Original article

The significance of the early detection of clinical symptoms in the overall survival of patients with pancreatic cancer

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SUMMARY

In order to identify whether early detection of clinical symptoms of pancreatic cancer may lead to earlier diagnosis and prolonged survival, the overall survival of 62 patients diagnosed with adenocarcinoma of the pancreas in the period January 1994-1996 and followed up until January 2000 was determined by Kaplan Meier analysis. In 25 patients clinical symptoms led the physician to the appropriate laboratory and radiological investigation to the final diagnosis and in the remaining 37 another initial diagnosis was established. Survival was compared between patients with stage IV disease. Median survival in the group of 25 patients where suspicion of pancreatic cancer was implemented earlier was 6.5 months and in those where final diagnosis was delayed was 4 months (p: 0.025). Median delay of the implication of the final diagnosis in the later group of patients was 3 months. Both groups of patients did not differ concerning the disease stage of their patients, being stage IV in the majority of cases. It is concluded that early detection of the clinical symptoms of pancreatic cancer may prolong survival even in patients with stage IV disease.

Key Words: Pancreatic cancer, survival

INTRODUCTION

Pancreatic cancer is a devastating disorder leading to early death accompanied by a poor quality of life for the majority of patients. This is a reality even in cases

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when initial diagnosis reveals the absence of metastasis.[1] Recent studies on the 5-year survival of patients with pancreatic cancer conclude that the over-time documented increase of the survival of these patients is probably attributed to the more accurate methods of diagnosis than to the amelioration of the methods of management.[2] If this is the case, then the early recognition of the primary clinical manifestations of the pancreatic cancer might contribute considerably to the prolongation of the survival of these patients. In order to verify that hypothesis the present study was undertaken, including mainly patients with stage IV pancreatic cancer, so as to reveal whether early detection might be more important than novel treatment modalities in the overall survival of these cases.

PATIENTS AND METHODS

A total of 62 patients - 40 male and 22 female - aged 69.1 ± 9.8 years were enrolled in the prospective study starting in January 1994 and ending in January 2000. According to its design all patients presenting in our department during the two-year period of January 1994 and January 1996 diagnosed with adenocarcinoma of the pancreas were recorded for all their clinical, laboratory and radiological findings. Diagnosis of pancreatic adenocarcinoma was based on histological findings after needle biopsy of one or several metastatic foci or of tumor sections selected after laparotomy. Patients were also questioned about the exact time period one or several clinical symptoms related to their illness presented, leading them to the initial visit to the doctor. Cancer was staged by the TNM system according to UICC as in other studies[3] and patients were followed up until January 2000 when follow-up stopped and final survival was determined in months. Patients with stage IV disease were subject to chemotherapy.

Patients were then divided into two categories according to the data collected from each one; those where clinical suspicion of cancer of the pancreas was raised leading the patients to the appropriate laboratory and radiological investigation of their illness; and those where no clinical suspicion of their illness was raised and where diagnosis was established later when either symptoms persisted or new symptoms were arisen. In both groups of patients total survival was determined in months and was expressed as the median values for each group of patients. Mean and median survival time were determined and survival plots were designed after Kaplan Meier analysis. Comparisons of the survival times was performed only between patients with stage IV disease by the Mann Whitney rank sum test. Any value of p below 0.05 was considered as significant.

RESULTS

The main clinical symptoms and laboratory and radiological findings of patients enrolled in the study are shown in Table1. It should be mentioned that these symptoms refer to those with which patients presented on their first visit. Overall survival of the group of patients where an early clinical suspicion of pancreatic carcinoma was raised was of a median value of 6.5 months ranging between two and 66 months. Overall survival of the group of patients without an early clinical suspicion of pancreatic carcinoma was of a median value of 4.0 months ranging between two and 26 months. Comparisons between both groups of patients are given in Table 2 and their survival curves in Figure 1.

Table 1. Main clinical symptoms, laboratory and radiological findings of patients enrolled in the study

	Number (%) of patients	
	Early Clinical Suspicion	No Clinical Suspicion
Clinical symptoms		
Epigastric pain	12 (48.0)	19 (51.4)
Weight loss	12 (48.0)	19 (51.4)
Jaundice	12 (48.0)	15 (40.5)
Nausea	4 (16.0)	9 (24.3)
Vomiting	7 (28.0)	9 (24.3)
Ascites	5 (20.0)	3 (8.1)
Fever	3 (12)	5 (13.5)
Laboratory findings		
Elevated transaminases	15 (60.0)	9 (24.3)
Elevated γGT and alkaline phosphatase	18 (72.0)	34 (91.9)
Hyperbilirubenemia	16 (64.0)	11 (29.7)
Hyperglycemia	8 (32.0)	15 (40.5)
Elevated Ca 19-9 (>39 IU/ml)	11 (44.0)	18 (48.6)
Radiological findings		
Ultrasound findings		
• Head mass of decreased echogeny	8 (32.0)	16 (43.2)
• Hypodense mass of the tail	0 (0)	1 (2.7)
• Biliary duct dilatation	1 (4.0)	3 (8.1)
• Liver foci of decreased echogeny	4 (16.0)	4 (10.8)
CT scan findings		
• Hypodence mass of the head	11 (44.0)	20 (54.0)
• Hypodense mass of the body	0 (0)	6 (16.2)
• Hypodense mass of the tail	1 (4.0)	1 (2.7)
• Hypodense liver foci	12 (48.0)	6 (16.2)
• Enlargement of mesenteric lymph nodes	6 (24.0)	3 (8.1)

Table 2. Survival of patients where clinical suspicion of pancreatic cancer occurred early compared to those where no clinical suspicion of pancreatic cancer was raised

	Early Clinical Suspicion of Pancreatic Cancer	No Clinical Suspicion of Pancreatic Cancer	
	Number of patients		P
Number of patients in each group	25	37	
Stage II	3 (12.0)	0 (0)	0.048
Stage III	2 (8.0)	2 (5.4)	NS
Stage IV	20 (80)	35 (94.6)	NS
Initial Diagnosis			
Pancreatic Cancer	25 (100)	9 (0)	
Peptic Ulcer	0 (0)	19 (51.3)	
Diabetes Mellitus	0 (0)	7 (18.9)	
Lumbar Pain	0 (0)	4 (10.8)	
Median Delay of Start of Follow-Up	1 month	1.4 months	NS
Start of Follow-Up Median Delay in Final Diagnosis	0 months	3 months	<0.001
Median Survival from Presentation of Symptoms	6.5 months	4.0 months	0.025

DISCUSSION

Cancer of the pancreas is accompanied by poor prognosis which might be attributed to the lack of clinical findings in the early stages of the disease; symptoms usually appear in the late stages of pancreatic cancer.[4] Recent findings indicate that the prolonged survival of patients with malignancies today, compared to the past, is mainly attributable to the improvement of diagnostic techniques[2] and not to the improvement of therapeutic modalities. On that basis the present study aimed to evaluate the significance of the early detection of clinical symptoms in the overall survival of patients with adenocarcinoma of the pancreas.

The study was conducted in a prospective trial involving a total of 62 patients, the majority with stage IV disease (Table 2). Among those patients, median survival was 4 months whenever no early clinical suspicion occurred and 6.5 months whenever an early clinical suspicion was raised (Figure 1). It is considered that overall survival of patients with pancreatic cancer is significantly greater in patients without metastasis either in lymph nodes or in solid organs.[5] The existence of metastatic foci does not appear to influence overall prognosis in the present study since among the total number of 62 patients enrolled, only three patients presented without any metastasis at all. However difficult might be to change the overall prognosis of a malignant neoplasm only by its early detection; especially in the field of metastasis it should be born in mind that the real importance of this median prolongation of survival of 2.5 months is questionable.
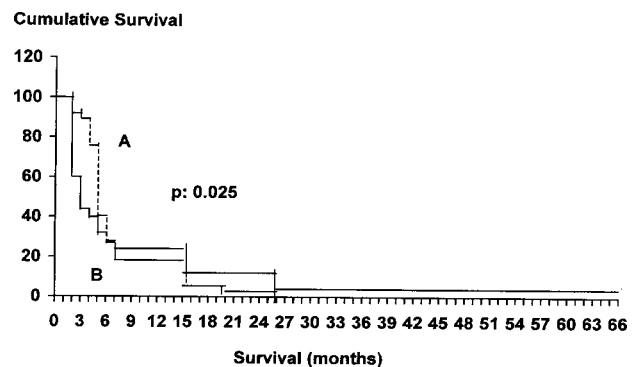

Figure 1. Kaplan Meier survival curves of patients with adenocarcinoma of the pancreas A) where physicians performed an early clinical suspicion of the final diagnosis; and B) where diagnosis was delayed due to misdiagnosis of early clinical findings (dashed line). Differences were statistically significant (p: 0.025)

Results revealing a statistically significant difference in the overall survival of these patients (Table 2) might be explained by the fact that their therapeutic management was immediately initiated contrary to the rest of patients where median delay in the diagnosis and the subsequent start of treatment was three months. It should be emphasized that the overall survival of patients suffering mainly from stage IV disease with delay in the diagnosis is equal to the survival found in larger series of patients with stage IV cancer of the pancreas.[6]

The initial diagnosis in the majority of cases where

diagnosis was delayed was either peptic ulcer or diabetes mellitus easily explained by the symptoms of epigastric pain, nausea and vomiting and the laboratory finding of hyperglycemia (Table 1). However, symptoms of weight loss and jaundice seem to contribute to the early diagnosis of the disorder.

The presented data seem to accentuate the significance attributed by other authors to the early detection of pancreatic cancer in the prolongation to the survival[2], even in cases where solid organ metastasis occur. However early evaluation of clinical symptoms is mainly based on primary care physicians giving emphasis to their needs for further education.[7]

REFERENCES

1. Paulino AC, Latona C. Unresectable adenocarcinoma of the pancreas: patterns of failure and treatment results. Cancer Invest 2000; 18:309-313.
2. Welch HG, Schawrtz LM, Woloshin S. Are increasing 5-year survival rates evidence of success against cancer ? JAMA 2000; 14:2975-2978.
3. Bakkenvold KE, Kambestad B. Staging of carcinoma of the pancreas and ampulla of Vater. Tumor (T), lymph node (N) and distant metastasis (M) as prognostic factors. Int J Pancreatol 1995; 17;249-259.
4. Furikawa H, Okada S, Saisho H, Ariyama J, et al. Clinicopathologic features of small pancreatic adenocarcinoma. A collective study. Cancer 1996; 78:986-990.
5. Banassai G, Mastrorilli M, Quarto G, Cappiello A, et al. Factors influencing survival after resection for ductal adenocarcinoma of the head of the pancreas. J Surg Oncol 2000; 73:212-218.
6. Mohiudn M, Rosato F, Schuricht A, Barbot D, et al. Carcinoma of the pancreas-the Jefferson experience 1975-1988. Eur J Surg Oncol 1994; 20:13-20.
7. Garcia AA, Egner JR. Pancreatic cancer and primary care providers. Cancer Invest 1995; 3:37-41.