We are IntechOpen,
the world's leading publisher of
Open Access books
Built by scientists, for scientists

5,200
Open access books available

128,000
International authors and editors

150M
Downloads

Our authors are among the

154
Countries delivered to

TOP 1%
most cited scientists

12.2%
Contributors from top 500 universities

Interested in publishing with us?
Contact book.department@intechopen.com

Numbers displayed above are based on latest data collected.
For more information visit www.intechopen.com

2

Acute Biliary Pancreatitis

Morgan Rosenberg[1], Ariel Klevan[2] and Eran Shlomovitz[1]
[1]University of Toronto,
[2]University of Miami,
[1]Canada
[2]USA

1. Introduction

More than 220,000 patients are admitted to hospital each year with acute pancreatitis in the United States alone.[1] The most common etiology of acute pancreatitis is gallstones. This chapter will focus on diagnostic and management issues related to acute biliary pancreatitis (ABP). Differentiating gallstone-induced acute pancreatitis from other etiologies (alcohol, medication induced, hypertriglyceridemia) should be prioritized in the initial investigation of acute pancreatitis as ABP has its own specific management considerations.

2. Epidemiology

Cholelithiasis, or gallstones, are present in up to 10% of the general population. Risk factors for developing gallstones include female sex, advancing age, ethnicity and genetics, obesity and the metabolic syndrome, rapid weight loss, high fat low fiber diet, pregnancy, and certain disease states such as cirrhosis and Crohn's disease.[2] Gallstones are present in 35-75% of all patients with acute pancreatitis in developed nations.[3,4] Up to 8% of patients with symptomatic gallstones will develop biliary pancreatitis due to migration into the bile duct, and ABP may be the initial presentation of gallstones in up to 40% of previously asymptomatic patients.[5] The yearly incidence of ABP is estimated at 4.9-80.0 cases per 100,000 population in the United States. Although most cases of ABP are mild and self-limited, case fatality rates as high as 15% have been reported in severe cases.[6] Risk factors for ABP include female gender with a ratio of 2:1 over males, age, with an incidence of ABP

---

[1] Whitcomb DC. Clinical practice. Acute pancreatitis. *NEJM*. 2006;354:2142-2150.

[2] Shaffer SA. Epidemiology of gallbladder stone disease. *Best Practice and Research Clinical Gastroenterology* 2006;20:981-996.

[3] van Geenen EJM, van der Preet DL, Bhagirath R, et al. Etiology and diagnosis of acute biliary pancreatitis. *Gastroenterology & Hepatology*. 2010;7:495-502.

[4] Agrawal S, Jonnalagadda S. Gallstones, from gallbladder to gut. Management options for diverse complications. *Postgraduate Medicine*. 2000;108:143-153.

[5] van Erpecum KJ. Complications of bile-duct stones: acute cholangitis and pancreatitis. *Best Practice & Research Clinical Gastroenterology*. 2006;20:1139-1152.

[6] Kaw M, Al-Antably Y, Kaw P. Management of of gallstone pancreatitis: cholecystectomy or ERCP and endoscopic sphincterotomy. *Gastrointestinal Endoscopy*.2002;56:61-65.

over 3 times higher at age 75 compared with age 20, and ethnicity, with increased incidence in those of white and Hispanic backgrounds.[7]

3. Pathogenesis

The exact pathogenesis of acute biliary pancreatitis is unclear. Several structural and genetic explanations are supported in the current literature.

3.1 Structural

One mechanism involves obstruction of the common bile and pancreatic ducts as gallstones migrate down and become impacted in the ampulla of Vater. Classic observational studies revealed gallstones may be retrieved from the stool of patients with biliary pancreatitis in >90% of cases as compared to approximately 10% of patients with symptomatic gallstones in the absence of pancreatitis, and in no patients with alcohol induced pancreatitis.[8,9] The precise mechanism of how the gallstones passing through the ampulla initiate and sustain pancreatic inflammation is unknown. It seems just the passage of material through the ampulla of Vater without overt obstruction may be enough to initiate pancreatitis as in the case of sludge containing microlithiasis. In this situation, passage of material through the ampulla may lead to spasm or local edema of the sphincter of Oddi resulting in temporary obstruction. Episodes of recurrent acute pancreatitis caused by microlithiasis may be significantly reduced by cholecystectomy or endoscopic sphincterotomy (ES).

A second mechanism involves reflux of infected bile into the pancreatic duct. The inflammation associated with cholangitis may extend as far as the pancreas initiating the episode of acute pancreatitis. Normal pressures in the pancreatic duct are well above pressures in the common bile duct (CBD), preventing reflux of bile into the pancreatic duct under physiologic conditions. With ampullary obstruction secondary to passing gallstones, pressure gradients may shift, allowing flow of bile and pancreatic juice back into the pancreatic duct. Studies have shown sterile refluxate does not cause acute pancreatitis, however infected bile (especially with *Escherichia coli*) or mixtures of bile and pancreatic juice can lead to acute pancreatitis.[10]

Gallstone-related factors have also been implicated as they relate to the number and frequency of gallstones that pass into the common bile duct and through the ampulla of Vater as well as the likelihood of obstruction. These factors include small size (<2-5mm), higher number (>20) of gallstones in the gallbladder, irregular surface of the gallstones, good emptying of the gallbladder with meals, and cystic duct width over 5mm. Next, bile duct anatomy including an enlarged CBD (>1.3mm), a wide angle between the CBD and pancreatic duct, and a common pancreaticobiliary channel may also predispose to acute

---

[7] van Geenen EJM, van der Preet DL, Bhagirath R, et al. Etiology and diagnosis of acute biliary pancreatitis. *Gastroenterology & Hepatology*. 2010;7:495-502.
[8] Acosta JM, Ledesma CL. Gallstone migration as a cause of acute pancreatitis. NEJM. 1974;290:484-487.
[9] Acosta JM, Rossi R, Ledesma CL. The usefulness of stool screening for diagnosing cholelithiasis in acute pancreatitis. A description of the technique. *American Journal of Digestive Diseases*. 1977;22:168-172.
[10] van Geenen EJM, van der Preet DL, Bhagirath R, et al. Etiology and diagnosis of acute biliary pancreatitis. *Gastroenterology & Hepatology*. 2010;7:495-502.

biliary pancreatitis. Patients with a history of ABP were found to be twice as likely to have a common pancreaticobiliary channel when compared to those with choledocholithiasis and cholelithiasis without a history of pancreatitis.[11]

3.2 Genetic

Genetic variations and mutations have been well described in idiopathic pancreatitis, and it appears that genetics may play a role in selected circumstances of biliary pancreatitis as well. Marschall et al. recently published a review of the genetic basis for gallstone formation and symptomatic gallstone disease including the development of biliary pancreatitis.[12] Using data from 43,141 mono- and dizygotic twins born between 1900 and 1958, they calculated that genetics account for up to 25% of the phenotypic variation among twins. As cholesterol stones account for over 90% of all gallstones, metabolic pathways involved in the formation of cholesterol stones have been studied. Bile is made up of water and three lipid components, namely cholesterol (4%), phospholipids (24%), and bile salts (72%). Genes encoding for transport proteins have been identified for each of these components with varying significance for the risk of ABP.

One such susceptibility locus is the D19H variant of *ABCG8*, a cholesterol transport protein. This allele increases the *ABCG5/8* mediated transfer of cholesterol into bile, resulting in biliary cholesterol hypersaturation, a necessary pre-requisite for cholesterol stones. Marschall et al. determined an odds ratio of 2.5 (95% CI 1.3-4.8) for the formation of symptomatic gallstones disease in 341 Swedish twins with at least one D19H allele.

Cases of recurrent ABP have been associated with a mutation in the *ABCB4* gene, which encodes for multidrug resistant p-glycoprotein MDR3, a protein involved translocation of phospholipids from the inner to the outer leaflet of the canalicular membrane of hepatocytes. Point mutations in *ABCB4* have been associated with low phospholipid-associated cholelithiasis syndrome, which is characterized by early gallstone disease (<40 years old), intrahepatic sludge and microlithiasis, and recurrent biliary disease after cholecystectomy. Mutations in *ABCB4* have also been associated with several other hepatobiliary diseases including intrahepatic cholestasis of pregnancy, progressive familial intrahepatic cholestasis type 3, and adult biliary cirrhosis.[13,14]

Bile salts are the third lipid component with several susceptibility loci identified. The *ABCB11* gene, encoding the bile salt export pump (BSEP), has been found as a rare cause of cholesterol stones with less than 2% of young adults being heterozygous for functionally relevant mutations. Expression of ABC transporters *ABCB11* and *ABCB4* are induced by the farnesoid X receptor (FXR), a bile acid sensor that regulates hepatic bile acid synthesis, uptake, and excretion genes, as well as other genes involved with turnover of cholesterol

---

[11] van Geenen EJM, van der Preet DL, Bhagirath R, et al. Etiology and diagnosis of acute biliary pancreatitis. *Gastroenterology & Hepatology*. 2010;7:495-502.

[12] Marschall HU, Katsika D, Rudling M, Einarsson C. The genetic background of gallstone formation: an update. *Biochemical and Biophysical Research Communications*. 2010;396:58-62.

[13] van Geenen EJM, van der Preet DL, Bhagirath R, et al. Etiology and diagnosis of acute biliary pancreatitis. *Gastroenterology & Hepatology*. 2010;7:495-502.

[14] Marschall HU, Katsika D, Rudling M, Einarsson C. The genetic background of gallstone formation: an update. *Biochemical and Biophysical Research Communications*. 2010;396:58-62.

and glucose homeostasis. The reduction in bile acid synthesis that results is associated with increased cholesterol gallstone formation. The A105G variant of the *SLC10A2* gene, encoding the apical sodium-dependent bile acid transporter (ASBT) was also identified as a risk factor for cholesterol stones with an odds ratio of 2.04 (95% CI 1.19-3.55).[15]

4. Diagnosis

The presentation of acute pancreatitis may be quite similar whether the etiologic basis is biliary or non-biliary in origin. This makes distinguishing acute biliary pancreatitis from other etiologies somewhat challenging. Certain clues may exist on history and physical examination, however laboratory investigations and abdominal imaging are often required for a more definitive diagnosis.

4.1 Clinical presentation

Abdominal pain, classically severe epigastric pain radiating to the back that is worse in the supine position, is a hallmark of acute pancreatitis of any etiology. The abdominal pain may worsen over the course of several hours and may be associated with nausea and vomiting. Patients may also report worsening of their pain following meals. Due to the significant inflammatory process and release of cytokines, fever is another common manifestation. Still, most patients will have a mild, self-limited course of their biliary pancreatitis. In one early series of 153 patients with ABP, only twenty-two (14%) were febrile and thirty (20%) were volume depleted. Eighty-one (53%) had right upper quadrant tenderness, and seventy-one (46%) had mid-epigastric tenderness. Notably, twenty-one (14%) had completely benign abdominal examinations, and only nine patients (6%) had diffuse peritonitis.[16]

During an episode of acute pancreatitis, pancreatic enzymes, vasoactive materials such as kinins, and other toxic substances extravasate from the pancreas into surrounding areas resulting in chemical irritation and contribute to third space losses that may lead to hypovolemia, tachycardia, and hypotension. In this situation, the abdomen may also become distended and tympanic due to paralytic ileus. When toxic mediators reach the systemic circulation, the corresponding systemic inflammatory response syndrome (SIRS) may be severe and result in end-organ damage including acute respiratory distress syndrome (ARDS) and acute kidney injury. Hemorrhagic pancreatitis may lead to the classic Cullen's sign, with ecchymosis in the periumbilical region, and Grey Turner's sign, with ecchymosis of the flank.

History of known gallstones, especially symptomatic gallstone disease such as biliary colic may indicate a biliary etiology, although it cannot rule out other etiologies of acute pancreatitis, nor can the absence of gallstones rule out a biliary source, as pancreatitis can be the first presentation of gallstone disease, and sludge and microcalculi are still a possibility. The absence of other associated etiologies including significant alcohol intake, initiation of medications known to be associated with pancreatitis, recent endoscopic retrograde cholangiopancreatography (ERCP), and known hypertriglyceridemia or hypercalcemia may

---

[15] Marschall HU, Katsika D, Rudling M, Einarsson C. The genetic background of gallstone formation: an update. *Biochemical and Biophysical Research Communications*. 2010;396:58-62.
[16] Frel G, Frel V, Thirlby R, McClelland R. Biliary pancreatitis: clinical presentation and surgical management. *American Journal of Surgery* 1986;151:170-175.

also lead to the diagnosis of ABP. Scleral icterus or overt jaundice may be associated with acute pancreatitis in select cases due to edema of the head of the pancreas or an obstructing stone in the case of biliary pancreatitis. History and physical examination should also aim to rule out mimickers of pancreatitis including acute cholecystitis, perforated duodenal ulcer, intestinal obstruction, mesenteric ischemia, or ruptured aneurysm amongst other etiologies.

4.2 Biochemistry

The diagnosis of pancreatitis of any etiology is classically made with elevations in serum amylase and lipase. Enzyme levels tend to rise within 4 - 8 hours of onset, peak around 24 hours, and return to normal between 2 - 14 days after onset of acute pancreatitis. Lipase has a longer half-life, up to 12 hours, compared to a half-life of only 2 hours for serum amylase, and thus lasts several days longer in the bloodstream. Most would consider elevations in amylase and lipase upwards of three times the upper limit of normal significant in the diagnosis of acute pancreatitis. However, in one retrospective study of 284 patients with a first episode of acute pancreatitis, over 30% of patients had amylase levels below three times the upper limits of normal and 18% had lipase levels below three times the upper limit of normal.[17] They did show that patients with a biliary origin of their acute pancreatitis were significantly (p = 0.007) more likely to have elevations in serum amylase over three times the normal limit compared to non-biliary etiologies. This study also determined that there was no association between level of elevation of enzymes and severity of disease looking at factors such as development of pseudocysts, renal impairment and need for dialysis, ICU admission requiring ventilatory support, need for surgery, and overall mortality.[18]

It is important, however, to remember that a long differential diagnosis exists for elevations in serum amylase and lipase. Other pancreatic diseases, acute cholecystitis or cholangitis, post-ERCP, trauma, bowel obstruction or ischemia, and medications may lead to elevations in both serum amylase and lipase. Additionally, renal impairment, penetrating peptic ulcer disease, salivary disease, several solid tumors and multiple myeloma, and gynecologic disease can raise serum amylase but not serum lipase, making lipase a more specific serum marker.

With a diagnosis of acute pancreatitis made, biliary etiology may be determined using several serum markers, especially serum alanine aminotransferase (ALT). As with serum amylase and lipase, elevations over three times the upper limit of normal are considered significant, however, up to 15% of patients with biliary pancreatitis will have normal liver enzymes.[19] There is also a differential diagnosis for elevations in ALT, most significantly alcohol (the second leading cause of acute pancreatitis in Western countries), viral hepatitis, and non-alcoholic fatty liver disease.

There have been several studies looking at the diagnosis of biliary pancreatitis through the use of ALT, either alone or in combination with other serum markers. Early studies looked

---

[17] Lankisch PG, Burchard-Reckert S, Lehnick D. Underestimation of acute pancreatitis: patients with only a small increase in amylase/lipase levels can also have or develop severe acute pancreatitis. *Gut*. 1999;44:542-544.

[18] Lankisch PG, Burchard-Reckert S, Lehnick D. Underestimation of acute pancreatitis: patients with only a small increase in amylase/lipase levels can also have or develop severe acute pancreatitis. *Gut*. 1999;44:542-544.

[19] van Geenen EJM, van der Preet DL, Bhagirath R, et al. Etiology and diagnosis of acute biliary pancreatitis. *Gastroenterology & Hepatology*. 2010;7:495-502.

at using multiple serum and urine biomarkers and occasionally clinical data to distinguish biliary from non-biliary etiologies. One such study developed a scoring system using seven variables including serum and urine amylase, serum AST and ALT, ALP, lipase/amylase ratio, and erythrocyte mean corpuscular volume (MCV) to differentiate biliary from alcoholic pancreatitis.[20] Each parameter was given a single point, and a score of 4 or greater out of 7 was significantly correlated to a biliary etiology of pancreatitis (p < 0.0001), and a score below 4/7 correlated with alcoholic etiology with a sensitivity of 92% and specificity of 94%. On the other hand, Davidson et al. argued against multi-factor systems in their study that compared test characteristics of a one-, three-, and five-factor test for biliary pancreatitis.[21] The one-factor test used serum ALT and aspartate aminotransferase (AST) alone, the three-factor test used alkaline phosphatase (ALP) and bilirubin in addition to transaminases, and the five-factor test included clinical data such as age and female sex, as well as amylase, alkaline phosphatase, and transaminases. In their study, the one- and three-factor tests performed slightly better than the five-factor test, and thus using serum transaminases alone were recommended for simplicity.

More recent studies have lent support for single-factor systems. One study looked at serum ALT ≥ 80 (U/L) in a cohort of 68 patients with acute pancreatitis, of which 44 (65%) had a biliary etiology.[22] They demonstrated that serum ALT ≥ 80 (two times the upper limit of normal) had a sensitivity of 91%, specificity of 100%, positive predictive value (PPV) of 100% and negative predictive value (NPV) of 86%. Combined with abdominal ultrasound, test characteristics improved somewhat with a sensitivity of 98%, specificity of 100%, PPV of 100% and NPV of 96%. A subsequent study looked at a cohort of 213 patients, of which 62% had ABP confirmed with endoscopic ultrasound (EUS), and found serum ALT levels over two times the upper limit of normal had a sensitivity of 74%, specificity of 84%, PPV of 88%, and NPV of 66% for predicting a biliary etiology, whereas serum ALT levels over three times the upper limit of normal had a sensitivity of 61%, specificity of 91%, PPV of 92%, and NPV of 59%.

4.3 Abdominal imaging

The contribution of medical imaging to the diagnosis and evaluation of pancreatitis has evolved substantially. Early plain film description of the effects of pancreatic inflammation on the intra-abdominal bowel gas pattern has emerged over 50 years ago. Despite today's widespread use of modern imaging technology including MRCP, these alterations in bowel gas patterns remain an occasional useful adjunct in the diagnosis of pancreatitis.

Various abdominal film patterns have been described and may be occasionally seen in the setting of pancreatitis. One of the better described is the "colon cutoff sign". In this pattern a dilated transverse colon appears to be abruptly cutoff occasionally simulating the appearance of colonic obstruction. This pattern is likely related to inflammation of the phrenicocolic ligament causing spasm or occasionally actual mechanical narrowing in the

[20] Stimac D, Lenac T, Marusic Z. A scoring system for early differentiation of the etiology of acute pancreatitis. *Scandinavian Journal of Gastroenterology* 1998;33:209-211.

[21] Davidson BR, Neoptolemos JP, Leese T, Carr-Locke DL. Biochemical prediction of gallstones in acute pancreatitis: a prospective study of three systems. *British Journal of Surgery* 1988;75:213-215.

[22] Ammori BJ, Boreham B, Lewis P, Roberts SA. The biochemical detection of biliary etiology of acute pancreatitis on admission: a revisit in the modern era of biliary imaging. *Pancreas* 2003;26(2):e32-e35.

region of the splenic flexure. This appearance is further accentuated on the background of an adynamic colon. Additional imaging findings may include a mottled appearance of the peripancreatic region secondary to fat necrosis or peripancreatic gas in the setting of suppurative pancreatitis. Numerous other non-specific signs in the setting of pancreatitis have been described including ascites, left sided pleural effusion and diaphragmatic elevation. Needless to say all these signs require additional imaging modalities, clinical and biochemical correlation for to establish the diagnosis.

4.3.1 Ultrasonography

Despite its dependence on operator skill and patient's body habitus ultrasonography has become a mainstay in the imaging of suspected biliary pancreatitis. In the setting of acute inflammation the pancreas may appear focally or diffusely enlarged, as well as relatively hypoechoic secondary to parenchymal edema. This is a reversal of the normal pattern in which the pancreas is echogenic relative to the adjacent liver. The main utility of sonography however is in its ability to image the biliary system in the search for cholelithiasis/choledocholithiasis as the etiology in order to guide further management. The widespread availability, sensitivity and relatively low cost of ultrasonography makes it particularly suitable for this role. Biliary stones typically appear as echogenic foci with posterior clean shadowing (Figure 1). Small stones and sludge however may not demonstrate posterior shadowing. Stones are more easily appreciated in the setting of biliary dilatation although distal CBD stones may remain obscured by overlying bowel gas.
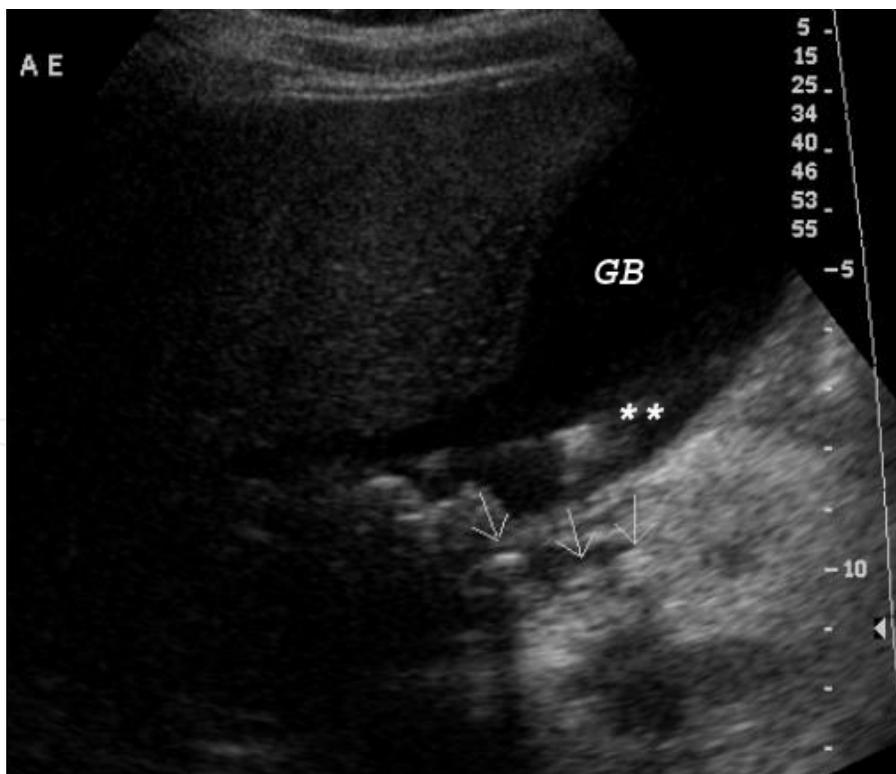

Fig. 1. Sonographic image demonstrating the typical appearance of CBD stones. Three stones (arrows) are visualized within a mildly dilated distal CBD. The stones appear as echogenic foci with posterior shadowing (best appreciated in the most proximal stone). Layering sludge and stones (asterisks) are also appreciated within the gallbladder (GB).

4.3.2 Computed tomography

Computed tomography (CT) has unique advantages in the evaluation of pancreatitis. It is relatively cheaper, non-invasive and more available as compared to ERCP and its sensitivity does not depend on the sonographer or the patient's body habitus as is the case with ultrasound. An inflamed pancreas may appear enlarged and heterogeneous with surrounding inflammatory changes. CT is also particularly useful is the evaluation of pancreatic necrosis, pseudocyst formation or other secondary complications of pancreatitis.

In the evaluation of a biliary cause of pancreatitis, CT however does have a significant weakness as up to 25% of biliary stones may be isodense to bile and therefore poorly visualized. Visible CBD stones may appear as a dense intraluminal mass with the so called "target sign" (Figure 2). As with other modalities, CBD dilatation may signal an underlying obstructing stone or mass and may require further evaluation with other methods in order to elucidate the underlying cause.
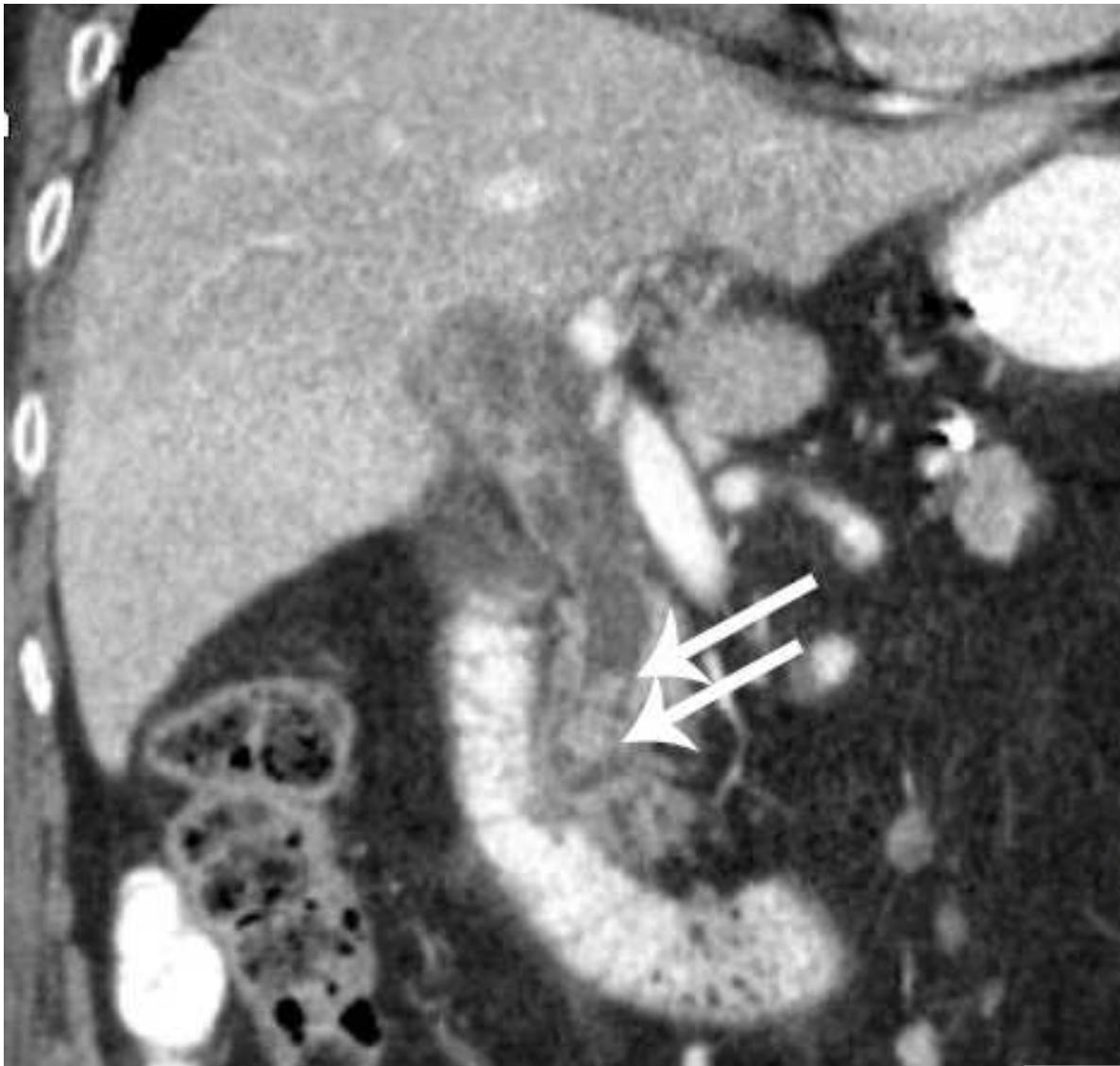

Fig. 2. Coronal reformatted CT centered on the distal CBD. Two dense stones(arrows) are noted in the distal CBD. The CBD is dilated secondary to the obstructing stones.

4.3.3 Magnetic resonance cholangiopancreatography

Magnetic resonance cholangiopancreatography (MRCP) is the most sensitive and specific non-invasive method of assessing the biliary system for choledocholithiasis as an underlying etiology for pancreatitis. MRCP uses a heavily T2 weighted sequence which highlights the biliary ducts due to their high water content. The signal of the surrounding soft tissues saturates out, thus allowing for exquisite visualization of the bright bile ducts in the background of low intensity surrounding soft tissues (Figure 3). In this setting biliary duct stones appear as dark signal voids within the bright bile fluid (Figure 4).

MRCP is comparable to ERCP with respect to its sensitivity in the detection of choledocholithiasis (Table 1). Although MRCP has lower special resolution as compared to ERCP and therapeutic interventions cannot be performed, it does afford several advantages. MRCP is non-invasive, it is less operator dependent, does not use ionizing radiation, and allows for visualization of the surrounding tissues when combined with additional MR sequences. Major disadvantages of MRCP include increased cost, decreased availability in many centers, and it requires a compliant patient to lie still and flat for 30-60 minutes, which may be difficult in the setting of acute pancreatitis when patients are in a significant amount of pain that may be worsened by a supine position.
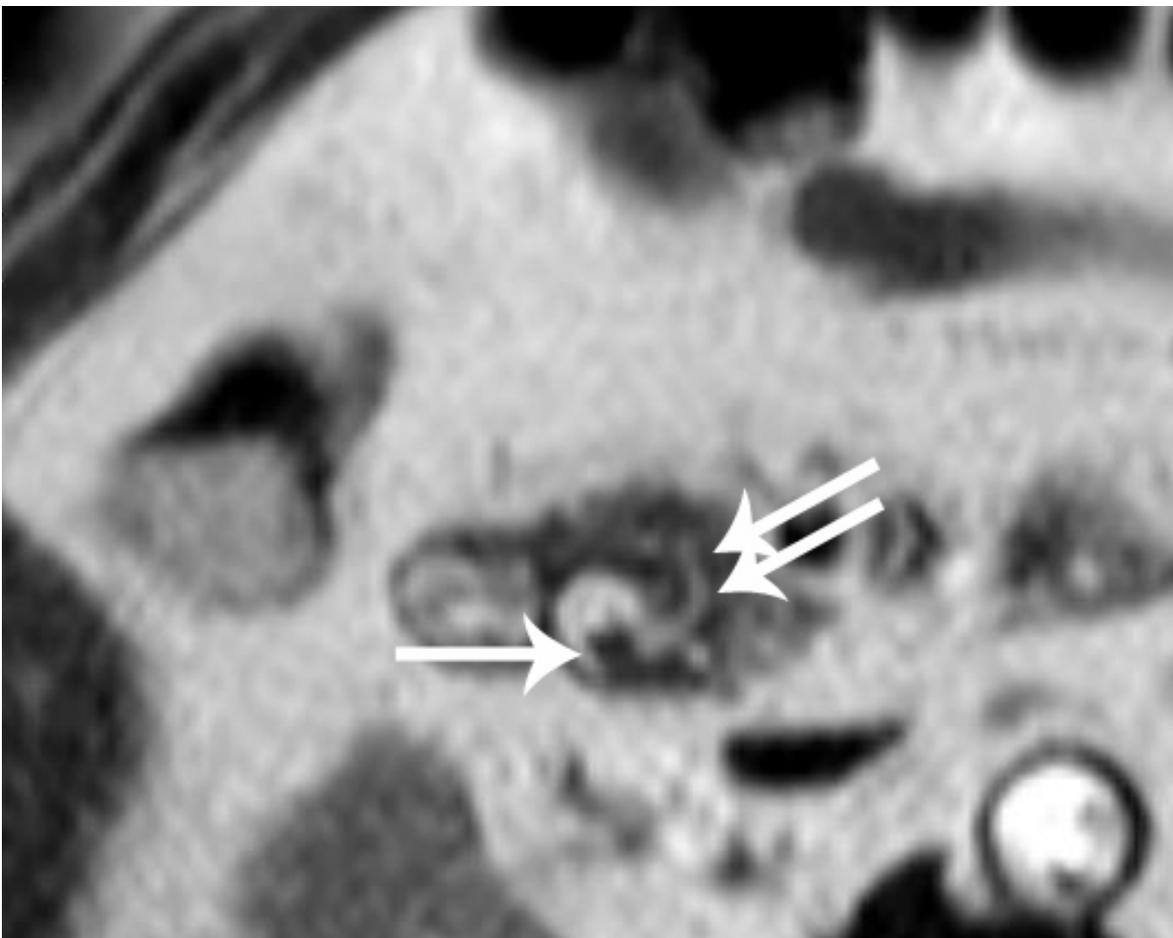

Fig. 3. Axial T2 image obtained as a part of the MRCP study demonstrating a stone at the distal CBD (arrow). The insertion point of the pancreatic duct into the distal CBD near the ampulla is also well visualized (double arrows). *Courtesy of Dr. Y. Krakowsky.*
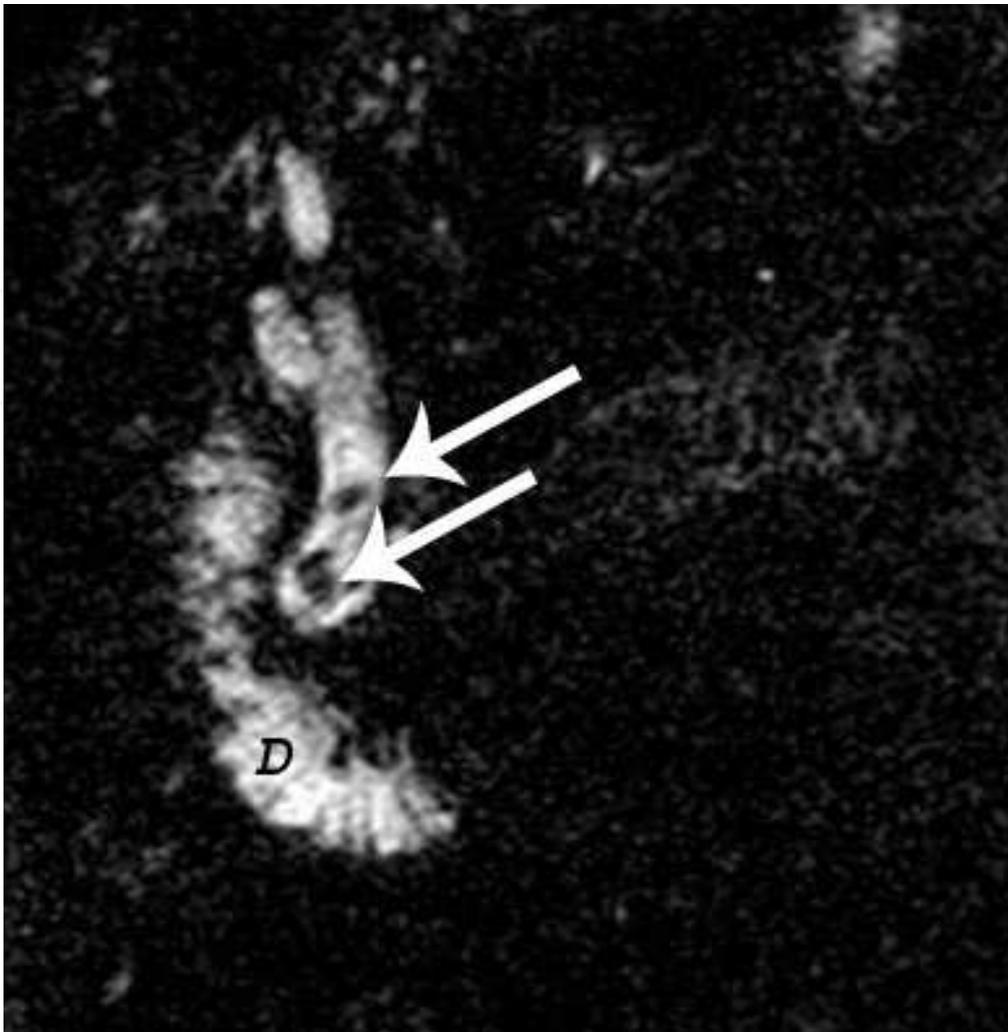
Fig. 4. Coronal MRCP image in the same patient at Figure 2. Image demonstrates two signal voids (arrows) on the background of the high intensity bile in the dilated CBD. The high water content intraluminal fluid in the duodenum (D) is also well appreciated.

4.3.4 Endoscopic retrograde cholangiopancreatography

Endoscopic Retrograde Cholangiopancreatography (ERCP) is a highly sensitive and specific test for assessing the biliary tree and in particular looking for choledocholithiasis (Table 1). Using a side-viewing endoscope, the ampulla is identified and cannulated, after which dye is injected into the biliary tree. Stones in the common bile duct show up as a filling defect on fluoroscopic imaging (Figure 5). During ERCP, endoscopic sphincterotomy (ES) may be performed to allow for improved passage of sludge and stones into the duodenum.

ERCP is the only imaging modality that can also be used therapeutically for removing CBD stones and sludge from the common bile duct. However, the major disadvantage to using ERCP for the initial diagnosis of a biliary etiology of pancreatitis is the potential for exacerbating the acute episode of pancreatitis, and therefore this modality should only be used in conjunction with endoscopic sphincterotomy for treatment of impacted stones in jaundiced patients, those with signs and symptoms of biliary sepsis or potentially in severe ABP.

Fig. 5. Fluoroscopic image demonstrating a dilated common bile duct and several common bile duct stones seen as filling defects (arrows) at the time of ERCP.

4.3.5 Endoscopic ultrasound

Endoscopic ultrasound (EUS) has the highest sensitivity and specificity of any imaging modality for the identification of choledocholithiasis (Table 1). It is also a very sensitive technique for visualization of pancreatic lesions, pseudocysts, and elucidating pancreatic ductal anatomy. Like transabdominal ultrasound, EUS is somewhat operator dependent, and access to EUS may be limited in some centers.

Imaging Modality	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
U/S – Gallstones	67-87	93	100	75-80
U/S – CBD Stones	20-50	83	67	39
CT	40	92	89	48
MRCP	80-100	83-98	89	71-100
ERCP	90-100	92	95	85
EUS	91-100	85-100	92-98	88-92

PPV = positive predictive value, NPV = negative predictive value, U/S = ultrasound, CBD = common bile duct, CT = computed tomography, MRCP = magnetic resonance cholangiopancreatography, ERCP = endoscopic retrograde cholangiopancreatography, EUS = endoscopic ultrasound

Table 1. Test characteristics of the common abdominal imaging modalities

5. Assessment of severity

Determining whether a given case of acute pancreatitis is mild or severe has important management and prognostic implications. Those with severe disease (up to 20% of ABP) may require admission to a monitored setting as they have morbidity rates of 30-50% and mortality rates up to 10-30% despite ICU management.[23] Several scoring systems exist, including Ranson's score, which combines 11 clinical data criteria, 5 from the first 24 hours, and the remaining 6 at 48 hours (Table 2). Each criterion is assigned 1 point, with scores ≥3 points representing severe pancreatitis, correlating with a 15% mortality rate, and scores more than 6 points carrying a mortality rate upwards of 50%.

	Non-biliary Pancreatitis	Biliary Pancreatitis
On Admission		
Age	>55	>70
WBC (mm^3)	>16,000	>18,000
Blood glucose (mg/dl)	>200	>220
LDH (U/L)	>350	>400
AST (U/L)	>250	>250
48 Hours		
Fall in hematocrit (%)	>10	>10
Rise in BUN (mg/dl)	>5	>2
Calcium (mg/dl)	<8	<8
PaO$_2$ (mmHg)	<60	<60
Base deficit (mEq/L)	>4	>5
Fluid sequestration (L)	>6	>4

WBC = white blood cell count, LDH = lactate dehydrogenase, AST = aspartate amino-transferase, BUN = blood urea nitrogen, PaO$_2$ = arterial partial pressure of oxygen

Table 2. Ranson's Criteria of severity for non-biliary and biliary origin of pancreatitis

A second scoring system validated for use in acute pancreatitis is the Acute Physiology and Chronic Health Evaluation (APACHE-II), calculated by adding 12 individual variable points, age points, and chronic health points. A score over 8 represents severe pancreatitis, and a score below 8 is unlikely to result in a fatal outcome. Although the APACHE-II score is cumbersome to calculate, its benefit over Ranson's score is that it can be repeated over the course of illness, whereas Ranson's score applies only to the initial 48 hours after presentation. Another commonly used scoring system is the CT severity index (CTSI), which combines CT grade with extent of necrosis to assign a score that reliably correlates with morbidity and mortality rates (Table 3). A score of 3 or above represents severe pancreatitis with scores 3-6 corresponding to a 35% morbidity and 6% mortality rate, and scores 7-10 corresponding to morbidity and mortality rates of 92% and 17% respectively.[24]

[23] Howard T. (2008) Management of gallstone pancreatitis, In: *Current surgical therapy, 9th ed.* Cameron J. pp. 477-480. Mosby Elsevier Inc., ISBN: 978-1-4160-3497-1, Philadelphia.
[24] Howard T. (2008) Management of gallstone pancreatitis, In: *Current surgical therapy, 9th ed.* Cameron J. pp. 477-480. Mosby Elsevier Inc., ISBN: 978-1-4160-3497-1, Philadelphia.

CT Grade	Points	Necrosis (%)	Points	Total CTSI score
A	0			0
B	1	0	0	1
C	2	<30	2	4
D	3	30-50	4	7
E	4	>50	6	10

Grade A = normal pancreas, B = pancreatic enlargement, C = inflammation of the pancreas and/or peripancreatic fat, D = single peripancreatic fluid collection, E = two or more peripancreatic fluid collections and/or retroperitoneal air.

Table 3. CT Severity Index (CTSI).

6. Management

Initial management of biliary pancreatitis is mainly directed at supportive care, limiting complications, and prevention of infection in the case of pancreatic necrosis. All patient are treated with bowel rest, fluid resuscitation, as well as appropriate analgesia and anti-emetics. Attempts should be made to re-institute oral nutrition, preferably post-pyloric with a jejunal nasoenteric feeding tube, however if oral nutrition is to be withheld for more than 5-7 days on the basis of ongoing fever, tachycardia, nausea, vomiting, severe abdominal pain, or leukocytosis, nutritional support with parenteral nutrition should be considered. Severe pancreatitis or development of systemic complications should be managed in a monitored setting such as the intensive care unit. There may be a role for urgent ERCP in select situations with patients who present jaundiced or have evidence of biliary sepsis.

Unique to a biliary origin of pancreatitis is the requirement for definitive removal of the etiologic trigger with cholecystectomy (or ERCP/ES). In severe cases of pancreatitis, cholecystectomy should be delayed at least 3 weeks to minimize the risk of infecting the pancreatic necrosis at the time of surgery. Also, in patients with evidence of large peripancreatic fluid collections, cholecystectomy may be delayed up to 6 weeks to allow for the maturation of a pseudocyst that can be drained at the time of surgery. In a study by Kelly and Wagner, 165 patients presenting with ABP were randomized to early surgery within 48 hours after admission or delayed surgery after 48 hours. The early surgery group was associated with higher rates of morbidity and mortality when compared to the late group with 83 versus 48% for morbidity and 18 versus 12% for mortality.[25]

In the case of mild biliary pancreatitis, practice guidelines from several international societies have recommended early cholecystectomy, but the definition of early has not been clearly defined and varies between the different guidelines. The International Association of Pancreatology has recommended cholecystectomy should be ideally performed prior to discharge from the initial hospitalization for pancreatitis.[26] The UK Working Party on Acute Pancreatitis have recommended that cholecystectomy not be delayed more than two weeks

---

[25] Kelly T, Wagner D. Gallstone pancreatitis: a prospective randomized trial of the timing of surgery. *Surgery* 1988;104:600-605.

[26] Uhl W, Warshaw A, Imrie C, et al. IAP Guidelines for the surgical management of acute pancreatitis. *Pancreatology* 2002;2:565-573.

after discharge from the index admission,[27] whereas the American Gastroenterological Association guidelines allow for 2-4 weeks after discharge.[28] Guidelines from the American College of Gastroenterology state early cholecystectomy should be performed, but do not define a particular target.[29] Perhaps the reason for the lack of consensus is due to that evidence for these recommendations is largely based on single-center observational studies and not large randomized clinical trial data. Studies done to date have demonstrated a risk of recurrent biliary pancreatitis from 25 to 63% when cholecystectomy was delayed until after discharge from the index hospitalization.[30,31,32]

In a retrospective observational study of 281 patients with ABP, Ito et al. demonstrated gallstone-related complications in 33% of patients who did not have index cholecystectomy, with recurrent ABP found in 13.4% of patients (versus no recurrences in the index cholecystectomy group). Of note, almost one third of recurrences occurred within 2 weeks after discharge, and half of recurrences occurred within 4 weeks.[33] They also looked at ERCP with ES as definitive treatment in 42 out of the 119 patients who did not have index cholecystectomy. A significant reduction in recurrence of ABP was noted in the ES group compared to no intervention group with rates of 4.8 versus 18.2% respectively. However, rates of biliary complications such as acute cholecystitis, jaundice, and cholangitis did occur with greater frequency in the ES group versus no intervention group. This trend of decreased recurrence of ABP but increased biliary complications has been replicated in several other studies, and as such, ERCP with ES should not be used in place of cholecystectomy for definitive treatment except in the case of patients who are deemed to be poor surgical candidates.[34]

Other than reduced recurrence rates, several benefits have been identified with early cholecystectomy during index hospitalization. A recent randomized prospective study has suggested that early cholecystectomy may actually reduce length of index hospitalization. This study looked at 50 patients who were admitted with mild ABP, with half randomized to the early group where cholecystectomy was performed within 48 hours of admission regardless of whether abdominal pain had subsided or laboratory values had normalized. They found that hospital length of stay was shorter for the early cholecystectomy group with an average of 3.5 days as compared to the control group with an average stay of 5.8

---

[27] UK Working Party on Acute Pancreatitis. UK guidelines for the management of acute pancreatitis. *Gut* 2005;54(Suppl 3):iii1-9.

[28] Forsmark CE, Baillie J. AGA Institute technical review on acute pancreatitis. *Gastroenterology* 2007;132(5):2022-44.

[29] Banks PA, Freeman ML. Practice guidelines in acute pancreatitis. *American Journal of Gastroenterology* 2006;101(10):2379-400.

[30] Uhl W, Muller CA, Krahenbuhl L, Schmid SW, Scholzel S, Buchler MW. Acute gallstone pancreatitis: timing of laparoscopic cholecystectomy in mild and severe disease. *Surg Endo* 1999;13:1070-1076.

[31] Ranson JH. The role of surgery in the management of acute pancreatitis. *Ann Surg* 1990;211:382-393.

[32] Ranson JH. The timing of biliary surgery in acute pancreatitis. *Ann Surg* 1979;189:654-663.

[33] Ito K, Ito H, Whang E. Timing of cholecystectomy for biliary pancreatitis: do the data support current guidelines? *Journal of Gastrointestinal Surgery* 2008;12:2164-2170.

[34] Kimura Y, Arata S, Takada T, et al. Gallstone-induced acute pancreatitis. *Journal of Hepatobiliary Pancreatic Sciences* 2010;17:60-69.

days (p=0.0016).[35] Of note, they did not find any statistically significant differences in the need to convert to open cholecystectomy or peri-operative complications between the two groups. Previous observational studies have also shown similar results. One of the largest series is that of 281 patients, of which 162 underwent cholecystectomy during index admission, where length of stay was 5 days for the early group compared to 7 days for the post-discharge cholecystectomy group. This difference was exaggerated further by the fact that 33% of the post-discharge cholecystectomy group required at least one other pre-cholecystectomy admission for gallstone-related events, resulting in an average of 3 additional days in hospital.[36]

Despite the decrease in biliary complications, reduced length of stay, and reduced readmissions, several studies have shown that most jurisdictions are still not following guidelines for early cholecystectomy. One retrospective study looked at 100 consecutive patients admitted with ABP and found only 40 had surgery within the index admission, with another 38 who were discharged for interval cholecystectomy. Two of the 38 were re-admitted while waiting for surgery with biliary complications.[37] Nguyen et al. explored whether lack of resources was a contributing factor to low compliance with guidelines, and they demonstrated that the rate of cholecystectomy during index admission increased at centers with the highest annual volume of cholecystectomies, decreased at centers with the highest volumes of acute pancreatitis, and decreased in centers with the highest volumes of ERCP.[38] These results confirm the hypothesis that resource intensification may be necessary to more consistently meet international guidelines.

7. References

Aboulian A, Chan T, Yaghoubian A, et al. Early cholecystectomy safely decreases hospital stay in patients with mild gallstone pancreatitis: a randomized prospective study. *Annals of Surgery* 2010;251(4):615-19.

Acosta JM, Ledesma CL. Gallstone migration as a cause of acute pancreatitis. *NEJM* 1974;290:484-487.

Acosta JM, Rossi R, Ledesma CL. The usefulness of stool screening for diagnosing cholelithiasis in acute pancreatitis: a description of the technique. *American Journal of Digestive Diseases* 1977;22:168-172.

Agrawal S, Jonnalagadda S. Gallstones, from gallbladder to gut. Management options for diverse complications. *Postgraduate Medicine* 2000;108:143-153.

Ammori BJ, Boreham B, Lewis P, Roberts SA. The biochemical detection of biliary etiology of acute pancreatitis on admission: a revisit in the modern era of biliary imaging. *Pancreas* 2003;26(2):e32-e35.

---

[35] Aboulian A, Chan T, Yaghoubian A, et al. Early cholecystectomy safely decreases hospital stay in patients with mild gallstone pancreatitis: a randomized prospective study. *Annals of Surgery* 2010;251(4):615-619.

[36] Ito K, Ito H, Whang E. Timing of cholecystectomy for biliary pancreatitis: do the data support current guidelines? *Journal of Gastrointestinal Surgery* 2008;12:2164-2170.

[37] Sanjay P, Yeeting S, Whigham C, et al. Management guidelines for gallstone pancreatitis. Are the targets achievable? *Journal of the Pancreas* 2009;10(1):43-7.

[38] Nguyen GC, Boudreau H, Jagannath SB. Hospital volume as a predictor for undergoing cholecystectomy after admission for acute biliary pancreatitis. *Pancreas* 2010;39:e42-e47.

Banks P, Freeman M. Practice guidelines in acute pancreatitis. *American Journal of Gastroenterology* 2006;101:2379-2400.

Davidson BR, Neoptolemos JP, Leese T, Carr-Locke DL. Biochemical prediction of gallstones in acute pancreatitis: a prospective study of three systems. *British Journal of Surgery* 1988;75:213-215.

Forsmark CE, Baillie J. AGA Institute technical review on acute pancreatitis. *Gastroenterology* 2007;132(5):2022-44.

Frel G, Frel V, Thirlby R, McClelland R. Biliary pancreatitis: clinical presentation and surgical management. *American Journal of Surgery* 1986;151:170-175.

Howard T. (2008) Management of gallstone pancreatitis, In: *Current surgical therapy, 9th ed.* Cameron J. pp. 477-480. Mosby Elsevier Inc., ISBN: 978-1-4160-3497-1, Philadelphia.

Ito K, Ito H, Whang E. Timing of cholecystectomy for biliary pancreatitis: do the data support current guidelines? *Journal of Gastrointestinal Surgery* 2008;12:2164-2170.

Kaw M, Al-Antably Y, Kaw P. Management of gallstone pancreatitis: cholecystectomy or ERCP and endoscopic sphincterotomy. *Gastrointestinal Endoscopy* 2002;56:61-65.

Kelly T, Wagner D. Gallstone pancreatitis: a prospective randomized trial of the timing of surgery. *Surgery* 1988;104:600-605.

Kimura Y, Arata S, Takada T, et al. Gallstone-induced acute pancreatitis. *Journal of Hepatobiliary Pancreatic Sciences* 2010;17:60-69.

Lankisch PG, Burchard-Reckert S, Lehnick D. Underestimation of acute pancreatitis: patients with only a small increase in amylase/lipase levels can also have or develop severe acute pancreatitis. *Gut* 1999;44:542-544.

Marschall HU, Katsika D, Rudling M, Einarsson C. The genetic background of gallstone formation: an update. *Biochemical and Biophysical Research Communications* 2010;396:58-62.

Nguyen GC, Boudreau H, Jagannath SB. Hospital volume as a predictor for undergoing cholecystectomy after admission for acute biliary pancreatitis. *Pancreas* 2010;39:e42-e47.

Ranson JH. The role of surgery in the management of acute pancreatitis. *Annals of Surgery* 1990;211:382-393.

Ranson JH. The timing of biliary surgery in acute pancreatitis. *Annals of Surgery* 1979;189:654-663.

Sanjay P, Yeeting S, Whigham C, et al. Management guidelines for gallstone pancreatitis. Are the targets achievable? *Journal of the Pancreas* 2009;10(1):43-7.

Shaffer SA. Epidemiology of gallbladder stone disease. *Best Practice & Research Clinical Gastroenterology* 2006;20(6):981-996.

Stimac D, Lenac T, Marusic Z. A scoring system for early differentiation of the etiology of acute pancreatitis. *Scandinavian Journal of Gastroenterology* 1998;33:209-211.

Uhl W, Muller CA, Krahenbuhl L, Schmid SW, Scholzel S, Buchler MW. Acute gallstone pancreatitis: timing of laparoscopic cholecystectomy in mild and severe disease. *Surgical Endoscopy* 1999;13:1070-1076.

Uhl W, Warshaw A, Imrie C, et al. IAP Guidelines for the Surgical Management of Acute Pancreatitis. *Pancreatology* 2002;2:565-573.

UK guidelines for the management of acute pancreatitis. *Gut.* 2005;54(S3):iii1-iii9.

van Erpecum KJ. Complications of bile-duct stones: acute cholangitis and pancreatitis. *Best Practice & Research Clinical Gastroenterology* 2006;20:1139-1152.

van Geenen E, van der Peet D, Bhagirath P, et al. Etiology and diagnosis of acute biliary pancreatitis. *Gastroenterology and Hepatology* 2010;7:495-502.

Whitcomb DC. Clinical practice. Acute pancreatitis. *NEJM* 2006;354:2142-2150.
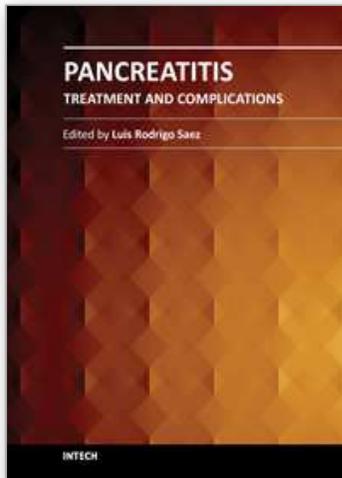
Pancreatitis - Treatment and Complications

Edited by Prof. Luis Rodrigo

ISBN 978-953-51-0109-3

Hard cover, 212 pages

Publisher InTech

Published online 02, March, 2012

Published in print edition March, 2012

Pancreatitis may be acute or chronic. Although they can be caused by similar aetiologies, they tend to follow distinct natural histories. Around 80% of acute pancreatitis (AP) diagnoses occur as secondary to gallstone disease and alcohol misuse. This disease is commonly associated with the sudden onset of upper abdominal that is usually severe enough to warrant the patient seeking urgent medical attention. Overall, 10 to 25% of AP episodes are classified as severe, leading to an associated mortality rate of 7 to 30%. Treatment is conservative and consists of general medical support performed by experienced teams, sometimes in ICUs. Although most cases of acute pancreatitis are uncomplicated and resolve spontaneously, the presence of complications has significant prognostic importance. Necrosis, hemorrhage, and infection convey rates of up to 25%, 50%, and 80% mortality, respectively. Other complications such as pseudocyst formation, pseudoaneurysm formation, or venous thrombosis increase morbidity and mortality to a lesser degree. The presence of pancreatic infection must be avoided.

How to reference

In order to correctly reference this scholarly work, feel free to copy and paste the following:

Morgan Rosenberg, Ariel Klevan and Eran Shlomovitz (2012). Acute Biliary Pancreatitis, Pancreatitis - Treatment and Complications, Prof. Luis Rodrigo (Ed.), ISBN: 978-953-51-0109-3, InTech, Available from: http://www.intechopen.com/books/pancreatitis-treatment-and-complications/acute-biliary-pancreatitis-2

INTECH
open science | open minds