

Improved Survival in Small Pancreatic Cancer

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Key Words

Pancreatic cancer · Small pancreatic cancer

Abstract

Background: Although the incidence of pancreatic cancer is relatively low compared with other tumors (2.4%), the death rate is high. Tumor detection and treatment at an early stage is necessary to improve the poor prognosis of patients, as is demonstrated by some reports showing a 5-year survival rate varying between 19 and 41% for patients undergoing radical pancreatectomy with the highest survival in patients with small tumors.

Methods: In our study we retrospectively reviewed the histologic and demographic data of 596 patients who were admitted to the surgical units of the Careggi Hospital (University of Florence-AOC of Florence) between 1988 and 1994 with the incoming diagnosis of pancreatic cancer. **Results:** Results are reported as the mean \pm standard deviation. The postoperative survival rate was calculated by the Kaplan-Meier method and statistical analysis was performed by the log rank test (significance $p < 0.05$). 247 patients had surgery, 110 with a curative intent. Postoperative mortality was 5.45%. The crude 5-year survival rate for patients who underwent curative surgery was 16.36% (18 patients), but for patients with

small lesions confined to the pancreas (T1N0M0, 29 patients) this was even 31.03% (9 patients; $p < 0.01$, χ^2 test). **Conclusions:** Our results indicate that it seems reasonable to consider these cancers as 'small', with survival reported in literature from 35 to 41%, so they probably represent the only curable condition at the present time.

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Pancreatic cancer is one of the most significant clinical challenges at the beginning of the millennium. Despite its relatively low incidence compared with other tumors (2.4%) [1, 2], the death rate is very high. Each year 28,000 cases occur in the United States, accounting for 26,000 deaths and making this cancer the fourth leading cause of death [3–5]; the fifth in Japan [6] with annual increase in death rate [7], and the sixth in Italy [8]. Throughout the world this cancer accounts for well over 185,000 new cases per year with an incidence ratio of about 0.99 [3]. The peak is found in the seventh to the eighth decades [9]. Five-year survival increased from 1% in the 1960–1963 period to 4–5% in the 1986–1993 [9–12].

Tumor detection and treatment at an early stage seem to be essential in order to improve the poor prognosis of patients. As is demonstrated by some reports [6, 9, 13–19], there is a 5-year survival rate varying between 19 and 41% for patients undergoing radical pancreatectomy with the highest survival in patients with small (≤ 2 cm) tumors confined to the pancreas (N0M0).

Unfortunately, despite technological advances [20–22], a delay in diagnosis remains high. Diagnosis is often

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made when the disease is at an advanced stage, with poor therapeutic opportunities since the diagnostic technologies do not affect the time of patient presentation and hence the stage of the disease.

Early clinical features are vague and nonspecific, often misunderstood by both the patient and the physician; symptoms can be attributed to other common abdominal disorders or even stress-correlated disorders of the gastrointestinal tract.

High-risk groups recently identified by genetic research are still few and confined to rare conditions [23]. Furthermore, neither simple cost-effective nor invasive and highly sensitive tests are presently available on a large scale and at an early stage [24]. Surgical resection remains the main treatment with curative potential.

In our study we retrospectively reviewed the histologic and demographic data of pancreatic cancer patients admitted to the surgical units of Careggi Hospital (University of Florence-AOC of Florence) to assess the impact on survival of surgical extirpation of small lesions, confined to the pancreas, that can be defined as 'early' pancreatic cancer [25].

Materials and Methods

Between January 1988 and December 1994, 596 patients suffering from pancreatic cancer were admitted to the Departments of Surgery of the University of Florence and Azienda Ospedaliera Careggi. Patients with cystadenocarcinoma, tumors of the endocrine pancreas and cancer of the bile duct, duodenum or ampulla of Vater as final diagnosis were excluded from this study. Paraffin-embedded specimens and histopathological data retrieved at the time of surgery were reviewed by the pathologists (G.N. and I.R.) and restaged according to the TNM system (UICC) [26–28]. All the cancers were ductal adenocarcinoma. Preoperative diagnosis and staging was based on the results of laboratory tests and imaging procedures. Tumor size was determined by histologic measurement. Local spread and metastases to the regional lymph nodes were histologically evaluated. Results are reported as mean \pm standard deviation. The postoperative survival rate was calculated by the Kaplan-Meier [29] method and statistical analysis was performed by the log rank test (significance $p < 0.05$) [30]. Statistical analysis of overall survival for 'curative' surgery and surgery of small lesions was performed by χ^2 test. Operative mortality was defined as any death occurring within 30 days after surgery.

Results

There were 375 men and 221 women with a mean age of 65.51 ± 12.17 years for the men and 69.97 ± 10.93 years for the women.

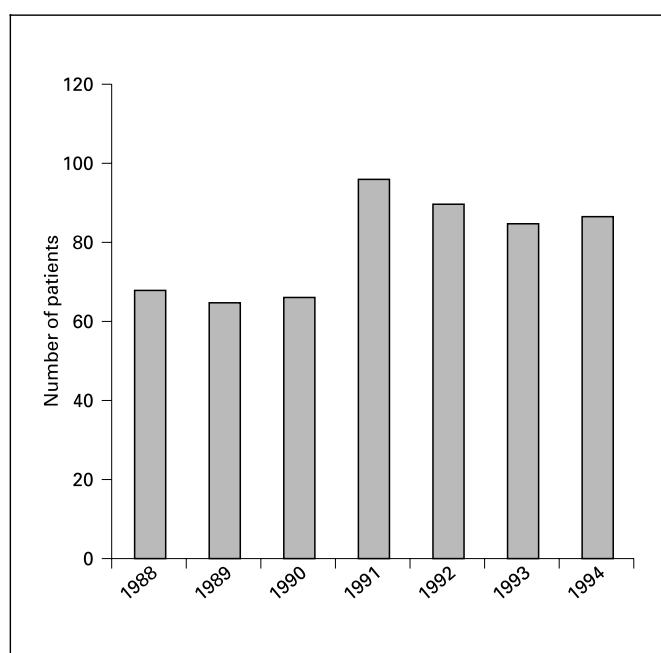


Fig. 1. Pancreatic cancer distribution per year.

Table 1. Stage distribution

Stage	Number of patients
I	95 (17.7%)
II	156 (29.0%)
III	176 (32.8%)
IV	110 (20.5%)

Table 2. Summary of surgical procedures

	n
Surgery with curative intent	
Pancreaticoduodenectomy	51
Left pancreatectomy	23
Total pancreatectomy	36
Total	110
Other surgical procedures	
Exploratory laparotomy	28
Hepaticojejunostomy and other biliary bypass procedures	68
Cholecystectomy	40
Gastric resection	8
Intestinal resection	7
Kherr biliary bypass	15
Gastrojejunostomy	14

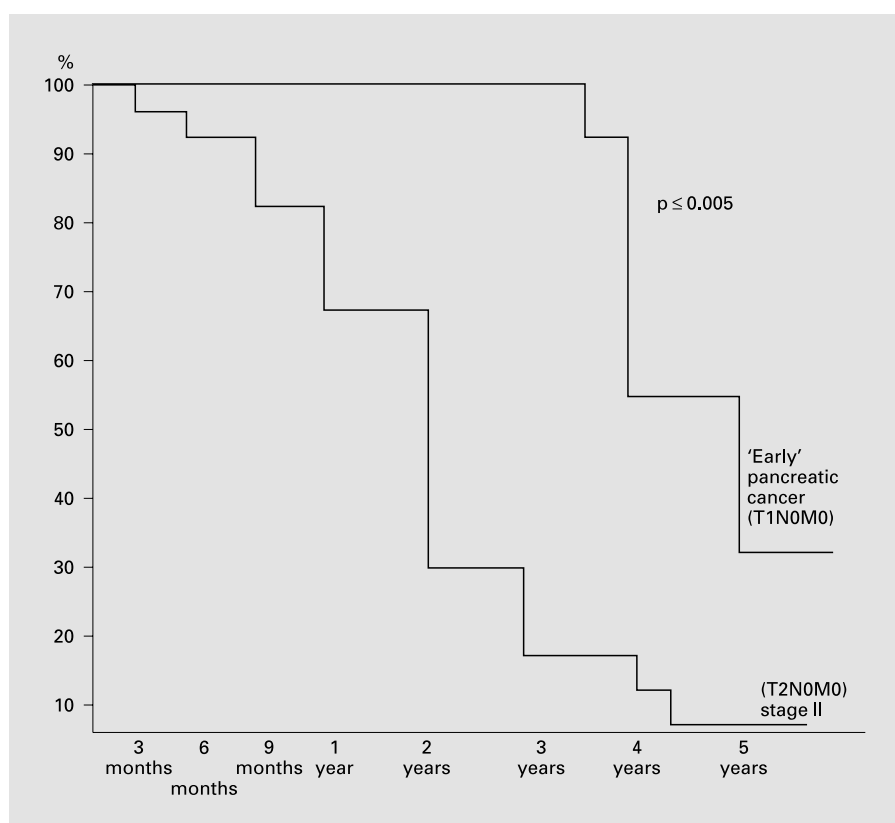


Fig. 2. Actuarial survival for 'early' pancreatic cancer and T2N0M0 stage II.

Table 3. Resected patients: demographics

	Men	Women
Number of patients	67	43
Age, years		
Mean	61.73 ± 12.62	68.27 ± 8.41
Median	64	70
Range	50 (29–79)	34 (45–79)

Table 4. Long-term survivors (T1N0M0)

Survival, years	Number of patients
10	5
9	5
8	6
7	6
6	6
5	9

Data of 59 patients were incomplete and thus excluded from the study. The annual distribution is depicted in figure 1.

The mean delay in diagnosis from initial symptoms was 4.3 ± 0.3 months. The preoperative stage distribution is reported in table 1.

247 patients had percutaneous biliary diversion, palliative surgery and/or adjuvant therapies. 110 patients had surgery with a curative intent (table 2, 3). The postoperative mortality was 5.45%.

The cumulative 5-year survival rate for patients who underwent curative surgery was 15.36% (18 patients), but

for patients with small lesions confined to the pancreas (T1N0M0, 29 patients) it rose to 31.03% (9 patients; $p < 0.01$, χ^2 test).

The actuarial survival of patients operated for curative surgery is depicted in figure 2, where the 2 groups are classified as: (1) 'early' pancreatic cancer (pT1N0M0), and (2) pT2N0M0 and stage II.

Five patients are alive after more than 10 years. The others are reported in table 4.

Table 5. Reports on survival following small lesion resection

Authors	Year	Total patients	Patients studied	Staging system	Small lesions	Survival rate
Tsuchiya et al. [18]	1986	3,315	753	JPS	45	37% (5 years)
Manabe et al. [19]	1988	335	125	JPS	5	37% (4 years)
Cameron et al. [51]	1991	168	95		29	29.7 months of median survival
Niederhuber et al. [34]	1995	17,490	9,715	AJCC	1,826	20% (2 years)
Yeo et al. [39]	1995	208	201		91 (<3 cm diameter)	28% (5 years)
Furukawa et al. [7]	1996	735	31	UICC	13	77.9 (4 years)
Fortner et al. [50]	1996	97	97		12 (<2.5 cm diameter)	33% (5 years)
Sperti et al. [8]	1996	549	113	UICC	20	26% (5 years)
Janes et al. [37]	1996	16,942	14,826	AJCC	2,263	18%
Mosca et al. [33]	1997	513	221	UICC	49	15.9%
Hirata et al. [49]	1997	1,013	1,001	JPS	102	50% (3 years)

Discussion

It is well known that pancreatic cancer is a common and deadly disease that is rarely cured. Review of the past 50 years of surgery reveals dismal results with a minimal impact on survival. Long-term survival in patients with a proven histologic diagnosis is found to be virtually confined to those undergoing tumor resection. Among these, patients with small tumors had a 5-year survival improvement that reached about 35% [31–51] (table 5).

Recently some authors [25] suggested the definition of ‘early’ pancreatic cancer as a small tumor (= 2 cm) confined to the pancreas (NOM0), and supported by the clinical behavior of this type of lesion. However, this encouraging outcome for survival has mainly been reported by surgeons from the Far East, and is derived from a different approach to patients affected by pancreatic cancer [52–54]. In fact the different classification and documentation systems hinder the comparison between institutions and do not allow multicenter analysis. The first classification for pancreatic malignancies was reported in the 1987 TNM classification [55]. In Japan, a different staging system was proposed by the Japanese Pancreatic Society (JPS) in 1986 [56, 57]. Major differences between these two classifications concern local tumor spread and the extent of lymph node involvement. Attempts to re-stage patients postoperatively according to the JPS classification or vice versa have not produced comparable results [58, 59]. Moreover the difficulties in comparing outcomes are the consequence of the lack of a proper defi-

inition of the different surgical techniques and extension of lymph node dissection [60, 61]. With regard to this last aspect, prospective studies have shown no statistical difference in the 5-year survival between traditional and extended lymphadenectomy, although patients with positive lymph nodes had an improved survival in the extended lymphadenectomy group [62–66].

Finally, the different types of classifications imply a difference in tumor staging due to the lack of consensus on the method for pathomorphological examination of the specimens [58, 59, 61].

According to the definition of a recent Consensus Conference, we considered our patients as having been operated by a standard procedure, and only the restaged patients were reexamined according to the UICC classification. In an attempt to overcome the difficulties in restaging all the patients as ‘early cancer’, as reported by Urrutia and Di Magno [25] in 1996, we define a pancreatic cancer as ‘small’ when it is ≤ 2 cm in greatest dimension and limited to the pancreas with no involvement of the lymph nodes that are evaluated for each patient, even if we always consider the operation as a standard one. Since our results are also rather consistent with the survival rate reported in literature (from 35 to 41%), we think it is reasonable to consider these small cancers as ‘early’ as they probably represent the only curable condition.

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