SELECTED VIGNETTES

OR

THE EMERGING ROLE OF ENDOSCOPIC THERAPY IN PANCREATIC DISEASE

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Summary

The past decade has seen the introduction of a number of new treatment options for pancreatic disease. Optimal treatment requires selecting that mode of therapy best suited for a particular patient. In acute pancreatitis, approximately 80% of patients will respond to conservative management. Therefore, the challenge is to select that group of patients which will have a severe and prolonged illness. This usually requires a combination of clinical assessment, multifactorial analysis and invasive and laboratory measures. CAT scanning, although not a reliable index of physiological severity of disease, does select a population of patients who are likely to develop complications from acute pancreatitis. Those patients who suffer a severe episode of acute pancreatitis should be considered for surgical or endoscopic therapy.

In chronic pancreatitis, pilot studies suggest that endoscopic stenting of the pancreatic duct may alleviate symptoms. Larger controlled studies are being initiated. In patients suffering from pancreatic cancer, percutaneous and endoscopic stenting of the common bile duct provides alternative methods to operative palliation of symptoms of obstructive jaundice. Again, matching the treatment option to the patient's clinical status is important for optimal results.

Introduction

The aim of this discussion is to highlight new approaches to the management of pancreatic disease, and to discuss the emerging role of endoscopic therapy. I also hope to place these new therapies in perspective with regard to current concepts in pancreatic disease. The talk will focus on acute pancreatitis, its diagnosis and treatment, and the palliation of benign and malignant pancreatic disease. Before proceeding to endoscopic therapy, I wish to set the background by discussing some commonly held concepts.

Acute Pancreatitis

We all think that acute pancreatitis is relatively easy to diagnose. Once the diagnosis has been made, little intervention is required. Surprisingly, the literature does not support these assumptions. The diagnosis of acute pancreatitis is not always evident. Wilson, Imrie and Carter reviewed the diagnosis of acute pancreatitis recorded at Glasgow Royal Infirmary between 1974 and 1984. During that period they identified 126 patients who died of acute pancreatitis. Of these, 53 [42%] had the diagnosis made only at necropsy (1).

In a further study, Corfield and Cooper (2) looked at the incidence of acute pancreatitis in the Bristol Clinic area between 1968 and 1979. They studied 650 patients who had suffered 737 attacks of pancreatitis. They found that the sex distribution was equal and the mean age was 60. They compared the mean annual incidence with the previous decade and showed that there had been an increase from 53.8 to 73 cases per million. The mortality rate, however, had remained unchanged. In no less than 35% of fatal cases the diagnosis was first made at necropsy (2). Furthermore, Corfield et al (3) looked at 114 patients and

attempted to predict the severity of each episode of acute pancreatitis. They found that clinical assessment alone identified the severity of the episode of acute pancreatitis in only 34% of patients.

Evidence for a multi-faceted approach to the diagnosis of acute pancreatitis comes from a study by Spechler et al (4) who looked at acute alcoholic pancreatitis as a clinical syndrome in which hyperamylasemia was not a necessary criterion for making the diagnosis. Over a one-year period they studied patients who they suspected had acute alcoholic pancreatitis. They used ultrasonography and computerized tomography to help support their diagnosis. In 68 episodes of acute alcoholic pancreatitis, serum amylase was normal at the time of hospital admission in 32%. In 40 episodes, ultrasonography and computerized tomography were performed within 48 hours of admission. Ultrasonographic findings for the diagnosis of acute pancreatitis were found in 43% and computerized tomography in 68%. They found that ultrasonography and computerized tomography supported the diagnosis as frequently in patients with normal serum amylase levels as in patients with hyperamylasemia. These workers concluded that patients with alcoholic pancreatitis frequently have normal serum amylase levels, and that the use of hyperamylasemia alone to establish the diagnosis of acute alcoholic pancreatitis was inadequate (4).

Having pointed out that the diagnosis of acute pancreatitis is quite often missed and that one cannot rely on any single factor, clinical or laboratory, to make this diagnosis, what are the methods for confirming the diagnosis of acute pancreatitis?

Definitive diagnostic criteria for acute pancreatitis include (1) an elevation of plasma levels of two pancreatic enzymes (e.g. amylase, lipase) greater than five times the upper limit of normal [greater than ten standard deviations above the laboratory mean], and (2) evidence of acute pancreatitis from ultrasonography, computer tomography, surgical or autopsy findings. The complete description of an attack of acute pancreatitis includes degree of severity, occurrence of local complications (e.g. abscess, pseudocysts, bleeding) and systemic complications (e.g. acute renal failure, adult respiratory distress syndrome), initial or recurrent episode and, if possible, the etiology. After the acute attack, exocrine and endocrine pancreatic function may remain impaired for variable periods of time. Morphologically, the pancreas usually recovers completely although pseudocysts and limited scarring may persist. Histologic criteria are useful in the categorization of many other diseases but are of little value in the clinical decision process because pancreatic tissue rarely becomes available for histologic study during the evolution of pancreatitis. Some centers use less stringent criteria, e.g. values of at least three times the upper limit of the reference range of either amylase or lipase.

Laboratory Assessment of Acute Pancreatitis

Total amylase activity in the serum or urine is the most commonly used test for evaluating abdominal symptoms. This is because it is a relatively easy and inexpensive test to perform. However, absolute values do not indicate the severity of the attack and they may not be helpful in monitoring convalescence

or deterioration and sometimes may not be elevated in acute pancreatitis, as previously discussed (2).

Clavien et al (5), in a series of 352 attacks of acute pancreatitis in 318 patients, made the diagnosis using CT criteria in 314 patients and at operation or autopsy in four patients. Sixty-seven (19%) of these cases had normal serum amylase on admission. There was no difference in clinical course, parameters used to assess severity, and CT findings between the two groups (those with a normal amylase and those with hyperamylasemia). Serum lipase levels were helpful in determining the diagnoses in two-thirds of patients with normal amylase levels. Normal serum amylase levels were more likely in those patients with pancreatitis of alcoholic origin; patients who had had multiple previous attacks; and where there had been a long duration between onset of symptoms and admission (5).

In an attempt to improve diagnostic accuracy, Mayer and McMahon performed diagnostic peritoneal lavage on 247 patients with suspected acute pancreatitis. The procedure enabled an erroneous clinical diagnosis to be corrected in seven patients (2.8%) and confirmed a tentative diagnosis in two other patients (0.8%). Lavage also identified 90% of the patients who died of fulminant pancreatitis or of the later effects of pancreatic necrosis. Peritoneal lavage is one of the few techniques that allows the clinician to assess the severity of an acute attack of pancreatitis at presentation. The greater the volume and the darker the color of any free peritoneal fluid, the worse the prognosis (6).

Attempts have been made to improve the diagnostic accuracy of serum amylase estimations by measuring isoenzyme alterations. In a prospective study, Swensson et al (7) measured amylase isoenzymes in 65 patients with abdominal pain and hyperamylasemia. They used an electrophoretic technique and concluded that elevated serum amylase with a predominant P-type pattern suggests pancreatic disease; elevation of S-type isoenzymes suggests but is not conclusive for a diagnosis other than pancreatitis.

Table I

They divided their study population into two diagnostic groups:

Group I	42 patients with clinical findings of pancreatitis
P-type -	isoenzymes elevated in 31 of these patients - 74%
S-type -	isoenzymes elevated in 11 of these patients - 26%
Group II	23 patients with abdominal pain attributed to causes other than pancreatitis
P-type -	isoenzymes were elevated in 4 patients - 17%
S-type -	isoenzymes were elevated in 19 patients - 83%

They concluded that isoenzyme determinations cannot unequivocally determine the cause of hyperamylasemia, but they can enhance the diagnostic specificity of the serum amylase.

In one study, serum and urine total amylase activity was measured on admission to hospital, just before surgery, and a week later in 40 patients treated with pancreatic resection (60-90% of the gland) for acute necrotizing pancreatitis. The extent of parenchymal necrosis was estimated histologically from serial sections of the surgical specimen. Serum and urine amylase levels did not differ between cases with necrosis of 0-25%, 26-50%, 51-75% or 76-100% of the pancreatic parenchyma. Serum amylase activity and with three exceptions urine amylase activity decreased from time of admission to time of surgery. Time related decrease was not greater in those patients estimated to have extensive (51-100%) versus limited (0-50%) necrosis. Serum amylases fell to normal in 5-6 days and urine amylases were normal by 7-8 days after the onset of symptoms irrespective of the clinical condition (8). Similar findings of lack of correlation between degree of elevation of serum amylase and the severity of pancreatitis has also been reported in experimental acute pancreatitis (9,10). It has been postulated that the initial increase in serum amylase is due to absorption of enzymes into the pancreatic venous blood but later the rise is due to the passage of enzyme from the pancreas into the peritoneal fluid with collection into the thoracic duct and thence into the blood. It is postulated that with cell death at hemorrhagic pancreatitis there is presumably a once only release of amylase, and the serum amylase tends to fall to normal within a few days of the onset of the pancreatitis, irrespective of the clinical condition (11).

Imaging in Acute Pancreatitis

It is common knowledge that a KUB may be helpful in the diagnosis of acute pancreatitis, giving evidence of ileus, gastric outlet obstruction, sentinel loop, colon cut-off sign, pancreatic calcification, and occasionally calcified gallstones. However, for most practical purposes, its role has been superceded by sonography and computerized tomography. Sonography is useful for diagnosing cholecystolithiasis but not accurate for choledocholithiasis, while computerized tomography can confirm the diagnosis and may give an indication of those patients who are predisposed to a prolonged hospitalization and complications of the illness such as pseudocysts, abscesses and necrosis.

Sonography

The paralytic ileus and small bowel distension which accompany acute pancreatitis often limit the usefulness of sonography. For optimal diagnosis, patients must be examined in multiple anatomical positions from various acoustic windows. Sonography may be useful in evaluating the gallbladder and biliary tree and establishing an etiology for an attack of pancreatitis. A normal sonogram does not exclude the diagnosis of acute pancreatitis, nor does it exclude choledocholithiasis. Doppler ultrasound may help detect vascular complications of acute pancreatitis such as pseudoaneurysm formation and splenic vein thrombosis. Doppler sonography may be of value in establishing the diagnosis of

pseudoaneurysms larger than 1 cm. Small pseudoaneurysms usually require angiography for detection. Doppler sonography is also useful for assessing splenic vein patency.

Typical Findings in Acute Pancreatitis

1. May appear normal
2. Diffusely enlarged hypoechoic gland denoting parenchymal edema.
3. Dilation of the pancreatic duct.
4. Masses (phlegmon, hematoma, pseudocyst, aneurysm).

When compared to CT, sonography is less precise in defining complex extrapancreatic spread of pancreatitis along fascial planes and within parapancreatic compartments. It is particularly limited in visualizing lesions of the transverse mesocolon.

CT Diagnosis of Acute Pancreatitis

Findings reflect the presence and extent of the retroperitoneal inflammatory process and are usually similar, regardless of etiology (trauma being the main exception where pancreatic lacerations associated with high density hematomas can sometimes be detected).

Mild Changes

Relatively normal or slight to moderate increase in the size of the gland.
Pancreas is diffusely enlarged.
Parapancreatic fat becomes hazy secondary to inflammatory infiltrate.

Extensive Changes

Small or large fluid collections are seen in the gland.
Amount of parapancreatic inflammatory exudate is increased (a solid mass of indurated pancreas and adjacent retroperitoneal tissues secondary to the inflammatory process is termed a phlegmon).
The pancreas may be massively enlarged and may show patchy areas of diminished enhancement (pancreatic necrosis).

There may be total obliteration of the parapancreatic fat by large amounts of solid elements mixed with high density ($20\text{-}40^{HU}$) fluid collections. These collections represent a mixture of inflammatory exudate, necrotic tissues and blood. They have been called pancreatic fluid collections or, if higher in density, phlegmons. These exudates may involve the anterior perirenal space; may extend inferiorly along the perirenal spaces bilaterally, continue over to psoas muscles and into the pelvis; they may involve mesocolon, mesentery, posterior perirenal space and the mediastinum, and pericardium.

Other Findings

Segmental pancreatitis - 18% of patients
Pleural effusions - 20-32% of patients
Pancreatic ascites - 7% of patients

CT sensitivity for diagnosing pancreatitis has been reported to be between 77-92% with a specificity of 100%. CT scanning is not a replacement for clinical assessment, but may indicate groups of patients who require close monitoring for specific complications. In a study of 83 patients, Balthazar et al (12) found that one could select those patients who were predisposed to suffer from complications such as pancreatic abscess and pseudocysts. Other workers have described CT scanning as a useful tool for selecting patients with pancreatic necrosis and differentiating this from patients with pancreatic phlegmon, and CT scanning has also been used as an aid to detecting those patients who develop superimposed infection on pancreatic necrosis. Consideration may be given to serial CT scanning in patients who show extensive changes in their initial examination.

CT Grading of Acute Pancreatitis (Balthazar et al, 12)

Study of 83 patients
Grade A: Normal pancreas
Grade B: Focal or diffuse pancreatic enlargement
Grade C: Intrinsic pancreatic abnormalities associated with haziness and densities representing inflammatory changes in the parapancreatic fat.
Grade D: Single ill-defined fluid collection or phlegmon.
Grade E: Two or more poorly defined collections or presence of gas in or adjacent to the pancreas.

Patients with grades D and E were predisposed to pancreatic abscesses. There was not a close correlation between CT grading in this manner and the patient's clinical status (as assessed by physiological parameters). Other workers have supported the concept that local complications requiring surgical intervention (abscess, pseudocyst, necrotic tissue) tended to develop in patients with CT evidence of moderate to severe parapancreatic fluid collections. Classen et al (31) performed a prospective evaluation of 76 patients following assessment of the initial CT scan. In this study, CT scan appearances were divided into edematous and phlegmonous (phlegmonous equated to groups D and E described above). Phlegmonous extrapancreatic spread in one or two anatomic areas was associated with 4 percent mortality, while extrapancreatic involvement of three or more areas was associated with a mortality rate of 42%.

CT of the pancreas using a rapid bolus contrast injection or by a prolonged bolus injection using a large amount of contrast allows an estimate of pancreatic necrosis to be made. Infected necrotic tissue and fluid collections occur in 3-21% of patients with acute pancreatitis. In mild pancreatitis, there is a rapid rise in the density of the entire gland (40-50^{HU}). In contrast, in pancreatic necrosis there is little enhancement following contrast injection. CT estimates of pancreatic necrosis are found to be fairly accurate in patients who underwent

subsequent surgery. Note there is little or no correlation between the presence and extent of a pancreatic phlegmon and pancreatic necrosis.

CT scanning with contrast has an overall sensitivity of 85% for pancreatic necrosis. Patients with pancreatic necrosis appear to be the ones most predisposed to developing septic complications.

Infectious Complications in Acute Pancreatitis

Infectious complications account for 80 percent of deaths from acute pancreatitis. Because there is very limited knowledge regarding the role of antibiotics in acute pancreatitis, and very little is known about prophylactic antibiotic usage. Methods are required to differentiate sterile from infected masses and collections. Fine needle aspiration of inflammatory mass and fluid collections is one method for detecting pancreatic infection and can help rationalize therapy. When pancreatitis progresses to pancreatic and parapancreatic necrosis, the ultimate outcome is determined by the amount of necrosis, the extent of extrapancreatic necrosis and bacterial contamination of necrosis. The mortality for patients with infected pancreatic necrosis is high, approximately 32 percent.

Gerzof, Banks et al (13) performed 92 percutaneous needle aspirations of pancreatic inflammatory masses in 60 patients suspected of harboring pancreatic infection. Sixty percent of these patients were found by gram stain and culture to have a total of 41 separate episodes of pancreatic infection. These observations were confirmed by surgery or indwelling catheter drainage except in one patient who expired prior to intervention. Among 50 aspirates judged to be sterile, no subsequent evidence of infection was found. Further studies are required in this area; however, this technique holds promise for the detection of pancreatic infection. It should also help rationalize therapy and allow the majority of patients with acute pancreatitis to be treated conservatively. Selection for surgery which has a significant morbidity and mortality in patients with acute pancreatitis can be confined to that subpopulation with severe necrotizing pancreatitis or one of the complications of the disease.

Clinical Staging

The need to select those patients with progressive acute pancreatitis for more intensive therapy and consideration for surgical intervention has promoted the search to objectively categorize the severity of attacks of acute pancreatitis. Initially, severity was assessed clinically. The presence of clinical parameters such as fever, dyspnea, oliguria, tense abdomen, hypotension, and failure to respond to treatment were considered poor prognostic indicators. Based only on the clinical evaluation, however, McMahon and coworkers (6) were successful in identifying only 39 percent of patients with severe pancreatitis. It should be noted that the accuracy of clinical assessment improves following a second examination 48 hours after presentation (14). In search of a more accurate and objective evaluation, several methods have been assessed and reported. The levels of serum cyclic adenosine monophosphate, albumin, and methemalbumin have been mentioned as possible indicators of disease severity.

Warshaw and colleagues have correlated pancreatic necrosis to the levels of serum ribonuclease, while McMahon's group (15) suggested that the severity of pancreatitis can be estimated by the volume and color of fluid aspirated at paracentesis and peritoneal lavage on admission. More recently, Buchler and coworkers (16) have noted that the C-reactive protein level can predict the presence of pancreatic necrosis with a sensitivity of 95 percent when 100 g per 100 ml is taken as the discriminating point. It has also been suggested that the determination of serum catalytic phospholipase A_2 activity may determine the patients who develop pancreatic necrosis and pulmonary failure. These tests are not readily available in all laboratories.

The most common method used in the past decade for assessing clinical severity has been the statistical analysis of early objective measurements of multiple risk factors, described by Ranson (17). These workers assessed 100 consecutive patients with acute pancreatitis. In 27 patients the diagnosis was proven at laparotomy or autopsy and in 73 the diagnosis rested on the clinical picture of pain in the upper abdomen, tenderness and guarding with vomiting and serum amylase levels which were above 200 Somogyi units/percent. There were 21 women and 79 men. Pancreatitis was associated with alcoholism in 74 and biliary tract disease in 14. Following the measurement of multiple biochemical parameters, they divided the study population into two groups.

Group I included 69 patients who required less than seven days of intensive care and recovered, and group II consisted of 31 patients with severe pancreatitis. Included in group II were 15 patient who died, and a further 16 who required more than seven days treatment in the intensive care unit. The following admission criteria were associated with a worse prognosis:

>55 years of age
blood glucose >200 mg%/100 ml
WBC >16,000
serum lactate dehydrogenase >350 IU/l (normal up to 225 IU/l)
SGOT >250 Sigma Frankel units/l (normal up to 40)

and over the initial 48 hours

fall in hematocrit >10%
serum calcium below 8 mg/100 ml
base deficit greater than 74 meq/l
BUN increase greater than 75 mg/100 ml
arterial PO_2 <60 mm Hg
fluid retention estimated to be greater than 6 liters.

Among 450 patients prospectively studied, an increasing number of risk factors (grave signs or prognostic signs) correlated statistically with the more severe forms of pancreatitis. For example, the mortality associated with 0 to 2 prognostic signs was less than 1 percent, 3 to 4 signs was 16 percent, 5 to 6 signs was 40 percent and 7 signs or over was 100 percent. It should be stressed, however, that these indicators have no diagnostic value. The assessment only attempts to identify a subgroup of patients at risk of increased morbidity and mortality who should be targeted for more drastic and specific therapeutic measures.

Imrie's modification of prognostic factors resulted in patients being considered to have severe pancreatitis if within the first 48 hours of admission three or more of the following were present:

1. WBC >15 x 10^9/l
2. PaO_2 <60 mm Hg (8 KPa)
3. Plasma glucose >10 mmol/l in the absence of diabetes
4. Blood urea >15 mmol/l and not responding to intravenous fluid therapy
5. Serum calcium <2.0 mmol/l
6. Serum albumin <32 g/l
7. Serum LDH >600 u/l
8. Serum transaminases (SGOT/SGPT) >100 u/l
9. Age >55 years

In an attempt to make this system more applicable for gallstone pancreatitis, these workers further modified their grading system. In this revised grading system, the age factor is removed and serum transaminases are considered of prognostic significance only if greater than 200 u/l. Over the years several further modifications to these prognostic matrices have been made. Assessing pancreatitis using multiple variables in this fashion has approximately 80% predictive value for all episodes of pancreatitis. It may be slightly less accurate for classifying gallstone pancreatitis.

Surgery and Acute Pancreatitis

Patients with extended intrapancreatic necrosis (greater than 50% of the pancreas) or infected pancreatic necrosis should be considered for surgery. The development of an acute surgical abdomen, shock, persistent or increasing organ dysfunction are usually indicators for surgery. There is a swing away from pancreatic resection in this situation because classic resection techniques have been associated with high complication rates and a hospital mortality greater than 30 percent. The currently favored technique is necrosectomy ± lavage. This involves debridement of demarcated, devitalized tissue. This is accompanied by intra-operative peritoneal lavage and the placement of large bore drainage tubes. Preliminary experience with necrosectomy followed by local lavage appears to be associated with decreased mortality (less than 10%). Controlled clinical studies are required to confirm these findings.

With regard to biliary pancreatitis, the timing of surgery on the biliary tree is controversial. Acosta et al (20) favored early intervention whereas Ranson (21) observed a high mortality in patients operated during the acute attack of gallstone pancreatitis. Subsequently Stone et al (22) performed a randomized, prospective trial and observed no difference in mortality when comparing patients treated surgically early versus those treated late after the pancreatitis has subsided. This discrepancy in findings is partially explained by the fact that patients were not stratified and compared according to disease severity.

It appears that selection of those patients with progressive changes of severe acute pancreatitis for intervention is the key to management. Many patients with acute gallstone pancreatitis will improve with observation for 24

hours. It is possible that the determining factor for this difference is whether the patient has passed a common duct stone or whether the patient has a retained common duct stone, especially if it is impacted in the ampulla. There are several theories proposed to explain how a stone passing through or becoming lodged in the terminal bile duct might precipitate an attack of acute pancreatitis. Opie (23) proposed the common channel theory, suggesting the presence of a common biliary pancreatic duct proximal to an obstructing stone in the ampulla could allow bile to flow into the pancreatic duct, triggering acute pancreatic inflammation. A second explanation for the development of acute pancreatitis is that it results from the reflux of duodenal contents through an incompetent sphincter of Oddi. This could be secondary to the passage of a large stone (24).

The currently favored hypothesis is that outflow obstruction secondary to a stone lodged in the ampulla or by edema and sphincter spasm associated with the passage of a stone leads to pancreatic ductal hypertension. Ductal hypertension causes either extravasation of pancreatic juice into the parenchyma of the gland followed by enzyme activation. More recently it has been proposed that this enzyme activation is an intracellular event precipitated by lysosomal enzymes (e.g. Cathepsin B) (25).

Selection of Patients with Possible Biliary Pancreatitis

Gallstone pancreatitis continues to have a mortality rate that approaches 10%. In a review of 132 fatal cases of acute pancreatitis, Carter found that one-third of the gallstone associated cases were diagnosed for the first time at autopsy. Cholangiography is the only definitive means of confirming the diagnosis of biliary pancreatitis. Schoelmerich, Gross et al (27) compared laboratory tests, ultrasound, computed tomography and ERCP in 50 consecutive patients with acute pancreatitis in an attempt to see whether they could predict which cases were biliary in origin. ERCP, surgery, and autopsy were used to define biliary pancreatitis.

Ultrasound and CT could not reliably diagnose biliary pancreatitis in the 10 patients found to have biliary disease. None of the laboratory tests had sufficient sensitivity and specificity to determine the diagnosis. Although all tests showed higher mean values in biliary pancreatitis, SGPT (ALT) gave the best discrimination (positive predictive value 53%, negative predictive value 94%, cut-off 60 units/liter).

In a further study, Neoptolemos et al (28) found a positive correlation between acute biliary pancreatitis and the patient's age as well as CBD diameter and pancreatic duct diameter. This same group also analyzed prospectively three clinico-biochemical systems for their ability to predict gallstone pancreatitis:

System 1	based on serum transaminase alone ($\geq$60 IU/l)
System 2	using alkaline phosphatase and bilirubin in addition to transaminase
System 3	using female gender, age, amylase and alkaline phosphatase in addition to transaminase.

The following table summarizes their findings:

Table II

Laboratory Data in Pancreatitis 1983 - 1986

	Biliary Pancreatitis	Non-biliary Pancreatitis
Gender	139 female	59 female
Age	65 ± 17	52 ± 19
Amylase	6041 ± 6335	4546 ± 3990
Alkaline phosphatase	257 ± 225	141 ± 137
Alanine transaminase	221 ± 227	72 ± 119
Bilirubin	40 ± 39	24 ± 30

Total patients 368; total number of episodes of pancreatitis 39; biochemical analysis performed within 48 hours

From Neoptolemos, Carr-Locke (39)

Sensitivity and specificity of the one factor system was 75% and 74%; for the three factor system was 74% and 78%; for the five factor system was 62% and 80%. The predictive value of a positive result was 78.8%, 81.5% and 80.1%, and of a negative result was 69.4%, 70.1% and 62.3% for the three systems, respectively. The performances of the one and three factor systems were marginally better than the performance of the five factor system. The one factor system had the advantage of simplicity. These workers concluded that finding a raised serum alanine aminotransaminase (ALT, SGPT) (more than 60 IU/liter) was simple and useful in the clinical setting with a predictive value of 75%.

These observations have been confirmed and corroborated by Mayer and McMahon. In evaluating the diagnostic potential of plasma aspartate aminotransferase (AST), alkaline phosphatase and bilirubin on the day of admission, these authors found the optimal cut-off for AST was 60 IU/l was recorded in 111 (84%) of 132 attacks associated with gallstones but in only 12 (14.5%) of 83 attacks without stones and was unrelated to the severity of the attack. Elevated levels of alkaline phosphatase and bilirubin were more common in attacks of pancreatitis associated with gallstones but were less reliable for the identification of cholelithiasis than AST.

Endoscopy and Non-Malignant Pancreatic Disease

Endoscopic retrograde cholangiopancreatography (ERCP) and the use of biliary endoprostheses in the treatment of benign and malignant biliary strictures is now a well-established and acceptable alternative to surgical

therapy. Although diagnostic ERCP is a routine investigation in the assessment of pancreatic disease, the use of endoscopic therapy in acute and chronic pancreatitis is experimental. The following reports are preliminary, and their role in the treatment of pancreatic diseases remains to be determined by prospective controlled studies. Because alternative methods for the treatment of pancreatic disorders are so unsatisfactory and because early results of endoscopic therapy are sufficiently encouraging, further studies are warranted.

In the past, acute pancreatitis was a contraindication to ERCP. Recently diagnostic and therapeutic ERCP have been performed in patients with acute pancreatitis thought to be secondary to choledocholithiasis. Many reports now attest to the safety of these procedures in acute biliary pancreatitis. In a recent study, Escourrou et al (29) reviewed their experience with ERCP and acute pancreatitis in 118 patients. ERCP showed choledocholithiasis in 78% of cases, and endoscopic sphincterotomy was possible during initial endoscopy in 95% of patients. Two patients died from post-sphincterotomy hemorrhage; however, no other complications were reported.

These results correspond with earlier reports by Cotton and Classen (30) and indicate that ERCP and sphincterotomy can be safely performed during an acute attack of pancreatitis without greater risk than is usually entailed by the procedure. These studies draw attention to the difficulty in diagnosing choledocholithiasis using conventional techniques. Non-invasive techniques for detecting common bile duct stones are generally unpredictable. In a recent report comparing ultrasound and ERCP in patients presenting with acute pancreatitis, ultrasound detected common bile duct stones in 18% of patients compared with a 78% detection rate by ERCP (32). An attempt has been made to use a multivariate analysis to determine which biochemical values would most accurately predict the presence of common bile duct stones. Common bile duct stones were predictable in 85% of the cases where the patient had severe pancreatitis [Blamey's criteria (29) and a bilirubin greater than 40 μmol/l (2.35 mg/dl)]. In these cases the diagnosis was confirmed by ERCP. However, the accuracy of prediction was less in cases of mild pancreatitis. For practical purposes, the finding of a raised serum alanine aminotransferase (ALT, SGPT) (more than 60 IU/liter) should raise the suspicion of choledocholithiasis.

Problems have included the absence of good criteria as to the best time to intervene with ERCP, and the lack of critical appraisal as to whether instrumentation of the papilla and injection of contrast into the pancreatic duct makes a serious case of pancreatitis worse. Some European investigators circumvented these concerns and advocated ERCP in all patients. The earlier report of Cremer et al (34) and Gelin et al (35) have not been substantiated by others. Both investigators advocated routine ERCP in all patients with acute pancreatitis. There was no reported increase in the overall incidence of complications following these procedures. Nonetheless, in most medical institutions there is limited experience in the routine use of urgent ERCP in all patients presenting with acute pancreatitis.

An important argument against such a universal approach is that most patients with biliary pancreatitis have self-limited episodes (approximately 80%) that permit elective intervention after the acute illness has subsided. This feature of the disease has also contributed to the absence of a clear consensus

among surgeons as to the timing of operation in biliary pancreatitis, despite extensive discussion in the surgical literature that predates endoscopists' concerns with this issue.

Recently the first randomized, controlled trial of emergency ERCP and sphincterotomy versus conservative treatment was reported by Neoptolemos et al (33). In patients with predicted severe attacks according to a multifactorial prognostic system, morbidity, mortality and hospital stay were significantly reduced by ERCP and sphincterotomy. In contrast, in patients with mild attacks the outcome was not significantly altered. This study assessed the outcome in 121 patients treated by emergency endoscopic sphincterotomy (33) or by conventional supportive therapy. There were no differences in complication rates (12%) or mortality (none) in those patients with a predicted mild attack, based on a modified Glasgow prognostic scoring system. However, in severe attacks the difference was dramatic, with a 61% versus 24% morbidity and 18% versus 5% mortality in favor of the endoscopic sphincterotomy group. There was no increased morbidity associated with the endoscopic intervention itself, and the authors concluded that patients with a high likelihood of a gallstone etiology who are predicted to have severe attacks should undergo urgent endoscopic sphincterotomy.

Acute Recurrent Pancreatitis

An etiology for acute pancreatitis can be identified in 60-88% of patients with acute recurrent pancreatitis (40). Small gallstones, minimal pancreatic duct abnormalities, and sphincter of Oddi dysfunction have been suggested as causes of pancreatitis in the remaining 12-40% of patients (44,45). In a recent study extending the findings of Katon et al (46) and Cotton (47), Venu et al (48) reviewed 116 patients who had acute recurrent pancreatitis, normal hepatobiliary ultrasound, and normal oral cholecystogram studies. Forty-five patients were found to have a possible cause for their pancreatitis at ERCP (Table III). Twenty-seven patients were found to have a structural abnormality at diagnostic ERCP, and 17 patients were found to have significantly elevated sphincter of Oddi basal pressure (50 ± 4.5 mmHg versus 15 ± 4.5) at ERCP manometry.

Table III

ERCP Findings in 116 Patients with Idiopathic Recurrent Pancreatitis (n=116)

Sphincter of Oddi dysfunction	17
Pancreas divisum	11
Choledochocele	4
Cholelithiasis	8
Papillary tumor	3
Malignant structure/pancreatic duct	1

From Venu RP et al (48)

Cremer and colleagues (34,35) suggested that pancreatography was useful in defining those patients with "chronic" pancreatitis who were having an "acute" attack of pancreatitis. The significance of this information is questionable. It has also been claimed that this technique combined with CT and ultrasound gives a precise definition of pancreatic necrosis, should surgery be necessary. This line of reasoning has been reinforced by a published small series which advocates ERCP in acute hemorrhagic necrotizing pancreatitis as a preoperative guide (37). It was suggested that this aids surgical dissection and may help overcome the problem of assessing the extent of pancreatic necrosis at laparotomy. Further studies in this area are anticipated.

Chronic Pancreatitis

There are preliminary reports indicating that pancreatic endoprostheses may be beneficial in patients with ductal abnormalities who are having recurrent episodes of pancreatitis or chronic pain. Huibregtse et al (49) inserted pancreatic stents in patients with chronic pancreatitis of varying etiologies (Tables IV and V). These patients had either recurrent episodes of pancreatitis or chronic pain. In 22 of the 32 patients referred with the diagnosis of chronic pancreatitis, a sphincterotomy of the pancreatic sphincter was performed to facilitate deep cannulation. A guidewire was placed prior to insertion of a nasopancreatic drain or endoprosthesis. Stents were successfully placed in eight out of 11 patients with pancreatic strictures, six of seven patients with pseudocysts, and six of 11 patients with pancreatic duct stones. Of three patients with papillary stenosis and ductal dilation, a pancreatic sphincterotomy

Table IV

Pancreatic Endoprosthesis Treatment
(n=32)

Abnormalities	Recurrent pancreatitis (n=21)	Chronic pain (n=11)
Dominant strictures	9	2
Stricture + stones	1	5
Pancreatic stones	4	1
Papillary stenosis	3	0
Pseudocyst	4	3

From Huibregtse et al (49)

was performed in three, and a stent placed in one. Among the patients receiving long-term endoscopic treatment, all 17 with recurrent episodes of acute pancreatitis improved, while seven of the ten patients with chronic pain due to pancreatitis also improved. These results suggest that the provision of a conduit to improve pancreatic drainage may be an important factor in treating certain cases of pancreatitis. The overall complication rate in this study was 22%. There was one death from perforation, and two patients required surgery for infectious complications subsequent to endoscopic therapy.

In a similar study carried out by the author (50), pancreatic stents were successfully inserted in a small group of 14 patients with benign pancreatic disorders (Figure 1). There was symptomatic improvement in approximately 50% of patients (Table VI). Soehendra et al (58) also reported encouraging results following endoscopic papillotomy of the sphincter of Oddi and the pancreatic duct component in patients with chronic obstructive pancreatitis. No serious complications were reported following this procedure, and it appeared to be very effective in relieving pancreatic pain. Fuji et al (52) also reported that pancreatic sphincterotomy is safe in chronic pancreatitis and that it can be combined with pancreatoscopy and endoprosthesis insertion. In this study a pancreatic sphincterotomy was successfully performed in 10 out of 13 patients with chronic pancreatitis; pancreatoscopy was performed in three cases to exclude

Table V

Pancreatic Endoprostheses Treatment:
Etiology of Chronic Pancreatitis

Etiologic factor	Patients
Alcohol	18
Gallstones	2
Pancreas divisum	3
Benign papillary tumor	1
Congenital ductal anomaly	1
Idiopathic	7

From Huibregtse et al (49)

Table VI

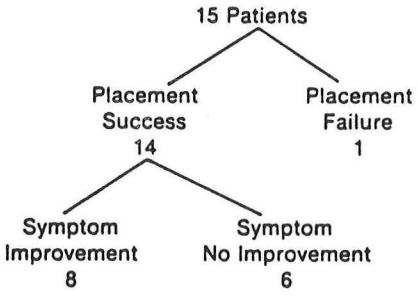
Stent Placement in Benign Pancreatic Disease

Indications for stents	No. patients with stents	No. Patients with symptomatic improvement
ETOH and stricture	5	4
Acute recurrent pancreatitis with papillary stenosis	7	3
Idiopathic chronic	2	1

calculi and pancreatic stents were placed in three cases. Clinical symptoms improved in nine out of ten patients following sphincterotomy and in one case after stent placement. In one case the stent had to be removed following the development of severe abdominal pain, and one patient did not benefit at all from stent placement.

Figure 1

Stent Placement in Benign Pancreatic Disease



The accumulated experience to date involves only small numbers of patients. Problems to be resolved involve the optimal time for stent insertion, the duration of treatment of stent placement, and the interval between stent removal and replacement. It has been the authors' policy to routinely exchange pancreatic stents at 6-month intervals. In a total of 30 stent placements during two years, five stents were found to be occluded at the time of removal, two stents had

dislodged and passed spontaneously through the gut, and two stents had to be removed following insertion because of an exacerbation of the patients' pain.

There have been preliminary reports indicating that the removal of pancreatic debris is helpful for pain relief in chronic pancreatitis (53,54). Several endoscopists (49,55,56,57) also proposed endoscopic drainage of pancreatic cysts as an alternative to the usual internal or external operative drainage techniques. Liguory (55) attempted endoscopic drainage in four patients outside the pancreas proper. Two patients had chronic alcoholic pancreatitis and two patients had acute pancreatitis, both complicated by pseudocyst formation. The cysts were localized with ultrasound and/or abdominal computed tomography, and they were found to be bulging into the stomach or duodenum at the time of endoscopy. Two endoscopic cystogastrostomies and two cystoduodenostomies were performed using a straight-wire sphincterotome and nasocystic drainage. The two patients with chronic pancreatitis benefitted from this form of therapy, but the two patients with acute pancreatitis subsequently underwent an operation because of complications.

Sahel et al (56) attempted to perform endoscopic cystoduodenostomy in 19 patients with chronic calcific pancreatitis with a success rate of 90%. The only two failures, as well as two perforations, occurred in patients without a visible bulge created by the cyst on the duodenum, and the authors recommended avoidance of this approach in such patients.

Table VII

Endoscopic Stent Failure in Pancreatic Diseases*

Occluded stents	5
Spontaneous passage	2
Early pain	2

*Stents changed at 6-month intervals. Total stent placements, 30.

Cremer et al (57) performed endoscopic cystoduodenostomy, using diathermy, on 22 patients and cystogastrostomy on 11, all of whom had cysts bulging into the wall of the appropriate adjacent structure. The success rates for the two groups were 95-100% with only a 10-20% long-term recurrence rate. Of the 33 patients, one with attempted cystoduodenostomy developed retroperitonitis treated with antibiotics followed by surgical cystojejunostomy. Two others undergoing cystogastrostomy developed infected pseudocysts treated nonsurgically. One of these had self-limited arterial bleeding at the time of the initial endoscopic excision.

It remains to be seen how many patients with pseudocysts will have the appropriate anatomy for endoscopic treatment. More data from additional centers

are needed to establish the efficacy and safety of this approach compared with surgery before this approach can be considered beyond the investigational stage.

In contrast to the above studies, Huibregtse et al (49) worked within the pancreas, positioning endoprostheses into the pseudocysts in five patients with chronic pancreatitis via the main pancreatic duct. Four patients experienced relief of their complaints and resolution of their cysts. In one patient a cystoduodenal fistula was created with an excellent result. Again, it is yet to be determined whether these techniques are superior to CT or ultrasound-directed needle aspiration or operative drainage.

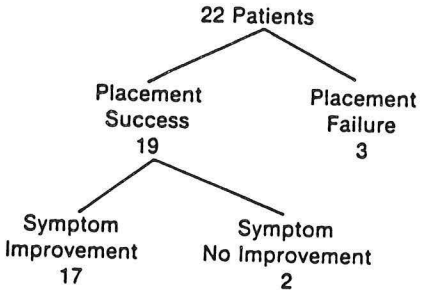
Pancreatic Divisum

During early embryologic development, the head of the pancreas develops separately from the body and tail. It has its own drainage, the duct of Wirsung. The duct of Santorini drains the body and tail. Following mid-gut rotation, the head fuses with the body of the pancreas, and the duct of Wirsung connects to the duct of Santorini. Drainage of pancreatic secretion usually takes place through the duct of Wirsung via the major papilla. The duct of Santorini draining via the minor papilla is thought to be no longer functional in the majority of patients. The situation where the body and tail continue to drain via the duct of Santorini is known as pancreas divisum. This can be complete pancreas divisum where the duct draining the head of the gland has no communication with the duct draining the body and tail of the gland, or incomplete, where there is a vestigial connection. The association between pancreatitis and pancreas divisum is controversial. The exact incidence of this congenital anomaly in the general population is unknown. It has been variously estimated to be between 6-14% of the population depending on whether these are pancreatographic or post-mortem surveys. However, there does appear to be a group of patients with this anomaly who suffer from acute recurrent pancreatitis or abdominal pain. Whether this is a causal association has never been established. There have been two approaches to treating this problem - one surgical, one endoscopic. Warshaw et al (26) took 100 patients with episodic acute pancreatitis or pancreatic pain and this anomaly or one of its variants and performed accessory sphincteroplasty. They found a symptomatic improvement in 70% of patients. They also found that ultra-sound with secretin formed the basis of a predictive test to determine which patient would benefit from intervention. Another approach to this problem has been endoscopic dilation and stent placement in the minor papilla of these patients.

There have been continuing reports (54) that dilation and stent placement in the minor papilla of patients with pancreas divisum relieves their symptoms. In an attempt to determine if pancreatic stent therapy is beneficial in patients with pancreas divisum, 22 of our patients underwent stent insertion either for pancreas divisum and acute recurrent pancreatitis or for pancreas divisum and severe abdominal pain (50). Six of these patients had a previous operation on the minor papilla before being referred to us. A stent was successfully placed endoscopically in 19 of these 22 patients (Figure 2). Stents were changed at six-month intervals. Of these 19 patients, 17 had symptomatic improvement with marked decrease in pain, decrease in number of attacks of pancreatitis, and fewer visits to the emergency room. The two patients who did not have symptomatic improvement had their stents replaced twice before this treatment was abandoned.

Figure 2

Stent Placement in Pancreas Divisum



Paradoxically, serial pancreatograms showed the development of dorsal ductal changes consistent with chronic pancreatitis in two patients during stent therapy despite their symptomatic improvement. These patients have been followed for six months to three years. Over this period, a total of 48 stents have been placed in the dorsal duct. At the time of the six-month stent exchange, it was noted that 10 stents had become occluded, and four stents had passed spontaneously out of the GI tract. Two stents had migrated into the body of the pancreas. Attempts to remove them with a minisnare retriever were successful in one patient. The other patient with the stent retained inside the pancreas has had no problems to date (Table VIII). Following endoscopic stenting, there were five episodes of pancreatitis, three of which responded spontaneously to conservative management, and two in which the stents had to be removed. One stent was removed 24 hours after insertion, and the other five days after insertion.

This preliminary experience with the endoscopic insertion of transpapillary stents in pancreatic diseases corroborates the report of Soehendra et al (58). Furthermore, it demonstrates that manipulation of the dorsal pancreatic duct is comparatively safe and less hazardous than formerly believed. Symptomatic improvement in the patients treated by transpapillary stent placement is encouraging, but a careful clinical trial is needed. Endoscopic therapy may provide an effective way of obtaining symptomatic relief in a select group of patients with benign pancreatic problems.

Table VIII

Problems Associated with Stent Placement in Patients with Pancreas Divisum

Total stent placements	48
Occluded stents	10
Spontaneous passage	4
Migration into pancreas	2
Early pain	2

Techniques

The technique for placing a stent in the pancreatic duct is similar to that used for inserting nasobiliary stents and drainage tubes. A diagnostic pancreatogram is performed. Following this, a 0.025 inch guidewire is inserted into the pancreatic duct and advanced midway toward the tail of the pancreas. A 5-Fr or 7-Fr barbed stent is then introduced over the guidewire into the pancreatic duct and positioned so that its distal end protrudes into the duodenal lumen. The stents are 5-7 cm in length.

In patients with suspected pancreas divisum, a dorsal duct pancreatogram can be obtained by cannulating the minor papilla with either a tapered-tip catheter, a needle-tip catheter, or a 3-Fr angiocatheter which may or may not require prior insertion of a 0.018 inch guidewire. The identification of the minor papilla is assisted by the long endoscopic approach and/or the injection of secretin which stimulates pancreatic juice outpouring and demarcation of the orifice (1 unit/kg). When a stent is to be placed into the dorsal pancreatic duct via the minor papilla, it is preferable to cannulate the papilla with a 3-Fr angiographic catheter through which a 0.018 inch guidewire is inserted. The guidewire is then advanced toward the tail of the pancreas and the stent positioned over the guidewire in the usual methods.

In those cases where the stent has migrated into the body of the pancreas, a minisnare can be inserted into the pancreatic duct and used to retrieve the stent. Using this technique, the authors managed to retrieve all but one of the stents that migrated into the body of the pancreas.

Dilation of the major and minor papilla is not routinely undertaken prior to stent placement. In the authors' experience, approximately 50% of cases required dilation prior to stent insertion. Dilation appears to be associated with an increased risk of pancreatitis as compared to a diagnostic ERCP study. In some patients with acute recurrent pancreatitis and papillary stenosis who have not benefitted from conventional sphincterotomy, dilation of the pancreatic sphincter with angiographic catheters has been undertaken with some improvement in symptoms. A larger, controlled study is required to elucidate the value of dilation at the pancreatic sphincter in patients with papillary stenosis.

Pancreatic sphincterotomy is not routinely practiced by the author. In a preliminary study, four patients with papillary stenosis and acute recurrent pancreatitis and two patients with papillary stenosis and chronic pancreatitis underwent pancreatic sphincterotomy. All patients had failed to improve following sphincterotomy on the common bile duct. Of this group of six patients, two developed pancreatitis and one bled following the procedure. None of this group of patients had lasting benefit following endoscopic pancreatic sphincterotomy. One patient with idiopathic pancreatitis benefitted from sphincterotomy. The significant incidence of complications has made us cautious about embarking on a larger study of endoscopic pancreatic sphincterotomy.

Obstructive Jaundice Secondary to Pancreatic Carcinoma

Carcinoma of the pancreas is the most common tumor causing biliary obstruction. In the United States more than 20,000 persons present with this problem each year (59). This is a disease of the elderly. The median age at onset for carcinoma of the pancreas in the United Kingdom in 1982 was over 70 years. The age distribution for these lesions is similar in the United States.

The results of surgical therapy for carcinoma of the pancreas are disappointing. Ideally, we would like to resect the tumor and cure the patients. However, this is not possible in the majority of patients. Carcinoma of the pancreas presents late, and in the vast majority of patients (90%) it has extended beyond the pancreas or metastasized at the time of presentation (60). In a survey of the literature over 50 years Gudjonsson (61) reported that pancreatic resection has had no practical impact on survival. He reported that 40% of those found to have cancer of the pancreas will be dead within three months, 65% within 6 months, and approximately 90% within one year of diagnosis. The five year survival rate in this survey was 0.4%. Thus, most patients require palliation rather than resection. This will involve a variety of treatments. The spectrum of therapy includes surgical bypass, endoscopic or percutaneous drainage for biliary obstruction, and analgesics or celiac plexus blocks for pain.

Surgical bypass is the established method for relieving biliary obstruction. However, surgery has a substantial morbidity and mortality. The risk of surgery increases with increasing age and in the presence of extensive metastatic disease. Age greater than 60 years has been reported as a risk factor in biliary surgery (62), and Ransohoff (63) found that the mortality for cholecystectomy and exploration of the common bile duct increases rapidly over 70 years of age. The operative mortality for pancreatic resection in patients over 65 and 70 years of age has been reported as 41 and 58 percent, respectively (64,65). The risk of surgery also increases in the presence of extensive metastatic disease. Blievernich (66) reports a mortality for bypass surgery for carcinoma of the pancreas of 12.3% for patients with local extension of the disease, rising to 20% with liver metastases and 43% for patients with peritoneal metastases and ascites. Operative mortalities of 28% in the presence of liver metastases and 59% with extensive metastatic disease have also been reported (67,68). Many patients presenting with malignant obstructive jaundice are elderly with extensive metastatic disease, and thus are at high risk for bypass surgery. Here at Parkland (69), operative management of pancreatic cancer has been associated with significant mortality. Several non-surgical techniques have been developed to establish biliary drainage in the hope of reducing the morbidity and mortality, and hospitalization time for patients with carcinoma of the pancreas, and also for patients who are unfit for general anesthesia. One of the physician's responsibility is to select those patients which are most suited for the different types of therapy currently available.

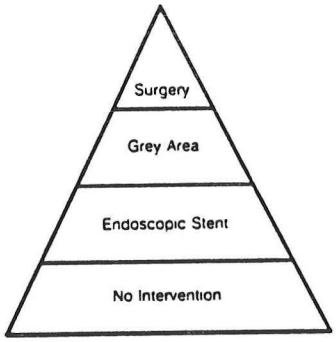
Nonsurgical Palliation

Initially, nonsurgical palliation was accomplished through external drainage by percutaneous transhepatic insertion of a catheter (70). Later a

guidewire and drainage catheter were manipulated through the stricture, allowing both internal and external bile flow (71). However, external biliary drainage has several disadvantages including pain at the catheter site, the risk of spontaneous catheter dislodgement, and leaks of ascitic fluid and bile around the catheter and bleeding (72). The use of nonsurgical techniques was advanced by the description of the transhepatic insertion of an indwelling stent without an external catheter (73). Endoscopic insertion of a biliary stent through the papilla was described more recently (74). At first it was not obvious which would be the best technique. The endoscopic approach seems technically more difficult than the percutaneous transhepatic method, but is possibly less traumatic for the patient. Variations in technique and patient selection make it difficult to compare these methods from published retrospective series.

Figure 3

The Spectrum of Approach to Malignant Obstructive Jaundice



The Middlesex group recently published results of the first prospective randomized trial comparing the two methods (75). Between February 1983 and March 1985, 75 patients with biliary obstruction due to malignancy were randomized to receive either an endoscopic or a percutaneous transhepatic stent. A total of 29 patients had hilar strictures due to cholangiocarcinoma or carcinoma of the gallbladder, and the remainder had low biliary strictures due to carcinoma of the pancreas. The lesions were not resectable, and the patients were considered to be unsuitable for bypass surgery because of their age, the extent of the disease, or associated medical conditions. The patients were elderly (median age 73), deeply jaundiced, and 20% had renal impairment associated with prolonged biliary obstruction. The two groups were well matched apart from a higher incidence of hilar strictures in the endoscopic group. This was allowed for by stratifying the statistical analysis for the site of the obstruction.

Endoscopic stents were significantly more successful in relieving jaundice and had a significantly lower 30-day mortality. The higher mortality with percutaneous stents was due to the high incidence of complications, mainly those of puncturing the liver with large-bore tubes, causing hemorrhage and bile leak. This suggests that the endoscopic approach should be attempted first when there are clinical indications for a biliary stent. The percutaneous method should be

reserved for those patients in whom the endoscopic approach fails. These results are comparable with those of other published series (75-85).

Table IX

Results of Prospective Randomized Trial Comparing Endoscopic and Percutaneous Stenting for Malignant Obstructive Jaundice in Patients Judged Not Fit for Surgery

	Endoscopic stents (n=39) (%)	Percutaneous stents (n=36) (%)
Successful stent insertion	89	76
Successful relief of jaundice	81	61*
Early complications	19	67
30-Day mortality	15	33**

* p=0.017 Mantel-Haenszel analysis
**p=0.016 Log-rank analysis

Experience with Endoscopic Stents and Pancreatic Malignancy

Since its introduction in 1979, endoscopic stenting has been used mainly for patients considered unfit for palliative bypass surgery. There was an initial learning phase where endoscopists developed the technique and equipment. There have been two major series describing the early results with this technique, one from Amsterdam and the other from London. At the Middlesex Hospital between March 1983 and March 1986, 102 patients with carcinoma of the pancreas were assessed for endoscopic stenting. The diagnosis was made by finding a mass in the pancreas on abdominal ultrasound and obstruction of the bile duct and pancreatic duct at ERCP. If there was doubt about the diagnosis, computed axial tomography and endoscopic ultrasound were also used. The lesions were judged to be not resectable because of the size of the tumor or spread of the tumor beyond the pancreas. The patients were considered to be unfit for bypass surgery because of their age, associated medical conditions, or extent of disease. Histologic confirmation of adenocarcinoma was obtained in 76 (76%) of the patients, usually by ultrasound-guided fine-needle aspiration biopsy.

Table X

Results of Endoscopic Stenting for Carcinoma of the Pancreas in Patients Who Are High Risks for Surgery

	The Middlesex Hospital (n=99)	University of Amsterdam (n=221)
Relief of jaundice	88%	87%
30-Day mortality	9%	10%
Mean survival	25 weeks	26 weeks
Late duodenal stenosis	6%	7.5%

The patients were deeply jaundiced; a quarter had renal impairment due to prolonged biliary obstruction. Seventeen patients (17%) had had previous unsuccessful surgical or percutaneous attempts at biliary drainage. Four of these patients had a biliary fistula. Three patients were so sick that further intervention was considered meddlesome and all three died within one week. Stenting was attempted in 99 patients, and a stent was successfully inserted in 88 (89%). Jaundice was relieved in all but one of the patients. The stents used were 10 Fr (n=71) with some 11.5 Fr (n=9) and 8 Fr (n=8). Eight patients with successfully inserted stents died within 30 days of the procedure. Three died with complications of the procedure: one cholangitis, one pancreatitis, and one patient died during the procedure, probably from oversedation. Three patients died with disseminated disease between days 6 and 26 following the procedure. One patient died with a bleeding gastric ulcer and another with bleeding gastric erosions. Those patients with failed procedures were managed by percutaneous intervention (n=4), bypass surgery (n=4), and no further treatment (n=3). Five of these patients died within 30 days.

The median survival of patients with successfully inserted stents was 21 weeks (mean 25 weeks). Late complications were stent blockage and duodenal obstruction. Stent replacement was required on at least one occasion in 20 patients, i.e. 29.5% of those at risk. These patients presented with a recurrence of their jaundice and/or cholangitis. The blocked stents were easily replaced endoscopically in all cases, and this required a hospital admission of 2-3 days. Duodenal obstruction requiring bypass surgery occurred in five patients, 6 percent of those at risk.

These results are similar to those obtained by Huibregtse at the University of Amsterdam in a large series of patients with carcinoma of the pancreas palliated with endoscopic stents (86). The incidence of duodenal stenosis in both series is lower than expected. A review of a series of patients undergoing biliary bypass surgery without prophylactic gastroenterostomy found reoperation

for duodenal stenosis in a mean of 16 percent (range 6-50%) of patients (87). The lower incidence in endoscopic series may be due to patient selection.

The quality of palliation is often difficult to judge. After successful stent insertion, pruritus is rapidly relieved, usually within 2-3 days. Jaundice resolves over several weeks. Nutrition is improved by returning bile to the duodenum and many patients without extensive metastatic disease gain weight. Renal impairment due to biliary obstruction resolves after stenting and renal function returns to normal.

The first prospective, randomized trials comparing palliation of malignant biliary obstruction with endoscopic endoprostheses versus surgical biliary bypass have just been published (88). These endoscopic techniques compare favorably with traditional surgical bypass. Further studies are required where patients are stratified according to performance status and tumor mass prior to being enrolled in studies. The concern with all current studies is that two different groups of patients are being compared.

Complications of Non-Surgical Biliary Drainage

The most important early complication is cholangitis. This is more common with hilar strictures, the exact incidence depending on the definitions used and how carefully patients are reviewed. Endoscopes must be carefully cleaned and disinfected, and accessory equipment should be sterilized (89). The incidence of cholangitis was high with the 7- and 8-Fr stents used initially and decreased when larger stents were introduced. It is recommended that stents of at least 10-Fr diameter should be used. Occasionally, stenting in a patient with multiple intrahepatic strictures will be complicated by cholangitis in an undrained segment of liver. It is difficult to selectively cannulate and drain the infected segments endoscopically. These patients are best managed by percutaneous drainage of these ducts.

Hemorrhage and pancreatitis have been reported following sphincterotomy for stent insertion. The incidence of these can be reduced by performing a small sphincterotomy or, if possible by inserting the stent without a sphincterotomy. Perforation complicating stenting may be due to the sphincterotomy or may occur in the bile duct at or below the stricture. Strictures should be gently negotiated with the guidewire. A hydrophilic, coated, steerable guidewire also helps negotiations of difficult structures. The wire usually passes easily once the correct position and angle are located. Perforations can usually be managed conservatively by obtaining adequate drainage of the bile duct with an endoscopic stent or percutaneously if this is not possible.

Post-Stent Management

Antibiotics are continued until it is clear that the stent is draining adequately, which is usually 24-48 hours. Bilirubin levels are performed daily; a falling bilirubin indicates adequate stent function. Abdominal ultrasound may be performed at 24-48 hours to assess stent function. Decompression of the biliary tree and the presence of air in the ducts indicates a functioning stent.

The histological diagnosis of malignancy can be confirmed by ultrasound- or CT-guided fine-needle aspiration biopsy. The patients need only be hospitalized for a few days after the procedure; however, the stay may be prolonged due to their poor general condition or the need for further investigations. After a successful stent insertion, pruritus is usually relieved in 2-3 days and jaundice will resolve over 2-3 weeks depending on initial bilirubin levels and hepatocellular function. In the absence of liver metastases or advanced cirrhosis, liver function tests should return to normal. On discharge, patients are advised that a recurrence of the jaundice or cholangitis should prompt an immediate return for further management. They are also briefed about relevant symptomatology that may occur following stent blockage. Consideration should be given to exchanging stents prophylactically at about 4 months in patients who remain vital (and in any patient with benign disease). The blocked stent can easily be replaced endoscopically.

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