adjusted rates. Cancer Causes Control 2000;11:31–35.

2 Otsubo T, Kobayashi S, Sano K, Misawa T, Ota T, Katagiri S, Yanaga K, Yamaue H, Kokudo N, Unno M, Fujimoto J, Miura F, Miyazaki M, Yamamoto M: Safety-related outcomes of the Japanese Society of Hepato-Biliary-Pancreatic Surgery board certification system for expert surgeons. J Hepatobiliary Pancreat Sci 2017;24:252–261.

3 Miura F, Yamamoto M, Gotoh M, Konno H, Fujimoto J, Yanaga K, Kokudo N, Yamaue H, Wakabayashi G, Seto Y, Unno M, Miyata H, Hirahara N, Miyazaki M: Validation of the board certification system for expert surgeons (hepato-biliary-pancreatic field) using the data of the National Clinical Database of Japan: part 1 – hepatectomy of more than one segment. J Hepatobiliary Pancreat Sci 2016;23:313–323.

4 Miura F, Yamamoto M, Gotoh M, Konno H, Fujimoto J, Yanaga K, Kokudo N, Yamaue H, Wakabayashi G, Seto Y, Unno M, Miyata H, Hirahara N, Miyazaki M: Validation of the board certification system for expert surgeons (hepato-biliary-pancreatic field) using the data of the National Clinical Database of Japan: part 2 – pancreatoduodenectomy. J Hepatobiliary Pancreat Sci 2016;23:353–363.

5 Kneuertz PJ, Pitt HA, Bilimoria KY, Smiley JP, Cohen ME, Ko CY, Pawlik TM: Risk of morbidity and mortality following hepato-pancreato-biliary surgery. J Gastrointest Surg 2012;16:1727–1735.

6 Nishikawa H, Kimura T, Kita R, Osaki Y: Treatment for hepatocellular carcinoma in elderly patients: a literature review. J Cancer 2013;4:635–643.

7 Sato M, Tateishi R, Yasunaga H, Horiguchi H, Yoshida H, Matsuda S, Koike K: Mortality and morbidity of hepatectomy, radiofrequency ablation, and embolization for hepatocellular carcinoma: a national survey of 54,145 patients. J Gastroenterol 2012;47:1125–1133.

8 Sperti C, Moletta L, Pozza G: Pancreatic resection in very elderly patients: a critical analysis of existing evidence. World J Gastrointest Oncol 2017;9:30–36.

9 Mann CD, Palser T, Briggs CD, Cameron I, Rees M, Buckles J, Berry DP: A review of factors predicting perioperative death and early outcome in hepatopancreaticobiliary cancer surgery. HPB (Oxford) 2010;12:380–388.

10 Ouchi Y, Rakugi H, Arai H, Akishita M, Ito H, Toba K, Kai I; Joint Committee of Japan Gerontological Society (JGLS) and Japan Geriatrics Society (JGS) on the definition and classification of the elderly: Redefining the elderly as aged 75 years and older: proposal from the Joint Committee of Japan Gerontological Society and the Japan Geriatrics Society. Geriatr Gerontol Int 2017;17:1045–1047.

11 Sadamori H, Yagi T, Shinoura S, Umeda Y, Yoshida R, Satoh D, Nobuoka D, Utsumi M, Yoshida K, Fujiwara T: Risk factors for organ/space surgical site infection after hepatectomy for hepatocellular carcinoma in 359 recent cases. J Hepatobiliary Pancreat Sci 2013;20: 186–196.

12 Takagi K, Yagi T, Yoshida R, Shinoura S, Umeda Y, Nobuoka D, Kuise T, Watanabe N, Sui K, Fujii T, Fujiwara T: Surgical outcome of patients undergoing pancreaticoduodenectomy: analysis of a 17-year experience at a single center. Acta Med Okayama 2016; 70:197–203.

13 Takagi K, Yoshida R, Yagi T, Umeda Y, Nobuoka D, Kuise T, Fujiwara T: Radiographic sarcopenia predicts postoperative infectious complications in patients undergoing pancreaticoduodenectomy. BMC Surg 2017; 17:64.

14 Utsumi M, Sadamori H, Shinoura S, Umeda Y, Yoshida R, Nobuoka D, Takagi K, Fujiwara T, Yagi T: Risk factors of morbidity and predictors of long-term survival after hepatopancreatoduodenectomy for biliary cancer. Hepato-Gastroenterology 2014;61:2167–2172.

15 Bilimoria KY, Liu Y, Paruch JL, Zhou L, Kmiecik TE, Ko CY, Cohen ME: Development and evaluation of the universal ACS NSQIP surgical risk calculator: a decision aid and informed consent tool for patients and surgeons. J Am Coll Surg 2013;217:833–842. e831–e833.

16 Clavien PA, Barkun J, de Oliveira ML, Vauthey JN, Dindo D, Schulick RD, de Santibañes E, Pekolj J, Slankamenac K, Bassi C, Graf R, Vonlanthen R, Padbury R, Cameron JL, Makuuchi M: The Clavien-Dindo classification of surgical complications: five-year experience. Ann Surg 2009;250:187–196.

17 Scholz AF, Oldroyd C, McCarthy K, Quinn TJ, Hewitt J: Systematic review and meta-analysis of risk factors for postoperative delirium among older patients undergoing gastrointestinal surgery. Br J Surg 2016;103:e21–e28.

18 Murakawa K, Kitamura Y, Watanabe S, Hongo S, Shinomiya K, Sendo T: Clinical risk factors associated with postoperative delirium and evaluation of delirium management and assessment team in lung and esophageal cancer patients. J Pharm Health Care Sci 2015;1:4.

19 Lassen K, Coolsen MM, Slim K, Carli F, de Aguilar-Nascimento JE, Schäfer M, Parks RW, Fearon KC, Lobo DN, Demartines N, Braga M, Ljungqvist O, Dejong CH; ERAS® Society; European Society for Clinical Nutrition and Metabolism; International Association for Surgical Metabolism and Nutrition: Guidelines for perioperative care for pancreaticoduodenectomy: enhanced Recovery After Surgery (ERAS®) Society recommendations. Clin Nutr 2012;31:817–830.

20 Melloul E, Hübner M, Scott M, Snowden C, Prentis J, Dejong CH, Garden OJ, Farges O, Kokudo N, Vauthey JN, Clavien PA, Demartines N: Guidelines for perioperative care for liver surgery: enhanced recovery after surgery (ERAS) society recommendations. World J Surg 2016;40:2425–2440.

21 Coolsen MM, van Dam RM, van der Wilt AA, Slim K, Lassen K, Dejong CH: Systematic review and meta-analysis of enhanced recovery after pancreatic surgery with particular emphasis on pancreaticoduodenectomies. World J Surg 2013;37:1909–1918.

22 Kagedan DJ, Ahmed M, Devitt KS, Wei AC: Enhanced recovery after pancreatic surgery: a systematic review of the evidence. HPB (Oxford) 2015;17:11–16.

23 Xiong J, Szatmary P, Huang W, de la Iglesia-Garcia D, Nunes QM, Xia Q, Hu W, Sutton R, Liu X, Raraty MG: Enhanced recovery after surgery program in patients undergoing pancreaticoduodenectomy: a PRISMA-compliant systematic review and meta-analysis. Medicine (Baltimore) 2016;95:e3497.

24 Takagi K, Yoshida R, Yagi T, Umeda Y, Nobuoka D, Kuise T, Hinotsu S, Matsusaki T, Morimatsu H, Eguchi J, Wada J, Senda M, Fujiwara T: Effect of an enhanced recovery after surgery protocol in patients undergoing pancreaticoduodenectomy: a randomized controlled trial. Clin Nutr 2018;pii:S0261-5614(18)30002-5.

25 Zhao Y, Qin H, Wu Y, Xiang B: Enhanced recovery after surgery program reduces length of hospital stay and complications in liver resection: a PRISMA-compliant systematic review and meta-analysis of randomized controlled trials. Medicine (Baltimore) 2017; 96:e7628.

26 Pan W, Bai H: Propensity score interval matching: using bootstrap confidence intervals for accommodating estimation errors of propensity scores. BMC Med Res Methodol 2015;15:53.

27 Hosmer D, Lemeshow S: Applied Logistic Regression, ed 2. New York, Wiley-Interscience, 2000.