Ann Surg Oncol
DOI 10.1245/s10434-016-5089-3

Annals of
SURGICAL ONCOLOGY
OFFICIAL JOURNAL OF THE SOCIETY OF SURGICAL ONCOLOGY

ORIGINAL ARTICLE – PANCREATIC TUMORS

Elderly Patients Strongly Benefit from Centralization of Pancreatic Cancer Surgery: A Population-Based Study

Lydia G. M. van der Geest[1], Marc G. H. Besselink, MD, PhD[2], Olivier R. C. Busch, MD, PhD[2], Ignace H. J. T. de Hingh, MD, PhD[3], Casper H. J. van Eijck, MD, PhD[4], Cees H. C. Dejong, MD, PhD[5], and Valery E. P. P. Lemmens, PhD[1,6]

[1]Department of Research, Netherlands Comprehensive Cancer Organisation (IKNL), Utrecht, The Netherlands; [2]Department of Surgery, Amsterdam Medical Center, Amsterdam, The Netherlands; [3]Department of Surgery, Catharina Hospital, Eindhoven, The Netherlands; [4]Department of Surgery, Erasmus University Medical Center, Rotterdam, The Netherlands; [5]Department of Surgery, Maastricht University Medical Center, Maastricht, The Netherlands; [6]Department of Public Health, Erasmus University Medical Center, Rotterdam, The Netherlands

ABSTRACT

Background. Series from expert centers suggest that pancreas cancer surgery is safe for elderly patients but nationwide data, taking hospital volume into account, are lacking.

Methods. From the Netherlands Cancer Registry, all 3420 patients who underwent pancreatoduodenectomy (PD) for primary pancreatic or periampullary carcinoma in 2005–2013 were selected. Associations between age (<75, ≥75 years), hospital volume (tertiles), and postoperative mortality (30, 90 day) were evaluated by χ^2 tests and logistic regression analyses. Overall survival was investigated by means of Kaplan–Meier and Cox proportional hazard regression analyses.

Results. The proportion of elderly patients (≥75 years) undergoing PD increased from 15 % in 2005–2007 to 20 % in 2011–2013 ($p = 0.009$). In low (<15 per year), medium (15–28 per year), and high (>28 per year) hospital volume tertiles, the proportion of elderly patients was 16, 20, and 17 %, respectively ($p = 0.10$). With increasing hospital volume, 30-day postoperative mortality was 6.0–4.5–2.9 % ($p = 0.002$) and 90-day mortality 9.3–8.0–5.3 % ($p = 0.001$), respectively. Within each volume tertile, adjusted 30- and 90-day mortality of elderly patients was 1.6–2.5 times higher compared to outcomes of younger patients. Adjusted 30-day mortality in elderly patients was higher in low-volume hospitals (odds ratio = 2.87, 95 % confidence interval 1.15–7.17) compared to high-volume hospitals. Similarly, elderly patients had a worse overall survival in low-volume hospitals (hazard ratio = 1.28, 95 % confidence interval 1.01–1.63). Postoperative mortality of elderly patients in high-volume hospitals was similar to mortality of younger patients in low- and medium-volume hospitals.

Conclusions. Elderly patients benefit from centralization by undergoing PD in high-volume hospitals, both with respect to postoperative mortality and survival. It would seem reasonable to place elderly patients into a high-risk category; they should only undergo surgery in the highest-tertile-volume hospitals.

At diagnosis, over half of patients with primary pancreatic or periampullary cancer is aged 70 years or older.[1] Although pancreatic resection is the only treatment option with curative intent, only 15–20 % of pancreatic cancer patients are eligible for surgery.[2,3] Pancreatic surgery is regarded as low-volume, high-risk surgery. Many studies have shown a strong and consistent relation between high procedural volumes and favorable postoperative outcomes after pancreatic surgery.[4–6] Hospital volume represents various interdepending structure and process characteristics of hospitals influencing morbidity rates, management of complications, and postoperative mortality.[7] In the past

For the Netherlands Comprehensive Cancer Organisation and the Dutch Pancreatic Cancer Group.

Electronic supplementary material The online version of this article (doi:10.1245/s10434-016-5089-3) contains supplementary material, which is available to authorized users.

First Received: 8 October 2015

L. G. M. van der Geest
e-mail: L.vanderGeest@iknl.nl

Published online: 21 January 2016

decade, after centralization of pancreatic surgery, a decreased postoperative mortality after pancreatic surgery was observed in the Netherlands.[8–10]

Together with improving postoperative mortality, an increased resection rate was observed in elderly pancreatic cancer patients in the United States.[11] Generally, elderly patients experienced worse postoperative outcomes compared to younger patients.[11–13] Because of higher rates of comorbid diseases and a decreased physiologic reserve, elderly patients may experience difficulties to counter complications after major surgery. Several studies showed a more than two times higher postoperative mortality in elderly patients who underwent pancreatic surgery, which is also found in the era of centralization.[10,14] However, little is known about the magnitude of the influence of hospital volumes on surgical outcomes of elderly patients. In addition, it is not known whether the centralization process of pancreatic surgery differs between younger and elderly patients.

Therefore, the purpose of this study was to investigate centralization, hospital volume, and postoperative mortality in elderly patients who underwent pancreatoduodenectomy (PD) for primary pancreatic or periampullary adenocarcinoma in the Netherlands.

METHODS

Data Source

The nationwide Netherlands Cancer Registry (NCR) covers nearly 17 million inhabitants and comprises population-based data on newly diagnosed malignancies. The primary source of notification of the NCR is the automated nationwide pathologic archive (PALGA), supplemented with data from the National Registry of Hospital Discharge Diagnoses. Since 1989, trained registration administrators collected data on patient, tumor, and treatment characteristics from the medical records in all Dutch hospitals. Topography and morphology were coded according to the International Classification of Diseases for Oncology (ICD-O).[15] Tumor stage was based on the tumor, node, metastasis classification system (TNM) that was applicable (6th edition in 2003–2009 and 7th edition thereafter).[16] Follow-up of vital status was obtained by annual linkage with the Municipal Personal Records Database, which contains the information of all Dutch inhabitants (dead or alive, or emigrated).

Patients and Outcome Measures

All patients who underwent PD (pylorus-preserving and Whipple procedures) for primary pancreatic (ICD-O code C25.0–9) or periampullary [located in ampulla of Vater (C24.1), distal extrahepatic bile duct (C24.0) or duodenum (C17.0)] adenocarcinoma in the period 2005–2013 were selected and included in this study.

Patients were divided into two age groups: younger ($<$75 years at time of diagnosis) and elderly ($\geq$75 years) patients. Because of the nature of the NCR, data on prior cancer diagnoses were available. Because information on other comorbid diseases was lacking in the majority of patients, data on socioeconomic status (SES) were used.[17,18] 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 4-digit postal code, and were broken into three SES categories (high, first to third deciles; intermediate, fourth to seventh deciles; low, eighth to 10th deciles). Pathologic tumor stage (TNM) was categorized as stage I, II, III, and IV according to tumor location.

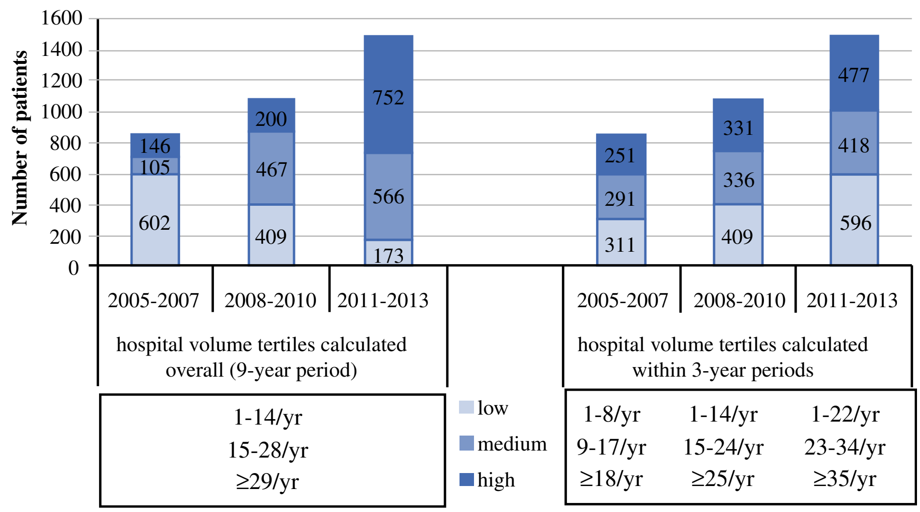
Hospital volumes were defined as the number of PDs that were performed per hospital per year and were broken evenly into volume categories by tertile: low hospital volumes (LHV, $<$15 resections per year), medium hospital volumes (MHV, 15–28 per year), and high hospital volumes (HHV, $>$28 per year), to obtain a similar number of patients in each volume category. In sensitivity analysis, hospital volume tertiles were calculated within 3-year periods of surgery (2005–2007, 2008–2010, 2011–2013, Fig. 1) to reduce the influence of many LHVs in the first time period.

To account for late fatal outcomes of postoperative complications, both 30- and 90-day mortality of any cause after date of resection were calculated.[14] Survival time was defined as the time between date of surgery and date of death. Patients alive as of January 1, 2015, were censored.

Statistical Analysis

To compare categorical characteristics of patients who underwent PD by age and by hospital volume, Pearson's χ^2 tests were used. A p value of $<$0.05 was considered significant. χ^2 tests were also used to compare postoperative outcomes (30 and 90 days) of younger and elderly patients within each hospital volume category. Univariable and multivariable logistic regression analyses were performed to investigate the association of age and hospital volume with postoperative mortality (30 and 90 days) after PD for pancreatic and periampullary carcinoma. Kaplan–Meier and Cox proportional hazard regression analyses were used to evaluate survival. All multivariable models were adjusted for the (possible) influence of year of surgery, sex, prior cancer, SES, and tumor location, stage, and grade. Multivariable Cox models were additionally adjusted for the use of adjuvant chemotherapy. All analyses were repeated with higher cutoff levels for age. Because of low

FIG. 1 Hospital volume tertiles of 3420 patients who underwent pancreatoduodenectomy for primary pancreatic or periampullary adenocarcinoma in 2005–2013 in the Netherlands, calculated in two different ways



numbers of octogenarians ($n = 163$) reducing the statistical power, an intermediate cutoff point at the 90th age percentile was also used (≥78 years, $n = 303$). All analyses were performed by STATA/SE 13.0 (StataCorp, College Station, TX).

RESULTS

Patients

Of all 3420 patients who underwent PD for primary pancreatic or periampullary carcinoma, the proportion of elderly patients (≥75 years, 18 %) increased over time from 15 % in 2005–2007 to 20 % in 2011–2013 ($p = 0.009$). Elderly patients more often had a periampullary carcinoma (46 vs. 42 %, $p = 0.05$) and a prior cancer (25 vs. 14 %, $p < 0.001$) compared to younger patients. In Table 1, patient and tumor characteristics are compared between tertiles of hospital resection volumes. Between hospital volume tertiles, borderline significant age differences were found (≥75 years: 16, 20, and 17 %, $p = 0.10$). However, over time, the strongest increase in the proportion of elderly patients was found at LHV (from 15 % in 2005–2007 to 24 % in 2011–2013, $p = 0.02$; MHV, 17–20 %, $p = 0.72$; HHV, 14–18 %, $p = 0.25$). A similar pattern was found for higher age cutoffs (≥80 years: LHV, 3–8 %, $p = 0.02$; MHV, 5–6 %, $p = 0.37$; HHV, 2–6 %, $p = 0.12$) and for hospital volume tertiles calculated within 3-year periods (≥75 years: LHV, from 14 % in 2005–2007 to 21 % in 2011–2013, $p = 0.009$; MHV, 16–19 %, $p = 0.57$; HHV, 15–19 %, $p = 0.43$). Furthermore, the use of adjuvant chemotherapy in patients with pancreatic carcinoma increased with increasing hospital volumes for both younger (<75 years: 39–47–57 % in LHV–MHV–HHV, $p < 0.001$) and elderly patients (≥75 years: 9–10–19 %, $p = 0.07$; volume tertiles within 3-year periods).

Postoperative Outcomes

Over time, 30-day mortality in elderly patients showed a tendency to decrease, from 10.2 % (13/127) in 2005–2007 to 5.1 % (15/296) in 2011–2013 ($p = 0.15$); in younger patients, a decrease was found, from 4.3 % (31/726) to 3.3 % (40/1195) ($p = 0.31$). At 90 days after surgery, a similar pattern was found in younger (6.9–5.7 %, $p = 0.26$) and elderly patients (15.0–10.8 %, $p = 0.47$).

Overall, HHV showed the most favorable 30-day ($p = 0.002$) and 90-day postoperative mortality rates ($p = 0.001$). As shown in Table 2, within all hospital volume tertiles, mortality was less favorable for elderly patients compared to younger patients. After adjustment for confounding factors, in LHV 30-day postoperative mortality of elderly patients was more than double that of younger patients, while differences in MHV and HHV were less pronounced ($p = 0.10$ and $p = 0.31$, respectively). Adjusted 90-day mortality in elderly patients was significantly increased within each hospital volume tertile (Table 2). Furthermore, in all hospital volume tertiles, elderly patients had a worse overall survival compared to younger patients (Table 3). After supplemental adjustment for adjuvant chemotherapy, the strongest reduction of the hazard ratio (HR) of mortality was found in HHV.

Age and Hospital Volume Combined

Age groups and volume tertiles were combined in each model, taking as the reference group the category elderly patients who underwent PD in HHV (Fig. 2). The adjusted 30-day mortality of elderly patients was worse in

Table 1 Patient, tumor and treatment characteristics of patients who underwent pancreatoduodenectomy (PD) for primary pancreatic or periampullary adenocarcinoma (ampulla of Vater, duodenum and distal bile duct) in 2005–2013 in the Netherlands, by hospital volume tertiles (Low, Medium, High hospital volume (HV))

Characteristic	All patients ($n = 3420$) n (%)	Low volume ($n = 1184$), %	Medium volume ($n = 1138$), %	High volume ($n = 1098$), %	p value
Sex					0.08
Male	1928 (56)	59	55	56	
Female	1491 (44)	41	45	44	
Age					0.10
<75 years	2811 (82)	84	80	83	
≥75 years	609 (18)	16	20	17	
History of cancer					0.14
No	2873 (84)	86	83	84	
Yes	547 (16)	14	17	16	
Socioeconomic status					0.006
High	1026 (30)	29	28	34	
Intermediate	1371 (40)	41	39	40	
Low	1.023 (30)	30	33	27	
Location of primary tumor					0.13
Pancreas	1960 (57)	58	59	55	
Periampulla	1460 (43)	42	41	45	
Tumor stage (TNM)					0.001
I	656 (19)	23	18	16	
II	2313 (68)	63	68	72	
III	367 (11)	11	11	9.8	
IV	61 (1.8)	1.7	1.7	2.0	
X	23 (0.7)	0.8	0.5	0.6	
Tumor grade					<0.001
Moderate/well differentiated	1835 (54)	58	51	51	
Poorly differentiated	1041 (30)	26	31	34	
Unknown	544 (16)	15	18	14	
Adjuvant chemotherapy (pancreas only, % yes)	810 (41)	22	48	56	<0.001

Low hospital volume, <15 resections per year; medium, 15–28 resections per year; and high, >28 per year

TNM tumor, node, metastasis classification system

LHV compared to HHV [odds ratio (OR) 2.87, 95 % confidence interval (CI) 1.15–7.17]. Ninety days after surgery, younger patients in HHV had a lower adjusted mortality (OR 0.46, 95 % CI 0.26–0.84) compared to elderly patients at HHV, but no significant difference was found between elderly patients in LHV and HHV ($p = 0.16$). Although elderly patients treated in HHV showed a better overall survival compared to elderly patients in LHV (HR 1.28, 95 % CI 1.01–1.63), they had a worse survival compared to younger patients in HHV (HR 0.77, 95 % CI 0.63–0.94) (Fig. 2). In a second regression model including adjuvant chemotherapy, the worse survival of elderly patients in LHV persisted (HR 1.29, 95 % CI 1.02–1.64). Postoperative mortality and overall survival of elderly patients at HHV did not differ statistically from outcomes of younger patients at LHV and MHV ($p \geq 0.16$). In sensitivity analyses, with hospital volume tertiles calculated within 3-year periods, a similar pattern was found (Supplementary Table 1 and Supplementary Fig. 1). Also, an age cutoff point at the 90th percentile (9 % of patients) showed a worse postoperative mortality and overall survival for elderly patients at LHV compared to elderly patients at HHV [30 days: OR (≥78 years in LHV vs. ≥78 years in HHV) = 2.29, 95 % CI 1.53–34.59; 90 days: OR = 2.93, 95 % CI 1.11–7.75; overall survival: HR = 1.43, 95 % CI 1.00–2.03]. Comparisons of other age–volume combinations with elderly patients in HHV did not reach statistical significance. Analyses of octogenarians compared to younger patients showed similar results.

TABLE 2 Univariable and multivariable logistic regression analyses predicting 30- and 90-day postoperative mortality of patients who underwent PD for primary adenocarcinoma, by age of patients within each hospital volume tertile

				Univariable analysis			Multivariable analysis		
	n	Proportion	*p*	OR	95 % CI	*p*	OR	95 % CI	*p*
30-day mortality									
Low HV	1184	6.0							
Age < 75 years	989	5.2	0.006	1	–	0.007	1	–	0.007
Age ≥ 75 years	195	10.3		2.10	1.22–3.61		2.13	1.23–3.70	
Medium HV	1138	4.5							
Age < 75 years	913	3.9	0.08	1	–	0.08	1	–	0.10
Age ≥ 75 years	225	6.7		1.74	0.94–3.24		1.72	0.91–3.25	
High HV	1098	2.9							
Age < 75 years	909	2.8	0.48	1	–	0.48	1	–	0.31
Age ≥ 75 years	189	3.7		1.36	0.58–3.19		1.59	0.65–3.88	
90-day mortality									
Low HV	1184	9.3							
Age < 75 years	989	8.4	0.02	1	–	0.02	1	–	0.01
Age ≥ 75 years	195	13.9		1.75	1.10–2.79		1.81	1.13–2.91	
Medium HV	1138	8.0							
Age < 75 years	913	6.6	<0.001	1	–	<0.001	1	–	0.001
Age ≥ 75 years	225	13.8		2.27	1.43–3.60		2.28	1.42–3.65	
High HV	1097	5.3							
Age < 75 years	908	4.5	0.01	1	–	0.008	1	–	0.004
Age ≥ 75 years	189	9.0		2.05	1.20–3.50		2.46	1.32–4.59	

HV hospital volume, <15 resections per year; medium, 15–28 resections per year; and high, >28 per year; *p* value by χ^2 test, *n* number of patients

OR odds ratio, *CI* confidence interval

TABLE 3 Univariable and multivariable Cox proportional hazard analyses predicting overall survival of patients who underwent PD for primary adenocarcinoma, by age of patients within each hospital volume tertile

Hospital volume and patient age	Univariable analysis		Multivariable analysis		Multivariable analysis + adjuvant chemotherapy	
	HR (95 % CI)	*p*	HR (95 % CI)	*p*	HR (95 % CI)	*p*
Low HV						
≥75 versus <75 years	1.29 (1.09–1.52)	0.004	1.27 (1.07–1.51)	0.006	1.21 (1.02–1.44)	0.03
Medium HV						
≥75 versus <75 years	1.24 (1.04–1.47)	0.02	1.45 (1.21–1.73)	<0.001	1.31 (1.09–1.57)	0.004
High HV						
≥75 versus <75 years	1.24 (1.01–1.51)	0.04	1.32 (1.08–1.61)	0.007	1.16 (0.94–1.43)	0.17

HV hospital volume, <15 resections per year; medium, 15–28 resections per year; and high, >28 per year

HR hazard ratio, *CI* confidence interval

DISCUSSION

This nationwide study of 3420 patients who underwent PD for primary pancreatic or periampullary carcinoma in the Netherlands found lower 30- and 90-day mortality in elderly patients treated at HHV compared to lower hospital volumes. Within each hospital volume tertile, postoperative mortality of elderly patients was 1.6–2.5 times higher compared to younger patients. Mortality rates of elderly patients in high-volume hospitals equaled mortality rates of younger patients in low- and medium-volume hospitals, while mortality rates of elderly patients in low-volume hospitals were worse.

In earlier reports from the Netherlands based on data until 2009, centralization of pancreatic surgery was observed, but no change was found in the age

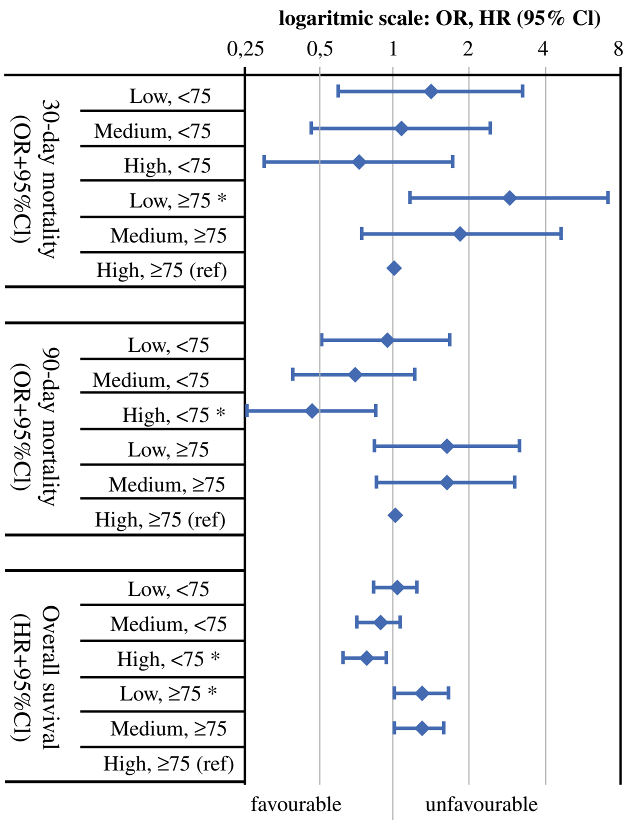


FIG. 2 Multivariable analyses predicting postoperative 30- and 90-day mortality and overall survival of 3420 patients who underwent pancreatoduodenectomy for primary adenocarcinoma by age of patients (<75 years, ≥75 years) and hospital volume tertiles (low, medium, high) combined; $*p < 0.05$. *OR* odds ratio, *HR* hazard ratio, *CI* confidence interval, *Ref* reference category

distribution of patients undergoing resection.[10,19] With ongoing centralization (the number of hospitals performing PDs decreased from 42 in 2005 to 21 of 91 hospitals in 2013), our study showed that the age of patients undergoing PD increased, especially from 2011 onward. The 2011 Dutch evidence-based guideline on pancreatic and periampullary carcinoma state that advanced age by itself should not be a contraindication for pancreatic surgery.[20] Also in 2011, the Dutch Healthcare Inspectorate (IGZ) and Dutch Society for Surgery (NVvH) set a minimum hospital volume standard for pancreatic surgery (benign and malignant) at 20 PD procedures per year.[21] In our study, over time, a steeper increase of the age of patients who underwent PD for cancer was found in low-volume hospitals. This finding suggests that treatment guidelines and volume standards have stimulated pancreatic surgery in the elderly, especially in low-volume hospitals. One may speculate that low-volume hospitals may have had more trouble attaining the national volume standard for pancreatic surgery, while high-volume hospitals may have room to select fit elderly patients. On the other hand, patients who seek care at low-volume hospitals may be older compared to patients seeking care at high-volume (university) hospitals. In recent years, an increasing proportion of this reservoir of eligible elderly patients in low-volume hospitals may have been offered pancreatic surgery.

We also found that patients who underwent pancreatic resection in high-volume hospitals more often had a high SES. In studies on treatment decision making, especially elderly and low-educated patients seem less likely to take active roles in the treatment decision-making process.[22] Elderly or low-SES patients may hesitate to leave "their" nearby hospital with doctors who know their comorbid diseases well, or they may prefer the nearest hospital because of the short travel distance.[23] Also, referral patterns may already differ by age or SES at the level of general practitioners before the first hospital visit. With ongoing centralization of pancreatic surgery, a better understanding is needed of factors influencing referral and treatment decision making in elderly patients.[22] The centralization process should not stimulate referral of only younger patients to hospitals with higher volumes.

Despite the rising age of patients who underwent PD, a slight decrease of postoperative mortality was found during our study period. Older age and the presence of comorbid diseases are important risk factors for early postoperative mortality.[12,24] In several studies a (more than) doubled postoperative mortality was found in elderly patients who underwent pancreatic surgery.[10,14] Mortality differences between hospital volume tertiles in our study may be the result of differences in the incidence of complications and the ability to manage them (failure to rescue).[7] Generally, morbidity rates were high after pancreatic surgery.[25,26] In studies that differentiated between surgical and nonsurgical complications, age differences were particularly found with respect to nonsurgical complications.[13,25,27] In our study, age differences in nonsurgical complications and failure-to-rescue rate may have contributed to the strong additive relation of age and hospital volume concerning postoperative mortality. Furthermore, the mortality difference between elderly and younger patients seemed to increase slightly between 30 and 90 days after surgery, especially in medium- and high-volume hospitals. These results suggest that in medium- and high-volume hospitals, a better ability to manage postoperative complications may have delayed some mortality beyond the 30-day period. Despite a possible delayed mortality, 90-day postoperative mortality of elderly patients in high-volume hospitals in our study remained similar to that of younger patients in low- and medium-volume hospitals. Therefore, elderly patients may benefit from undergoing pancreatic surgery in high-volume hospitals.

Overall, chemotherapy use after resection for pancreatic carcinoma was low in the Netherlands (41 %). Adjuvant chemotherapy after resection of pancreatic carcinoma is now considered the standard of care.[20,28,29] Elderly patients and patients in low-volume hospitals in our study were less likely to receive adjuvant chemotherapy. Adjustment for variation of chemotherapy only slightly explained the decreased survival of elderly patients in low-volume hospitals. In these hospitals, other factors like postoperative complications may have contributed to both postoperative mortality and the omission of adjuvant chemotherapy.[24]

The Netherlands is characterized by good access to health care facilities as a result of its well-organized health insurance. After diagnosis of pancreatic cancer, physicians should inform elderly patients about volume–outcome patterns in pancreatic surgery. Furthermore, when discussing minimum volumes of pancreatic surgery, special attention should be paid to the elderly and potentially other high-risk groups, such as patients with premalignant or extensive disease. These patients may be regarded as comprising specific high-risk categories; they should be operated on only in the highest tertile volume hospitals. In this way, high-risk patients are provided with similar operative risks as low-risk patients such as younger patients.

Our study has some major limitations, especially the lack of detailed data on the health status of patients. Adjustment for number and type of comorbid diseases may limit the magnitude of mortality differences between younger and elderly patients after PD surgery.[12] However, available data on SES and a prior diagnosis of cancer that were included in the multivariable models hardly influenced the association of age with postoperative outcomes after PD. SES may have little (additional) impact because patients who were offered high-risk pancreatic surgery will be relatively fit. Furthermore, comorbidity information had only limited impact on survival in cancers with poor prognosis like pancreatic cancer.[30] Second, in the NCR, no data were available on surgical and nonsurgical postoperative complications after PD. In 2013, the Dutch Pancreatic Cancer Audit (DPCA) was launched, and in the future, this will provide more extensive case mix correction and investigation of postoperative complications.[31]

CONCLUSIONS

Over time, the age of patients undergoing PD for primary pancreatic or periampullary adenocarcinoma increased. In low-volume hospitals, this increase was slightly more pronounced compared to medium- and high-volume hospitals. A better understanding is needed of the dynamics of centralization and factors influencing referral and treatment decision making in elderly patients. Furthermore, both older age and lower hospital volume were independently and strongly related to increased postoperative mortality after PD for primary adenocarcinoma (additive effect). To improve postoperative mortality and overall survival, elderly patients should undergo pancreatic surgery in hospitals with low baseline risks, i.e., the highest volume tertile facility. In this way, these patients are offered an operative risk comparable to that of younger patients.

DISCLOSURE The authors declare no conflict of interest.

REFERENCES

1. Netherlands Cancer Registry (NCR): Dutch cancer figures (2013) http://www.cijfersoverkanker.nl/. Accessed 13 April 2015.
2. Abraham A, Al-Refaie WB, Parsons HM, Dudeja V, Vickers SM, Habermann EB. Disparities in pancreas cancer care. *Ann Surg Oncol.* 2013;20:2078–87.
3. Bilimoria KY, Bentrem DJ, Ko CY, et al. Validation of the 6th edition AJCC pancreatic cancer staging system: report from the National Cancer Data Base. *Cancer.* 2007;110:738–44.
4. Birkmeyer JD, Siewers AE, Finlayson EV, et al. Hospital volume and surgical mortality in the United States. *N Engl J Med.* 2002;346:1128–37.
5. Gooiker GA, van Gijn W, Wouters MW, et al. Systematic review and meta-analysis of the volume–outcome relationship in pancreatic surgery. *Br J Surg.* 2011;98:485–94.
6. van Heek NT, Kuhlmann KF, Scholten RJ, et al. Hospital volume and mortality after pancreatic resection: a systematic review and an evaluation of intervention in the Netherlands. *Ann Surg.* 2005;242:781–8.
7. Birkmeyer JD, Dimick JB. Understanding and reducing variation in surgical mortality. *Annu Rev Med.* 2009;60:405–15.
8. Gooiker GA, van der Geest LG, Wouters MW, et al. Quality improvement of pancreatic surgery by centralization in the western part of the Netherlands. *Ann Surg Oncol.* 2011;18:1821–9.
9. Lemmens VE, Bosscha K, van der Schelling G, Brenninkmeijer S, Coebergh JW, de Hingh IH. Improving outcome for patients with pancreatic cancer through centralization. *Br J Surg.* 2011;98:1455–62.
10. de Wilde RF, Besselink MG, van der Tweel I, et al. Impact of nationwide centralization of pancreaticoduodenectomy on hospital mortality. *Br J Surg.* 2012;99:404–10.
11. Riall TS, Sheffield KM, Kuo YF, Townsend CM Jr, Goodwin JS. Resection benefits older adults with locoregional pancreatic cancer despite greater short-term morbidity and mortality. *J Am Geriatr Soc.* 2011;59:647–54.
12. van Gestel YR, Lemmens VE, de Hingh IH, et al. Influence of comorbidity and age on 1-, 2-, and 3-month postoperative mortality rates in gastrointestinal cancer patients. *Ann Surg Oncol.* 2013;20:371–80.
13. Sukharamwala P, Thoens J, Szuchmacher M, Smith J, DeVito P. Advanced age is a risk factor for post-operative complications and mortality after a pancreaticoduodenectomy: a meta-analysis and systematic review. *HPB (Oxford).* 2012;14:649–57.

14. Swanson RS, Pezzi CM, Mallin K, Loomis AM, Winchester DP. 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.* 2014, 21(3):4059–67.
15. Fritz A, Percy C, Jack A, et al. International classification of diseases for oncology (ICD-O). 3rd ed. Geneva: World Health Organization; 2000.
16. Wittekind C, Greene FL, Hutter RVP, Klimpfinger M, Sobin LH. TNM atlas. Berlin: Springer-Verlag; 2004.
17. Louwman WJ, Aarts MJ, Houterman S, van Lenthe FJ, Coebergh JW, Janssen-Heijnen ML. A 50 % higher prevalence of life-shortening chronic conditions among cancer patients with low socioeconomic status. *Br J Cancer.* 2010;103:1742–8.
18. Reames BN, Birkmeyer NJ, Dimick JB, Ghaferi AA. Socioeconomic disparities in mortality after cancer surgery: failure to rescue. *JAMA Surg.* 2014;149:475–81.
19. Gooiker GA, Lemmens VE, Besselink MG, et al. Impact of centralization of pancreatic cancer surgery on resection rates and survival. *Br J Surg.* 2014;101:1000–5.
20. Netherlands Comprehensive Cancer Organisation (IKNL). National evidence-based guideline for pancreatic carcinoma. 2011. http://www.oncoline.nl/. Accessed 13 Apr 2015.
21. Dutch Society for Surgery (NVvH). Normering Chirurgische Behandelingen [Standards for surgical treatment]. 2011. http://www.heelkunde.nl/nvvh. Accessed Dec 10, 2014.
22. Tariman JD, Berry DL, Cochrane B, Doorenbos A, Schepp KG. Physician, patient, and contextual factors affecting treatment decisions in older adults with cancer and models of decision making: a literature review. *Oncol Nurs Forum.* 2012;39:E70–83.
23. Stitzenberg KB, Sigurdson ER, Egleston BL, Starkey RB, Meropol NJ. Centralization of cancer surgery: implications for patient access to optimal care. *J Clin Oncol.* 2009;27:4671–8.
24. Mayo SC, Gilson MM, Herman JM, et al. Management of patients with pancreatic adenocarcinoma: national trends in patient selection, operative management, and use of adjuvant therapy. *J Am Coll Surg.* 2012;214:33–45.
25. Belyaev O, Herzog T, Kaya G, et al. Pancreatic surgery in the very old: face to face with a challenge of the near future. *World J Surg.* 2013;37:1013–20.
26. Turrini O, Paye F, Bachellier P, et al. Pancreatectomy for adenocarcinoma in elderly patients: postoperative outcomes and long term results: a study of the French Surgical Association. *Eur J Surg Oncol.* 2013;39:171–8.
27. Lee DY, Schwartz JA, Wexelman B, Kirchoff D, Yang KC, Attiyeh F. Outcomes of pancreaticoduodenectomy for pancreatic malignancy in octogenarians: an American College of Surgeons National Surgical Quality Improvement Program analysis. *Am J Surg.* 2014;207:540–8.
28. Oettle H, Neuhaus P, Hochhaus A, et al. Adjuvant chemotherapy with gemcitabine and long-term outcomes among patients with resected pancreatic cancer: the CONKO-001 randomized trial. *JAMA.* 2013;310:1473–81.
29. Neoptolemos JP, Stocken DD, Bassi C, et al. Adjuvant chemotherapy with fluorouracil plus folinic acid vs gemcitabine following pancreatic cancer resection: a randomized controlled trial. *JAMA.* 2010;304:1073–81.
30. Read WL, Tierney RM, Page NC, et al. Differential prognostic impact of comorbidity. *J Clin Oncol.* 2004;22:3099–103.
31. Dutch Pancreatic Cancer Group (DPCG). Dutch pancreatic cancer audit. 2011. http://dpca.clinicalaudit.nl. Accessed 13 Apr 2015.