

# PANCREATIC CANCER IS THE BEST OUTCOME A GOOD DEATH?

Pancreatic cancer remains a captain of death among us having gained notoriety for being universally fatal. Nine in ten persons diagnosed with pancreatic cancer will be lost within five years of diagnosis despite best available treatment. The disease affects more than 330,000 persons a year worldwide and the incidence is rising.



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## EARLY SYMPTOMS ARE SUBTLE

**P**art of the problem in treating pancreatic cancer is that in the early stages, it is quite subtle.

Removed from the mainstream gastrointestinal tract, a pancreatic growth remains without symptoms until much later in its course. Early symptoms, if any,



Did you know

The peak age of incidence for pancreatic cancer is in the 60-70 years age group.

are often ignored or treated as indigestion. These early symptoms include epigastric or upper abdominal discomfort radiating to the back. As the tumor enlarges more dramatic symptoms such as jaundice (the yellowish discoloration of the skin and whites of the eyes), vomiting and weight loss occur. Another often noted symptom is the occurrence of diabetes or glucose intolerance. Although not all patients with diabetes have a pancreatic tumor, a recent onset of diabetes in one of the susceptible age group, should sound an alarm.

including Hereditary Breast and Ovarian Cancer Syndrome and Lynch Syndrome (Hereditary Non-polyposis Colorectal Cancer). Certain types of pancreatic cysts are also pre-malignant lesions, mucinous cysts, in particular, have a tendency towards malignant change.

## CHALLENGE FOR DOCTORS

Pancreatic cancer poses a challenge to doctors treating it in all aspects of its management. Early diagnosis of pancreatic cancer represents a masterclass in medical diagnostics. The onus is on general practitioners to exercise a high degree of suspicion. However, a battery of tests for every patient is unlikely to be efficient owing to the rarity of the disease. As such a clever history and physical examination remain the cornerstone of early diagnosis. A close follow-up for patients started on empirical treatment for dyspepsia with further investigation for persisting symptoms is a prudent course of action.

Blood tests and radiological imaging have improved tremendously over the last decade. The availability of liver function tests, tumor markers, ultrasonography and computed tomography (CT) imaging to the population at risk no doubt greatly enhances the likelihood of an early diagnosis. However a word of caution, an accurate interpretation of the results is required for the best effects.

Transabdominal ultrasonography of the abdomen is a widely available, cost efficient and non-invasive means of imaging the abdomen.

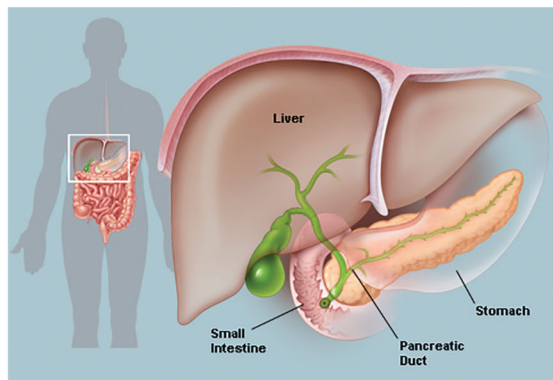
Unfortunately, the location of the pancreas behind the air-filled stomach and colon make visualising the entire pancreas difficult. None the less, in expert hands, subtle, indirect signs such a dilated bile duct or pancreatic duct may provide valuable clues.

**Tumor markers are neither sensitive nor specific for pancreatic cancer, as such a negative result does not rule out the diagnosis by any means.**

## WARNING SIGNS OF PANCREATIC CANCER

- Jaundice or yellowing of the skin and eyes
- Dark urine, pale stools and itchy skin
- Loss of appetite, weight and fatigue for some patients
- Back pain if the cancer has spread to the upper abdomen
- Other symptoms include fullness after eating, change in bowel habits e.g. loose bowel movement and recent new or worsening existing diabetes

Some people are more likely than others to develop pancreatic cancer. Smoking and obesity are known risk factors. A strong family history defined as having two first-degree relatives suffering the disease is another. Some inherited genetic syndromes are associated with pancreatic cancer



The investigation of choice to image the pancreas in its entirety is contrast enhanced CT. The present generation of spiral CT scanners can complete a multiphasic, holistic examination of the pancreas in seconds. With expert interpretation, mass lesions in the pancreas



can be identified, staged and planned for treatment. Although more freely available than before, CT scans are still expensive and carry a small risk of complications.

Changes in the pancreatic duct, a slim conduit which traverses the length of the pancreas can be a strong sign for pancreatic cancer. The pancreatic duct can be visualized by pancreatography which can be done endoscopically (endoscopic retrograde cholangio-pancreatography, ERCP) but with the advent of magnetic resonance imaging (MRI), can now be done non-invasively where facilities are available.

Another recent addition to the modes of diagnosis of pancreatic cancer is the endoscopic ultrasound. This involves passing a fiber-optic cable with a small ultrasound probe at its tip through the mouth of a patient under sedation. The probe is brought to lie adjacent the pancreas in the stomach or duodenum providing a vivid image of the pancreas. Furthermore, using ultrasound guidance, a needle can be passed through the pancreas to obtain tissue from lesions noted which can be analysed in the laboratory to clinch the diagnosis.

## DIFFICULT CHOICES

The diagnosis of pancreatic cancer is devastating. Time and space must be afforded to the patient and their families to absorb and accept the challenges that lie ahead. It is not uncommon for patients to seek advice outside the medical fraternity

before choosing the next course of action. Decision making is a crucial step in obtaining a good outcome for patients afflicted with pancreatic cancer. The patient remains at the core of this process and is provided with adequate information to make these difficult choices. The best outcomes are achieved by a multidisciplinary team working together in the patients' best interests. Although surgery and chemotherapy are the mainstay of treatment, support from many other fields of medicine are required for successful treatment.

Surgery aimed at removal of the tumor is the only treatment known to cure

**Surgery remains the only chance of cure. Recent developments have greatly improved the results of surgery.**

the disease, and initial investigations are aimed at determining if surgery is feasible. Incomplete removal is not helpful and can lead to complications which further affect the patient's quality of life. Some patients may have resectable tumors but

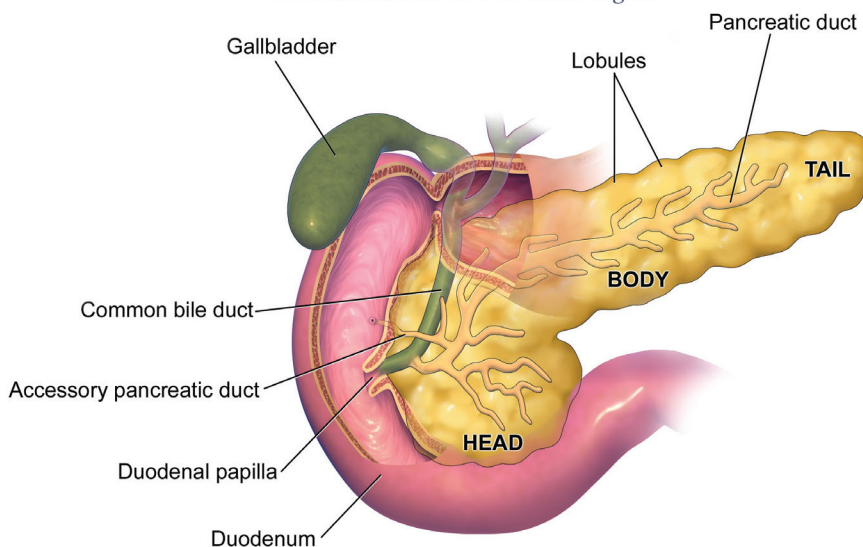
co-existing chronic disease and severe malnutrition that make them poor candidates for major surgery.

Treatment of pancreatic cancer depends largely on the stage at diagnosis. The vast majority of pancreatic tumors are aggressive lesions which spread easily and early in the course of the disease. Complete excision of a lesion before this has occurred is the only means to cure the disease. Surgery of the pancreas presents a formidable

**Specifically, the endoscopic ultrasound has revolutionised the management of pancreatic cysts, allowing for proper characterisation and decision making on treatment.**

## LOCATION OF PANCREAS CANCER

- 60 to 70 percent of exocrine pancreatic cancers are localised to the head;
- 20 to 25 percent are in the body/tail; and
- the remainder involve the whole organ.



challenge due to the location of the pancreas and its nature. Recent developments have greatly improved the results of surgery with high volume centers reporting 95-100% post-operative survival with acceptable morbidity. The Achilles heel of surgery, however, remains the aggressive nature of the disease

which often leads to early recurrence and death. Clinical trials have proven that the results of surgery are optimised by adjuvant chemotherapy. The five-year survival of patients with successful treatment is between 20-25%.

The majority of patients will have the disease at a stage where surgery

will no longer be of benefit. Efforts are then best directed towards improving the quality of life of the patient. Chemotherapy has been shown to increase survival. Some common complications of advanced pancreatic cancer such as jaundice and intestinal obstruction can be effectively relieved with endoscopy.

### WORLD CANCER RESEARCH FUND INTERNATIONAL, LONDON

- The estimated 5-year prevalence of people in the world living with pancreatic cancer is 4.1 per 100,000. This cancer is almost always fatal.
- Using the new findings from the Continuous Update Project show that about 19% of cases of pancreatic cancer in the US can be prevented by being a healthy weight.
- About 55 per cent of pancreatic cancer cases occurred in more developed countries.
- The highest incidence of pancreatic cancer was in Northern America and Europe; and the lowest incidence in Africa and Asia.

	WITHOUT SURGERY	SUCCESSFUL CURATIVE RESECTION (ABOUT 205 PATIENTS)
<b>Median survival rate</b>	<b>4-6 months</b>	<b>12-19 months</b>
<b>1 year survival rate</b>	<b>24%</b>	
<b>Overall 5 year survival rate</b>	<b>5%</b>	<b>15-20%</b>

### 5 YEAR SURVIVAL AFTER SUCCESSFUL SURGERY ➔ NOT GUARANTEE OF CURE

LOCATION	TIME OF PRESENTATION	PROGNOSIS
<b>HEAD and NECK</b>	<b>Earlt presentation-ob-structive jaundice</b>	<b>Better prognosis</b>
<b>Body and Tail</b>	<b>Late presentation (Mass)</b>	<b>Worse prognosis</b>

The pain associated with cancer can be managed with medication and coeliac plexus neurolysis. Pain medication for cancer is prescribed in a step ladder pattern with stronger opioid analgesics used in advanced stages of the disease. Coeliac plexus neurolysis is a procedure with

which pain-sensitive nerve tissue is chemically destroyed to reduce the back pain associated with pancreatic cancer.

Pancreatic cancer is the subject of intense research worldwide. Areas of interest include early diagnosis where genetic study hopes to identify

early pre-malignant changes in the pancreas by sampling pancreatic fluids. Other recent advances include targeted therapy such as the growth factor inhibitor, erlotinib which has recently been approved for use with standard chemotherapy. Parallel to the advances in systemic treatment,



surgeons are pushing the boundaries of resectability using vascular resection and reconstruction in cases that were not too long ago deemed unresectable.

## PROMISING RESEARCH PROGRESS

Promising results are seen in immune-based strategies to treat pancreatic cancer. Immune checkpoint inhibitors, therapeutic vaccines and combination immunotherapies are showing promise where other approaches have failed. For pancreatic cancer, early studies suggest that vaccines can induce T cells that have the potential to recognise and kill pancreatic cancer cells. For most significant clinical benefit, these immunotherapies will have to be refined.

In another development, for the first time researchers have shown how controlling cholesterol metabolism in pancreatic cancer cells reduces metastasis, pointing to a potential new treatment using drugs previously developed for atherosclerosis.

Researchers from MIT and Massachusetts General Hospital have now developed a small, implantable device that delivers chemotherapy drugs directly to pancreatic tumors. They found that this approach was up to 12 times more effective than giving chemotherapy drugs by intravenous injection, which is how most pancreatic cancer patients are treated. **IM**



### SOME CURIOSITIES OF PANCREATIC CANCER:

- Pancreatic cancer is the 12th most common cancer worldwide but the 4th commonest cause of cancer death. Every year an estimated 300,000 persons are diagnosed and another 30,000 die from it, indicating the lethal nature of the disease.
- Although the commonest form of pancreatic cancer is pancreatic adenocarcinoma (which accounts for 90% of pancreatic cancers), there are several other types of pancreatic cancer which carry a more favourable prognosis such as neuroendocrine tumors, solid pseudopapillary neoplasms and cancers of the Ampulla of Vater.
- The symptoms of pancreatic cancer depend on the location of the tumor. Tumors involving the head of the pancreas are prone to cause jaundice due to infiltration of the common bile duct. Tumors arising from the body of the pancreas tend to present with back pain.
- Surgery for tumors of the head of the pancreas is called a pancreatoduodenectomy which involves the removal of the head of the pancreas with the adjacent duodenum, gallbladder and surrounding lymph nodes.
- Surgery for the removal of tumors of the body and tail of the pancreas is called a distal-pancreatectomy which involves removal of the body and tail of the pancreas, the spleen and surrounding lymph nodes.