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Outcome of surgical treatment of pancreatic, peri-ampullary and ampullary cancer diagnosed in the south of The Netherlands: A cancer registry based study

F.J. van Oost[a,*], E.J.T. Luiten[b], L.V. van de Poll-Franse[a], J.W.W. Coebergh[a,c], A.J.M. van den Eijnden-van Raaij[a]

[a]*Comprehensive Cancer Centre South (IKZ), P.O. Box 231, 5600 AE Eindhoven, The Netherlands*
[b]*Department of Surgery, St Anna Hospital, Geldrop, The Netherlands*
[c]*Department of Public Health, Erasmus University Medical Centre, Rotterdam, The Netherlands*

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Abstract

Aims: To gain insight into the quality of pancreatic cancer surgery in 10 low-volume (median sized) hospitals, each serving 150,000–250,000 people, in the Comprehensive Cancer Centre South (CCCS) area and of referred patients to academic centres to determine the need for further regionalization.

Method: The population-based Eindhoven Cancer Registry was used to select all patients in the CCCS area with pancreatic, peri-ampullary and ampullary cancer diagnosed between January 1, 1995 and April 30, 2000 ($N=1130$). Of those, 124 patients (11%) underwent surgical resection (of which 40 were treated in university hospitals outside the region).

Results: For all pancreatic carcinoma resections, the 3-month survival rate was 82%, varying from 95% for referred patients to 76% for patients treated within the region ($p=0.014$). One- and two-year survival rates showed no difference between both groups ($p=0.36$ and $p=0.55$, respectively). Surgically treated patients who were referred to university hospitals outside the CCCS area were younger, more often male, more often diagnosed with pTNM stage III, exhibited less comorbidity and had a higher socio-economic status than patients surgically treated within the region.

Conclusion: Although the results are based on small numbers and patient selection probably influenced these outcomes, these data seem to support further hospital specialisation, to which the surgeons of the CCCS area have committed themselves.

Keywords: Pancreatic cancer; Surgery; Hospital volume; Mortality; Regionalization

Introduction

There are approximately 200 new patients per year in the southern part of The Netherlands, with an incidence of pancreatic and distal choledochal duct tumours of about 10 per 100,000 persons a year (in total almost 1800 new patients per year in The Netherlands[1]). Per hospital location approximately 10–15 new patients per year are diagnosed with carcinoma of the pancreas.[2] A Dutch study showed that less than five radical resections took place annually in most community hospitals.[3] Many studies find that 'volume' has a favourable influence on peri-operative mortality.[3–8] During the early 1990s this peri-operative mortality was reported to be 1.5% for patients in high-volume centres (≥ 25 resections/year) in The Netherlands in contrast to 16% for low-volume hospitals (<5 resections/year).[3] However, patient selection (on the basis of age, tumour stage, subsite, comorbidity and functional status) also tends to affect the outcome of many observational studies.[3,5,8–10]

The aim of this project was to review the extent and quality of surgical management of pancreatic cancer in 10 general hospitals in the Comprehensive Cancer Centre South (CCCS) area (where no university hospital is present and no official referral centre had been appointed), in order to determine the need for regionalization.

* Corresponding author. Tel.: +31 40 2971616; fax: +31 40 2971610.

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Patients and methods

Patients

The database of the population-based Eindhoven Cancer Registry was used to select all patients diagnosed between January 1, 1995, and April 30, 2000, with an invasive carcinoma of the pancreas, the peri-ampullary region (including Vater's ampulla) or the extrahepatic choledochal ducts (excluding Klatskin tumours). If cancer of the extrahepatic choledochal duct was not localized in the distal choledochal duct, the patient was excluded from the study. These tumours will subsequently be referred to as 'pancreatic cancer'. Moreover, only patients were selected who were initially diagnosed in a hospital in the CCCS area ($N=1130$). Patients who underwent a curative resection are further referred to as 'surgically treated' patients ($N=124$); patients who did not undergo a curative resection are further referred to as 'not surgically treated' patients. Due to merging, during the study period the number of hospitals in this area decreased from 17 to 10 (still at 17 locations) each serving 150,000–250,000 people. The sizes of these hospitals ranged from 425 hospital beds to 1370 and the number of gastrointestinal oncological surgeons ranged from 2 to 6. No university hospital is present and at the time of this study no official referral centre was appointed.

Surgical treatment and covariates

The four types of resections registered were (1) pylorus-preserving pancreaticoduodenectomy (PPPD), (2) 'classical' Whipple's resection, (3) total pancreatectomy and (4) pancreas tail resection. Information on referred patients was obtained from academic centres and other Cancer Registries.

In the analyses, patients were divided into age categories '<60 years', '60–69 years' and '≥ 70 years'. Carcinomas were separated into the groups 'peri-ampullary' and 'other', because peri-ampullary tumours, like carcinomas of Vater's ampulla, have a better prognosis than other pancreatic tumours.[2] Carcinomas that were localized partly in the peri-ampullary region and partly in the pancreatic head or the distal choledochal duct were classified as 'peri-ampullary'. Socio-economic status was estimated on the basis of the postal code, using an indicator developed by Statistics Netherlands.[11] This indicator takes into account the mean values of the homes and the mean incomes of households at a specific postal code. The influence of type of comorbidity and peroperative and post-operative complications on in-patient mortality was also studied. Comorbidity is registered since 1993 by the Eindhoven Cancer Registry according to an adapted version of the Charlson classification scheme.[12,13]

Statistics

The Wilcoxon-test and Chi-square or Fisher's exact test were used to detect differences between patient groups. Two-sided p-values <0.05 were regarded as statistically significant. To study risk indicators of in-patient mortality, logistic regression analyses were used with adjustment for age. In-patient mortality was defined as dying before discharge to the patients own home, a nursing home or rehabilitation centre. No information was available on in-patient mortality for most patients who were referred to university clinics. Crude survival was analysed with the life-table method using the log-rank test to report p-values. Active follow-up of cancer patients by the Eindhoven Cancer Registry consists of systematic checks on survival through hospitals, community registries and the Central Genealogical Office. Follow-up was complete as of January 1, 2004. Data were analysed by means of SAS (version 8.02, SAS Institute Inc., Cary, North Carolina, USA).

Results

Between January 1, 1995, and April 30, 2000, 1130 patients were diagnosed with pancreatic cancer in the CCCS area. Of 124 patients (11%) who underwent surgical resection, 40 were treated in university hospitals outside the region. Two other patients were excluded from the analyses (medical records could not be found/tumour origin unclear). The remaining 82 patients underwent surgical resection in a hospital in the CCCS area.

Patient characteristics

Surgically treated patients (including referred patients) were generally younger and more often had peri-ampullary carcinomas (Table 1). Surgically treated patients who were referred to university hospitals outside the CCCS area were younger, more often male, more often diagnosed with pTNM stage III, exhibited less comorbidity and had a higher socio-economic status than patients surgically treated within the region.

Diagnosis and resections

The diagnosis of pancreatic cancer and/or the indication for exploratory laparotomy was based on computer tomography (CT), endoscopic retrograde cholangiopancreaticography (ERCP), ultrasound and/or pathological examination in approximately two-thirds of the patients surgically treated in the CCCS area. Gastroduodenoscopy was the diagnostic procedure most often used after these techniques.

In eight of 10 hospitals pancreatic carcinoma resections were performed (range: 5–17 per hospital). Two patients were referred for resection within the region and the 40

Table 1
Patient characteristics before and after surgical resection

	Treatment		
	No surgery ($n=1006$)	Surgery; CCCS[a] area ($n=82$)	Surgery; university hospitals ($n=40$)
Mean age (range)	69 (29–94)	64 (41–78)	60 (42–76)
Gender			
Male	503	43	27
Female	502	39	13
pTNM-stage			
I	–	27	4
II	–	16	1
III	–	30	27
IV	–	5	4
Unknown	–	4	1
Tumour localisation			
Peri-ampullary	31	29	14
Pancreatic head	580	41	16
Distal choledochal duct[b]	121	6	5
Distal pancreas	134	5	4
Pancreas not specified	140	1	1
Comorbidity[c]			
None	316	29	18
1	297	26	8
2	168	10	3
≥ 3	100	5	0
Cardiovascular diseases	348	26	5
Diabetes mellitus	180	12	1
Pulmonary diseases	94	6	1
Gastro-intestinal diseases	75	5	1
Socio-economic status[d]			
Low	325	30	8
Moderate	341	32	9
High	230	18	12
Peroperative complications	–	8	Not available
Postoperative complications[e]	–	59	Not available
Re-interventions	–	31	Not available
In-patient mortality	–	20	Not available

[a] CCCS, Comprehensive Cancer Centre South.
[b] For not surgically treated patients: all invasive tumours of the extrahepatic bile ducts, except Klatskin tumours.
[c] Excluding 'comorbidity unknown' (no surgical treatment, $n=125$; surgical treatment in Comprehensive Cancer Centre South area, $n=12$; surgical treatment in university hospitals, $n=11$).
[d] Excluding 'unknown' (no surgical treatment, $n=32$; surgical treatment in university hospitals, $n=8$).
[e] Accumulation of abdominal fluid ($n=29$); gastro-intestinal event ($n=26$); pulmonary failure ($n=17$); haemorrhage ($n=10$); cardiac event ($n=9$); renal failure ($n=6$); wound infection ($n=5$); fustula ($n=4$); pancreatitis ($n=4$).

referred patients came from eight hospitals (range: 2–9 per hospital).

Eight of the 82 resections in the CCCS area were accompanied by peroperative complications, which involved a haemorrhage in six cases. Post-operatively, 59 patients suffered complications, mostly accumulation of abdominal fluid ($n=29$) and gastro-intestinal problems ($n=26$), less often cardiac events ($n=9$) or pancreatitis ($n=4$), leading to one or more re-interventions in 31 cases.

In-patient mortality and survival

Patients surgically treated within the region exhibited an in-patient mortality rate which increased with age (<60: 13%; 60–69: 24%; ≥ 70: 34%). The in-patient mortality rate was affected by occurrence of peroperative complications (50%), post-operative accumulation of abdominal fluid (52%) and cardiac events (89%) and/or pancreatitis (75%). Gender, presence of comorbidity, tumour localisation and pTNM-stage showed no clear relationship with in-patient mortality (data not shown).

Among patients surgically treated in the CCCS area the 2-year survival rate was 56% for patients with a peri-ampullary carcinoma and 24% for patients with other tumour localisations (Fig. 1). The 1-year survival rate for all patients surgically treated in the Comprehensive Cancer Centre South area (including in-patient mortality) was 55% in comparison to 13% for not surgically treated patients.

The 3-month survival rate for all surgically treated patients was 82% and this varied from 95% for patients

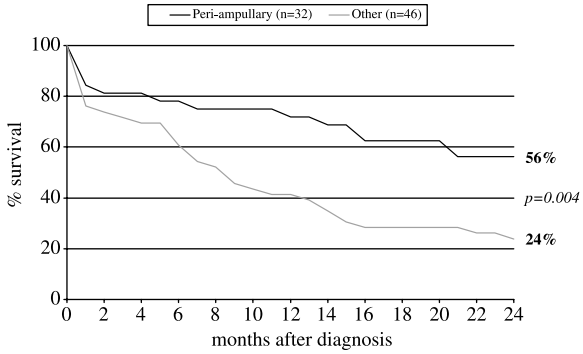

Figure 1. Overall survival (including in-patient mortality) of patients treated surgically within the Comprehensive Cancer Centre South area according to tumour localisation.

referred to university hospitals outside the CCCS area to 76% for patients surgically treated within the region. One- and two-year survival rates showed no difference between both groups (Fig. 2).

Discussion

The 3-month survival rate after a pancreatic carcinoma resection was 95% for patients referred to university hospitals outside the CCCS area and 76% for patients treated within the region (performed in eight so-called 'low-volume' hospitals: less then five resections a year). Although these results are based on small numbers and patient selection probably influenced these outcomes, these data seem to support further hospital specialisation. Nevertheless, 1- and 2-year survival rates showed no significant difference between both groups.

Patients with a peri-ampullary carcinoma were more often surgically treated. Furthermore, surgically treated patients were younger, and this was even more true for referred patients, who also had less comorbidity and were of a higher socio-economic status than patients surgically treated in the CCCS area. Another study in our area[14] revealed that those with a lower educational level were less likely to visit specialists. It is, therefore, possible that patient selection had taken place, either upon referral, but also due to application of strict selection criteria for the health status of patients and better staging in university hospitals. Unfortunately, we do not have information about the number of patients who have been turned down by the specialist centres for medical or logistical reasons.

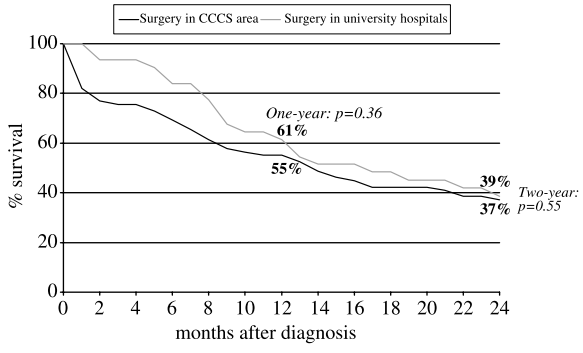

Figure 2. Overall 2-year survival (including in-patient mortality) of patients treated surgically within the Comprehensive Cancer Centre South (CCCS) area and in university hospitals.

In the CCCS area approximately 20–25 patients with pancreatic cancer would annually qualify for tumour resection (including referred patients). Because of these small numbers, potentially important differences between patients and hospitals could hardly be observed. Peroperative and post-operative complications were registered retrospectively based on information in the medical records at the Departments of Internal Medicine and Surgery. In a prospective study clearly defined rules for the registration of complications could be established,[15] whereas the registration of complications in the current study depended upon the probably imperfect reporting of complications.

The current study showed that age and type of post-operative complication affected in-patient mortality. The literature also indicates that age is an important risk indicator for in-patient mortality.[3,5,8,9,16] The presence of comorbidity in general and the number of comorbid conditions seemed to have little influence on in-patient mortality. Tumour localisation (peri-ampullary vs other) clearly affected 2-year survival.

Approximately, half of all patients in The Netherlands who underwent a pancreatic cancer resection during the early 1990s were treated in low-volume hospitals[3] similar to those in the CCCS area. Several studies have shown better outcomes of high-risk surgical procedures in specialized high-volume centres compared with medium and low-volume hospitals.[6–8,16,17] As in this study, patients in high-volume centres were most often younger, had a lower comorbidity index score and a higher socio-economic status than patients in low-volume hospitals.[6,7,16] However, differences in case-mix could not fully explain the variation in peri-operative mortality between high-volume and medium/low-volume hospitals.[6–8,16]

Although referral of patients to high volume centres seems obvious, delay of necessary surgical treatment may occur in these centres due to waiting lists and prevailing of acute surgical patients. The shown variation has led the surgeons in the south of The Netherlands to further regionalize surgical management for pancreatic cancer.

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References

1. Visser O, Coebergh JWW, Van Dijck JAAM, Siesling S, editors. *Incidence of cancer in The Netherlands 1998*. Utrecht: Association of Comprehensive Cancer Centres; 2002.
2. Coebergh JWW, Janssen-Heijnen MLG, Louwman WJ, Voogd AC, editors. *Cancer incidence, care and survival in the south of The Netherlands, 1955–1999: a report from the Eindhoven Cancer Registry (IKZ) with cross-border implications*. Eindhoven: Comprehensive Cancer Centre South (IKZ); 2001.
3. Gouma DJ, De Wit LT, Van Berge Henegouwen MI, Van Gulik TH, Obertop H. Hospital experience and hospital mortality following partial pancreaticoduodenectomy in The Netherlands. *Ned Tijdschr Geneeskd* 1997;**141**:1738–41.
4. Birkmeyer JD, Finlayson SR, Tosteson AN, Sharp SM, Warshaw AL, Fisher ES. Effect of hospital volume on in-hospital mortality with pancreaticoduodenectomy. *Surgery* 1999;**125**:250–6.
5. Lieberman MD, Kilburn H, Lindsey M, Brennan MF. Relation of perioperative deaths to hospital volume among patients undergoing pancreatic resection for malignancy. *Ann Surg* 1995;**222**:638–45.
6. Sosa JA, Bowman HM, Gordon TA, Bass EB, Yeo CJ, Lillemoe KD, et al. Importance of hospital volume in the overall management of pancreatic cancer. *Ann Surg* 1998;**228**:429–38.
7. Gordon TA, Bowman HM, Bass EB, Lillemoe KD, Yeo CJ, Heitmiller RF, et al. Complex gastrointestinal surgery: impact of provider experience on clinical and economic outcomes. *J Am Coll Surg* 1999;**189**:46–56.
8. Glasgow RE, Mulvihill SJ. Hospital volume influences outcome in patients undergoing pancreatic resection for cancer. *West J Med* 1996; **165**:294–300.
9. Bachmann MO, Alderson D, Peters TJ, Bedford C, Edwards D, Wotton S, et al. Influence of specialization on the management and outcome of patients with pancreatic cancer. *Br J Surg* 2003;**90**:171–7.
10. Bakkevold KE, Kambestad B. Morbidity and mortality after radical and palliative pancreatic cancer surgery. Risk factors influencing the short-term results. *Ann Surg* 1993;**217**:356–68.
11. van Duijn C, Keij I. *Sociaal-economische status indicator op postcode niveau*. Heerlen/Voorburg: CBS; 2002.
12. Coebergh JW, Janssen-Heijnen ML, Post PN, Razenberg PP. Serious co-morbidity among unselected cancer patients newly diagnosed in the southeastern part of The Netherlands in 1993–1996. *J Clin Epidemiol* 1999;**52**:1131–6.
13. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis* 1987;**40**:373–83.
14. van der Meer JB, van den Bos J, Mackenbach JP. Socioeconomic differences in the utilization of health services in a Dutch population: the contribution of health status. *Health Policy* 1996;**37**:1–18.
15. Bassi C, Falconi M, Salvia R, Mascetta G, Molinari E, Pederzoli P. Management of complications after pancreaticoduodenectomy in a high volume centre: results on 150 consecutive patients/with invited commentary. *Dig Surg* 2001;**18**:453–8.
16. Hodgson DC, Zhang W, Zaslavsky AM, Fuchs CS, Wright WE, Ayanian JZ. Relation of hospital volume to colostomy rates and survival for patients with rectal cancer. *J Natl Cancer Inst* 2003;**95**: 708–16.
17. Neoptolemos JP, Russell RC, Bramhall S, Theis B. Low mortality following resection for pancreatic and periampullary tumours in 1026 patients: UK survey of specialist pancreatic units. UK Pancreatic Cancer Group. *Br J Surg* 1997;**84**:1370–6.