ORIGINAL ARTICLE

Volume−outcome relationships in pancreatoduodenectomy for cancer

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Abstract

Background: Volume−outcome relationships in pancreatic surgery are well established, but an optimal volume remains to be determined. Studies analyzing outcomes in volume categories exceeding 20 procedures annually are lacking.

Study design: A consecutive 3420 patients underwent PD for primary pancreatic or periampullary carcinoma (2005−2013) and were registered in the Netherlands Cancer Registry. Relationships between hospital volume (<5, 5−19, 20−39 and ≥40 PDs/year) and mortality and survival were explored.

Results: There was a non-significant decrease in 90-day mortality from 8.1 to 6.7% during the study period (p = 0.23). Ninety-day mortality was 9.7% in centers performing <5 PDs/year (n = 185 patients), 8.9% for 5−19 PDs/year (n = 1432), 7.3% for 20−39 PDs/year (n = 240) and 4.3% for ≥40 PDs/year (n = 562, p = 0.004). Within volume categories, 90-day mortality did not change over time. After adjustment for confounding factors, significantly lower mortality was found in the ≥40 category compared to 20−39 PDs/year (OR = 1.72 (1.08−2.74)). Overall survival adjusted for confounding factors was better in the ≥40 category compared to categories under 20 PDs/year: HR (≥40 vs 5−19/year) = 1.24 (1.09−1.42). In the ≥40 category significantly more patients received adjuvant chemotherapy and had >10 lymph nodes retrieved compared to lower volume categories.

Conclusions: Volume−outcome relationships in pancreatic surgery persist in centers performing ≥40 PDs annually, regarding both mortality and survival. The volume plateau for pancreatic surgery has yet to be determined.

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Introduction

Pancreatic carcinoma affects 10 per 100,000 persons annually.[1] Resection offers the only chance for cure in patients with pancreatic or periampullary (duodenum, ampulla, distal bile duct) carcinoma. Pancreatic surgery is traditionally regarded as low-volume, high-complex surgery. Many studies have clearly demonstrated improved postoperative outcomes following pancreatoduodenectomy (PD) in centers with higher procedural volumes compared to low volume hospitals. However, most studies examine volume−outcome relationships up to more than

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Lydia G.M. van der Geest and L. Bengt van Rijssen contributed equally to this work.

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20 procedures per year, and an optimal volume cut-off level is currently unknown.[2–5]

Over the past decade, centralization of pancreatic surgery has occurred in The Netherlands which was accompanied by improved postoperative and long-term survival.[6–9] Nationwide minimum volumes have been set for various procedures and are reviewed periodically. For PD, in 2011 the Dutch Society for Surgery has set a minimum volume level of 20 procedures per center annually.[10] The question was raised whether further increasing the volume cut-off for PD from 20 to 40 could further improve outcomes. The aim of this study was to examine postoperative mortality and long-term survival in patients who underwent PD for primary pancreatic or periampullary malignancy in The Netherlands with hospital volume categories higher than previously examined.

Methods

Patient selection

This study was approved by the review board of the Netherlands Comprehensive Cancer Organization (IKNL), which was established to protect the privacy rights of patients and hospitals in the Netherlands Cancer Registry (NCR). Newly diagnosed malignancies in The Netherlands are registered in the population-based NCR, covering 17 million inhabitants. Completeness is estimated to be at least 95%. Topography and morphology are coded according to the international Classification of Diseases for Oncology (ICD-O).[11] The tumor – lymph node – metastasis (TNM) classification was used to record tumor stage at diagnosis.[12] Survival data was obtained from the Municipal Personal Records Database.

All patients who underwent a PD (either pylorus-preserving or Whipple-Kausch) for primary pancreatic (C25), ampulla of Vater (C24.1), extrahepatic bile duct (C24.0) or duodenal (C17.0) adenocarcinoma between 2005 and 2013 were selected from the NCR. Patients residing or resected abroad, other (pancreatic) resections and age under 18 years old were excluded. Tumor location was categorized as pancreas or periampullary (ampulla, distal bile duct and duodenum). Tumor stage (TNM 6th (2005–2009) and 7th (2010–2013) edition) was based on pathological TNM. Socioeconomic status (SES) was based on The Netherlands Institute for Social Research and deciles were collapsed into three categories (high: 1st–3rd, intermediate: 4th–7th, low: 8th–10th deciles).

Hospital volume and outcome measures

Hospital volume was categorized as <5, 5–19, 20–39 and ≥40 PDs per year. The highest volume category was based on doubling of the current volume cut-off of 20 PDs per year.[6,9] Hospital volume classification was based on the number of PDs for primary malignancies. The volume category per hospital was calculated for each years separately. For each hospital, the volume category could vary per year. To account for late fatal outcomes of postoperative complications, postoperative mortality was defined as death from any cause within 90 days postoperatively. Patients with metastatic disease undergoing PD (n = 61) were excluded from the analysis of survival. Overall survival (OS) was defined as the time between PD and death. Patients alive after December 31st, 2014 were censored. To minimize the influence of postoperative mortality on results of long-term survival, patients alive at 90 days postoperatively were included in the analysis of conditional survival (CS).

Statistical analysis

Baseline patient characteristics (gender, age, prior cancer, SES), tumor characteristics (location, stage, grade) and treatment characteristics (margin status, lymph nodes, chemotherapy) were compared between hospital volume categories using Pearson's chi-square tests. A p-value <0.05 was considered statistically significant. The chi-square test was used to investigate the association between hospital volume and postoperative outcomes. Univariable and multivariable logistic regression analyses were performed to investigate hospital volume and the influence of patient and tumor characteristics on 90-day postoperative mortality. Supplementary multilevel analysis did not reveal relevant clustering within hospitals (likelihood ratio test, p = 0.14) and was discarded. Cox proportional hazard regression analysis was used to evaluate the relation between hospital volume and (conditional) survival. Characteristics with a $p < 0.10$ in univariable analysis were entered into multivariable models, as well as period of surgery to adjust for possible time effects of (high) hospital volumes. Hospital volume was entered in all models. Analyses were performed using STATA/SE (version 13.0; STATA Corp., College Station, Texas, USA).

Results

Patient and hospital characteristics

In total 3420 patients were included. The nationwide total volume of PDs for primary pancreatic or periampullary carcinoma doubled from 270 patients in 2005 to 538 patients in 2013. Between 2005 and 2013, an increase was found in the proportion of patients receiving PD aged 65 years or older (from 54 to 64%, p = 0.003) and the proportion of stage II pancreatic carcinoma (T3 or N1, 66–73%, $p < 0.001$). Patient and hospital characteristics are shown in Table 1. Patients in high volume centers more often had high SES (37 vs 24–30%, p = 0.002). In the lowest volume category the tumor was more often located in the periampullary region (50 vs 40–44%, p = 0.012).

Between 2005 and 2013, the number of hospitals performing PD for pancreatic or periampullary carcinoma halved from 42 to 21. The median annual number of PDs per hospital increased from 4 (interquartile range [IQR] 2–7) to 23 (IQR 20–32). The highest volume category of ≥40 procedures per year contained 4% of all hospital-years (5 different hospitals), while the lowest volume category consisted of 30% of all hospital-years. The

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Table 1 Baseline characteristics of patients who underwent pancreatoduodenectomy (PD) for primary pancreatic or periampullary carcinoma between 2005 and 2013 based on volume of PDs/year

	All	<5/year	5–19/year	20–39/year	≥40/year	p-value
Hospital-years n=	*286*	*87*	*139*	*48*	*12*	–
Patients n=	3420	185	1432	1241	562	–
Patient	N (%)	%	%	%	%	
Gender						0.459
Male	1929 (56)	58	57	57	53	
Female	1491 (44)	42	43	43	47	
Age						0.085
<65 years	1426 (42)	49	43	40	40	
65–74 years	1385 (41)	40	39	42	42	
≥75 years	609 (18)	11	18	18	18	
History of cancer						0.025
No	2873 (84)	90	85	82	85	
Yes	547 (16)	10	15	18	15	
SES						0.002
High	1026 (30)	24	30	28	37	
Medium	1371 (40)	40	41	40	38	
Low	1023 (30)	36	30	32	25	
Tumor						
Location of primary tumor						0.012
Pancreas	1960 (57)	50	60	56	56	
Periampullary	1460 (43)	50	40	44	44	
Tumor invasion (T)						<0.001
T1–2	1185 (35)	43	39	31	29	
T3–4	2205 (64)	56	60	69	70	
TX	30 (0.9)	1	1	1	1	
Lymph node status (N)						<0.001
N0-X	1376 (40)	48	44	3628	34	
N1	2044 (60)	52	56		66	
Distant metastasis (M)						0.36
M0-X	3359 (98)	99	98	98	98	
M1	61 (1.8)	1	2	2	2	
Tumor grade						<0.001
Moderate/well diff.	1835 (54)	64	56	50	51	
Poor diff.	1041 (30)	26	26	35	33	
Unknown	544 (16)	9.2	18	15	15	
Treatment						
Lymph nodes (per cent 10 or more examined)	1660 (49)	23	39	55	66	<0.001
Margin status (T1-2-3N0-1M0 only; per cent R0)	2270 (75)	69	74	78	77	0.024
Chemotherapy (pancreas only; per cent yes)	810 (41)	15	30	50	61	<0.001

SES, socioeconomic status; Diff., differentiation.

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highest annual number of PD's performed for pancreas or periampullary carcinoma by a single center was 57 in 2013. The number of patients undergoing surgery in a >40 PDs/year center increased from 14% in 2009 to 36% in 2013 ($p < 0.001$).

Postoperative mortality

Between 2005 and 2013, no significant decrease in 90-day mortality was found (8.1–6.7%, p = 0.23). The 90-day mortality was 9.7% in centers performing <5 resections annually (n = 185 patients), 8.9% for 5–19 resections (n = 1432), 7.3% for 20–39 resections (n = 1240) and 4.3% for ≥40 resections (n = 562, p = 0.004). Within volume categories, 90-day mortality did not change over time. After adjustment for confounding factors including period of surgery (Table 2), significantly worse 90-day mortality was found in each volume category compared to the highest (≥40) volume category: OR = 2.59 (95%CI 1.32–5.09) for the <5 category, OR = 2.11 (1.32–3.38) for the 5–19 category and OR = 1.72 (1.08–2.74) for the 20–39 category, respectively.

Treatment characteristics

With increasing hospital volume, there were significant differences in treatment characteristics (Table 1). Following adjustment for period of surgery, age, SES, prior cancer, tumor location, stage and grade, and excluding metastatic disease, in the ≥40 category significantly more often 10 or more lymph nodes were found at pathological analysis compared to each lower volume category: OR = 0.22 (95%CI 0.15–0.33) compared to the <5 category, OR = 0.41 (0.33–0.51) compared to the 5–19 category, and OR = 0.66 (0.54–0.82) compared to the 20–39 category. Also, significantly more patients received adjuvant chemotherapy in the highest volume category compared to each lower category: OR = 0.22 (95%CI 0.11–0.43) compared to the <5 category, OR = 0.45 (0.32–0.60) compared to the 5–19 category, and OR = 0.70 (0.52–0.95) compared to the 20–39 category. Furthermore, a radical resection (R0) was achieved significantly more often in the highest volume category compared to the <5 category but not to respective higher categories: OR = 0.62 (95%CI 0.41–0.93) compared to the <5 category, OR = 0.89 (0.69–1.15) compared to the 5–19 category, and OR = 1.12 (0.87–1.43) compared to the 20–39 category.

Overall survival and conditional survival

Median OS was 16.8 months for patients undergoing resection for pancreatic carcinoma, and 31.9 months for patients with periampullary carcinoma. Older age, pancreatic tumors, advanced tumor stage, poor differentiation, and positive margins were associated with worse OS. After adjustment for confounding factors including the period of surgery, OS was better in the ≥40 volume category compared to hospital volumes under 20 procedures per year (Table 3): HR = 1.34 (95%CI 1.09–1.65) compared to the <5 category, HR = 1.24 (1.09–1.42) compared to the 5–19 category, and HR = 1.10 (0.97–1.26) compared to the 20–39 category (Table 3). When using the 20–39 volume category as reference category, significantly better OS was found in this reference category compared to volumes under 20 procedures per year: HR = 1.21 (95%CI 1.01–1.46) compared to the <5 category and HR = 1.13 (1.02–1.24) compared to the 5–19 category.

Besides aforementioned confounding factors, in CS (n = 3160), the use of adjuvant chemotherapy was associated with improved survival. In a multivariable model predicting CS, survival of patients alive at 90 days after resection was significantly better in the ≥40 volume category compared to hospital volumes under 20 procedures per year: HR = 1.30 (95%CI 1.04–1.61) compared to the <5 category and HR = 1.19 (1.04–1.37) compared to the 5–19 category. No significant difference was found compared to the 20–39 hospital volume category: HR = 1.06 (95%CI 0.93–1.22). When using the 20–39 volume category as reference category, significantly better CS was found in this reference category compared to volumes under 20 procedures per year: HR = 1.22 (95%CI 1.01–1.49) compared to the <5 category and HR = 1.12 (1.01–1.25) compared to the 5–19 category.

Discussion

In this nationwide population-based study including over 3400 PDs for primary pancreatic and periampullary carcinoma, an improved postoperative mortality, increased use of adjuvant chemotherapy and higher number of retrieved lymph nodes was observed in centers performing >40 PDs/year, compared to each lower volume category. Significantly favorable OS and CS were found in centers performing 20 or more procedures annually. These results were not confounded by time periods of surgery.

Our findings regarding 90-day mortality are consistent with a recent study using the National Cancer Data Base, in which the unadjusted 90-day mortality rate for PD was 7.4%. Similarly, also in our study 90-day mortality was significantly lower in each higher hospital volume category, up to a category of more than 40 procedures annually.[5] The US study did not report survival outcomes. To our knowledge, this study is the first to examine long-term (survival) volume–outcome relationships including hospitals performing >40 PDs annually. A long-term volume-outcome effect may reflect better quality of surgery (e.g. high percentage R0 resection is associated with lower local recurrence rate), but also better management of late-follow up events (e.g., late postoperative morbidity, disease progression).

Conditional survival reflects the probability of surviving an additional period of time, based on a specific length of time already survived. For patients with pancreatic carcinoma it was previously demonstrated that CS is a better estimator of survival compared to traditional survival estimates.[13] In our study, CS reflects the survival of patients following the initial short-term mortality zone of 90 days and was significantly improved in both volume categories beyond 20 procedures per year compared

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Table 2 Univariable and multivariable logistic regression analyses predicting 90-day postoperative mortality following PD for primary pancreatic or periampullary carcinoma between 2005 and 2013

Characteristics	N (%) 3419[a] (100)	Univariable			Multivariable		
		OR	95%CI	p-value	OR	95%CI	p-value
Hospital volume				0.002			
<5/year	185 (5)	2.41	1.28–4.56		2.59	1.32–5.09	0.006
5–19/year	1432 (42)	2.18	1.39–3.41		2.11	1.32–3.38	0.002
20–39/year	1240 (36)	1.75	1.11–2.78		1.72	1.08–2.74	0.023
≥40/year	562 (16)	1			1	–	
Period of surgery				0.232			
2005–2007	853 (25)	1	–		1	–	
2008–2010	1075 (31)	1.04	0.75–1.44		1.08	0.77–1.52	0.646
2011–2013	1491 (44)	0.82	0.59–1.12		0.93	0.65–1.33	0.695
Gender				0.006			0.006
Male	1929 (56)	1	–		1	–	
Female	1490 (44)	0.69	0.53–0.90		0.69	0.53–0.90	
Age				<0.001			
<65 years	1425 (42)	1	–		1	–	
65–74 years	1385 (41)	2.07	1.51–2.83		2.14	1.56–2.93	<0.001
≥75 years	609 (18)	3.03	2.14–4.31		3.17	2.23–4.52	<0.001
History of cancer				0.921			
No	2872 (84)	1	–				
Yes	547 (16)	1.02	0.72–1.44				
SES				0.378			
High	1026 (30)	1	–				
Medium	1370 (40)	1.071.25	0.78–1.47				
Low	1023 (30)		0.90–1.73				
Location of primary tumor				0.566			
Pancreas	1959 (57)	1	–				
Periampullary	1460 (43)	1.08	0.84–1.39				
Tumor invasion (T)				0.082			
T1–2	1185 (35)	1	–		1	–	
T3–4	2204 (64)	1.07	0.81–1.40		1.12	0.85–1.48	0.422
TX	30 (0.9)	3.24	1.29–8.13		3.47	1.34–8.98	0.010
Lymph node status (N)				0.912			
N0-X	1375 (40)	1	–				
N1	2044 (60)	0.99	0.76–1.28				
Distant metastasis (M)				0.277			
M0-X	3358 (98)	1	–				
M1	61 (1.8)	1.60	0.72–3.55				
Tumor grade				0.150			
Moderate/well diff.	1834 (54)	1	–				
Poor diff.	1041 (30)	1.09	0.82–1.46				
Unknown	544 (16)	1.41	1.00–1.97				

SES, socioeconomic status; Diff, differentiation.
[a] N = 1 lost to follow up due to emigration before 90 days postoperatively.

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Table 3 Univariable and multivariable proportional hazard (Cox) regression analyses predicting overall survival following PD for primary pancreatic or periampullary carcinoma between 2005 and 2013

Characteristics	N 3359	Univariable			Multivariable		
		HR	95%CI	p-value	HR	95%CI	p-value
Hospital volume				0.002			
<5/year	184	1.31	1.08–1.59		1.34	1.09–1.65	0.006
5–19/year	1404	1.23	1.09–1.40		1.24	1.09–1.42	0.002
20–39/year	1222	1.10	0.97–1.26		1.10	0.97–1.26	0.14
≥40/year	549	Ref	–		Ref	–	
Period of surgery				0.320			
2005–2007	843	Ref	–		Ref	–	
2008–2010	1051	0.93	0.84–1.03		1.02	0.92–1.14	0.70
2011–2013	1465	0•94	0.84–1.04		1.03	0.91–1.15	0.68
Gender				0.208			
Male	1898	Ref	–				
Female	1461	0.95	0.87–1.03				
Age				<0.001			
<65 years	1396	Ref	–		Ref	–	
65–74 years	1362	1.17	1.07–1.28		1.16	1.06–1.27	0.001
≥75 years	601	1.35	1.21–1.51		1.31	1.16–1.47	<0.001
History of cancer				0.551			
No	2824	Ref	–				
Yes	535	1.03	0.93–1.16				
SES				0.314			
High	1006	Ref	–				
Medium	1345	1.05	0.95–1.16				
Low	1008	0.98	0.88–1.09				
Location of primary tumor				<0.001			<0.001
Pancreas	1921	Ref	–		Ref	–	
Periampullary	1438	0.55	0.50–0.60		0.60	0.55–0.66	
Tumor invasion (T)				<0.001			
T1–2	1174	Ref	–		Ref	–	
T3–4	2157	1.51	1.38–1.65		1.20	1.09–1.32	<0.001
TX	28	1.32	0.85–2.06		1.60	1.01–2.52	0.04
Lymph node status (N)				<0.001			<0.001
N0-X	1363	Ref	–		Ref	–	
N1	1996	2.11	1.93–2.30		1.92	1.75–2.11	
Tumor grade				<0.001			
Moderate/well diff.	1801	Ref	–		Ref	–	
Poorly diff.	1022	1.53	1.40–1.67		1.52	1.39–1.66	<0.001
Unknown	536	0.94	0.83–1.06		0.99	0.88–1.12	0.90
Chemotherapy				0.78			
No	2399	Ref	–		Ref	–	
Yes	960	0.99	0.90–1.08		0.70	0.66–0.81	<0.001
Radical resection				<0.001			
Yes (R0)	2481	Ref	–		Ref	–	
No	756	2.07	1.89–2.28		1.54	1.49–1.82	<0.001

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Table 3 (*continued*)

Characteristics	N 3359	Univariable			Multivariable		
		HR	95%CI	p-value	HR	95%CI	p-value
Unknown	122	1.80	1.48–2.20		1.26	1.13–1.69	0.002
>10 LN examined				0.67			
No	1621	Ref	–		Ref	–	
Yes	1623	1.031.08	0.95–1.12		0.89	0.81–0.97	0.008
Unknown	115		0.87–1.34		1.09	0.87–1.36	0.46

SES, socioeconomic status; Diff., differentiation. LN, lymph nodes.
Excluding patients with metastatic disease (n = 61).

to lower hospital volumes, and no statistically significant difference was found in volume categories beyond 40 procedures per year compared to a 20–39 hospital volume category. As such, in the present study improved long-term outcomes required a lower threshold than improved short-term outcomes. Long-term outcomes are influenced by more factors than just short-term postoperative complications. Many patients undergoing surgery in high volume hospitals will receive both adjuvant therapy and management of follow-up events in their referring hospitals. Therefore, to provide high-quality care pathways to all patients, centralization of surgical treatment should be accompanied by close collaboration between pancreatic (surgery) centers and referring hospitals.

Patient (SES), tumor and prognostic treatment characteristics differed between hospital volume categories. Although higher volume hospitals resected less patients with TNM Stage I disease, patient SES was higher. Possibly, patients with a higher SES prefer surgery in higher volume, mainly academic centers. Furthermore, with increasing hospital volume, more favorable margin status (R0), number of examined lymph nodes and use of adjuvant chemotherapy were found. More experience with the disease in higher volumes centers might be associated with this finding.[14] However, differences between hospital volumes regarding these important prognostic treatment features did not explain the hospital volume effect in long-term survival.

Increasing capabilities to support patients with postoperative complications may delay some postoperative mortality beyond the 30-day period.[15,16] Hospitals may differ in their capability to timely recognize and adequately manage severe complications after pancreatic surgery ('failure-to-rescue').[17] In a previous study, doubled mortality rates at 90- compared to 30-post-operative days following resection for pancreatic carcinoma were found in all hospital volume categories.[5] In our study, the most favorable 90-day mortality was found in >40 PDs/year centers. There was non-significant improvement in mortality during the study period. However, as was previously demonstrated, during the study period there was an increase in the number of T3 and N1 patients being resected and an increasing age of resected patients.[9,18] Especially elderly patients were at increased risk of postoperative mortality.

Due to an almost doubling of pancreatic resections in the Netherlands within eight years, hospital volumes in our study automatically increased over time ('volume creep').[19] However, a further decrease in the number of hospitals performing pancreatic surgery in most recent years indicates an ongoing centralization of pancreatic surgery in the Netherlands.[4,6,9] Based on the current data a volume-plateau for 90-day mortality and overall survival cannot yet be determined. Furthermore, learning curves of hospitals with still increasing volumes could influence outcomes.

This study has some limitations mainly related to the available data in the NCR-database. First, no comorbidity data were available. Negative impacts of comorbid conditions on outcomes following pancreatic surgery have been described and may differ between hospital volume categories.[16,20,21] Second, a hospital volume classification based on the number of PDs for primary malignancies was used while the actual volume standard in the Netherlands is based on PD for benign and malignant diagnoses. Therefore, volume categories of hospitals might be slightly underestimated. However, the vast majority of PDs are performed for pancreatic malignancy.[7] With ongoing centralization, future registry studies can investigate the association between outcomes of PD and hospital volumes at still higher cut-offs. Based on the current data we cannot determine whether the plateau for 90-day mortality and overall survival has been reached with 40 PDs annually.

Concluding, the volume–outcome relationship for PD persists also in centers who perform $\geq$40 procedures annually, both for lower 90-day mortality rate and overall survival, as compared to lower volume categories. The volume plateau for pancreatic surgery has yet to be determined. Ultimately, research should extend beyond solely hospital volume numbers. Including adequate case-mix correction, surgeon volume, completeness of multidisciplinary care, traveling distances, patient preferences, and other factors all contribute to a more nuanced but complex discussion regarding the volume–outcome relationship in pancreatic surgery.

Financial declarations/Conflicts of interest

None declared.

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References

1. Rahib L, Smith BD, Aizenberg R, Rosenzweig AB, Fleshman JM, Matrisian LM. (2014 Jun 1) Projecting cancer incidence and deaths to 2030: the unexpected burden of thyroid, liver, and pancreas cancers in the United States. *Cancer Res* 74:2913–2921.
2. Birkmeyer JD, Siewers AE, Finlayson EVA, Stukel TA, Lucas FL, Batista I *et al*. (2002 Apr 11) Hospital volume and surgical mortality in the United States. *N Engl J Med* 346:1128–1137.
3. Gooiker GA, van Gijn W, Wouters MWJM, Post PN, van de Velde CJH, Tollenaar RAEM *et al*. (2011 Apr) Systematic review and meta-analysis of the volume-outcome relationship in pancreatic surgery. *Br J Surg* 98: 485–494.
4. van Heek NT, Kuhlmann KFD, Scholten RJ, de Castro SMM, Busch ORC, van Gulik TM *et al*. (2005 Dec) Hospital volume and mortality after pancreatic resection: a systematic review and an evaluation of intervention in the Netherlands. *Ann Surg* 242:781–788. discussion 788–90.
5. Swanson RS, Pezzi CM, Mallin K, Loomis AM, Winchester DP. (2014 Dec) The 90-day mortality after pancreatectomy for cancer is double the 30-day mortality: more than 20,000 resections from the national cancer data base. *Ann Surg Oncol* 21:4059–4067.
6. de Wilde RF, Besselink MGH, van der Tweel I, de Hingh IHJT, van Eijck CHJ, Dejong CHC *et al*. (2012 Mar) Impact of nationwide centralization of pancreaticoduodenectomy on hospital mortality. *Br J Surg* 99:404–410.
7. Gooiker GA, van der Geest LGM, Wouters MWJM, Vonk M, Karsten TM, Tollenaar RAEM *et al*. (2011 Jul) Quality improvement of pancreatic surgery by centralization in the western part of the Netherlands. *Ann Surg Oncol* 18:1821–1829.
8. Lemmens VEPP, Bosscha K, van der Schelling G, Brenninkmeijer S, Coebergh JWW, de Hingh IHJT. (2011 Oct) Improving outcome for patients with pancreatic cancer through centralization. *Br J Surg* 98: 1455–1462.
9. Gooiker GA, Lemmens VEPP, Besselink MG, Busch OR, Bonsing BA, Molenaar IQ *et al*. (2014 Jul) Impact of centralization of pancreatic cancer surgery on resection rates and survival. *Br J Surg* 101:1000–1005.
10. Normering Chirurgische Behandelingen 3.0, Nederlandse Vereniging voor Heelkunde, www.heelkunde.nl.
11. Fritz A, Percy C, Jack A, Shanmugaratnam K, Sobin L, Parkin DM *et al*. (2000) *International Classification of Diseases for Oncology (ICD-O)*. Geneva: World Health Organization.
12. Wittekind C, Greene FL, Hutter RVP, Klimpfinger M, Sobin LH. (2004) *TNM Atlas*. Berlin: Springer-Verlag.
13. Kent TS, Sachs TE, Sanchez N, Vollmer CM, Callery MP. (2011 Dec) Conditional survival in pancreatic cancer: better than expected. *HPB* 13: 876–880.
14. Esposito I, Kleeff J, Bergmann F, Reiser C, Herpel E, Friess H *et al*. (2008 Jun) Most pancreatic cancer resections are R1 resections. *Ann Surg Oncol* 15:1651–1660.
15. van Gestel YRBM, Lemmens VEPP, de Hingh IHJT, Steevens J, Rutten HJT, Nieuwenhuijzen GAP *et al*. (2013 Feb) Influence of co-morbidity and age on 1-, 2-, and 3-month postoperative mortality rates in gastrointestinal cancer patients. *Ann Surg Oncol* 20:371–380.
16. Hyder O, Dodson RM, Nathan H, Schneider EB, Weiss MJ, Cameron JL *et al*. (2013 Dec) Influence of patient, physician, and hospital factors on 30-day readmission following pancreatoduodenectomy in the United States. *JAMA Surg* 148:1095–1102.
17. Tamirisa NP, Parmar AD, Vargas GM, Mehta HB, Kilbane EM, Hall BL *et al*. (2016 Feb) Relative contributions of complications and failure to rescue on mortality in older patients undergoing pancreatectomy. *Ann Surg* 263:385–391.
18. van der Geest LGM, Besselink MGH, van Gestel YRBM, Busch ORC, de Hingh IHJT, de Jong KP *et al*. (2015 Nov 9) Pancreatic cancer surgery in elderly patients: balancing between short-term harm and long-term benefit. A population-based study in the Netherlands. *Acta Oncol*, 1–8. [Epub ahead of print].
19. Finks JF, Osborne NH, Birkmeyer JD. (2011 Jun 2) Trends in hospital volume and operative mortality for high-risk surgery. *N Engl J Med* 364: 2128–2137.
20. Dias-Santos D, Ferrone CR, Zheng H, Lillemoe KD, Castillo CF-D. (2015 May) The Charlson age comorbidity index predicts early mortality after surgery for pancreatic cancer. *Surgery* 157:881–887.
21. Hill JS, Zhou Z, Simons JP, Ng SC, McDade TP, Whalen GF *et al*. (2010 Jul) A simple risk score to predict in-hospital mortality after pancreatic resection for cancer. *Ann Surg Oncol* 17:1802–1807.

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