Gallstone Pancreatitis

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Introduction

Gallstone disease is the most common cause of acute pancreatitis in the Western hemisphere, accounting for 35–75 % of cases [1]. Although it is a disease that often has a mild course, which typically subsides in 3–5 days, it can be severe and have an associated mortality as high as 5–10 % [2]. The recognition and diagnosis of acute pancreatitis is essential. Understanding the underlying etiology, severity of disease, and available therapeutic options are all equally important in the treatment of patients affected with this disease.

Epidemiology

Gallstone pancreatitis is most common in women in their sixth or seventh decade of life. It is less common in men and younger individuals. The annual incidence in the United States is 40 cases per 100,000 adults, and the incidence is increasing, both in the United States and in the United Kingdom [2–4]. Many have speculated that this observed increase is related to the ongoing obesity epidemic [5, 6]. As the incidence has risen, so too have the number of hospital admissions. The financial impact related to hospitalizations for acute pancreatitis now totals $2.2 billion annually [7, 8].

Risk factors for gallstone pancreatitis are the same risk factors we attribute to gallstone formation. These include: rapid weight loss, female gender, age >60, obesity, pregnancy, cholesterol-reducing drugs, cirrhosis, and diabetes. A large cystic duct >5 mm, greater than 20 stones, and small stones <0.5 mm have been proposed as additional risk factors [9].

Etiology and Pathogenesis

In the United States and the rest of the Western world, gallstone disease is the most common cause of acute pancreatitis. Gallstones, microlithiasis, and biliary sludge account for 35–75 % of cases [10]. Alcohol is the second leading cause, and should be considered in patients with chronic pancreatitis or a history of alcohol abuse even when concurrent cholelithiasis is found.

The association between gallstones and pancreatitis was first described in 1901 by Opie [11]. Subsequently, many have sought to better understand exactly how gallstones elicit the inflammatory response in acute pancreatitis. Gallstones are found in the feces of up to 85–90 % of patients with gallstone pancreatitis as compared to only 10 % of patients with symptomatic

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S.R. Eachempati, R.L. Reed II (eds.), *Acute Cholecystitis*, DOI 10.1007/978-3-319-14824-3_10

cholelithaisis with no pancreatitis [12]. This suggests that the pancreaticobiliary obstruction is transient and stones often pass spontaneously into the duodenum.

The obstruction of the bile or pancreatic duct by an impacted or passing stone is the most widely accepted mechanism behind gallstone pancreatitis. Reports of early autopsy specimens published in the 1890s described the morphologic appearance of the pancreas in cases of acute pancreatitis suggesting the disease is caused by autodigestion [13]. Even now, after years of investigation and an impressive body of research, the process of autodigestion and activation of intracellular enzymes within the pancreas is not fully understood. Under normal conditions cholecystokinin (CCK) stimulates the acinar cells of the pancreas, triggering its exocrine function. The biogenesis of pancreatic digestive enzymes includes several proteolytic steps, with the final step and activation occurring in the luminal space of the duodenum [14]. Enterokinase located on the duodenal mucosa converts trypsinogen to trypsin, and once in its active form trypsin is responsible for converting the inactive pancreatic enzymes (zymogens) into their active state.

There are several protective mechanisms in place to prevent the premature activation of these enzymes within the pancreas. These include the delayed luminal activation of trypsinogen in the duodenum, the pancreatic sphincter, and exocrine secretions and mucosal barriers aimed at inhibiting protease activity. However, in gallstone pancreatitis at least one of these mechanisms fails, leading to premature enzyme activation and acinar cell damage and inflammation. Recent animal studies suggest that a lysosomal cystein proteinase, cathespin B, plays an important role in intrapancreatic trypsinogen activation leading to acute pancreatitis [15]. This activation causes systemic effects and resultant multiple organ dysfunction, similar to the cascade of events observed in trauma, severe burns and sepsis. Key inflammatory mediators involved in acute pancreatitis include: TNF-alpha, IL-1beta, IL-6, IL-8, PAF, IL-10, C5a, ICAM-1, and substance P [16].

Presentation

Pain is the most common presenting complaint in patients with gallstone pancreatitis. Pain often begins abruptly, and is severe and unrelenting. It can be localized to the right upper quadrant or epigastric region, but can also be more diffuse. Approximately 50 % of patients will also complain of pain radiating to the back [17]. Like acute cholecystitis, pain is often exacerbated with eating, and patients generally present with anorexia. Patients with severe gallstone pancreatitis may present with symptoms of severe dehydration and SIRS, such as altered mental status. Nausea and vomiting are frequent associated symptoms. Few patients will provide a history of biliary colic, and a thorough history should be obtained to help rule out less common causes of pancreatitis, such as alcohol abuse, recent endoscopic retrograde cholangiopancreatography (ERCP), medication use, and recent viral/bacterial infections.

Physical examination findings vary based on the severity of disease. In mild cases, patients will have minimal to moderate abdominal tenderness. In severe cases of gallstone pancreatitis, patients may have impressive abdominal tenderness, with an abdominal examination mimicking a surgical abdomen. Severe peripancreatic inflammation may cause a generalized ileus and hypoactive bowel sounds on examination. Patients with severe dehydration due to fluid sequestration and vomiting may show signs of shock such as hypotension, tachycardia, tachypnea, and lethargy.

Diagnosis

Laboratory Evaluation

Although there is not a single biochemical "gold standard," laboratory testing is useful in both diagnosing gallstone pancreatitis and in assessing the severity of disease. Serum amylase and lipase are important markers of pancreatic inflammation. Advantages of measuring serum amylase include that it is easy to measure and consequently is widely available. Serum amylase increases 2–12 h after onset and normalizes in 3–5 days.

Though it has a high sensitivity for the diagnosis of pancreatitis, perhaps its greatest disadvantage is a relatively low specificity and thus, a high false positive rate. The pancreas is not the only source of amylase, and in fact, in normal circumstances, as much as 65 % of amylase arises from the salivary glands. In contrast, serum lipase has a higher sensitivity (85–100 %) and specificity (95–100 %) [18, 19]. Lipase is primarily produced by pancreatic acinar cells. However, it should be noted that nonspecific elevations in lipase have been reported in many conditions, slightly decreasing its specificity for acute pancreatitis. Serum lipase peaks at 24 h after onset and stays elevated longer than amylase, and thus is a better marker for pancreatitis in patients who present days after the onset of their pain [20]. The degree of elevation of amylase and lipase does not correlate with severity of disease, and once the diagnosis of acute pancreatitis is made, daily measurement should be discouraged. The trend of amylase and lipase does not correlate with clinical progress or overall prognosis [21].

A basic metabolic panel is valuable in detecting metabolic derangements, including acute kidney injury, hyperglycemia, and hypocalcemia. Obtaining a complete blood count will identify the degree of leukocytosis and hemoconcentration. These markers are essential in determining disease severity (see section "Severity of Disease"). A serum triglyceride level and calcium level should be examined to rule out hypertriglyceridemia and hypercalcemia as possible causes of pancreatitis. If autoimmune pancreatitis is suspected, IgG4 should be examined [22].

Liver function testing may reveal a transaminitis and elevation in serum bilirubin. While gallstone pancreatitis inevitably involves some degree of biliary obstruction, in most cases this is transient and thus there is variability in liver function test (LFT) abnormality. LFTs may be normal in up to 10 % of patients with gallstone pancreatitis [23]. A serum alanine aminotransferase (ALT) three times the normal value has a positive predictive value (PPV) of 95 % in distinguishing gallstone pancreatitis from other causes of acute pancreatitis [24].

Imaging Modalities

Imaging in patients with acute pancreatitis can help determine etiology (e.g., gallstones, neoplasms, and anatomic variants such as pancreas divisum). In patients with gallstone pancreatitis, imaging helps complement physical examination findings and laboratory testing to stratify patients and provide appropriate care. Imaging can also be used to assess the severity of disease and degree of peripancreatic inflammation or parenchymal necrosis and, in many cases, identify complications such as pseudocysts, fluid collections, or hemorrhage.

All patients presenting with pancreatitis without an obvious source should undergo dedicated right upper quadrant ultrasonography. Ultrasound can identify cholelithiasis with greater than 95 % sensitivity, and this widely available, noninvasive test offers the advantage of speed at little cost. Ultrasound may fail to detect stones smaller than 4 mm, and its sensitivity in detecting choledocholithiasis ranges from 40 to 60 % [25]. Although ultrasound can identify pancreatic edema, it is a poor study to gauge disease severity of pancreatitis. Despite its limitations, ultrasound remains the first test of choice to make a diagnosis of gallstone pancreatitis. When severe disease or common bile duct stones are suspected, further imaging is indicated.

Contrast-enhanced computed tomography (CT) has a high sensitivity in detecting pancreatic necrosis, and thus is useful in moderate and severe cases. A repeat CT at 3–4 days can also be helpful in determining progression of disease. Obtaining a pancreas protocol CT entails thin cuts (2–3 mm) through the pancreas during two phases. The first phase is referred to as the arterial or pancreas phase, during which the pancreas parenchyma, celiac plexus, and superior mesenteric artery are filled with contrast. Later, the venous phase allows for visualization of the superior mesenteric, portal, and splenic veins [26]. CT is less sensitive than ultrasound in detecting cholelithiasis; however, it is 75–95 % sensitive in detecting a dilated common bile duct or choledocholithiasis. Routine use of CT on admission is not recommended, as traditional

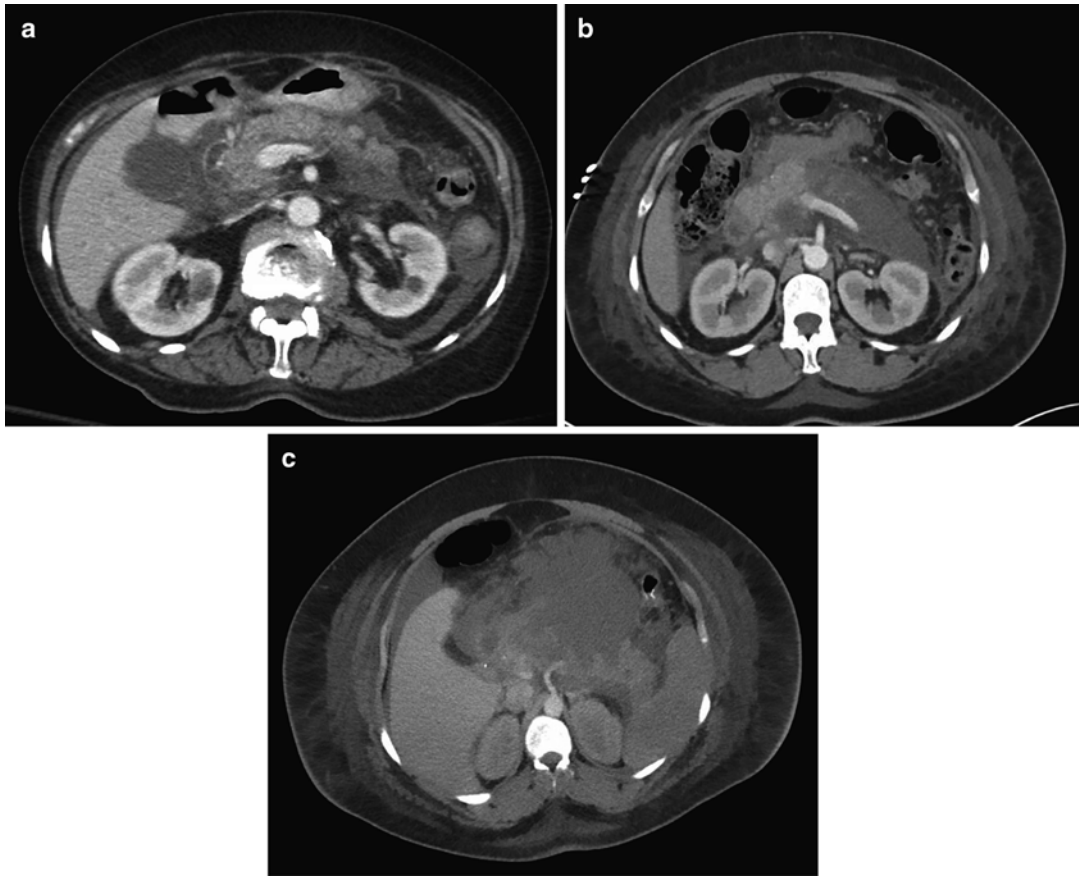

Fig. 10.1 (**a**) Peripancreatic inflammation and fluid. (**b**) Irregular heterogenous enhancement of the pancreatic gland with peripancreatic inflammation and fluid suggestive of pancreatic necrosis, along with mesentery infiltration. (**c**) Severe pancreatic necrosis with surrounding fluid and phlegmon

scoring systems to estimate severity have been shown to be equally effective [27, 28]. However, in patients with severe disease who present with an acute abdomen, CT can provide key information to establish a diagnosis, and determine the degree of inflammation, necrosis, presence of complications such as fluid collections, or evaluate for signs of superinfection (Fig. 10.1). Balthazar et al. developed a grading system based on CT features of acute pancreatitis to stratify patients [29] (see section "Severity of Disease").

Although more expensive and less available, magnetic resonance imaging (MRI) with gadolinium contrast is a reliable method in the evaluation of acute pancreatitis. MRI has fewer contraindications than CT, and is an ideal substitute in pregnant patients or those with renal insufficiency. It is especially useful in visualizing complications of gallstone pancreatitis such as hemorrhage and has the ability to differentiate fluid collections from liquefied necrosis [30]. Magnetic resonance cholangiopancreatography (MRCP) involves a specific MRI protocol designed to enhance the fluid signal within the biliary system allowing for more accurate delineation of biliary and pancreatic anatomy. Filling defects and anatomic disruptions in the pancreatic duct can be better appreciated, and many clinicians use MRCP as a screening tool to select patients for ERCP. The sensitivity of MRCP for detecting choledocholithiasis has been reported to be 85–90 %, making it an ideal study when CBD stones are suspected [31].

Severity of Disease

In gallstone pancreatitis there is a wide spectrum of disease. Although as many as 80 % of patients will have a benign course, the remaining 20 % can have severe disease with a mortality rate in this group as high as 30 % [32, 33]. Mortality associated with this disease is often due to multisystem organ failure (MOF) and later to septic complications of pancreatic necrosis. Many have sought to develop prognostic scoring systems or markers in order to identify patients most at risk. Multiple studies have evaluated the ability of clinicians alone to differentiate between mild and severe AP. Sensitivity of clinical assessment alone ranges from 34 to 64 %, suggesting that without additional disease severity stratification tools, many patients with severe pancreatitis might not be triaged to the appropriate level of care [34, 35].

Ranson Criteria

Ranson Criteria (Table 10.1) is the most frequently used multifactorial scoring system in the United States. It was first introduced by Ranson et al. in 1974 to score the severity of alcoholic-induced pancreatitis and later modified for gallstone pancreatitis in 1979 [36]. It is based on 11 clinical and laboratory data points in nonbiliary pancreatitis, and ten data points in gallstone pancreatitis (arterial oxygen saturation (PaO_2) is omitted from the original scoring system). Data points are collected at presentation and at 48 h into the hospital course. A score of three or more is the cutoff for severe pancreatitis, however, mortality predictions are not accurate until 48 h into the course of acute pancreatitis.

Table 10.1 Ranson criteria

	Gallstone pancreatitis	Nongallstone pancreatitis
At admission		
Age (years)	>70	>55
WBC (cells/μL)	>18 K	>16 K
Blood glucose (mg/dL)	>220	>200
Serum AST (U/L)	>250	>250
Serum LDH (U/L)	>400	>350
At 48 h		
Serum calcium (mmol/L)	<8	<8
Hematocrit fall (%)	>10	>10
PaO_2 (mmHg)	Omitted	<60
BUN increase (mg/dL)	>2	>5
Base deficit (mEq/L)	>6	>4
Sequestration of fluid (L)	>4	>6

APACHE-II

The Acute Physiology and Chronic Health Evaluation II (APACHE-II) scoring system was developed by Knaus et al. in 1985 [37]. It was initially developed to estimate mortality in all patients admitted to an intensive care unit (ICU) but has been widely applied to patients with acute pancreatitis. It offers a distinct advantage over Ranson Criteria because it can be calculated at any time during the hospital admission, and changes in the APACHE-II score have been shown to correlate with clinical improvement or deterioration. The score is a composite of 12 individual variable points, age points, and chronic health points (Table 10.2). Calculating an

Table 10.2 APACHE-II parameters and units of measurement

Age (years)
Temperature (°C)
Mean arterial pressure (mmHg)
pH
Heart rate (beats per min)
Respiratory rate (breaths per min)
Serum sodium (mEq/L)
Serum potassium (mEq/L)
Serum creatinine (mg/dL)
Hematocrit (%)
WBC (cells/μL)
Glasgow-coma-scale (points)
A—a gradient (if $FiO_2 \geq 0.5$) (mmHg)
PaO_2 (if $FiO_2 < 0.5$) (mmHg)
History of organ insufficiency
History of immunocompromise

Table 10.3 The APACHE-II severity of disease classification system

Physiologic variable	+4	+3	+2	+1	0	+1	+2	+3	+4
Temperature—rectal (°C)	≥41	39–40.9		38.5–38.9	36–38.4	34–35.9	32–33.9	30–31.9	≤29.9
Mean arterial pressure (mmHg)	≥160	130–159	110–129		70–109		50–69		≤49
Heart rate	≥180	140–179	110–139		70–109		55–69	40–54	≤39
Respiratory rate (nonventilated or ventilated)	≥50	35–49		25–34	12–24	10–11	6–9		≤5
Oxygenation (mmHg) a. $FiO_2 > 0{,}5$ use $A\text{-}aDO_2$	a ≥500	350–499	200–349		<200				
b. $FiO_2 < 0{,}5$ use PaO_2	b				>70	61–70		55–60	<55
Arterial pH	≥7.7	7.6–7.69		7.5–7.59	7.33–7.49		7.25–7.32	7.15–7.24	<7.15
Serum sodium (mmol/L)	≥180	160–179	155–159	150–154	130–149		120–129	111–119	<110
Serum potassium (mmol/L)	≥7	6–6.9		5.5–5.9	3.5–5.4	3–3.4	2.5–2.9		<2.5
Serum creatinine (mg/dL, Double point score for acute renal failure)	≥3.5	2–3.4	1.5–1.9		0.6–1.4		<0.6		
Hematocrit (%)	≥60		50–59.9	46–49.9	30–45.9		20–29.9		<20
White blood count (in 1000/mm^5)	≥40		20–39.9	15–19.9	3–14.9		1–2.9		<1
Glasgow-Coma-Scale (GCS)	Score = 15 minus actual GCS								
Serum HCO_3 (venous, mmol/L, use if no ABGs)	≥52	41–51.9		32–40.9	22–31.9		18–21.9	15–17.9	<15
A = Total Acute Physiology Score APS		Sum of the 12 individual variable points							
B = *Age points*		*C = Chronic Health Points*							
≤44 years	0 points	If the patient has a history of severe organ system insufficiency or is immunocompromised, assign points as follows:							
45–54 years	2 points								
55–64 years	3 points	a. For nonoperative or emergency postoperative patients—5 points							
65–74 years	5 points	b. For elective postoperative patients—2 points							
≥75 years	6 points								
APACHE-II Score = Sum of A (*APS points*) + B (*Age points*) + C (*Chronic Health points*)									

APACHE-II score can be cumbersome (Table 10.3), and this difficulty in clinical practice is often cited as its greatest shortcoming. An APACHE-II score of eight or above is indicative of severe disease [38].

(From: Knaus WA, Draper EA, Wagner DP, Zimmerman JE. APACHE-II: a severity of disease classification system. Crit Care Med 1985; 13(10):818-29)

Glasgow Score

The Glasgow Score, also known as the Glasgow-Imrie Score, is a modification of Ranson's criteria, that includes age and laboratory data points with alerted cut offs. Hematocrit, base deficit, and fluid sequestration are omitted from this system, while albumin is included. It was published by Imrie et al., in 1984, but its current use is lim-

Table 10.4 Glasgow score parameters

P	– PO_2 (mmHg)		<60
A	– Age (years)		>55
N	– Neutrophills/WBC (cells/μL)		>15 K
C	– Calcium (mmol/L)		<2
R	– Renal function/Urea (mmol/L)		>16
E	– Enzymes	ALT (U/L)	>100
		LDH (U/L)	>600
A	– Albumin (g/L)		<32
S	– Sugar/glucose (mg/dL)		>180

Table 10.5 CT severity index (CTSI)

Grading of pancreatitis		Score		Degree of necrosis	Score
A	Normal pancreas	0	+	0 %	0
B	Enlargement of the pancreas	1		≤30 %	2
C	Inflammatory changes in the pancreas and peripancreatic fat	2		30–50 %	4
D	Findings of grade C plus 1 fluid collection	3		>50 %	6
E	Findings of grade C plus 2 or more fluid collections, and/or the presence of gas in or adjacent to the pancreas	4			

ited to Europe. The Glasgow score has been shown to be equally effective in predicting mortality and is as accurate (though not better than) Ranson's criteria [35, 39]. Like the Ranson criteria the Glasgow score also requires 48 h to complete; and a score of three or greater is indicative of severe pancreatitis (Table 10.4).

CT Severity Index

Balthazar et al. introduced the CT Severity Index (CTSI). Its aim is to grade the severity of acute pancreatitis radiographically and does not take into account clinical parameters [29]. CTSI combines the morphologic features of the pancreas including the degree of pancreatic and peripancreatic inflammation with the degree of necrosis (Fig. 10.1 and Table 10.5). Subsequent modifications of the CTSI have been proposed, but when compared head-to-head with the CTSI of Balthazar, no significant differences were noted in their ability to evaluate the severity of acute pancreatitis. The CTSI score not only correlates with disease severity and mortality, it has also been shown to correlate with the duration of hospitalization, and need for necrosectomy [28]. The CT findings are scored from 0 to 10, and a score of two or greater is indicative of moderate disease. Scores greater than six are associated with higher rates of complications and death [40, 41].

Biochemical Markers of Severity

C-reactive protein (CRP) is the best laboratory marker of disease severity. In a multicenter prospective study, CRP levels of >150 mg/L at 48 h after symptom onset was significant in differentiating cases of mild and severe acute pancreatitis [42]. Although CRP is unable to identify necrotizing pancreatitis or predict mortality, serial measurements can help to identify the development of localized complications. CRP is widely used in Europe but has not been adopted as standard practice in the United States. Several initial studies showed promising results with regard to the predictive value of procalcitonin (PCT), however, newer evidence suggests that the measurement of PCT is of limited value [42]. Several new serologic and urinary markers of severity are being investigated but remain experimental. These include, urinary trypsinogen activation peptides, and cytokines IL-6 and IL-8.

Revised Atlanta Classification (2012)

In 1992, the Atlanta Symposium attempted to standardize and create a globally accepted classification of acute pancreatitis and its complications. Better understanding of the etiology and pathophysiology of this disease has led to the most recent 2012 revision [43] (Table 10.6).

Table 10.6 Atlanta criteria for severity of acute pancreatitis

Grades of severity		Supplemental definitions	
Mild	– No organ failure	Organ failure	– SBP <90 mmHg, not responsive to fluid
	– No local or systemic complications		– Serum Cr >2 (after resuscitation)
			– PaO_2/FiO_2 <200
Moderate	– Transient organ failure (<48 h) and/or	Local complications	– Peripancreatic fluid collections
	– Local or systemic complications without persistent organ failure		– Acute necrotic collections
Severe	– Persistent organ failure (>48 h), single or multiple organ failure	Systemic complications	– Exacerbations of underlying comorbidities

Treatment

Mild Disease

Initial management in patients with gallstone pancreatitis with mild disease (Ranson <3, APACHE-II <8, CTSI <2) is largely centered on supportive care. This involves correcting metabolic derangements, aggressive fluid resuscitation with intravenous fluids, and pain control. Patients can be triaged to a regular floor or monitored unit. These patients are generally kept NPO until pain control is optimized and enteral feeding can be tolerated. Early enteral feeding has been shown to be safe and effective in reducing hospital length of stay [44]. However, feeding should be avoided if it interferes with early cholecystectomy. In patients with mild disease, and without concomitant cholecystitis, use of prophylactic antibiotics does not reduce morbidity or mortality [45, 46].

The clinical practice and management of potential CBD stones in patients with mild disease varies greatly. Some surgeons image the CBD routinely preoperatively with MRCP, ERCP, or endoscopic ultrasound (EUS), while others routinely perform intraoperative cholangiogram (IOC) or laparoscopic ultrasound. The current trend is towards a more selective approach when clinical suspicion is high. As many as 95 % of stones in gallstone pancreatitis pass spontaneously and routine imaging is often unnecessary and costly. Previous data promoting ERCP in the first 24 h for all-comers of gallstone pancreatitis has been challenged [47]. There is now ample evidence to show that ERCP has no diagnostic or therapeutic role in patients with mild gallstone pancreatitis and no evidence of biliary obstruction [48, 49].

Historically, surgical intervention was delayed 6–8 weeks following an acute attack of pancreatitis to allow for inflammation to subside [50]. This approach led to high readmission rates and complications of recurrent attacks. If cholecystectomy is not performed, the risk of recurrence of biliary pancreatitis or other biliary events is as high as 75 %, with 50 % of the recurrent episodes occurring in the first 90 days [51–53]. These data have led to the widely accepted principal that cholecystectomy should be performed during the index hospitalization. Most surgeons choose to schedule surgery when the pancreatitis and peripancreatic inflammation is improving, using resolution of pain and normalization of liver chemistries and pancreatic enzymes as their guide. Aboulian et al., demonstrated that early laparoscopic cholecystectomy within 48 h of admission, regardless of pain or laboratory values, did not compromise patient safety and resulted in shorter hospitalizations [54]. Several subsequent studies have supported these conclusions [55]. Thus, in patients with mild disease, early cholecystectomy should be considered when laboratory values are trending toward normal.

Severe Disease

Patients with severe disease (Ranson >3, APACHE-II >8, CTSI >2) require admission to an intensive care unit (ICU). In addition to standard laboratory exams, an ABG should be obtained and repeated to ensure proper tissue oxygenation. A nasogastric tube (NGT) and Foley catheter should also be placed. The correction of metabolic derangements, aggressive fluid resuscitation with intravenous fluids, and pain control are again the guidelines of supportive care. Low serum bicarbonate and base deficit are signs of underresuscitation, while a continual decrease in hematocrit or SaO_2/PaO_2 during resuscitation can be signs of worsening inflammation. The use of prophylactic antibiotics in patients with severe gallstone pancreatitis without concomitant cholangitis is controversial. Previous data in the 1990s suggested that prophylactic antibiotic use in patients with pancreatic necrosis decreased the rates of infectious complications, but did not alter overall mortality. Subsequent trials, and a recent systemic review and meta-analysis, however, failed to demonstrate a reduction in mortality or infectious events [56]. Current use of prophylactic antibiotics is not recommended.

Repeat imaging with CT or MRI should be obtained in 48–72 h to monitor for disease progression and detect complications such as peripancreatic fluid collections, necrosis, or signs of infection (air bubbles in areas of necrosis). Pancreatic necrosis can occur in as many as 50 % of patients with severe gallstone pancreatitis. Close clinical observation and a high degree of suspicion for infected pancreatic necrosis should be pursued in patients with fever, persistent leukocytosis, or signs of sepsis. Infection of peripancreatic fluid or areas of necrosis can occur in 30–70 % of cases of necrotizing pancreatitis, and usually occurs 2–3 weeks after the onset of disease. The diagnosis can be made by CT-guided fine-needle-aspiration (FNA) or via specimens obtained at the time of surgery. Once the diagnosis is made, necrosectomy, surgical debridement, or immediate radiographically guided-drainage, should be strongly considered.

Acute cholangitis is seen in 10 % of patients with severe gallstone pancreatitis, and urgent ERCP is indicated [57]. The role and timing of ERCP in severe gallstone pancreatitis in patients without cholangitis remains controversial despite extensive investigation. Currently, the use of ERCP should be targeted to those patients with severe gallstone pancreatitis complicated by biliary sepsis and cholangitis [49, 58]. Unlike mild gallstone pancreatitis, early surgical intervention in severe gallstone pancreatitis is associated with increased mortality, and increased infectious complications and sepsis [59, 60]. Suggested time intervals for delayed cholecystectomy range from 3 weeks to 3 months. Imaging may be useful to help guide surgical timing and aid in diagnosing complications such as pseudocysts.

Special Patient Populations

Unfit surgical candidates due to age and comorbid conditions can be managed with ERCP with endoscopic sphincterotomy (ES) as an alternative to laparoscopic cholecystectomy. Although recurrent attacks of pancreatitis are low, two randomized controlled trials have shown a high incidence of recurrent biliary disease and both advocate for cholecystectomy when patients are able to undergo the procedure [61, 62].

Pregnancy increases the risk of gallbladder disease, and its incidence, including acute cholecystitis and gallstone pancreatitis, in pregnancy ranges from 0.05 to 0.8 % [63]. If there is need for CBD imaging MRI/MRCP or EUS is recommended over diagnostic ERCP and CT to limit fetal exposure to radiation. Previous recommendations regarding surgical management warned against operative intervention during the first and third trimesters. Recent guidelines produced by the Society of American Gastrointestinal and Endoscopic Surgeons promote the use of laparoscopic surgery in any trimester of pregnancy [64]. They cite considerable data pointing to the improved safety of surgical intervention, and the significant morbidity and mortality associated with untreated gallbladder

disease and recurrent attacks. They propose that the indications for laparoscopic cholecystectomy for the general population be applied to the pregnant patient as well.

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