

Survival following pancreatic carcinoma: a follow-up study of all cases recorded in Malmö, Sweden, 1977–1991

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Background The aim of this follow-up study was to assess whether there has been any increase in the percentage of patients offered attempted curative surgery for pancreatic carcinoma and whether the overall survival rate has improved, during the time period 1977–1991.

Methods Details of new cases of pancreatic carcinoma arising in the population of Malmö during the study period were retrieved from the Local Tumour Register in Lund, Sweden. In all, 740 patients were found; 575 of these were diagnosed before death. Kaplan–Meier analysis was used to calculate overall survival rates, and Cox regression analysis was used to assess survival in relation to year of diagnosis after adjustment for sex, age at diagnosis and stage of disease.

Results Cytological or histopathological evidence of the disease was given in 95 per cent of cases. The overall 5-year survival rate was 0.5 per cent (three of 575). Curative surgery was attempted in 24 patients (4.2 per cent); the proportion undergoing curative surgery increased in the last part of the study. Two of the 24 patients in this group survived for 5 years.

Conclusion The prognosis in pancreatic carcinoma remains dismal. Attempted curative surgery still is the only hope for cure, but the group of patients that can be offered this possibility is very limited. In this study, an increase was found in the proportion of patients who were offered attempted curative surgery, but there was no statistically significant increase in the 5-year survival rate following surgery.

The high survival rates, given by several follow-up studies of patients operated on for pancreatic carcinoma, may be interpreted as evidence of an improved prognosis^{1–3}. Other studies have, however, presented results indicating that no or extremely few patients can be cured by surgery^{4–7}.

The objective of this study on pancreatic carcinoma from Malmö University Hospital, Sweden, was to assess whether there had been any increase in the percentage of patients offered attempted curative surgery and whether the overall survival rate improved during the time period 1977–1991.

Patients and methods

Few patients were offered attempted curative surgery before the end of the 1970s, and therefore the period 1977–1991 was chosen for study. This also permits an actual 5-year follow-up time. The study comprised all individuals belonging to the Malmö population who had carcinoma of the pancreas diagnosed during the period, as reported to the Local Tumour Register for Southern Sweden, in Lund. Reporting of cancer cases is compulsory, and is done by the surgeon or physician at the hospital, or by the local GP, as well as by the pathologist.

Of 740 reported carcinomas, 575 were diagnosed before death. Only pancreatic adenocarcinomas judged to be of ductal origin were included. The city of Malmö had a population that ranged between 229 107 and 240 220 during the study interval. The University Hospital is the only hospital in Malmö for admission of patients with somatic diseases, and so all patients with pancreatic carcinoma were seen by the surgeons there. All cytological and histopathological examinations, as well as autopsies, were performed at the Department of Pathology. During the 1970s and 1980s the clinical autopsy rate in the city was 65 per cent and in carcinoma cases it was 80 per cent or

higher^{8,9}. The material was entirely unselected. Three patients referred from outside Malmö were operated on in the early years of the study and were excluded. No other patients with pancreatic carcinoma were referred to this hospital from outside the city. No patients from Malmö were identified who were treated surgically outside the city. All cases have been followed from the time of diagnosis, as reported to the Local Tumour Register, until death or the end of 1996. No case was lost to follow-up.

To verify the diagnosis in all patients with pancreatic carcinoma surviving more than 2 years ($n = 19$), hospital charts including results from cytological and histopathological examinations and/or autopsy records were retrieved. All patients who had been operated on with attempted radical surgery ($n = 24$) were identified, and their charts were retrieved and scrutinized to verify that the operation was actually done with curative intent. This was true for all patients; these cases have already been reported in part¹⁰.

Statistical analysis

The Kaplan–Meier method¹¹, with the generalized Wilcoxon rank sum test, was used for the computation of survival in relation to time at diagnosis, divided into three 5-year periods, and in relation to attempted curative surgery. Cox's proportional hazards model was used to estimate the probability of survival after attempted curative surgery during the two latest 5-year periods after adjustment for sex, age at diagnosis and stage of disease¹².

Results

During the 15-year study period, 740 patients with pancreatic adenocarcinoma were reported to the Local Tumour Register for Southern Sweden. One hundred and sixty-five patients (22.2 per cent) were diagnosed at autopsy. In 114 (69.1 per cent) of these, the underlying cause of death, according to death certificate, was pancreatic carcinoma.

Paper accepted 9 June 1998

was not done owing to a severe inflammatory reaction in the surrounding tissues. The specimen has been re-evaluated and the diagnosis confirmed.

more^{7,15,17}. The main reason for the difference is probably that material in the present study was entirely unselected. The local or national attitude to resectional surgery may also be more conservative, and may be reflected in lower resection rates.

The median age of the 575 patients diagnosed while alive was 72 (range 38–96) years. In 411 (71.5 per cent) of these, the diagnosis was based on histopathology, in a further 138 (24.0 per cent) on cytology and in the remaining 26 (4.5 per cent) the diagnosis was made by ultrasonography, computed tomography (CT) or surgical exploration without a cytological or histopathological examination.

For the whole cohort of 740 patients, there was no difference in survival between the 5-year periods (Fig. 1) (cases identified at autopsy were included and given a fictive survival of 0.1 month). Patients selected for attempted radical surgery were younger at diagnosis and survived longer than those treated by palliative surgery or no surgery at all (Table 1). The resection rate during the first 8 years of study was 1.9 per cent (five of 261) and in the last 7 years it was 6.1 per cent (19 of 314) ($P < 0.05$). The 19 patients who survived more than 2 years all had

cytological or histopathological confirmation of adenocarcinoma of the pancreas. Eight of these were operated on with curative intent; the rest were generally treated with bypass surgery.

Palliative operations (biliary or gastric bypasses) were undertaken in 281 patients (48.9 per cent). In 95 per cent of the operated cases this meant a biliodigestive shunt and/or a gastrojejunostomy. Laparotomy without additional procedures was performed in five patients (0.9 per cent). Endoscopic stenting, in patients jaundiced as a result of pancreatic tumour obstructing the common bile duct, was not in regular use at this time. During the 3 years preceding 1991, an endoscopic stent was used in five patients.

Twenty-four patients (4.2 per cent) were selected for attempted curative surgery and underwent a Whipple procedure ($n = 21$); in one case a total and in two a distal pancreatectomy was performed. The presenting symptoms for these patients are shown in Table 2. Only one patient was operated on in the first time period, eight in the second and 15 patients in the third. All had findings of ductal adenocarcinoma (Table 3), in 22 cases in the head and in two in the tail of the pancreas¹³. All survived for 30 days. One patient died after 52 days and several reoperations. Twenty-two of the 24 patients died within 5 years, all from recurrent disease; in 16 patients there was locoregional recurrence and 15 had distant

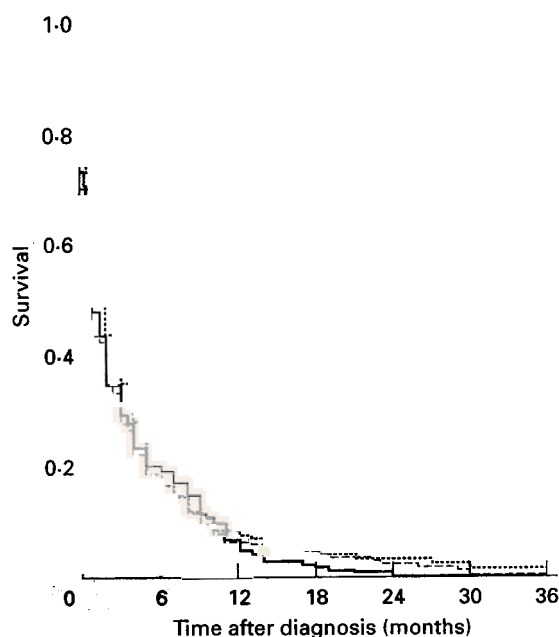


Fig. 1 Kaplan-Meier survival curves, illustrating survival for 740 new patients with pancreatic carcinoma diagnosed in 1977–1981 (—), 1982–1986 (---) and 1987–1991 (.....). The number of patients remaining alive and in the study at the beginning of each 6-month period is shown below the graph

Table 1 Age and survival related to mode of treatment

	Age (years)	Survival (months)
Attempted radical surgery ($n = 24$)	60 (42–74)	11 (2–109)
Palliative or no surgery ($n = 551$)	72 (38–96)	2 (0–71)
Cases identified at autopsy ($n = 165$)	80 (60–101)	
All cases ($n = 740$)	74 (38–101)	(0–109)

Values are median (range)

Table 2 Presenting symptoms in patients undergoing pancreatic resection. Symptoms were present for a median of 1 (range 0.5–9) months

Symptom	No. of patient
Jaundice	18
Pain	12
Nausea and vomiting	3
Diarrhoea	2
Weight loss	8

Eighteen patients were admitted on an emergency basis

Table 3 Tumour grade, tumour node metastasis classification and stage in patients who had a pancreatic resection

	No. of patients
Tumour grade	
High	
Intermediate*	
Low	
TNM classification†	4
T ₁ N ₀	
T ₁ N ₁	
T ₂ N ₀	
T ₂ N ₁	
T ₃ N ₀	
T ₃ N ₁	
T ₄ any N	
Stage‡	
I	
II	
III	

* Intermediate differentiation; † Union Internacional Contra la Cancrum tumour node metastasis (TNM) classification, 1987; ‡ stage I, T₁T₂N₀M₀; stage II, T₃N₀M₀; stage III, any T₁N₁M₀. One patient (stage I/T₂N₀) died in hospital 52 days after operation. The two 5-year survivors had stage I(T₂N₀) and stage III(T₁N₁) disease

metastases. The diagnosis of recurrent disease was based on autopsy in 13 cases, and in the remaining nine on CT or ultrasonography, often together with fine-needle aspiration biopsy. Median survival time was 11 months. Two patients, at the time of writing aged 59 and 81 years, are still alive and free from disease 8 and 9 years after resection; one of these patients had a distal carcinoma.

The 5-year survival rate for patients operated on between 1987 and 1991 was not statistically significantly different from that of those undergoing operation between 1982 and 1986 (Fig. 2) (relative risk 0.5 (95 per cent confidence interval 0.2–1.4); $P = 0.2$).

For all patients diagnosed while alive, the 5-year survival rate was 0.5 per cent (three of 575); for the entire cohort, i.e. including the cases detected at autopsy, it was 0.4 per cent (three of 740).

Among those not operated on, or not operated on for cure, three patients (0.5 per cent) lived longer than 3 years and one is still alive 6 years later. This patient had an adenocarcinoma *in situ* in a surgical biopsy. Resection was not done owing to a severe inflammatory reaction in the surrounding tissues. The specimen has been re-evaluated and the diagnosis confirmed.

Discussion

Pancreatic carcinoma was in this study associated with an overall 5-year survival rate close to zero. From this perspective the survival rate of 8 per cent (two of 24) in patients who were offered attempted curative surgery may be considered a great therapeutic achievement.

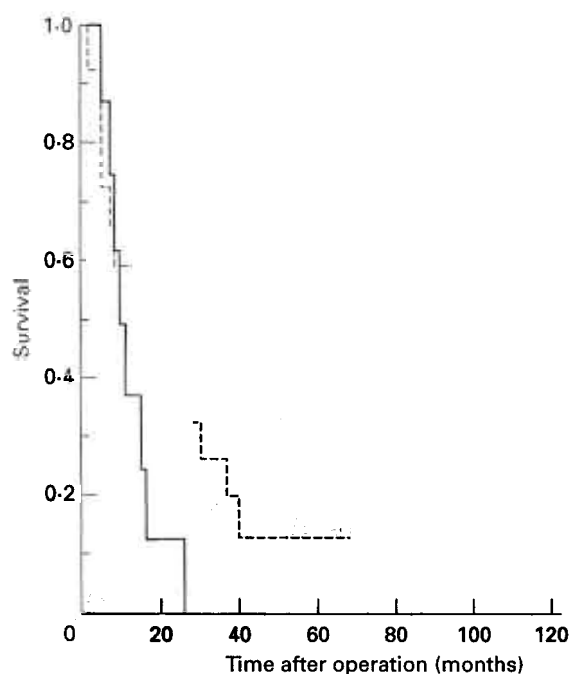


Fig. 2 Kaplan-Meier survival curves, illustrating survival following attempted radical surgery for pancreatic carcinoma for the periods 1982-1986 (—) and 1987-1991 (---). The number of patients remaining alive and in the study at the beginning of each 20-month period is shown below the graph

These figures are, however, far from the 25–55 per cent survival rates reported in other follow-up studies⁷. It is likely that these discrepancies do not reflect differences in therapeutic success, but rather the selection of cases used for assessment of survival rates. In this study all cases of pancreatic carcinoma during the time period 1977–1991 were included. As the university hospital is the only referral unit for somatic disorders and as the autopsy rate during the study period was almost 70 per cent, the authors are confident that the patients included can be considered a representative sample of the population with pancreatic carcinoma in Malmö.

The low number of survivors in this study was not the result of inadequate surgical technique or perioperative care. The 30-day mortality rate was zero and one patient died in hospital following resection; these figures are comparable to results from units doing pancreatic surgery on a regular basis^{14–16}.

The resection rate in this study was 4.2 per cent, whereas the usual reported figure is around 10 per cent or more^{7,15,17}. The main reason for the difference is probably that material in the present study was entirely unselected. The local or national attitude to resectional surgery may also be more conservative, and may be reflected in lower resection rates.

The lack of significant differences in 5-year survival rates for patients operated on in the periods 1982–1986 and 1987–1991 must be considered in relation to the small numbers of patients.

The high rate of local recurrence is well documented, and is probably due to local spread of the tumour before diagnosis^{18,19}. Adjuvant treatment directed towards the peripancreatic region could possibly improve survival^{20–22}. The large multicentre trial, being conducted by the European Study Group of Pancreatic Cancer, may clarify the role of adjuvant treatment²³. However, an adjuvant treatment will have to be extremely effective for that alone to result in an improvement on the dismal survival figures of today. A reduced death rate of 30 per cent with adjuvant treatment has been indicated for colonic cancer²⁴. A corresponding effect in pancreatic carcinoma would, with the present resection rate, result in a change of survival rate from 8 per cent to about 30 per cent in patients operated on with curative intent. In actual numbers this is equal to six more 5-year survivors, an increase from two to eight.

Is the present resectability rate low, or is it representative of the true rate in an unselected population of carcinoma cases? A large epidemiological study on the outcome of nearly 14 000 unselected cases of pancreatic carcinoma in the West Midlands, UK, recently reported a resection rate of 2.6 per cent²⁵. There are considerable differences between the two studies. The age-standardized incidence of the disease was 10.1 and 8.4 per 10⁵ for men and women respectively in the Midlands²⁵. In Malmö the incidence was 20.6 and 13.4 per 10⁵ respectively during the 1980s²⁶. The number of patients included in the Swedish study was substantially lower than in the UK study, but the diagnosis was to a high degree verified by cytological (24.0 per cent) or histological (71.5 per cent) examination. Despite these differences, both studies arrived at the same rate of palliative procedures, as well as similar resection and survival rates. As in this study, the British group also found an increased 5-year survival rate after resection in the most recent period.

Resection rates in unselected patients with pancreatic carcinoma do not seem to be higher than 5–10 per cent,

and the 5-year survival rate after attempted curative surgery is less than 10 per cent. The resection rate during the last 7 years of the present study was not far from the 7 per cent reported from a Norwegian national study²⁷. This means that, up to 1991, one in 200 patients with pancreatic carcinoma was 'cured' by surgery, at best. Low resection rates may be due to a nihilistic view of the possibilities of surgery, but the authors believe that resection rates over 10 per cent are probably the result of patient selection.

In this urban population, the proportion of patients with pancreatic carcinoma who may be offered attempted curative surgery has increased from 1.9 per cent in 1977–1984 to 6.1 per cent in 1985–1991. The seemingly improved 5-year survival rate was not statistically significant in the Cox analysis after adjusting for sex, age at operation and stage of disease. It must be emphasized, however, that this part of the study was based on a very limited number of patients.

Acknowledgements

This study was supported by grants from the Swedish Medical Research Council project no. 17X-8305 and the Foundations for Research at Malmö University Hospital.

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