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The safety and risk factors of major hepatobiliary pancreatic surgery in patients older than 80 years

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Purpose: Recently, the number of elderly patients has increased due to a longer life expectancy. Among these elderly patients, more octogenarians will be diagnosed with major hepatobiliary pancreatic (HBP) diseases. Therefore, we need to evaluate the safety and risk factors of major HBP surgery in patients older than 80 years.
Methods: From January 2000 to April 2015, patients who underwent major HBP surgery were identified. The patients were divided into 2 groups according to their age at the time of surgery: Group O (≥80 years) and group Y (<80 years). The patient characteristics and intra- and postoperative outcomes were retrospectively investigated in the 2 groups.
Results: The median age was 84 years (range, 80–95 years) in group O and 61 years (range, 27–79 years) in group Y. group O had worse American Society of Anesthesiologists (ASA) physical status (ASA ≥ III: 23% *vs*. 7%, P = 0.002) and was associated with a higher rate of hypertension and heart problems as comorbidities. There were significant differences in albumin and BUN, favoring group Y. The length of intensive care unit stay was longer in group O, whereas the overall complication and mortality rates did not show statistical difference. But, there was a significant difference in systemic complication of both Clavien-Dindo classification grade ≥II and ≥III as complications were divided into surgical site complication and systemic complication.
Conclusion: Major HBP surgery can be performed safely in patients older than 80 years if postoperative management is appropriately provided.
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Key Words: Aged, Safety, Postoperative complications, Mortality

INTRODUCTION

The elderly population has increased worldwide. In 2000, the percentage of the population aged 65 years and older in the United States was 12.4%. In 2010, the percentage of the population aged 65 years and older in the United States was 13.0% [1]. In South Korea, the percentage of the population aged 65 years and older was 12.7% in 2014. In 2020, the percentage of the population aged 65 and older in South Korea is projected to exceed 20% [2]. The proportion of the population aged 80 years and over was 2.52% as of January 1, 2015 in South Korea [3].

As the population ages, more octogenarians will be diagnosed with major hepatobiliary pancreatic (HBP) diseases such as intrahepatic duct or extrahepatic duct stone, cholangitis and benign or malignant tumor, etc. For treatment, major HBP surgery should be performed. However, the risk of postoperative complication increases with advanced age because of the high comorbidity in elderly patients [4-11]. Therefore, it is difficult to make the decision to perform major HBP surgery in elderly patients.

On the other hand, recent reports have found acceptable morbidity and mortality in specific HBP surgeries with patients older than 80 years [4,12-16]. In these recent reports, the type of surgery was limited to a specific major surgery such

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as pancreatico-duodenectomy and/or distal pancreatectomy. Therefore, we included various types of major HBP surgery in our study.

The hypothesis of this study is that major HBP surgery can also be performed safely in patients older than 80 years. Thus, we conducted this study to evaluate the safety and risk factors of major HBP surgery in patients older than 80 years.

METHODS

From January 2000 to April 2015, the patients who underwent major HBP surgery were identified in Ewha Womans University Mokdong Hospital. We found a variety of major HBP surgeries. As a concept of major HBP surgery, we included laparoscopic common bile duct exploration with cholecystectomy, or laparoscopic common bile duct exploration, or open common bile duct exploration, distal pancreatectomy, subtotal pancreatectomy and extended cholecystectomy as well as pancreaticoduodenectomy (PD), hepatic segmentectomy, hemihepatectomy or greater, extrahepatic bile duct resection with hepaticojejucostomy or choledochojejunostomy and hepatopancreaticoduodenectomy [17]. We excluded minor HBP surgeries such as laparoscopic cholecystectomy, open cholecystectomy, internal drainage of pancreatic pseudocyst and fenestration of hepatic cyst as well as liver transplantation, trauma-related surgery and pediatric surgery.

We analyzed 100 patients who underwent major HBP surgery in patients older than 80 years at the time of surgery. These 100 patients were classified into three types according to the performed operation: lower-case hepatectomy included hepatic segmentectomy or hemihepatectomy or greater (10 patients); lower-case pancreatectomy included pylorus-preserving pancreatoduodenectomy or Whipple operation or a distal pancreatectomy or subtotal pancreatectomy (18 patients); lower-case other major operation included laparoscopic common bile duct exploration with cholecystectomy or laparoscopic common bile duct exploration or open common bile duct exploration or hepaticojejucostomy or choledochojejunostomy or extended cholecystectomy (72 patients). A total of 100 patients aged ≥80 years (group O) were matched with 100 patients aged <80 years (group Y) who were randomly selected as a control group for comparison. The number of patient group of each type of surgery was the same with the number of randomly selected control group of each type of surgery. Then, the patient characteristics and intra- and postoperative outcomes were retrospectively investigated in the 2 groups.

Patient characteristics included age, sex, American Society of Anesthesiologists (ASA) physical status, disease malignancy, performed operation type, comorbidities, preoperative laboratory findings, and previous laparotomy history. Comorbidities included diabetes mellitus (DM), hypertension, obstructive lung disease (OLD), heart problem, chronic kidney disease (CKD), cerebrovascular accident (CVA) history, sepsis at the time of surgery, and previous cancer history. OLD included chronic obstructive pulmonary disease, asthma, and pulmonary emphysema. Heart problem included coronary artery disease, congestive heart failure, atrial fibrillation, aortic stenosis, unstable angina, myocardial infarction, severe heart wall hypokinesia, and sick sinus syndrome. Prostate cancer, thyroid cancer, and skin cancer except for melanoma were not included in the category of previous cancer history. Open or laparoscopic appendectomy was not included in the category of previous laparotomy history, but gynecological surgeries such as cesarean section, uterine myomectomy, and total hysterectomy were included.

Intraoperative (IO) outcomes included operation time, portal vein or superior mesenteric vein (SMV) resection, IO organ injury, IO packed red blood cells (p-RBC) transfused, and estimated blood loss (EBL).

The primary end-point of the study was overall complication and mortality rates. The second end-point was the postoperative recovery course such as length of postoperative stay, length of intensive care unit (ICU) stay, postoperative diet starting day, and severity of complication.

Postoperative outcomes included length of postoperative stay, length of ICU stay, postoperative diet starting day, mortality, and overall complication. Severity of complication was classified by Clavien-Dindo grade [18]. Clavien-Dindo grade II or more was considered significant. Complications were also investigated by dividing them into surgical site complication and systemic complication. Postoperative complications were investigated for 30 days after surgery. Mortality was defined as death within 90 days of surgery.

Categorical variables are presented as number (percentage). Continuous variables are presented as median (range). Differences between groups were evaluated by univariate analyses using the chi-square and independent samples t-test for categorical and continuous variables, respectively. All statistical significances were determined at $P < 0.05$.

RESULTS

Patient characteristics and comorbidities

The median age was 84 years (range, 80–95 years) in group O and 61 years (range, 27–79 years) in group Y. There was no difference in terms of gender composition and disease malignancy. However, ASA physical status was worse in group O (ASA ≥ III: 23% *vs.* 7%, $P = 0.002$).

Patient comorbidities were compared between the 2 groups at the time of surgery. There were no significant differences between the groups in terms of DM, OLD, CKD, CVA history, sepsis at the time of surgery and previous cancer history.

However, group O was associated with a higher rate of hypertension (48% *vs.* 30%, P = 0.009) and heart problem (17% *vs.* 3%, P = 0.001).

Preoperative laboratory findings were compared between the 2 groups. There were no significant differences in terms of creatinine levels, hemoglobin levels, total bilirubin, and glucose levels. However, there were significant differences in terms of albumin (3.3 ± 0.5 *vs.* 3.5 ± 0.5, P = 0.012) and BUN (17.5 ± 7.2 *vs.* 14.4 ± 12.2, P = 0.027), favoring the younger group (Table 1).

IO outcomes

There were no differences in operation time, rate of portal vein resection or SMV resection, IO organ injury, IO p-RBC transfused, and EBL (Table 2).

Postoperative outcomes

There were no differences in terms of length of postoperative stay, postoperative diet starting day, and mortality rate (lower-case length of postoperative stay: 15.8 ± 11.5 days *vs.* 14.8 ± 11.0 days, P = 0.527; postoperative diet starting day: 5.0 ± 4.9 days *vs.* 4.4 ± 2.6 days, P = 0.366). Ninety-day mortality was the same, as the number of dead patients was three in both groups (P = 0.999). However, the length of ICU stay was longer in group O (2.9 ± 5.2 days *vs.* 1.6 ± 2.1 days, P = 0.019) (Table 3).

There was no significant difference in overall complication rate by Clavien-Dindo grade ≥ II (28% *vs.* 17%, P = 0.063) as

Table 1. Baseline characteristics of study patients

Characteristic	≥80 Years (n = 100)	<80 Years (n = 100)	P-value[a]
Sex, male:female	43:57	51:49	0.257
Age (yr)	84 (80–95)	61 (27–79)	<0.001
ASA physical status classification			
I	0	3	0.002
II	77	90	
III	23	7	
IV	0	0	
V	0	0	
VI	0	0	
Malignancy	26	25	0.871
Type of operation			
Hepatectomy	10	10	0.999
Pancreatectomy	18	18	
Other major operation	72	72	
Comorbidities			
Diabetes mellitus	19	20	0.831
Hypertension	48	30	0.009
OLD[b]	7	3	0.194
Heart problem[c]	17	3	0.001
CKD	1	1	0.999
CVA history	6	2	0.149
Sepsis	2	4	0.407
Previous cancer history[d]	11	9	0.637
Albumin (g/dL)	3.3± 0.5	3.5 ± 0.5	0.012
BUN (mg/dL)	17.5 ± 7.2	14.4 ±12.2	0.027
Creatinine (mg/dL)	0.9 ± 0.3	0.9 ± 0.9	0.996
Hemoglobin (g/dL)	11.9 ± 1.5	12.1 ± 1.8	0.433
Total bilirubin (mg/dL)	3.5 ± 4.0	3.5 ± 4.1	0.947
Glucose (mg/dL)	140.2 ± 49.8	132.5 ± 51.6	0.286
Previous laparotomy[e]	27	39	0.071

Values are presented as number, median (range), or mean±standard deviation.
ASA, American Society of Anesthesiologists; OLD, obstructive lung disease; CKD, chronic kidney disease; CVA, cerebro-vascular accident.
[a]Fisher exact test or chi-square test for discrete variable and Mann-Whitney U-test for continuous variable. [b]OLD included a chronic obstructive lung disease, asthma and pulmonary emphysema. [c]Heart problem included a coronary artery disease, congestive heart failure, atrial fibrillation, aortic stenosis, unstable angina, myocardial infarction, severe heart wall hypokinesia and sick sinus syndrome. [d]Prostate cancer, thyroid cancer and skin cancer except for melanoma were not included in the category of previous cancer history. [e]Open or laparoscopic appendectomy was not included in the category of previous laparotomy history, but gynecological surgeries such as cesarean section, uterine myomectomy and total hysterectomy were included.

Table 2. Intraoperative outcomes

Outcome	≥80 Years (n = 100)	<80 Years (n = 100)	P-value[a]
Operation time (min)	258 ± 128.6	285.7 ± 138.8	0.157
PV or SMV resection	0	4	0.121
IO organ injury	0	0	0.999
IO p-RBC transfused (unit)	0.3 ± 0.9	0.5 ± 1.6	0.467
Estimated blood loss (mL)	275.1 ± 285.0	427.4 ± 912.9	0.114

Values are presented as mean ± standard deviation or number.
PV, portal vein; SMV, superior mesenteric vein; IO, intraoperative; p-RBC, packed red blood cells.
[a]Fisher exact test or chi-square test for discrete variable and Mann-Whitney U-test for continuous variable.

Table 3. Postoperative outcomes and complication

Outcome	≥80 Years (n = 100)	<80 Years (n = 100)	P-value[a]
Length of postoperative stay (POD)	15.8 ± 11.5	14.8 ± 11.0	0.527
Length of ICU stay (day)	2.9 ± 5.2	1.6 ± 2.1	0.019
Diet start (POD)	5.0 ± 4.9	4.4 ± 2.6	0.366
Mortality	3	3	0.999
Complication			
CD grade ≥ II[b]	28	17	0.063
Surgical site complication	13	11	0.663
Systemic complication	19	7	0.012
CD grade ≥ III[c]	19	12	0.171
Surgical site complication	11	10	0.818
Systemic complication	12	3	0.016

Values are presented as mean ± standard deviation or number.
POD, postoperative day; ICU, Intensive care unit; CD grade, Clavien-Dindo classification grade.
[a]Fisher exact test or chi-square test for discrete variable and Mann-Whitney U-test for continuous variable. [b]CD grade ≥ II means grade II, III, IV, and V. [c]CD grade ≥ III means grade III, IV, and V.

well as Clavien-Dindo grade ≥ III (19% *vs.* 12%, P = 0.171). Although the difference in overall complication rate was not statistically significant, the overall complication rate by Clavien-Dindo grade ≥ II and Clavien-Dindo grade ≥ III showed high tendency in group O.

As the complication was divided into surgical site complication and systemic complication, systemic complication rates of both Clavien-Dindo grade ≥ II and grade ≥ III was higher in group O (Clavien-Dindo grade ≥ II: 19% *vs.* 7%, P = 0.012; Clavien-Dindo grade ≥ III: 12% *vs.* 3%, P = 0.016) while surgical site complication rates showed no difference between the 2 groups.

Three patients in group O died: the first case was due to acute respiratory distress syndrome, the second case was due to hospital acquired pneumonia and acute renal failure, and the third case was due to septic shock. Also, 3 patients in group Y died: the first case was due to intra-abdominal surgical site bleeding, the second case was due to septic shock, and the third case was due to atrial fibrillation (Table 4).

DISCUSSION

In this study, there was a significant difference in terms of ASA physical status, the worse being in group O. Furthermore, group O was associated with a higher rate of hypertension and heart problem as comorbidities. For preoperative laboratory findings, there were significant differences in terms of albumin and BUN, favoring group Y. There were no differences in the IO outcomes such as operation time, rate of portal vein or SMV resection, IO organ injury, IO p-RBC transfused, and EBL. For postoperative outcomes, the length of ICU stay was longer in group O, whereas overall complication and mortality rates did not show statistical difference. However, when the complications were divided into surgical site complication and systemic complication, there was a significant difference in the rate of systemic complication of both Clavien-Dindo grade ≥ II and grade ≥ III.

The elderly population has increased worldwide. With this increase, surgeons are increasingly faced with the prospect of performing major HBP surgery in patients older than 80 years. In this study, we attempted to determine the safety and risk

Table 4. Comparison of mortality cases between the 2 groups

Case	Age/sex	Type of operation	Comorbidity	Preoperative history	ICU stay (day)	Complication
≥80 Years						
Case 1	80/female	LCBDE	Hypertension RA	No	14	ARDS, pneumonia, atrial fibrillation
Case 2	84/male	PPPD	Hypertension CVA	No	8	Ventricular tachycardia, hospital acquired pneumonia, ARF, pulmonary edema
Case 3	81/male	CBDE	Previous traumatic ICH	Stereotactic aspiration of ICH	36	Septic shock due to biliary sepsis, AKI due to ischemic event, intra-abdominal fluid collection, splenic infarction, CBD stricture
<80 Years						
Case 1	63/female	CBDE	DM Biliary sepsis	Partial hepatectomy d/t IHD stone	3	Intra-abdominal surgical site bleeding
Case 2	69/female	PPPD	Hypertension RA	No	6	Surgical site bleeding, septic shock, renal failure, pulmonary edema, wound infection-candida albicans, VRE
Case 3	56/male	PPPD	Hypertension RCC Hypothyroidism	No	11	Atrial fibrillation

ICU, intensive care unit; LCBDE, laparoscopic common bile duct exploration; RA, rheumatoid arthritis; ARDS, acute respiratory distress syndrome; PPPD, pylorus-preserving pancreatoduodenectomy; CVA, cerebrovascular accident; ARF, acute renal failure; CBDE, common bile duct exploration; ICH, intracranial hemorrhage; AKI, acute kidney insufficiency; CBD, common bile duct; DM, diabetes mellitus; IHD, intrahepatic duct; VRE, vancomycin resistant enterococcus; RCC, renal cell carcinoma.

factors of major HBP surgery and demonstrate herein that major HBP surgery can be performed safely in patients older than 80 years. We used the age of 80 years as a cutoff in our study to allow comparisons with other studies and have found acceptable outcomes in morbidity and mortality after major HBP surgery in patients older than 80 years [4,12-16,19]. As summarized in Table 5, rates of postoperative mortality and overall complication rates in patients over the age of 80 years appeared similar to younger patients [13-15,19]. Contrary to the results of our study, the study by Makary et al. [20] showed significantly higher overall complication as well as mortality rate in the older group (52.8% *vs.* 41.6% and 4.1% *vs.* 1.7%, respectively, both $P < 0.05$). In the study by Melis et al. [4], the overall complication was higher in octogenarians than younger patients (68% *vs.* 44%, $P = 0.03$), whereas mortality did not show statistical difference ($P = 0.23$).

In our study, there were no significant differences in overall complication and postoperative mortality rates. Dividing the complications into surgical site complication and systemic complication, there was also no significant difference in terms of surgical site complication of both Clavien-Dindo grade ≥ II and grade ≥ III. However, systemic complication of both Clavien-Dindo grade ≥ II and grade ≥ III showed significant difference in the 2 groups (Clavien-Dindo grade ≥ II: 19% *vs.* 7%, $P = 0.012$; Clavien-Dindo grade ≥ III: 12% *vs.* 3%, $P = 0.016$). In other words, systemic complication was higher in group O. The reason that systemic complication was higher in the old age group seems to be that physical tolerance that fights against surgical trauma becomes weaker due to aging. Also, the result may be associated with the longer stay in ICU. However, there was no significant difference in the length of hospital stay after the operation; the reason for this result may be that recent medical improvements made it possible for systemic complications to be overcome with postoperative care. This is also shown by the same mortality rate in the 2 groups.

In the future, it seems necessary to actively perform preoperative physical examination, carefully select the cases, and cautiously administer premedication to reduce the rate of complication in elderly patients, especially in that of systemic complication. Also, even if systemic complication occurs, postoperative management should be appropriately provided.

Furthermore, we need to actively use the National Surgical Quality Improvement Program (NSQIP) in order to reduce overall complication and mortality rate [21-25]. Lower-case, careful preoperative selection and appropriate postoperative management can be possible if based on the predictive value of NSQIP, which will eventually lead to reduction in overall complication as well as mortality rate.

Performance status is a good preoperative assessment tool for determining surgical risk in elderly patients [26]. Therefore, the limitation of our study is that preoperative Eastern Cooperative

Table 5. Literature review

Source	Operations performed	Age (yr)	No.	Complication (%)	Mortality (%)
Chen et al. 2003 [14]	PD only	≥80	16	51	13
		<80	82	56	12
Makary et al. 2006 [20]	PD only	≥90	10	50	0
		80–89	197	52.8*	4.1*
		<80	2,491	41.6	1.7
Hardacre et al. 2009 [19]	PD and DP	≥80	32	66	0
Lee et al. 2010 [13]	PD only	≥80	74	47.3	5.4
		<80	703	51.1	3.8
Hatzaras et al. 2011 [15]	PD and DP	≥80	27	52	3.7
		<80	490	59	3.7
Melis et al. 2012 [4]	PD only	≥80	25	68*	4.0
		<80	175	44	0.6
Present study	Major HBP surgery	≥80	100	28	3
		<80	100	17	3

PD, pancreaticoduodenectomy; DP, distal pancreatectomy; HBP, hepatobiliary pancreatic.
*P < 0.05 compared with patients < 80 years.

Oncology Group (ECOG) scale performance status was not used to evaluate the difference between the 2 groups, since there was no data in the patient records. Instead, we used ASA physical status, which is as standard as ECOG score, to evaluate the performance status in this study. Also, the main limitations of our study are its retrospective nature and selection bias.

In conclusion, major HBP surgery can be performed safely in patients older than 80 years if postoperative management is appropriately provided.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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