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Surgery for perihilar cholangiocarcinoma from a viewpoint of age: Is it beneficial to octogenarians in an aging society?

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ABSTRACT

Background: Whether operative treatment provides benefits for elderly patients with perihilar cholangiocarcinoma is unknown. The aim of this study was to review resection of perihilar cholangiocarcinoma according to age and to clarify its value for octogenarians.

Methods: Between April 1977 and December 2015, we reviewed consecutive patients who underwent resection for perihilar cholangiocarcinoma with a special focus on patient age.

Results: During the study interval, 831 patients underwent resection for perihilar cholangiocarcinoma. The median age of the resected patients increased by 11 years over approximately 40 years. Before 2001, no octogenarians underwent operative intervention; however, the proportion of operations for octogenarians increased to 9% after 2010. Further analyses were performed on 643 resected patients between 2001 and 2015. The resectability rate was not different between the octogenarians and the other age groups (71% vs 72.4%). The Charlson Comorbidity Index and preoperative laboratory data were similar between the 2 groups. A less advanced tumor was a predominant feature in the octogenarians compared to the other age groups. Consequently, the procedure used in the octogenarians were less extensive, but the proportion of R_0 resection was greater in the octogenarians than in the other age groups (95.% vs 78.3%, $P = .008$). The ratio of patients who died of other diseases was also greater among octogenarians (29% vs 6.0%, $P < .001$). Overall survival was similar between the 2 groups (41% vs 38.9% at 5 years).

Conclusion: Resection of perihilar cholangiocarcinoma can be performed with low mortality irrespective of age with careful patient selection and offers long-term survival even in octogenarians.

Introduction

The wave of aging has been surging both in Eastern and Western countries. Specifically, Japan is now the highest aging society in the world. According to the 2016 statistics of the Ministry of Health, Labour and Welfare,[1] the proportion of the population aged 65 years or older is 26.7%, and this proportion is expected to reach approximately 40% in 2050. Along with this marked trend of aging, the number of aged patients with cancer requiring surgical treatment has increased dramatically.[2,3] Unlike younger patients, elderly patients often have age-related issues, including decreased organ function, comorbidity, sarcopenia, hypobulia (less interest in engagement in society), or cognitive impairment. These issues should be evaluated carefully when treating older patients with cancer.

Perihilar cholangiocarcinoma (PHCC) is a devastating disease that still remains one of the most difficult challenges for hepatobiliary surgeons.[4–9] Although the incidence of PHCC has been increasing worldwide, hepatectomy has rarely been offered to elderly patients with PHCC, primarily due to the difficulty, risks, and complexity of resection.[5–9] Another concern is that aging leads to a number of structural and functional changes in the liver that may make hepatectomy less tolerable.[10] Nevertheless, a better understanding of liver anatomy, improved perioperative management, and innovated technical devices have enhanced the safety of hepatectomy, expanding its indication. To the best of our knowledge, only 2 studies have reported surgical outcomes of elderly patients with resectable PHCC.[11,12] Thus, whether complex hepatobiliary resection truly provides merit for elderly patients in aging society is unknown.

The aim of the present study was to review our experiences with resection for PHCC, to assess the effect of patient age on surgical outcomes, and to clarify the clinical value of complex hepatobiliary resection for elderly patients with PHCC in our current aging society.

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Methods

Between April 1977 and December 2015, consecutive patients who underwent resection for PHCC in the First Department of Surgery, Nagoya University Hospital were reviewed retrospectively, with a focus on patient age. This study was approved by the Human Research Review Committee of Nagoya University Hospital (Approval No. 2017-0350).

Preoperative management

Preoperative management has been described in detail in our previous report.[4] Briefly, cholangiography, computed tomography, and ultrasonography were used as a preoperative workup.[4] Patients who had jaundice and/or dilated bile ducts in the future remnant lobe routinely underwent percutaneous or endoscopic biliary drainage.[13,14] Portal vein embolization has been introduced since 1990 and was performed when the liver remnant was less than 40%, according to a previously reported method.[15] Liver function was evaluated consistently by the indocyanine green test.[16] Since the late 1990s, preoperative autologous blood donation has been used in patients with hemoglobin concentrations of $\geq$11 g/dL.[17] Replacement of externally drained bile has been used since the late 1990s.[18] Perioperative symbiotic treatment has also been used since 2005.[19] In principle, preoperative management was the same, irrespective of patient age. In the very elderly patients, the following characteristics were a prerequisite for operative consideration: ambulating well, no cognitive/mental disorder, strong will to undergo operation, and appropriate support from the patient's family.

Surgery

All operations were performed after the serum total bilirubin concentrations had decreased to $<$2 mg/dL. The type of hepatectomy was determined based on the location of the primary tumor, as reported previously.[4] Combined pancreatoduodenectomy[4,20] and/or combined vascular resection[4,21,22] were performed when needed to achieve curative resection. The parenchymal transection was performed using cavitron ultrasonic surgical aspirator or instrument fracture technique, under both hepatic artery and portal vein clamping for 15 or 20 minutes (according to surgeon's preference) at 5-minute intervals.

The pathologic findings of resected specimens were documented prospectively according to the 7th edition of the American Joint Committee on Cancer Staging Manual and the 5th edition of the Japanese General Rules for Cancer of the Biliary Tract.

Follow-up

A physical examination and blood tests including tumor markers were performed every 2 to 3 months in principle. Computed tomography was performed at least twice a year for the first 5 years. As adjuvant treatment, Gemzar (Gemcitabine hydrochloride, Eli Lilly and Company, Indianapolis, IN) or TS-1 (tegafur-gimeracil-oteracil potassium, Taiho Pharmaceutical Co Ltd, Tokyo, Japan) was used, mainly in patients with lymph node metastasis after 2007 because these agents were authorized for use in 2006 and 2007. Radiation therapy was also used in patients with positive surgical margins.

Statistics

The results are expressed as the median with ranges unless otherwise specified. Statistical analysis was performed using the Mann-Whitney *U* test for continuous variables and the χ^2 analysis or Fisher exact test for categorical variables. Patient survival was determined from the time of operation to the time of death or the most recent follow-up and was calculated using the Kaplan-Meier product-limit method. Differences in the survival curves were compared using the log-rank test.

Results

Changes in patients' ages over time

During the study period, 831 consecutive patients underwent resection for PHCC. The distribution of patient age over time is summarized in Fig. 1. Before 1991, patients aged 50 to 59 years and those aged less than 50 years accounted for 31% and 22%, respectively; however, these proportions gradually decreased to 10% and 6%, respectively, after 2010. In sharp contrast, patients aged 70 to 79 years accounted for only 13% before 1991, while this age group represented 41% of those resected after 2010. Before 2001, no patients aged 80 to 89 years (octogenarians) underwent resection, but after 2000, the proportion of octogenarians increased and reached nearly 10% after 2010. Consequently, the median patient age gradually increased; it was 59 years in 1979 to 1990, 65 years in 1991 to 2000, 65 years in 2001 to 2005, 68 years in 2006 to 2010, and 70 years in 2011 to 2015. Thus, patient age at time of operation increased by 11 years during the study period.

To evaluate surgical outcomes in the very elderly patients (octogenarians), further analyses were performed using data obtained from 643 patients who underwent resection in 2001 or later. In addition, unresected patients during the same period were also analyzed.

Resectability according to age

Between 2001 and 2015, a total of 889 patients with PHCC were treated at our clinic, 643 (72.3%) of these patients underwent resection, and the remaining 246 did not undergo resection (Table 1). Of those resected, 40 were octogenarians. The resectability rate was not different between groups stratified according to patient age with approximately 70% in each group. Reasons for unresectability, however, were different in different age groups. Distant metastasis was a major reason in patients aged $<$60 years but became a minor reason at a more advanced age. In contrast, poor general/liver function was a minor reason in patients aged $<$60 years but became a major reason at a more advanced age. Three of the 16 octogenarians who did not undergo resection and 1 of the 82 nonresected septuagenarians refused to undergo operation despite possible resection. There were no such patients aged $<$70 years.

Patients' characteristics according to age

Preoperative biliary drainage and portal vein embolization were used equally irrespective of patient age (Table 2). As for comorbidity, the incidence of hypertension and chronic renal disease was greater in the octogenarians compared to the other patients, while the incidence of other comorbidity, including diabetes mellitus, chronic liver disease, chronic pulmonary disease, and cardiovascular disease, was not different. Consequently, the Charlson Comorbidity Index was similar among each patient group. Most of the laboratory data were also similar. The plasma disappearance rate of indocyanine green alone was significantly less in the octogenarians, but the difference was very slight.

Surgical outcomes according to age

As to the operative procedures performed (Table 3), bile duct resection without hepatectomy was performed more frequently in

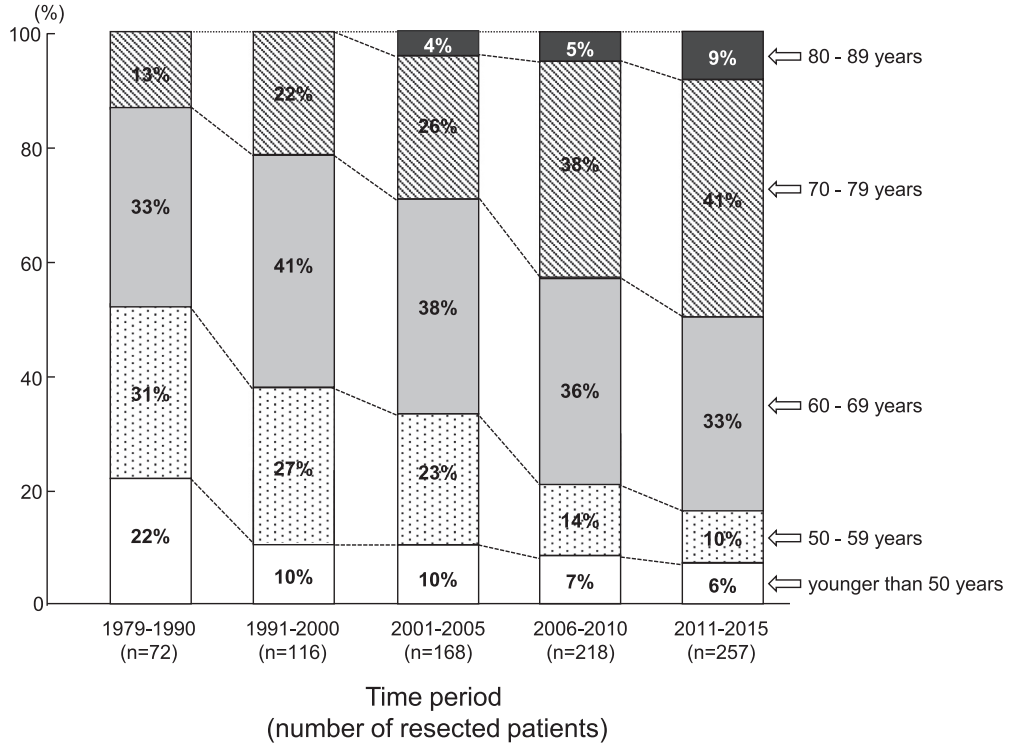

Fig. 1. Changes in age distribution of 831 resected patients according to time period.

Table 1
Resectability according to age (between 2001 and 2015).

	Total	Patients' age (y)				*P*
		<60	60–69	70–9	≥80	
Number of patients treated, *n*	889	210	309	314	56	
Resected	643	143	228	232	40	-
Nonresected	246	67	81	82	16	-
Resectability	72.3%	68.1%	73.8%	73.9%	71.4%	.876
Reason for nonresectability, *n*						<.001
Distant metastasis	123 (50.0%)	43 (64.2%)	39 (48.1%)	36 (43.9%)	4 (25%)	
Locally far advanced	75 (30.5%)	20 (29.9%)	31 (38.3%)	20 (24.4%)	4 (25%)	
Poor general/liver function	44 (17.9%)	4 (6.0%)	11 (13.6%)	25 (30.5%)	5 (31 %)	
Refusal to undergo operation	4 (1.6%)	0	0	1	3 (19%)	

Note that *P* indicates the statistical difference between the octogenarians (≥80 years) and the others (<80 years).

Table 2
Preoperative characteristics of resected patients according to age (between 2001 and 2015).

	Total ($n=643$)	Patients' age (y)				*P*
		<60 ($n=143$)	60–69 ($n=228$)	70–79 ($n=232$)	≤80 ($n=40$)	
Sex (male/female), *n*	402/241	90/53	144/84	147/85	21/19	.176
Body mass index	21.2 (13.1– 35.2)	21.6 (15.2– 34.9)	21.1 (14.9– 35.2)	21.2 (13.1– 33.6)	21.4 (16.2– 26.6)	.988
Biliary drainage, *n*	572 (89.0%)	131 (91.6%)	203 (89.0%)	204 (87.9%)	34 (85%)	.410
Portal vein embolization, *n*	377 (58.6%)	81 (56.6%)	144 (63.2%)	133 (57.3%)	19 (48%)	.190
Comorbidity, *n*						
Hypertension	217 (33.7%)	16 (11.2%)	79 (34.6%)	100 (43.1%)	22 (55%)	.003
Diabetes mellitus	82 (12.8%)	13 (9.1%)	31 (13.6%)	31 (13.4%)	7 (18%)	.331
Chronic liver disease	29 (4.5%)	5 (3.5%)	8 (3.5%)	14 (6.0%)	2	.700
Chronic pulmonary disease	27 (4.2%)	3 (2.1%)	4 (1.8%)	19 (8.2%)	1	>.999
Cardiovascular disease	25 (3.9%)	3 (2.1%)	13 (5.7%)	7 (3.0%)	2	.664
Chronic renal disease	11 (1.7%)	0	1	7 (3.0%)	3 (8%)	.026
Charlson Comorbidity Index	0 (0–8)	0 (0–6)	0 (0–6)	0 (0–8)	0.5 (0–5)	.757
Laboratory data						
Hemoglobin (g/dL)	11.5 (8.2–16.0)	11.9 (8.8–15.4)	11.5 (8.6–16.0)	11.3 (8.2–14.7)	11.3 (9.4–13.7)	.322
Albumin (g/dL)	3.6 (2.4–4.7)	3.8 (2.7–4.7)	3.6 (2.5–4.6)	3.5 (2.4–4.5)	3.6 (2.5–4.3)	.245
Cholesterol (mg/dL)	157 (75–328)	158 (89–248)	157 (87–328)	155 (75–265)	158 (87–281)	.541
Glucose (mg/dL)	94 (58–244)	89 (65–224)	94 (58–188)	96 (62–221)	91 (74–157)	.920
Prothrombin time (%)	99 (38–148)	100 (55–138)	100 (63–148)	99 (38–145)	96 (75–126)	.163
KICG	0.158 (0.087–0.307)	0.174 (0.102–0.307)	0.162 (0.099–0.242)	0.150 (0.087–0.225)	0.151 (0.103–0.201)	.049

Note that *P* indicates the statistical difference between the octogenarians (≥80 years) and the others (<80 years).
KICG, plasma disappearance rate of indocyanine green.

Table 3
Operative procedures and outcomes according to age (between 2001 and 2015).

	Total ($n=643$)	Patients' age (y)				P
		<60 ($n=143$)	60–69 ($n=228$)	70–79 ($n=232$)	≥80 ($n=40$)	
Type of hepatectomy,* n						<.001
S1, 4, 5, 6, 7, 8	52 (8.1%)	13 (9.1%)	25 (11.0%)	14 (6.0%)	0	
S1, 5, 6, 7, 8	202 (31.4%)	40 (28.0%)	68 (29.8%)	81 (34.9%)	13 (33%)	
S1, 2, 3, 4, 5, 8	170 (26.4%)	43 (30.1%)	68 (29.8%)	52 (22.4%)	7 (18%)	
S1, 2, 3, 4	189 (29.4%)	45 (31.5%)	55 (24.1%)	73 (31.5%)	16 (40%)	
S1, 4, 5, 8/S1, 5, 8/S1, 4/S1	17 (2.6%)	2	8 (3.5%)	7 (3.0%)	0	
Without hepatectomy	13 (2.0%)	0	4 (1.8%)	5 (2.2%)	4 (10%)	
Combined resection, n						
Pancreatoduodenectomy	82 (12.8%)	19 (13.9%)	28 (12.3%)	34 (14.7%)	1	.048
Portal vein resection	234 (36.4%)	64 (44.8%)	87 (38.2%)	75 (32.3%)	8 (20%)	.027
Hepatic artery resection	129 (20.1%)	33 (23.1%)	46 (20.2%)	44 (19.0%)	6 (15%)	.541
Operative time (min)	600 (344–1,150)	645 (344–1140)	600 (348–1090)	595 (376–1,150)	554 (353–867)	.003
Blood loss (mL)	1,340 (46–11,115)	1,393 (345–11,115)	1,292 (46–7100)	1,381 (209–10,349)	1,018 (362–3,397)	.020
Homologous blood transfusion,† n	233 (36.2%)	40 (28.0%)	74 (32.5%)	98 (42.2%)	21 (52%)	.027
Postoperative complication, n						
Liver failure¶	195 (30.3%)	42 (29.4%)	65 (28.5%)	77 (33.2%)	11 (28%)	.688
Pneumonia	9 (1.4%)	2 (1.4%)	2 (0.9%)	2 (0.9%)	3 (8%)	.014
Renal failure	8 (1.2%)	2 (1.4%)	4 (1.8%)	1 (0.4%)	1	.404
Bacteremia	42 (6.5%)	7 (4.9%)	16 (7.0%)	17 (7.3%)	2	>.999
Wound sepsis	64 (10.0%)	14 (9.8%)	22 (9.6%)	24 (10.3%)	4 (10%)	>.999
Intra-abdominal abscess	125 (19.4%)	18 (12.6%)	41 (18.0%)	55 (23.7%)	11 (28%)	.184
Intra-abdominal bleeding	14 (2.1%)	5 (3.5%)	6 (2.6%)	3 (1.3%)	0	>.999
Relaparotomy, n	20 (3.1%)	7 (4.9%)	6 (2.6%)	5 (2.2%)	2	.357
Postop hospital stay (d)§	30 (12–218)	29 (12–155)	29 (12–129)	32 (12–218)	30 (15–202)	.444
Mortality,# n	13 (2.0%)	4 (2.8%)	4 (1.8%)	4 (1.7%)	1	.570

* Expressed as Couinaud's hepatic segments resected.
† Homologous blood includes packed red blood cell and fresh frozen plasma during intra- and postoperative period.
¶ Grade B or C according to the International Study Group of Liver Surgery.
§ Excluding 13 deaths related to surgery.
# Including all deaths related to surgery. Note that P indicates the statistical difference between the octogenarians (≥80 years) and the others (<80 years).

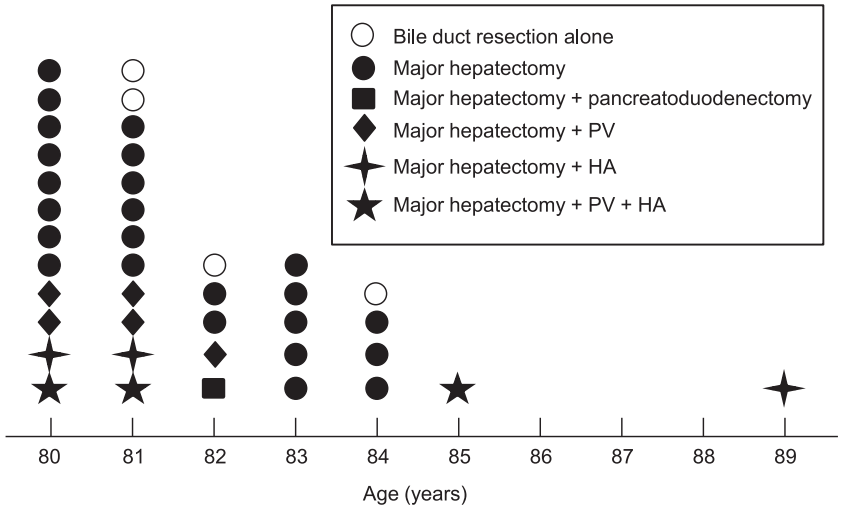

Fig. 2. Operative procedures performed in 40 octogenarians with perihilar cholangiocarcinoma (PHCC). *PV*, portal vein resection with reconstruction; *HA*, hepatic artery resection with reconstruction.

the octogenarians compared to the other patients (10% vs 1.5%). In contrast, extended hepatectomies such as right trisectionectomy (0% vs 8.6%) and left trisectionectomy (18% vs 27.0%) were also performed less frequently in the octogenarians. Combined resections, including pancreatoduodenectomy or vascular resection, were also performed less frequently in the octogenarians. Regarding the less extensive procedures performed in the octogenarians, operative time was the shortest, and blood loss was the least in this age group. Fig. 2 shows the details of operative procedures performed in 40 octogenarians. Four patients underwent bile duct resection alone, and the remaining 36 patients underwent some form of hepatectomy with or without combined resection. The oldest patient in this series was an 89-year-old male who underwent left trisectionectomy with hepatic artery resection and reconstruction.

Postoperative pneumonia developed more frequently in the octogenarians (8% vs 1.0%), while the incidence of the other postoperative complications was not different among each age group (Table 3). The duration of postoperative hospital stay was similar at approximately 30 days. In addition, mortality was also similar at approximately 2% in each age group. In the 40 octogenarians, an 80-year-old male who had undergone a left trisectionectomy with simultaneous resection of the portal vein and hepatic artery died of aspiration pneumonia on day 29, and the remaining 39 were

Table 4
Bismuth type, tumor stage, and curability according to age (between 2001 and 2015).

	Total ($n=643$)	Patients' age (y)				P
		<60 ($n=143$)	60–69 ($n=228$)	70–79 ($n=232$)	≥80 ($n=40$)	
Bismuth type, *n*						.031
I/II	111 (17.3%)	22 (15.4%)	34 (14.9%)	42 (18.1%)	13 (32.5%)	
III	244 (37.9%)	50 (35.0%)	85 (37.3%)	96 (41.3%)	13 (32.5%)	
IV	288 (44.8%)	71 (49.7%)	109 (47.8%)	94 (40.5%)	14 (35.0%)	
pT,* *n*						.003
1–3	286 (44.5%)	59 (41.3%)	91 (39.9%)	109 (47.0%)	27 (67.5%)	
4	357 (55.5%)	84 (58.7%)	137 (60.1%)	123 (53.0%)	13 (32.5%)	
pN,* *n*						.019
0	335 (52.1%)	63 (44.1%)	123 (53.9%)	121 (52.2%)	28 (70.0%)	
1	308 (47.9%)	80 (55.9%)	105 (46.1%)	111 (47.8%)	12 (30.0%)	
pM,* *n*						.048
0	560 (87.1%)	124 (86.7%)	199 (87.3%)	198 (85.3%)	39 (97.5%)	
1	83 (12.9%)	19 (13.3%)	29 (12.7%)	34 (14.7%)	1 (2.5%)	
pStage,* *n*						.002
I/II	173 (26.9%)	39 (27.3%)	53 (23.2%)	61 (26.3%)	20 (50.0%)	
III	93 (14.5%)	15 (10.5%)	34 (14.9%)	37 (15.9%)	7 (17.5%)	
IVA	294 (45.7%)	70 (49.0%)	112 (49.1%)	100 (43.1%)	12 (30.0%)	
IVB	83 (12.9%)	19 (13.3%)	29 (12.7%)	34 (14.7%)	1 (2.5%)	
Curability, *n*						.008
R_0†	510 (79.3%)	117 (81.8%)	178 (78.1%)	177 (76.3%)	38 (95.0%)	
$R_1/_2$	133 (20.7%)	26 (18.2%)	50 (21.9%)	55 (23.7%)	2 (5.0%)	

* According to 7th edition.
† Including positive ductal margin with carcinoma in situ. Note that *P* indicates the statistical difference between the octogenarians (≥80 years) and the others (<80 years).

Table 5
Cause of death according to age (between 2001 and 2015).

	Total ($n=643$)	Patients' age (y)				P
		<60 ($n=143$)	60–69 ($n=228$)	70–79 ($n=232$)	≥80 ($n=40$)	
Number of death, *n*	423 (65.8%)	96 (67.1%)	146 (64.0%)	157 (67.7%)	24 (60.0%)	.426
Died of postoperative complication	13	4	4	4	1	
Died of recurrence	379	88	132	143	16	
Died of other disease	31 (7.4%)	4 (4.3%)	10 (6.9%)	10 (6.4%)	7 (29.2%)	<.001
Other malignancies	15	1	8	3	3	
Cardiovascular disease	4	0	2	1	1	
Suicide	3	3	0	0	0	
Senility	3	0	0	2	1	
Aspiration pneumonia	3	0	0	1	2	
Rupture of esophageal varices	2	0	0	2	0	
Sudden death due to unknown cause	1	0	0	1	0	

Note that *P* indicates the statistical difference between the octogenarians (≥80 years) and the others (<80 years).

discharged from the hospital and returned home in good health. They could enjoy active social life without hospitalization for postoperative rehabilitation.

Tumor stage and curability according to age

Bismuth type was different between the octogenarians and the other patients who had operative intervention; type I/II was more frequent in the octogenarians, and type IV was less frequent in the octogenarians (Table 4). The extent of tumor progression, expressed as pT, pN, pM, and pStage, was also different between the octogenarians subjected to operative intervention and the other patients; in the former, less advanced tumor was predominant. Consequently, the proportion of R_0 resection was greater in the octogenarians than in the other patients (95.0% vs 78.3%).

Survival

At this writing, a total of 423 patients died of postoperative complication (n = 13), disease recurrence (n = 379), or other diseases (n = 31) (Table 5). The ratio of patients who died of other diseases was significantly greater in the octogenarians; it was as high as 29% in the octogenarians, but <7% in the other patients. Other malignancies, including lung, pancreas, prostate, or colon cancer, were a major cause of death among other disease deaths, followed by cardiovascular disease. Postoperative overall survivals were nearly identical between the octogenarians and the other patients (41% vs 38.9% at 5 years; $P=.467$). In contrast, disease-specific survival for the octogenarians was somewhat better compared to the other patients (50% vs 40.2% at 5 years; $P=.067$) (Fig. 3).

The survival for the 246 nonresected patients was nearly identical among the 16 octogenarians and the other 230 patients (31% vs 42.0% at 1 year, 13% vs 12.4% at 2 years, 6% vs 1% at 3 years; $P=.779$). All 4 patients who refused to undergo operative intervention despite possible resection died within 3 years (7, 12, 23, and 32 months, respectively).

Discussion

The present study demonstrated that the median age of patients undergoing resection for PHCC increased by 11 years (from 59 to 70 years) over the 40 years from 1977 to 2015. According to the Japan National Statistics,[1] the average human life expectancy was 72.7 years for males and 78.0 years for females in 1977, at the beginning of the study period; at the end of the study period in

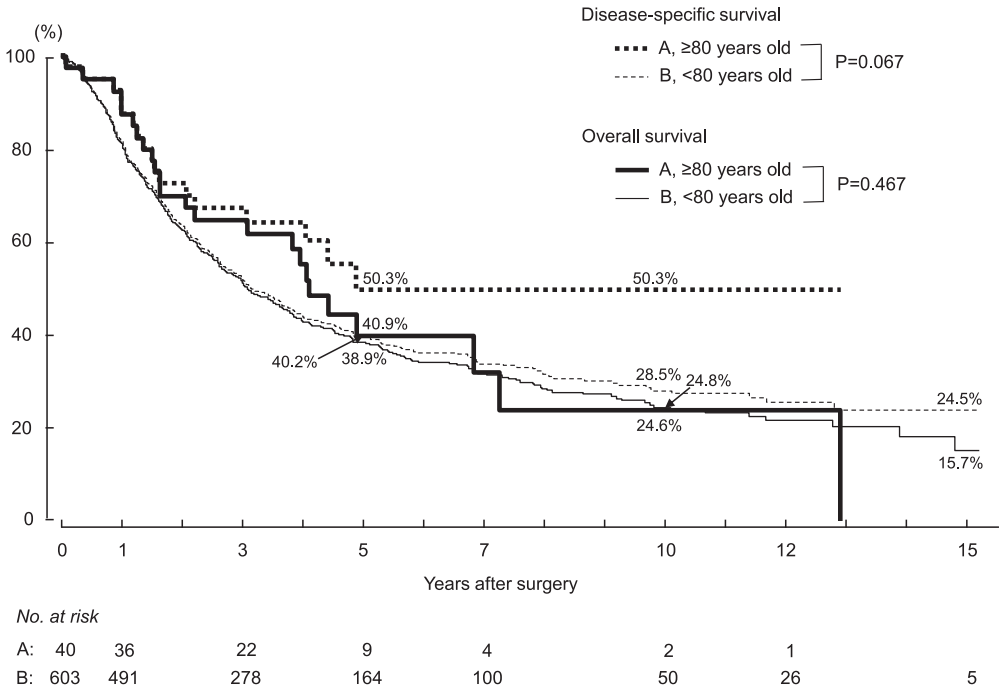

Fig. 3. Overall and disease-specific survivals for the octogenarians and the other patients.

2015, the life expectancy had increased to 80.8 years for males and 87.0 years for females. Thus, the life expectancy at birth increased by 8 years for Japanese males and by 9 years for Japanese females during the study period. These findings indicated that the increase in age of resected patients with PHCC was natural and inevitable. Although the authors did not investigate this parameter, this trend (i.e., an increase in patient age) is presumed to be true in other gastrointestinal malignancies.[2]

Unexpectedly, resectability rates were nearly similar, approximately 70%, in each patient group stratified by age. The authors originally anticipated that the resectability rate in octogenarians would be much less compared to the other groups, but the results were different. Regarding the reasons for unresectability, cancer-related factors, including distant metastasis or locally far advanced disease, accounted for over 90% in patients aged <60 years, while it decreased to 50% in the octogenarians who were considered for operative intervention. In contrast, poor general condition/liver function increased with age. In addition, refusal to undergo operative treatment was found in 19% of the octogenarians, while it was not common in younger patients. Overall, reasons for unresectability were different between the octogenarians and the other patients. Although the reason that the resectability rates were similar is unclear, likely it was due to prereferral "unintentional" selection caused by a biased view of the local doctors, patient family, or patients themselves that the elderly are beyond indication for complex surgery.

The operative procedures performed in the octogenarians also were different compared to the other groups. Bile duct resection without hepatectomy was performed only rarely in the younger patients, while it was used in 4 of the 40 octogenarians. Combined pancreatoduodenectomy or portal vein resection was performed much less frequently in the octogenarians. This difference in selection of surgical procedures reflects the fact that less advanced tumors were dominant in the octogenarians receiving operative intervention, again suggesting a selection bias. For example, 3 of the 4 octogenarian patients who underwent bile duct resection alone had early papillary cancer, and the remaining patient had limited nodular tumor. Thus, bile duct resection alone was chosen; eventually, all patients underwent R_0 resection. In contrast, when planning the operative procedure, surgeons must consider the balance between safety and radicality. Because elderly patients are more fragile and have less physiologic reserve than younger patients, it seems logical to adopt a less extensive procedure for elderly patients. In this regard, the decision on the type of resection probably entertained a less extensive resection at the expense of radicality. Nevertheless, our selection for the octogenarians was aggressive and appropriate, which is supported by the observation that R_0 resection was achieved in as high as 95% of the octogenarians.

Many studies[23–28] have reported no differences in surgical outcomes after hepatectomy between older and younger patients, but some reports have shown a difference. Adam et al[29] analyzed a prospective registry of more than 7,000 patients with colorectal liver metastasis and found that advanced age (≥70 years, $n = 1624$) was associated with greater postoperative morbidity (32.3% vs 28.7%; $P < .001$) and mortality (5.0% vs 2.2%; $P < .001$), because chronic comorbidity increased with increased age. Reddy et al[10] studied 856 patients undergoing major hepatectomy at 2 high-volume centers and showed that increasing age was not associated with postoperative morbidity but was associated with mortality (1.5% in <50 years, 7.0% in 50–64 years, 8.4% in 65–74 years, and 8.4% in ≥75 years; $P < .001$). The present study demonstrated that postoperative morbidity and mortality were similar regardless of age. These findings are consistent with the results from many previous studies of hepatectomy for multiple reasons and not just PHCC.[23–28] Caution, however, is needed for interpretation because nearly all previous studies involved patients who underwent simple hepatectomy without bilioenteric anastomosis. Preoperative diagnosis, operative procedure, and perioperative management for PHCC are very complicated; thus, the appropriate operative procedure to treat PHCC, particularly for elderly patients, should be performed only at high-volume centers with high expertise.

An important finding arising from the present study is that long-term survival for the octogenarians was nearly identical to that of younger patients. The disease, however, was generally less advanced in the octogenarians than in younger patients, but the long-term deaths caused by other diseases were more common in

the octogenarians. Therefore, disease-specific survival was somewhat better in the octogenarians. When treating elderly patients, surgeons should consider the remaining expected years of life. The remaining life expectancy at 80 years is 11.6 years for Japanese females and 8.6 years for Japanese males,[1] suggesting that octogenarians with malignancy should be treated in the same manner as younger patients provided they are good operative candidates.[26] Although there are several scoring systems to predict postoperative mortality and morbidity, such as Estimation of Physiologic Ability and Surgical Stress,[28] Physiologic and Operative Severity Score for the Study of Mortality and Morbidity,[30] and Preoperative Assessment of Cancer in the Elderly,[31] there is no evidence to indicate whether these systems are applicable for PHCC. Indeed, the present authors did not use these scoring systems for decision-making concerning the indications for operative intervention in elderly patients, which was largely dependent on the authors' experience.

In the present study, many variables were examined comprehensively in terms of patient age. Some variables changed gradually with an increase in patient age. In contrast, other variables showed large differences between the octogenarians and septuagenarians or younger patients: for example, (1) the extent of tumor, expressed as pT, pN, pM, and pStage; (2) curability; (3) the planned operative procedures to be performed; and (4) cause of death. These observations suggest that in an aging society, octogenarians should be focused on and studied as "truly aged patients,"[26] although there were individual differences. In this respect, statistical significance tests for variables in the present study were performed between the octogenarians and the other patients, aiming at exploring the features of very elderly patients.

The present study had several limitations, including its retrospective nature and the use of a single center; therefore, unexpected bias cannot be completely ruled out; however, the cohort was homogeneous, the number of involved patients was large, and the analyses were comprehensive. Another limitation, as mentioned earlier, was the lack of use of scoring systems to determine the operative indications in elderly patients, although there most likely was some element of appropriate selection bias in the octogenarians subjected to operative therapy. Further prospective studies are needed on this issue.

In conclusion, operative therapy with resection of PHCC under careful patient selection can be performed with low mortality irrespective of age and offers a better chance of long-term survival even in octogenarians. In the current aging society, surgeons are increasingly treating more elderly patients with cancer. Elderly patients with PHCC should not be precluded from appropriate resection of PHCC solely due to age.

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