



## Scientific Review

# Should We Deny Surgery for Malignant Hepato-Pancreatico-Biliary Tumors to Elderly Patients?

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Published Online: August 11, 2005

**Abstract.** Malignant hepato-pancreatico-biliary (HPB) tumors have their highest incidence within the sixth to eighth decades of life. The aging of the world population has resulted in a dramatic increase in the number of elderly patients considered for resection of malignant HPB tumors. Because elderly patients are more likely to have more co-morbidities, cognitive impairment, and decreased life expectancy, the benefit and appropriateness of these procedures must be scrutinized for geriatric patients. Therefore, many surgeons have compared the perioperative and long-term outcome of hepatic and pancreatic resections for elderly and younger patients. In most series the elderly population was defined by an age of 70 years or older. The results demonstrate that hepatic resection for hepatocellular carcinoma and colorectal liver metastases can be safely performed in well-selected elderly patients with long-term outcome comparable to younger patients. Similar findings are also reported for pancreatic resection in elderly patients with either ampullary or pancreatic cancer. Although the survival benefit of pancreatico-duodenectomy is limited in all age groups, the absence of competitive therapy justifies this procedure as the sole curative option in younger as well as older patients. Data on resection of gallbladder cancer and hilar bile duct cancer in the elderly are sparse, but there is evidence from large series on resection of these types of tumors that advanced age per se is not a risk factor for reduced outcome. Therefore, surgical options should not be denied to elderly patients with a malignant HPB tumor, and the evaluation should include surgeons expert in HPB surgery.

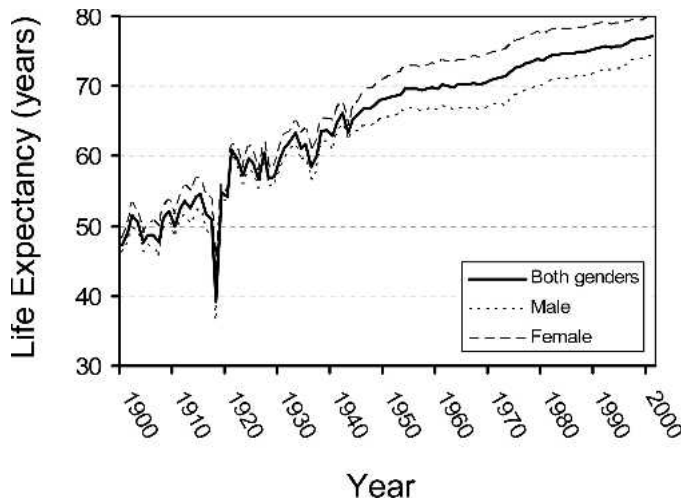
Life expectancy in developed nations increased dramatically over the 20th century as a result of improvements in working conditions, nutrition, public health, and medicine (Fig. 1). In 1900, life expectancy at birth was 47.8 years in the United States [1]. In 2001, approximately 100 years later, it was 77.2 years in the United States, 78.8 years in Europe, and 80.9 years in Japan [1, 2]. This development has resulted in an increase in the older population, reflected by the fast-growing age segments  $\geq 65$  years and  $\geq 85$  years (Fig. 2). While the age group  $\geq 65$  years comprised only 4.1% (3.1 million persons) of the total U.S. population in 1900, it reached 12.7% (34.8 million persons) in 2000 [3]. Thus, the population of this age segment has grown eightfold in the last century. This trend of aging will continue for the next decades.

Projections predict that the age group  $\geq 65$  years will increase to 70.3 million persons by 2030, representing 20.0% of total U.S. population. Similar aging profiles are observed for Europe and Japan.

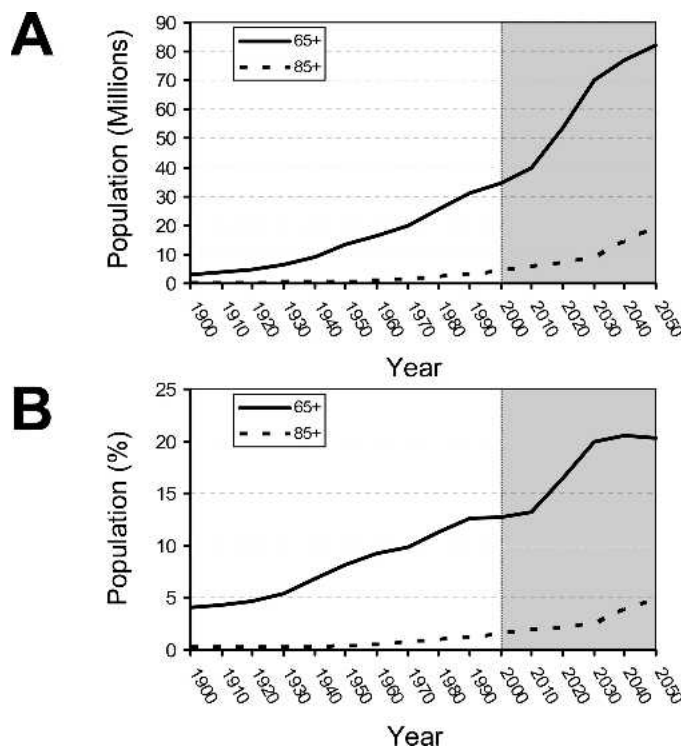
Malignant hepato-pancreatico-biliary (HPB) tumors have their highest incidence within the sixth to the eighth decades of life (Fig. 3). The median age at diagnosis of a malignant HPB tumor in the United States was, except for male patients with hepatocellular carcinoma, 70 years or older, implying that more than 50% of patients with hepatocellular carcinoma (female patients), gallbladder, bile duct, and pancreatic cancer are over 70 years old [4] (Table 1). Similar aging profiles are also observed for colorectal liver metastases. The median age at diagnosis for colorectal cancer was 72 years (male 70 years, female 74 years). Because most liver metastases (70%) present as metachronous lesions [5, 6], it is evident that the median age at diagnosis of a patient with colorectal liver metastases is over 72 years.

Surgical resection is the only potentially curative treatment option for most types of malignant HPB tumors as far as the disease is resectable and limited. The aging of the population and the peak incidence of malignant HPB tumors in the age segment 65–85 years have resulted in a dramatic increase in the number of elderly patients considered for resection of these tumors (Fig. 2 and 3). Unfortunately, many physicians consider advanced age to be a contraindication for surgery, for fear that extended resections of HPB tumors are too risky, with only limited survival benefit for elderly patients. Surgery is often not offered to these patients, who are not presented to experienced HPB surgeons, and as a consequence they receive either no treatment or inappropriate treatment. The question therefore arises whether advanced age represents a risk factor for inadequate treatment of malignant HPB tumors. For breast cancer, it was reported that elderly patients are more likely to receive inadequate treatment even if co-morbidities and functional status are controlled [7, 8]. One inappropriately applied argument for the aged-biased treatment decision might be the lower life expectancy of elderly patients compared to younger patients. However, the actual life expectancy in the United States in 2001 of a person at 65 years and 75 years of age was still 18.1 years and 11.5 years, respectively [9]. These demographic data alone should justify offering adequate treatments for elderly patients with malignant HPB tumors

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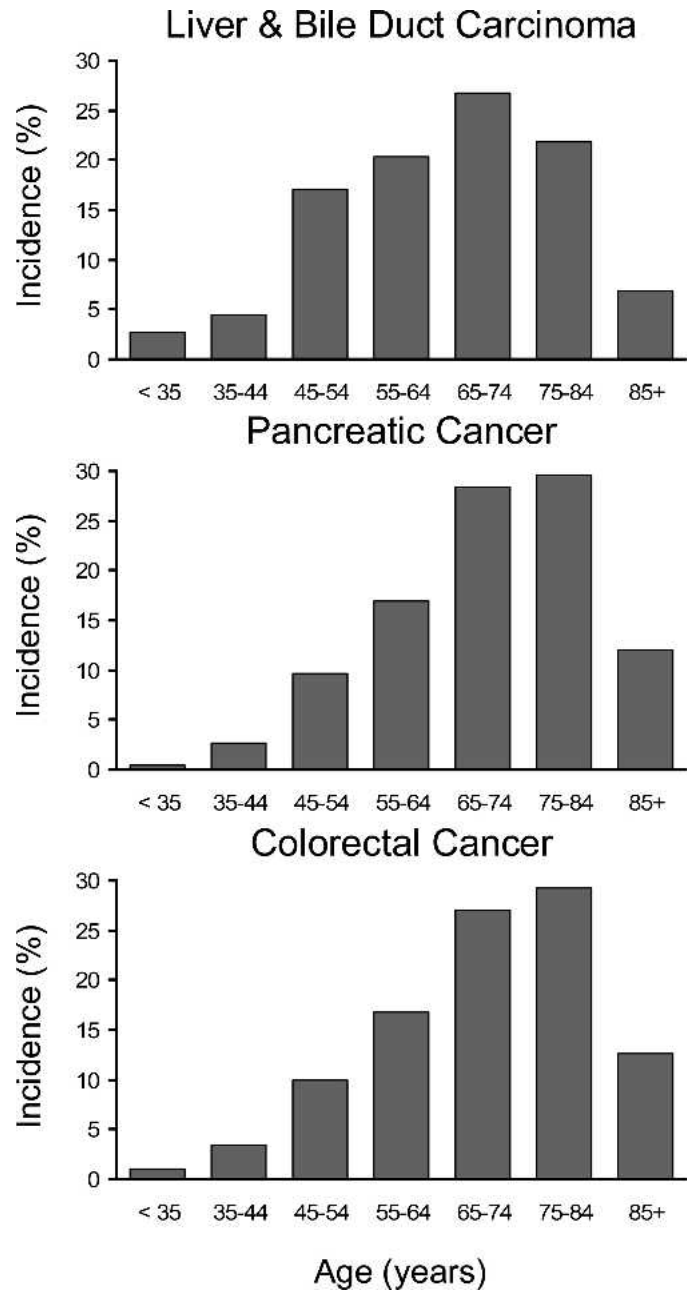
**Fig. 1.** Estimated life expectancy at birth in the United States from 1900 to 2001. Data extracted from the National Vital Statistics Reports 2004 [1].



**Fig. 2.** Actual and projected estimates of the total population (A) and percentage (B) of age segments  $\geq 65$  years (65+) and  $\geq 85$  years (85+) in the United States [3]. Data of the period 2000–2050 represent middle-series projections (gray area). All data refer to the resident US population.

as long as the disease is limited and co-morbidities and functional status are controlled.

Another important issue that may influence future treatment decisions in elderly patients in many health care systems is the need to control costs. This consideration is of special relevance for HPB surgery because liver and pancreatic resections are



**Fig. 3.** Age distribution of incidence of 10,395 liver and bile duct carcinoma cases, 18,790 pancreatic cancer cases, and 91,850 colorectal cancer cases in the United States during the period 1997–2001. Data extracted from the Surveillance, Epidemiology, and End Results (SEER) Program of the National Cancer Institute for the period 1997–2001 [4].

among the most expensive abdominal surgical procedures. The rising economic pressure on health care costs raises the question of how much of health care resources should be allocated to the older population. This question is being intensively debated, and it is likely to become one of the most controversial aspects of health care delivery [10].

This editorial update review analyzes studies on elderly patients who have undergone surgical resection of malignant HPB tumors. Perioperative and long-term outcomes were compared between elderly and younger patients to assess the risk and benefit of

**Table 1.** Median age at diagnosis of primary malignant hepato-pancreatico-biliary tumors.

Tumor site	Median age (years)		
	Males	Females	Total
Liver	64	70	66
Gallbladder	73	73	73
Intrahepatic bile duct	71	76	73
Extrahepatic bile ducts	71	74	73
Pancreas	70	74	72

Data from the Surveillance, Epidemiology, and End Results (SEER) Program of the National Cancer Institute for the period 1997–2001 [4].

surgical resection of malignant HPB tumors in elderly patients. The analysis are presented separately for resection of hepatocellular carcinoma (HCC), colorectal liver metastases (CLM), pancreatic and ampullary carcinomas, gallbladder cancer, and hilar cholangiocarcinoma.

### Liver Resection for Hepatocellular Carcinoma

Approximately 427,000 patients die annually from HCC, which ranks HCC as the 4th most common cause of death from cancer worldwide [11]. Surgical resection is the preferred standard treatment for HCC, as long as the tumor is resectable, the disease limited, and the hepatic function preserved. The peak incidence of HCC around the 6th decade of life, combined with the aging of the world population, results in a dramatically increasing elderly population of patients with HCC considered for hepatic resection. In Asia, HCC is a major problem, with more than 326,000 deaths annually, which corresponds to 76% of all HCC-related deaths worldwide [11]. These demographic data indicate that the greatest experience with hepatic resection for HCC in elderly patients is in Asia. Therefore it is not surprising that 10 of 11 identified studies comparing risk and benefit of hepatic resection for HCC between young and elderly patients are from Asia [12–21] (Table 2). The only European study, which is published in the current issue of the *World Journal of Surgery*, comes from Italy [22].

Most of the studies analyzed here compared the outcome of hepatic resection in patients younger and older than 70 years of age [14, 16–18, 20–22]. Most patient characteristics were homogeneously distributed between younger and older patients, but the elderly patients had significantly lower hepatitis B (HBV) and higher hepatitis C (HCV) infection rates, as well as higher proportions of female patients (Tables 2, 3) suggesting a different hepato-carcinogenesis in geriatric patients [28, 29].

Operative data demonstrated similar operative times and blood loss for older and younger patients [13–16, 20, 21]. Yeh et al. reported even a significantly lower mean blood loss in elderly patients [18]. Although the older patients had more co-morbidities, this had no impact on the postoperative complication rates, which were similar in the two groups. Interestingly, the Italian study observed significantly fewer complications in elderly patients [22]. Mortality rates of 3%–43% are reported for elderly patients after hepatectomy for HCC (Table 2). Two Asian studies had an unacceptably high mortality rate of greater than 40% for elderly patients [13, 14]. However, mortality rates reported in the recently published cohort studies of the past five years were below 10% and were not significantly different between elderly and young patients (Table 2). These data underscore that hepatic

resections for HCC can be safely performed in elderly patients with comparable risk with younger patients. This seems to be true even for octogenarians [15].

Regarding long-term outcome, there was a large range of 5-year survival rates in elderly patients ranging between 18% and 76% [12, 15–19, 21, 22]. Cirrhosis and Child-Pugh B/C were predictors of poor survival in elderly patients, as is proven for the general patient population [19–21]. Despite the statistical lower life expectancy of elderly patients, the long-term outcome after hepatic resection for HCC was comparable between older and younger patients (Table 3). Furthermore, Hanazaki et al. observed a survival benefit for elderly patients with hepatic recurrent disease who underwent repeat hepatic resection [21]. The favorable perioperative and long-term outcome demonstrates that selected elderly patients benefit from hepatic resection for HCC in the same way as younger patients. Therefore, surgical treatment, including extended hepatectomies, is justified in elderly patients with HCC.

### Liver Resection for Colorectal Liver Metastases

Approximately 437,000 patients die annually from colorectal cancer, which ranks colorectal cancer as the third most common cause of death from cancer worldwide [11]. The liver is the most common organ for distant metastases from colorectal cancer, which is affected in approximately 50%–60% of patients with colorectal cancer. At present, liver resection is the only curative therapy option for patients with isolated colorectal liver metastases. Although only 10%–20% of patients with liver metastases are candidates for surgical resection, as with HCC, the peak incidence of this disease occurs beyond the age of 70 years, and the growing life expectancy results in an increasing elderly population considered for hepatic resection. In contrast to HCC, elderly patients with colorectal liver metastases represent a predominantly non-cirrhotic population.

Hepatic resection for colorectal liver metastases in elderly patients is safe, as demonstrated by a low mortality rate of 3.9%–7.3% in patients 70 years of age or older (Table 2). When elderly ( $\geq 70$  years) and younger ( $< 70$  years) patients were compared, mortality and complication rates were not significantly different between both age groups. Interestingly, in one study a subgroup analysis of patients older than 70 years of age revealed similar mortality and complication rates for the age segments 70–74 years, 75–79 years, and  $\geq 80$  years [24]. Despite advanced age, elderly patients had no prolonged hospital stay compared to that of younger patients. Although three studies had a selection bias in terms of a higher frequency of major resections in younger patients [23, 25, 26], the largest series, by Fong et al., reported an equivalent distribution of major procedures in young and elderly patients [24].

Elderly patients had a 5-year overall survival after hepatic resection of 16–46 months, which was similar to that of younger patients (Table 4). There is additional evidence from two large series on hepatic resection for colorectal liver metastases that age per se is not a risk factor for long-term outcome [30, 31]. These findings indicate that elderly patients with colorectal liver metastases benefit from hepatic resection to a similar degree as younger patients. Therefore, hepatic resection for colorectal liver metastases should be the preferred therapeutic option for elderly patients as long as co-morbidities are controlled.

**Table 2.** Perioperative outcome after hepatic resection for primary and secondary malignant tumors in young and elderly patients.

Author year [ref.]	Underlying disease	Age (years)	No. of patients	Female (%)	Mortality rate (%)	Complication rate (%)	Operative time (hours)	Blood loss (ml)	Hospital stay (days)
Ezaki et al. 1987 [12]	HCC	56–65	44	11.4	11.4	34.1	—	—	—
		≥ 66	37	18.9	5.4	24.3	—	—	—
Yanaga et al. 1988 [13]	HCC	< 65	127	13.4	22.0	21.3	2.7 <sup>b</sup>	3000 <sup>b</sup>	—
		≥ 65	27	29.6	40.7	40.7	3.0 <sup>b</sup>	3500 <sup>b</sup>	—
Nagasue et al. 1993 [19]	HCC	≤ 50	26	—	0.0	26.9	—	—	—
		≥ 70	32	21.9	12.5	28.1	—	—	—
Takenaka et al. 1994 [16]	HCC	< 70	229	18.8	0.9	49.8	4.9 <sup>b</sup>	1592 <sup>b</sup>	—
		≥ 70	39	30.8	5.1	51.3	4.7 <sup>b</sup>	1560 <sup>b</sup>	—
Yamamoto et al. 1997 [14]	HCC	50–69	40	12.5	5.0 <sup>a</sup>	—	4.6 <sup>b</sup>	1718 <sup>b</sup>	—
		> 70	7	28.6	42.9 <sup>a</sup>	—	4.2 <sup>b</sup>	1507 <sup>b</sup>	—
Poon et al. 1999 [17]	HCC	< 70	299	14.7 <sup>a</sup>	3.0	40.0	—	—	—
		≥ 70	31	32.2 <sup>a</sup>	6.0	48.0	—	—	—
Wu et al. 1999 [15]	HCC	< 80	239	20.5	2.1	15.5	5.5 <sup>b</sup>	1507 <sup>b</sup>	13.5 <sup>a,b</sup>
		≥ 80	21	9.5	0.0	14.3	5.1 <sup>b</sup>	1471 <sup>b</sup>	17.8 <sup>a,b</sup>
Lui et al. 1999 [20]	HCC	< 70	98	16.3	3.1	33.7	6.4 <sup>b</sup>	2710 <sup>b</sup>	16.7 <sup>b</sup>
		≥ 70	24	12.5	8.3	20.8	6.5 <sup>b</sup>	3519 <sup>b</sup>	17.5 <sup>b</sup>
Hanazaki et al. 2000 [21]	HCC	< 70	283	21.5	6.0	23.3	—	1959 <sup>b</sup>	—
		≥ 70	103	31.1	9.7	28.2	—	1476 <sup>b</sup>	—
Yeh et al. 2004 [18]	HCC	< 70	398	22.1	10.5	—	—	1616 <sup>a,b</sup>	—
		≥ 70	34	20.6	7.7	—	—	1058 <sup>a,b</sup>	—
Ferrero et al. 2005 [22]	HCC	≤ 70	177	18.1	9.6	42.4 <sup>a</sup>	—	—	14.8 <sup>a,b</sup>
		> 70	64	26.6	3.1	23.4 <sup>a</sup>	—	—	11.2 <sup>a,b</sup>
Zieren et al. 1994 [23]	CLM	≤ 70	72	—	2.8	25.0	—	—	—
		> 70	18	61.1	5.5	27.8	—	—	16.0 <sup>b</sup>
Fong et al. 1995 [23]	CLM	< 70	449	43.2	4.2	39.9	—	—	12.0 <sup>a,c</sup>
		≥ 70	128	36.7	3.9	42.2	—	—	13.0 <sup>a,c</sup>
Brunken et al. 1998 [25]	CLM	< 70	141	—	3.5	26.2	—	—	14.0 <sup>b</sup>
		≥ 70	25	—	4.0	28.0	—	—	15.0 <sup>b</sup>
Brand et al. 2000 [26]	CLM	< 70	126	—	2.4	30.9	4.7 <sup>b</sup>	1973 <sup>b</sup>	16.6 <sup>b</sup>
		≥ 70	41	—	7.3	39.0	4.0 <sup>b</sup>	1575 <sup>b</sup>	13.1 <sup>b</sup>
Cosenza et al. 1995 [27]	HCC, CLM, Others	< 59	22	50.0	0.0	31.8	—	900 <sup>c</sup>	9.8 <sup>b</sup>
		> 66	20	45.0	5.0	25.0	—	625 <sup>c</sup>	9.0 <sup>b</sup>

<sup>a</sup>*p* < 0.05.<sup>b</sup>mean.<sup>c</sup>median.

HCC: hepatocellular carcinoma; CLM: colorectal liver metastase.

**Table 3.** Long-term outcome after hepatic resection for hepatocellular carcinoma in young and elderly patients.

Author year [ref.]	Age (years)	No. of patients	Cirrhosis (%)	HBV (%) +	HCV + (%)	Survival (months)	5-year survival (1%)
Ezaki et al. 1987 [12]	56–65	44	93.2	—	—	—	28
	≥ 66	37	67.6	—	—	—	18
Nagasue et al. 1993 [19]	≤ 50	26	84.6	—	—	—	49
	≥ 70	32	68.8	9.4	—	—	24
Takenaka et al. 1994 [16]	< 70	229	83.8	18.3	59.0 <sup>a</sup>	—	52
	≥ 70	39	79.5	5.1	88.2 <sup>a</sup>	—	76
Wu et al. 1999 [15]	< 80	239	77.8	58.5 <sup>a</sup>	—	—	59
	≥ 80	21	81.0	28.6 <sup>a</sup>	—	—	41
Poon et al. 1999 [17]	< 70	299	48.8	85.9 <sup>a</sup>	—	42 <sup>c</sup>	40
	≥ 70	31	25.8	51.6 <sup>a</sup>	—	38 <sup>c</sup>	29
Hanazaki et al. 2000 [21]	< 70	283	54.8	23.7	40.7 <sup>a</sup>	33 <sup>b</sup>	40
	≥ 70	103	45.6	18.4	55.4 <sup>a</sup>	39 <sup>b</sup>	51
Yeh et al. 2004 [18]	< 70	398	48.9	74.0 <sup>a</sup>	31.8 <sup>a</sup>	28 <sup>c</sup>	32
	≥ 70	34	54.5	25.8 <sup>a</sup>	63.2 <sup>a</sup>	40 <sup>c</sup>	40
Ferrero et al. 2005 [22]	≤ 70	177	100.0	21.4	38.9 <sup>a</sup>	—	32
	> 70	64	100.0	10.9	60.9 <sup>a</sup>	—	49

<sup>a</sup>*p* < 0.05.<sup>b</sup>mean.<sup>c</sup>median.

HBV: hepatitis B Virus; HCV: Hepatitis C Virus.

**Table 4.** Long-term outcome after hepatic resection for colorectal liver metastases in young and elderly patients.

Author year [ref.]	Age (years)	No. of patients	Survival (months)	5-year survival (%)
Fong et al.	< 70	449	44 <sup>c</sup>	39
1995 [24]	≥ 70	128	40 <sup>c</sup>	35
Brunken et al.	< 70	141	—	31
1998 [25]	≥ 70	25	—	46
Brand et al.	< 70	126	35 <sup>a,b</sup>	21
2000 [26]	≥ 70	41	22 <sup>a,b</sup>	16

<sup>a</sup>*p* < 0.05.  
<sup>b</sup>mean.  
<sup>c</sup>median.

**Table 5.** Preoperative outcome of pancreatic resection in young and elderly patients.

Author year [ref.]	Age (years)	No. of patients	Mortality rate (%)	Complication rate (%)	Operative time (hours)	Blood loss (ml)	Hospital stay (days)
Kairaluoma et al.	< 70	47	8.5	29.8	—	—	—
1987 [32]	≥ 70	21	9.5	47.6	—	—	—
Hannoun et al.	< 70	179	10.0	34.6	—	—	25.0 <sup>b</sup>
1993 [33]	≥ 70	44	4.5	36.0	—	—	22.0 <sup>b</sup>
Kayahara et al.	< 70	102	6.9	48.0	9.8 <sup>a,b</sup>	3618 <sup>a,b</sup>	—
1994 [34]	≥ 70	28	17.8	53.6	7.6 <sup>a,b</sup>	1735 <sup>a,b</sup>	—
Fong et al.	< 70	350	4.0	38.3	—	—	20.0 <sup>c</sup>
1995 [24]	≥ 70	138	5.8	44.9	—	—	20.0 <sup>c</sup>
DiCarlo et al.	< 70	85	3.5	32.9	6.7 <sup>b</sup>	700 <sup>b</sup>	16.5 <sup>b</sup>
1998 [35]	≥ 70	33	6.1	39.4	6.2 <sup>b</sup>	750 <sup>b</sup>	17.0 <sup>b</sup>
Magistrelli et al.	< 70	73	6.8	27.4	4.2 <sup>b</sup>	—	23.5 <sup>b</sup>
1998 [36]	≥ 70	29	0.0	31.0	4.1 <sup>b</sup>	—	19.3 <sup>b</sup>
Sohn et al.	< 80	681	1.6	39.6	7.0 <sup>c</sup>	650 <sup>c</sup>	16.9 <sup>a,b</sup>
1998 [37]	≥ 80	46	4.3	56.5	6.4 <sup>c</sup>	500 <sup>c</sup>	21.1 <sup>a,b</sup>
Bottger et al.	≤ 70	243	2.9	39.5	5.7 <sup>c</sup>	1500 <sup>c</sup>	18.0 <sup>c</sup>
1999 [38]	> 70	57	5.3	56.1	4.9 <sup>c</sup>	1500 <sup>c</sup>	21.0 <sup>c</sup>
Al Sharaf et al.	< 70	47	4.2	46.8	6.0 <sup>c</sup>	2500 <sup>c</sup>	16.0 <sup>c</sup>
1999 [39]	≥ 70	27	7.4	44.4	5.7 <sup>c</sup>	1500 <sup>c</sup>	13.0 <sup>c</sup>
Bathe et al.	65–74	54	3.7	52.0	7.0 <sup>b</sup>	867 <sup>b</sup>	18.0 <sup>b</sup>
2000 [40]	≥ 75	16	25.0	69.0	7.2 <sup>b</sup>	741 <sup>b</sup>	25.0 <sup>b</sup>
Bathe et al.	65–74	47	2.1	38.3	7.2 <sup>b</sup>	973 <sup>b</sup>	15.0 <sup>b</sup>
2001 [41]	≥ 75	19	21.0	57.9	7.5 <sup>b</sup>	750 <sup>b</sup>	25.0 <sup>b</sup>
Hodul et al.	< 70	74	1.4	35.1	6.8 <sup>b</sup>	1138 <sup>b</sup>	10.8 <sup>b</sup>
2001 [42]	> 70	48	0.0	39.6	6.3 <sup>b</sup>	1071 <sup>b</sup>	11.9 <sup>b</sup>
Richter et al.	< 70	426	2.8	21.6	6.0 <sup>c</sup>	1000 <sup>c</sup>	19.0 <sup>c</sup>
2002 [43]	< 70	93	3.2	23.6	5.6 <sup>c</sup>	700 <sup>c</sup>	21.5 <sup>c</sup>
Lightner et al.	< 75	188	3.2	56.4	—	—	15.0 <sup>b</sup>
2004 [44]	≥ 75	30	3.0	70.0	—	—	16.0 <sup>b</sup>

<sup>a</sup>*p* < 0.05.  
<sup>b</sup>mean.  
<sup>c</sup>median.

**Pancreatic Resection for Pancreatic and Ampullary Cancer**

Approximately 168,000 patients die annually from pancreatic cancer, which ranks this cancer type as the ninth most common cause of death from cancer worldwide [11]. The world cancer statistics demonstrate that most deaths occur in developed nations, with 69,000 deaths (41%) annually in Europe and 28,000 (17%) in North America [11]. The poor prognosis of this disease is reflected by the high mortality-incidence ratio of 0.98. The risk to develop pancreatic and ampullary cancer dramatically increases with age, with a median age of 72 years at the time of diagnosis (Table 1). Thus, as for HCC and colorectal liver metastases, the epidemiology of the disease combined with the growth of the older population results in an increasing number of elderly patients to be considered for pancreatic surgery. Despite the limited survival benefit of surgery, pancreatoduodenectomy

remains the standard treatment in the absence of other effective therapies. Because pancreatic surgery is seen as one of the most extensive abdominal procedures, many physicians scrutinize the appropriateness of this operation in geriatric patients.

During the past two decades, pancreatic surgeons have made a particular effort to investigate the benefit of surgery, mostly for cancer of the pancreas and the ampullary region (Tables 5 and 6). Most studies compared perioperative and long-term outcome in patients younger than 70 years versus those older than 70 years of age [24, 32–36, 38, 39, 42, 43]. Operative data demonstrated that intra-operative blood loss and operative times were similar for younger and older patients, implying that the extent and difficulty of surgical procedures are independent of age. Also, most studies demonstrated that pancreatoduodenectomy can be safely performed in elderly patients, with a mortality rate below 10% (Table 5). Only 3 of 14 identified studies reported an unacceptably

**Table 6.** Long-term outcome after pancreatic resection for malignant pancreatic and ampullary tumors in young and elderly patients.

Author year [ref.]	Tumor type	Age (years)	No. of patients	Median survival (months)	5-year survival (%)
Kairaluoma et al. 1987 [32]	Pancreatic cancer	< 70	24	8	—
	Pancreatic cancer	≥ 70	11	9	—
	Ampullary cancer	< 70	19	36	58
	Ampullary cancer	≥ 70	8	20	25
Hannoun et al. 1993 [35]	Pancreatic cancer	< 70	71	16	19
	Pancreatic cancer	≥ 70	21	16	17
	Ampullary cancer	< 70	39	30	45
	Ampullary cancer	≥ 70	10	36	38
Fong et al. 1995 [24]	Pancreatic, ampullary, bile duct and duodenal cancer	< 70	350	24 <sup>a</sup>	29
		≥ 70	138	18 <sup>a</sup>	21
DiCarlo et al. 1998 [37]	Pancreatic cancer	< 70	85	16	9
		≥ 70	33	14	—
Sohn et al. 1998 [37]	Pancreatic cancer	< 80	282	17	36 <sup>b</sup>
		≥ 80	25	18	46 <sup>b</sup>
	Ampullary cancer	< 80	454	20	27
		≥ 80	41	32	19
Al Sharaf et al. 1999 [39]	Pancreatic cancer	< 70	14	8	11
		≥ 70	27	10	0
Bathe et al. 2000 [40]	Ampullary cancer	65–74	54	24	23
		≥ 75	16	9	31
Bathe et al. 2001 [41]	Pancreatic cancer	65–74	47	25 <sup>a</sup>	—
		≥ 75	19	11 <sup>a</sup>	—
Richter et al. 2002 [43]	Pancreatic cancer	< 70	205	14	—
		≥ 70	42	23	—
		< 70	106	46	—
	Ampullary cancer	≥ 70	28	57	—

<sup>a</sup>*p* < 0.05.<sup>b</sup>2-year survival rate.

high mortality rate of 18%–25% in elderly patients [34, 40, 41]. Elderly patients had also higher complication rates and longer hospital stay in these studies. However, complication rates and hospital stay were comparable between the younger and older populations in the majority of the studies [24, 33–36, 39, 42–44]. Although the elderly population has a higher prevalence of comorbidities, American Society of Anesthesiologists (ASA) scores and co-morbidities were evenly distributed between the two age groups [36, 39, 40, 42, 43]. Furthermore, patients with ASA grade IV were either excluded from pancreatic resection or were in the minority [24, 32–34, 38, 39]. Therefore, careful patient selection appears to be the key criterion for a favorable perioperative outcome in elderly patients undergoing pancreaticoduodenectomy.

Regardless of age, the long-term prognosis after pancreaticoduodenectomy for pancreatic head cancer is discouraging. The prognosis of patients undergoing pancreaticoduodenectomy for ampullary tumors is significantly better, but is also associated with frequent tumor recurrence. As shown in Table 6, the improved patient survival of resected ampullary tumors compared to pancreatic cancer is present in both the younger and older populations. Of note, median survival after pancreaticoduodenectomy for ampullary and pancreatic cancer was comparable between younger and older patients in most studies [32, 33, 35, 38, 39, 43]. This was even true for octogenarian patients who underwent pancreaticoduodenectomy [37]. These data demonstrate that pancreaticoduodenectomy can be performed safely in carefully selected elderly patients, and that survival is comparable to that observed in younger patients. Therefore, the decision to perform pancreatic resection should be independent

of chronological age but rather should be based on the best chance for a curative pancreatic resection in a healthy geriatric patient.

#### Radical Resection of Gallbladder Cancer

Gallbladder cancer occurs infrequently in Europe and in the United States, and has a dismal prognosis. Although gallbladder cancer is a disease of the elderly, with a median age of more than 70 years at diagnosis (Table 1), only one study was identified which analyzed the outcome of radical resection for gallbladder cancer in younger (< 75 years) versus older (≥ 75 years) patients [45]. In that study, 87 younger patients and 32 elderly patients underwent extended cholecystectomy for T1–3 gallbladder cancer. Clinico-pathological characteristics and perioperative mortality were comparable between the two age groups. The long-term outcome measured by the 5-year overall survival was 61% in the elderly group and was not statistically different from that of younger patients. In contrast, elderly patients (*n* = 22) who underwent only simple cholecystectomy for gallbladder cancer had a poor 5-year overall survival of 14%. Although not primarily focused on elderly individuals, another large series on curative resection of gallbladder cancer reported similar mortality and complication rates among patients <70 years and >70 years of age [46]. This study failed to identify age as an independent risk factor of long-term outcome. Despite the poor prognosis of gallbladder cancer, these data demonstrate that selective elderly patients might benefit from adequate surgical treatment, and therefore an aggressive treatment strategy is justified in the elderly population.

### Resection of Hilar Bile Duct Cancer

Hilar bile duct cancer (Klatskin tumor) represents the most common form of bile duct cancer [47, 48]. The peak incidence of this disease occurs within the seventh decade of life (Table 1). The natural history of untreated Klatskin tumor is dismal, and results in exceptional 5-year survivors [49]. Although the surgical management of this disease is difficult and should unquestionably be limited to specialized centers, radical resection is the only potential chance for cure. Bile duct resection combined with liver resection is the most commonly performed curative procedure. Because a significant proportion of patients are diagnosed at an advanced age, the questions arise whether this kind of extended procedure can be safely performed in elderly patients, and whether such treatment will result in extended survival in the elderly population. Unfortunately, no published study addressing these important issues is currently available. Therefore, data on perioperative outcome after extended resection of Klatskin tumors are not available for elderly patients. However, information on long-term outcome of elderly patients could be extracted from few series on surgical resection of hilar bile duct cancer. Launois et al. reported a comparable 5-year survival rate for patients > 70 years (22%) and < 60 years (17%) [50]. Kawasaki et al. found a similar mean survival in patients  $\geq$  70 years (32.6 months) and < 70 years (36.6 months) [51]. Despite the absence of age-comparing studies, the survival data from these series demonstrate that elderly patients may benefit from extended resection as much as young patients do.

### Economic Considerations of HPB Surgery in the Elderly

Hepatic and pancreatic resections are undoubtedly among the most expensive abdominal procedures performed. The forces of cost control on health care may scrutinize the benefit of extended resections of HPB tumors in elderly patients. In terms of survival, the present review illustrates that elderly patients with malignant liver and pancreas tumors benefit from curative surgery as much as younger patients do (Tables 3, 4, and 6). Furthermore, the cost-related variables of geriatric patients such as operative time, complication rate, and hospital stay were similar to those of their younger counterparts in most series. These findings alone suggest that hospital costs for patients undergoing hepatic and pancreatic resections might not be significantly higher for elderly patients. This issue was addressed by Vickers et al., who performed a cost-analysis of pancreaticoduodenectomy in patients  $\geq$  70 years of age versus those > 70 years of age [52]. The authors analyzed separately anesthesia, laboratory, pharmacy, and operating room costs, as well as the total costs for both age populations. Costs of anesthesia, laboratory, and pharmacy, as well as total costs, were comparable between the younger and older population. Interestingly, operating room-related costs were significantly lower for the elderly population. These favorable findings seem to be attributable to a careful patient selection in this study as the preoperative risk profiles were not significantly different between older and younger patients. Logically, this also resulted in comparable perioperative complication profiles for the two age groups. This illustrates that careful selection of geriatric patients is of paramount importance, not only for the perioperative and long-term outcome of hepatic and pancreatic resections but also for the cost efficiency of these procedures.

### Conclusions

The present review demonstrates that extended resections of malignant HPB tumors can be safely performed in patients over 70 years of age. Despite the lower statistical life expectancy of elderly patients, the long-term outcome was comparable between younger patients and the geriatric population. Although the survival benefit of pancreaticoduodenectomy is limited for patients with pancreatic cancer, the absence of any other effective therapy justifies this procedure as the unique curative option not only in younger patients but also in the elderly. However, the preoperative risk evaluation and the extent of the disease appear to be the most important criteria for selecting elderly patients who will benefit from surgery. If the selection process takes these criteria into account, resections of malignant HPB tumors can be performed in elderly patients without generating higher costs as compared to younger patients. Therefore, chronological age alone should not be a contraindication to extended resections of malignant HPB tumors or a risk factor for inadequate surgical therapy. Surgery should be denied to elderly patients only after discussion with expert HPB surgeons.

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