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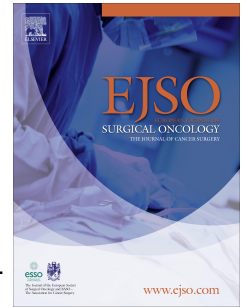


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**REDUCTION OF IN-HOSPITAL MORTALITY FOLLOWING REGIONALIZATION OF
PANCREATIC SURGERY IN THE SOUTH-EAST OF THE NETHERLANDS**

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Abstract

Background: In the late nineties of the former century, surgery for pancreatic and peri-ampullary cancer in the southern part of The Netherlands was performed mainly in low-volume hospitals (<5 resections/year). Results reported by the Comprehensive Cancer Center South (CCCS) in 2005 revealed the clearly disappointing results of this practice. The former stimulated the regionalization of pancreatic surgery by 3 collaborating surgical units into one non-academic teaching hospital in the eastern part of the CCCS-region starting from July 2005.

Methods: All of the 76 patients in this regional cohort group in whom a resection of a (peri-)pancreatic tumour was performed with curative intent have been followed up prospectively. The results of surgical morbidity and in-hospital mortality were compared with the results of the CCCS cohort group which were reported previously.

Results: Ever since the regionalization the annual number of patients undergoing resection of a pancreatic tumour increased from 10 to 33, resulting in a total number of 76 patients. Postoperative complications, reoperation rate and in-hospital mortality decreased significantly to 34,2%, 18,4% and 2.6% respectively, as compared to 71,9%, 37,8 and 24,4% in the time period before regionalisation ($p < 0.01$).

Conclusion: These unique comparative prospective data derived from daily practice in a collaborative surgical region in The Netherlands (CCCS) support the need for centralisation of pancreatic surgery in order to improve standard of care in pancreatic surgery. This can be achieved by collaboration in a large regional hospital.

Key-words: regionalization – pancreaticoduodenectomy – pancreatic cancer – mortality

Introduction

Surgical resection is currently the only potential curative treatment available for patients diagnosed with localized pancreatic cancer. However, surgery for pancreatic cancer is challenging and usually regarded as a “high-risk procedure”. During the last decade, several authors have reported that surgery-related mortality and morbidity can be reduced significantly when performed in high-volume centers(1-5). In spite of the aforementioned, referral patterns of patients with operable pancreatic cancer have not changed impressively since. Up to today many patients are still treated in low-volume centres with varying results(6-9).

In the southern part of The Netherlands, 10 hospitals spread over 17 locations each serving a population between 150.000-250.000 people are joined in the Comprehensive Cancer Center South (CCCS). Until recently, no official referral center for pancreatic surgery was appointed. Pancreatic surgery used to be performed in 8 hospitals, none of them performing more than 4 resections a year. In an effort to determine the need for regionalization of pancreatic surgery, the CCCS reviewed the quality of surgery for pancreatic cancer delivered from 1995-2000(10). The results were reported in 2005 and demonstrated a disappointing 24% overall postoperative mortality after pancreatic surgery.

In an effort to improve the quality of surgical care for pancreatic cancer, collaboration by regionalization was initiated in the eastern part of the CCCS-region shortly thereafter. The latter was accomplished by establishing a team of 5 dedicated surgeons from 3 collaborating surgical departments. These faculty level surgeons are all certified oncological surgeons with special interest in abdominal oncology and were all responsible for pancreatic surgery in their own hospital prior to regionalisation. All procedures involving the pancreas were performed by at least 2 surgeons from this team. Initial pre-operative work-up was performed by the referring hospital. However, all surgical procedures and postoperative care was concentrated in one single hospital (Catharina Hospital Eindhoven), while it was abandoned in the hospitals joining regionalization. The results of this procedure are reported in this prospective study.

Methods:

In order to analyse the impact of regionalisation of pancreatic surgery on surgical outcome, results with regard to postoperative morbidity and mortality before regionalisation (period A: January 1995 until April 2000) were compared with similar data prospectively collected from the start of regionalisation (period B). Results with regard to period A have been reported previously in 2006 which were derived from the population based database of the CCCS (10).

Similarly as for period A, data of all patients from July 2005 to July 2009 (period B), diagnosed and operated on for a (pre-)malignant tumour of the pancreas, Vater's ampulla or the extra-hepatic ducts were collected prospectively. Cholangiocarcinomas of the upper main bile duct, necessitating a Klatskin-type resection as well as duodenal tumours were excluded. All of these patients were operated on in the Catharina Hospital Eindhoven by a regional surgical team of 5 dedicated oncologic surgeons. Primary endpoint was in-hospital mortality defined as mortality before discharge to the patient's home, a nursing home or rehabilitation centre. The recently published ISGPS-definitions were used for scoring of postoperative complications(11-13).

Statistics

Categorical variables were expressed in numbers and/or proportions. Continuous variables were provided with median value and range. The Fisher's exact test was used to analyze categorical data. A p-value less than 0.05 was considered statistically significant. For the present series actual survival rates were calculated. Numbers of survivors and at risk per follow-up were provided. Follow-up was completed until July 2009.

Results

Patients and referral pattern

Before regionalisation (period A), 82 patients underwent a resection for a pancreatic tumour in the CCCS-region. These resections were performed in 8 hospitals. None of the hospitals performed more than 4 resections per year at that time. Regionalisation in the south-eastern part of the CCCS-region started in July 2005 (period B) when surgeons from 2 surgical departments joined efforts for patients with pancreatic cancer. During the first year in total 10 pancreatic resections for malignancy were performed. Shortly thereafter, neighbouring hospitals started to refer patients with pancreatic cancer to our hospital. In total 10 hospitals, all within the CCCS-region have referred at least 1 patient since the regionalisation. In January 2008 two surgeons from a third hospital joined the pancreatic team. Subsequently the number of pancreatic resection increased to 33 in the most recent year, leading to 76 resections for pancreatic cancer in this period (B).

Characteristics

Patient and tumour characteristics are comparable for before and after regionalisation (Table 1).

Morbidity and mortality

The results with regard to both operative and postoperative morbidity and mortality are demonstrated in table 2. The results concerning period A were published previously(10). Peroperative complications, mainly comprising haemorrhage (9.8 vs. 3.9%) occurred less in patients operated by a regional surgical team although not statistically different ($p=0.21$). The number of re-operations decreased significantly: 31 re-operations (38%) before and 14 (18%) after regionalisation ($p < 0.008$). Reasons for reoperation were: early postoperative haemorrhage (3 grade B, 1 grade C), drainage of intra-abdominal abscesses (4 patients), drainage of grade C pancreatic leakages (4 patients) and delayed gastric emptying grade C due to adhesions (2 patients). Besides these operatively corrected complications another 5

patients suffered from a grade A (4 patients) or grade B (1 patient) delayed gastric emptying, grade B pancreatic leakage (5 patients) and pneumonia (3 patients). Taken together, postoperative complications were significantly reduced after regionalisation (34,2% vs. 71,9%, $p < 0.0001$).

Postoperative in-hospital mortality was significantly reduced following regionalisation from 24.4% to 2.6% ($p < 0.0001$). Two patients died after regionalisation. The first patient, a 72-year-old female, developed a fatal haemorrhagic cerebrovascular accident on the 6th postoperative day following a Whipple's procedure for a T3N1 adenocarcinoma of the pancreatic head. A second 79-year-old male patient died of severe ARDS on the 6th postoperative day following a pylorus preserving pancreaticoduodenectomy for a T2N0 distal cholangiocarcinoma complicated by a grade C leakage of the pancreaticojenostomy.

Results with regard to both short term and long-term survival are shown in Table 3. Both 3-month (75% vs. 97%; $p < 0.001$) as well as 1 year survival (55% vs. 76%; $p = 0.02$) are significantly increased following regionalisation. There is a trend towards an improved survival after two years but this did not reach statistical significance (37% vs. 52%, $p = 0.23$).

Discussion

This prospective cohort study on the effect of regionalisation of surgery for pancreatic cancer in the eastern part of the CCCS region in The Netherlands demonstrates that concentration in a high volume center and surgical treatment by a dedicated surgical team results in reduction of postoperative morbidity and mortality.

During the last decade several large population based studies have also demonstrated that hospital and surgeon-volume results in less post-operative complications and mortality (1-9;14;15). In some states in the USA this awareness has resulted in formal centralisation of pancreatic surgery and a subsequent decrease in postoperative mortality(7;16). However, nationwide effects of centralisation in the USA are not seen yet(17). Also in Europe most patients are still operated in low-volume centers as has been reported in recently published population-based studies from Italy, Belgium and the Netherlands (6;8;9). Without exception, these studies again confirm the inverse correlation between the number of resections per hospital and postoperative mortality. All authors of these studies invariably advocate further centralisation of pancreatic surgery in their countries. In the Netherlands the plea for centralisation has been initiated since 1995. Nevertheless, nationwide referral patterns over the last decade have not changed significantly since(6;15). The improvement of quality of care for surgical patients with pancreatic cancer is challenged by some authors claiming excellent results from low-volume hospitals(18) as well as by the observation that also high-volume centres may not always fulfil high standards of qualitative care(19). Finally, opponents of centralisation claim that at least a part of the beneficial results obtained by specialized centres may be due to case selection. Indeed, in a previous report we have also shown that patients seeking surgery in specialized centres outside our region more often were male, younger, in a better health and higher socioeconomic status as compared to patients who do not(10). The latter is also confirmed by a study from the USA, reporting that patients referred to high-volume centres were more often white and had a better insurance as compared to patients treated in low volume centres(1).

Besides these objective data, more subjective arguments probably play an essential role in the reluctance of surgeons to refer patients to other hospitals. The complexity of pancreatic surgery is generally regarded as an interesting and alluring aspect of abdominal oncologic surgery by most surgeons. These surgeons feel that their profession may become less attractive once pancreatic surgery is no longer part of their surgical practice leaving them to carry on practising pancreatic surgery even with low patient volume.

The aforementioned has been daily practice for a long time in the CCCS-region where surgeons from 10 hospitals performed less than 5- resections per year. It was only after the publication of the disappointing results that an initiative was undertaken to improve the regional quality of care for this kind of surgery. One of the solutions might have been to prohibit pancreatic surgery at all within the CCCS-region and to refer all patients to established centres for pancreatic surgery in the Netherlands. Due to logistics (e.g. travelling time and the waiting lists in the referral centres) this option was regarded as unattractive. Instead, regional collaboration was sought which resulted in the successful establishment of a referral centre within the south-eastern part of the CCCS-region. In our opinion, the main reason for the current successful regionalization is that certified oncological surgeons with experience in pancreatic surgery from neighbouring hospitals were invited to participate in one collaborating surgical team. By doing so, they could refer the patients to a neighbouring centre but at the same time could continue to perform pancreatic surgery, even at a higher level,

The current study shows that this initiative of regional collaboration has improved both the short term and long term outcome of these patients. Several factors have probably contributed to this improvement. First of all, due to the higher exposure of the participating surgeons the surgical technique has improved. This is illustrated by a decrease in complications both during the operation and in the early postoperative period. Despite the decrease in postoperative complications, still a significant proportion of the patients suffer from a variety of complications. This is a well-known phenomenon in pancreatic surgery and is reported by many expert centres(20). The higher index of suspicion and early recognition

of complications by medical and nursing staff due to higher exposure resulting in early treatment of these complications is of utmost importance in order to prevent postoperative mortality. The former may probably be the most important explanation for the success of regionalisation. Apart from earlier detection of complications, expanding experience with regard to minimal invasive treatment of complications, i.e. intervention radiology, results in a significant decrease in the need for reoperations. In the absence of experience with the non-operative minimal invasive treatment of complications at the start of the regionalisation most complications were treated by reoperation resulting in a decreased but still high reoperation rate of 18% in the current series. However, with growing experience intervention radiologists currently treat most intra-abdominal fluid collections by CT-guided percutaneous drainage and the endoscopic treatment of anastomotic bleeding by gastroenterologists has become standard of care. Therefore, we expect that the number of reoperations will continue to fall with increasing experience. Also medical oncologists have become more familiar with this patient category and adjuvant chemotherapy is currently offered more frequently. The former may in part also contribute to the slight improvement in the two year survival observed in the recent period. Finally, there is evidence from several studies that also pathological examination of the resection specimen improves with growing experience resulting in better staging(21;22). Taken all together, treatment of patients who are operated on for pancreatic cancer has become an even more multi-disciplinary effort which benefits this group of patients. Recently, the multi-disciplinary approach was regarded as the most important contributory to the improved long-term survival of patients undergoing pancreatic resection in the MD Anderson Cancer Center(23).

The beneficial effects of concentration of surgical care is not only limited to pancreatic surgery but involves many other procedures once regarded as “general surgery” such as for instance complex colorectal(24) and vascular surgery(25). It is likely that patient organisations and health care authorities will pursue concentration of such complex procedures in the near future. The present study shows that centralisation of complex surgical treatment not automatically implies that these patients should be referred to

nationwide expert centres but that through collaboration high quality of care can be achieved in a high volume regional hospital. The call for centralisation should therefore no longer be regarded as a threat by general hospitals but as a chance to improve results through regional collaboration for this complex and challenging surgical pathology.

TABLES

Table 1		A	B	p value
Total (n)		82	76	
Mean age (range)		64 (41-78)	65 (42-81)	
Gender				
	male	43	46	
	female	39	30	.338
pTNM-stage				
	I	27	19	
	II	16	17	
	III	30	23	
	IV	5	9	
	Metastasis other origin	0	1	
	Premalignant lesions	0	7	
	Not classified	4	0	.205
Tumour localisation				
	Peri-ampullary	29	21	
	Pancreatic head	41	38	
	Distal Choledochol duct	6	9	
	Distal pancreas	5	8	
	Pancreas not specified	1	0	.483

Table 2		A	B	p value
Total (n)		82	76	
Complications	Peroperative complications	8 (9.8%)	3 (3.9%)	.214
	Postoperative complications	59 (71.9%)	26(34.2%)	<.0001
	Re-operations	31 (37.8%)	14 (18.4%)	.008
	In-hospital mortality	20 (24.4%)	2 (2.6%)	<.0001

Table 3		A	B	p value
	3-month survival (%)	75	97	<.0001
	1-year survival (%)	55	76	.023
	2-year survival (%)	37	52	.230

Group B: survivors and number of patients at risk with 3-months follow-up n=65 and 67, 1-year n=34 and 45 and 2-years n=12 and 23

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