“PLATELET LYMPHOCYTE RATIO AS A DIAGNOSTIC MARKER IN PANCREATIC MALIGNANCY”

Dissertation
Submitted in partial fulfillment of the regulations of

M.S. DEGREE EXAMINATION

BRANCH I GENERAL SURGERY

Department of General Surgery

GOVT. STANLEY MEDICAL COLLEGE AND HOSPITAL

CHENNAI - 600001

THE TAMILNADU DR.M.G.R MEDICAL UNIVERSITY

CHENNAI

APRIL 2015

CERTIFICATE

This is to certify that this dissertation titled

"PLATELET LYMPHOCYTE RATIO AS A DIAGNOSTIC MARKER IN PANCREATIC MALIGNANCY"

is the bonafide work done by **Dr Praveen Kumar Arumugam ,** Post Graduate student (2012 – 2015) in the Department of General Surgery, Government Stanley Medical College and Hospital, Chennai under my direct guidance and supervision, in partial fulfillment of the regulations of The Tamil Nadu Dr. M.G.R Medical University, Chennai for the award of M.S., Degree (General Surgery) Branch - I, Examination to be held in April 2015.

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DECLARATION

I, **DR. PRAVEEN KUMAR ARUMUGAM** solemnly declare that this dissertation titled **"PLATELET LYMPHOCYTE RATIO AS A DIAGNOSTIC MARKER IN PANCREATIC MALIGNANCY"**

is a bonafide work done by me in the Department of General Surgery, Government Stanley Medical College and Hospital, Chennai under the guidance and supervision of my unit chief.

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This dissertation is submitted to The Tamilnadu Dr. M.G.R. Medical University, Chennai in partial fulfillment of the university regulations for the award of M.S., Degree (General Surgery) Branch - I, Examination to be held in April 2015.

Place: Chennai.

Date: September 2014. **DR.PRAVEEN KUMAR ARUMUGAM**

ACKNOWLEDGEMENT

I am grateful to **Prof.Dr.A.L.Meenakshi Sundaram ,**Dean, Govt. Stanley Medical College for permitting me to conduct the study and use the resources of the College.

My sincere thanks to **Prof.Dr.S.Viswanathan,** Professor and HOD, Department of General Surgery, for his valuable guidance throughout the study.

I am highly indebted to my guide**Prof.Dr.M.Abdul Kader,** Professor of Surgery for his constant help, inspiration and valuable advice in preparing this dissertation.

I express my deepest sense of thankfulness to my Assistant Professors **Dr.Abraham Jebakumar and Dr.Shanmugham** for their valuable inputs and constant encouragement without which this dissertation could not have been completed.

I consider it a privilege to have done this study under the supervision of my beloved former Professor and Head of the Department **Prof.Dr.K.Kamaraj**, who has been a source of constant inspiration and encouragement to accomplish this work.

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I am particularly thankful to my fellow postgraduate colleagues for their valuable support in the time of need throughout this study.

I would be failing in my duty without acknowledging the contribution of my friends Dr. Jeevanantham ,Dr .Rakesh Chandru, Dr. Anbarasan, Dr.Palani, Dr.Jeevan prakash in helping me in completing this dissertation

It is my earnest duty to thank my parents without whom accomplishing this task would have been impossible.

I am extremely thankful to my patients who consented and participated to make this study possible.

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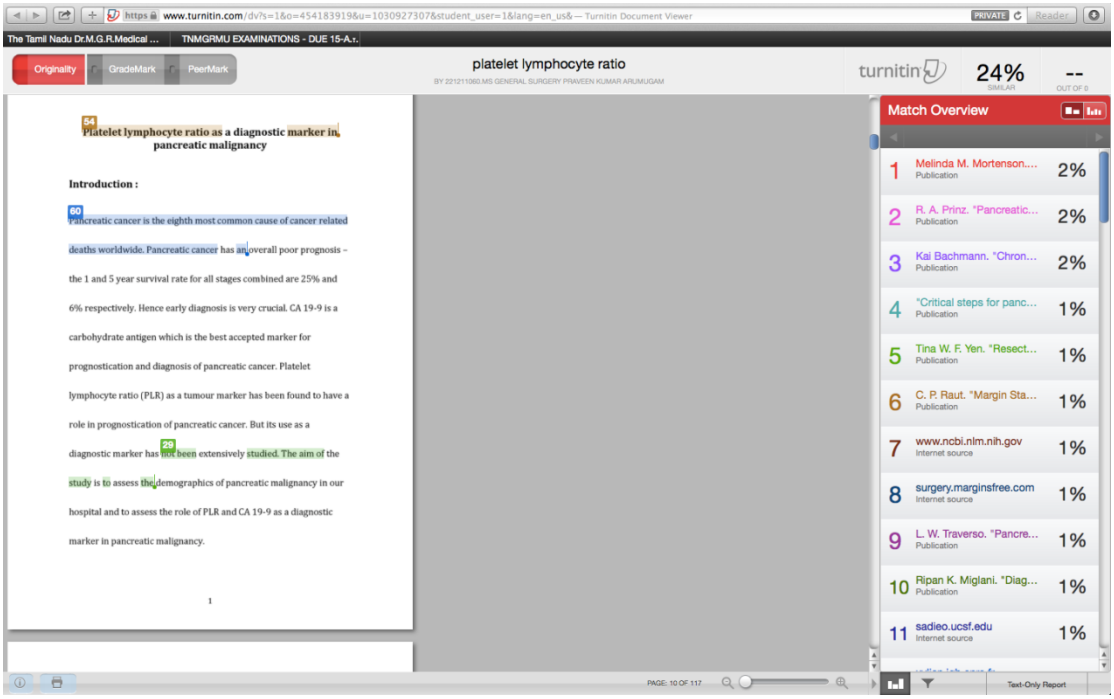
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Platelet lymphocyte ratio as a diagnostic marker in pancreatic malignancy
Introduction :
Pancreatic cancer is the eighth most common cause of cancer related deaths worldwide. Pancreatic cancer has an overall poor prognosis – the 1 and 5 year survival rate for all stages combined are 25% and 6% respectively. Hence early diagnosis is very crucial. CA 19-9 is a carbohydrate antigen which is the best accepted marker for prognostication and diagnosis of pancreatic cancer. Platelet lymphocyte ratio (PLR) as a tumour marker has been found to have a role in prognostication of pancreatic cancer. But its use as a diagnostic marker has not been extensively studied. The aim of the study is to assess the demographics of pancreatic malignancy in our hospital and to assess the role of PLR and CA 19-9 as a diagnostic marker in pancreatic malignancy.
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Title of the Work : Platelet Lymphocyte ratio as a diagnostic marker in pancreatic Malignancy.

Principal Investigator : Dr. Praveen Kumar Arumugam

Designation : PG in MS (General Surgery)

Department : Department of General Surgery
Government Stanley Medical College,
Chennai-01

The request for an approval from the Institutional Ethical Committee (IEC) was considered on the IEC meeting held on 11.02.2014 at the Council Hall, Stanley Medical College, Chennai-1 at 2PM

The members of the Committee, the secretary and the Chairman are pleased to approve the proposed work mentioned above, submitted by the principal investigator.

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Platelet lymphocyte ratio as a diagnostic marker in pancreatic malignancy

Introduction :

Pancreatic cancer is the eighth most common cause of cancer related deaths worldwide. Pancreatic cancer has an overall poor prognosis – the 1 and 5 year survival rate for all stages combined are 25% and 6% respectively. Hence early diagnosis is very crucial. CA 19-9 is a carbohydrate antigen which is the best accepted marker for prognostication and diagnosis of pancreatic cancer. Platelet lymphocyte ratio (PLR) as a tumour marker has been found to have a role in prognostication of pancreatic cancer. But its use as a diagnostic marker has not been extensively studied. The aim of the study is to assess the demographics of pancreatic malignancy in our hospital and to assess the role of PLR and CA 19-9 as a diagnostic marker in pancreatic malignancy.

Aims and Objectives :

1. To asses the demographics of histologically proven pancreatic malignancy in our hospital.

2.To assess the role of Platelet lymphocyte ratio and CA 19-9 in the diagnosis and management of pancreatic malignancy.

Study design :

Cross sectional study.

Inclusion criteria :

1.All patients admitted with impression of pancreatic malignancy indicated by imaging (pancreatic mass on USG abdomen/ CECT abdomen) and with/without clinical features of malignancy such as jaundice, abdominal mass, pruritis.

Exclusion criteria :

1. Patients with clinical of biochemical features of cholangitis.

2. Patients in whom histopathological confirmation was not available.

Methodology :

Cross sectional study for the period Nov 2013 to Nov 2014 was done in Govt. Stanley Hospital. The patients admitted in Govt. Stanley hospital during this period were included.

Method of collection of data :

Details of the patients, detailed history, clinical examination, symptoms and signs of pancreatic malignancy were recorded.

Parameters taken into account were :

Jaundice

Loss of weight(>10% of body wt in the last six months or less)

Previous history of pancreatitis

Alcohol intake (equal to or more than 80g of ethanol per day for 5 years was considered significant)

Patients admitted with features of pancreatic malignancy were subjected to the following investigations:

Blood:

- Complete blood count
- Liver function test (SGOT, SGPT, ALP, S.Bilirubin)
- CA19-9 (normal value < 39 U)
- PLR (cut off at 150)

The following imaging investigations were done:

- Ultrasound (transabdominal)
- Doppler USG (where indicated)
- CECT abdomen (pancreas protocol CT)
- MRI/MRCP (where indicated)

Other investigations

Esophagogastroduodenal scopy – end or side viewing scopy.

ERCP (where indicated)

FNAC – USG or CT guided.

Statistical methods :

Derivations from continuous measurements were presented on mean +/- standard deviation, and from categorical measurements were presented in number (%).

Significance – 5% level of significance.

Significance on parameters on continuous scale – student t test was usedand for intergroup analysis chi squared test was used.

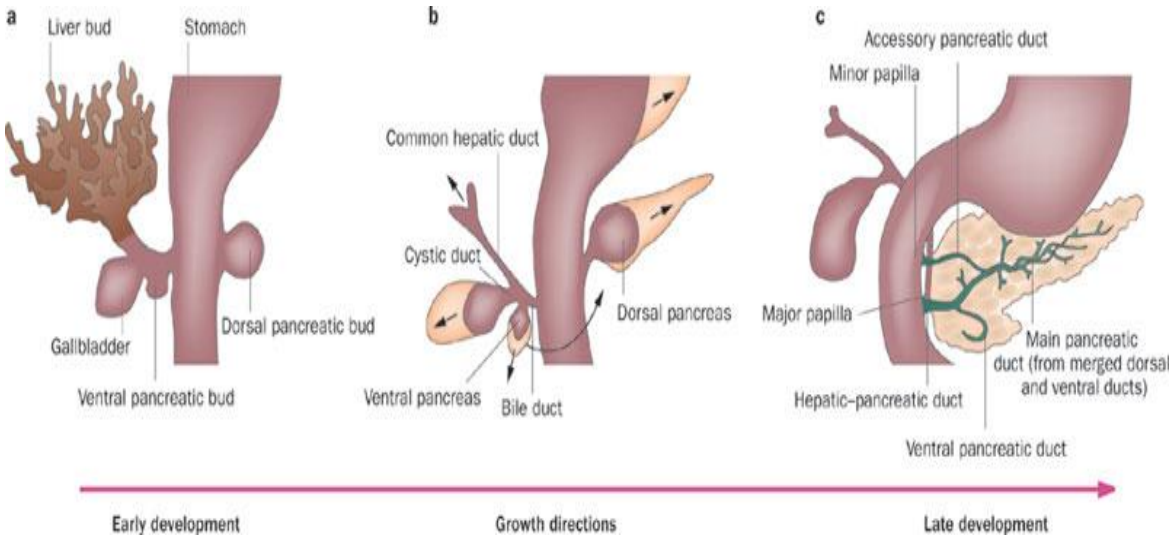
Diagnostic statistics such as sensitivity, specificity, ppv, npv were calculated for CA 19-9 and PLR . Statistical software – XLSTAT and Socialstatistics.com were used.

Review of literature

Anatomy

Embryology

The pancreas and liver begin as epithelial buds from the primitive gut and reach their mature form through proliferation and differentiation of multiple cell types. Early in embryonic development the endoderm folds into a tube, the anterior part of which is the foregut. At the same time the precursors of major blood vessels form in the surrounding mesenchyme, which is important in early pancreatic development. The primitive aorta, paired anteriorly and fused into a single vessel in the region of the foregut, lies immediately dorsal to the gut. Primitive vitelline veins lie ventral to the gut. The primitive gut and the primitive vessels are, at this stage, tubes consisting solely of a single layer of epithelium. Interaction of the epithelium of the aorta with that of the gut induces proliferation of endodermal epithelium and the beginning of differentiation to form the dorsal primordium of the pancreas. A similar inductive process occurs where vitelline vein endothelium touches gut endoderm to produce ventral buds. The proliferating pancreatic buds express the *Pdx1* gene,providing an early marker of pancreatic differentiation.



Development of the pancreas

The epithelium of the dorsal and ventral buds proliferates to form thegrowing dorsal and ventral pancreatic primordia.

The liver, gallbladder, and associated ducts also develop from the right ventralprimordium. The epithelium expands as primordial tubules that branch as they grow into the surrounding mesenchyme. Mesenchyme is cellular at first. Adult connective tissue is derived from mesenchyme. Cells become more dispersed as differentiation toward adult extracellular matrix proceeds. Extracellular matrix plays a distinct role in the changes accompanying chronic pancreatitis and pancreatic cancer.
The pancreas initially grows within a free mesentery, but subsequent changes convert it into a retroperitoneal organ. Rotation of the gut moves the duodenum from the midline to the right side, its middle segment

pressed against the dorsal abdominal wall. The pancreas, carried along in the duodenal mesentery, similarly acquires a retroperitoneal position as the mesenteric layers fuse.

Its location at the dorsal abdominal wall just posterior to the diaphragm places the pancreas into close association with a myriad of major vessels and nerves. The aorta gives off the celiac trunk on leaving the thoracic cavity and before passing along the dorsal surface of the pancreas. The superior mesenteric artery arises dorsal to the pancreas to pass ventrally over the duodenum. The supe- rior mesenteric vein, paralleling the artery, passes to the dorsal surface of the pancreas where it is joined by the splenic vein to form the hepatic portal vein. The thinner part of the pancreas over the superior mesenteric– hepatic portal vein is its neck,

separating the head from the body.

The endocrine and exocrine components of the pancreas derive from the same population of cells. Differentiation of the cells comprising the primitive ducts leads along three main pathways. At intervals cells bud off the primitive ducts, proliferate into spheroidal groups, lose their contact with the lumens, and become the islets of Langerhans. At the ends and along the sides of the primitive ducts, differentiating cells produce the spheroidal and elongate collections that constitute the acini.

The remaining cells stay approximately in their original relationship to become the mature ducts.

In the mature pancreas, acinar tissue is most prominent.

Islets of Langerhans are interspersed among the acinar tissue, as are smaller (intralobular) ducts.

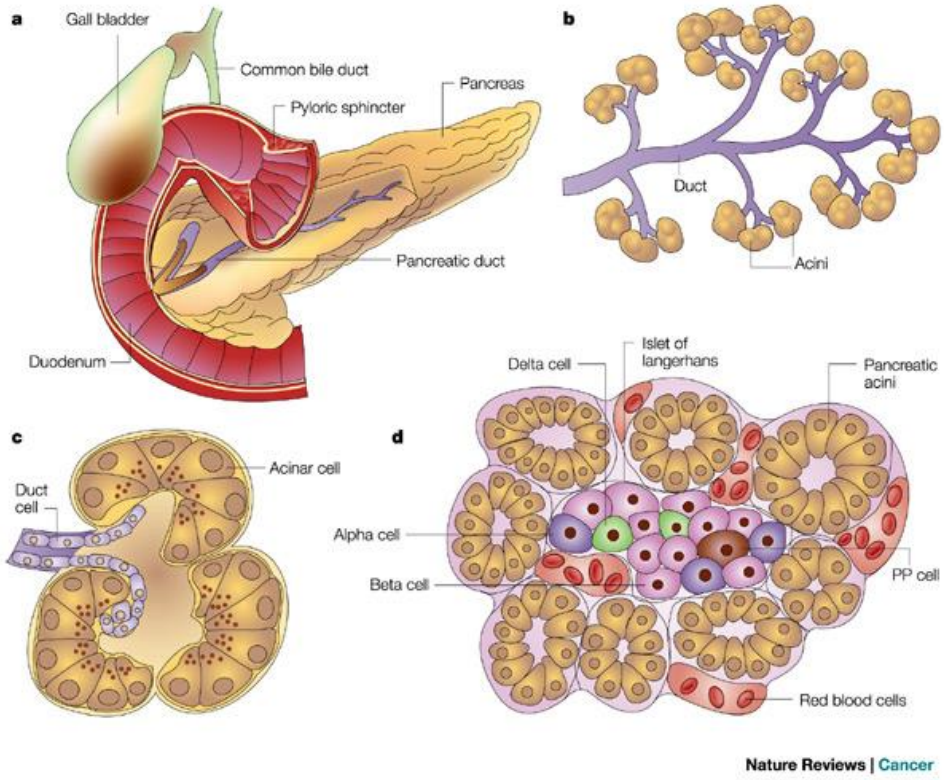
Mature ducts form a barrier between the secretion products they carry in their lumens and the surrounding extracellular matrix. The epithelium constitutes a continuous layer lining the ducts. Ductal epithelial cells lie side-by-side with the apposing membranes at the luminal surface joined by tight junctions. Therefore interchange of fluid and ions between duct lumen and extracellular space must be a transcellular event regulated by the cells traversed. Larger ducts present a smooth, undulating surface toward the lumen. Tightly joined ductal cells display microvilli projecting into the lumen between tight junctions. In the absence of pancreatic disease, the ducts are surrounded by a connective tissue matrix with a small number of cells. With disease, however, such as chronic pancreatitis, the epithelial barrier may be missing in places,with accumulation of inflammatory cells and proliferation of blood vessels exposed directly to the lumen. In this condition interchange of substances and cells between lumen and the extracellular space of the pancreas can occur without the regulation normally provided by the ductal epithelium.

Acinar cells

Acinar tissue constitutes the greatest proportion of the mature normal pancreas. Like islet cells, early acinar cells are derived from primitive ducts. Continued proliferation and differentiation produce the cells specialized to synthesize, store, and secrete digestive enzymes. Acinar cells are present by the 4th month of gestation. However, the relative proportions of enzymes change with time. At birth, trypsinogen levels are less than normal adult levels, lipase is only a fraction of adult levels, and amylase is almost absent.Enzymes are synthesized in an abundant rough endoplasmic reticulum prominent in the base of acinar cells and packaged in the Golgi apparatus for storage. Many of the enzymes are stored in granules as precursor products (zymogens) mainly in the apex of acinar cells. Stimulation of the acinar cell releases zymogen granules at the cell membrane bordering on the acinar lumen. Activation of the enzymes occurs on entry into the duodenal lumen where enterokinase acts on the pancreatic juice conducted there through the pancreatic ductal system. Trypsin is activated, in turn activating other zymogens.

Pancreatic ducts branch and rebranch, producing progressively more and smaller ducts. The smallest ducts are intimately associated with acini.

Some duct cells form tight junctions with adjacent acinar cells. The result is a continuous lumen, surrounded by a continuous epithelium, from the ductal system through the acinar system . A duct may terminate on an acinus that is formed by a spheroidal accumulation of acinar cells. Alternately, a duct may contact one acinus, then continue on the other side to contact a second acinus.Acini can be elongate, bifurcated, or multilobed. An acinus may contact a duct at two places, forming a looped lumen. Small ductal cells that are located within an acinus are referred to as centroacinar cells. Acini are grouped into microscopic lobules. Collections of these microscopic lobules are grouped together and surrounded by connective tissue septa to produce the lobulated pattern visible on the pancreatic surface.

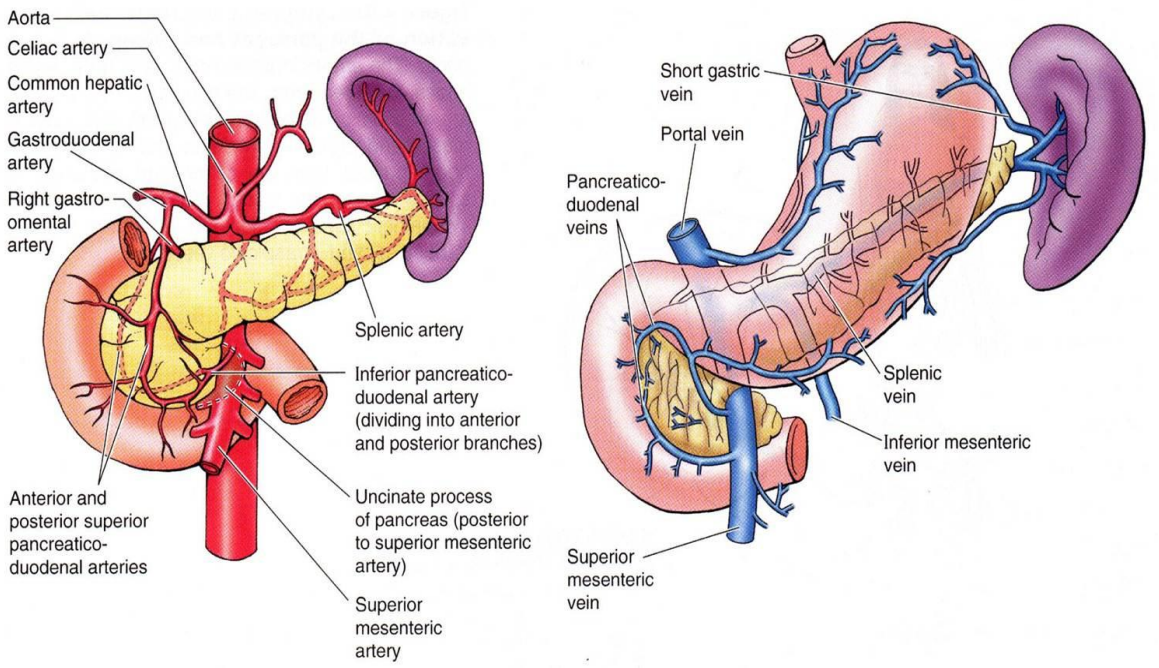


Blood Supply

The abundant blood supply of the pancreas comes from branches of the aorta that also serve adjacent abdominal organs. Arteries originating in the aorta branch to serve liver, stomach, spleen, and intestine in common with the pancreas. The celiac and superior mesenteric arteries constitute the primary arteries from which others are derived. The splenic and common hepatic arteries branch from the celiac. Dorsal and greater pancreatic arteries, in addition to smaller ones, branch from the splenic artery. The gastroduodenal artery branches from the common hepatic to form anterior and posterior superior branches that form loops by anastomosing with anterior and posterior pancreaticoduodenal branches of the inferior pancreaticoduodenal artery, a branch of the superior mesenteric artery . Arteries running in the region where the head of the pancreas apposes the duodenum supply both organs.

Abundant anastomoses of arteries provide alternate routes of circulation. The microcirculation within the pancreas is supplied by arteries that continue to branch. The arteries that penetrate the surface of the pancreas do not parallel the main ductal system. They derive from a peripheral location distinct from the ducts that originate in the duodenum and branch from central locations within the pancreas.Part of the microcirculation

supplies the ductal system. Vessels are numerous in the connective tissue surrounding ducts. A capillary plexus supplies the acinar tissue and drains into the venous system.



Blood supply of the pancreas

Veins of the pancreas drain eventually into the hepatic portal system , so may become involved in the spread of pancreatic cancer to the liver. Cancer may invade the hepatic portal vein along its path dorsal to the pancreas.

Lymphatic system

The lymphatic system of the pancreas complements the drainage system provided by veins and serves as a route for cellular migration. Lymphatic vessels lie mostly in the connective tissue septa of the pancreas. They are not particularly numerous, they have thin walls, and they tend to collapse when not in situ, so they are difficult to observe. A few intralobular lymphatic vessels drain into the interlobular plexus. These, in turn, coalesce into larger vessels which tend to parallel the blood vessels serving the pancreas.Lymphatic vessels emerge on the surface of the pancreas to enter lymph nodes. Efferent vessels from multiple nodes empty eventually into the thoracic duct.
In the normal situation the lymphatics carry mostly excess interstitial

fluid so could be considered to serve as an overflow.In pathologic situations, other things gain access and are conducted. Lymph-borne metastases of pancreatic cancer are found in primary and secondary lymph nodes interposed between the pancreas and the thoracic duct. Lymph nodes surround the pancreas and lie before and along the sides of the aorta and its branches. Many of the nodes are associated with blood vessels and may be described according to the vessel. Celiac, splenic, hepatic, gastroduodenal, pancreaticoduodenal, and superior mesenteric groups of nodes are described. Suprapancreatic and infrapancreatic

groups lie immediately outside the pancreas.Numeric designation and grouping are also used to describe nodes of importance to metastasis.

Nervous System

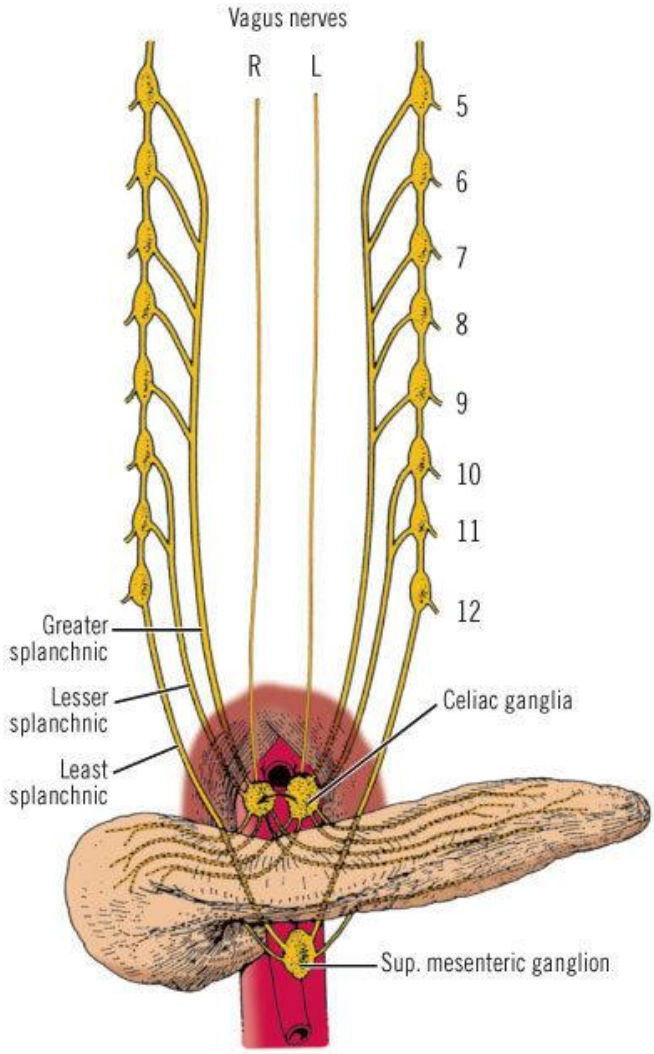
Nerves control normal pancreatic function and serve as pain pathways and routes of cancer spread in the presence of disease. The principal nerve groups serving the pancreas are parts of the sympathetic and parasympathetic divisions along with their accompanying sensory fibers . Sympathetic fibers carried primarily in the splanchnic nerves originate in the intermediolateral cell column of the spinal cord. Accompanying sensory fibers have their cell bodies in the dorsal root ganglia. Parasympathetic fibers are carried with accompanying sensory fibers in the vagus nerve, which is attached to the brain. Sympathetic innervation affects pancreatic vasculature. Parasympathetic innervation modulates secretion. However, normal control of pancreatic function is complex and relies on simultaneous regulated activity of all mechanisms, so that a defect in one component can affect another. Physiologic control of and response by the pancreas is mediated in part by peptidergic innerva- tion.Among these neurotransmitters are substance P, neuropeptide Y, calcitonin gene-related peptide, and vasoactive intestinal polypeptide.

Splanchnic and vagus nerves pass through a plexus of nerve fibers and ganglia distributed around the base of the celiac artery. The sympathetic fibers synapse on sec- ondary neurons in the celiac ganglia in addition to contributing to the celiac plexus. The parasympathetic fibers and sensory fibers pass through the celiac plexus without synapse. Parasympathetic fibers synapse on cell bodies of secondary neurons that form ganglia within the pancreas.

The pancreas is connected to the enteric neural system in addition to the brain and spinal cord. The enteric nervous system is an organized and interconnected network of nerve cell bodies and fibers found within and regulating the alimentary tract proper. Nerve cells in the lower stomach and duodenum extend fibers into the pancreas. A direct connection is thereby established between the enteric nervous system and that of the pancreas.

Nerve fibers combine in the celiac plexus and are distributed to the substance of the pancreas as networks surrounding the arteries of supply.The nerves that are distributed thus are mixed; that is, a nerve may contain sympathetic, parasympathetic, and sensory fibers. The nerves are mainly unmyelinated; that is, unlike the larger nerves supplying muscles in which nerve fibers are surrounded by layers of myelin, the nerve fibers in the pancreas are surrounded immediately by

Schwann cells and contained in a protected environmentthat is separated from the surrounding milieu by a perineurium .



Nerve supply

On direct intense stimulation of nerves, or because of damage to the perineurium and nerve fibers by invasion of pancreatic cancer or chronic inflammation accompanying chronic pancreatitis, pain may be induced and sustained. A logical approach to the treatment of unremitting pain is

to interrupt the pathway conducting it. Common approaches have been to block the celiac plexus or to interrupt the splanchnic nerves since they are the principal pathways for pain conduction from the pancreas.

The severity and breadth of pain generation may lead to incorporation, at least potentially, of other nerves that are less central to pain conduction from the pancreas.It is possible that sensory nerves in the vagus may contribute to pain generation under appropriate circumstances. The pancreas lies on the posterior abdominal wall, and pancreatic cancer may extend from the pancreas proper to involve spinal nerves. Branches of the phrenic nerve could become involved in pain transmission.

After the nerve fibers carrying the impulses enter the spinal cord, they are carried to the brain where they are interpreted as pain. These are thought to travel primarily in the spinothalamic tract. There is some evidence, however, that fibers in the dorsal columns of the spinal cord may also carry chronic pain and that interruption of these fibers can provide relief.

Pancreatic cancer

Pancreatic and periampullary carcinomas include a group of malignant neoplasms arising in or near the ampulla of Vater or in the pancreas. The initial pattern of symptoms is determined by the location of the primary lesion. Lesions that grow near the bile duct tend to cause obstructive jaundice, whereas pancreatic lesions that grow in the body or tail tend to be manifested as pain or a mass effect. The great majority of tumors that occur in these areas are adenocarcinomas arising from either the pancreas, ampulla of Vater, distal common bile duct, or duodenum. Pancreatic and periampullary carcinomas are a major public health problem throughout most of the world. Pancreas cancer is the fourth leading cause of cancer death in the United States, with 31,800 deaths in 2005 as opposed to 163,510 deaths for lung cancer, 56,290 deaths for colorectal cancer, and 40,870 deaths for breast cancer.In the United States, the incidence of pancreas cancer rose dramatically from the 1930s until the 1970s, nearly doubling. Since the mid-1970s the incidence has remained stable at about 8 to 9 cases per 100,000 population. Pancreatic cancer is a highly lethal malignancy with the yearly mortality approaching the incidence (32,180 in 2005). In the United States, demographic risk factors for pancreas cancer include age, with the majority of patients in or beyond their sixth decade of life; sex, with a

slight male preponderance; and race, with African American males having the highest overall incidence.

In Europe, pancreas cancer is the sixth leading cause of cancer death, and the incidence is similar to that in the United States. The incidence in Europe has also remained stable during the past 3 decades. The Japanese, however, have seen a dramatic increase in the incidence of pancreas cancer over the past 3 decades, although the overall incidence is still less than that observed in the West. India and parts of the Middle East have the lowest recorded incidence of pancreas cancer. Worldwide, more than 200,000 people die of pancreas cancer every year.

Ampullary carcinoma is the second most common periampullary carcinoma, with an overall incidence of 6 cases per 1 million or approximately 1800 cases per year in the United States.Although it constitutes between 7% and 19% of periampullary carcinomas, it accounts for a higher percentage of operative cases because these lesions are more amenable to complete resection.Distal bile duct carcinoma and periampullary duodenal carcinoma occur less frequently than pancreas and ampullary carcinoma. The actual incidence of these two carcinomas is much more difficult to estimate because they occur less frequently and are often lumped together with other malignancies. For example, distal bile duct carcinomas are often combined with all cholangiocarci- nomas (perihilar and intrahepatic), as well as with gallbladder carcinoma.

Likewise, periampullary duodenal carcinomas are often combined with all duodenal carcinomas or all small bowel carcinomas.

Risk factors for pancreatic adenocarcinoma :

Established	Tobacco
	Inherited susceptibility
Associated	Chronic pancreatitis
	DM type 2
	Obesity
Possible	Physical inactivity
	Certain pesticides
	High carbohydrate or sugar intake

Clinical Findings

Symptoms depend on the location of the lesion, with most patients having vague symptoms early in the course of their disease. Patients with lesions that occur near the bile duct, such as those near the ampulla, head of the pancreas, and uncinate process, are much more likely to have obstructive

jaundice. Those with lesions in the body or tail of the pancreas are more likely to complain of pain.

The majority of patients with pancreatic (head), periampullary, distal common bile duct, or duodenal (near the region of the ampulla) adenocarcinoma have the classic constellation of jaundice, pruritus, acholic stools, and tea-colored urine. Patients with a common bile duct adenocarcinoma usually distal or adenocarcinoma of the ampulla are the most to have obstructive jaundice because the lesion does not need to grow to very large size before it completely obstructs the bile duct. In addition to the classic symptoms, vague upper abdominal discomfort often develops and sometimes radiates to the back. Late in the course of the disease this pain can progress to be very debilitating. Other general symptoms include anorexia, fatigue, malaise, and weight loss. Nausea and vomiting can be a sign of gastric outlet obstruction from duodenal involvement. Patients may also have acute pancreatitis secondary to obstruction of the pancreatic duct. Elderly patients with acute pancreatitis but without a history of alcohol use or gallbladder stones should be screened for a neoplasm.

Patients with pancreatic cancer involving the body or the tail of the gland are more in favour to have weight loss and abdominal pain as their initial complaints. These lesions can grow to a larger size before producing

symptoms and are often diagnosed at a later stage with a poorer prognosis.

Physical findings on examination include scleral icterus, jaundice, and a palpable gallbladder (Courvoisier's sign). Signs of advanced disease include cachexia, palpable metastatic lesions within the liver, palpable disease in the left supraclavicular fossa near the confluence of the subclavian vein and thoracic duct (Virchow's nodule), palpable periumbilical metastatic disease (Sister Mary Joseph's nodule), and pelvic metastatic disease palpable anteriorly on rectal examination (Blumer's shelf nodule).

Laboratory Findings

In addition to the clinical signs and symptoms, patients early in the course of their disease may have subtle laboratory findings such as mildly elevated liver function test results, mildly elevated bilirubin levels, or elevated alkaline phosphatase levels, or they may have new onset diabetes or anemia. If the disease has progressed and jaundice is apparent, patients generally have elevated serum levels of bilirubin and alkaline phosphatase, usually associated with only a mild elevation in liver transaminases. Ongoing obstruction of the biliary tree may lead to an

inability to absorb vitamin K and resultant coagulopathy because of the lack of intrinsic pathway clotting factors. It is important to replete vitamin K in these patients.

There are no definitive serum markers for any of the pancreatic or periampullary adenocarcinomas. Markers that tend to be used are carbohydrate antigen 19-9 (CA 19-9) and carcinoembryonic antigen (CEA). CA 19-9 is elevated in up to 75% of patients with pancreas adenocarcinoma, but levels are also elevated in benign conditions of the pancreas, liver, and bile ducts, as well as in smokers. CEA levels may be elevated with any of the periampullary adenocarcinomas, but more typically with bile duct and duodenal adenocarcinoma. Because nearly 100% of pancreas adenocarcinomas have a mutation in K-*ras*, several groups have tried to detect these mutations from aspirates obtained by endoscopic techniques or in stool.

Imaging Studies

The imaging modalities most frequently used for patients with suspected periampullary cancer are right upper quadrant ultrasound (RUQ US), computed tomography (CT), magnetic resonance imaging (MRI), including magnetic resonance cholangiopancreatography (MRCP), endoscopic retrograde cholangiopancreatography (ERCP), and

percutaneous transhepatic cholangiography (PTC). The benefit of positron emission tomography (PET) has not been clearly defined. Over the past 15 years there has been a general trend away from invasive imaging studies (ERCP and PTC) toward noninvasive imaging studies. This trend has occurred for two reasons. First, there have been studies that have documented an increased rate of both preoperative and postoperative complications with the routine use of these modalities.Second, surgeons have become more willing to operate on jaundiced patients as long as they are not septic or malnourished from their biliary obstruction.

Clinicopathological staging

Patients with cancer of the pancreas, ampulla, distal bile duct, and duodenum are staged according to the American Joint Committee on Cancer (AJCC) staging system. These staging criteria are based on the size and extent of the primary tumor (T), lymph node involvement (N), and the presence of distant metastases (M). Patients are stratified into stage groupings that guide prognosis and treatment. Pancreas adenocarcinomas are staged with the AJCC exocrine pancreas guidelines,

distal common bile duct cancers are staged with the AJCC extrahepatic bile
duct guidelines, ampullary cancers are staged with the AJCC ampulla of Vater guidelines, and duodenal cancers are staged with the AJCC small intestine guidelines.

Operative technique of pancreaticoduodenectomy

The first successful resection of a periampullary tumor was performed by Halsted in 1898 at the Johns Hopkins Hospital. He described a local ampullary resection with reanastomosis of the pancreatic and bile ducts into the duodenum in a woman with obstructive jaundice.Codivilla performed the first en bloc resection of the head of the pancreas and duodenum for periampullary carcinoma, but the patient did not survive beyond the postoperative period.The first successful two-stage pancreaticoduodenectomy was performed by Kausch in 1909.In 1914, Hirschel reported the first successful one-stage pancreaticoduodenectomy.In the first part of the 20th century, most periampullary cancers were managed by a transduodenal approach similar to that first reported by Halsted.

Whipple and colleagues in 1935 reported three successful 2 stage resections of the head of the pancreas along with the duodenum.Ten years

later, modifications and improvements were made in the procedure, including - first one-stage pancreaticoduodenectomy in the United States by Trimble in 1941. The technique was not so popular and was less practised due to the morbidity and mortality acoosiated with the surgery.

Pancreaticoduodenectomy

Pancreaticoduodenectomy involves removal of the pancreatic head, duodenum, gallbladder, and bile duct with or without removal of the gastric antrum.

The surgical resection is divided into the following clearly defined steps.

- The purpose of step 1 is to isolate the infrapancreatic SMV and separate the colon (and its mesentery) from the duodenum and pancreatic head. The omental bursa is entered by taking the greater omentum off the transverse colon; the lesser sac is entered, and the loose attachments of the posterior gastric wall to the anterior surface of the pancreas are taken down. The hepatic flexure of the colon is mobilized from its retroperitoneal attachments. The mesentery along the inferior border of the pancreas from a point medial to (to the patient's left) the middle colic vessels is incised and carried out laterally and inferiorly to expose the junction of the middle colic vein and the SMV. The middle colic vein may enter directly into the anterior surface of the infrapancreatic SMV or

arise as a common trunk with the gastroepiploic vein (gastrocolic trunk). If the middle colic vein and gastroepiploic vein share a common trunk, the common trunk can be divided; otherwise, the gastroepiploic vein is left intact and divided later in the operation following pancreatic transection. When necessary, the middle colic vein is divided proximal to its junction with the SMV. Division of the middle colic vein allows greater exposure of the infrapancreatic SMV and prevents iatrogenic traction injury to the SMV during dissection of the middle colic vein-SMV junction, especially when dealing with large tumors or tumors extending inferiorly from the uncinate process. In fact, the base of the transverse mesocolon and the anterior leaf of the small bowel mesentery can be left attached to the tumor and resected en bloc with the pancreatic head. Such caudal or inferior tumor extension is not a contraindication to pancreaticoduodenectomy but does add complexity to the operation during this step when the infrapancreatic SMV is identified.

Mobilization of the retroperitoneal attachments of the small bowel and right colon mesentery is performed in patients with uncinate tumors extending into the small bowel mesentery and in those patients who require venous resection and reconstruction. This maneuver was first described by Cattell and Braasch for exposure of the duodenum. The

visceral peritoneum of the small bowel mesentery is incised to the ligament of Treitz, thereby mobilizing the small bowel mesentery. When complete, this maneuver allows cephalad retraction of the right colon and small bowel, exposing the third and fourth portions of the duodenum.

- Occasionally, when there is extensive inflammatory change or scarring at the root of mesentery, usually the result of a prior attempt at resection, we may not identify the SMV early in the operation. In such a case, the SMV will be exposed during step 6 when the pancreas is divided in a caudal direction from the level of the portal vein. This can be a dangerous maneuver because of the lack of vascular control; however, it is a valuable technique for the experienced surgeon who deals with more complicated pancreatic resections, often in the reoperative setting.
- The Kocher maneuver is begun at the transverse portion (third portion) of the duodenum by identifying the inferior vena cava. All fibrofatty and lymphatic tissue medial to the right ureter and anterior to the inferior vena cava is elevated, along with the pancreatic head and duodenum. The Kocher maneuver is continued to the left lateral edge of the aorta, with care taken to identify the left renal vein. The right gonadal vein is usually preserved as it courses anterior to the right ureter and serves as a good landmark to help prevent inadvertent injury to the ureter. A complete Kocher

maneuver is necessary for the subsequent dissection of the pancreatic head from the SMA . Particularly important is the division of the leaf of peritoneum that is posterior to the mesenteric vessels; incision of this portion of peritoneum is necessary prior to performing the SMA dissection. Traditionally, the relationship of the tumor to the SMA would be assessed by manual palpation following a completed Kocher maneuver. As previously stated, preoperative MDCT more accurately predicts resectability and obviates this maneuver.

The portal dissection is initiated by exposing the common hepatic artery (CHA) proximal and distal to the right gastric artery and the gastroduodenal artery (GDA). The CHA is exposed by removing the large lymph node that lies directly anterior to this vessel. The right gastric artery and then the GDA are ligated and divided. The GDA often has a small proximal branch, which may originate anteriorly or just along its lateral border. It is often helpful to ligate and divide this branch separately to obtain adequate length on the proximal GDA to perform a safe ligation and division. If there is tumor extension to within a few millimeters of the GDA origin, one should obtain proximal and distal control of the hepatic artery and divide the GDA flush at its origin. The resulting arteriotomy can be closed with interrupted 6-0 Prolene sutures. Overly aggressive dissection at the GDA origin can result in intimal

dissection of the hepatic artery; this is usually the result of blunt dissection and inadequate vascular control of the proximal and distal hepatic artery. Dissection of the hepatic artery should be performed with gentle, sharp dissection, especially in patients who have received prior external-beam radiation therapy and in those with extensive scar formation from prior surgery. Division of the GDA allows mobilization of the hepatic (common, proper) artery off of the underlying PV, which can be found within the triangle formed by the CHA, GDA, and superior border of the pancreas. The PV should always be exposed prior to dividing the common hepatic duct. Cholecystectomy is then performed and the common hepatic duct is transected at its junction with the cystic duct.

- Review of the preoperative CT scan and careful palpation of the porta hepatis prior to division of the bile duct should alert one to the possibility of anomalous hepatic arterial circulation. A replaced or accessory right hepatic artery arising from the proximal SMA may course posterolaterally to the PV. Rarely, the entire CHA may arise from the SMA (type IX hepatic arterial anatomy). If the foramen of Winslow was initially closed because of adhesions, it should have been re-established at the time of the Kocher maneuver .
- Access to the foramen of Winslow is necessary to palpate the porta hepatis and appreciate anomalous hepatic arterial circulation.

Rarely, the right hepatic artery arising from the proper hepatic artery courses posterior to the PV. In addition, a low-lying right hepatic artery may be injured when the bile duct is divided in an inflamed porta hepatis. Following transection of the bile duct, bile fluid cultures are sent for evaluation and the indwelling biliary stent, when present, is removed. Intraoperative bile cultures are used to guide therapeutic antibiotic treatment postoperatively in the event of an intra-abdominal or superficial wound infection. When possible, we place a gentle bulldog clamp on the transected bile duct to prevent bile spillage until the time of bile duct reconstruction. The anterior wall of the PV is further exposed following division of the common hepatic duct and medial retraction of the CHA. The PV itself should be identified but not extensively mobilized, at which time the stomach and pancreas have been divided. The superior pancreaticoduodenal vein is a constant venous tributary of the PV, which drains the cephalad aspect of the pancreatic head and is located at the superolateral aspect of the PV. Bleeding caused by traction injury to this venous tributary may be difficult to control at this time in the operation.

- The stomach is transected with a linear gastrointestinal stapler at the level of the third or fourth transverse vein on the lesser curvature and at the confluence of the gastroepiploic veins on the greater

curvature so as to perform a standard antrectomy. Care should be taken to ligate and divide the terminal branches of the left gastric artery along the lesser curvature of the stomach prior to gastric transection. However, when opening the lesser omentum and one should specifically look for an accessory or replaced left hepatic artery arising from the left gastric artery. Overly aggressive division of the filmy lesser omentum (with the cautery) in a caudal direction can easily injure a replaced left hepatic artery. The omentum is then divided at the level of the greater curvature transection with the harmonic scalpel. Pylorus preservation may be considered in patients with small periampullary neoplasms, but should not be performed in patients with bulky pancreatic head tumors, duodenal tumors involving the first or second portions of the duodenum, or lesions associated with grossly positive pyloric or peripyloric lymph nodes. To ensure adequate blood supply to the duodenojejunostomy (if pylorus preservation is performed), the anastomosis is created 1.0 to 1.5 cm from the pylorus.

- The loose attachments of the ligament of Treitz are taken down with care to avoid injury to the inferior mesenteric vein. The jejunum is then transected with a linear gastrointestinal stapler approximately 10 cm distal to the ligament of Treitz, and its mesentery is sequentially ligated and divided . It is preferred to tie the

mesenteric (staying) side and use the harmonic scalpel on the serosal (bowel) side. This dissection is continued proximally to involve the fourth and third portions of the duodenum. The duodenal mesentery is divided to the level of the aorta, allowing the devascularized segment of duodenum and jejunum to be reflected beneath the mesenteric vessels.

- The most oncologically important and difficult part of the operation is the next step. After traction sutures are placed on the superior and inferior borders of the pancreas, the pancreas is transected with electrocautery at the level of the PV. If there is evidence of tumor adherence to the PV or SMV, the pancreas can be divided at a more distal location in preparation for segmental venous resection. The specimen is separated from the SMV by ligation and division of the small venous tributaries to the uncinate process and pancreatic head . Complete removal of the uncinate process from the SMV is required for full mobilization of the SMPV confluence and subsequent identification of the SMA. Failure to fully mobilize the SMPV confluence risks injury to the SMA and usually results in a positive margin of resection caused by the incomplete removal of the uncinate process and the mesenteric soft tissue adjacent to the SMA. In addition, without complete mobilization of the SMV, it is difficult to expose the SMAa maneuver necessary for direct

ligation of the inferior pancreaticoduodenalartery or arteries. Mass ligation of this vessel (or vessels) with mesenteric soft tissue is the major cause of postoperative hemorrhage as this vessel retracts from its poorly placed tie or ligature.

Once the pancreatic head and uncinate process are completely separated from the SMV and SMPV confluence, one may experience bleeding from the specimen because of the resulting venous hypertension (the inferior pancreaticoduodenal arteries from the SMA are still intact). One option we occasionally employ is to leave the superior pancreaticoduodenal vein (located at the superolateral aspect of the PV) intact until the more caudal inferior pancreaticoduodenal artery is ligated. This usually does not limit the mobilization of the SMV at the level of the uncinate process and therefore still allows exposure of the SMA.

Proper mobilization of the SMV involves identification of the jejunal branch of the SMV (referred to by some as the first jejunal branch). This branch originates from the right posterolateral aspect of the SMV (at the level of the uncinate process), travels posterior to the SMA, and enters the medial (proximal) aspect of the jejunal mesentery. Very rarely, the jejunal branch may course anterior to the SMA, a situation that greatly facilitates this dissection. The jejunal branch usually gives off one or two venous tributaries to the uncinate process; these tributaries should be divided. If tumor involvement of the SMV (at the level of the jejunal

branch) prevents dissection of the uncinate process from the SMV, the jejunal branch should be divided. Injury to the distal SMV at this level, or a tangential laceration in its jejunal branch (as it courses posterior to the SMA), is difficult to control and probably represents the most frequent cause of iatrogenic SMA injury as one attempts to suture a venous injury prior to full exposure of the SMA. Once the uncinate process is separated from the distal SMV, medial retraction of the SMPV confluence allows one to expose the SMA. The specimen is then separated from the right lateral wall of the SMA, which is dissected to its origin at the aorta. Direct exposure of the SMA avoids iatrogenic injury and ensures direct ligation of the inferior pancreaticoduodenal artery or arteries.

Most patients have one or two pancreaticoduodenal arteries that are identified and ligated in continuity at their origin from the SMA. Failure to accurately identify and ligate these vessels may be a common cause of early postoperative bleeding. As mentioned previously, the soft tissue adjacent to the proximal SMA represents the SMA (or retroperitoneal) margin. A grossly positive SMA margin should not occur if high-quality preoperative imaging is performed. A microscopically positive SMA margin will occur in 10% to 20% of cases; margin positivity can result from tumor spread along perineural sheaths and does not always result from direct extension of the primary tumor.

Frozen-section evaluation of the pancreaticoduodenectomy specimen is

limited to analysis of the pancreatic and common hepatic duct transection margins. Positive resection margins on the bile or pancreatic duct mandate further resection until clear margins are achieved. However, changes caused by pancreatitis should not be confused with margin positivity. Pancreatitis usually involves the entire body and tail of the pancreas distal to the tumor within the pancreatic head. This may result in dysplastic cells at the pancreatic transection margin on frozen-section evaluation. Further resection of the pancreas should be performed only if there is histologic evidence of invasive carcinoma (on frozen-section analysis) at the margin; dysplasia in the absence of carcinoma is not an indication for further pancreatic resection. Invasive carcinoma extending along the main pancreatic duct is uncommon.

Complete permanent-section analysis of the pancreaticoduodenectomy specimen requires that it be oriented for the pathologist to enable accurate assessment of the SMA margin of excision and other standard pathologic variables. Because we remove all tissue to the right of the SMA, further resection at this margin is not possible. However, the SMA margin must be identified and inked with the pathologist; it cannot be assessed retrospectively.

The operation as described here emphasizes full mobilization of the SMPV confluence, exposure of the SMA, and removal of all mesenteric soft tissue and perineural tissue to the right of this vessel. The high

incidence of local recurrence following pancreaticoduodenectomy mandates that greater attention be paid to the SMA margin (the soft tissue margin along the right lateral border of the proximal 3 to 4 cm of the SMA). During step 6 of pancreaticoduodenectomy, full mobilization of the SMPV confluence is necessary to allow complete exposure of the SMA. Dissection of the specimen from the proximal SMA is necessary to obtain a negative SMA margin; therefore, this is the most important technical aspect of this operation. Direct exposure of the SMA should be a routine part of pancreaticoduodenectomy, will minimize the risk for iatrogenic injury of this vessel, and will ensure direct ligation of the inferior pancreaticoduodenal artery(s), thereby minimizing the risk for postoperative intra-abdominal hemorrhage.

Pancreatic, Biliary, and Gastrointestinal Reconstruction

Reconstruction after pancreaticoduodenectomy proceeds first with the pancreatic anastomosis.

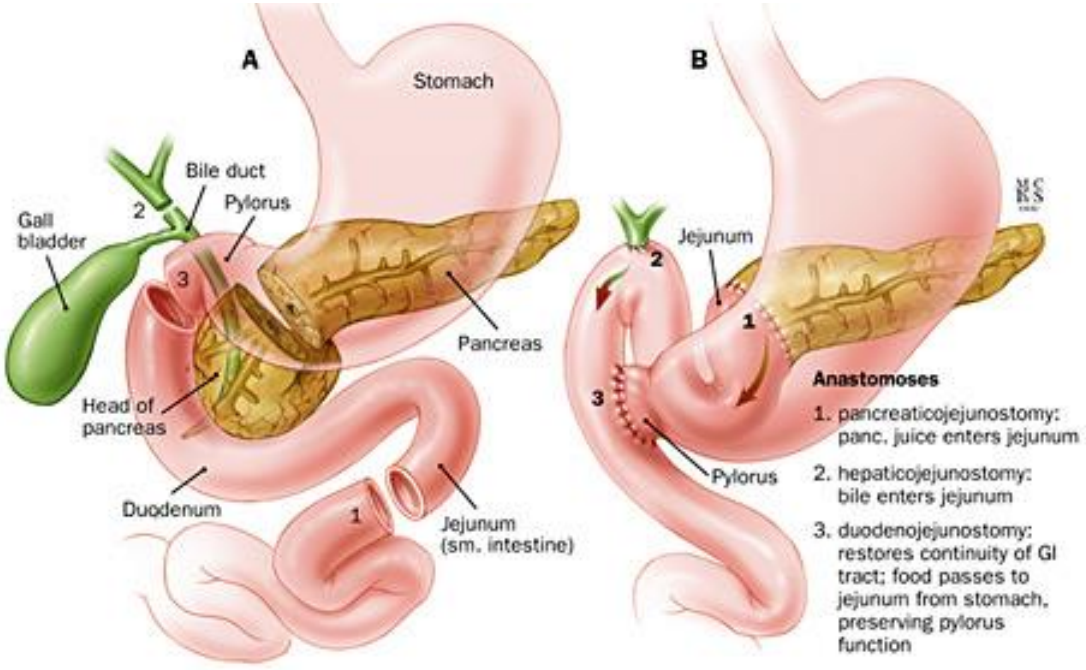
- The pancreatic remnant is mobilized from the retroperitoneum and splenic vein for a distance of 2 to 3 cm. Failure to adequately mobilize the pancreatic remnant results in poor suture placement at the pancreaticojejunal anastomosis. Injury to the proximal splenic artery can occur when mobilizing the pancreatic remnant if one does not appreciate the location of this vessel. The transected

jejunum is brought through a generous incision in the transverse mesocolon to the left of the middle colic vessels. We prefer to bring the jejunum retrocolic rather than retroperitoneal (posterior to the mesenteric vessels in the bed of the resected duodenum). A two-layer, end-to-side, duct-to-mucosa panceaticojejunostomy is performed over a small Silastic stent. If the pancreatic duct is dilated, a stent is not employed. Following completion of the posterior row of interrupted 4-0 seromuscular monofilament sutures, a small full-thickness opening is made in the bowel. The anastomosis between the pancreatic duct and the small bowel mucosa is completed with 4-0 or 5-0 monofilament sutures. Each stitch incorporates a generous bite of the pancreaticduct and a full-thickness bite of the jejunum. The posterior knots are tied on the inside, and the lateral and anterior knots are tied on the outside. Prior to the anterior sutures being tied, the stent is placed across the anastomosis so that it extends into the pancreatic duct and small bowel for a distance of approximately 2 to 3 cm. The anastomosis is completed with placement of an anterior row of 4-0 seromuscular monofilament sutures. When the pancreatic parenchyma is soft, we often use vascular pledgets for the anterior row of sutures to prevent them from causing a tear in the pancreatic tissue.

- When the pancreatic duct is not dilated and/or the pancreatic substance is soft (not fibrotic), one can perform a two-layer anastomosis that invaginates the cut end of the pancreas into the jejunum. The outer posterior row of 4-0 sutures is placed as outlined previously. The bowel is then opened for a length equal to the transverse diameter of the pancreatic remnant. Using a running, double-armed, 4-0 nonabsorbable monofilament suture, the pancreatic remnant is sewn to the jejunum. The anastomosis is completed with placement of an anterior row of 4-0 seromuscular sutures. However, we rarely use this technique because even a nondilated pancreatic duct can usually be anastomosed using the duct-to-mucosa technique.
- A single-layer biliary anastomosis is performed using interrupted 4-0 absorbable monofilament sutures. It is important to align the jejunum with the bile duct to avoid tension on the pancreatic and biliary anastomoses. A stent is rarely used in the construction of the hepaticojejunostomy.
- An antecolic, end-to-side gastrojejunostomy is constructed in two layers. Starting from the greater curvature, 6 to 8 cm of the gastric staple line is removed. A posterior row of 3-0 silk sutures is followed by a full-thickness inner layer of running monofilament sutures; the anterior row of silk sutures completes the anastomosis. The distance between the biliary and gastric anastomoses should be

at least 50 cm, thereby allowing the jejunum to assume its antecolic position (for the gastrojejunostomy) without tension, and also preventing bile reflux cholangitis. We prefer an antecolic gastrojejunostomy to prevent possible outlet obstruction caused by the colonic mesentery. Lastly, the jejunal limb should be aligned so that the efferent limb is adjacent to the greater curvature of the stomach. A No. 10 French feeding jejunostomy tube may be placed distal to the gastrojejunostomy. We rarely use a gastrostomy tube for postoperative gastric decompression. Prior to abdominal closure, the abdomen is carefully irrigated in all four quadrants. In patients with a previous indwelling endobiliary stent, the bile is contaminated and often has had free access to at least the right upper quadrant of the abdomen; careful irrigation may prevent postoperative infectious complications. In addition, in patients who have contaminated bile from an endobiliary stent or a previous biliary bypass, we often place one drain in the right upper quadrant; we no longer place a drain near the pancreatic anastomosis. The use of drains remains an active area of controversy in the field of pancreatic surgery, and many surgeons still drain the pancreaticojejunostomy. Finally, we place the mobilized falciform ligament (carefully preserved when the abdomen was opened) between the hepatic artery, at the level of

the GDA stump, and the afferent jejunal limb to cover the GDA stump . This is one simple strategy to minimize the risk for pseudoaneurysm formation at the site of the GDA stump in the event of a pancreatic anastomotic leak and resultant abscess formation.



Whipples procedure

Adjuvant therapy

In 1985 the Gastrointestinal Tumor Study Group (GITSG) trial was reported and demonstrated that patients undergoing resection for pancreas

cancer who received adjuvant chemoradiotherapy had better survival.This prospective randomized trial compared observation (control) and split-course radiotherapy (4000 cGy, 20 fractions, over a 6-week period) with bolus 5-fluorouracil (5-FU), 500mg/m^2 intravenously on each of the first 3 days of the 200-cGy sequence of radiotherapy, in patients with pancreas cancer. Additionally, patient receiving adjuvant therapy underwent bolus 5-FU administration every week for 2 years.

It has also been demonstrated that multiagent 5- FU–based chemotherapy regimens can be combined with radiotherapy. The group at the Virginia Mason Clinic have combined 5-FU, cisplatin, interferon alfa, and radiotherapy and have shown significant activity in the adjuvant setting, albeit with increased toxicity.A randomized controlled trial performed by the European Study Group for Pancreatic Cancer (ESPAC-1) demonstrated that systemic chemotherapy alone is superior to chemoradiation therapy in the postoperative setting.The role of adjuvant chemoradiotherapy in the treatment of distal bile duct, ampullary, and duodenal cancer is even less well understood than for pancreas cancer because of the relative infrequency of these diseases.

Palliative chemotherapy

5-FU was considered the standard therapy for advanced pancreas cancer before approval of gemcitabine by the Food and Drug Administration (FDA). Although response rates greater than 20% were reported for treatment with 5-FU, most of these reports predated the era of CT imaging and were based primarily on clinical tumor evaluation. Modern phase II trials have reported response rates of less than 10% for 5-FU alone or with leucovorin.

Gemcitabine was approved by the FDA because of its ability to alleviate tumor-related symptoms. A pivotal phase III trial was completed to quantify this effect in patients with metastatic, symptomatic pancreatic cancer.[81] One hundred twenty-six patients who had not received previous chemotherapy for metastatic disease were randomized to weekly gemcitabine ($n = 63$) or weekly bolus 5-FU ($n = 63$). Overall survival in patients treated with gemcitabine was significantly improved over those treated with 5-FU (median survival, 5.7 versus 4.4 months, respectively; $P < .0025$). One-year survival rates were 18% for patients treated with gemcitabine versus 2% for patients treated with 5-FU.

Operative palliation

As discussed previously, current preoperative staging and imaging modalities allow resection in approximately 80% of patients explored for periampullary cancer. When a patient undergoes exploration and the cancer is found to be unresectable, a decision must be made regarding whether to operatively palliate the patient. Operative palliation is most beneficial in patients without widespread metastatic disease and with a life expectancy of more than several months. The potential morbidity and mortality associated with operative palliation should be weighed against the more durable palliation achieved with biliary bypass with or without gastrojejunostomy. Additionally, open chemical splanchnicectomy can be added to the operative palliative procedure.

Chronic pancreatitis

Natural course and pathogenesis of pain in chronic pancreatitis

The main rationale for conservative approaches in the past derives from the assumption that most patients with long-standing chronic pancreatitis will become pain- free due to a progressive “burning out” of the organ.However, studies showing that pain alleviation did not occur in more than 50% of the patientsas well as the unpredictability of the course of the disease,the considerable socioeconomic implications of frequent hospitalization in these mostly young patients,and last, the implementation of more customized surgical techniques has led, at least in part, to a reconsideration of this view.

Pain is the most common symptom for which the patient commonly becomes a surgical candidate. Many theories have been put forth for the cause of pain in these patients.

Ductal and parenchymatous hypertension

The ductal hypertension theory is based on several observations. Ductal dilation is a common finding that is suggestive for an increased pressure in the pancreatic ductal system, which may be observedin these patients.

Patients with the “small duct pancreatitis” also have ductal and parenchymatous hypertension.Hence, elevated intrapancreatic pressureor, in other terms, a retroperitoneal compartment syndrome yielding reduced pancreatic blood flow and reduction of the intrapancreatic pH level, especially after stimulation of the exocrine pancreatic secretion,has been assumed to cause pain or to interact with its intensity. As a logical consequence of these findings, the concept of surgical and, later, endoscopic, decompression of the main pancreatic duct system arose that leads at least to temporary pain relief.

Complications of chronic pancreatitis

In the course of chronic pancreatitis, several complications with less or more life-threatening potential may occur. Extrahepatic cholestasis as well as duodenal obstruction may be a result of an inflammatory tumor, a fibrotic scarring, or both, occurring in the head of the pancreas. Acute inflammatory episodes can lead to chronic pancreatic pseudocysts or internal pancreatic fistula to the abdominal or thoracic cavities. Finally, thrombosis of the splenic vein can occur as a result of the inflammatory reaction of chronic pancreatitis, which results in splenomegaly and localized (so-called left- sided) portal hypertension. The pathophysiology, clinical presentation, and management of these complications of chronic pancreatitis are reviewed in this chapter.

Common Bile Duct Stenosis

Biliary strictures have been recognized as characteristic complications of chronic pancreatitis. In hospitalized patients with pancreatitis, the incidence of biliary stricture accounts for about 5% to 9% and drastically increases to up to 35% in surgical series.The main factor for the development of common bile duct stenosis is the close anatomic relationship of the distal common duct to the head of the pancreas, thereby increasing the risk of secondary common bile duct stricture in these patients by cephalic irregularities of any reason. Even though pseudocysts are common in chronic pancreatitis, compression of the common bile duct by pseudocysts is rare. The spectrum of clinical presentation of these patients ranges from being asymptomatic with only biochemical findings such as elevated alkaline phosphatase or bilirubin level, or both, to being septic with cholangitis. Interventional (i.e., surgical) therapy is clearly indicated in patients with common bile duct strictures secondary to chronic pancreatitis. Endoscopic stenting plays a role in patients who are unfit for surgery, but it is not recommended as definitive therapy, particularly with regard to the necessity of repeated endoscopic interventions due to infection, stent displacement, or stent occlusion.Of greatest importance is to rule out that biliary obstruction in

these patients is a result of a concomitant malignancy in the periampullary region.

Duodenal Obstruction

In patients requiring an operation for chronic pancreatitis, the incidence of duodenal obstruction, which can
be either transient or permanent, accounts for 12%.Duodenal obstruction can also occur secondarily to pancreatic pseudocysts.Patients typically present with a history of nausea, vomiting, upper abdominal pain, and weight loss. Endoscopy shows a concave-shaped extraluminal impression without mucosal involvement beginning at the descending portion of the duodenum. Warshaw found that 25% of the patients with common bile duct stenosis caused by chronic pancreatitis also required surgical treatment of duodenal obstruction.In duodenal obstruction, operation is indicated for patients with failure to resolve the obstruction with 1 to 2 weeks of conservative therapy, suggesting the presence of an irreversible duodenal obstruction necessitating further (surgical) treatment. The surgical procedure of choice should definitively address all the individual existing complications of chronic pancreatitis at once. Therefore, combined drainage procedures or resection are used to manage these findings. Gastric outlet obstruction can result from various mechanisms. The most frequent cause in addition to an inflammatory mass due to chronic pancreatitis is a duodenal involvement by pancreatic cancer. If

surgery is indicated, the therapeutic aim should be to eliminate the cause of the duodenal stricture, such as an enlarged pancreatic head or an encasement of the duodenum by inflammatory adhesions.

Internal Pancreatic Fistulas

Pancreatic ascites and pancreaticopleural fistulas are known as *internal pancreatic fistulas.* They result from a disruption of the pancreatic duct or leakage from a pseudocyst. Internal pancreatic fistulas are rare but well recognized conditions associated with a significant morbidity and mortality.Misdiagnoses such as in cases of pancreaticopleural or pancreaticobronchial fistula are not uncommon. Three main types of thoracic manifestations include mediastinal pseudocysts, pancreaticopleural fistulas, and pancreaticobronchial fistulas.Once an internal pancreatic fistula is suspected, laboratory testing of pleural effusions with special respect to their amylase concentration should be performed. Diagnostic evaluation should in particular address a possibly underlying ductal pathology. Conservative treatment may be indicated in patients with mild to moderate ductal anatomic alterations.

Conservative treatment has an efficacy of 30% to 60%, a recurrence rate of 15%, and a mortality rate of 12%.Interventional endoscopic therapy would be the next step in patients with persisting fistulas and pleural effusion. Endoscopic treatment is based on the concept that main pancreatic duct disruption arises as a consequence of an increase in

intraductal pressure or within a pseudocyst and aims at the reduction of the ductal pressure. In most patients, a pancreatic sphincterotomy via the major papilla is performed to facilitate transpapillary endoscopic placement of a pancreatic duct stent.In selected cases, this may be combined with the use of tissue glue for the closure of pancreatic fistulas.Surgical treatment has to focus on the elimination of ductal hypertension that inhibits spontaneous closure of fistulas.

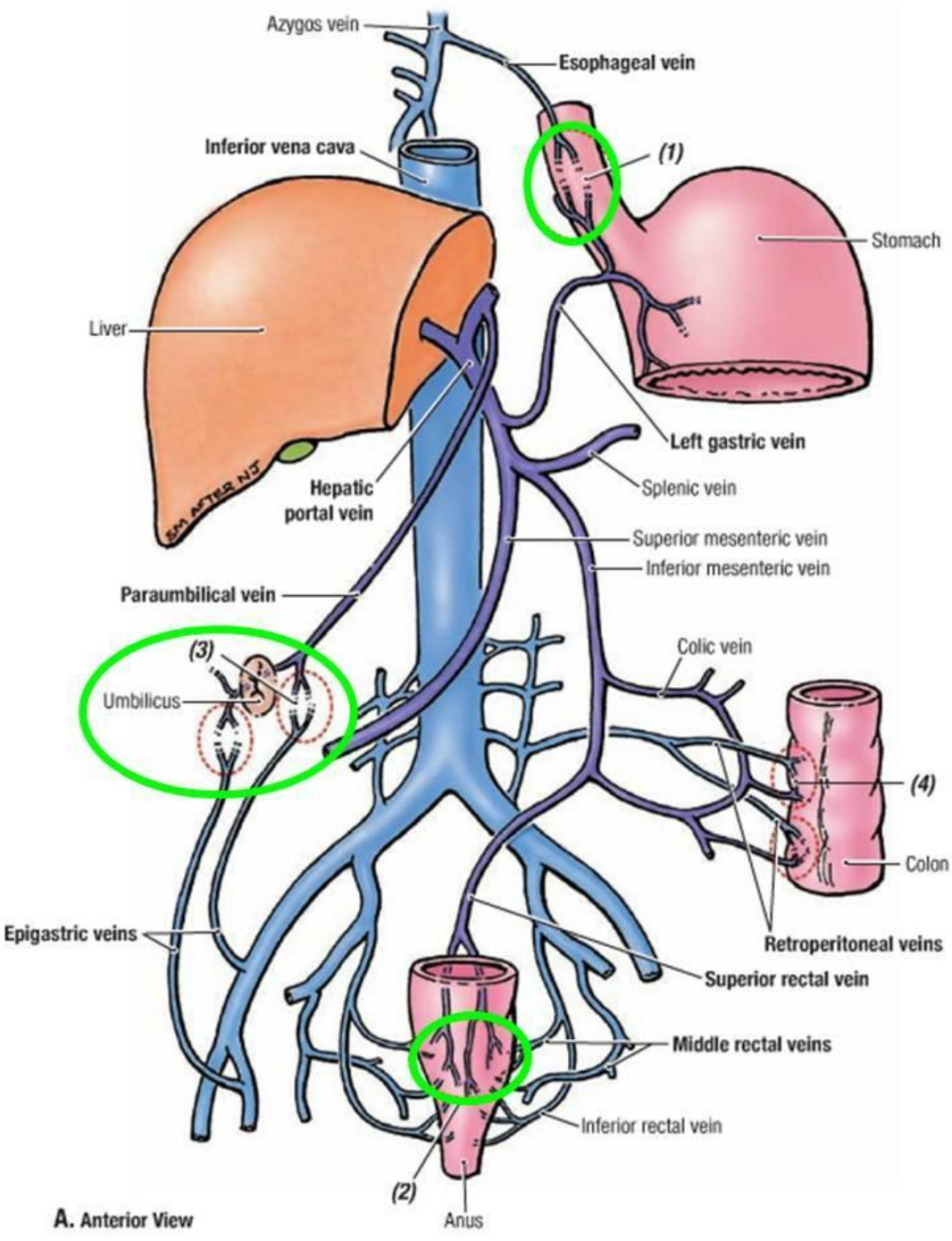
Pancreatic Ascites

Pancreatic ascites is defined as massive accumulation of pancreatic fluid in the peritoneal cavity. The level of amylase in the ascitic fluid is typically above 1000 IU/L and the ascitic fluid to serum amylase ratio is approxi- mately 6.0.It has been described in approximately 4% of patients with chronic pancreatitis and in 6% to 14% of those with pancreatic pseudocysts. Sometimes an attack of acute pancreatitis or a traumatic injury to the pancreas can be held responsible; however, two thirds of patients do not give a history of a recent episode of pancreatitis.The establishment of diagnosis is often difficult because pain or symptoms of pancreatic disease may be absent. Especially in patients with alcohol abuse, the diagnosis may be confused with ascites due to cirrhosis and portal hypertension. Diagnostic paracentesis should be per- formed in

every patient with ascites. If pancreatic ascites is suspected, routine tests of ascitic fluid such as cell count, culture, Gram stain, amylase, albumin, and total protein should be obtained. Once the diagnosis has been established, the evaluation of the pancreatic duct morphology is mandatory. There is agreement that endoscopic retrograde cholangiopancreatography should be performed to localize the site of leakage and to perform endoscopic therapy (transpapillary stenting of the pancreatic duct or sealing of the leak) if possible as the procedure of first choice.Although there are no data on the role of magnetic resonance cholangiopancreatography for the diagnosis of this condition, this test can accurately demonstrate the normal pancreatic duct and detect any abnormalities arising from it.Treatment with somatostatin or octreotide together with diuretics and repeated paracentesis may be beneficial for some patients.The stent can facilitate healing of ductal disruptions by partially occluding the leaking duct or bypassing the pancreatic sphincter, thereby decreasing the intrapancreatic duct pressure. Some patients fail medical therapy, ultimately requiring surgery.Indications for surgery include persistent or recurrent accumulation of ascites and/or sudden deterioration of clinical status. The type of surgical intervention depends on the ductal anatomy, the site of the leakage from the pancreatic duct or pseudocyst, and the operative findings.

Vascular Irregularities - Portal Hypertension

Extrahepatic portal hypertension (EPH) is defined as extra- hepatic hypertension of the portal venous system in the absence of liver cirrhosis.



Sites of collateral flow

In cases of portal hypertension, the collateral routes include the short gastric veins which may present as gastric varicies in the fundus the stomach. The esophageal veins shif blood to the azygos system and may manifest as esophageal or gastric varicies. The left gastroepiploic veins pushes blood into the inferior mesenteric and left colic veins. Rarely the right gastroepiploic vein drains into the retroperitoneum, renal, and intercostal veins.

Thrombosis of the Portal Vein with Cavernous Transformation

Dealing with patients with chronic pancreatitis and coexistent portal vein thrombosis with cavernous transformation complicates the decision-making process enormously . Pancreatitis is the most common extrahepatic, inflammatory disease that causes portal vein thrombosis. Preoperative assessment of patients should routinely include a high-resolution computed tomographic scan and magnetic resonance device providing information with regard to arterial supply and venous drainage. As for other abdominal operations, such as surgery for gastric or duodenal ulcer disease, portal vein thrombosis with cavernous transformation was identified as a major operative risk factor, accounting for prolonged operative time and substantial intraoperative blood loss. What is the ideal operative strategy for a patient with chronic pancreatitis

and an inflammatory pancreatic head tumor who has developed portal vein thrombosis with cavernous transformation? Basically, the goals of the operation in patients with or without cavernous transformation do not differ. Hence, the essential landmarks of the surgical strategy resemble those in patients without irregularities of the portal flow. However, any operation in these patients carries particular risks. This notably applies for technical steps that are associated with a dissection of portal collaterals, thereby increasing the amount of postoperative ascites. A transection of the pancreatic parenchyma above the portal vein as required for the Beger procedure, Whipple resection, and duodenum-preserving pancreatic head resection should be avoided by all means because this carries unpredictable risks.

In conclusion, EPH with coexistent cavernous transformation entails a substantial risk in pancreatic surgery for chronic pancreatitis. The mere presence of portal vein thrombosis with cavernous transformation does not justify surgery in chronic pancreatitis. When surgery is considered in a symptomatic patient, surgical strategy is determined more by pancreatic morphology than by the intent to restore portal blood flow. The approach to chronic pancreatitis with associated portal vein thrombosis with cavernous transformation is multidisciplinary,

tailoring the various therapeutic options to meet the individual patient’s needs.

Pancreatic Cancer in chronic pancreatitis

Perhaps the most challenging aspect of the management of presumed chronic pancreatitis is distinguishing it from *pancreatic carcinoma*. Patients initially seen with biliary obstruction, duodenal obstruction, or an inflammatory mass in the head of the pancreas may all have benign complications of chronic pancreatitis, but the possibility of pancreatic or other periampullary malignant disease must always be considered. Furthermore, evidence suggests that patients with chronic pancreatitis are at increased risk for the development of pancreatic cancer. Lowenfels and colleagues reported on a cohort of 2015 patients with chronic pancreatitis.The risk for pancreatic cancer increased in linear fashion from the time of diagnosis of chronic pancreatitis, with the incidence increasing from 1.8% at 10 years to 4% at 20 years. Other groups have confirmed these findings in similar studies and have concluded that chronic pancreatitis increases the risk for pancreatic cancer by up to three times the risk in the general population.

Much effort has been expended to clarify which imaging modalities and diagnostic procedures best distinguish pancreatic cancer from chronic pancreatitis. Conventional CT and ERCP have traditionally been used to distinguish these two diagnoses, with a combined diagnostic accuracy of

about 65% to 80%.Because of the high rate of both false-positive and false-negative results, other techniques have been advocated to aid in the diagnosis. EUS is available in many centers. Advocates of this technique claim high sensitivity for the detection of pancreatic masses; Barthet and colleagues claimed 100% sensitivity in detecting pancreatic masses in patients with chronic pancreatitis.Certainly, such a 100% sensitivity rate does not translate into a 100% accuracy rate. EUS is thought to be particularly helpful in the detection of masses smaller than 2 cm, many of which are missed on CT scan.EUS is also reported to allow accurate characterization of the relationship of pancreatic masses to the superior mesenteric vessels and portal vein and thus to predict resectability. However, one study reported that newer high-resolution spiral CT is at least as accurate in determining resectability based on vascular involvement and that CT may be more accurate in determining involvement of the superior mesenteric artery.EUS is an invasive procedure, but it may allow for the establishment of a tissue diagnosis by fine-needle aspiration cytology. However, a negative cytologic study should not delay resection in a patient with an appropriate clinical history and a mass suggestive of pancreatic cancer. Moreover, patients with chronic pancreatitis have been found to have an extremely high rate of false-positive EUS studies that detect a focal mass, so the positive predictive value of EUS for pancreatic cancer is as low as 60%.

MRCP has also been advocated for distinguishing pancreatic cancer from chronic pancreatitis. As with many of its applications, studies of the use of MRCP in diagnosing pancreatic cancer are small, and it is too early to determine the accuracy of this technique. Studies in the radiologic literature have unfortunately found similar MRI enhancement of pancreatic cancer and chronic pancreatitis, a finding that makes a definitive diagnosis difficult.Other groups support the use of positron emission tomography (PET) with fluorodeoxyglucose for the diagnosis of pancreatic cancer. Rose et al. reported that PET scanning was more sensitive and specific than CT in the detection of small pancreatic tumors and that PET scan results led to a change in management in 43% of the patients in their series.Unfortunately, the patients with false-positive results in this series all had chronic pancreatitis, so these findings call into question whether PET offers useful data in the diagnosis of pancreatic cancer in patients with chronic pancreatitis. Imdahl and colleagues argued that the level of glucose uptake in pancreatic masses as measured by PET allowed for differentiation of pancreatic cancer and chronic pancreatitis in a small group of patients.Whether these results would make a difference in the eventual treatment is not clear because patients with concerning clinical findings all underwent resection in this series. Clearly, no current diagnostic test is sufficiently accurate to differentiate chronic pancreatitis from pancreatic cancer. In the future, molecular

genetic techniques focusing on ductal precursor lesions and the characteristic molecular fingerprint of pancreatic cancer may allow better differentiation between benign and malignant pancreatic disease. At present, patients in whom the diagnosis is unclear but the clinical symptoms of pain, jaundice, and weight loss with a noncalculous distal biliary obstruction make the diagnosis of malignant disease possible should undergo surgical exploration with planned pancreaticoduodenectomy. Because the mortality rate of pancreaticoduodenectomy has fallen significantly, particularly in experienced centers, proceeding with surgical resection is one approach.Patients found to have chronic pancreatitis without malignant disease have also been shown to benefit from this procedure, particularly regarding quality-of-life issues.Duodenum-preserving resection of the pancreatic head is another possible approach to patients with severe chronic pancreatitis.

Surgical procedures

The evolution of the lateral pancreaticojejunostomy began in 1908 when Coffey first performed distal pancreatectomy with pancreaticoenterostomy in dogs. He accurately suggested that this procedure would be beneficial in various clinical situations. Link first

performed drainage of the pancreatic duct for chronic pancreatitis in 1911. Several decades later, Duval described distal pancreatectomy, splenectomy, and distal pancreaticojejunostomy for patients with chronic pancreatitis. The distal pancreaticojejunostomy was performed in an end-to-end fashion. His premise for this procedure was that increased pressure in the main pancreatic duct produced pain, which could be alleviated by draining the pancreas by a retrograde route. Criteria for the procedure to proceed included intraoperative documentation of increased pancreatic duct pressure. Duval's procedure addressed the distal pancreatic duct, but it neglected the proximal duct. Puestow and Gillesby addressed the more proximal portions of the duct by longitudinally opening the pancreatic duct in addition to splenectomy and distal pancreatectomy. A pancreaticojejunostomy was formed by the anastomosis of the open end of the jejunum and the proximal pancreas. Although a greater extent of the duct was decompressed, the head of the pancreas remained undrained as the jejunum was not able to be brought to the right of the superior mesenteric vessels.

The Puestow Gillesby procedure was later modified by Partington and Rochelle, who described a side-to-side anastomosis created from a longitudinal opening in the jejunum as well as the pancreatic duct. Mobilization and resection of the spleen and distal pancreas were not necessary and drainage of the pancreas from the head to the tail was

achieved. Most recently, Frey described local resection of the head of the pancreas that has been used in concert with lateral pancreaticojejunostomy. This procedure is important for situations in which the head of the pancreas has become enlarged and contains multiple strictures and retention cysts, which make complete ductal decompression exceedingly difficult.

The procedure :

A broad-spectrum intravenous antibiotic active against Gram-negative enteric organisms is usually administered preoperatively because cultures of pancreatic duct fluid yield organisms in approximately one fourth of patients. A mechanical and antibiotic bowel preparation is advisable, particularly in reoperative cases, because the transverse colon and its vascular supply may be adherent. Sequential compression devices are placed on the legs for the prevention of deep vein thrombosis.

Radiographic capability should be available in case intraoperative cholangiography or pancreatography is needed. Digital fluoroscopy is preferred but standard static exposures may suffice.

A bilateral subcostal incision is our preferred method for entering the peritoneal cavity, but a midline incision may be appropriate, depending on the patient's body habitus and the location of previous incisions. A thorough initial exploration should confirm findings of chronic pancreatitis. The pancreas typically has a uniform, firm, and fibrotic

consistency. A directed search should be made for evidence of malignancy. Any suspicious liver, peritoneal, or mesenteric frozen section must be done. If unusually hard areas or a mass is encountered in the pancreas, fine-needle aspiration can be performed with an 18-guage needle, and immediate cytologic analysis of the specimen can be obtained if an experienced cytologist is available. Cancer may also be detected as an area of breakthrough on the substance of the pancreas or mesentery. Superficial shave biopsies of these areas can be obtained. Patients undergoing pancreaticojejunostomy for chronic pancreatitis, a few will have cancer diagnosed intraoperatively or within several months.

The entry into the lesser sac can be technically demanding if previous pseudocyst disease has been treated by cystgastrostomy. The splenic artery can be palpated at the superior margin of the gland. The firm inferior edge of the pancreas also can be readily identified. The gastrocolic attachments must be divided all the way to the left, and the transverse colon and splenic flexure must be mobilized downward to provide sufficient access to the more lateral tail of the gland.

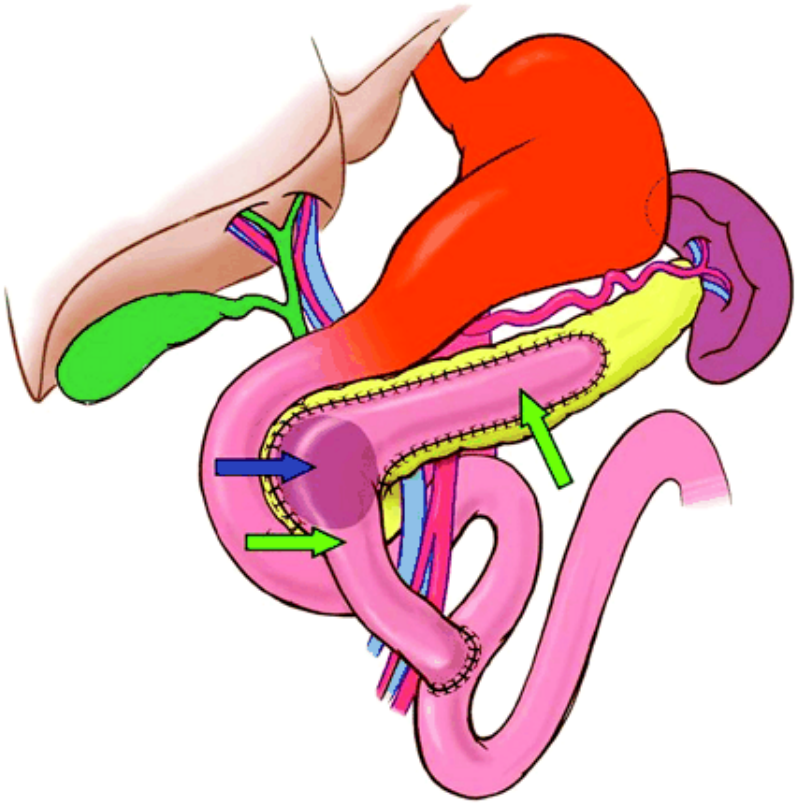
The pancreatic head is mobilized by a wide Kocher maneuver. The hepatic flexure of the colon must be mobilized inferiorly to allow complete exposure for this procedure. With normal tissue planes, the duodenum can be delivered bluntly from the retroperitoneum, but in chronic pancreatitis it is best accomplished by sharp dissection to avoid

tearing retroperitoneal vessels. The superior mesenteric vein is approached cautiously because it may be obscured by fibrotic reaction and is easily torn or punctured. Tracing the middle colic veins downward helps to identify its location. During this phase of the dissection, the head of the pancreas is exposed, and the adherent mesocolon is mobilized downward. Troublesome bleeding from the mesocolic veins is controlled by fine suture-ligation or venorrhaphy. Division of the gastrocolic ligament and extended kocherization permit complete bimanual palpation of the pancreatic head and evaluation of the uncinate process.

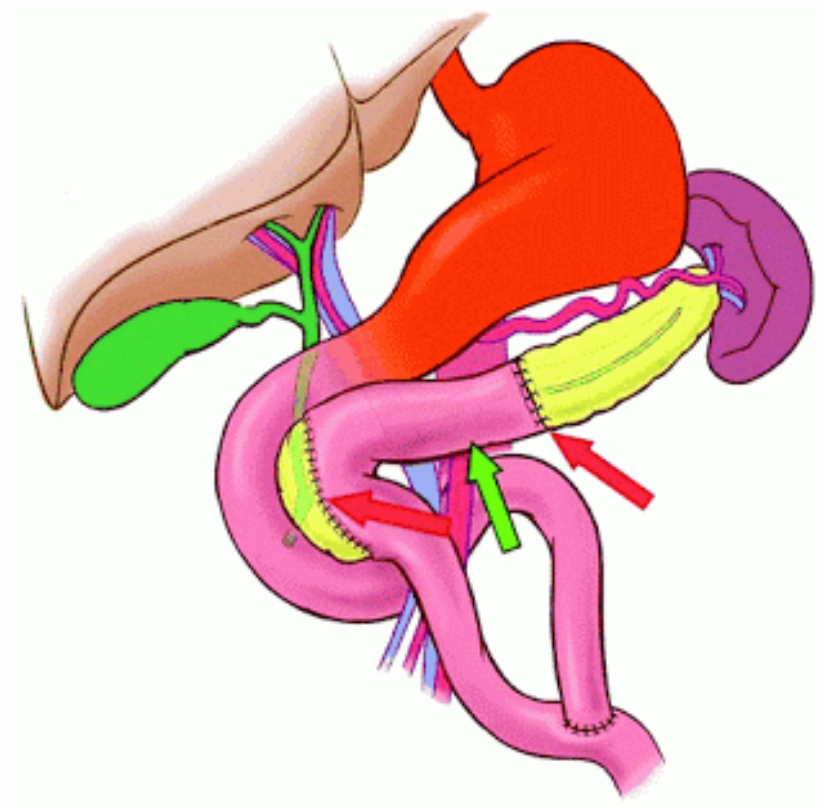
The duct is identified. This is confirmed by needle aspiration that yields water-clear pancreatic fluid. If a vessel has been punctured during attempted aspiration, the duct fluid may be sanguineous, but it still will be dilute. Cautery is used to cut down directly on the aspirating needle until the duct is entered. If the duct cannot be identified by this method, intraoperative ultrasonography can be used to determine its location. If intraoperative ultrasonography is not available, a vertical incision perpendicular to the expected course of the duct can be made in the midbody of the gland. The incision should be to the left of the course of the superior mesenteric vein as this can be injured if the posterior margin of the gland is violated. If the duct is unusually difficult to locate, the preoperative imaging studies should be reviewed again to make certain the duct is suitably dilated for the planned operation.

The duct has a more anterior position toward the tail of the gland and dives posteriorly within the head. Thus, the depth of parenchyma that has to be divided is variable. The duct is opened to within approximately 1 cm of the tip of the tail.

The most important and difficult site for decompression is the pancreatic head. The ducts of Wirsung and Santorini are opened as close to the wall of the duodenum as possible. Failure to unroof both the duct of Wirsung and duct of Santorini is a common cause of persistent postoperative pain. Anterior pancreaticoduodenal or gastroepiploic veins that run vertically over the pancreatic head toward the superior mesenteric vein are suture-ligated and divided as the ductotomy is extended to the duodenum. Because the main pancreatic duct dives posteriorly and inferiorly to the right of the superior mesenteric vein, and because the head of the pancreas is frequently bulky and enlarged in patients with chronic pancreatitis, anterior ductotomy alone may not be adequate for drainage of the proximal main pancreatic duct and uncinate process.



Frey's procedure



Beger's procedure

Local resection of the pancreatic head described by Frey provides better

decompression in this situation. With the fingers of the left hand behind the head of the gland and using cautery, the anterior capsule of the gland and the underlying pancreatic tissue are removed to the level of the duct of Wirsung. Care must be taken to excise sufficient overlying parenchyma to expose the posterior, inferior, and medial extent of the ducts. The posterior wall of the pancreatic duct is within millimeters of the posterior capsule and identifies the posterior extent of the dissection. The superior mesenteric vein and portal vein must be identified during this dissection. A rim of adjacent fibrous tissue of approximately 0.5 cm is preserved for the anastomosis. A probe or balloon catheter can be placed through the cystic duct or a choledochotomy to identify and protect the intrapancreatic common bile duct if there is uncertainty about its location. By palpating the gland with the left fingers posterior and the left thumb anteriorly, the surgeon can identify residual undrained areas and preserve a posterior rim of pancreatic tissue.

A frozen section is routinely obtained on a portion of the resected head or a slice of parenchyma removed during the ductotomy. This is done not only to confirm the diagnosis but also to rule out a malignancy. Any area in the gland that is suspicious for cancer should be biopsied and evaluated with frozen section. An effort should be made to remove all ductal calculi and debris. This is particularly important in the head of the gland, where they can be the cause of persistent obstruction of tributaries entering the

main duct. Concretions of calcium carbonate often extend into the parenchyma and must be firmly extracted. Obviously, not all intraparenchymal calcifications can be removed. Caution is necessary to avoid bleeding. If pancreatic bleeding occurs, it is controlled with cautery, carefully placed suture ligatures, or application of topical hemostatic agents.

A number of authors have emphasized that the pancreaticojejunal anastomosis must be at least 6 to 10 cm to provide optimal results. Focus on a specific length is misplaced because even a long anastomosis is not adequate if portions of the gland are incompletely decompressed. The surgeon's task is to drain the ductal system as thoroughly as possible, with particular attention to the head of the gland. More complete ductal decompression should be associated with better pain relief.

A 50- to 60-cm Roux-en-Y limb is constructed after dividing the jejunum 20 to 30 cm distal to the ligament of Treitz. This can be performed quickly with a gastrointestinal stapler. The end staple line closure of the transected distal jejunum is reinforced with sutures. The Roux-en-Y limb is brought up by a conventional route, often in a retrocolic position through a mesenteric window between the right and middle colic vessels. A longer Roux-en-Y limb may be necessary for concomitant drainage of associated pseudocysts or an obstructed biliary tract. An enterotomy is made along the antimesenteric border of the jejunal loop. The length of

the enterotomy should be shorter than that the pancreatic opening because the bowel will stretch. The jejunal opening can easily be extended if necessary.

There have been different recommendations as to the preferred technique for the pancreaticojejunal anastomosis. Alternatives

include the use of one or two layers of sutures, the use of continuous or interrupted sutures, and incorporation of the pancreatic capsule, transected edge of parenchyma, or duct mucosa on the pancreatic side. No single method has been proven superior. The technique should be adapted to the size of the duct and thickness of the gland. Interrupted sutures of 3-0 silk have long been used for this anastomosis, but our current preference is for a single-layer continuous anastomosis that uses an absorbable but long-lasting monofilament suture. Bites are taken through the full thickness of the jejunum and pancreatic capsule. The pancreatic stitch may include a small portion of the transected parenchymal edge. We do not attempt to sew directly to the mucosa of the pancreatic duct, although this may be done toward the tail, where the parenchyma often becomes thin. Sewing the jejunum to the capsule of the pancreas instead of performing a mucosa-to-mucosa anastomosis can allow enhanced decompression of less-dilated ducts. It is thought that sutures placed deep into the gland in an attempt to reach the duct mucosa

may occlude side branches and lead to a postoperative leak of pancreatic fluid or limit pancreatic decompression.

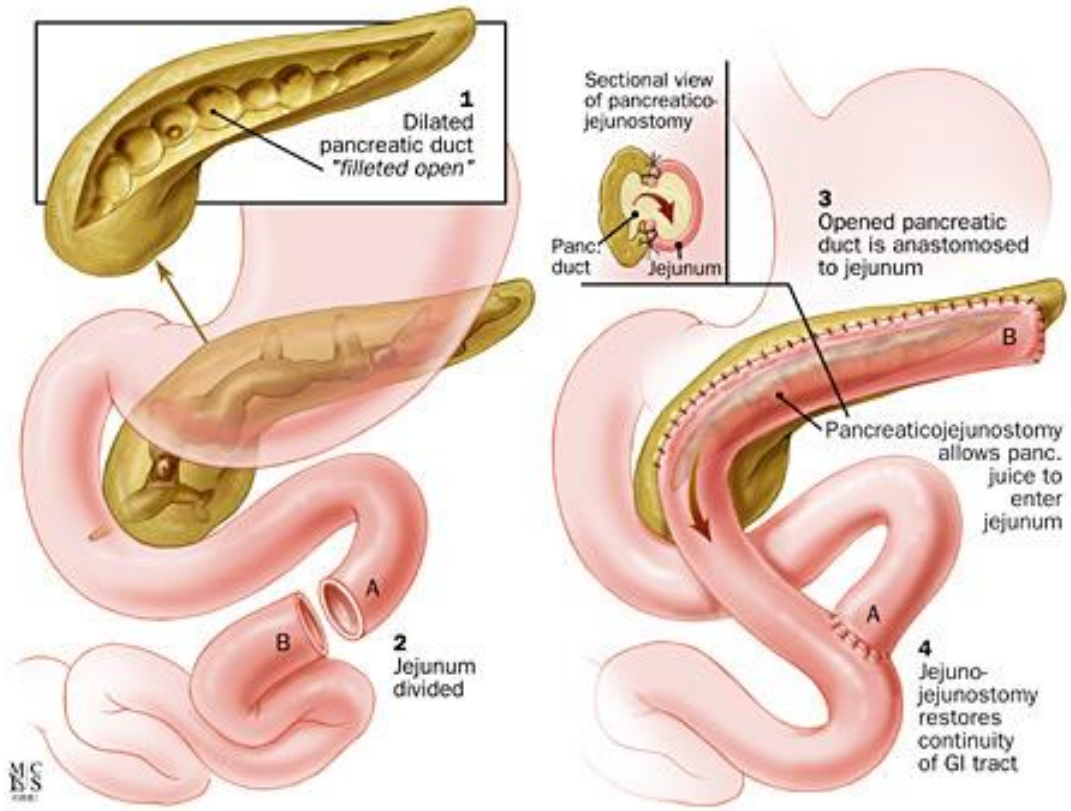
The continuous anastomosis is performed by placing two sutures next to each other at the middle of the posterior row. Because access to the tail is more difficult, the left suture is run first. This establishes the left posterior row and a portion of the anterior row after the corner has been reached. Alternatively, the suture line may be started at the tail of the gland. The right suture is then run toward and around the pancreatic head. The anastomosis is completed by tying the two sutures where they meet anteriorly. Care must be taken when performing the anastomosis in the head of the gland to avoid placing sutures through the pancreaticoduodenal vessels, which can cause troublesome bleeding that must be controlled before completing the anastomosis. Rarely, only the head of the pancreas is diseased. In this unusual instance, coring out the head of the pancreas may be all that is required to achieve adequate decompression. The Roux limb is then used as previously described to drain the pancreatic head.

As many as 40% of patients with chronic pancreatitis who undergo lateral pancreaticojejunostomy have associated pancreatic pseudocysts. Concomitant drainage of the pseudocyst and dilated pancreatic duct is the most effective method for treating patients with these coexisting conditions. Intrapancreatic pseudocysts can be drained by extending the

ductal incision into the pseudocyst and incorporating the opening into the jejunal limb. Extrapancreatic pseudocysts can be drained either by using the side or the end of the jejunal limb, depending on their location. When necessary, biliary drainage can be accomplished by choledochoduodenostomy or by anastomosis of the bile duct to the Roux-en-Y limb of jejunum. A gastrojejunostomy can be constructed proximal to the enteroenterostomy for the Roux-en-Y limb if bypass of a fixed duodenal obstruction is required. Pancreaticoduodenectomy is appropriate for management of combined biliary and gastric obstruction in chronic pancreatitis.

Construction of the Roux-en-Y limb is completed by an end-to-side enteroenterostomy that is accomplished with either sutures or stapling devices. The opening of the transverse mesocolon is closed around the Roux-en-Y limb to prevent internal small bowel herniation. Likewise, the small bowel mesenteric defect adjacent to the enteroenterostomy is closed. Cholecystectomy is typically performed during lateral pancreaticojejunostomy. A feeding jejunostomy is placed selectively in patients who are extremely malnourished or have had long-standing gastric outlet obstruction. Closed suction drains may be used if there is concern about leakage of bile or pancreatic secretions. The likelihood of this is small, and drains are not usually

necessary. Nasogastric decompression is continued postoperatively until bowel function resumes. Oral intake is resumed as after any major abdominal procedure.



Peustow's procedure

Operative Modifications of Duodenum- Preserving Resectional Procedures

Modifying the Beger procedure, Warren and coworkers suggested to combine a duodenum-preserving pancreatic head resection with

denervation of the body and tail of the pancreas by ligating and dividing the splenic vein at its junction with the superior mesenteric vein.The splenic artery is divided as it approaches the pancreas from the celiac axis. Viability of the spleen is ensured through its extensive arterial and venous collateral circulation, principally the gastroepiploic and short gastric vessels. The entire flap (pancreas, splenic artery and vein, and associated nerve fibers) is freed from all tissue until the pancreas is attached only to the vessels at the hilus of the spleen. This maneuver supposedly severs all somatic and autonomic nerve fibers. Finally, a Roux- en-Y loop of jejunum is prepared and the pancreatic duct anastomosed with a small mucosal opening. Kimura et al. suggested a different modification of a duodenum- preserving pancreatic head resection with detailed description of how to preserve the duodenal blood supply.After a complete Kocher maneuver is performed, the pancreas is cut above the portal vein and removed from the third potion of the duodenum. Then the posterior surface of the pancreatic head is removed from the connective tissue membrane, which should be left intact to ensure blood flow to the duodenum. The main pancreatic duct is cut at its junction with the terminal portion of the bile duct. The pancreas is cut on the left aspect of the anterosuperior pancreaticoduodenal artery. Hence, the pancreatic tissue between the duodenum and the common bile duct is left intact to preserve sufficient blood flow to the papilla. After carefully

suturing the cut surface of the pancreas with nylon monofilament strings, the remaining body of the pancreas is anastomosed in the posterior wall of the stomach. Nakao described a pancreatic head resection with segmental duodenectomy including minor and major papilla in 1998.After cholecystectomy, the pancreas is divided above the portal vein. The extrapancreatic nerve plexus between the uncinate process and the superior mesenteric artery is preserved, so the inferior pancreaticoduodenal artery is preserved. The posterior inferior pancreaticoduodenal artery is ligated and divided. The anterior inferior pancreaticoduodenal artery is divided near the major papilla. The common bile duct is divided at the upper border of the pancreas. Two to three centimeters of ischemic area of the duodenum is observed including the major and minor papilla. The oral side of the duodenum is divided at 5 to 7 cm from the pyloric ring. The distal part of the duodenum is divided at the margin of the anteroinferior pancreaticoduodenal artery ligation. The gastroduodenal artery is completely spared. The length of the resected duodenum ranges from 3 to 5cm. The reconstruction of the alimentary tract is

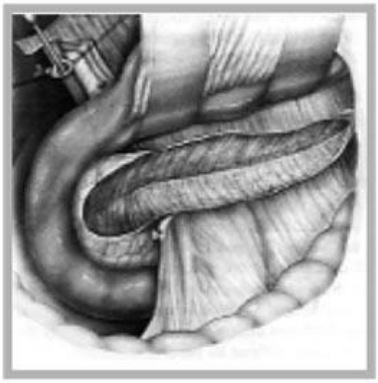
performed with pancreaticogastrostomy, duodenoduodenostomy, and choledochoduodenostomy. Most recently, another modification (Bern procedure) has been added to the surgical armamentarium for treatment of chronic pancreatitis.It combines some aspects of the Beger and Frey

procedures since it refrains from transection above the portal vein but excises the pancreatic head to a much larger extent than the Frey procedure, therefore potentially preventing a recurrence and definitely decompressing the common bile duct. Early results are promising and randomized trials are under way, but late follow-up results are not available yet. It is our firm belief that the optimal surgical treatment consists of an individually tailored approach (Hamburg procedure). The head of the pancreas should always be cored out to a variable extent including a decompression of the intrapancreatic bile duct. This ensures the removal of altered tissue and includes "inflammatory altered" as well as "hypertensive" tissue. In addition, the procedure can be further customized regarding the pancreatic duct system. If ductal irregularities are present in the pancreatic head and tail, the operation can be extended as a drainage operation much in the way of a Partington- Rochelle procedure into the pancreatic tail.

Salvage Procedures

Even though pancreatic surgery for chronic pancreatitis yields excellent results, recurrences may occur. Most frequently, recurrence develops in the remnant of the pancreatic head indicating either insufficient surgical resection of the head of the pancreas or aggressive disease. In these

instances, salvage procedures may be indicated ranging from “re-do” pancreas head resections to partial pancreaticoduodenectomy (Whipple procedure, pylorus-preserving pancreaticoduodenectomy). In selected patients (i.e., re-recurrence), even total splenopancreaticoduodenectomy has to be considered. This applies, for instance, to patients in which partial pancreaticoduodenectomy, additional interventional nerve blocks, and surgical denervation fail to achieve definitive pain relief.



For small duct disease v shaped excision of the length of the pancreas was described by Izbicki et al.

New developments in chronic pancreatitis

The principles of treatment for chronic pancreatitis are based on the following clinical and anatomic patterns:

1. The head of the gland is usually the pacemaker of chronic pancreatitis; any treatment must be designed around this area.
2. Almost every patient seeks treatment for abdominal pain (a few have chronic fistulas).
3. Surgery is considered only after all conservative treatments methods have failed.

In our institution, surgery is used only after “endotherapy” has failed. Endotherapy is an evolving concept that should be utilized only in pancreaticobiliary centers with extensive endoscopic retrograde cholangiopancreatography (ERCP) experience and where proficient management of complicated pancreatitis is already practiced.

Whether one uses surgical or endoscopic treatment, the patient will not have relief of pain unless the following criteria are met:

1. Chronic pancreatitis is documented using the 1963 Marseille definitionof “residual pancreatic damage, either anatomic or functional, that persists even if the primary cause or factors are eliminated.” The irreversible change in the pancreas is usually fibrosis.
2. The cause of the chronic pancreatitis (e.g., gall- stones, alcohol use, or autoimmune pancreatitis) must have been remedied or eliminated.
3. Imaging studies must show an anatomic defect.

4. The Cambridge classification of image severityof “marked” has been documented (e.g., at least a

main pancreatic duct stricture with or without stones) .

The treatment is designed to address this anatomy, which is almost always in the pancreatic head. It is unusual for the epicenter of the disease to be isolated in the tail. Consider then a neoplastic cause or that the patient is currently abusing alcohol.

5. Onceendotherapyhasfailed,thetreatmentishead resection if the patient is a surgical candidate; pylorus-preserving pancreaticoduodenectomy (PPPD), but there are several “head resection” techniques that are options depending on surgeon preference.

Using the algorithm just presented, the patient considered for head resection is highly selected. However, after long-term follow-up, these highly selected patients will achieve significant reduction in their disabling pain, and three fourths of them will have complete pain relief.We have preferentially used PPPD for head resection in an attempt to accrue a 20-year follow-up after this procedure. If the head of the pancreas is the pacemaker of chronic pancreatitis, then removal of the entire head should produce the best pain relief. This percentage of pain relief with complete head resection should be the benchmark that other, less extensive, head resection procedures should achieve.

The evolution of endoscopic therapy to treat pancreatic disorders has moderated the need for resection in some centers. Although unable to duplicate the results of pancreatic head resection in patients with multiple strictures and stones associated with pseudotumors of the pancreatic head, endotherapy can nevertheless improve pain as well as decrease relapsing attacks of pancreatitis by approaching *obstructing calculi* and isolated *inflammatory stenoses*. This treatment is not done by endoscopists acting independently but requires access to various forms of lithotripsy, interventional radiologic support, and surgical salvage when endotherapy fails. Head resection is the final option and is the default after multiple sessions in patients where stone extraction is unsuccessful or if he patient remains stent dependent despite repeated treatment of obstructing stenoses. But how good is endotherapy? The purpose of this chapter is to describe the efficacy for pain relief with endotherapy and, when required, salvage by head resection using PPPD.

Endotherapy

The endoscopic approach to strictures and stones presupposes access to the pancreas through the major or minor papilla. Sphincterotomy can be done using either a conventional or needle knife sphincterotome, usually with a pure cutting current to minimize the chance of cautery transmission. When approaching the pancreatic duct through the major

papilla, most endoscopists undertake an initial biliary sphincterotomy to expose the pancreaticobiliary septum and help define the length of the subsequent pancreatic duct (PD) sphincter incision.Slick guidewires (e.g., Tracer or Metro, or Jagwire) are used to provide access and orientation and as the “rail” for all subsequent treatment.

Prior to consideration of endotherapy one must ensure that a pancreatic stricture is benign. The patient will have already had a computed tomographic scan of the “pancreas protocol” variety, an endoscopic ultrasound, and brush cytology of any stricture potentially malignant. These anatomic criteria will have been correlated with the clinical presentation as well as blood tumor markers such as CA 19-9. Clinical follow-up is also a mandatory part of endotherapy as any neoplastic process can masquerade as chronic pancreatitis.

Benign strictures may be dilated by 4- to 6-, 5- to 7-, or 8- to 10-French dilating catheters but are more commonly treated by 4- to 8-mm hydrostatic dilating balloons. Occasionally, extremely tight strictures, particularly those associated with an upstream stone, may need to be breached by a screwlike device called a *Soehendra stent extractor*. Following dilation to a size approximating the downstream pancreatic duct, most endoscopists attempt to place a 7- to 10-French prosthesis across the stricture. This stent is usually retrieved in 2 to 4 months and, if persistent, the stricture is re-treated with additional dilation and

replacement of the prosthesis. If initial stent insertion is not helpful to relieve pain, then most endoscopists seek surgical consultation. If the stent insertion is helpful, then the process can be repeated several times over a year's time frame. If the patient becomes stent dependent for symptom relief, most endoscopists consider surgical referral. In contrast to placement of a single stent for a stricture, our practice has evolved into placement of multiple smaller prostheses (5 to 7 French) across the stenosis. Not only does this allow drainage between the stents at time of inevitable stent occlusion, but also, as has been demonstrated in the endoscopic treatment of biliary strictures,multiple stents appear to improve subsequent stricture patency rates.

The removal of obstructing pancreatic calculi is considerably more difficult than the endoscopic removal of bile duct stones.Not only are pancreatic stones frequently associated with downstream strictures but they

may also lodge at acute angulations of the duct and result in upstream ductal disruption in the form of a pseudocyst or pancreatic ascites. Approximately half of main pancreatic ductal stones can be removed after PD sphincterotomy, with or without dilation of a concomitant stricture, using conventional biliary stone baskets or an extraction balloon over a guidewires.In the remaining cases, fragmentation is required.

Extremely large, impacted, and irregularly shaped calculi require fragmentation prior to removal. Although the latter can take the form of electrohydraulic, mechanical, or laser lithotripsy, most centers, including our own, prefer extracorporeal shock wave lithotripsy (ESWL).Stones can be targeted prior to ERCP, if sufficiently calcified, or may require a baseline ERCP with insertion of a stent or nasopancreatic drain for localization. Once the stone or stones have been localized and fragmented, the fragments must be removed transampullary during an additional endoscopic procedure. Following fragment extraction, prosthesis placement is usually undertaken to minimize obstructive pancreatitis from edema at the site of previously impacted fragments or the sphincterotomy site. In addition, small side-branch calculi frequently migrate into the main pancreatic duct after decompression, and the prosthesis keeps the ductal system decompressed.

Results after endotherapy for stricture without stones

Multiple recent series have reported a 60% to 80% reduction in attacks of relapsing pancreatitis as well as a comparable relief in chronic pain complaints following endoscopic treatment of pancreatic strictures, although three or four treatment sessions may be required. These results are consistent with the authors' experience.

Several caveats need to be mentioned. Stents themselves can cause “ductitis” and parenchymal injury as a consequence of side-branch occlusion or direct stent pressure by the upstream end or side prongs.Additionally, stent placement invariably leads to bacterial colonization within the ductal system. Stent occlusion can occasionally result in upstream duct blowout or even sepsis.

The results of endotherapy for pancreatic duct stricture have to be considered in two categories: persistence of stricture and symptom relief. Anatomically, stricture resolution approximates only 20% to 30% in published series, even when therapy has been undertaken for up to 1 year.Clinically, most series suggest that only 10% to 20% of patients fail to get relief with initial stent placement, particularly those without upstream ductal dilation or those with multiple stones. In the remaining patients, most achieve a relatively asymptomatic level after stent removal, whereas a minority become stent dependent (15% to 20%) for pain relief. The reason for stent depen- dence is uncertain but may be related, in part, to loca- tion (strictures in the head are more pernicious) or the original cause (those strictures that are a consequence of severe pancreatitis with ductal disruption are often problematic).

Results after endotherapy for stones

About half of the patients will have strictures with stones. In contrast to some of the uncertainty associated with endoscopic treatment of pancreatic duct strictures, data are reasonably good that endotherapy for calculi is associated with short- and long-term symptom relief.This is obviously contingent on successful clearance of stones from the main pancreatic duct, the treatment of concomitant biliary and/or pancreatic ductal stenosis, and patient selection (patients with a pseudotumor have problems not necessarily related to stones and should be excluded from endotherapy).

During the period of 1995-2000 we began our series of pancreatic duct stone extraction.Thirty-five of 40 patients required a single ESWL session, while a total of 86 ERCPs were required to completely clear the main pancreatic duct. There was a 20% rate of minor procedural complications. After a mean follow-up of 2.4 ± 0.6 years, 80% of the patients avoided surgery. Four of these patients died of a cause unrelated to chronic pancreatitis. There was a statistically significant decrease in analog pain scores, oxycodone-equivalent narcotic use, and yearly pancreatitis-related admissions.

Since that time, an additional 90 cases have been added with comparable results. The utilization of endoscopy to approach pancreatic strictures and stones since 1995 has not been associated with an increase in operative

drainage or resective procedures for pancreatic duct stones; despite a relative increase in referrals for evaluation of chronic pancreatitis problems. The lack of an increase in surgical procedures may be due to endotherapy. However, as some have suggested, endotherapy might simply delay an inevitable resective or more effective decompressive procedure.

Immunology (concept of PLR)

Lymphocytopenia is presentin systemic inflammation as a result of cancers that release mediators such as interleukin-10 (IL-10) and transforming growth factor-beta – they are inhibitory mediators. This resultsin immunosuppressive effect where the lymphocyte function is reduced .These two inhibitory cytokines interleukin 10 and transforming growth factor beta are secreted by pancreatic cancer cells.

Lymphocytopenia is associated with pancreatic adenocarcinoma – and this has been demonstrated by various studies. The association is more strong camparing it to colorectal or gastic adenocarcinoma, inference being, adenocarcinoma of the pancreas elicits an immune respone that is different from other gastrointestinal malignancies such as stomach or colorectal.

When the surgical specimen showed lower amount of lymphocyte infiltration after resection for pancreatic malignancy, it resulted in worse

prognosis for the patient resulting in lower overall survival. Cancer cells are able to evade the immune system as the lymphocytes get trapped within the peritumoural fibrosis.

Increase in platelet counts, occurs in adenocarcinoma of the pancreas and causes a hypercoagulable state. As a result, it leaves the person at a higher risk of thromboembolic events. A few proinflammatory mediators such as interleukin 1,3 and 6 are known to stimulate the megakaryocyte proliferation. Hence there is a relation between the increased platelet count and the overall survival in adenocarcinoma of the pancreas, as this reflects systemic inflammation that is an index brought about by the tumour.

Smith et al. suggested that preoperative PLR the tumor invasiveness and merits evaluation as an adjunctive investigation to CA19-9 that helps in identifying the need for laparoscopic staging in patients with potentially resectable periampullary carcinoma.

So, in these types of cancers (pancreatic – head of pancreas or periampullary), increase in the platelet count and decrese in lymphocyte count occurs. Although these absolute values were not found to be important as prognostic markers, the ratio (platelet lymphocyte ratio) was used as a prognostic marker of malignancy.

Platelet lymphocyte ratio is identified as a marker that can predict the invasiveness of a malignancy.

In this study, PLR is analysed as a diagnostic tool.It has been done previously in a study with 43 patients by Miglani et al – published in the Indian Journal of Surgery.

Observation and results

Total number of patients in the study - 44

Out of the total of 44 patients analysed 26 were found to have malignancy, 16 were diagnosed as chronic pancreatitis, 1 patient was diagnosed as cystadenoma of pancreas and 1 patient was diagnosed with Koch's disease.

The demographics of the patients with pancreatic cancer and chronic pancreatitis are represented below in percentage of the total :

Age intervals	Pancreatic cancer (%)	Chronic pancreatitis (%)
21-30	-	2 (12.5%)
31-40	3 (10.7%)	3 (18.8%)
41-50	9 (32.1%)	7 (43.8%)
51-60	11 (42.3%)	4 (25%)
61-70	3 (10.7%)	-
Total	26	16
Male	17 (60.7%)	13 (81.3%)
Female	11 (39.3%)	3 (18.7%)

Out of all the malignant cases which were 26 in number, 15 of them were diagnosed as carcinoma head of pancreas. Whipples procedure was done for 6 of them – diagnosis was confirmed with histopathology.

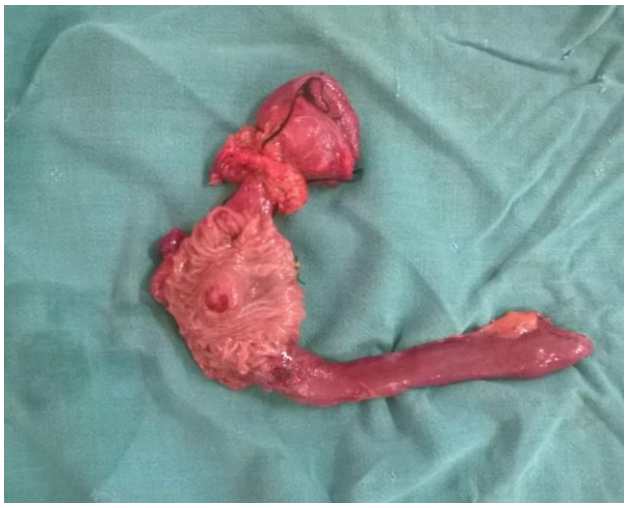
3 of the patients were found to have unresectable disease on table and hence resorted to palliative triple bypass.

6 patients had metaststic disease – mostly liver, these patients were managed with palliative chemotherapy. Tissue biopsy was obtained by ultrasound guided biopsy (FNAC) of the liver metastasis.

11 patients were diagnosed with periampullary carcinoma, out of which whipples procedure was done in 9 of them. Tissue biopsy was obtained from upper gi scopy (side viewing scopy).

2 out of these 11 were found to have disseminated disease – liver metastasis and hence managed with palliative chemotherapy.All malignant case had tissue diagnosis.

Management	**Ca head of pancreas**	**Periampullary ca**
Whipples procedure (pancreaticoduodenectomy)	6 (40%)	9 (82%)
Palliative triple bypass	3 (20%)	-
Palliative chemotherapy	6 (40%)	2 (18%)
Total	15	11



Whipple specimen

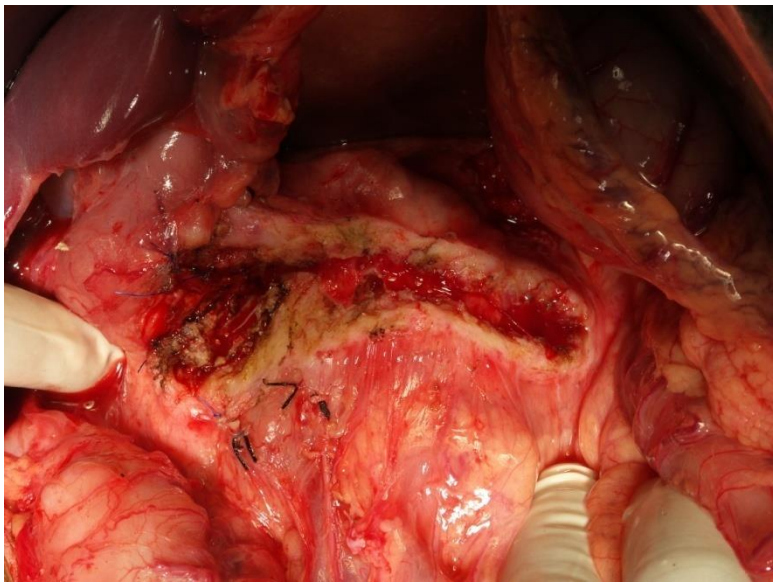
In the benign causes of mass lesions of the pancreas, the total was 18. Out of this 16 were chronic pancreatitis.

Preoperative dignosis was obtained in all the patients with either ultrasound or CT guided FNAC from the lesion.

Out of the 16 patients, 10 were treated with Freys procedure.

The remaining were managed conservatively.

	Chronic Pancreatitis
Freys procedure	10 (62.5%)
Conservative	6 (37.5%)
Total	16



Intraoperative finding – Frey's procedure

The various clinical parameters studied in groups – pancreatic cancer and chronic pancreatitis are displayed below

Study Variables	Pancreatic cancer	Chronic pancreatitis	P value
Age, mean ± Sd	51.4 ± 9.1	43.9±8.7	0.005
Gender, (Male : Female)	15:11	15:3	0.116
Alcoholic %	11 (42%)	12 (75%)	0.04
Jaundice %	23 (88%)	2 (13%)	<0.001
Prev. attack of pancreatitis %	3 (12%)	13 (81%)	<0.001
Weight loss %	25 (96%)	14 (88%)	0.29
Bilirubin,(mg/dl) mean ± Sd	7.4±6.1	0.9±0.5	<0.001
Lymphocytes (/cumm) mean ± Sd	2259.6±1059.7	2386±756.7	0.335
Platelet (/cumm) mean ± Sd	290730.8±103153	223187.5±56820.4	0.001
CA19-9(U/L) mean ± Sd	612.8±964.2	104.9±293.9	0.024
PLR mean ± Sd	149.9±83.7	98.9±31	0.012

Age :

The mean age was higher in patients with pancreatic cancer than with chronic pancreatitis. The age difference came out to be statistically significant.

Gender :

There was no statistical difference in the male to female ratio in the two groups.

Alcohol intake :

The chronic pancreatitis group had significantly more alcoholics (75%), compared to the pancreatic cancer group (42%), it was statistically significant.

Jaundice :

There were more patients with jaundice in the pancreatic cancer group (88% vs 13%) than the chronic pancreatitis group, this was statistically significant.

Previous attacks of pancreatitis :

The chronic pancreatitis group had a statistically significant percent (81% vs 12%) of patients with previous history of pancreatitis.

Weight loss :

This parameter was present in both groups, but was more for pancreatic cancer group but this did not reach statistical significance.

Bilirubin :

The serum bilirubin was grossly more in the cancer group and was statistically significant.

Lymphocyte count :

The mean lymphocyte count for cancer group was 2259±1059.7, and the pancreatitis group was higher with 2386±756.7, but the difference did not reach statistical significance.

Extreme lymphocytopenia (< 1000 /cumm) was observed only in one patient (2.3%) with cancer head of pancreas – which was resectable – whipples was done for this patient.

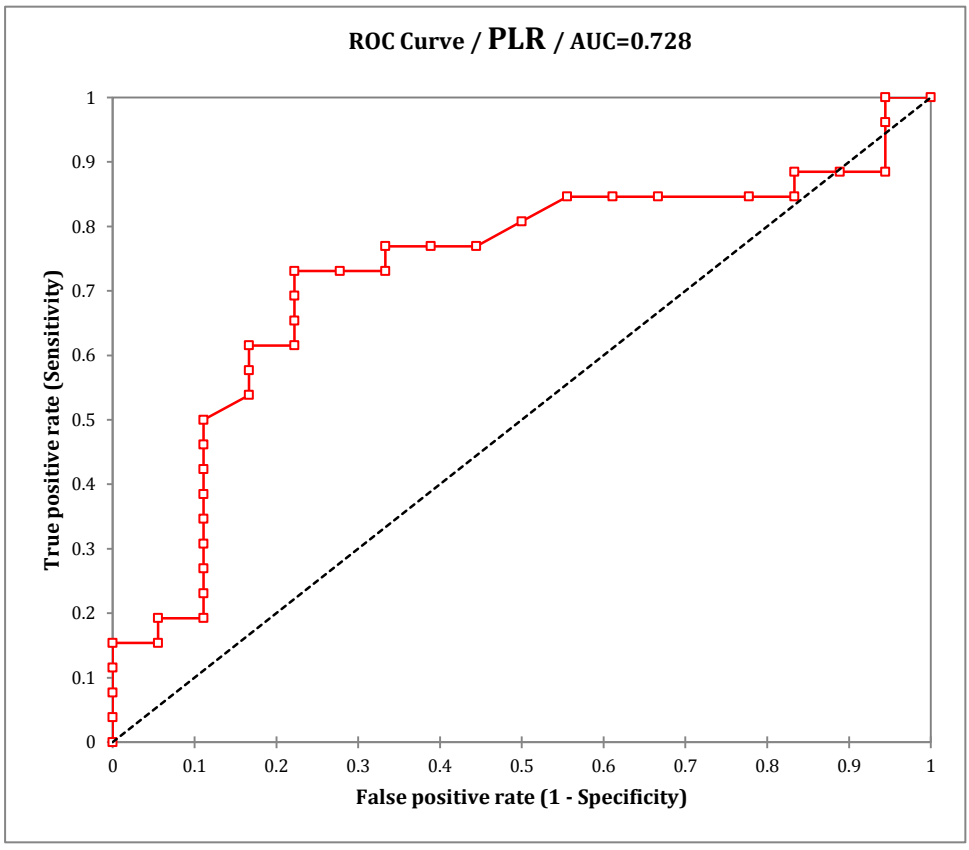
Platelet count :

The mean platelet count measured in the cancer group was 290730.8±103153 and in the pancreatitis group was 223187.5±56820.4. Thrombocytosis was more in the cancer group and this was statistically significant.

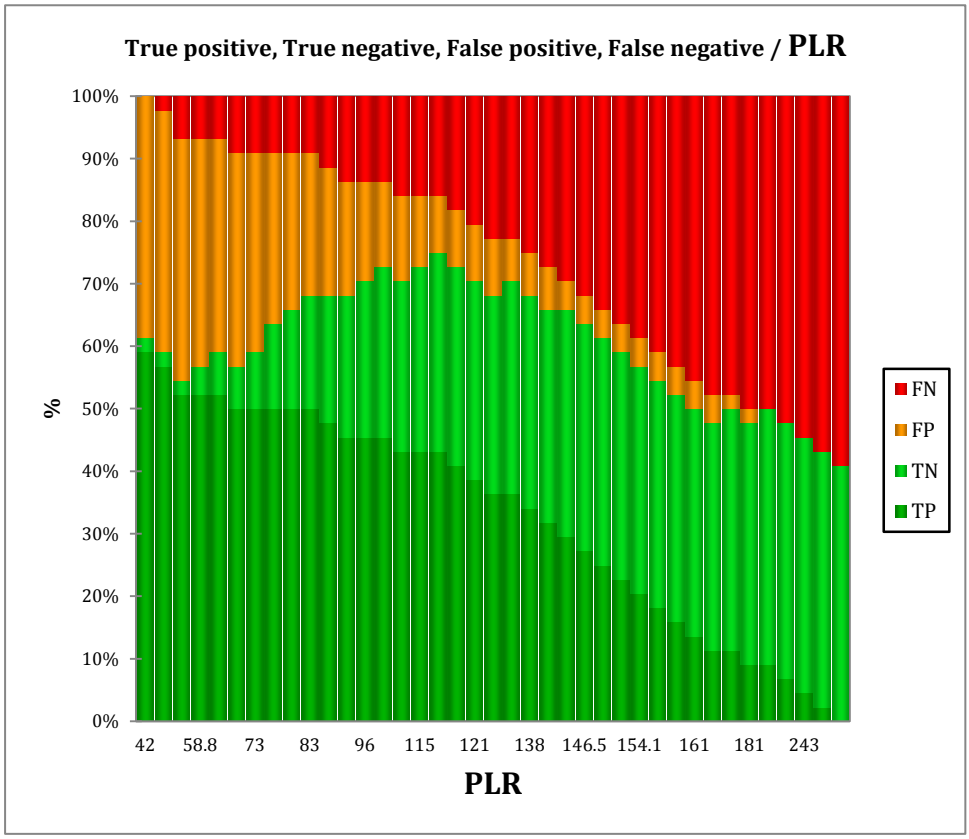
Marked thrombocytosis (>4L) was seen in 2 patients (45.5%), both of them were diagnosed as periampullary carcinoma, resectable – whipples was done.

Platelet lymphocyte ratio :

Platelet lymphocyte ratio (PLR) was used as a marker – to differentiate malignancy from the pancreatitis group. The cut off value was set at 150.The mean value in the cancer group was 149.9±83.7 and the mean value of the pancreatitis group was 98.9±31. The difference was statistically significant (p =0.012).



ROC curve for PLR

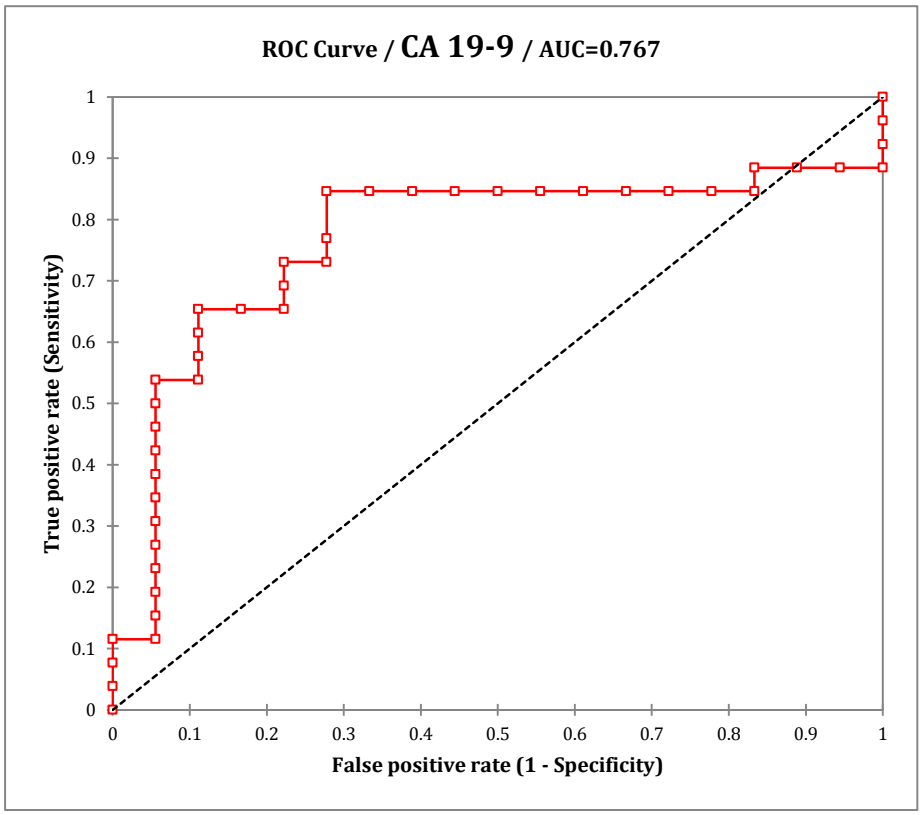


The sensitivity, specificity, NPV, PPV and accuracy of PLR were as follows : 73.1, 77.8, 66.7, 82.6 and 75

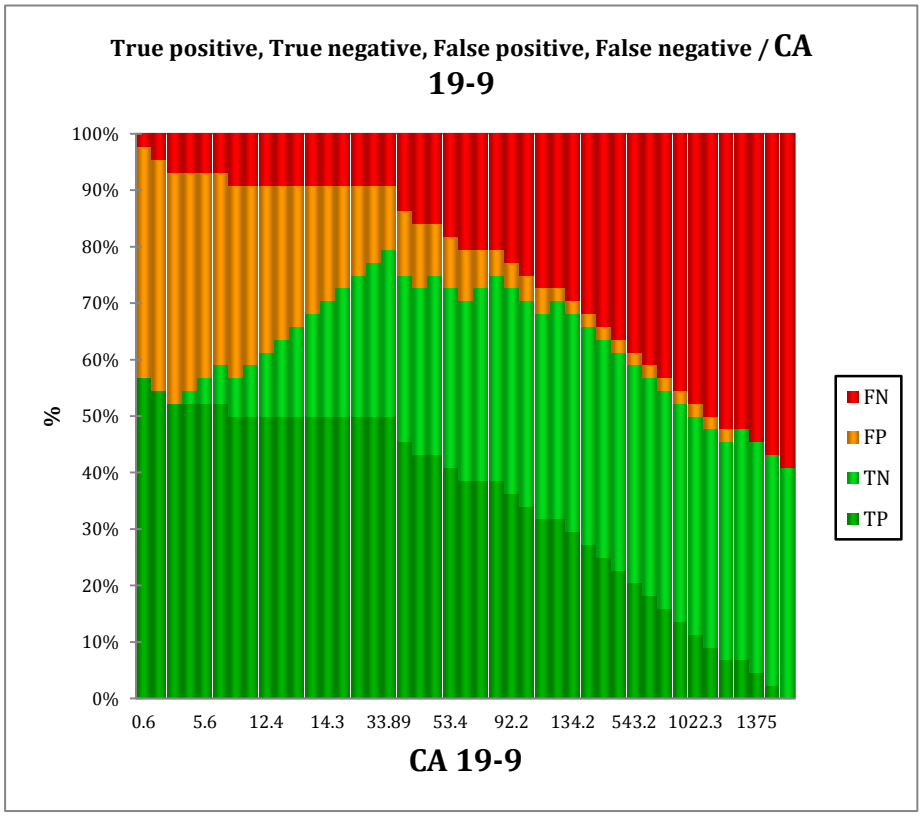
CA 19-9 :

CA 19-9 was used as a marker for malignancy and the cut off was 37U/ml. The mean value for cancer group was 612.8±964.2 and the mean for pancreatitis group was 104.9±293.9, the difference was statistically significant (p=0.024)

The sensitivity, specificity, NPV, PPV and accuracy of CA 19-9 were as follows :84.6, 65.7, 76.5, 81.5 and 79.5



ROC curve for CA19-9



Discussion

Pancreatic carcinoma is generally diagnosed late and the candidates for surgery are fewer. It becomes important to recognize lesions that are malignant and they should be differentiated from mass lesions of chronic pancreatitis as these lesions mimic carcinoma.

Parameters such as age of the patient, loss of weight – in the recent past (three to six months), and level of jaundice (serum bilirubin) are helpful in separating malignant lesions from those due to chronic pancreatitis.

Similar inferencesfound in this study were age of the patients, loss of weight, and serum bilirubin level-These parameters were significant when both the groups were compared. Other blood parameters that were analysed were platelet count and lymphocyte count.

When these markers were used undividually, the interpretations did not reach statistical significance. Hence even in the presence of marked lymphopenia or thrombocytosis, these values were not useful as markers of malignancy.

These two blood indices when combined as Platelet lymphocyte ratio (PLR) gives us a new marker.

There was a study done in 2008 by Smith et al. The purpose was to find out if platelet lyphocyte ratio could be used along with CA19-9 for patients with periampullary carcinoma and whether they would require staging laparoscopy. The number of patients selected were twohundred and sixty three. The sensitivity, specificity and respectability values for CA19-9 less than150 and for platelet lymphocyte ratio were

CA19-9	PLR
Sensitivity – 51%	51%
Specificity – 73%	72%
PPV– 83%	81%
NPV- 36%	38%

These two parameters were combined and the inference was that both ppv (95 %) and specificity (96 %) were much better.

It was also observed that features of histopathological examination such as increasing T stage, vascular invasion in the specimen, perineural invasion, and resection margin involvement were all associated with a

higher value of platelet lyphocyte ratio done preoperatively in periampullary carcinoma going in for resection.

Another study was done in which there one hundred and ten patients were operated for pancreatic cancer.

The inference was that platelet lyphocyte ratio was a marker of prognosis in overall survival – which was significant with a p value of 0.001. This was more significant than the values taken separately, ie, lyphocyte count or platelet count.

PLR value	Overall survival (median)
<=150	19.7 months
151 - 300	13.7 months
>300	5.8 months

The preoperative PLR was significant on multivariate analysis (P<0.001), along with size of the tumour (P=0.010) and LN ratio (P=0.013).

Neutrophil-lymphocyte ratio was also studied and found to be insignificant.

In this study, platelet lyphocyte ratio was studied as a tumour marker to differentiate pancreatic cancer from chronic pancreatitis. The cut off was chosen as 150 based on the many studies done on this subject earlier.

The carbohydrate antigen 19–9 (CA19-9) is an accepted tumour marker which helps in diagnosis and prognostication of cancer pancreas.

But CA19-9 can be elevated in inflammatory lesions of the pancreas also.

It is the most accepted and widely used marker for pancreatic cancer diagnosis and prognosis.

The sensitivity ranges from 70 to 90%, and the specificity values are between 70 to 98%. The cut off is usually set at 37U/ml. With the increase in cut off values, sensitivity drops but specificity improves.

Similar inferences were shown by Ramesh et al. The values of sensitivity, specificity, ppv and npv were:

CA19-9	Sensitivity%	Specificity%	PPV	NPV
37 U/ml	68	70	61	76
100 U/ml	41	86	67	68
300 U/ml	15	100	100	63

CA19-9 levels were found to increase in the presence of cholangitis. So, patients with cholangitis were excluded from the study.

In this study – patients with chronic pancreatitis exhibited a rise in CA19-9 which was 12.5 %.

The results of this study comparing PLR and CA19-9

	Sensitivity	Specificity	PPV	NPV	Accuracy
PLR	**73.1**	**77.8**	**82.6**	**66.7**	**75**
CA19-9	**84.6**	**65.7**	**81.5**	**76.5**	**79.5**

From the above numbers it is clear that the values are comparable and we can infer that PLR is at least comparable to CA 19-9 as a diagnostic test – as it had a better specificity and positive predictive value.

Conclusion :

In this study of 44 patients, 18 having benign lesions due to chronic pancreatitis/ Kochs/ Benign tumour and 26 having malignancy, platelet lyphocyte ratio which has been widely published as a prognostic marker has been shown to have diagnostic implications as well.

Platelet lymphocyte ratio did not prove to be better than CA19-9 but was as good as CA19-9 in differentiating malignancy and chronic pancreatitis with an accuracy of 75 (compared to accuracy of CA 19-9 of 79.5 which is comparable).

The accuracy may be increased by the combination of both these markers.

Malignancy developing in chronic pancreatitis as an important subset where diagnosis is difficult and platelet lymphocyte ratio may prove a good marker in diagnosing these cases as the sensitivity of CA19-9 in these cases is not high.

Larger sample sized studies are necessary for the confirmation of the results obtained here.

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Annexures :

Proforma :

" PlateletLymhocyte Ratio As A Diagnostic Marker In Pancreatic Malignancy "

Investigator: **Dr.Praveen Kumar Arumugam**, PG - MS (General Surgery)

Guide : Prof. Dr. K. Kamaraj MS

Sl. No. :

- NAME :
- AGE /SEX:
- ADDRESS WITH CONTACT NUMBER:

- IP NO:
- DATE OF ADMISSION:
- DATE OF SURGERY:

HISTORY OF PRESENTING ILLNESS:

Abdominal Pain –

Jaundice –

Pruritis –

Weight loss (>10% in last 3-6 mo) -

Any other relevant history

PAST/P ERSONAL/ FAMILY HISTORY:

DM HT Epilepsy Asthma Tb

Prev h/o pancreatitis

Smoking – Y / N

_____ cig/ day for _____yrs

Alcohol – Y / N

_____ ml / day for _____ yrs

Family history

GENERAL EXAMINATION:

P.R: **B.P:**

Icterus/ Cy/ Cl/ PE/ LA

BMI

SYSTEMIC EXAMINATION:

CVS - RS - PA –

PR -

Clinical diagnosis -

Investigations:

CBC
Hb%
TC
DC
Lymphocyte count
Platelet count
ESR

LFT
S. Bilirubin Direct Indirect
SGOT
SGPT
SAP
T.Proteins
S.Albumin

CA 19 - 9
PLR

Other investigations:

USG Abd

CECT Abd

MRI/MRCP

UGI Endoscopy

HPE

Information Module

You are being invited to be a subject in this study.

Before you participate in this study, I am giving you the following details about this study, which includes the aims, methodology, intervention, possible side effects, if any and outcomes:

All patients with features of pancreatic malignancy by imaging and clinical features will be included in this study. A detailed clinical history will be taken following a standardized proforma. A detailed clinical examination will be done and relevant investigations, basic and special investigations will be done at the time of admission.Platelet, lymphocyte count, CA 19-9 and imaging studies would be done .The results arising from this study will be analyzed and used for academic purposes. You will be given clear instructions at every step and you are free to ask/ clarify any doubts. Your identity will remain confidential. You are free to withdraw from this trial at any point of time, without any prior notice &/ or without any medical or legal implications.

I request you to volunteer for this study.

Thanking You,

(Dr.Praveen Kumar Arumugam)

Name:

Informed Consent

Name:

Age/ Sex:

IP No:

I herewith declare that I have been explained in a language fully understood by me regarding the purpose of this study, methodology, proposed intervention, plausible side effects, if any and sequelae.

I have been given an opportunity to discuss my doubts and I have received the appropriate explanation.

I understand that my participation in this study is completely voluntary and that I am free to withdraw from this study at anytime without any prior notice &/ or without having my medical or legal rights affected.

I permit the author and the research team full access to all my records at any point, even if I have withdrawn from the study. However my identity will not be revealed to any third party or publication.

I herewith permit the author and the research team to use the results and conclusions arising from this study for any academic purpose, including but not limited to dissertation/ thesis or publication or presentation in any level.

Therefore, in my full conscience, I give consent to be included in the study and to undergo any investigation or any intervention therein.

Patient's Sign

Investigator's Sign

(Dr.Praveen Kumar Arumugam)

Masterchart :

Name	Age	Sex	IP no	Jaundi	Prev h/	Wt loss	Smoker	Alcoholic	Bilirubin	Lymphocyte C	Platelet C	PLR	CA 19-9	Diagnosis	Treatment
Jeyaraman	54	m	33081	n	n	n	y	y	0.39	1919	356000	185	33.89	Cystadenoma head of pancr	Conservative
Kesavamoorth	54	m	47015	n	n	y	n	y	0.98	5472	232000	42	11	Kochs disease head of pancr	Conservative on Att
Manikam	45	m	1445512	y	n	y	y	y	8.6	1740	255000	146.5	134.2	Ca head of pancreas/ liver n	Palliative chemo
Shanthi	43	f	1422489	y	n	y	n	n	23.8	3488	312000	89	1105	Ca head of pancreas	Whipples
Sathyanadhan	47	m	1448521	n	y	y	y	y	1.2	2118	342000	161	1375	Ca head of pancreas/CCP	Whipples
Shanthi	52	f	1435800	y	n	y	n	n	12.9	602	86000	142	53.4	Ca head of pancreas	Whipples
Madhavan	52	m	15913	Y	n	y	y	y	9.6	3042	166000	54	742	Ca head of pancreas/ liver n	Palliative bypass/ surface mets
Ruthraiya	70	m	1445675	y	n	y	y	y	1.3	2360	170000	72	92.2	Ca head of pancreas/ with li	Whipples
Jayalalitha	62	f	1447245	y	n	y	n	n	6.5	1822	290000	159	543.2	Ca head of pancreas/ liver n	Palliative chemo
Murugesan	48	m	15438	y	y	y	n	n	3.3	1547	202000	130	573	Ca head of pancreas unrese	Palliative triple bypass
Shankaran	45	m	39117	y	y	y	n	y	17.23	1280	232000	181	65	Ca head of pancreas/CCP	Whipples
Suseela	42	f	1402925	y	n	y	n	n	4.5	1564	396000	253	258.4	Ca head of pancreas/ with li	Palliative chemo
Thomas	40	m	46820	n	n	y	n	y	1.21	2656	320000	121	0.7	Ca head of pancreas/ liver n	Palliative chemo
Shanthi	60	f	1422478	y	n	y	n	n	15.8	2025	312000	154.1	1052	Ca head of pancreas	Whipples
Balakrishnan	55	m	1443752	y	n	y	n	n	2.9	2042	310000	152.7	96.4	Ca head of pancreas unrese	Palliative triple bypass
Balan	58	m	1443767	y	n	y	y	y	8.5	1748	290000	165	1022.3	Ca head of pancreas/ liver n	Palliative chemo
Nagaraj	70	m	1443745	y	n	y	y	y	9.2	1776	270000	152	530.6	Ca head of pancreas unrese	Palliative chemo
Jeyalakshmi	52	f	18299	y	n	y	n	n	18.05	5610	306000	54	4105	Periampullary ca	Whipples
Unnamalai	45	f	30715	y	n	y	n	n	5.4	3840	200000	52.1	157	Periampullary ca with liver n	Palliative chemo
Varathammal	55	f	29262	y	n	y	n	n	5.66	2139	521000	243	2923	Periampullary ca	Whipples
Abraham	40	m	43216	y	n	y	n	n	12.5	3904	329000	84	0.6	Periampullary ca	Whipples
Murugan	58	m	24307	n	n	y	n	n	0.9	2210	306000	138	10.3	Periampullary ca	Whipples
Gunasekaran	60	m	1443110	y	n	y	y	y	2.8	1256	246000	195	105.5	Periampullary ca	Whipples
Ambu	45	f	6498	y	n	y	n	n	5.6	2668	280000	104.9	42	Periampullary ca	Whipples
Srinivasan	57	m	1448567	y	n	y	y	y	8.6	1724	270000	156	860.6	Periampullary ca/ liver mets	Palliative chemo
Sulochana	48	f	32851	y	n	n	n	n	2.5	2898	348000	120	43.3	Periampullary ca	Whipples
Malliga	55	f	1441932	y	n	y	n	n	2.6	1448	210000	145	0.8	Periampullary ca	Whipples
Raman	33	m	50017	y	n	y	n	y	1.5	1242	590000	475	42	Periampullary ca	Whipples
Saleem Ravut	54	m	13034	n	n	y	y	y	0.8	3392	327000	96	20.4	CCP	Conservative
Satish	28	m	532147	n	n	y	n	n	0.8	1548	210000	135	3.4	CCP	Conservative
Kalaimoorthy	45	m	1436798	n	y	y	y	y	0.4	1885	149000	79	1200	CCP	Freys
Venkatachalar	42	m	1435867	n	y	y	y	y	0.36	2556	372000	145	13.15	CCP	Freys
Selvam	45	m	1436518	n	y	y	n	y	0.8	3012	220000	73	12.4	CCP	Freys
Murugesan	36	m	1434132	n	y	y	y	y	2.9	2232	189000	84	109.2	CCP	Freys
Somasundara	38	m	23508	n	y	n	y	y	1.33	1216	216000	174	82	CCP	Conservative
Sulochana	45	f	14721	y	n	n	n	n	0.8	2184	156000	71	48	CCP	Conservative
Mani	35	m	1446730	n	y	y	n	y	0.9	2245	230000	102	12.5	CCP	Conservative
Loganathan	50	m	1448150	n	y	y	y	y	1	1476	170000	115	13.2	CCP	Freys
Thilaga	52	f	1443155	n	y	y	n	n	0.9	2658	210000	79	5.6	CCP	Freys
Kannlappan	56	m	1445382	n	y	y	y	y	0.8	1860	220000	118	14.3	CCP	Conservative
Arumugam	56	m	1443345	n	y	y	n	y	0.9	2470	220000	89	23.4	CCP	Freys
Manimuthu	45	m	6439	n	y	y	y	y	0.8	4250	252000	58.8	22.4	CCP	Freys
Vidhya	30	f	1438666	y	y	y	n	n	0.9	2568	210000	81	90	CCP	Freys
Kripakaran	45	m	1446933	n	y	y	n	y	0.8	2624	220000	83	8.6	CCP	Freys