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Pancreatic Cancer – Clinical Course and Survival

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1. Introduction

The incidence of pancreatic carcinoma varies from 6-20/100.000 in different countries and ethnic groups, but is considered to be on the average 10/100.000 (Gudjonsson 1987) and causes a significant economic burden on health resources (Gudjonsson 1995, Du 2000).

Cancer of the pancreas is the 13th in frequency in the USA but fourth most frequent cause of death from cancer (Jemal 2010) fifth most frequent cause of death in Japan and sixth in China.

Adenocarcinoma constitutes 90% of pancreatic malignancies. Only 50% of patients in tumor registries had histologic confirmation (Gudjonsson 1987).

The cause of pancreatic cancer is unclear but it is more frequent among cigarette smokers. Chronic pancreatitis leads to increased frequency.

2. Genes

Mutations in K-ras genes are found in up to 90% of cases of cancer of the pancreas but are not specific and are also found in patients with chronic pancreatitis. The suppressor genes p16 and p53 are inactivated and DPC4 deleted in 50% of cases of pancreatic cancer. (Cowgill 2003).

3. Clinical features

The disease is slightly more frequent among males than females.

Patients may occasionally be under thirty years of age. Forty percent are between 60-70 years. Thirty percent are between 50-60 years old and twenty percent between 70-80 years old (Gudjonsson 1987).

4. Clinical features

Majority of patients complain of weight loss which is on the average 10 kg. Most complain of pain, which may be deep seated, in a third of patients the pain radiates to the back, a fifth experience relief by bending forward, and 10-15% it is worsened with eating.

Anorexia may be present in half of patients. A third may complain of vomiting. A third complain of acholic stools and dark urine. One in four may report jaundice (Gudjonsson 1987).

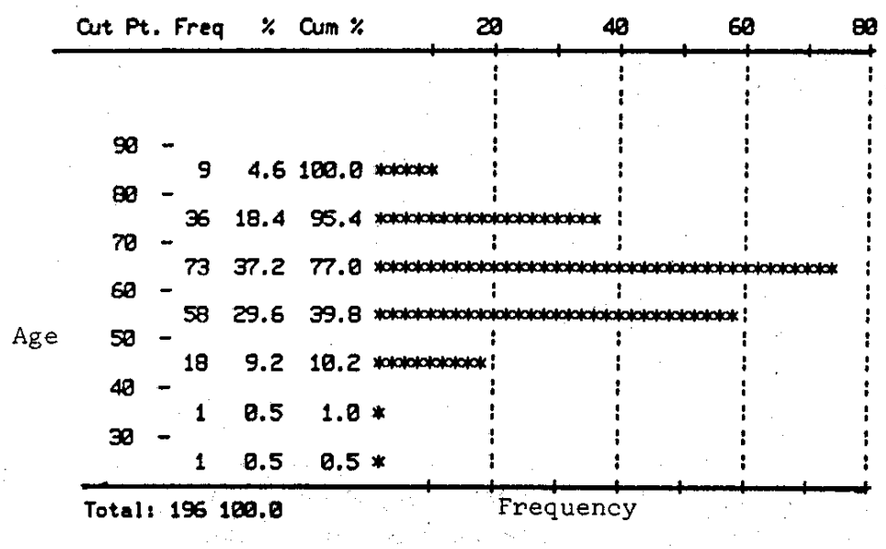

Fig. 1. Age distribution.

Duration of symptoms is variable but 40% have had symptoms less than 1 month, 20% 2 months and 10% 3 months.

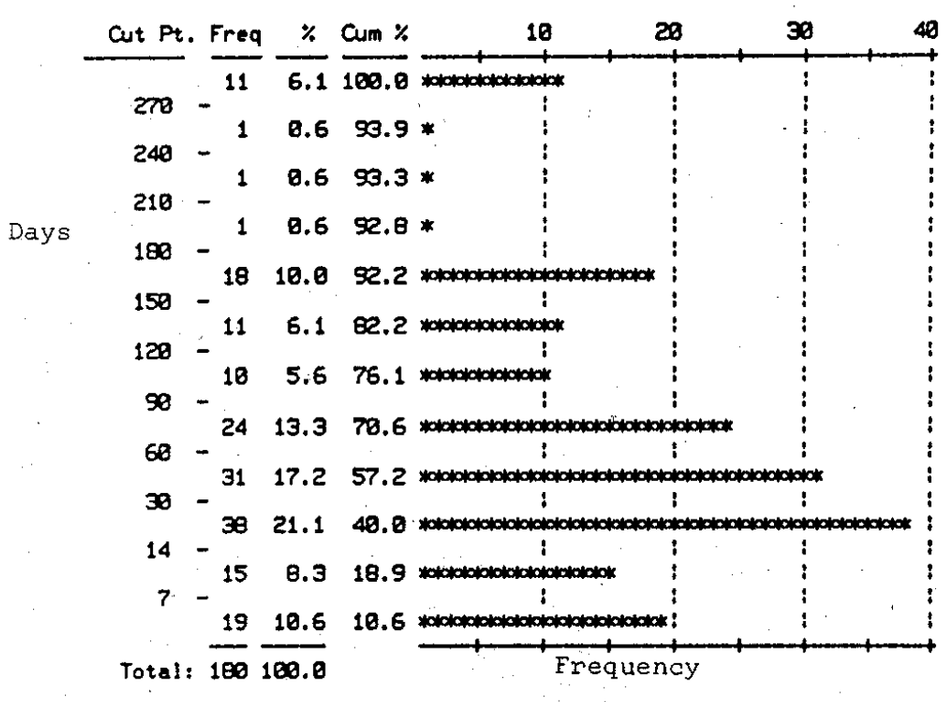

Fig. 2. Duration of symptons.

5. Physical findings

Hepatomegaly may be present in over 50% of patients, 40% may have clinical jaundice, blood in stool may be found in one in four, abdominal mass found in one in five and ascites in more than one in ten.

6. Laboratory values

Elevated alkaline phosfatase and gamma GT are the most frequent abnormalities or in close to 80% of patients, while 60% have elevated SGOT.

Fasting hyperglycemia may be found in close to 60% of patients. Hyperbilirubinemia is initially found in approximately 50%, anemia and elevated lipase in a third.

CA 19-9 may be elevated in 80-90% but is mainly of benefit in monitoring the progress of the disease.

7. Differential diagnosis

The main differential diagnosis are gastric pathology, i.e. cancer or ulcers, gallstones, chronic pancreatitis, or ampullary ca.

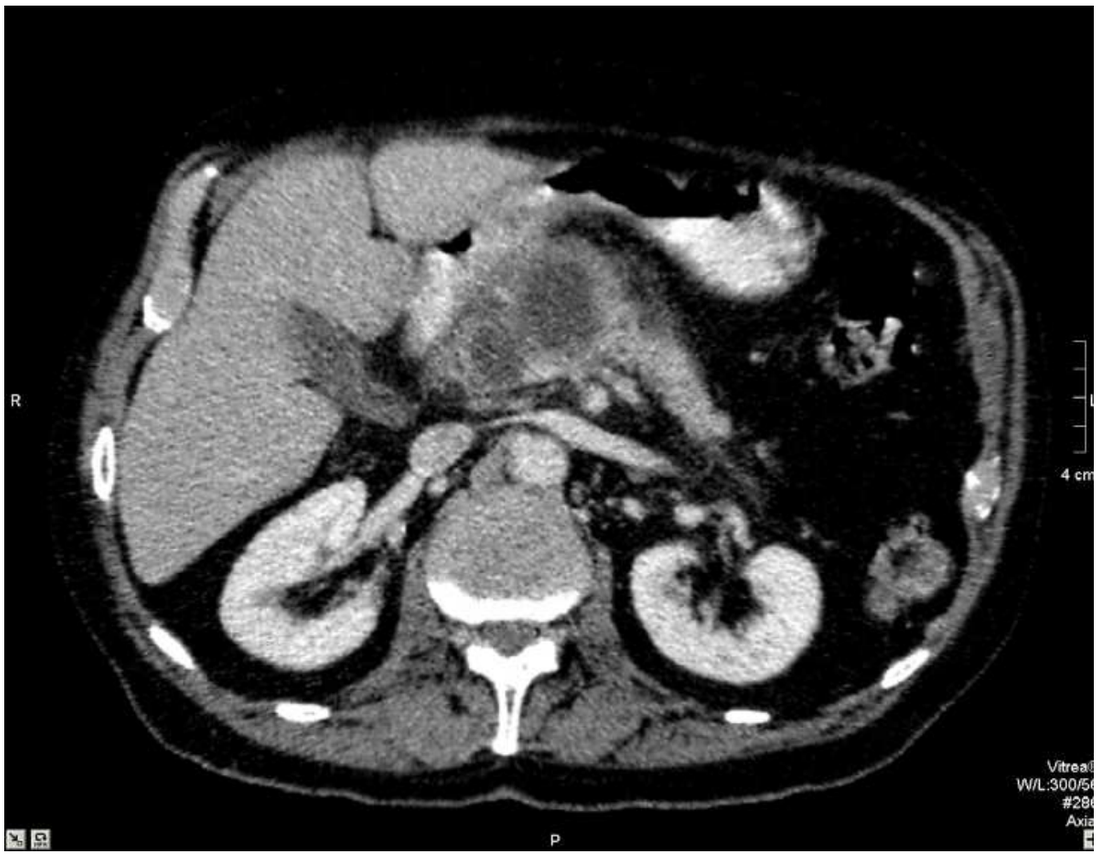

Fig. 3. CT. Pancreatic cancer. Axial view.

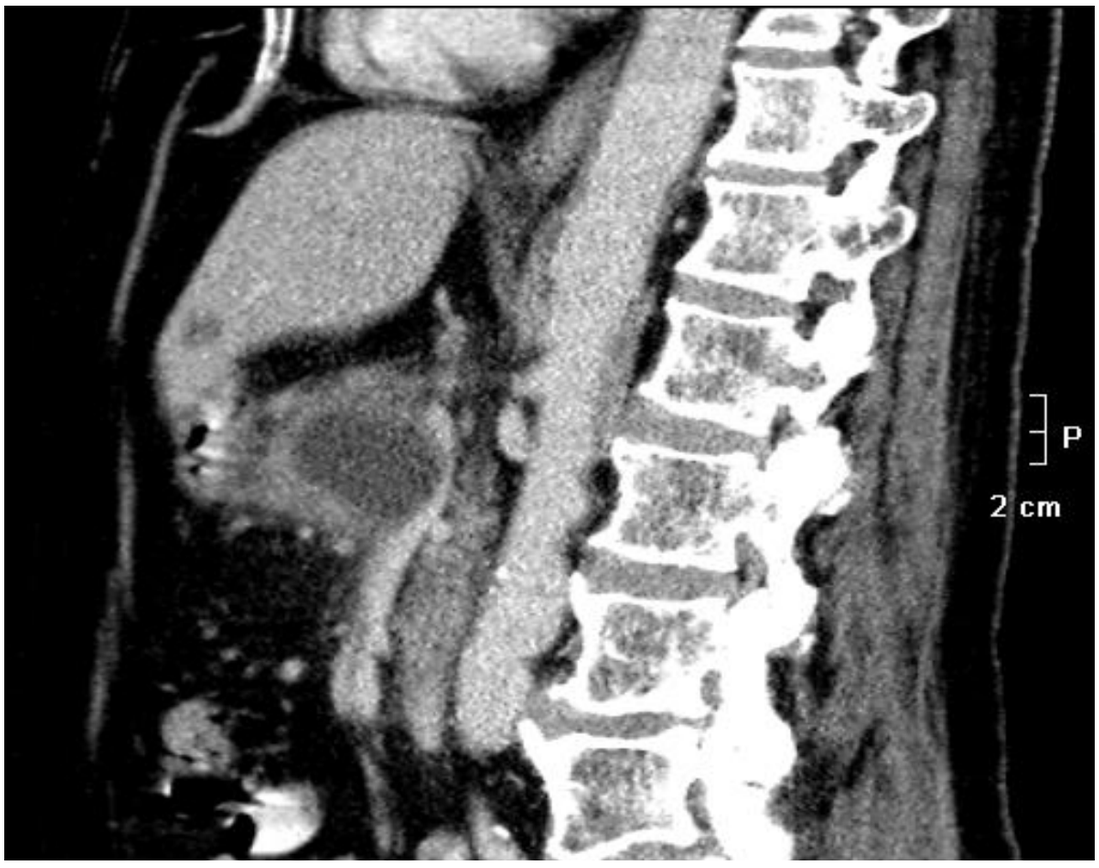

Fig. 4. CT. Pancreatic cancer, Sagital view. Metastases in liver.

8. Diagnostic procedure

In non-jaundice patients it is appropriate to start with upper endoscopy or radiographic upper gastrointestinal studies. In a jaundiced patient ultrasound would establish or rule out gallstones, but also make large tumors and liver metastases obvious. Computerised Tomography, especially the helical form would best confirm the extent of tumor mass and growth beyond the boundaries of the gland. MRI, EUS or ERCP would further delineate the extent of the disease. Angiography and a PET scan are of lesser value (Bipat 2005).

Attempts should be made to obtain tissue diagnosis from the tumour mass or liver by Fine Needle Biopsy guided by CT, US or EUS.

9. Prognosis, statistics

Before doctors embark on attempts at vigorous curative therapy the documented course of this disease and survival statistics so far should be borne in mind (Gudjonsson 1987, 1995).

In 90% of cases it has been found that the disease has progressed beyond the boundaries of the gland to adjacent lymph nodes, liver, omentum, stomach or duodenum.

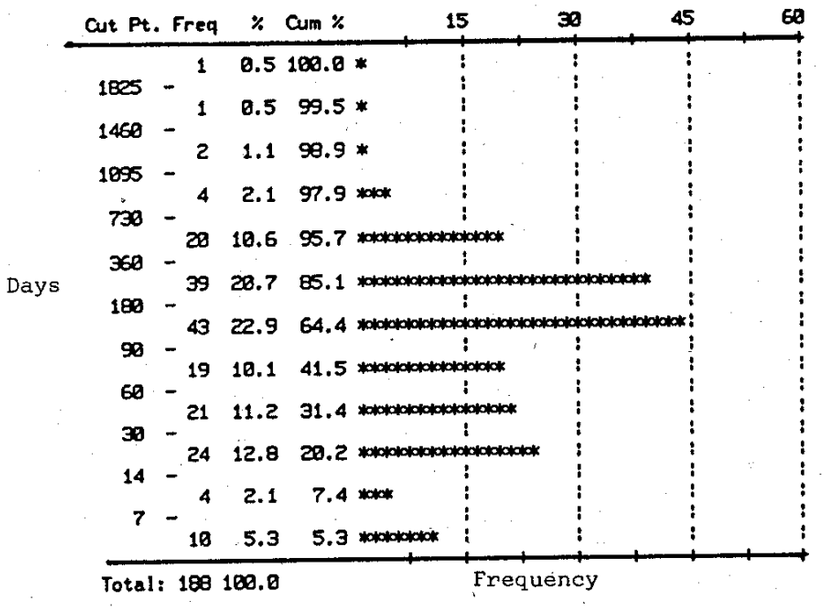

Fig. 5. Survival distribution.

Overall five-year survival is well below 1%. Close to 50% of patients with pancreatic adenocarcinoma will be dead within approximately 3 months, 65-70% within 6 months and 85-90% within 12 months, but an occasional patient may still survive 5 years with or without resection.

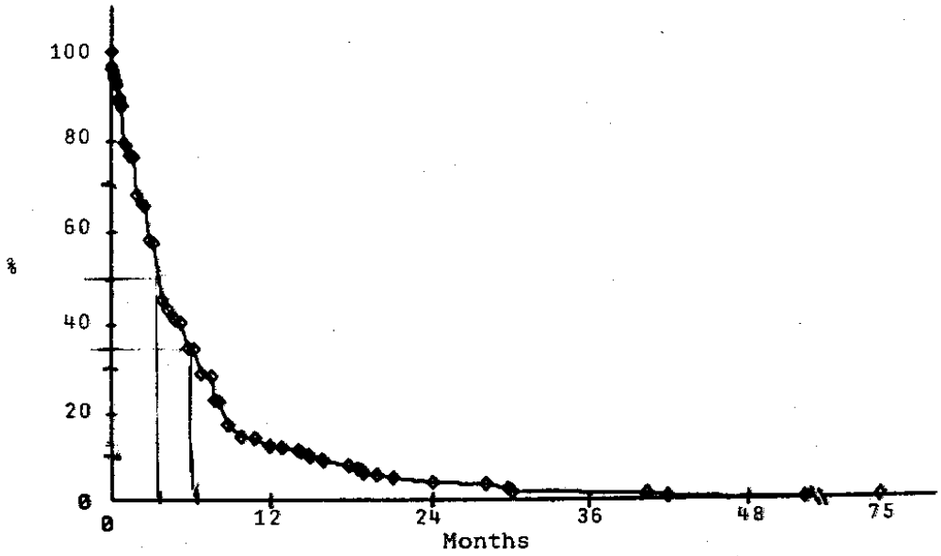

Fig. 6. Survival curve.

The disease will cause pain and obstruction of the biliary and/or gastroduodenal system.

A full 90% of patients will therefore primarily need palliation in the form of relief of pain and relief of the obstruction of the biliary and gastroduodenal system which may occur.

10. Operative findings

Earlier on approximately 80% of patients would have had a surgical laparotomy after imaging studies and in a third of those only a biopsy would have been feasible. Half of those operated on would have had a biliary bypass performed and some of those also a gastric bypass with 5-10% undergoing only a gastric bypass (Brooks 1976).

Now laparoscopy is increasingly used to stage the extent of disease and obtain a biopsy (Nagorney 1999). Either method would reveal that in 2/3 of established cases the tumor would be located in the head of the pancreas and one third in the body and/or tail and have progressed beyond the boundaries of the pancreas. Only about 10% of patients are resectable.

Jaundice will be a significant problem in these patients as the disease progresses. Advances in endoscopic palliative therapy have been significant and stents can now be inserted by skilled hands endoscopically or transhepatically in the biliary system but are associated with complications and primarily have role in those patients who have a short term prognosis (Costamagna 2004).

Many patients will still have laparotomy but are then found to be unresectable. A surgical biliary bypass is then advisable and an operative bypass of the hepatic or common duct is preferred over the gallbladder (Nagorney 1999). If there is no gastric outlet obstruction at that stage the value of a prophylactic gastric bypass is debated but it is well documented that a significant number of those patients who have longer prognosis and initially have only a biliary bypass will later develop gastroduodenal obstruction and will need a second intervention (Gudjonsson 1987).

When a gastroduodenal obstruction occurs later in patients with biliary endoscopic stents, operative gastrojejunostomy may be required, but progress continues in both laparoscopic gastrojejunostomies and also insertion of duodenal stents (Maetani 2004).

Pain is in most cases a major problem. If a laparotomy is performed an intraoperative chemical neurolytic splanchnic block should be done (Lillemoe 1999).

In non-operated patients progress is being made in performing percutaneous, transthoracic (thoracoscopic) splanchnicectomy and endoscopic ultrasonographic splanchnic plexus blocks.

The value of a laparotomy should not be underestimated as by then biopsy, biliary-, gastroduodenalbypass and splanchnic resection can be accomplished (Mann 2009).

Resection is claimed by many to be the only chance of “cure”, but is only applicable in 10% of cases. Survival statistics based only on resected patients with actuarial methods and significant censoring are misleading (Yeo 1995, Gudjonssn 2009).

Resections were initially fraught with a high mortality rate but that has certainly decreased at the relatively few centres with high volume, though morbidity is still high.

The poor results of resections is not surprising considering that even in those who are considered resectable, 20-50% of resection margins are positive for cancer (Willet 1993) and nodes are positive in up to 80% of cases and tumor cells can be found in the bone marrow in

up to 50% of cases (Z'graggen 2001). Biopsy proof should be mandatory before resections are performed. Radical cancer surgery of 6-10 hours duration for chronic pancreatitis is not justified.

An occasional resected patient may certainly survive 5 years but will then most likely be reported over and over in the literature (Gudjonsson 2009).

Half of those who survive 5 years after resections have recurrence of cancer (Conlon 1996). The post op course of resected patients is not smooth and they may need many readmissions to hospitals (Gudjonsson 1995, Reddy 2009). The value of resections as palliation is unproven.

True cure of pancreatic cancer after resection is exceptional.

11. Chemotherapy

Cancer of the pancreas is a very chemoresistant disease. Gemcitabine and 5 fluoruracil have been used in different forms in numerous trials of resected and nonresected patients and may add to quality of life and prolong life and exceptionally contribute to 5-year survival (Neoptolemos 2004).

Radiation therapy has been used pre- intra- and postoperatively in various forms alone or in conjunction with chemotherapy but has not had any significant effect on survival.

Novel diagnostic and therapeutic approach is needed (Yokoyama 2009).

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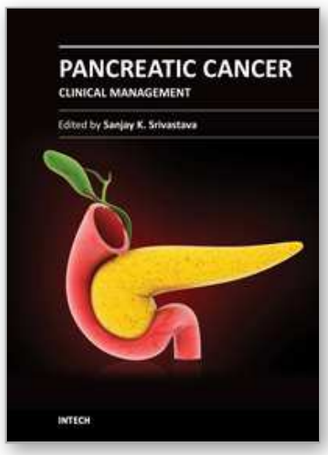

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This book covers pancreatic cancer risk factors, treatment and clinical procedures. It provides an outline of pancreatic cancer genetic risk factors, biomarkers and systems biology for the better understanding of disease. As pancreatic cancer suffers 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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