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ORIGINAL ARTICLE

## Pancreatic cancer surgery in elderly patients: Balancing between short-term harm and long-term benefit. A population-based study in the Netherlands

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### ABSTRACT

**Background:** At a national level, it is unknown to what degree elderly patients with pancreatic or periampullary carcinoma benefit from surgical treatment compared to their younger counterparts. We investigated resection rates and outcomes after surgical treatment among elderly patients. **Methods:** From the Netherlands Cancer Registry, 20 005 patients diagnosed with primary pancreatic or periampullary cancer in 2005–2013 were selected. The associations between age (<70, 70–74, 75–79, ≥80 years) and resection rates were investigated using  $\chi^2$  tests, and surgical outcomes (30-, 90-day mortality) were evaluated using logistic regression analysis. Overall survival after resection was investigated by means of Kaplan-Meier and Cox proportional hazard regression analysis. **Results:** During the study period, resection rates increased in all age groups (<70 years: 20–30%,  $p < 0.001$ ; ≥80 years: 2–8%,  $p < 0.001$ ). Of 3845 patients who underwent tumour resection for pancreatic or periampullary carcinoma, the proportion of octogenarians increased from 3.5% to 5.5% ( $p = 0.03$ ), whereas postoperative mortality did not increase (30-day: 6–3%,  $p = 0.06$ ; 90-day: 9–8%,  $p = 0.21$ ). With rising age, 30-day postoperative mortality increased (4–5–7–8%, respectively,  $p < 0.001$ ), while 90-day mortality was 6–10–13–12% ( $p < 0.001$ ) and three-year overall survival rates after surgery were 35–33–28–31%, respectively ( $p < 0.001$ ). After adjustment for confounding factors, octogenarians who survived 90 days postoperative exhibited an overall survival close to younger patients [hazard ratio (≥80 vs. <70 years) = 1.21, 95% confidence interval (0.99–1.47),  $p = 0.07$ ]. **Conclusion:** Despite higher short-term mortality, octogenarians who underwent pancreatic resection showed long-term survival similar to younger patients. With careful patient screening and counselling of elderly patients, a further increase of resection rates may be combined with improved outcomes.

### HISTORY

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Pancreatic cancer is one of the most fatal types of cancer, with both incidence and mortality rates close to 10 cases per 100 000 European inhabitants [1]. Incidence rates rise with increasing age from less than one case per 100 000 Dutch inhabitants under 40 years of age up to 70 cases per 100 000 inhabitants aged 75 years or older. At time of diagnosis, over half of patients diagnosed with pancreatic cancer are aged 70 years or older.

For pancreatic and periampullary carcinoma, tumour resection is the only treatment option with a curative intent. Unfortunately, tumour resection is possible in only 15–20% of patients due to locally advanced or metastatic disease at time of diagnosis. Pancreatic surgery is considered highly complex due to relatively high morbidity and mortality rates. Therefore, in the past this type of surgery was restricted to relatively young patients. Together with centralisation of pancreatic surgery, postoperative mortality after pancreatic surgery has

decreased; with in-hospital and 30-day mortality rates reported under 5% [2,3]. With improving postoperative mortality risk, more elderly patients, including fit octogenarians, may be offered pancreatic surgery [4]. Although several specialised institutions reported an absence of an impact of very old age on postoperative mortality [5–8], some population-based studies on this topic showed unfavourable postoperative outcomes in octogenarians compared to younger patients [4,9–12]. However, less is known about octogenarians compared to other elderly age groups.

In the Netherlands, between 2000 and 2009 an increased resection rate has been observed in patients with pancreatic head carcinoma [13]. And although postoperative mortality after pancreatic surgery decreased between 2004 and 2009, elderly patients showed a twice as high mortality rate compared to patients younger than 70 years of age [14]. It is unknown, however, to what extent elderly patients

benefitted from increasing resection rates and improving outcomes.

Therefore, the objective of this nationwide study is to examine resection rates, and short- and long-term outcomes among elderly patients who underwent pancreatic resection for primary pancreatic or periampullary carcinoma, with special attention to octogenarians.

## Methods

### Data collection

The nationwide Netherlands Cancer Registry (NCR) records data on all patients with newly diagnosed cancer in the Netherlands, a country with nearly 17 million inhabitants. Since 1989, the NCR is based on notification of all newly diagnosed malignancies in the Netherlands by the automated pathological archive (PALGA), supplemented with data from the National Registry of Hospital Discharge Diagnoses. Completeness is estimated to be at least 95%. Information on patient characteristics (e.g. gender and date of birth), as well as tumour characteristics (e.g. date of diagnosis, site and subsite [International Classification of Diseases for Oncology (ICD-O-3)] [15], histology, stage (TNM classification) [16] and grade), and primary treatment are collected routinely from the medical records in all Dutch hospitals. Actual vital status (dead or alive) was routinely obtained from the Municipal Personal Records Database, which contains information on the vital status of all Dutch inhabitants.

### Patients

For this study all patients diagnosed with primary pancreatic, ampulla of Vater, extrahepatic bile duct and duodenum cancer (ICD-O C25, C24.1, C24.0, C17.0) in the period 2005–2013 were selected from the NCR. Patients with diagnosis at autopsy, age under 18 years, residing abroad, histologically confirmed neuroendocrine and non-epithelial malignancies were excluded. Before 2010 no distinction was available between diagnosis of distal and proximal extrahepatic bile duct carcinoma (both C24.0). Therefore, for analysis of resection rates patients diagnosed with extrahepatic bile duct carcinoma (C24.0) were excluded. To analyse outcomes, we selected all patients who underwent resection for histologically proven pancreatic (C25), ampulla of Vater (C24.1) and duodenum (C17.0) carcinoma as well as patients who underwent pancreatic surgery for extrahepatic bile duct carcinoma (C24.0). We excluded patients who underwent endoscopic tumour resection only ( $n=51$ ) and patients who underwent tumour resection abroad ( $n=63$ ).

To evaluate outcomes of elderly patients in more detail, the age of patients at diagnosis was divided into four groups: <70 years, 70–74 years, 75–79 years and  $\geq 80$  years. Patients aged 70 years and older were considered 'elderly' patients. Socioeconomic status (SES) was based on reference data from The Netherlands Institute for Social Research. Scores on social deprivation were derived from income, education and occupation per four-digit postal code, and were broken into three SES-categories (high: 1st–3rd, intermediate: 4th–7th, low: 8th–10th deciles). Due to the nature of the NCR, data on prior

cancer diagnoses were available in all patients. In addition, comorbidity data was available in 13% of surgically treated patients in our study. Comorbidity was recorded according to a slightly modified version of the Charlson classification in all patients diagnosed in a NCR region (different time periods in three of nine NCR regions of the Netherlands). Serious comorbid conditions included previous malignancies, chronic obstructive pulmonary diseases, cardiovascular diseases, cerebrovascular diseases, digestive tract diseases, diabetes mellitus and other serious diseases. The number of comorbidities were categorised in three groups (0, 1,  $\geq 2$ ). Tumour stage (TNM) was categorised as 'loco-regional' (T1–2–3 or N+, M0), 'extended' (T4M0), 'metastatic' (M1) or 'unknown' (X), based on pathological TNM and irrespective of tumour location. To account for late fatal outcomes of postoperative complications [3], both 30- and 90-day mortality of any cause after date of tumour resection were evaluated. Survival time was defined as the time from the date of tumour resection to the date of death. Patients who were alive at 1 January 2015 were censored.

### Statistical analysis

To compare resection rates in the four age groups and to compare categorical patient (gender, SES), tumour (location, stage, grade) and treatment characteristics of patients who underwent tumour resection, two-sided Pearson's  $\chi^2$ -tests were used. Until 2012, analyses of two-year periods smoothed the resection rates. To control for potential incompleteness of non-resected patients in the most recent available year of diagnosis, sensitivity analyses were performed excluding 2013. A  $p$ -value <0.05 was considered significant. Univariate and multivariate logistic regression analyses were performed to investigate the association of age with 30- and 90-day postoperative mortality. Kaplan-Meier and Cox proportional hazard regression analyses were used to evaluate the relation between age and overall survival. Characteristics with a  $p < 0.10$  in the univariate analysis were entered into the multivariate models. In sensitivity analyses, the influence of the number and type of comorbid conditions was investigated. All analyses were performed using STATA/SE (version 13.0; STATA Corp., College Station, TX, USA).

## Results

### Resection rates

The median age of the 20 005 patients diagnosed with pancreatic ( $n=17\ 742$ ), ampulla of Vater ( $n=1427$ ) and duodenum carcinoma ( $n=836$ ) in the period 2005–2013 was 71, 71 and 70 years, respectively (range 19–101 years). Of all these patients, 46% was younger than 70 years of age and 21% was aged 80 years or older.

Over time, the proportion of patients undergoing tumour resection increased from 14% in 2005–2006 to 24% in 2013 ( $p < 0.001$ ). This increase was more prominent in patients diagnosed with pancreatic (from 10% to 20%,  $p < 0.001$ ) or ampulla of Vater carcinoma (from 52% to 69%,  $p = 0.006$ ) than in patients with duodenum carcinoma (from 37% to 36%,  $p = 0.26$ ).

Overall, resection rates have increased in all age groups [ $< 70$  years: from 20% to 30%; 70–74 years: 16–29%; 75–79

years: 10–22%;  $\geq 80$  years: 2.1–7.5% (all  $p < 0.001$ ). As shown in Figure 1, resection rates of patients diagnosed with pancreatic carcinoma and aged 70–74 years (11–24%,  $p < 0.001$ ) approached resection rates of patients under 70 years of age (15–25%,  $p < 0.001$ ). In octogenarians with pancreatic carcinoma, resection rates were lowest and an increase especially took place in most recent years (1–2–2–4–5% in consecutive periods,  $p < 0.001$ ). For ampulla of Vater and duodenum carcinoma together, an increase was only found in patients of  $\geq 80$  years (7–23%,  $p = 0.02$ ). Significance levels remained similar after excluding patients diagnosed in 2013.

### Patients who underwent tumour resection

The median age of the 3845 patients who underwent resection for pancreatic [ $n = 2260$  (59%)] or periampullary [ $n = 1585$  (41%); ampulla of Vater, duodenum and distal bile duct] carcinoma was 67 years (range 19–90 years). Over time, the proportion of patients younger than 70 years of age decreased from 66% in 2005–2006 to 59% in 2013 and the proportion of octogenarians nearly doubled from 3.5% to 5.5% ( $p = 0.03$ ). Patient and tumour characteristics per age group of resected patients are shown in Table I. Compared to younger age groups, octogenarians more often had resection for periampullary carcinoma ( $p = 0.01$ ). The prevalence of a prior cancer diagnosis and the number of comorbid conditions increased with older age (both  $p < 0.001$ ), particularly an increase of cardiac and vascular diseases (both  $p < 0.001$ ). With rising age, a decreasing proportion of patients with pancreatic carcinoma received adjuvant chemotherapy (48–36–15–3%,  $p < 0.001$ ).

### Postoperative mortality

Overall, 4.6% of patients died within 30 days of surgery (from 5.7% in 2005–2006 to 3.2% in 2013,  $p = 0.06$ ) and at time of 90 days postoperatively 7.8% of patients had deceased (9.2–7.5%,  $p = 0.21$ ). Over time, 30-day mortality of elderly patients ( $\geq 70$  years) halved from 9.2% in 2005–2006 to 4.5% in 2013 ( $p = 0.06$ ) and 90-day mortality slightly decreased from 14.0% to 11.9% ( $p = 0.27$ ). Less improvement of postoperative outcomes was observed in patients under 70 years of age (30-day mortality: 3.8–2.2%,  $p = 0.52$  and 90-day mortality: 6.3–4.5%,  $p = 0.39$ ).

With rising age, 30-day mortality worsened ( $p < 0.001$ , Figure 2). The highest 90-day mortality was found in the age group of 75–79 years of age ( $p < 0.001$ ). However, postoperative outcomes of the three elderly age groups did not differ significantly from each other ( $\geq 70$  years: 30-day  $p = 0.33$ ; 90-day  $p = 0.37$ ). In multivariate logistic regression models, after adjustment for confounding factors, all elderly patient groups showed significantly worse 30- and 90-day mortality compared to patients under 70 years of age (Table II). No significant associations were found between number or types of comorbid conditions and postoperative mortality.

### Survival

Patients with resected pancreatic carcinoma exhibited a worse one-, three- and five-year overall survival (OS; 63%, 24% and

16%, respectively) compared to patients with resected periampullary carcinoma (74%, 47% and 36%). Elderly patients had lower survival rates than patients younger than 70 years of age. Octogenarians had similar one-, three- and five-year OS (pancreas 53%, 21% and 13%; periampullary 73%, 40% and 28%) compared to both other elderly patient groups, especially in patients with pancreatic carcinoma (Table III).

Patient characteristics like SES, a prior cancer diagnosis and the number of comorbid conditions of surgically treated patients were not associated with OS (univariate  $p = 0.53$ ,  $p = 0.49$  and  $p = 0.87$ , respectively). After adjustment for differences in tumour location, stage and grade, adjuvant chemotherapy and period of diagnosis, OS of octogenarians who underwent pancreatic resection was similar to survival of other elderly patient groups (Table IV). In sensitivity analyses on type of comorbid conditions, only the presence of pulmonary diseases seemed independently associated with a poor OS (adjusted HR = 1.75, 95% CI 1.20–2.57).

Octogenarians who survived 90 days postoperative exhibited OS close to that of patients younger than 70 years of age [HR ( $\geq 80$  vs.  $< 70$  years) = 1.21, 95% CI (0.99–1.47),  $p = 0.07$ ].

### Discussion

This nationwide population-based study showed a 3–4 times increase of resection rates among octogenarians with pancreatic or periampullary carcinoma between 2005 and 2013 in the Netherlands. Among patients who underwent tumour resection, the proportion of octogenarians showed a 50% increase, while no increase of postoperative mortality was found. All elderly patient groups ( $\geq 70$  years) exhibited a higher short-term mortality risk compared to patients under 70 years of age, but no significant differences were found between the three elderly patient groups. Adjustment for other contributing factors did not change these results. Interestingly, (conditional) OS of surgically treated octogenarians approached survival of patients younger than 70 years of age.

In line with a recent population-based study in the USA [4], we found increasing resection rates in all age groups and especially in octogenarians. Although patients were less likely to be resected with older age, the resection rate of patients aged 70–74 years now has reached a level similar to that of younger patients. Our study confirmed an earlier report from the Netherlands attributing an increased resection rate in patients with pancreatic head carcinoma to more patients with advanced tumours (T3 and/or N1) undergoing resection (data not shown) [13]. At that time however, no significant change in the age of resected patients was found. In our study including additional years, particularly in the most recent years increasing resection rates were observed in elderly patients. As a result, age of resected patients has increased (median age from 65 to 67 years). Our findings are in accordance with the recent Dutch guideline on pancreatic cancer [17], stating that high age alone should not be a contraindication for pancreatic surgery. The proportion of octogenarians in our study (4.7%), however, was in the lower range compared to reports from specialised centres (4.5–17%) [5–8] and compared to population-based studies on this subject reporting 5.7–12.4% octogenarians [3,4,10].

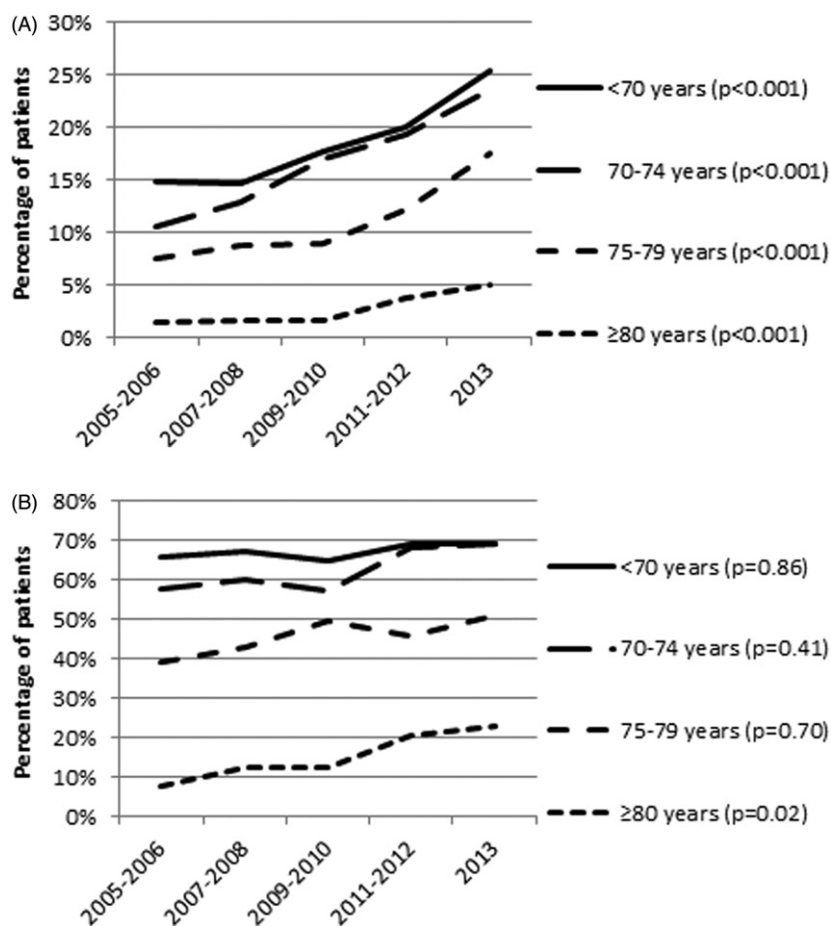


Figure 1. Resection rates by age group of patients diagnosed with primary pancreatic (A) and periampullary (B: ampulla of Vater, duodenum) carcinoma in the period 2005–2013 in the Netherlands.

Table I. Characteristics of patients who underwent tumour resection for primary pancreatic or periampullary (ampulla of Vater, duodenum and distal bile duct) carcinoma in the period 2005–2013 in the Netherlands, by age group.

	All patients N = 3845 %	<70 years N = 2373 %	70–74 years N = 781 %	75–79 years N = 510 %	≥80 years N = 181 %	$\chi^2$ p-value
Gender						
Male	2149 (56)	56	57	56	48	0.14
Female	1696 (44)	44	43	44	52	
Socioeconomic status (SES)						
High	1154 (30)	31	28	29	29	0.58
Intermediate	1538 (40)	39	41	44	34	
Low	1153 (30)	30	31	27	37	
History of cancer						
No	3212 (84)	87	81	78	72	<0.001
Yes	633 (16)	13	19	24	29	
Comorbid conditions <sup>a</sup>	(n = 426)	(n = 261)	(n = 91)	(n = 66)	(n = 8)	<0.001
0	122 (29)	35	20	17	13	
1	125 (29)	29	30	30	38	
2+	159 (37)	29	48	53	50	
Unknown	20 (5)	7	2	0	0	
Location of primary tumour						
Pancreas	2260 (59)	60	60	56	49	0.01
Periampullary	1585 (41)	40	40	44	51	
Tumour stage						
T1–2–3/N1 M0	3336 (87)	86	88	88	92	0.19
T4 M0	384 (10)	11	9	10	7	
M1	98 (3)	3	2	2	<1	
X	27 (1)	1	1	1	<1	
Tumour grade						
Moderate/well diff.	2044 (53)	53	52	54	54	0.57
Poorly diff.	1158 (30)	31	31	27	27	
	643 (17)	16	17	19	19	

<sup>a</sup>Available in three out of nine cancer regions (n = 426, 11% of all patients).



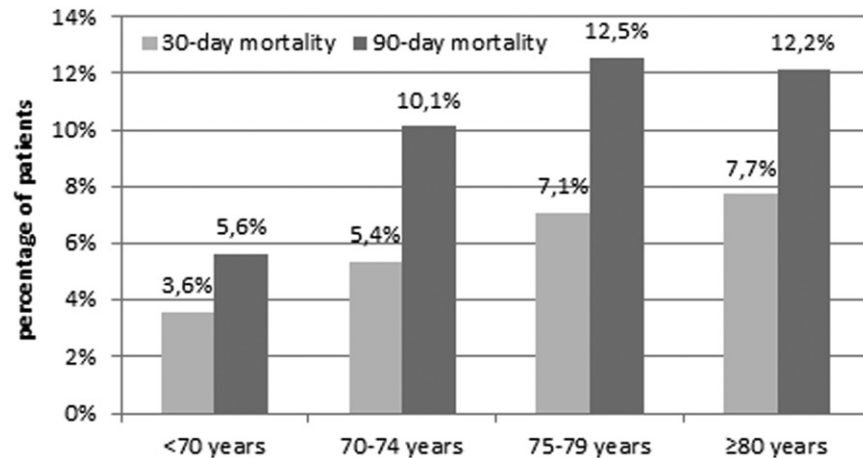


Figure 2. Unadjusted 30- and 90-day of patients who underwent resection for diagnosis of primary pancreas or periampullary carcinoma in 2005–2013 in the Netherlands, by age groups.

Table II. Univariate and multivariate logistic regression analyses predicting postoperative outcomes (30- and 90-day mortality) of patients who underwent resection for primary pancreatic or periampullary carcinoma in the period 2005–2013 in the Netherlands.

Characteristics	30-day mortality					90-day mortality				
	Univariate			Multivariate		Univariate			Multivariate	
	OR	95% CI	p-Value	OR	95% CI	OR	95% CI	p-Value	OR	95% CI
<b>Age</b>										
<70 years	1	–	<0.001	1	–	1	–	<0.001	1	–
70–74 years	1.53	1.05–2.24		1.57	1.07–2.29	1.88	1.41–2.52		1.91	1.42–2.55
75–79 years	2.04	1.37–3.06		2.07	1.38–3.10	2.40	1.75–3.28		2.45	1.78–3.36
≥80 years	2.26	1.25–4.06		2.44	1.35–4.41	2.31	1.43–3.73		2.48	1.53–4.02
<b>Period of diagnosis</b>										
2005–2006	1	–	0.06	1	–	1	–	0.21	1	–
2007–2008	0.84	0.51–1.37		0.82	0.50–1.34	0.84	0.57–1.25		0.84	0.57–1.25
2009–2010	1.02	0.65–1.60		1.01	0.65–1.59	1.00	0.69–1.43		1.00	0.69–1.43
2011–2012	0.65	0.41–1.04		0.62	0.39–0.99	0.69	0.48–1.00		0.69	0.48–1.00
2013	0.54	0.31–0.97		0.52	0.30–0.93	0.82	0.54–1.24		0.82	0.54–1.24
<b>Gender</b>										
Male	1	–	0.03	1	–	1	–	0.008	1	–
Female	0.71	0.52–0.97		0.71	0.51–0.97	0.72	0.56–0.92		0.71	0.57–0.91
<b>SES</b>										
High	1	–	0.89	1	–	1	–	0.25	1	–
Medium	1.04	0.72–1.50		1.04	0.72–1.50	1.10	0.82–1.47		1.10	0.82–1.47
Low	1.10	0.75–1.63		1.10	0.75–1.63	1.29	0.95–1.75		1.29	0.95–1.75
<b>History of cancer</b>										
No	1	–	0.86	1	–	1	–	0.97	1	–
Yes	1.04	0.69–1.55		1.04	0.69–1.55	0.99	0.72–1.37		0.99	0.72–1.37
<b>Comorbid conditions<sup>a</sup></b>										
0	1	–	0.83	1	–	1	–	0.86	1	–
1	0.97	0.31–3.11		0.97	0.31–3.11	1.24	0.47–3.25		1.24	0.47–3.25
2+	1.30	0.46–3.67		1.30	0.46–3.67	1.27	0.51–3.17		1.27	0.51–3.17
Unknown	–	–		–	–	–	–		–	–
<b>Primary tumour</b>										
Pancreas	1	–	0.09	1	–	1	1	0.29	1	–
Periampullary	1.30	0.96–1.76		1.22	0.90–1.65	1.14	0.90–1.44		1.14	0.90–1.44
<b>Tumour stage</b>										
T1–2–3/N+M0	1	–	0.51	1	–	1	–	0.05	1	–
T4 M0	1.38	0.88–2.17		1.38	0.88–2.17	1.26	0.87–1.82		1.29	0.88–1.87
M1	1.17	0.47–2.91		1.17	0.47–2.91	2.09	1.17–3.74		2.40	1.33–4.32
X	1.74	0.41–7.39		1.74	0.41–7.39	2.18	0.75–6.36		1.90	0.64–5.67
<b>Tumour grade</b>										
Moderate/well diff.	1	–	0.80	1	–	1	0.92–1.58	0.05	1	–
Poorly diff.	1.12	0.80–1.58		1.12	0.80–1.58	1.20	1.07–2.00		1.22	0.92–1.60
Unknown	1.06	0.70–1.62		1.06	0.70–1.62	1.46	–		1.42	1.04–1.95

CI, confidence interval; N, number of patients; OR, odds ratio.

<sup>a</sup>Available in three out of nine cancer regions (n = 426, 11% of all patients).

Despite increasing resection rates in the course of our study, 30-day postoperative mortality slightly decreased in elderly patients who underwent resection for pancreatic or periampullary carcinoma. Thirty-day postoperative mortality in

octogenarians (7.7%) in our study was in line with previous population-based and multi-institutional studies showing a (30-day and/or in-hospital) postoperative mortality between 4.7% and 15.5% [3,4,10]. In concordance with a large

**Table III.** Crude 1-, 3-, 5-year survival of patients who underwent tumour resection for primary pancreatic and periampullary carcinoma in the period 2005–2013 in the Netherlands, by age group.

	All patients				Pancreas				Periampullary			
	N	1-year (%)	3-year (%)	5-year (%)	N	1-year (%)	3-year (%)	5-year (%)	N	1-year (%)	3-year (%)	5-year (%)
All ages	3845	68	33	24	2260	63	24	16	1585	74	47	36
<70 years	2373	71	35	27	1421	67	25	18	952	77	50	40
70–74 years	781	65	33	22	466	59	24	13	315	72	46	36
75–79 years	510	60	28	17	285	53	21	10	225	68	37	27
≥80 years	181	64	31	21	88	53	21	13	93	73	40	28
<i>p</i> -Value		<0.001	<0.001	<0.001		<0.001	0.001	<0.001		0.02	0.004	0.002

**Table IV.** Univariate and multivariate Cox proportional hazards analyses predicting survival of patients who underwent resection for primary pancreatic or periampullary carcinoma in the period 2005–2013 in the Netherlands.

Characteristics	Univariate analysis			Multivariate analysis		
	HR	95% CI	<i>p</i> -Value	HR	95% CI	<i>p</i> -Value
Age				Ref		
<70 years	Ref	–	<0.001	1.15	–	
70–74 years	1.14	1.04–1.26		1.31	1.05–1.27	0.004
75–79 years	1.32	1.18–1.48		1.25	1.17–1.47	<0.001
≥80 years	1.19	1.00–1.43			1.04–1.50	0.02
Period of diagnosis				Ref		
2005–2006	Ref	–	0.03	Ref	–	
2007–2008	0.85	0.75–0.96		0.86	0.76–0.98	0.02
2009–2010	0.87	0.77–0.97		0.91	0.81–1.03	0.13
2011–2012	0.85	0.76–0.96		0.90	0.79–1.01	0.08
2013	0.95	0.82–1.11		0.97	0.83–1.13	0.71
Gender						
Male	Ref	–	0.10			
Female	0.94	0.87–1.01				
SES						
High	Ref	–	0.53			
Medium	1.05	0.96–1.15				
Low	1.01	0.91–1.11				
History of cancer						
No	Ref	–	0.49			
Yes	1.04	0.94–1.15				
Comorbid conditions <sup>a</sup>						
0	Ref	–	0.87			
1	1.12	0.83–1.51				
2+	1.04	0.78–1.37				
Unknown	0.97	0.56–1.68				
Primary tumour						
Pancreas	Ref	1	<0.001	Ref	–	
Periampullary	0.56	0.52–0.61		0.49	0.44–0.53	<0.001
Tumour stage						
T1–2–3/N + M0	Ref	–	<0.001	Ref	–	
T4 M0	1.09	0.96–1.24		1.34	1.89–1.53	<0.001
M1	2.34	1.90–2.88		2.49	2.02–3.07	<0.001
X	0.75	0.46–1.22		0.82	0.50–1.34	0.43
Tumour grade						
Moderate/well diff.	Ref	–	<0.001	Ref	–	
Poorly diff.	1.49	1.37–1.62		1.47	1.35–1.61	<0.001
Unknown	0.93	0.83–1.03		0.90	0.80–1.01	0.07
Chemotherapy						
No	Ref	–	0.08	Ref	–	
Yes	0.93	0.85–1.00		0.73	0.66–0.80	<0.001

CI, confidence interval; HR, hazard ratio.

<sup>a</sup>Available in three out of nine cancer regions ( $n = 426$ , 11% of all patients).

observational study of patients undergoing pancreatoduodenectomy for cancer [12], short-term mortality risk of octogenarians in our study did not differ from that of other elderly age groups. In addition, our study showed that also long-term survival of octogenarians was similar to that of other elderly patient groups. Despite a high short-term mortality risk, long-term survival of octogenarians even approached survival of the youngest age group under 70 years of age. Although with increasing age the prevalence of prior cancer and

comorbidities increased, these factors were not associated with short- and long-term mortality after surgery. Our results therefore indicate that octogenarians who underwent pancreatic surgery in the Netherlands were carefully selected. It was not known, however, whether all fit elderly patients with resectable pancreatic or periampullary cancers were indeed offered pancreatic surgery or were referred to specialised centres to be evaluated for pancreatic surgery. Centralisation of pancreatic surgery, which has been observed in the

Netherlands in the past decade [14], may have unwanted side effects. Hospitals may increasingly differ in (patient and tumour) criteria to select or refer patients for surgery [18]. Therefore, possibly more elderly patients in the Netherlands could benefit from pancreatic surgery [2,10].

Several studies on surgical risks of patients with gastrointestinal cancers showed that postoperative mortality prolonged beyond the 30-day postoperative period [3,19–21]. In a recent study, a doubling of the 30-day mortality rate after pancreatic surgery was found by 90 days postoperative [3]. Our study population showed a 70% increase within the same time span, with 90-day mortality rates of elderly patients exceeding 10%. Major pancreatic surgery and postoperative complications itself may aggravate existing comorbid conditions or a fragile functioning, especially in elderly patients [22]. Preoperative use of geriatric assessment tools may provide additional insight in nutritional, physical, psychological and social risks of elderly patients [23]. Furthermore, the improved ability to support patients with severe postoperative complications may have resulted in delayed mortality beyond the 30-day period. However, extending the time window of postoperative mortality risks until 90 days postoperatively may include patients who die from progressive disease [21]. In our study, both elderly patients and resected patients with metastatic disease showed an elevated 90-day mortality risk. Therefore, an extended postoperative time window in pancreatic surgery for cancer will reflect quality of the perioperative surgical process as well as adequate preoperative diagnosis and selection of resectable patients.

A major limitation of our study on elderly patients is the lack of national data on comorbidity. However, available comorbidity data were collected region-wide and nearly complete. In sensitivity analyses the number and type of comorbid conditions were not significantly associated with short- and long-term mortality after pancreatic resection for cancer, possibly except for pulmonary diseases. Although these analyses may suffer from a lack of power due to small numbers in elderly age groups, available data in the total study population on prior cancer diagnoses showed similar associations with outcomes. In addition, the influence of comorbidity on survival seems of less importance in cancers with poor prognosis, such as pancreatic cancer [24]. Furthermore, no information was available on postoperative complications and cause of death. Overall, mixed results were found on the association of high age and morbidity after pancreatic surgery for cancer [2,5,8,12]. However, in studies that differentiated between surgical and non-surgical complications, age differences were particularly found in non-surgical complications [12,25].

## Conclusions

In the past decade, increased resection rates were observed in all age groups and especially in octogenarians with pancreatic or periampullary carcinoma on a nationwide level. Despite a high short-term mortality risk similar to other elderly patients, surgically treated octogenarians showed long-term survival similar to younger patients. Careful patient screening and ongoing centralisation may further increase resection rates

while improving postoperative mortality and survival. Selection for resection solely based on age seems not justified.

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