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Temporal Trends in Pancreatic Cancer

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1. Introduction

Pancreatic cancer is one of the most common malignancies of the digestive system and, depending on the geographic area, fourth or fifth leading cause of cancer deaths (Lillemoe *et al*, 2000; Simon & Printz, 2001). Between 1960 and 1980, the incidence rates had increased significantly in most industrialised countries, including Poland. Corresponding 5-year survival rates demonstrated only slight variations and remained stable at about 1-3%. Surprisingly, results obtained from some population databases suggest that only about 30% of patients registered as pancreatic cancer have been adequately verified by histopathology (Wood *et al*, 2006). Moreover, since many studies included only small groups of patients, previous reports did not properly reflect the actual changes, including long-term results of treatment (Gudjonsson, 1995). As incidence rates were relatively high and the efficacy of therapeutic methods was questionable, pancreatic cancer was subject to numerous clinical trials (Jafari & Abbruzzese, 2004). However, no clear conclusions could be drawn in terms of the best therapeutic approach due to marked differences between individual studies (Gudjonsson, 1995).

Many epidemiological studies published over the last 50 years provided detailed data for some general trends related to incidence and mortality rates for pancreatic cancer. Changes in other areas of interest, such as variation in surgical and systemic therapy or long-term outcomes are much less examined. Taking into account these facts, an analysis of temporal trends for some surgical aspects of pancreatic disorders may provide significant information supplementing the results of previous studies.

2. Methods

A literature search was performed using two bibliographic databases, i.e. PubMed and Ovid. Databases were searched using combinations of the following keywords: (pancreatic neoplasm or pancreatic cancer) and (trends or time related changes). Additionally all patients diagnosed with pancreatic duct cell cancer (*adenocarcinoma ductale*) treated between 1972 and 2003 at the 1st Department of General and GI Surgery of Jagiellonian University Medical College in Kraków were reviewed. Other pancreatic tumours verified as non-duct cell cancers and periampullary neoplasms were excluded. Clinical and demographic data, including age, gender and type of therapeutic interventions, were collected from medical records. Tumours were staged according to the TNM classification of *Union Internationale Contre Le Cancer* (UICC) of 1997. The type and extent of surgical treatment was categorised

based on commonly accepted criteria (Pedrazzoli *et al*, 1999). To analyse temporal trends for pancreatic cancer, the study interval was divided into three periods, i.e. period 1 (1972-1983), period 2 (1984-1993) and period 3 (1994-2003).

3. General epidemiological trends

Worldwide epidemiological studies on pancreatic cancer have demonstrated slightly higher incidence rates in males irrespectively of the geographic area (Katanoda & Dongmei, 2008; Katanoda & Yako-Suketomo, 2010; Levi *et al*, 2003; Michaud, 2004; Sahmoun *et al*, 2003).

		Period 1 1972-1983 (n=145)	Period 2 1984-1993 (n=294)	Period 3 1994-2003 (n=508)	P
Gender	female	70 (48%)	106 (36%)	222 (44%)	0.027†
	male	75 (52%)	188 (64%)	286 (56%)	
Age, median (95%CI)		58 (57-62)	60 (58-62)	63 (62-65)	<0.001‡
Location	head	89 (61%)	199 (68%)	341 (67%)	
	body	50 (35%)	71 (24%)	140 (28%)	0.147†
	tail	6 (4%)	24 (8%)	27 (5%)	
Stage	I	0 (0%)	7 (2%)	5 (1%)	
	II	3 (2%)	2 (1%)	16 (3%)	0.047†
	III	8 (6%)	11 (4%)	32 (6%)	
	IV	134 (92%)	274 (93%)	455 (90%)	
Therapy	surgical	117 (81%)	228 (78%)	376 (74%)	0.192†
	conservative	28 (19%)	66 (22%)	132 (26%)	
Type of surgical procedures					
	resective	11 (9%)	46 (20%)	115 (31%)	<0.001†
	non-resective	106 (91%)	182 (80%)	261 (69%)	
Type of pancreatic resections					
	PD	8 (73%)	22 (48%)	46 (40%)	
	PPD	0 (0%)	4 (8%)	14 (12%)	0.557†
	distal pancreatectomy	2 (18%)	10 (22%)	22 (19%)	
	total pancreatectomy	1 (9%)	10 (22%)	33 (29%)	
Type of non-resective surgery					
	laparotomy	38 (36%)	62 (34%)	81 (31%)	
	biliary bypass	55 (52%)	64 (35%)	19 (7%)	<0.001†
	gastro-enteric bypass	4 (4%)	13 (7%)	67 (26%)	
	biliary and enteric bypass	9 (8%)	43 (24%)	94 (36%)	
Chemotherapy					
	no	138 (95%)	222 (76%)	231 (45%)	<0.01†
	yes	7 (5%)	72 (24%)	277 (55%)	
Median survival, months (95%CI)					
	overall	5.2 (4.7-5.6)	6.2 (5.2-7.2)	7.6 (6.7-8.5)	<0.001§
	pancreatic resections	26.6 (10.4-42.8)	14.3 (11.2-17.4)	20.0 (13.7-26.3)	0.041§
	unresectable tumours	5.0 (4.5-5.6)	5.5 (4.6-6.5)	5.9 (5.1-6.6)	<0.001§

Table 1. Demographic and clinical data of patients with pancreatic cancer
(PD –pancreatoduodenectomy, PPPD – pylorus-preserving PD, † chi-square test;
‡ ANOVA analysis of variance, § log-rank test)

Most authors agree that this phenomenon is mainly related to the exposure to carcinogens, particularly smoking. The role of the latter factor has been confirmed by increasing incidence trends in populations with a high proportion of smoking individuals and lowering incidence in countries where smoking is decreasing, i.e. Sweden (Bobak, 2003; Flook & van Zanten, 2009; Luo *et al,* 2008; Mulder *et al*, 2002; Simon & Printz, 2001).

Between 1972 and 2003, a total of 1708 patients with chronic pancreatic and periampullary disorders were hospitalised, including 947 patients with histopathologically verified pancreatic duct cell cancer (Popiela et al, 2007). Fifty-eight per cent of 947 patients with pancreatic cancer were males (n=549) and 42% (n=398) females. Although the proportion of males increased temporarily to 64% in period 2, it subsequently decreased to values observed in period 1 (tab. 1). The median age was 62 years (95% confidence interval [CI] 61 – 62) and demonstrated a significant increasing trend over time. Similarly to other authors, we have recorded a significant increase in the proportion of females diagnosed with pancreatic cancer over the last twenty years. The significant increasing trend for the median age shown in our series was similar to other reports where growing numbers of pancreatic resections were carried out in elderly patients (Delcore *et al*, 1991; DiCarlo *et al*, 1998; Sohn *et al*, 1998).

4. Changes in pathological findings

Numerous changes have been observed worldwide in the diagnostics of pancreatic cancer during the last five decades. The number of cases diagnosed at laparotomy carried out due to jaundice or epigastric complaints decreased sharply as abdominal ultrasound was introduced into routine clinical practice (Soreide *et al*, 2010). Subsequently, ultrasound was gradually replaced by less operator-dependent imaging techniques, such as computed tomography (CT) and magnetic resonance imaging (MRI). A gradual increase in the use of endoscopic ultrasonography (EUS) and positron emission tomography (PET) has been observed over the recent years, but their application is usually limited to some specific clinical situations. The proportion of patients diagnosed solely with US and CT nowadays varies between 75% and 85%, while other imaging techniques (MRI, PET, EUS) are used less frequently (David *et al*, 2009; Ngamruengphong *et al*, 2010).

The majority of lesions treated in our centre was located in the head of the pancreas (n=629, 66%), whereas cancers of the body and tail were found in 28% (n=261) and 6% (n=57) of cases, respectively. There were no significant differences in the proportions of tumours located in the head, body and tail of the pancreas over time (Popiela *et al*, 2007). However, other authors suggested some variation over time. Based on 43,946 cases of pancreatic cancer recorded between 1973 and 2002 in the Surveillance, Epidemiology, and End Results (SEER), Lau et al. found a 46% increase in the incidence of body/tail cancers (Lau *et al*, 2010). Reports from other geographic areas mostly failed to demonstrate any significant change in the prevalence of distally-located cancers.

Technical improvements in imaging methods and their wider accessibility should theoretically allow for an earlier diagnosis of pancreatic cancer leading to reduced proportions of advanced tumours and increased resectability rates. Surprisingly, most cohort studies failed to demonstrate any marked increase in the proportion of cancers at a lower stage (Cress *et al*, 2006; Janes *et al*, 1996; Niederhuber *et al*, 1995; Riall *et al*, 2006; Sener *et al*, 1999). The percentage of patients with stage IV tumours in our series, similarly to other reports, showed only a slight lowering trend. Although this phenomenon was accompanied by increasing resectability rates,

the proportion of stage groups in patients undergoing pancreatic resections remained stable. Similarly to our findings, other authors reported only slight variations in staging patients with pancreatic cancer. In a population of 2986 cases of pancreatic cancer from the Digestive Cancer Registry of Burgundy (France) over a 30-year period (1976–2005) the overall proportion of stage I, II and III tumours was 1.3%, 2.2% and 5.4%, respectively (David *et al*, 2009). The proportion of stage I–II cancers slightly increased from 2.8% in the 1976–1980 period to 8.8% in the 2001–2005 period, though these changes were highly significant (P<0.001). Nevertheless, metastatic and/or non-resected cases decreased only by about 10% from 95.2% to 85.5%. The increasing trend of resectability rates found in this study was also confirmed by authors from various geographic areas. In a group of 16,758 patients treated between 1980 and 2000 in Sweden, the proportion of resectable tumours observed by Linder et al. increased from 7.2% to 15.1% (Linder *et al*, 2006). A similar trend was reported for the US population in a recent study involving 24,016 patients (Riall *et al*, 2006).

5. Surgical trends

Improved diagnostic methods increased the percentage of patients diagnosed with metastatic disease before surgery. Simultaneous development of endoscopic methods allows to perform biliary or duodenal stenting, and along with better imaging tests, has contributed to the decreasing rates of open surgery in patients with disseminated disease (Lefebvre *et al*, 2009).

Two hundred and twenty-six of 947 analysed patients (24%) were disqualified from surgical intervention. The remaining 721 (76%) patients were subject to surgical therapy and this proportion decreased insignificantly from 81% to 74% in the last decade. Pancreatic resections were performed in 172 (24%) patients and the resectability rate increased significantly from 9% to 31% between period 1 and 3, respectively. No significant changes in the type of pancreatic resections could be demonstrated for the whole cohort. However, an increasing proportion of pylorus-preserving pancreaticoduodenectomy (Traverso procedure) from 0% to 23% in the last period was found for lesions located in the head of the pancreas. The percentage of patients undergoing only exploratory laparotomy was stable over time with a mean value of 33%. The proportion of patients with biliary bypass significantly decreased with a concomitant increase in the ratio of gastro-enteric and double bypass procedures.

A gradual increase in endoscopic procedures is commonly reported in most reports. Linder et al. reported a significant reduction in the proportion of patient subject to surgical biliary bypass from 45.9% between 1980 and 1986 to 18.1% between 1994 and 2000 (Linder *et al*, 2006). These changes were accompanied by a lowering percentage of gastro-enteric bypass from 33.8% to 22.8%. Lefebvre et al. reported a similar decreasing trend for palliative surgery from 55% in 1978–1982 to 32% in 1998–2002 due to the more common use of endoscopic stenting (Lefebvre *et al*, 2009). We have found analogical variations in biliary bypass from 52% to 7%, but as opposed to Linder et al. the percentage of gastro-enteric and simultaneous biliary and enteric bypasses increased from 4% to 26% and from 8% to 36%, respectively. This change in the therapeutic strategy was related mainly to our analysis of patients requiring open surgery for upper gastrointestinal ileus and results of randomized clinical trials supporting the idea of prophylactic gastro-enteric bypass (Lillemoe *et al*, 1999; Popiela *et al*, 2002b; Van Heek *et al*, 2003). The increasing proportion of pylorus-preserving pancreaticoduodenectomy observed in the last decade for patients undergoing pancreatic head resections reflects the current belief that the procedure does not impair oncological radicality and, as suggest some authors, reduces adverse metabolic consequences of pancreatic resections (Schafer *et al*, 2002).

The most important aspect of surgery-related trends in pancreatic cancer is associated with markedly decreasing postoperative mortality. We have observed similar changes in the early postoperative outcomes and long-term survival as those reported by other authors (Popiela *et al*, 2002b; Sierzega *et al*, 2006). In particular, a significant lowering trend of postoperative mortality rates was found from values exceeding 10% in the early eighties to an average of 4.1% in the last decade (fig. 1) (Popiela, 1979; Popiela *et al*, 2004).

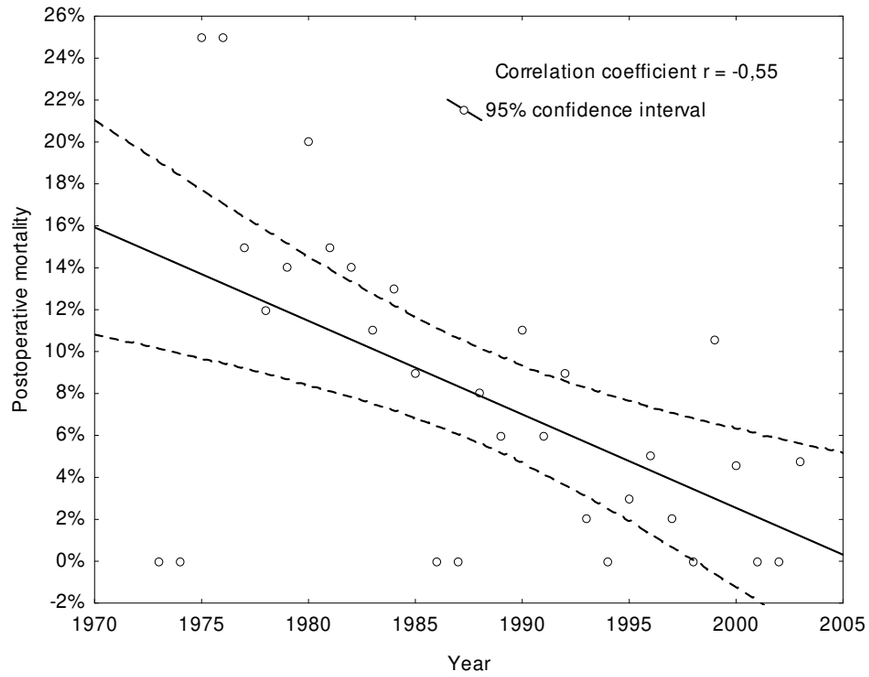


Fig. 1. Postoperative mortality rates for pancreatic resections in consecutive years

6. Trends in systemic therapy

Pancreatic surgery has reached a plateau in terms of long-term survival observed for patients with pancreatic cancer (Popiela *et al*, 2002a; Popiela *et al*, 2002c). Therefore, further improvements should only be expected from combined modality therapy. IN our series, various regimens of chemotherapy were used in 38% (n=356) of cases and the percentage of patients qualified of systemic therapy increased significantly from 5% in period 1 to 55% in period 3. Fluorouracil was the primary chemotherapeutic agent until 1997 and afterwards was replaced by multidrug regimens based on gemcitabine, cisplatin and irinotecan.

Although there is no uniform consensus on adjuvant therapy of pancreatic cancer, a recent meta-analysis of clinical trials have supported the benefits of chemotherapy found in our study (Stocken *et al*, 2005). The most recent analysis of data from the SEER registry in 1910 patients who underwent resections for pancreatic adenocarcinoma performed between 1991 and 2002 reflects the overall change in the proportion of patients qualified for systemic treatment after surgical intervention (Simons *et al*, 2010). The proportion of subjects receiving adjuvant chemoradiotherapy in US increased from 26% in 1991–1993 to 37% in 2000-2002. The role of palliative chemotherapy is also increasing as demonstrated in a recent

meta-analysis of clinical trials, where chemotherapy significantly prolonged survival compared to symptomatic therapy (Yip *et al*, 2009). Another meta-analysis on gemcitabine combined with platinum agents provided additional proofs for combination therapy, as the concomitant use of both drugs significantly increased response rates and prolonged time to progression (Xie *et al*, 2006). Results of our studies showed that any gemcitabine based regimen of palliative chemotherapy produced better results than observed in control groups and the combination of gemcitabine and cisplatin was the most effective regimen (Popiela *et al*, 2001; Popiela *et al*, 2005). Increased rates of adjuvant and palliative chemotherapy have been reported by several authors (David *et al*, 2009; Lefebvre *et al*, 2009).

7. Changes in prognosis

The overall median survival in our series was 7.1 months (95%CI 6.6 to 7.6) and was significantly longer after pancreatic resections (median 14.8 months; 95%CI 11.5 to 16.9) than in the remaining cases (median 5.8 months; 95%CI 4.4 to 6.9). The overall 5-year survival rate was 4.5% and increased to 14.3% for resective cases. No patient with unresectable tumour survived 5 years from the time of diagnosis. Pairwise comparisons of survival functions demonstrated statistically significant differences between each stage according to UICC 1997 (fig. 2).

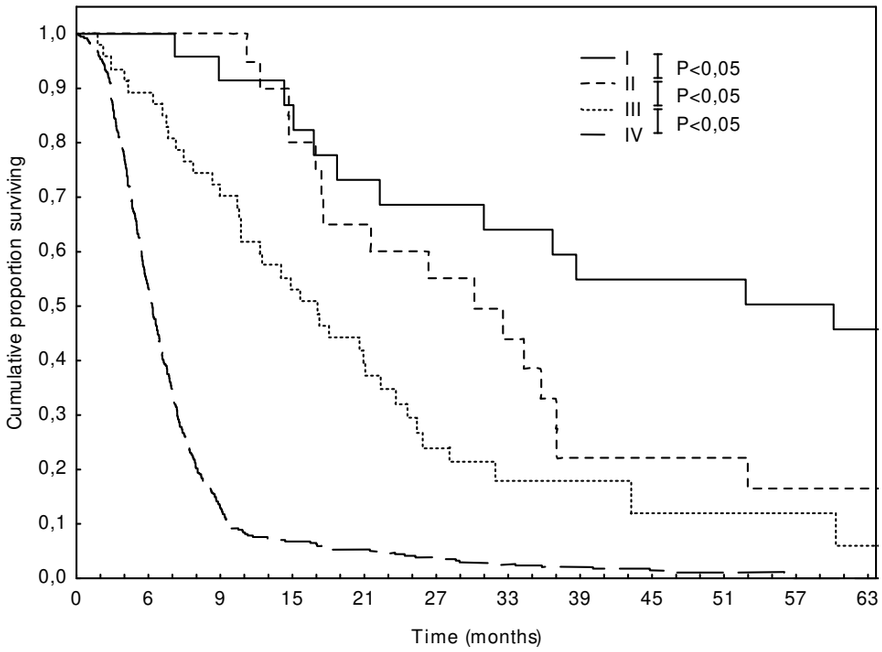


Fig. 2. Stage-specific survival for resectable pancreatic cancer

The 5-year survival rate for stage I was 50.3% with a median survival of 63.1 months (95%CI 7.6 to 118.6). Five-year survival rates of 16.5% and 5.9% for stage II and III, respectively, were significantly lower. Corresponding median survival times were 33.2 months (95%CI 21.0 to 45.5) and 20.1 months (95%CI 14.8 to 25.3). The median survival of patients with stage IV cancers was 6.2 months (95%CI 5.7-6.6) and no patient survived 5 years. The median and 5-year survival rates after curative resections (R0 according to UICC) were 27.9

months and 29.4%, respectively. The corresponding duration of median survival for microscopically (R1) and macroscopically (R2) non-radical resections of 11.4 and 11 months was significantly shorter. No patient survived 5 years after either R1 or R2 resection. A significant increasing trend for overall survival was found between period 1 and 3 (fig. 3, tab. 1). The correlation coefficient for the median survival of patients treated in consecutive years was 0.59 and this increasing trend was statistically significant (fig. 4). The median survival of patients undergoing pancreatic resections during the last decade (20 months, 95%CI 13.7 to 26.3) was significantly longer than for the period 1984-1993 (14.3 months, 95%CI 11.2 to 17.4). However, the differences between median survival during 1972-1983 and 1984-1993 or 1972-1983 and 1994-2003 were statistically insignificant (fig. 5). Nevertheless, the median survival of patients with unresectable tumours increased significantly between consecutive periods (fig. 6).

Long-term results in patients treated for pancreatic cancer demonstrate only slight variations over the last 30 years with 5-year survival rates of 1-3% (Gudjonsson, 1995; Lillemoe *et al*, 2000; Tsiotos *et al*, 1999). Nevertheless, the number of reports describing improving survival trends is growing (Riall *et al*, 2006; Wood *et al*, 2006). The 2.4-month increase in the overall median survival found in our patients was due to improvements observed in both resectable (from 14.3 months between 1984 and 1993 to 20 months between 1994 and 2003), and unresectable cases (from 5 months between 1972 and 1983 to 5.9 months in the last decade). The relatively high median survival (26.6 months) in resectable patients treated in period 1 was related to the small number of cases (11 patients). In a recent publication of 1423 patients undergoing pancreaticoduodenectomy for pancreatic cancer, the median survival increased significantly from 8 months in the eighties to 19 months in patients operated after 2000 with comparable proportions of stage groups (Winter *et al*, 2006). A similar trend was also reported by Riall et al. in a large study on unresectable

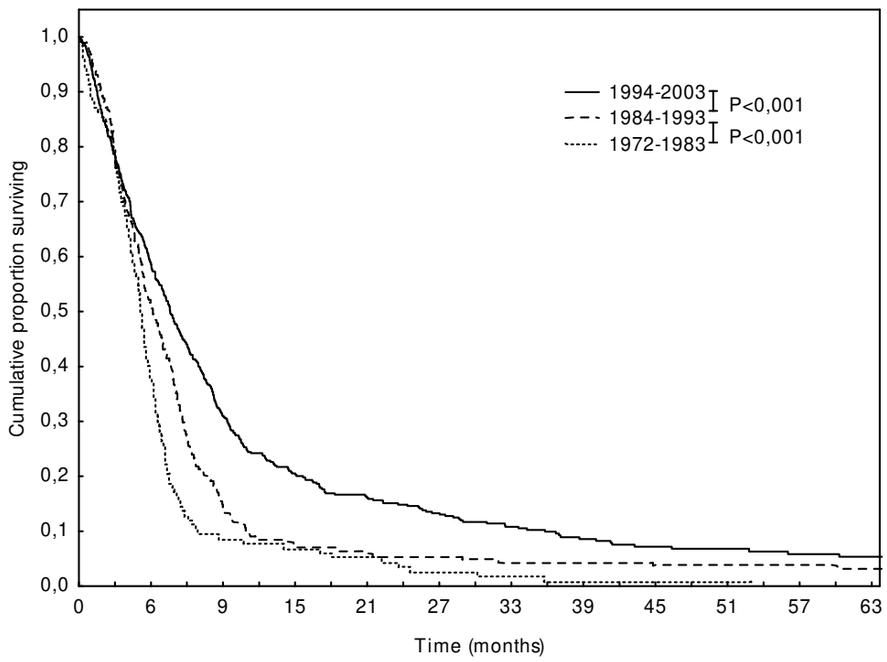


Fig. 3. Overall survival functions for individual time periods

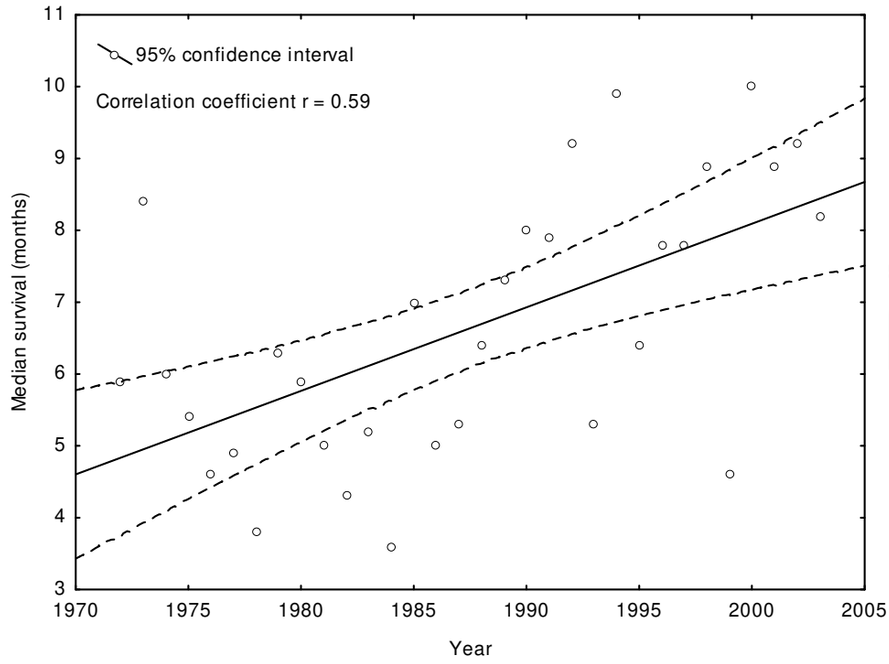


Fig. 4. Changes in median survival in consecutive years

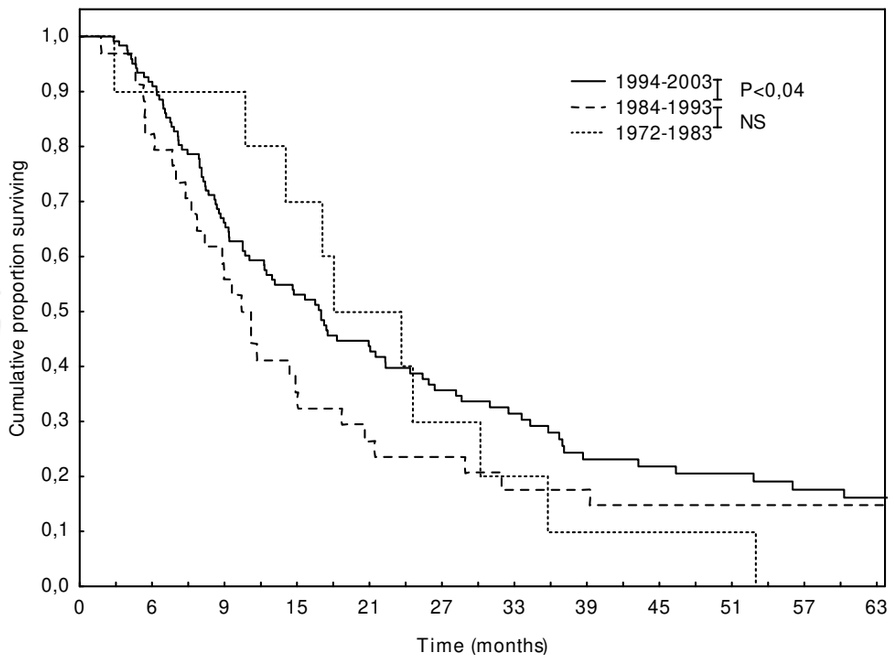


Fig. 5. Changes in survival in consecutive years for resectable tumours

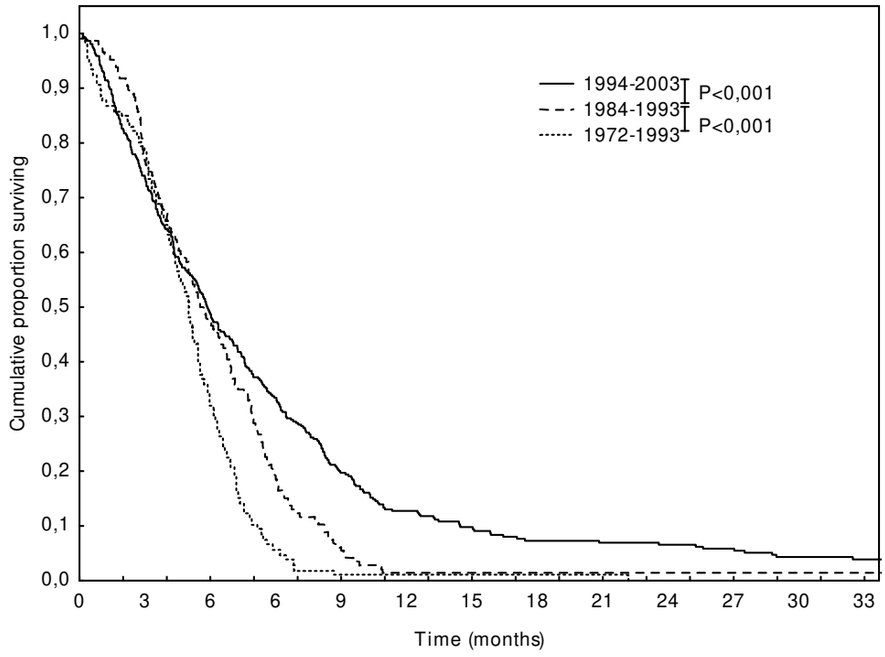


Fig. 6. Changes in median survival in consecutive years for unresectable tumours

pancreatic cancer (Riall *et al*, 2006). In 12043 cases of disseminated disease, the proportion of patients who survived 2 years increased from 1.4% between 1988 and 1991 to 2.3% between 1996 and 1999. A recent analysis of the SEER database showed a similar improving trend for overall survival in patients with pancreatic cancer (Lau *et al*, 2010). The overall 3-year survival rate increased from 4.3% to 6.2% from 1973 to 1987 to 1988 to 2002 for tumours of the pancreatic head and from 2.8% to 3.9% in pancreatic body/tail cancers. Similar observations were reported from the South Australian Cancer Registry covering the period from 1977 to 2006 with 4,166 pancreatic cancers (Luke *et al*, 2009) and 21,663 patients from the Cancer Registry of Norway for the period 1965–2007 (Soreide *et al*, 2010).

8. Conclusion

The analysis of 947 patients with pancreatic cancer treated between 1972 and 2003 demonstrated the existence of significant trends mainly for early postoperative and long-term outcomes. Postoperative mortality rates significantly decreased from values exceeding 10% in the early eighties to an average of 4.1% in the last decade. The overall median survival increased from 5.2 to 7.6 months and this change was reflected by improving outcomes in both resectable and unresectable disease. The observed changes are attributed mainly to the increasing role of combined therapy and emphasise the importance of such an approach.

Even with easily accessible imaging tests, the majority of patients with either cancer is still diagnosed at an advanced stage. Therefore, improved diagnostic procedures at the level of pre-hospital care are the key for actual improvement of patients' survival. Primary care physicians and specialists diagnosing patients with obstructive jaundice are of particular importance since endoscopic procedures commonly performed by gastroenterologists cannot be regarded as curative therapy and the need for surgical exploration should always be considered.

9. References

Bobak M (2003) Relative and absolute gender gap in all-cause mortality in Europe and the contribution of smoking. *Eur J Epidemiol* 18(1): 15-8

Cress RD, Yin D, Clarke L, Bold R, Holly EA (2006) Survival among patients with adenocarcinoma of the pancreas: a population-based study (United States). *Cancer Causes Control* 17(4): 403-9

David M, Lepage C, Jouve JL, Jooste V, Chauvenet M, Faivre J, Bouvier AM (2009) Management and prognosis of pancreatic cancer over a 30-year period. *Br J Cancer* 101(2): 215-8

Delcore R, Thomas JH, Hermreck AS (1991) Pancreaticoduodenectomy for malignant pancreatic and periampullary neoplasms in elderly patients. *Am J Surg* 162(6): 532-5; discussion 535-6

DiCarlo V, Balzano G, Zerbi A, Villa E (1998) Pancreatic cancer resection in elderly patients. *Br J Surg* 85(5): 607-10

Flook R, van Zanten SV (2009) Pancreatic cancer in Canada: incidence and mortality trends from 1992 to 2005. *Can J Gastroenterol* 23(8): 546-50

Gudjonsson B (1995) Carcinoma of the pancreas: critical analysis of costs, results of resections, and the need for standardized reporting. *J Am Coll Surg* 181(6): 483-503

Jafari M, Abbruzzese JL (2004) Pancreatic cancer: future outlook, promising trials, newer systemic agents, and strategies from the Gastrointestinal Intergroup Pancreatic Cancer Task Force. *Surg Oncol Clin N Am* 13(4): 751-60, xi

Janes RH, Jr., Niederhuber JE, Chmiel JS, Winchester DP, Ocwieja KC, Karnell JH, Clive RE, Menck HR (1996) National patterns of care for pancreatic cancer. Results of a survey by the Commission on Cancer. *Ann Surg* 223(3): 261-72

Katanoda K, Dongmei Q (2008) Comparison of time trends in pancreatic cancer incidence (1973-97) in East Asia, Europe and USA, from Cancer Incidence in Five Continents Vol. IV-VIII. *Jpn J Clin Oncol* 38(2): 165-6

Katanoda K, Yako-Suketomo H (2010) Comparison of time trends in pancreatic cancer mortality (1990-2006) between countries based on the WHO mortality database. *Jpn J Clin Oncol* 40(6): 601-2

Lau MK, Davila JA, Shaib YH (2010) Incidence and survival of pancreatic head and body and tail cancers: a population-based study in the United States. *Pancreas* 39(4): 458-62

Lefebvre AC, Maurel J, Boutreux S, Bouvier V, Reimund JM, Launoy G, Arsene D (2009) Pancreatic cancer: incidence, treatment and survival trends--1175 cases in Calvados (France) from 1978 to 2002. *Gastroenterol Clin Biol* 33(10-11): 1045-51

Levi F, Lucchini F, Negri E, La Vecchia C (2003) Pancreatic cancer mortality in Europe: the leveling of an epidemic. *Pancreas* 27(2): 139-42

Lillemoe KD, Cameron JL, Hardacre JM, Sohn TA, Sauter PK, Coleman J, Pitt HA, Yeo CJ (1999) Is prophylactic gastrojejunostomy indicated for unresectable periampullary cancer? A prospective randomized trial. *Ann Surg* 230(3): 322-8; discussion 328-30

Lillemoe KD, Yeo CJ, Cameron JL (2000) Pancreatic cancer: state-of-the-art care. *CA Cancer J Clin* 50(4): 241-68

Linder S, Bostrom L, Nilsson B (2006) Pancreatic cancer in sweden 1980-2000: a population-based study of hospitalized patients concerning time trends in curative surgery and other interventional therapies. *J Gastrointest Surg* 10(5): 672-8

Luke C, Price T, Karapetis C, Singhal N, Roder D (2009) Pancreatic cancer epidemiology and survival in an Australian population. *Asian Pac J Cancer Prev* 10(3): 369-74

Luo J, Adami HO, Reilly M, Ekbom A, Nordenvall C, Ye W (2008) Interpreting trends of pancreatic cancer incidence and mortality: a nation-wide study in Sweden (1960-2003). *Cancer Causes Control* 19(1): 89-96

Michaud DS (2004) Epidemiology of pancreatic cancer. *Minerva Chir* 59(2): 99-111

Mulder I, Hoogenveen RT, van Genugten ML, Lankisch PG, Lowenfels AB, de Hollander AE, Bueno-de-Mesquita HB (2002) Smoking cessation would substantially reduce the future incidence of pancreatic cancer in the European Union. *Eur J Gastroenterol Hepatol* 14(12): 1343-53

Ngamruengphong S, Li F, Zhou Y, Chak A, Cooper GS, Das A (2010) EUS and survival in patients with pancreatic cancer: a population-based study. *Gastrointest Endosc* 72(1): 78-83, 83 e1-2

Niederhuber JE, Brennan MF, Menck HR (1995) The National Cancer Data Base report on pancreatic cancer. *Cancer* 76(9): 1671-7

Pedrazzoli S, Beger HG, Obertop H, Andren-Sandberg A, Fernandez-Cruz L, Henne-Bruns D, Luttges J, Neoptolemos JP (1999) A surgical and pathological based classification of resective treatment of pancreatic cancer. Summary of an international workshop on surgical procedures in pancreatic cancer. *Dig Surg* 16(4): 337-45

Popiela T (1979) Early detection and surgical treatment of pancreatic cancer. *Pol Przeg Chir* 51: 1049-1054

Popiela T, Kedra B, Sierzega M (2001) Efficacy of gemcitabine in patients wit non-resectable pancreatic cancer: prospective clinical study. *Nowotwory* 51: 117-121

Popiela T, Kedra B, Sierzega M (2002a) Does extended lymphadenectomy improve survival of pancreatic cancer patients? *Acta Chir Belg* 102(2): 78-82

Popiela T, Kedra B, Sierzega M, Gurda A (2004) Risk factors of pancreatic fistula following pancreaticoduodenectomy for periampullary cancer. *Hepatogastroenterology* 51(59): 1484-8

Popiela T, Kedra B, Sierzega M, Kubisz A (2002b) Chirurgisch palliative Therapie beim Pankreaskarzinom: 25 Jahre Erfahrungen eines einzelnen Referenzzentrums. *Zentralbl Chir* 127(11): 965-70

Popiela T, Kedra B, Sierzega M, Kubisz A (2002c) Patienten mit nicht-fortgeschrittenen Pankreaskarzinomen profitieren von der ausgedehnten Lymphadenektomie. *Zentralbl Chir* 127(11): 960-4

Popiela T, Kulig J, Sierzega M, Legutko J (2005) A prospective randomized trial on two gemcitabine-based regimens of chemotherapy for unresectable pancreatic cancer. *Gastroenterology* 128(Supp 2): A-109

Popiela T, Kulig J, Sierzega M, Richter P, Legutko J (2007) Temporal trends of pancreatic cancer and cancer of the ampulla of Vater treated between 1972 and 2003. *Gastroenterol Pol* 14(4): 241-249

Riall TS, Nealon WH, Goodwin JS, Zhang D, Kuo YF, Townsend CM, Jr., Freeman JL (2006) Pancreatic cancer in the general population: Improvements in survival over the last decade. *J Gastrointest Surg* 10(9): 1212-23; discussion 1223-4

Sahmoun AE, D'Agostino RA, Jr., Bell RA, Schwenke DC (2003) International variation in pancreatic cancer mortality for the period 1955-1998. *Eur J Epidemiol* 18(8): 801-16

Schafer M, Mullhaupt B, Clavien PA (2002) Evidence-based pancreatic head resection for pancreatic cancer and chronic pancreatitis. *Ann Surg* 236(2): 137-48

Sener SF, Fremgen A, Menck HR, Winchester DP (1999) Pancreatic cancer: a report of treatment and survival trends for 100,313 patients diagnosed from 1985-1995, using the National Cancer Database. *J Am Coll Surg* 189(1): 1-7

Sierzega M, Popiela T, Kulig J, Nowak K (2006) The ratio of metastatic/resected lymph nodes is an independent prognostic factor in patients with node-positive pancreatic head cancer. *Pancreas* 33(3): 240-5

Simon B, Printz H (2001) Epidemiological trends in pancreatic neoplasias. *Dig Dis* 19(1): 6-14

Simons JP, Ng SC, McDade TP, Zhou Z, Earle CC, Tseng JF (2010) Progress for resectable pancreatic [corrected] cancer?: a population-based assessment of US practices. *Cancer* 116(7): 1681-90

Sohn TA, Yeo CJ, Cameron JL, Lillemoe KD, Talamini MA, Hruban RH, Sauter PK, Coleman J, Ord SE, Grochow LB, Abrams RA, Pitt HA (1998) Should pancreaticoduodenectomy be performed in octogenarians? *J Gastrointest Surg* 2(3): 207-16

Soreide K, Aagnes B, Moller B, Westgaard A, Bray F (2010) Epidemiology of pancreatic cancer in Norway: trends in incidence, basis of diagnosis and survival 1965-2007. *Scand J Gastroenterol* 45(1): 82-92

Stocken DD, Buchler MW, Dervenis C, Bassi C, Jeekel H, Klinkenbijl JH, Bakkevold KE, Takada T, Amano H, Neoptolemos JP (2005) Meta-analysis of randomised adjuvant therapy trials for pancreatic cancer. *Br J Cancer* 92(8): 1372-81

Tsiotos GG, Farnell MB, Sarr MG (1999) Are the results of pancreatectomy for pancreatic cancer improving? *World J Surg* 23(9): 913-9

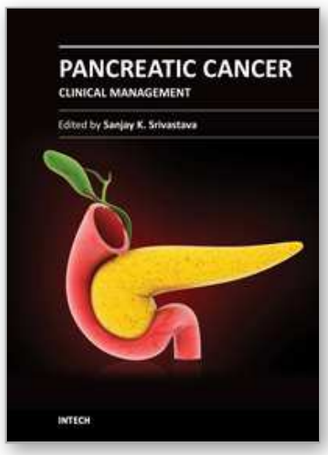
Van Heek NT, De Castro SM, van Eijck CH, van Geenen RC, Hesselink EJ, Breslau PJ, Tran TC, Kazemier G, Visser MR, Busch OR, Obertop H, Gouma DJ (2003) The need for a prophylactic gastrojejunostomy for unresectable periampullary cancer: a prospective randomized multicenter trial with special focus on assessment of quality of life. *Ann Surg* 238(6): 894-902; discussion 902-5

Winter JM, Cameron JL, Campbell KA, Arnold MA, Chang DC, Coleman J, Hodgin MB, Sauter PK, Hruban RH, Riall TS, Schulick RD, Choti MA, Lillemoe KD, Yeo CJ (2006) 1423 pancreaticoduodenectomies for pancreatic cancer: A single-institution experience. *J Gastrointest Surg* 10(9): 1199-210; discussion 1210-1

Wood HE, Gupta S, Kang JY, Quinn MJ, Maxwell JD, Mudan S, Majeed A (2006) Pancreatic cancer in England and Wales 1975-2000: patterns and trends in incidence, survival and mortality. *Aliment Pharmacol Ther* 23(8): 1205-14

Xie DR, Liang HL, Wang Y, Guo SS, Yang Q (2006) Meta-analysis on inoperable pancreatic cancer: a comparison between gemcitabine-based combination therapy and gemcitabine alone. *World J Gastroenterol* 12(43): 6973-81

Yip D, Karapetis C, Strickland A, Steer CB, Goldstein D (2009) Chemotherapy and radiotherapy for inoperable advanced pancreatic cancer. *Cochrane Database Syst Rev*(4): CD002093



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This book covers pancreatic cancer risk factors, treatment and clinical procedures. It provides an outline of pancreatic cancer genetic risk factors, biomarkers and systems biology for the better understanding of disease. As pancreatic cancer suffers from lack of early diagnosis or prognosis markers, this book encompasses stem cell and genetic makers to identify the disease in early stages. The book uncovers the rationale and effectiveness of monotherapy and combination therapy in combating the devastating disease. As immunotherapy is emerging as an attractive approach to cease pancreatic cancer progression, the present book covers various aspects of immunotherapy including innate, adaptive, active, passive and bacterial approaches. Management of anesthesia during surgery and pain after surgery has been discussed. Book also takes the reader through the role of endoscopy and fine needle guided biopsies in diagnosing and observing the disease progression.

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