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SRGS • BILIARY TRACT & PANCREAS, PART I

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Editorial and business offices
ACS-SRGS
633 N. Saint Clair St.
Chicago, IL 60611-3211
P 800-631-0033 or 312-202-5227
F 312-202-5009
srgs@facs.org | www.facs.org/publications/srgs

Managing editor:
Lynanne Feilen, lfeilen@facs.org

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The overview is compiled with the assistance of an 18-member, international board of editors who are experts in the various focus areas that comprise the specialty of surgery. In addition, the editorial board has representation and expertise in such important fields as medical evidence evaluation, surgical education, outcomes research, standard setting, and performance improvement. SRGS is a unique resource because the overview and selected full-text articles provide the reader with the most valuable and pertinent content illuminated with informed opinion and critique. Unnecessary material is eliminated. SRGS does not present itself as infallible and the editor-in-chief takes responsibility for the content that appears in each issue. The editor-in-chief and the editorial board recognize that there is no such thing as the “average” surgical patient, and that the information in the literature must be interpreted in the light of the clinical presentation of each individual patient.

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1. What proportion of patients with gallstones will become symptomatic over long-term followup?
   a) 1%
   b) 80%
   c) 30%
   d) 20%
   e) 45%

2. Available data indicate that surgeons practicing in rural areas of the United States will do how many biliary tract procedures each month?
   a) 5
   b) 20
   c) 14
   d) 7
   e) 26

3. Which of the following increases the risk of pigmented gallstone formation?
   a) Male gender
   b) Obesity
   c) Pregnancy
   d) Age < 25 years
   e) Cirrhosis

4. Which of the following is true of symptomatic cholelithiasis?
   a) Once cystic duct obstruction occurs, it becomes permanent
   b) Pain due to myocardial ischemia is rarely confused with biliary pain
   c) Large gallstones (> 10 mm diameter) are more likely to cause biliary pancreatitis
   d) Biliary pain can radiate to the interscapular area of the back
   e) Symptomatic cholelithiasis can be effectively treated with cholesterol-lowering drugs

5. A 34-year-old woman with no significant comorbid conditions is seen in the emergency department with her third episode of sharp, right upper quadrant pain with nausea. Which of the following is the most helpful test to confirm the presence of gallstones?
   a) Flat and upright abdominal radiographs
   b) Serum amylase and lipase levels
   c) Endoscopic retrograde pancreatography
   d) Abdominal ultrasound
   e) Complete blood count

6. The expected overall mortality risk for laparoscopic cholecystectomy is?
   a) 2%
   b) 4%
   c) 6.2%
   d) 3%
   e) 0.1%
7. At the time of laparoscopic cholecystectomy, a patient is found to have a severely inflamed gallbladder that is adherent to the duodenum. Laparoscopic dissection results in significant bleeding. Which of the following is appropriate?
   a) Abandon the operation
   b) Convert to open cholecystectomy
   c) Add additional laparoscopic ports
   d) Perform intraoperative endoscopic retrograde cholangiopancreatography (ERCP)
   e) Change to a 30-degree laparoscope

8. Which of the following has been shown to eliminate the risk of bile duct injury during laparoscopic cholecystectomy?
   a) Minimally invasive fellowship training
   b) Routine intraoperative cholangiography
   c) Immediate preoperative ERCP
   d) A surgeon and first assistant with laparoscopic training during residency
   e) None of the above

9. During laparoscopic cholecystectomy, the “critical view” refers to which of the following?
   a) Routine use of a zero-degree laparoscope
   b) Routine use of laparoscopic ultrasound
   c) Delaying division of any structure until the entry of the cystic duct into the gallbladder and entry of the cystic artery into the gallbladder wall have been visualized
   d) Routine intraoperative cholangiography
   e) Having abdominal ultrasound images available in the operating room

10. Laparoscopic single-site cholecystectomy is a term used to describe which of the following?
    a) Cholecystectomy done in only one hospital
    b) Cholecystectomy using transvaginal placement of the laparoscope
    c) Laparoscopic cholecystectomy using a single skin incision and two fascial incisions at the level of the umbilicus
    d) Cholecystectomy with the laparoscope passed orally with gallbladder removal via a gastrotomy
    e) Cholecystectomy with the laparoscope passed transrectally

11. Four days after laparoscopic cholecystectomy, a 34-year-old woman comes to the emergency room with complaints of feeling right upper abdominal fullness and bloating. Which of the following is the best diagnostic strategy?
   a) Flat and upright abdominal films
   b) Complete blood count
   c) ERCP
   d) Magnetic resonance cholangiography
   e) Abdominal ultrasound

12. The patient described in the previous question has an infrahepatic fluid collection discovered on imaging. Which of the following is the best approach?
    a) Immediate exploratory laparotomy
    b) HIDA scan
    c) Follow the collection with sequential ultrasound examinations
    d) CT scan with percutaneous drainage of the fluid
    e) Prescribe analgesics and schedule return office visit

13. The above patient has drainage of 350 mL of bile-stained fluid. Transhepatic cholangiography discloses a completely divided common bile duct. Which of the following is associated with high success for repair of the duct?
    a) Immediate reoperation by the primary surgeon
    b) Drainage for at least six months
    c) Choledochojejunostomy with anastomosis to healthy, unscarred proximal duct by a surgeon who has experience performing this procedure
    d) End-to-end reanastomosis of the duct
    e) Choledochoduodenostomy
14. Each of the following statements about management of bile duct injury during laparoscopic cholecystectomy is true except which one?

a) Complete anatomic definition of the injury contributes to successful repair
b) Repair 4–6 weeks after biliary drainage and imaging of the injury is associated with improved outcomes
c) Immediate exploration and repair once an injury is suspected is associated with the best results
d) Repair by experienced biliary surgeons is associated with improved outcomes
e) Choledochojejunalostomy is the preferred repair method for a completely divided common bile duct

15. A 70-year-old woman is admitted to the coronary care unit with substernal chest pain. After diagnosis of myocardial infarction, she undergoes coronary artery stenting. On the first post-stent day she still requires moderate doses of cardiotonic agents for support of cardiac output. On the second day she develops right upper quadrant pain and tenderness. Fever and leucocytosis are present. Abdominal ultrasound shows enlarged, fluid-filled gallbladder but no gallstones. Which of the following is the best management strategy?

a) Immediate ERCP
b) Transhepatic drainage of the biliary tract
c) Antibiotic therapy and continued support
d) Magnetic resonance cholangiography
e) Antibiotic therapy, continued support, and percutaneous cholecystostomy

16. Which of the following increases the likelihood that common bile duct stones will not pass spontaneously into the duodenum?

a) Periampullary duodenal diverticulum
b) Male gender
c) Body mass index > 30
d) Elevated amylase level
e) History of smoking

17. Which of the following is one of the most common serious complications of ERCP with sphincterotomy?

a) Bleeding
b) Myocardial infarction
c) Acute cholecystitis
d) Aspiration pneumonia
e) Esophageal perforation

18. According to the available literature, which of the following is associated with the best chance for long-term cure in patients with symptomatic choledocholithiasis?

a) ERCP with sphincterotomy and balloon extraction of stones without cholecystectomy
b) ERCP with sphincterotomy and balloon extraction of stones followed by cholecystectomy within one year
c) ERCP with sphincterotomy and balloon extraction of stones followed by laparoscopic cholecystectomy within six weeks
d) Laparoscopic cholecystectomy with concomitant common duct exploration
e) Laparoscopic cholecystectomy with postoperative ERCP

19. The Mirizzi syndrome is characterized by impaction of a gallstone in what location?

a) Cystic duct or distal gallbladder
b) Ampulla of Vater
c) Distal ileum
d) Duodenum
e) Periampullary duodenal diverticulum

20. Which of the following patient groups is likely to benefit from early ERCP?

a) Patients with biliary pancreatitis and cholangitis
b) Patients with biliary pancreatitis and large gallstones
c) Patients with alcoholic pancreatitis
d) Patients with hypercalcemia
e) Patients with pancreatitis due to hypertriglyceridemia

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The full-text reprints of articles cited in the literature review are included in some formats of SRGS. The boldface numbers at the end of each citation indicate the page numbers where each reprint can be found in the print subscription of SRGS. All of the articles reviewed in this issue can be found in the reference list at the end of the literature review.

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   The authors provide a valuable overview of the surgical management of gallstone disease.


   The authors developed a nomogram for predicting symptomatic gallstone disease in older patients.


   Strasberg provides valuable information to guide surgeons seeking to maximize patient safety and minimize risk of malpractice litigation.


   This classic article provides useful advice for increasing the safety of laparoscopic cholecystectomy.


   McKinley and coauthors provide useful educational concepts that can be incorporated into training for surgeons to become expert in laparoscopic cholecystectomy.


   This article describes the experience of a single, multidisciplinary team in treating post-cholecystectomy bile leak and bile duct injury.


   This article provides useful data supporting the use of enterotomy and stone removal as the preferred treatment for the typical patient with gallstone ileus.


   This is a useful review article describing the management of patients with acute pancreatitis.


   Dellinger and coauthors describe a scoring system for predicting pancreatitis severity and the need for intervention for pancreatic necrosis.


    This article describes a laparoscopic, transgastric approach for the management of pancreatic necrosis and pancreatic abscess.
New SRGS Log-in Procedures

On August 5, 2014, the American College of Surgeons (ACS) launched its new public website, facs.org, designed for easy access from desktops, tablets, and smartphones. ACS retired its members-only Web portal, efacs.org, migrating some features to the new public website, and replacing others with a new online community platform.

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The new ACS website is optimized for Microsoft Windows IE 8+, Apple Mac Safari 6+, Mozilla Firefox 14+, Google Chrome 26+, Apple Mobile Safari 6+, Google Android Internet Browser 4+, Google Android Chrome 20+.
With this issue of *SRGS*, we begin a two-part review of biliary tract and pancreatic conditions of importance to the general surgeon. In this first issue, we will focus on inflammatory gallbladder and biliary tract disease and the associated complications as well as biliary and non-biliary acute pancreatitis. In the second issue (Volume 41, Number 1), we will discuss chronic pancreatitis as well as congenital and neoplastic diseases of the biliary tract and pancreas. Editorial assistance for these two issues has been ably provided by Nicholas Zyromski, MD, FACS, Department of Surgery, Indiana University School of Medicine, Indianapolis, Indiana.

An overview of evidence-based practice for the management of patients with gallstones is by Duncan and Riall in the *Journal of Gastrointestinal Surgery*, 2012. This article is supplied as a full-text reprint accompanying some formats of *SRGS*. The structure of this report serves as a guide for the review of surgical management of cholelithiasis and the complications of gallstone disease. Clinical practice guidelines for the management of cholelithiasis have been promulgated by several professional groups, including the Society for Surgery of the Alimentary Tract (SSAT), the Society of American Gastrointestinal Endoscopic Surgeons (SAGES), and the World Gastroenterology Organization (WGO). The guideline documents are available free from the organizations’ websites (www.ssat.com, www.wgo.org, and www.sages.org).

Introductory comments in each of the documents confirm the significant health burden of gallstone disease and the complications associated with this group of disorders. Only 20% of patients with gallstones develop symptoms necessitating operative intervention. Data cited in the guidelines documents confirm that 750,000 biliary procedures are performed annually in the U.S.; 90% of these are laparoscopic operations. Data cited by Duncan and Riall estimate that 20 million Americans have gallstones and the annual cost of treatment of gallstone disease in the U.S. exceeds 5 billion dollars. Estimates from Europe indicate that 10% of the population have gallstones, with 30% of women reaching age 65 having the condition.

Biliary procedures represent a significant proportion of the practices of general surgeons (especially surgeons practicing in rural areas) in the U.S. Van Bibber and coauthors analyzed data from the National Inpatient Sample and reported surgeon specialty and organ system distributions of inpatient procedures performed by rural general surgeons in the *Journal of the American College of Surgeons*, 2006. Biliary tract procedures accounted for 24% of the inpatient procedures performed by rural general surgeons compared to 16% of the procedures performed by general surgeons practicing in urban areas. These proportions indicate that an understanding of biliary tract disease and knowledge of the management of biliary conditions is important for general surgeons. Additional data reported by Harris and coauthors in the *American Journal of Surgery*, 2010, supports the assertion that biliary tract disease is a major component of general surgery practice. These authors analyzed survey data from 43 general surgeons practicing in rural areas of North and South Dakota. They found that the care of patients with biliary tract disease comprised 6.3% of the 1,017 procedures performed annually by these surgeons. This would mean that, in a given year, a rural general surgeon would perform at least five biliary operations per month.

Although operations on the pancreas represent a much smaller proportion of the average general surgeon’s practice, the variety of urgent and emergent categories of pancreatitis and its complications means that general surgeons will be required to evaluate and participate in the care of patients with pancreatic diseases. Pancreatitis is an important complication of gallstone disease; since gallstone disease is particularly common in younger women, biliary pancreatitis will be encountered in this patient group, especially during pregnancy.
Cholelithiasis

Inflammatory conditions of the gallbladder and biliary tract are, in the main, complications of gallstone disease. Eighty percent of gallstones are cholesterol stones. These stones form when bile is supersaturated with cholesterol. Stones form around a crystal nucleus and factors in bile, such as mucin glycoprotein, transferrin and immunoglobulins, work to facilitate and accelerate stone formation. Gallbladder stasis that may result from vagotomy, fasting, and rapid weight loss (such as the weight loss observed after bariatric operations), prolonged total parenteral nutrition, and somatostatin therapy are contributing factors to gallstone formation as well. Pigment stones account for about 20% of biliary tract stones. These brown or black stones form as a result of increased unconjugated bilirubin caused by hemolytic states, bacterial infection of the biliary tract (particularly in Asian patients); pigment stones are also encountered in patients with cirrhosis. Abnormalities of biliary tract motility observed in cirrhotic patients and in patients with chronic biliary infection contribute to pigment stone formation.

Management of symptomatic versus asymptomatic cholelithiasis

Duncan and Riall note that the most common symptom of cholelithiasis is abdominal pain usually located in the right hypochondrium, often accompanied by nausea. Clinical diagnosis is occasionally challenging because some patients present with nonspecific symptoms such as dyspepsia or nonspecific upper abdominal and lower chest discomfort. In this patient group, biliary symptoms are difficult to distinguish clinically from other important conditions, such as acute peptic ulcer disease and myocardial ischemia. Pain from gallstone disease is thought to result from temporary obstruction of the cystic duct by gallstones, with pain occurring with contraction of the gallbladder against the obstruction. The pain typically occurs following a meal, is sharp, and located in the epigastrium and right upper quadrant of the abdomen. The pain may radiate to the right flank and/or interscapular area of the back and nausea frequently accompanies the pain.

Although pain from cholelithiasis is often called “biliary colic,” it is worth noting that the pain is not truly “colic” because it does not have a crescendo/decrescendo pattern. Because obstruction of the cystic duct is temporary, symptoms will frequently resolve spontaneously, although pain intervals may last for 30 minutes to 24 hours. Data from European studies cited in the WGO practice guidelines documented note that nocturnal pain is a common presentation in men and post-prandial pain is common in women. Confirmation of the diagnosis requires demonstration of gallstones with imaging in a patient with typical symptoms. Abdominal ultrasound is the most cost-effective means of confirming the presence of gallstones in symptomatic patients. Duncan and Riall cite data indicating that sensitivity and specificity for use of right upper quadrant ultrasound for imaging diagnosis of gallstones exceeds 95%.

Magnetic resonance imaging (MRI) may be helpful in evaluating patients with possible symptomatic gallstone disease presenting in the late stages of pregnancy. MRI has recognized value in the diagnostic process for patients with cholecystolithiasis and pancreatitis. These topics are reviewed in later sections of the overview. The authors cite data indicating that computerized tomography (CT) imaging is not useful as a diagnostic modality for patients with uncomplicated symptomatic cholelithiasis except in situations where there is significant diagnostic uncertainty and ultrasound examination has not confirmed the diagnosis. Sensitivity and specificity for CT imaging as a diagnostic tool for gallstone disease hovers around 50%. Of interest is that evidence presented in recent reports indicates that nearly 50% of patients with gallbladder symptoms are imaged with both ultrasound and CT imaging despite the poor accuracy of CT for these conditions. Patients presenting to the hospital at night were more likely to receive CT imaging compared with patients who presented during the day. Duncan and Riall hypothesize that availability of CT imaging during evening and night hours rather than diagnostic accuracy may be driving the increased use of CT imaging for patients presenting after 7 pm.

Recurrent symptoms along with confirmed gallstones are the most common indication for cholecystectomy. Duncan and Riall note that once a second episode of gallstone symptoms has occurred, 70% of patients will
have at least one more recurrence if the gallbladder is not removed. Cholecystectomy is the only effective intervention leading to cure of complications of gallstone disease; all other therapies are palliative and include such interventions as gallstone dissolution and biliary lithotripsy. Available clinical practice guidelines emphasize that cholecystectomy is more than 95% effective in providing complete relief of gallstone symptoms. Patients whose symptoms are not relieved by cholecystectomy are usually found, on further diagnostic evaluation, to have another condition causing the symptoms; the clinical practice guidelines stress the importance of informing patients that nonspecific symptoms, such as dyspepsia and diarrhea, are unlikely to resolve following cholecystectomy.

Cholecystectomy is generally not indicated for asymptomatic patients with gallstones. The risk of symptom development or the emergence of gallbladder malignancy is more than offset by the small, but significant, risk of mortality or morbidity from cholecystectomy. European data indicate that the risk for symptom development in a patient with initially asymptomatic gallstones is 0.3%–1.2% annually. The risk for developing gallbladder cancer is 0.3% over the course of 30 years in patients with asymptomatic gallstones.

Practice guidelines promulgated by the WGO recommend that cholecystectomy be avoided in patients who are asymptomatic except if patients are living in an area remote from available health care or in high-risk areas for biliary infection. Patients who are immunosuppressed are candidates for cholecystectomy. Duncan and Riall note that cholecystectomy is often recommended before heart transplantation. These authors also note that preemptive cholecystectomy is indicated in patients with hemolytic diseases, such as sickle cell disease, if gallstones are present. The WGO guidelines recommend cholecystectomy for elderly patients with insulin-dependent diabetes (high risk for inflammatory complications), but prospective data cited by Duncan and Riall confirm that preemptive cholecystectomy was not beneficial in diabetic patients. Cholecystectomy may be beneficial if patients have or are expected to have rapid weight loss (e.g., gallstones encountered during bariatric surgical procedures).

A recent report by Heida and coauthors in the International Journal of Obesity, 2014, presents evidence that children and adolescents undergoing behavioral modification therapy for obesity were at increased risk of developing gallstones if weight loss of more than 25% of baseline BMI occurred. Because of the increased risk for gallbladder cancer, patients with asymptomatic gallstones and a calcified (porcelain) gallbladder are candidates for preemptive cholecystectomy.

Increasing numbers of elderly patients in the U.S. have stimulated efforts to facilitate clinical decision-making for older patients with various surgical conditions including gallstones. The overall expected mortality of elective cholecystectomy is less than 0.1% but the mortality risk rises in elderly patients, particularly those requiring emergency operations, and in patients with severe comorbidities such as cardiac, renal, and vascular disease or coagulopathy. Insights into actual outcomes of elective laparoscopic cholecystectomy performed in older patients are offered by data presented in an article by Fry and coauthors in Surgery, 2014. The authors analyzed data from the national Medicare database for 90-day outcomes of elective laparoscopic cholecystectomy in patients over 65 years of age. In-hospital mortality was 0.7% and an additional 1.3% of patients died in the 90-day interval following hospital discharge. Complications that caused a prolonged hospital stay or hospital readmission occurred in 8% and 10.1% of patients, respectively. These data support the view that careful risk assessment is necessary so that patients are given a realistic view of expected outcomes. In very high risk or critically ill patients, especially those with septic shock, percutaneous cholecystostomy might offer a means of postponing operation until the overall condition of the patient improves (discussed in more detail later in the overview).

Determining the risk for development of symptoms and/or complications in older patients is challenging. An example of a potentially helpful algorithm for prediction of the clinical course of elderly patients with gallstones is presented in an article by Parmar and coauthors in Annals of Surgery, 2014. This article is supplied as a full-text reprint accompanying some formats of SRGS. The authors used Medicare claims data to identify patients who had a diagnosis of gallstones but did not undergo operation during the 10-week interval following the diagnosis. Risks for development of gallstone-related symptoms or complications were assessed for the ensuing 2 years after the initial period without operation. Data from nearly 93,000
patients were analyzed. The risk nomogram accurately identified 51% of patients who had less than a 10% risk for development of complications and 5.4% of patients who had a 2-year risk of > 40% for the development of gallstone complications. The main risk factors driving an increased statistical chance for complications were male gender, older age, complications of gallstone disease on initial diagnosis, and initial presentation to an emergency treatment area. An illustration and detailed instructions for using the nomogram are included in the text of the article. Readers are encouraged to review these.

**Preoperative preparation for cholecystectomy**

The SSAT practice guidelines emphasize that elective laparoscopic cholecystectomy is the preferred method for performing cholecystectomy in patients who are acceptable operative risks. Currently, more than 90% of cholecystectomies are performed laparoscopically. Details of the procedure as well as complications of laparoscopic cholecystectomy are discussed in detail in a subsequent section of the overview. Open cholecystectomy is a standardized procedure, learned during surgical training that has been performed by surgeons for more than a century. The morbidity of open cholecystectomy results from the need to make a midline, paramedian, or subcostal incision with attendant increased pain, increased hospital length of stay compared with laparoscopic cholecystectomy, and increased time to resumption of normal activities.

Certain subgroups of patients can be more safely treated with open cholecystectomy. Open cholecystectomy might be considered for patients with cirrhosis, patients with gallbladder necrosis, generalized peritonitis, or severe pancreatitis, patients with a history of extensive prior upper abdominal surgery, and women in the third trimester of pregnancy. A special subgroup of patients who might be candidates for open cholecystectomy include those with a suspected gallbladder mass or suspicion of gallbladder cancer. If the available surgeon is trained to perform open cholecystectomy but lacks laparoscopic skills, open cholecystectomy is preferred. There are important caveats involving the indications for open cholecystectomy and these are discussed in later sections of the overview. Gallbladder neoplasms are discussed in the next issue of *SRGS*.

**Laparoscopic cholecystectomy**

Laparoscopic cholecystectomy skills are acquired by surgeons who are trained in accredited residency programs, which leads to certification by a recognized specialist certification body. The American Board of Surgery currently requires satisfactory completion of the Fundamentals of Laparoscopic Surgery course jointly developed by SAGES and the American College of Surgeons, Division of Education, as a component of surgical residency training. Practice guidelines for laparoscopic management of biliary tract disease have been developed and revised several times since 1990 by SAGES; the guidelines document is available free of charge from the society website at [www.sages.org](http://www.sages.org). The guidelines note that the use of laparoscopic cholecystectomy for the management of patients with complications of gallstones has been standard treatment since an important consensus conference convened by the National Institutes of Health in 1992. The practice guidelines developed by SAGES are intended to reflect “best available approaches.”

Given the complexity of disease and the variability encountered in individual patients, practice guidelines are designed to offer advice to the surgeon and are not intended to be used by rote without consideration of patient preferences and the medical condition of the patient. The SAGES guidelines note that antibiotic prophylaxis is not required in the good-risk patient undergoing elective cholecystectomy. Data cited in the guidelines suggest that high-risk patients (age > 60 years, diabetes, acute cholecystitis, biliary colic within 30 days of operation, jaundice, and/or cholangitis) will probably benefit from a single dose of intravenous antibiotics given within one hour of the skin incision. Re-dosing of the chosen drug is indicated if the procedure duration exceeds four hours. Additional data cited in the SAGES guidelines suggest that ampicillin-sulbactam is an effective antimicrobial prophylaxis drug for high-risk patients undergoing laparoscopic cholecystectomy. Readers are encouraged to review the topic of antibiotic prophylaxis available in *SRGS*, Volume 39, Number 4. Separate SAGES guidelines outline the use of venous thromboembolism prophylaxis in patients undergoing laparoscopic cholecystectomy. In good-risk patients with anticipated operative duration of less than one hour, pharmacologic prophylaxis is probably unnecessary. Risk factors, such as a history of venous thrombosis...
or hypercoagulable state, will prompt administration of prophylactic anticoagulant drugs and the use of sequential compression stockings. Readers are encouraged to review the information in SRGS, Volume 38, Number 8, for a discussion on venous thromboembolism prophylaxis.

**Technique of laparoscopic cholecystectomy**

The guidelines proceed to a discussion of patient positioning and surgeon location. They note that the most popular approach in the U.S. is to have the patient supine with the left arm tucked next to the patient’s side. Video monitors are placed on each side of the patient at the head of the table. An alternate approach, more popular outside the U.S., is to have the patient in lithotomy position with the surgeon standing between the patient’s legs. Access to the peritoneal cavity to create a pneumoperitoneum can be achieved by the open transumbilical technique or with a Veress needle. Available data have not documented the superiority of one access approach over the other. The pneumoperitoneum is established at a pressure of 12–15 mmHg for most operations. Lower pressures may be desirable (12 mmHg) for pregnant patients (management of biliary disease in pregnancy is discussed later in this overview).

The guidelines emphasize that safety of laparoscopic cholecystectomy depends on precise identification of the gallbladder and bile duct anatomy in order to avoid bile duct injury. Identification is facilitated by retraction of the fundus of the gallbladder using a locking laparoscopic forceps (retracting laparoscopic forceps attached to the fundus of the gallbladder and pushed over the liver edge toward the diaphragm) and simultaneous lateral retraction of the infundibulum of the gallbladder. Inflammation and anatomic variation increase the difficulty of precise anatomic identification. Inflammation may cause adhesion of the fundus of the gallbladder to the hepatic hilum plate with the result that the main biliary ducts, hepatic arteries, and portal vein are encased in the inflammatory mass. They recommend that when severe inflammation and distortion of the anatomy is encountered, the temptation to switch to a fundus-to-porta dissection of the gallbladder be resisted and, when the conversion to an open procedure occurs, a lesser procedure such as cholecystostomy or subtotal cholecystectomy is preferred over fundus-down dissection. This report offers a valuable caution. The data do not provide us with any information on the frequency of this situation but it is clear that surgeons need to be aware of the potential hazards associated with fundus-to-porta dissection in the face of severe inflammation.

Data on the effectiveness of laparoscopic subtotal cholecystectomy in patients with severe inflammation encountered at the time of operation are presented in an article by Tamura and coauthors in *Hepatogastroenterology*, 2013. The authors report outcomes data on 89 patients. The patients were subdivided into three groups. Group 1 had the posterior wall of the gallbladder left attached to the liver. Group 2 had excision of the upper portion of the gallbladder, leaving the lower third of the gallbladder because the triangle of Calot was obscured by inflammation. Group 3 had the lower third of the
gallbladder closed with sutures after partial excision. All of the operations were completed successfully without perioperative mortality and no persistent bile leakage or bile duct injury. Over a follow-up interval extending out to eight years there have been no instances of gallbladder cancer. Gallstones recurred in three (11.3%) of the group 3 patients. The authors conclude that subtotal cholecystectomy is an effective method for dealing with severe gallbladder inflammation encountered at the time of laparoscopic cholecystectomy.

The guidelines from SAGES and from the Society for Surgery of the Alimentary tract note that a conversion-to-open-procedure rate of 2%–5% can be expected in large clinical experiences. Careful dissection is recommended until a single duct entering the gallbladder and a single artery entering the wall of the gallbladder are identified. Dissection of the ductal end of the gallbladder from the hepatic bed facilitates this “critical view.” A useful rule is that no structure should be divided until a satisfactory anatomic view is achieved. Methods for determining the anatomy of the important ductal and vascular structures to reduce the risk of bile duct injury are reviewed next. Once the cystic duct and cystic artery are identified, and occluded with laparoscopic vascular clips, the duct and artery are divided and the gallbladder is dissected from the liver bed. The specimen can be placed in a plastic bag and removed via the umbilical port. The area of the operation is inspected and any excess blood or bile is aspirated. The pneumoperitoneum is evacuated and ports are removed. Fascial openings are closed with sutures and skin closure is achieved with adhesive strips.

Most good-risk patients can be discharged on the day of the procedure or the following morning depending on adequacy of postoperative pain control, control of postoperative nausea and vomiting, and an adequate home care environment. A metaanalysis examining the evidence for or against ambulatory versus inpatient laparoscopic cholecystectomy is by Ahmad and coauthors in *Surgical Endoscopy*, 2008. This analysis identified seven clinical trials that met the criteria for inclusion; 598 patients were included in the trials. The data disclosed that ambulatory laparoscopic cholecystectomy was more cost-effective than an overnight stay because of shorter hospitalization. The rate of readmission after ambulatory laparoscopic cholecystectomy was less than 5%. The success of ambulatory laparoscopic cholecystectomy was ascribed to careful patient selection. Factors associated with successful ambulatory laparoscopic cholecystectomy included a patient who lived within a short distance from the hospital, younger patients, excellent patient education before the procedure, and absence of medical comorbidities. The success rate for ambulatory laparoscopic cholecystectomy dropped to 70% for patients older than 50 years, patients with ASA scores ≥ 3, or a procedure performed after noon. The analysis notes the importance of control of postoperative nausea and postoperative pain to ensure successful ambulatory procedures. The authors note that there are not strong data supporting the use of any specific anesthetic protocol or postoperative drug protocol to achieve success. They note that it is their practice to use local anesthetic infiltration into the port site areas to improve analgesia.

### Complications of surgical management of biliary tract disease

Postoperative intraabdominal complications of laparoscopic cholecystectomy primarily involve bile leakage usually due to cystic duct stump leakage or intrahepatic bile duct laceration in the gallbladder bed. The most severe, and most feared, complications of laparoscopic cholecystectomy are injuries to the bile duct and injuries to the blood supply to the liver. Overall, the risk of significant bile duct injury ranges from 1/200–1/400 cases for elective cholecystectomy. The SSAT practice guidelines document suggests that patients be informed that the risk of bile duct injury is 0.5%. Risk factors for bile duct injury include surgeon inexperience, inflammation of the bile duct area, patient obesity, bleeding, and variant anatomy of the right hepatic duct; procedures done for complex problems such as acute cholecystitis, pancreatitis, and choledocholithiasis have higher rates of bile duct injury.

Bile duct injury, even when recognized immediately, is associated with longer lengths of hospitalization and increased health care costs. Often, referral to a health care team located at a distance from the institution where the injury occurred is necessary and this adds cost and increases inconvenience for the patient and family. Bile duct injury has an important impact on long-term quality of life. This topic is reviewed in an article by Ejaz
and coauthors13 in the Journal of the American College of Surgeons, 2014. The authors report long-term (median followup of 169 months) results of a health-related, quality of life survey. A total of 167 patients were eligible for inclusion and the response rate to the survey was 37%. The analysis showed that patients experienced significant reduction in psychological quality of life (depression, low energy level) in the immediate period after the bile duct injury and during the recovery interval after definitive repair. Successful repair was achieved in more than 96% of patients and quality of life was normal over the long term in patients whose repair was successful.

Of interest is that more than 70% of patients entered into malpractice litigation; obtaining a favorable verdict or settlement did not seem to improve quality of life or accelerate recovery. The authors stress that their excellent clinical results are largely the result of multidisciplinary team of surgeons, endoscopists, interventional radiologists, and rehabilitation specialists who participated in the care of these patients. They also stress the importance of including and documenting a discussion of bile duct injury risk in the informed consent process for laparoscopic cholecystectomy.

An important question relevant to the problem of bile duct injury in patients undergoing laparoscopic cholecystectomy is what measures can be taken to eliminate or reduce the risk. In an editorial published in 2009, Fischer14 provided an analysis of the available research on bile duct injury during laparoscopic cholecystectomy. The data analyzed by Fischer suggested that bile duct injury resulted from “misperception” by operating surgeons and not by failure to apply, consistently, the basic principles of anatomic identification reviewed above. Fischer goes on to review the four avenues available to the surgeon to avoid bile duct injury. These include careful anatomic identification (as described above), fundus to infundibulum dissection, conversion to open cholecystectomy, and cholangiography. Fundus to infundibulum dissection may be difficult when an enlarged and/or inflamed gallbladder is encountered.

Fischer notes that the failure to establish, with strong data, that cholangiography lowers the risk of bile duct injury means that many surgeons performing laparoscopic cholecystectomy may lack the equipment, experience, and expertise to perform cholangiography efficiently. He further notes that there is significant resistance among surgeons to convert to an open cholecystectomy. The fact that bile duct injury continues to occur even in the practices of experienced laparoscopic surgeons, combined with the lack of sufficiently strong evidence of a protective role for cholangiography to convince the entire surgical community, leads to the conclusion, offered by Fischer, that the frequency of bile duct injury is at an irreducible minimum point. He concludes that a risk of 0.4%-0.7% of a bile duct injury may be the price paid for the reduced pain and more rapid recovery associated with laparoscopic cholecystectomy.

Bile duct injury occurring during laparoscopic cholecystectomy is a major cause of malpractice litigation. This topic is addressed in two related articles by Strasberg in the Journal of the American College of Surgeons, 2005.15,16 These articles are older but continue to be important assets for surgeons performing laparoscopic cholecystectomy. Both articles are supplied as full-text reprints accompanying some formats of SRGS. In the first article, the author describes the basic issues surgeons need to understand as they face malpractice suits. The legal definitions of “negligence” and “substandard care” are discussed and the importance of doctor-patient communication, combined with complete, honest, and timely entries in the medical record, is reviewed. This article is highly recommended for detailed review by readers.

In the second of the two articles, Strasberg discusses elements of the preoperative evaluation including obtaining informed consent. He notes that the specific indication for the operation, along with the clinical, laboratory, and imaging data that support the decision to operate, should be documented clearly in the medical record. He draws on his extensive experience as a medical-legal expert to note that a complication that occurs during a procedure that was not indicated is a situation at high risk for litigation. In the setting of symptomatic cholelithiasis presenting with biliary colic, it is necessary to document the type and frequency of symptoms along with the imaging data that confirm the presence of gallstones. Factors that bear on the operative risk of the patient are also included. For conditions that may not be as straightforward as biliary colic (biliary dyskinesia is one example), more detailed information is required.
Obtaining informed consent is of critical importance. Strasberg suggests the use of a checklist and an example of his checklist is reproduced as Figure 1. The four key categories to cover during the informed consent conversation with the patient are the rationale for the procedure (including the factors involved in choosing the particular procedure), followed by a description of how the procedure is performed. The risks and alternatives to the procedure should also be discussed. A realistic discussion of potential complications is necessary. This portion of the consent conversation should include a discussion of conversion to an open cholecystectomy as a safety measure. If there are factors that increase the risk of conversion, such as a history of acute cholecystitis, this discussion assumes even greater importance.

The author moves on to a discussion of technical features of the operation. He favors the “critical view” approach where no structure is divided until a single artery and duct leading to the gallbladder have been found on dissection. Strasberg considers the infundibular approach, where the anterior surface of the infundibulum of the gallbladder is progressively freed until the cystic duct is visualized, an “error trap.” He notes that a large distally located gallbladder stone can obscure the junction of the cystic duct. When the cystic duct runs parallel to the common duct and there is inflammation-causing adhesion of the cystic duct to the wall of the common duct, separation of the two structures may be difficult. This anatomic situation is illustrated in Figure 2.

Strasberg supports two final measures to increase the safety of laparoscopic cholecystectomy and decrease the risk of bile duct injury. The first of these is liberal use of cholangiography. The author notes the importance of having the equipment, a prepared imaging staff, and an informed operating team so that adequate visualization of the biliary tract can be obtained on images. Complete delineation of the extrahepatic and intrahepatic ducts is necessary, and it is important that no portion of the image is obscured by dye leakage.

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**Figure 1** Example of a consent checklist for laparoscopic cholecystectomy. Reproduced from Stasberg,16 with permission.

1. Rationale for the procedure or why cholecystectomy is being recommended
   - 1a. The basis for diagnosis – symptoms and investigations
   - 1b. The degree to which the operation can reasonably be expected to relieve symptoms and prevent complications when the diagnosis is choledolithiasis and relieve symptoms when the diagnosis is other than choledolithiasis e.g. biliary dyskinesia

2. Description of the procedure
   - 2a. How the gallbladder is removed laparoscopically
     What the procedure will be like for the patient
     Expectations regarding:
     - 2b. Length of stay
     - 2c. Pain
     - 2d. Return to normal functioning including work
     - 2e. Possible variations in this pattern based on need for conversion or other intraoperative events
   - Conversion to open cholecystectomy
     - 2f. Why it may be needed
     - 2g. How likely
     - 2h. Cholecystostomy and partial cholecystectomy – why it is rarely not safe to complete a cholecystectomy
   - Cholangiography
     - 2i. When it is done (indications)
     - 2j. What is done when bile duct stones are found and if they are not removed at time of surgery

3. Risks of the procedure: type, incidence, severity and consequences
   - 3a. Bile duct injury: potentially serious complication possibly requiring additional open surgery - 1/400 operations.
   - 3b. Other serious complications, e.g. injury to major blood vessel or intestine -1/1000
   - 3c. Wound infection – 1/100
   - 3d. Port site hernia -1/1000
   - 3e. Loss of gallstones from the gallbladder. Explain what is done when this occurs and possible consequences.
   - 3f. Other complications of abdominal surgery, pneumoperitoneum, and anesthesia e.g. atelectasis and urinary retention.
   - 3g. Life without a gallbladder. Only known sequel is postcholecystectomy diarrhea – incidence and chance of permanent alteration in bowel habit – 1/400.

4. Alternatives to laparoscopic cholecystectomy
   - 4a. Open cholecystectomy
   - 4b. Risks of no treatment (development of complications)

5. Opportunity to ask unanswered questions
6. The patient has affirmed that he/she understands
7. The patient has received a copy of this form
The value of intraoperative cholangiography is a frequently debated issue. Duncan and Riall\(^1\) note that the available data to support the routine versus selective use of intraoperative cholangiography as a means of preventing bile duct injury are conflicting. Some studies have shown significant increases in rates of bile duct injury when cholangiography is not used, while others have shown no significant difference. The authors note that since the rates of bile duct injury are low, single institution studies are likely to be underpowered to provide definitive guidance on this issue. Additional data on the use of intraoperative cholangiography is the focus of a report by Sheffield and coauthors\(^17\) in *JAMA, 2013*. The authors analyzed data from a single-state Medicare claims database over a nine-year interval. Data from nearly 93,000 patients were included. Intraoperative cholangiography was used in 40% of patients. The risk of bile duct injury was lower in the patients having intraoperative cholangiography but this difference was not statistically significant after adjustment for unknown confounders using the statistical technique of instrumental variables. The authors stress that the reasons for use of intraoperative cholangiography cannot be discerned from an analysis of administrative data. It is not possible to determine if cholangiography was done as a matter of routine, because of unclear anatomy, or because of a suspected bile duct injury. They also emphasize that the data analysis could not adjust for surgeon experience or technique. It is therefore possible that surgeons who used intraoperative cholangiography frequently were more experienced and, possibly, more technically skilled.

In an editorial that accompanied this article, Bilimoria and coauthors\(^18\) discuss the potential advantages of the use of the instrumental variables adjustment. They note that the perfect “instrument” would be randomization in a prospective trial. In the absence of this opportunity, an adequate instrument should be relevant but unrelated to the outcome of interest (bile duct injury). The authors note that the instrument chosen in the study by Sheffield and coauthors was the hospital/surgeon rate of cholangiography use. Bilimoria and colleagues emphasize this instrument faces potential hazards because no adjustment can be made for hospitals that mandate the use of intraoperative cholangiography as part of an overall safety program nor can any insight be made about the impact of cholangiography as a characteristic of more skilled surgeons. Despite these hazards, the data add to the knowledge base in this area. It is unlikely, however, that these data will end the debate over the value of intraoperative cholangiography as a means of reducing the risk of bile duct injury.

Strasberg\(^16\) notes that the techniques used in open cholecystectomy including fundus-to-porta dissection and dissection to isolate, completely, the junction of the cystic duct with the common bile duct are other alternatives. The fundus-to-porta dissection of the gallbladder from the gallbladder bed may be technically challenging in patients with a large and/or acutely inflamed gallbladder (see earlier discussion). Complete dissection of the junction of the cystic duct with the common bile duct increases the risk of injury to the common bile duct and is not recommended.

The final technique to maximize the safety of laparoscopic cholecystectomy and minimize the risk of bile duct injury is for the surgeon to have a low threshold for conversion of the operation to an open cholecystectomy. The concept of a “stop order” is introduced. Industries use a stop order to prompt a stoppage of current activity if the risk of an adverse event increases past a certain threshold. An example is presented of a commercial pilot choosing to land at an alternative airport because visibility prevented clear identification of the landing strip at the

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**Figure 2**

This figure illustrates how the association of the cystic duct and the common bile duct may be obscured when the cystic duct runs parallel to the common bile duct. Reproduced from Strasberg,\(^16\) with permission.
altitude designated as the minimum safe flight altitude during an approach. The author urges the adoption of a philosophy that states that the goal of the surgeon is to perform a large number of cholecystectomies safely, even if that means performing fewer laparoscopic cholecystectomies. Strasberg concludes by noting that conversion to an open cholecystectomy does not always solve the problems of anatomic definition. The surgeon should be prepared to use cholecystostomy and partial cholecystectomy if accurate anatomic definition is not possible.

Another potentially valuable means of identifying ductal and vascular anatomy that may reduce the risk of bile duct injury is the use of laparoscopic ultrasonography. Experience with this approach is described in by Gwinn and coauthors in *Surgery, 2013*. The authors report a prospectively gathered single-surgeon case series including 44 patients. Ultrasound was used intraoperatively to identify biliary ductal and hepatic vascular anatomy. Outcomes in this group of patients were compared with outcomes in 41 patients who underwent planned open cholecystectomy over the same time interval. The data analysis showed the use of ultrasound assistance was associated with a 100% rate of laparoscopic completion of the cholecystectomy despite the fact that severe inflammation made identification of anatomy difficult by gross visualization. The patients who had ultrasound used had lower volumes of blood loss, fewer complications, and a shorter length of hospital stay than did patients in the comparison group. Although this report suggests potential value for the use of laparoscopic ultrasound, the results need to be interpreted carefully because, for example, only one experienced surgeon used ultrasonography. Patients in the comparison group underwent operation on by other surgeons. Additional data suggest that changes in educational programs that can successfully teach expertise. This article is supplied as a full-text reprint accompanying some formats of *SRGS*. The authors note that successful acquisition of expertise requires education in the cognitive domain as well as the technical skills domain. The goals of education to achieve expertise will need to include efforts in both domains, with the aim of transferring the characteristics of expert surgeons to learners. This will require a careful “scaffolding” of expert surgeon characteristics so that these attributes can be learned and learning curves can be shortened. The topics presented by McKinley, et al., have significant potential value and readers are encouraged to review the text in its entirety.

The characteristics of the operative approach may contribute to the risk of bile duct injury. This topic is the focus of an article by Joseph and coauthors in *Annals of Surgery, 2012*. The authors conducted a systematic review of the literature relevant to rates of complications, including bile duct injury, in patients undergoing single-incision laparoscopic cholecystectomy. They were able to identify 45 acceptable studies supplying data on more than 2,600 patients. More than 90% of the procedures were elective.
and performed on patients without evidence of acute gallbladder inflammation. The overall complication rate was 4.2% and the bile duct injury rate was 0.7%. The authors concluded that single-incision laparoscopic cholecystectomy should be avoided in patients with evidence of acute gallbladder inflammation and that additional research is necessary to confirm the safety of this modification of laparoscopic cholecystectomy.

As noted previously, combination injuries that involve the bile duct and the hepatic vessels may lead to liver atrophy and major hepatectomy may be required to manage these complications. A clinical experience with major hepatectomy for post-laparoscopic cholecystectomy biliary/vascular injury is described by Laurent and coauthors\(^{19}\) in *Annals of Surgery*, 2008. This analysis reports a retrospective case series involving 18 patients seen over a 15-year interval in a specialized hepatobiliary surgery center. The injury involved the hilar confluence in all patients. Vascular injury was present with the bile duct injury in 72% of patients. Liver atrophy was present in 83%. The interval between the laparoscopic cholecystectomy and the major hepatectomy was almost four years. Two or more prior attempts at surgical repair of the injury had occurred in most of the patients. Preoperative biliary drainage procedures and/or stent placement had resulted in positive bile cultures in more than half of the patients. Various types of hepatic resection were needed, including one trisegmentectomy. There was no postoperative mortality but significant morbidity, including hemorrhage requiring reoperation, biliary fistula, and prolonged ascites, was observed in 61% of patients. The authors stress that patients with complex biliary/vascular injuries, with a history of failed prior attempts at repair or stent placement, should be considered candidates for liver transplantation. The reason is liver atrophy and the development of biliary cirrhosis. They did not observe any instance of clinical liver insufficiency in their patients, although biliary cirrhosis was present in several resected specimens. Their experience supports the contention that biliary cirrhosis is often found only in the resected liver tissue distal to the bile duct injury.

They further stress the desirability of resection before multiple episodes of cholangitis have occurred. The main advantage of hepatectomy is the complete removal of the abnormal liver tissue with a single biliary-enteric anastomosis. Thirteen of the 18 patients had excellent outcomes at a median follow-up interval of eight years. Three additional patients had good outcomes. The main complication leading to suboptimal outcomes was recurrent cholangitis and sepsis. The authors conclude that hepatic resection is a useful intervention for patients with complex biliary/vascular injury following laparoscopic cholecystectomy. Although significant short-term postoperative complications are encountered, mortality was low and long-term outcomes were good for more than 90% of patients.

**Factors associated with successful repair of bile duct injuries**

In a national survey reported by Archer and colleagues\(^{24}\) in *Annals of Surgery*, 2001, the most frequent site of bile duct injury was the common bile duct below the bifurcation of the hepatic ducts; a minority of injuries were at or above the bifurcation. Surgeons were more likely to describe the dissection as “difficult” in cases where injury occurred. Two-thirds of injuries were suspected, and confirmed, intraoperatively. Evidence from this survey suggests that routine performance of an intraoperative cholangiogram resulted in increased numbers of bile duct injuries diagnosed intraoperatively, but the data is less clear regarding the effectiveness of routine intraoperative cholangiography in reducing the risk of bile duct injury. The SAGES practice guidelines\(^{3}\) cite data indicating routine intraoperative cholangiography reduces the risk of bile duct injury but, as noted in earlier discussion, this issue is controversial.

As noted above, the majority of bile duct injuries are discovered during the laparoscopic cholecystectomy procedure. The SAGES guidelines stress the importance of injury identification and prompt repair by a surgeon experienced in biliary tract reconstructive procedures. The primary surgeon can usually manage minor tangential lacerations of the bile duct if they are identified at the time of the original procedure. Closure of the laceration with fine absorbable suture with drainage or intubation of the laceration with a biliary drain, followed by gradual drain removal once the tract has matured, will usually suffice. Placement of a T-tube in a small duct may increase the
severity of the injury; a smaller nasal-biliary drainage tube placed and brought out through the skin of the abdomen may be preferable.

For the most common severe injury pattern, division of the common bile duct below the bifurcation of the common hepatic duct, reconstruction is best achieved by choledochojejunostomy using the Roux-en-Y technique. Techniques of choledochojejunostomy will be discussed in the next issue of *SRGS*, Volume 41, Number 1. Recognition of bile duct transection below the bifurcation during the primary operation prompts conversion to open laparotomy and repair using choledochojejunostomy if the surgeon is skilled in this procedure.

Injuries not identified at the time of the primary operation present with a variety of symptoms ranging from mild symptoms of abdominal fullness and discomfort to biliary peritonitis with life-threatening shock. Stasberg has indicated that such mild postoperative symptoms are seriously by the surgeon to avoid delay in diagnosing postoperative complications. When the patient presents with symptoms raising suspicion of bile leak due to an open cystic duct, a lacerated intrahepatic duct in the gallbladder bed, a tangential laceration of a major bile duct, or a major bile duct transection, resuscitation of the patient followed by imaging of the biliary tree (usually with transhepatic cholangiography or magnetic resonance cholangiopancreatography) will define the area of injury.

The advantage of transhepatic cholangiography is its therapeutic potential. Tangential lacerations of the bile duct and open cystic ducts can be managed with indwelling biliary stents. Major bile duct transections or stenoses will require imaging for definition of the injury, transhepatic drainage, and definitive repair by a skilled surgical team. Once patients with bile duct injuries have been stabilized, and the injury has been documented with imaging, it is useful to classify the injuries so that communication between surgeons is facilitated if the patient requires transfer to another facility. Classification is useful, also, to facilitate reporting of data in the medical literature. Bile duct injuries are classified according to a straightforward, four level system, reported in a classic 1995 article by Stewart and Way. The class I injury is a tangential laceration of the common bile duct at the cystic duct/common bile duct junction. The class II injury is a partial excision of the lateral wall of the common bile duct. A class III injury is transection of the common bile duct that is the most common of the serious bile duct injuries. The class IV injury occurs when the right hepatic duct is mistaken for the cystic duct and transected. This injury can be complicated by an associated injury or occlusion of the right hepatic artery.

Data cited in the SAGES guidelines support laparoscopic drainage of the area of injury and transfer of the patient to a surgeon skilled in bile duct reconstruction if bile duct transection is identified. Success rates of bile duct injury repair when undertaken by an experienced, multidisciplinary team are presented by Pitt and coauthors in *Annals of Surgery*, 2013. This article is supplied as a full-text reprint accompanying some formats of *SRGS*. The authors report retrospective clinical record data from 528 patients treated over an 18-year interval. Bile leak was diagnosed in 45% of patients and bile duct injury in the remainder. Endoscopic interventions were successful in 96% of patients with bile leaks. These interventions consisted of endoscopic retrograde cholangiopancreatography (ERCP) with placement of biliary drains and/or biliary stents. Bile leaks most often occur in the cystic duct (failure of closure) or from injury to small duct structures in the gallbladder bed.

Injuries to ducts in the gallbladder bed have often been described as injuries to the duct of Luschka. This description is challenged in an article by Schnelldorfer and coauthors in the *Journal of Gastrointestinal Surgery*, 2012. The authors conducted a systematic review of the literature to determine the anatomic features of the biliary ducts that reside in the sub-vesical area of the gallbladder fossa. They note that these ducts are commonly referred to as ducts of Luschka. They refer to Luschka’s original description of ducts that were present on the peritoneal surface as well as the gallbladder fossa surface of the gallbladder. The authors hypothesize, based on review of current literature and modern histologic sections, that the ducts described by Luschka were actually lymphatic channels and that the bile-containing structures described in Luschka’s textbook which resided in the gallbladder fossa adjacent to the gallbladder wall were actually bile ducts. These are likely bile ducts that are part of the drainage system of
the right lobe or accessory ducts. Based on their review of the literature, Schnelldorfer and coauthors suggest that the ducts residing in the gallbladder fossa adjacent to the gallbladder wall be termed “sub-vesicle” ducts.

They propose a classification system that divides these ducts into groups termed “segmental” (common finding, a duct that is a part of the right lobe drainage system); “accessory” or “supernumerary” duct (most common type, aberrant duct not connected to the right lobe drainage system); and two final, very rare, subtypes “aberrant” (system of ducts within the connective tissue of the gallbladder fossa) and “hepatocholecystic” (duct draining into the gallbladder lumen). They recommend that the term “duct of Luschka” be replaced by this nomenclature of sub-vesicle bile ducts, which comprise a significant proportion of biliary injuries resulting in perioperative bile leak.

Pitt and coauthors note that bile duct injuries requiring surgical repair are accomplished with preoperative stenting followed by Roux-en-Y hepaticojejunostomy. In their series, only one patient required hepatic resection. Success rates for hepaticojejunostomy were 88% overall with success rates over the most recent five-year interval rising to 96%. The authors note that factors related to failure of bile duct reconstruction included endoscopic management six months or more after the injury and hepaticojejunostomy performed within 2–4 weeks of the injury. The authors conclude that repair of bile duct injuries and bile leaks using a multidisciplinary approach is safe and successful. Surgical repair in this series was most successful if preoperative stenting for 4-6 months was used.

Additional retrospective clinical record data on outcomes of primary and revisional hepaticojejunostomy are presented in two 2013 articles by Benkabbou and coauthors in Surgery, and Pekolj and coauthors in the Journal of the American College of Surgeons. These data confirm the high success rates with a multidisciplinary approach and use of Roux-en-Y hepaticojejunostomy. Overall success rates for primary and revisional surgery were in the range of 90% and defined by absence of biliary symptoms and no need for reintervention procedures over followup of more than three years.

The association of timing of repair and prior attempts at repair before referral to a specialized center is the topic of a retrospective case series review by de Reuver and coauthors in Annals of Surgery, 2007. The data presented are drawn from a medical record review of 151 patients. The data disclosed a higher rate of complications in patients who had undergone procedures prior to referral to the specialty center (26.4% versus 7.9%). There was no postoperative mortality. Anastomotic stricture occurred more often in patients repaired during the first six weeks following bile duct injury and in those patients who had undergone earlier repair procedures in other hospitals. The authors observed that many of the procedures performed prior to referral to the specialty center were performed without complete imaging to define the location and nature of the injury. De Reuver and colleagues recommend that percutaneous techniques be used to control bile leakage and potential infection. They stress that acute laparotomy should be restricted to patients with acute bile peritonitis. In this setting drainage and control of biliary leakage are accomplished and repair of the injury is delayed until inflammation is controlled and complete delineation of the injury type is established with imaging studies.

The complexity of the diagnostic and therapeutic process for bile duct injury and the fact that durations of illness are, in many cases, prolonged over several months, adverse effects on quality of life may be expected. De Reuver and coauthors updated their previously reported quality of life data in a detailed letter to the editor in Annals of Surgery, 2007. The authors note that there was an error made in calculating quality of life scores in their initial report and the error is corrected in the letter to the editor. The result of the correction was that revised scores did not show as large an impact of bile duct injury and its management on patient quality of life over more than 10 years of followup as the previous analysis had shown. Despite this, the quality of life for their patients was worse than for age-matched patients without a history of laparoscopic cholecystectomy and for age-matched patients who had undergone an uncomplicated laparoscopic cholecystectomy followed by full recovery.
The adverse effects on quality of life were statistically significant in six of the eight areas of function queried in their study. De Reuver and colleagues note that other reports have not consistently shown adverse effects on quality of life following successful repair of a bile duct injury (see previous discussion). They recommend continued research be conducted to document quality of life in patients who have had successful repair of bile duct injury.

**Editorial comment:** The success of laparoscopic cholecystectomy for symptomatic cholelithiasis and for other conditions causing biliary pain is undeniable. Nevertheless, complications occur and these should continue to be recorded and studied. Prevention is the desired means of dealing with these but, as noted by Fischer, the frequency of bile duct injury has been diminished by preventive measures, but the complication has not been eliminated.

The message from the articles reviewed and from my own practice experience is that a willingness to convert to open cholecystectomy whenever anatomic definition of the gallbladder/cystic duct junction is not achieved is a key component of the effort to minimize bile duct injury. When bile duct injury occurs, the primary effort should be to control bile leakage. Repair of any injury more severe than a small tangential laceration of the common bile duct should not be undertaken unless the surgeon has the experience and backup support to conduct successful bile duct reconstruction. Once bile leakage is controlled, anatomic definition of the injury using imaging is necessary. Although magnetic resonance imaging (MRI) is useful, the fact that percutaneous transhepatic cholangiography can define the area of injury and provide drainage of the biliary tract makes this approach preferable, in my opinion. Finally, surgeons should not be reluctant to consult with and transfer patients to colleagues with specific expertise in biliary tract reconstructive procedures.

**Postcholecystectomy pain**

A small proportion of patients undergoing laparoscopic cholecystectomy for cholelithiasis will have persistent right-sided abdominal pain. The clinical practice guidelines promulgated by the SSAT note that persistent biliary pain may be present in up to 5% of patients following cholecystectomy. In such patients, a thorough search for other causes of pain (peptic ulcer disease, irritable bowel syndrome) is indicated. A persistent question in this patient group has been whether sphincter of Oddi dysfunction contributes to this syndrome. A randomized prospective trial of endoscopic sphincterotomy in patients with postcholecystectomy pain is reported by Cotton and coauthors in *JAMA*, 2014. These authors report a randomized prospective trial comparing endoscopic sphincterotomy with usual care in a group of patients with postcholecystectomy pain. The data analysis showed that endoscopic sphincterotomy was no better than usual care in controlling symptoms. The authors concluded that dysfunction of the sphincter of Oddi is not a cause of postcholecystectomy pain.

**NOTES and single-site laparoscopic cholecystectomy**

Two approaches to laparoscopic biliary surgery of the future are worth watching as they develop. Natural orifice transluminal endoscopic surgery (NOTES) is done with the endoscope and instrumentation inserted into the peritoneal cavity via natural orifices, such as the oral route into the esophagus and stomach, the anal-rectal route, and the vagina. There have been a number of feasibility studies in animals and a few human case reports but the large case series necessary to make this procedure an acceptable component of the therapeutic armamentarium of surgeons has not been reported.

By contrast, clinical series of single-site laparoscopic procedures have been reported. The single site approach uses one or more entry points in the umbilical area for peritoneal access and instrument insertion. The goal, primarily, is to improve cosmesis and, perhaps, reduce postoperative pain. Recent data comparing outcomes of single-site laparoscopic cholecystectomy with conventional four-port laparoscopic cholecystectomy are presented in an article by Marks and coauthors in the *Journal*...
of the American College of Surgeons, 2013. The authors report results of a randomized, prospective, unblinded trial comparing the two procedures. A total of 200 patients were randomized with 119 patients undergoing single-site laparoscopic surgery. Cosmesis scores at one year following operation favored the single-site operation. Rates of incisional hernia were significantly higher (8.4% versus 1.2% for the conventional operation). The authors conclude that both operations are feasible and safe and that additional long-term follow-up data are required to confirm or refute the increased risk for incisional hernia with the single-site procedure.

Data on early outcomes of single-site laparoscopic cholecystectomy come from a comparative study of patients undergoing single-site procedures and conventional multiple-site procedures by Hodgett and coauthors\(^4\) in the Journal of Gastrointestinal Surgery, 2009. The authors present a retrospective comparison of 29 patients undergoing laparoscopic single-site cholecystectomy and compare the duration of operations, hospital length of stay, and short-term surgical outcomes to a group of 29 patients undergoing conventional laparoscopic cholecystectomy. The patients who were offered the single-site procedure were seen contemporaneously with the patients offered conventional laparoscopic cholecystectomy, but the choice of procedure was not randomized. A single surgeon performed all of the single-site procedures. A detailed description of the operative technique favored by this surgical group is included in the article and readers are encouraged to review this. There were no statistically significant clinical and demographic characteristics differences in the two groups of patients. The operative times and hospital lengths of stay were likewise not different. Three of the single-site patients required placement of additional trocars to facilitate safe completion of the operation. Three patients in the single-site group developed minor postoperative complications, including two patients who experienced significant right abdominal pain necessitating an extra hospital day. One single-site patient developed acute urinary retention. The authors offer no data concerning patient satisfaction or indices of cosmesis. They question, on the basis of this preliminary dataset, whether single-site operations are less painful than conventional laparoscopic cholecystectomy.

**Editorial comment:** The surgical approaches of the future will likely involve fewer incisions. Application of newer adjunctive devices, such as robotic instrumentation, will also expand. Practicing surgeons will need to be aware that these newer procedures are most likely applicable only to patients with straightforward anatomy, nonobese body habitus, and minimal inflammatory change. Data proving that single-site laparoscopic cholecystectomy is superior to conventional laparoscopic cholecystectomy in terms of patient satisfaction, reduced pain, and improved cosmesis are not yet available. That outcomes of single-site procedures are “not inferior” to outcomes for conventional laparoscopic cholecystectomy is suggested by the available data, but additional work is needed before broad application of these approaches occurs.

**Complications of gallstone disease**

Significant complications of gallstones include acute cholecystitis, choledocholithiasis, and the various complications of choledocholithiasis. These topics are reviewed in this section of the overview. Biliary pancreatitis, an important complication of choledocholithiasis, is discussed in a later section of the overview dealing with pancreatitis.

**Acute cholecystitis**

Ongoing obstruction of the cystic duct with gallstone impaction leads to inflammation in the gallbladder wall and, on occasion, bacterial infection of the gallbladder bile. Edema of the gallbladder wall occurs and pericholecystic fluid accumulates. Ischemia of the gallbladder wall may occur with ongoing inflammation. Clinically this process gives rise to the classic combination of symptoms and associated physical findings that are characteristic of acute cholecystitis. Right upper quadrant pain and tenderness with signs of peritoneal inflammation in the area of the inflamed gallbladder are requisite findings for
Complications of gallstone disease | BILIARY TRACT & PANCREAS, PART I

support of the diagnosis of acute cholecystitis. Depending on the individual patient, overt signs of systemic inflammation including fever, tachycardia, and leucocytosis may be present. Confirmation of the diagnosis is achieved with ultrasound imaging demonstration of gallstones, edema of the gallbladder wall, and pericholecystic fluid.

Duncan and Riall cite data that support the use of early cholecystectomy in patients with acute cholecystitis who are acceptable operative risks. Additional data cited by the authors confirm a risk of recurrence of gallbladder symptoms approaching 30% in patients who do not undergo early cholecystectomy. This finding is confirmed in a population-based study by de Mestral and coauthors in the Journal of Trauma and Acute Care Surgery, 2013. These authors report an analysis of data from a large single-region database. Outcomes for more than 25,000 patients were recorded. They found that recurrence of biliary symptoms necessitating acute care was observed in 29% of patients during a one-year interval after the initial evaluation. Of interest are the facts that nearly one-third of the recurrences were in the forms of biliary obstruction with cholangitis or biliary pancreatitis. Recurrences were most common in the 18-34 year age group. The authors concluded that early cholecystectomy should be considered, especially in younger patients, to prevent recurrent symptoms and potentially serious complications that may be associated with cholangitis and pancreatitis.

A randomized prospective trial comparing morbidity and cost of early (within 24 hours) versus delayed laparoscopic cholecystectomy is reported in an article by Gutt and coauthors in Annals of Surgery, 2013. The study included 618 patients from 34 European centers that were randomized (unblinded) to undergo early laparoscopic cholecystectomy with preoperative antibiotic coverage or a therapeutic course of antibiotics followed by laparoscopic cholecystectomy (at 7–45 days). The primary endpoint was overall perioperative morbidity. Secondary endpoints were length of hospital stay and overall costs. Overall mortality was 0.3%, the same for both groups. Overall morbidity was significantly lower in the early cholecystectomy group as were overall health care costs.

A systematic review of the literature comparing early versus late cholecystectomy for patients with acute cholecystitis is by Gurusamy and coauthors in the British Journal of Surgery, 2010. Five randomized trial were included and these involved 451 patients. The data analysis showed that hospital stay was significantly shorter in patients who underwent early cholecystectomy. The analysis further disclosed that the frequency of bile duct injury, conversion to open cholecystectomy, and other complications were not different when the groups were compared. Bile leaks were diagnosed in 3% of the early group, but there were no bile leaks recorded in the late group. Based on this analysis, the authors conclude that early cholecystectomy is as safe and effective as a therapeutic strategy for patients with acute cholecystitis who are candidates for laparoscopic cholecystectomy. Although the studies available suggest an increased rate of conversion to open cholecystectomy in patients undergoing early operation, this difference did not reach statistical significance. Based on the available data and their experience, Duncan and Riall provide a useful management algorithm for acute cholecystitis reproduced as Figure 3.

Because of the preponderance of young patients with acute cholecystitis, data that would support successful approaches for elderly patients and patients at high operative risk are needed. An article reviewing options for management of elderly patients with acute cholecystitis is by McGillicuddy and coauthors in the British Journal of Surgery, 2012. The authors report a retrospective clinical record review of 475 patients 65 years of age or older who were diagnosed with acute cholecystitis over a nine-year interval. Good-risk patients (n=290) had cholecystectomy performed during the index admission. Conversion to open operation was necessary in 20% of patients and 21% of patients had a major complication (pneumonia, myocardial infarction, respiratory failure, or sepsis). Nonoperative therapy was used in 185 patients. Of these, 65 patients underwent cholecystostomy and subsequent cholecystectomy was performed in 44 patients. No operative intervention was used in 128 patients and the recurrent symptom rate in this group of patients was 4%. The authors conclude that treatment with antibiotics and supportive care without cholecystectomy is feasible and safe in high-risk elderly patients if resolution of symptoms of acute cholecystitis occurs. In patients whose symptoms persist, non-cholecystectomy options (percutaneous cholecystostomy) should be considered.
Percutaneous cholecystostomy represents an alternative to laparoscopic or open cholecystectomy that has potential value for high-risk patients with acute cholecystitis. A review of national trends in the use of this option is the focus of a report by Duszak and Behrman in the *Journal of the American College of Radiology*, 2012. The authors reviewed data from the Medicare claims database for patients seen between 1994–2009 and determined changes in the rates of laparoscopic cholecystectomy, open cholecystectomy, and percutaneous cholecystostomy for patients diagnosed with acute cholecystitis. The authors note that rates of percutaneous cholecystostomy increased 567% over the interval of the study. Laparoscopic cholecystectomy increased by 3% and open cholecystectomy decreased by 7.5%. There was considerable regional variation in reported rates of use of percutaneous cholecystostomy; the rate in the Northeastern U.S. was 5.4% while the rate in one Rocky Mountain state was less than 2%. The authors note that there are multiple potential reasons for this variability including institutional preferences, differences in availability, and the presence of more advanced stages of disease in an aging population.

Outcomes of percutaneous cholecystostomy for acute cholecystitis in critically ill, high-risk patients are reported in two articles reviewed at this time. The first is by Atar and coauthors in *Clinical Radiology*, 2014. The authors retrospectively reviewed data on 81 patients seen over a four-year interval. The mean age of the group was 82 years and all satisfied criteria for critical illness. Calculous cholecystitis was diagnosed in nearly 90% of patients. Tube placement was successful in all patients and symptoms resolved in most patients. In-hospital mortality was 18%, with septic shock being the most common cause of death. Of the surviving patients, 78% underwent interval cholecystectomy but postoperative outcomes for these patients are not reported. The authors concluded that percutaneous cholecystostomy was an effective method for relieving symptoms of acute cholecystitis in high-risk patients who were not candidates for cholecystectomy at the time of treatment.

The second article reviewed is by Chang and coauthors in *Surgery*, 2014. The authors reviewed data on 183 patients from two Korean medical centers who were diagnosed with acute cholecystitis and who were deemed too high risk for early cholecystectomy. Mean age of the patients was 68 years. Tube placement was successful in all patients and symptoms improved in more than 95% of patients. Over a mean follow-up period of more than three years, symptom recurrence was observed in 12% of patients. No data on rates of death during followup are reported. Of note is that this group of patients was relatively young and less than 25% of the group was managed in the intensive care unit. The authors concluded that percutaneous cholecystostomy was effective in relieving symptoms of acute cholecystitis in this patient group.
Choledocholithiasis

Although much progress has been made in understanding the natural history of gallstone-related conditions, there are significant gaps in our knowledge about the expected array of clinical courses for patients with choledocholithiasis. We know that a significant proportion (up to one-third) of patients with choledocholithiasis will spontaneously pass stones into the duodenum. The presence of large stones (>0.5–1 cm diameter), fibrosis of the sphincter of Oddi, periductal duodenal diverticulum, and cholangitis increase the risk that stones will remain in the bile duct system and become symptomatic. Once symptoms occur and choledocholithiasis is suspected, a variety of management strategies are available to the clinician. In this section, provide a detailed review of the surgical aspects of choledocholithiasis.

Clinical manifestations of choledocholithiasis include upper abdominal pain and abnormal liver chemistries. If cholangitis is present, fever and leucocytosis may also be observed. Severe cholangitis and/or severe biliary pancreatitis (see later discussion) will manifest by signs of sepsis and possible hemodynamic instability. Elevations of serum bilirubin and clinical jaundice strongly suggest the presence of choledocholithiasis. Usually the serum bilirubin level is below 15 mg/dL. Hepatic enzymes such as alkaline phosphatase and gamma-glutamyl transaminase are elevated in more than 90% of patients with choledocholithiasis. Liver enzyme levels usually decrease over the course of the first three to six days of an episode of symptomatic choledocholithiasis. Abdominal ultrasound is usually the first imaging study obtained. Ultrasound is a dependable means of demonstrating gallbladder stones and may document bile duct dilation that is a predictive factor for choledocholithiasis. Ultrasound has low sensitivity for detection of bile duct stones, but a high specificity if stones are visualized. Magnetic resonance cholangiography and endoscopy with endoscopic ultrasound are very accurate means of documenting choledocholithiasis. Sensitivity of magnetic resonance cholangiography is 85%, with a specificity of 93%. Sensitivity of endoscopic ultrasound ranges from 93%–98%, with specificity of 97%–100%.

The guidelines presented in the article are promulgated by the British Society for Gastroenterology and were formulated following an extensive review of the literature that was evaluated and discussed by several expert panels. The guidelines recommend that strong consideration be given to the use of endoscopic ultrasound to document stones in the presence of a high probability of choledocholithiasis.

Data supporting the value of endoscopic ultrasound for the detection of common bile duct stones are found in an article by Petrov and Savides in the British Journal of Surgery, 2009. These authors conducted a systematic review of the literature and identified four trials with acceptable levels of quality. The trials involved 213 patients; the data analyzed document the dependability of endoscopic ultrasound. Sensitivity of magnetic resonance cholangiography was 85%, with a specificity of 93%. Sensitivity of endoscopic ultrasound ranges from 93%–98%, with specificity of 97%–100%.

Guidelines for the diagnosis and management of choledocholithiasis are found within the Society for Surgery of the Alimentary Tract guidelines for biliary tract disease as well as the SAGES guidelines for laparoscopic management of biliary disorders. Guidelines for managing patients with choledocholithiasis are discussed in an article by Williams and coauthors in Gut, 2008. These authors provide a probability diagram for the diagnosis of choledocholithiasis using data such as patient age, bilirubin elevation, and ultrasound detection of bile duct dilation. This diagram is reproduced as Figure 4.

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than one endoscopy procedure to achieve an adequate ultrasound examination. In further analysis of the data, the authors determined that an endoscopic ultrasound guided examination for bile duct stones was cost-effective if the probability of choledocholithiasis based on clinical features (or possibly the British Society of Gastroenterology decision support diagram) was less than 61%. The authors concluded that endoscopic ultrasound is a valuable adjunct to assist in determining the need for ERCP with sphincterotomy in patients at low or moderate risk for choledocholithiasis.

Available data indicate that ERCP and endoscopic ultrasound are safe interventions for use in elderly patients with medical comorbid conditions. This topic is discussed in an article by Benson and coauthors in *Digestive Diseases and Sciences*, 2010. These authors analyzed complications in a group of 1,000 patients. A cohort of the group older than 70 years, with a mean age of 80 years, was compared to patients younger than 70 years with a mean age of 54 years. No significant difference in procedure-related complications was noted. The British Society of Gastroenterology guidelines recommend against the use of ERCP solely for diagnosis.

Duncan and Riall note that approximately 10% of patients with gallbladder stones will have concomitant common bile duct stones discovered by preoperative imaging or suspected because of alterations in liver chemistries. Several options for management of these patients are available. These include ERCP with sphincterotomy and duct clearance followed by cholecystectomy, cholecystectomy with postoperative ERCP and duct clearance, cholecystectomy with intraoperative cholangiography and common bile duct exploration, and cholecystectomy with expectant treatment since most small (< 1.0 cm in diameter) bile duct stones will pass into the duodenum. Use of the various treatment strategies varies significantly and this variation is probably based on institutional practice patterns and availability of expertise and resources. Duncan and Riall cite data supporting the fact that ERCP prior to cholecystectomy is successful in achieving duct clearance in over 95% of patients, but more than one procedure may be necessary and this fact may prolong hospital stay and raise costs. If choledocholithiasis is discovered at operation by cholangiography or laparoscopic ultrasonography, postoperative ERCP is successful in 75% of patients. If postoperative ERCP fails, an additional operative procedure may be necessary. Intraoperative biliary imaging and common bile duct exploration is as effective as preoperative ERCP in achieving ductal clearance, according to data cited by the authors.

A Cochrane Collaboration database review of the literature comparing surgical versus endoscopic management of common bile duct stones is by Dasari and coauthors in *Cochrane Database of Systematic Reviews*, 2013. The authors included 16 randomized trials with more than 1,700 patients in the review. In trials comparing open cholecystectomy and common bile duct exploration with ERCP, there were significantly fewer instances of retained stones in the open surgery groups. Comparisons of laparoscopic common bile duct exploration with preoperative ERCP showed equivalent efficacy for both approaches with retained stones identified in approximately 8% of patients. When laparoscopic common bile duct exploration was compared with postoperative ERCP, there was a significant increased risk of retained stones for patients who underwent postoperative ERCP.

A recent randomized prospective trial comparing preoperative ERCP followed within 72 hours by laparoscopic cholecystectomy and common bile duct exploration is by Ding and coauthors in the *Journal of Gastrointestinal Surgery*, 2014. The study randomized 221 patients. The analysis of the data showed that both approaches were equally efficacious for clearance of bile duct stones, with success rates of 94% for both approaches. During long-term followup (median followup of 38 months), stone recurrence was observed in a significantly larger proportion of patients treated with preoperative ERCP (9.5% versus 2.1% recurrence). The authors hypothesize that endoscopic sphincterotomy may predispose to reflux of duodenal content into the bile duct with resultant bacterial colonization that could lead to stone formation.

A second randomized trial is described in an article by Rogers and coauthors in *Archives of Surgery*, 2010. The authors randomized 122 good-risk (ASA class 1 and 2) patients to have ERCP followed by laparoscopic cholecystectomy or one-stage laparoscopic management of choledocholithiasis. The authors found that mortality and morbidity rates were comparable between the two groups. The one-stage group had significantly shorter hospital lengths of stay and hospital and professional
charges were significantly lower in this group. The authors concluded that the one-stage approach was the most cost-effective means of managing choledocholithiasis.

An article dealing with a comparison of laparoscopic cholecystectomy performed within 72 hours of ERCP with operations performed 6-8 weeks after ERCP is by Reinders and coauthors50 in *Gastroenterology*, 2010. These authors conducted a randomized prospective trial involving 49 patients who underwent “early” laparoscopic cholecystectomy after ERCP compared to 47 patients having operation 6–8 weeks after ERCP. The authors found no difference in the operative duration, length of hospital stay, or rate of conversion to an open procedure when the groups were compared. Thirty-six percent of patients in the late group developed recurrent biliary symptoms during the waiting period. These events included 13 episodes of biliary pain and four episodes of acute cholecystitis. By contrast, one patient in the early group developed acute cholecystitis while awaiting laparoscopic cholecystectomy. These authors concluded that early cholecystectomy effectively protects patients from recurrent biliary symptoms after ERCP.

Duncan and Riall1 note that patients presenting with severe symptomatic choledocholithiasis (clinical evidence of bile duct obstruction, gallstone pancreatitis, or cholangitis) are preferentially treated with ERCP, with selective use of early cholecystectomy in patients with mild disease (cholangitis and gallstone pancreatitis are reviewed in later sections of the overview). Cholecystectomy should be performed in acceptable risk patients who present with symptomatic choledocholithiasis. Data cited by the authors confirm that recurrent symptomatic choledocholithiasis is observed in 40%—60% of patients treated with ERCP and duct clearance alone. Duncan and Riall supply a suggested treatment algorithm for patients with choledocholithiasis. This algorithm is reproduced as Figure 5.

![Figure 5](image)

**Figure 5 Management algorithm for patients with choledocholithiasis. Reproduced from Duncan and Riall,1 with permission.**

**Techniques of laparoscopic management of choledocholithiasis**

The practice of leaving a T-tube for drainage of the common duct following laparoscopic cholecystectomy and laparoscopic common bile duct exploration is a matter of some debate. This topic is the focus of an article by Yin and coauthors51 in *Annals of Surgery*, 2013. The authors note that laparoscopic common bile duct exploration has been shown to be safe and effective. The options available for laparoscopic common bile duct exploration include the trans-cystic duct approach and laparoscopic choledochotomy. Limitations of the trans-cystic duct approach include inability to deal with large stones and with stones located above the duct junction with common bile duct. Limitations of laparoscopic choledochotomy are primarily related to leaving a T-tube in place. Specific T-tube complications occur in approximately 15% of patients and include bile leakage, tube displacement, and cellulitis at the tube exit site. These complications have stimulated interest in avoiding T-tube placement and primary ductal closure. The authors conducted a systematic review of the literature focusing on the safety and effectiveness of primary ductal closure. Twelve acceptable studies involving nearly 1,000 patients were identified. The analysis showed
that primary ductal closure was associated with a 3% risk of bile leakage that was not significantly higher than the rate observed with T-tube drainage. Retained stones and other biliary-specific complications were not significantly different when primary closure and T-tube drainage were compared. Available data was not sufficient to support a recommendation for the use of adjunctive measures such as biliary stent placement. The authors concluded that current data in the literature support the safety and effectiveness of primary ductal closure.

A Cochrane review of the use of T-tube drainage following laparoscopic common bile duct exploration is by Gurusamy and Samraj in Cochrane Database of Systematic Reviews, 2008. Unfortunately, this systematic review could only identify one trial of sufficient quality. In the trial 55 patients were randomized; 27 were closed primarily and the remainder had a T-tube placed. The data show, as anticipated, that the patients with primary closure of the bile duct had a shorter hospital length of stay. This issue is examined further in a single-surgeon, prospective, randomized trial of 122 consecutive patients by El-Geidie in the Journal of Gastrointestinal Surgery, 2010. Sixty-one patients were randomized in each group to receive a T-tube or have primary closure. The data disclose that hospital length of stay, overall complications, and bile-duct-related complications were lower in the primary closure group. The author concludes that primary closure without T-tube drainage is safe and effective.

Complications of choledocholithiasis

Two major complications of choledocholithiasis, cholangitis and Mirizzi syndrome, are discussed here. The third major complication, gallstone pancreatitis, is reviewed in a later section.

Cholangitis

Duncan and Riall note that endoscopic ductal drainage is the preferred approach for the management of patients with acute cholangitis. Patients with mild cholangitis (satisfactory clinical response to antibiotics and fluid resuscitation) can have ERCP done electively. Moderate cholangitis (blunted response to fluid resuscitation and antibiotics but no evidence of organ dysfunction) can be managed with ERCP performed within 24 hours of admission. Patients with severe cholangitis should have urgent ERCP done as soon as possible after initial evaluation. The authors cite data supporting the use of percutaneous transhepatic biliary drainage if ERCP is not possible.

Management of cholangitis is discussed in a review by Attasaranya and coauthors in Medical Clinics of North America, 2008. The authors note that cholangitis can present in a variety of clinical patterns ranging from a mild infection to life-threatening suppurative cholangitis. Choledocholithiasis is the most important pathogenesis of cholangitis. Complications from a previous procedure performed on the common bile duct (e.g., stricture formation) are the second most common etiologic category for cholangitis. Increasingly, bile duct stricture resulting from biliary surgical procedures and liver transplantation are causes of cholangitis. The authors cite data that indicate that biliary obstruction with translocation of intraductal bacteria and endotoxin into the bloodstream cause the symptoms of cholangitis. Organisms enter the biliary tree from the duodenum, the portal vein, and/or the biliary lymphatics. Increasing biliary pressure facilitates the translocation process. The authors note that the Charcot triad (fever, right upper abdominal pain, and jaundice) occurs in up to 70% of patients with cholangitis. More severe forms may present with the Reynolds pentad, which adds hypotension and alteration of consciousness to the Charcot triad. The pain of cholangitis is less sharp and generally less severe than the pain of biliary obstruction. In high-risk patients, the typical symptoms may be absent. Elderly patients presenting with fever, leukocytosis, and abnormal liver chemistries should raise suspicion of cholangitis. Liver function studies and other blood tests are nonspecific. Bile cultures are frequently positive with coliform organisms, clostridia, staphylococcus, bacteroides, and streptococcus isolated frequently. CT imaging is useful to document biliary tract dilation and to detect liver abscesses.

Management of cholangitis depends on the severity of symptoms. Mild cases can be treated with antibiotics with biliary decompression using ERCP within 24–48
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hours. Severe cases require critical care, resuscitation, CT imaging, and urgent biliary decompression. An algorithm for management of cholangitis is reproduced as Figure 6. Ampicillin-sulbactam and piperacillin/tazobactam have excellent concentrations in bile. In high-risk patients who are severely ill, antimicrobial therapy directed toward anaerobic organisms should be added. Definitive culture results can be obtained from bile samples at the time of biliary decompression and antimicrobial therapy altered to fit the organisms recovered. Therapy continues for 7–14 days depending on the severity of the cholangitis. Biliary drainage can be accomplished with endoscopic, percutaneous, or surgical techniques. Endoscopic drainage is the most frequently employed intervention. Once access to the duct is obtained, bile samples are withdrawn. Contrast injections are minimized to keep biliary pressure low and an indwelling stent is placed to ensure biliary drainage. Later removal of stones is planned. Data cited by the authors disclose no difference in the effectiveness of biliary stenting and nasal biliary drainage. Surgical drainage with rapid placement of a T-tube drain is an effective treatment if ERCP or percutaneous drainage fails or is unavailable.

Mirizzi syndrome

The Mirizzi syndrome is an unusual form of obstruction of the common bile duct that results from impaction of a stone in the cystic duct or distal gallbladder with obstruction of the common bile duct produced by direct pressure on the duct (Type 1) or by the formation of a gallbladder-to-common-bile-duct fistula (Type 2). A review of experience with treatment of Mirizzi syndrome in a single center over a 23-year interval is by Erben and coauthors in the Journal of the American College of Surgeons, 2011. The authors review details of the clinical presentation, diagnostic evaluation, and treatment of 36 patients (0.18% of all patients requiring cholecystectomy). They note that Mirizzi syndrome is a rare complication of biliary disease first reported in the early years of the 20th century. Type 1 Mirizzi syndrome is characterized by external pressure on the common bile duct by a stone impacted in the distal gallbladder or cystic duct. When erosion of the walls of the gallbladder (or cystic duct) and common bile duct occurs and a fistula forms, the syndrome becomes Type 2 Mirizzi syndrome. The article contains a helpful illustration of the two types of Mirizzi syndrome; the illustration is reproduced as Figure 7. The authors note that the most
common presenting symptoms were upper abdominal pain and jaundice. Of interest is that 17% of patients had no clinical symptoms on presentation, but 75% of patients had abnormal liver chemistries; gallstone impaction in the duodenum and cholecystocolonic fistula was present in one patient each. Ultrasonography, CT imaging, and endoscopic cholangiography were used to confirm the diagnosis but the presence of Mirizzi syndrome was not confirmed preoperatively in 50% of patients. Laparoscopic cholecystectomy was attempted in patients with Type 1 Mirizzi syndrome, but conversion to open cholecystectomy was necessary in 67% of this patient group. Operative management included cholecystectomy alone for Type 1 Mirizzi syndrome; fistula closure in Type 2 Mirizzi syndrome was accomplished by ductal closure over a T-tube or Roux-en-Y anastomosis of the jejunum to the fistula opening. The authors concluded that laparoscopic cholecystectomy can be an acceptable approach in carefully selected patients but the conversion rate to open operation is high.

Additional data on management of Mirizzi syndrome is presented in an article by Zhong and Gong56 in the American Surgeon, 2012. These authors present a single-center, retrospective, clinical case series involving 25 patients. Preoperative diagnosis was possible in 50% of patients using ultrasonography and magnetic resonance biliary imaging. Most patients were treated with open cholecystectomy, and fistula closure in Type 2 Mirizzi syndrome was accomplished with closure over a T-tube. Three-year followup was available. All patients recovered with one patient developing recurrent jaundice due to biliary stricture nearly three years postoperatively. The authors concluded that open cholecystectomy is their preferred approach to these patients when the preoperative diagnosis can be made. When the diagnosis is made intraoperatively, conversion to open cholecystectomy is common.

This condition is discussed further in an article by Mithani and coauthors57 in the Journal of Gastrointestinal Surgery, 2008. These authors report a case series of 16 patients seen in a single center over the course of a 12-year interval. There was no mortality in this series, but 11 of 14 patients experienced conversion from a laparoscopic approach to an open approach. One patient had the diagnosis made at the time of open cholecystectomy. One patient diagnosed preoperatively underwent an open cholecystectomy. Relief of obstruction, and clearance of stones, was accomplished in 13 patients. Three patients required postoperative procedures. Lithotripsy was performed in two patients and ERCP in one. The authors conclude that successful management of this unusual syndrome requires a multidisciplinary approach and the understanding that most patients will require open cholecystectomy.

Special problems in biliary tract disease

In this section of the overview, a variety of special problems related to the biliary tract are discussed.

Biliary disease during pregnancy

Urgent and emergent general surgery procedures are occasionally required during pregnancy and complications of gallstone disease represent one of the most common of the conditions necessitating general surgery interventions. Traditionally, open cholecystectomy with management of associated choleodocholithiasis, according to the principles discussed in the preceding section of the overview, have been the preferred form of intervention and attempts to manage the conditions medically have been used to delay surgery until after delivery of the fetus. If no alternative to open intervention is available, consistent with patient safety, attempts are made to perform the intervention in the first or third trimester of pregnancy (although the clinical needs of the patient are paramount).

With the increasing use of laparoscopic operations for biliary tract diseases, reexamination of the safety of laparoscopy in the pregnant patient has occurred. Clinical knowledge about the use of laparoscopy in pregnant patients focused on the potential adverse effects of pneumoperitoneum on uterine blood flow and on the developing fetus. Concern over the use of imaging of the biliary tract has also led to limitations on the accuracy of diagnosis of these conditions.
An analysis of a clinical series of patients undergoing urgent general surgical interventions during pregnancy is by Corneille and coauthors in the American Journal of Surgery, 2010. The report begins with a discussion of the frequency and outcomes of urgent interventions during pregnancy. Data is cited which indicate these procedures are required in 1/635 pregnancies. Appendicitis is a common indication for operation and perforation of the appendix is more common during pregnancy than in the nonpregnant patient. Nearly half of the patients who develop symptoms of biliary tract disease during pregnancy will require operation before the pregnancy is completed. A 5% rate of fetal loss has been reported when urgent biliary operations are necessary. Biliary pancreatitis (discussed later in the overview) is a particularly severe complication with fetal loss in up to 60% of instances, with an associated maternal mortality rate of 15%.

To evaluate contemporary results for laparoscopic procedures in patients with biliary tract disorders, the authors conducted a retrospective medical record review of patients undergoing open and laparoscopic procedures in a single academic medical center. Between 1993 and 2007, 38 pregnant patients underwent laparoscopic cholecystectomy and one patient underwent open cholecystectomy. Twenty-nine of the 39 patients had the operation done in the second or third trimester of pregnancy. Gangrenous cholecystitis was encountered in two patients, one of whom had open cholecystectomy. Twenty-four of the patients who had biliary procedures had delivery records available. There was no maternal mortality and no fetal loss in the patients who had operation for biliary tract disease. For all procedures performed during pregnancy, the fetal loss rate was 7% and the pregnancy-related complication rate was 37% for laparoscopic procedures and 42% for open procedures. The authors stress that all of the instances of fetal mortality occurred in patients with extremely high-risk pregnancies. They note that there are several case series reports of laparoscopic biliary tract operations in pregnant patients that report no fetal loss. The authors did observe a higher frequency of placental/amniotic complications in the patients undergoing laparoscopic cholecystectomy. The clinical implications of this last observation are not clear from the data available. The authors conclude that laparoscopic cholecystectomy is an effective and safe intervention in pregnant patients.

SAGES has produced practice guidelines for the use of laparoscopic procedures during pregnancy. These guidelines are available at www.sages.org. The guidelines note that the main concerns about the use of laparoscopic surgical procedures during pregnancy have focused on changes in uterine and maternal blood flow during pneumoperitoneum, the potential for trocar injury to the fetus, and problems with attaining necessary exposure for safe conduct of the operation. The guidelines cite recent data indicating that laparoscopic surgery is safe during pregnancy and the benefits of laparoscopic surgery are preserved when the intervention is used in pregnant women. The use of imaging in the evaluation of abdominal disease in the pregnant patient is governed by the axiom that states that the successful diagnosis and management of abdominal disease in pregnancy leads to the greatest benefit for the mother and, therefore, the greatest benefit for the fetus.

The need to make an early definitive diagnosis to guide therapy takes precedence over concerns of the effects of imaging on the fetus. The guidelines recommend that abdominal ultrasound be used as the primary imaging modality to define the presence of gallstones. If other forms of imaging are necessary, the radiation dose to the fetus should be limited to five rads, especially during the first trimester of pregnancy when teratogenesis is the main risk. In later stages of pregnancy, concerns over delivery of radiation to the fetus center on the excess risk of malignant disease with cumulative radiation doses to the fetus in excess of 15–20 rads. The guidelines note that accepted cumulative dose of radiation to the fetus during pregnancy should be limited to 5–10 rads, with no procedure exceeding 5 rads. The guidelines note that the radiation doses to the fetus occurring with standard CT scans of the abdomen are within acceptable ranges. Magnetic resonance imaging can be used at any stage of pregnancy so long as gadolinium contrast material (which crosses the placenta) is not used. Although clear data to support specific defects related to the use of gadolinium are not available, controversy continues regarding the safety of this contrast material. Nuclear medicine studies are associated with acceptable radiation doses to the fetus. Preoperative and operative cholangiography is safe so long as fluoroscopy use is limited since the radiation dose to the patient can exceed 20 rads/minute of fluoroscopy.
The selective use of operative cholangiography with lead shielding of the uterus is recommended by the guidelines. Alternatives to fluoroscopy include intraoperative ultrasound and choledochoscopy.

Endoscopic retrograde cholangiopancreatography has potential value in the diagnosis of choledocholithiasis (see preceding discussion) and in biliary pancreatitis (although this is debatable and is discussed later in the overview). ERCP exposes the patient to the additional risk of bleeding and pancreatitis. The performance of non-radiation ERCP in pregnant patients for the purpose of clearing the bile duct of stones in cases of suspected choledocholithiasis and/or biliary pancreatitis has recently been introduced. Three reports of this technique are discussed at this time. The first report is an analysis of a single endoscopist experience with radiation-free ERCP. This report is by Shelton and coauthors in *Gastrointestinal Endoscopy*, 2008. Wire-guided cannulation of the papilla and bile duct permits introduction of a balloon catheter for stone clearance. Endoscopic ultrasound and choledochoscopy via the papillotome channel of the endoscopic device can assist in confirming clearance of stones from the bile duct. The report describes experience with this approach in 21 consecutive women. Successful cannulation of the bile duct and duct clearance was achieved in all patients. One episode of mild pancreatitis was recorded.

The second report is a review of the management of biliary tract disease in pregnancy with an emphasis on the role and technique of ERCP. The report is by Al-Hashem and coauthors in *Journal of Clinical Gastroenterology*, 2009. The authors note that use of MRI and endoscopic ultrasound has improved the accuracy of diagnosis of biliary duct stones without exposing the fetus to ionizing radiation. ERCP is useful so long as exposure to fluoroscopy is limited and the uterus is shielded. The authors cite data from a long-term follow-up study of patients undergoing ERCP during pregnancy. In a series of 18 patients, all had successful clearance of the duct. One patient had post-sphincterotomy bleeding and one had pancreatitis. There was one fetal loss. Eight-year follow-up data were available on 11 patients and all had healthy children without developmental problems. In this series, endoscopic ultrasound was the preferred method to document cannulation of the bile duct. The authors recommend ERCP for pregnant patients with biliary pancreatitis and patients with a high suspicion of choledocholithiasis. They recommend that endoscopic ultrasound be used to document the presence of stones and successful cannulation of the bile duct. Biliary stent placement may obviate the need for sphincterotomy. Cautious use of radiation is recommended. When possible, procedures should be performed during the second and third trimester of pregnancy (the decision regarding timing of the procedure should be based on the clinical needs of the patient rather than the gestational age of fetus).

The final report on the use of ERCP without radiation during pregnancy is by Akcakaya and coauthors in *World Journal of Gastroenterology*, 2009. This report confirms successful cannulation of the bile duct in 18 pregnant women, 17 of whom had choledocholithiasis. There were no instances of pancreatitis. One biliary stent was placed because of uncertain clearance of the bile duct. All deliveries were normal and no developmental defects were noted in the infants delivered. The authors recommend radiation-free ERCP for pregnant patients with biliary duct stones.

The SAGES guidelines note that the selection of the time of surgical intervention should be based on the clinical presentation of the patient. Contemporary data reviewed in the guidelines have failed to document an increased risk of adverse outcomes during any specific trimester. Laparoscopic procedures are associated with less pain and faster recovery, and both are beneficial to the fetus. The ultimate judgment regarding the use of laparoscopic or open cholecystectomy is based on the anatomy of the patient, the clinical presentation, the expertise of the surgeon, and the size of the uterus. If laparoscopic cholecystectomy is needed after the uterus has passed the level of the umbilicus, the patient should be placed in the left lateral position to minimize pressure on the inferior vena cava by the uterus. Trocar placement sites may need adjustment based on the size of the uterus. Inflation pressures for the pneumoperitoneum are restricted to 10–15 mmHg. The guidelines recommend reducing intraperitoneal pressure in patients with preexisting restrictive lung disease because of concern about upward displacement of the diaphragm causing worsened pulmonary function. Routine monitoring of end-tidal CO₂ is recommended. For the low-risk patient, intraoperative and postoperative sequential compression devices are recommended for ve-
nous thromboembolism prophylaxis. Early ambulation is encouraged. The guidelines note that data about the use of unfractionated and low molecular weight heparin are scarce. Available data suggest that unfractionated heparin is safe to administer to pregnant patients with careful monitoring.

The guidelines recommend laparoscopic cholecystectomy for patients with symptomatic gallstones. They note that nonoperative therapy has been documented to have very high symptom recurrence rates. The available data suggest that laparoscopic cholecystectomy performed for conventional indications is beneficial for the mother and the fetus. Patients with symptoms of choledocholithiasis can be managed with preoperative or postoperative ERCP (see foregoing discussion) or with intraoperative common bile duct evaluation and exploration according to the local availability of resources. There are no convincing data to support the use of one strategy over another although use of ERCP means that there is a risk of bleeding (if sphincterotomy is used), pancreatitis, and the imposition of multiple procedures.

**Gallbladder disease in cirrhotic patients**

Patients with cirrhosis are subject to the development of pigment stones. Population estimates suggest that the frequency of cholelithiasis in patients with cirrhosis is twice that of the general population. A systematic review of the literature relevant to the use of cholecystectomy for symptomatic gallstones in cirrhotic patients is by Laurence and coauthors in *HPB (Oxford)*, 2012. The authors identified 44 acceptable studies that reported data on more than 2,000 patients. The available studies reported outcomes on patients with mild or moderate (stable) cirrhosis. The reported mortality for laparoscopic cholecystectomy was 0.74% and the reported mortality for open cholecystectomy was 2%.

Case series data confirming the value of laparoscopic cholecystectomy in cirrhotic patients are available. Reports by Sleeman and coauthors and Mancero and coauthors provide information on 85 patients operated on in “safety net” public hospitals. Traditionally, these patients would be in higher risk categories than patients cared for in other environments. Both reports disclosed no operative mortality. Morbidity rates were higher in cirrhotic patients and averaged over 25%. Mancero and colleagues followed patients post-discharge from the hospital and noted a complication rate of 16% after discharge. Nonetheless, morbidity was successfully managed in all patients with complications and the effects of morbidity were offset by rapid recovery and decreased need for pain management. Overall, recent data confirm the value of laparoscopic cholecystectomy for cirrhotic patients in Child-Pugh class A and B. Three prospective randomized trials comparing outcomes for open and laparoscopic cholecystectomy were identified. These reported outcomes for 220 patients. Laparoscopic cholecystectomy was associated with fewer complications overall and fewer infectious complications as well as a shorter recovery interval. The risk of postoperative hepatic insufficiency was equivalent for both procedures.

An analysis of data from the National Inpatient Sample for cirrhotic patients undergoing cholecystectomy for symptomatic gallstones is by Chmielecki and coauthors in *HPB (Oxford)*, 2012. Demographic and outcomes data from 3,240 patients are reported. Laparoscopic cholecystectomy was performed in 2,587 patients and open cholecystectomy in 383 patients. Child’s class data are not reported, but coagulopathy and electrolyte abnormalities were observed in 16%–21% of all groups and differences among groups were not significant. Renal insufficiency was observed in 4%–8% of patients. The outcomes analysis showed that operative mortality was significantly higher for open cholecystectomy compared with laparoscopic cholecystectomy or laparoscopic cholecystectomy converted to an open procedure (8% versus 1.6%). Blood transfusion was more often used in open procedures and infectious complications were significantly higher in patients having open cholecystectomy. Hepatic insufficiency occurred in 7% of the open cholecystectomy group compared with 1.4% of the laparoscopic cholecystectomy group. The authors concluded that laparoscopic cholecystectomy was the safer approach for patients with cirrhosis.
A retrospective, single-center clinical series is reported by Nguyen and coauthors in HPB (Oxford), 2011. Data from 68 patients are reported. Only two patients were Child’s class C. No postoperative mortality of hepatic insufficiency was observed. Operating times and the overall rate of complications were lower and recovery times were shorter for patients undergoing laparoscopic cholecystectomy. The authors concluded that laparoscopic cholecystectomy is the preferred approach for patients with cirrhosis and symptomatic gallstones.

An article reporting results of a management strategy for patients with severe cirrhosis and acute cholecystitis is by Yao and coauthors in Gastroenterology Research and Practice, 2014. The authors report outcomes from 29 patients. Six patients were Child’s class A and 19 were Child’s class B. All patients had clinical evidence of gallstones and acute gallbladder inflammation. Patients were treated with supportive critical care and percutaneous transhepatic cholecystostomy, with cholecystectomy performed, on average, eight days later. All patients survived to hospital discharge. Hepatic insufficiency developed in 17% of patients. The authors conclude that cholecystostomy followed by delayed cholecystectomy is a safe and effective approach for patients with advanced cirrhosis and acute cholecystitis.

Acalculous cholecystitis

Acalculous cholecystitis is a challenging entity that complicates the care of critically ill patients. An increasing number of critically ill patients, increased awareness of acalculous cholecystitis and improved methods of imaging for diagnosis have combined to increase the numbers of patients reported in the literature with this condition. The diagnosis and management of acute acalculous cholecystitis is reviewed here.

A review of the clinical features of acute acalculous cholecystitis is by Huffman and coauthors in Clinical Gastroenterology and Hepatology, 2010. The authors note that this condition is a complication of critical illness that occurs usually in patients older than 60 years. The illness emerges usually within the second to fifth week of critical care. Symptoms are nonspecific and include upper abdominal discomfort and tenderness. Abdominal ultrasound is the most dependable diagnostic modality. Imaging will generally disclose gallbladder wall thickening, a dilated gallbladder, pericholecystic fluid, intraluminal gas, or emphysema of the gallbladder wall. The etiology of acute acalculous cholecystitis is believed to result from the systemic inflammatory process that characterizes critical illness. Histologic studies of the gallbladder have shown evidence of acute activation of the inflammatory immune response, common finding in other tissues involved in the systemic inflammatory response syndrome. Leucocyte margination, interstitial edema, and evidence of increased gallbladder wall permeability have all been confirmed by histologic examination. Early diagnosis is related to improved survival. Still, mortality rates hover around 30% in reported series. Definitive therapy of acute acalculous cholecystitis is cholecystectomy. In severely ill patients, bridging cholecystostomy is preferred. This procedure can relieve symptoms and provide valuable information to guide antibiotic therapy when culture of the bile is performed.

Outcomes data from an analysis of a health system database, including 1,725 patients with acute acalculous cholecystitis, is reported in an article by Simorov and coauthors in the American Journal of Surgery, 2013. The data analysis showed that bridging cholecystostomy followed by delayed cholecystectomy was associated with significantly lower in-hospital mortality (5% versus 8%) as well as faster recovery times and lower hospital costs. The authors recommend that acute acalculous cholecystitis in critically ill patients be diagnosed early using a high index of suspicion and imaging with ultrasonography. The preferred treatment approach is percutaneous cholecystostomy followed by delayed cholecystectomy.

Other informative review articles on acalculous cholecystitis are by Barie and Eachampati in Gastroenterology Clinics of North America, 2010, and Huffman and Schenker. The authors open their discussion by stressing that the development of acute cholecystitis is a serious complication in critically ill patients who have gallstones. Acalculous cholecystitis is a more lethal disease involving mostly male patients who are critically ill because of a process separate from the cholecystitis. Mortality rates of 30% continue to be reported. Contributing to the high death rate is delay in diagnosis that leads to high rates of gangrene of the gallbladder (50%) and perforation of the gallbladder (10%). Acalculous cholecystitis cases cluster in
patients who have had complex cardiac surgery or open/endovascular abdominal aortic surgery. Frequencies of acalculous cholecystitis ranging from 0.12%–0.9% are reported for these patient groups. Other vulnerable groups include men who have sustained major burn injury or multiple traumatic injuries. Other patient groups where acalculous cholecystitis has been diagnosed include patients with diabetes, cardiac arrest, and end-stage renal disease.

Commonly, the basic disease is complicated by a low cardiac output state preceding the development of acute acalculous cholecystitis. Secondary infection of the gallbladder during systemic sepsis can also lead to acute acalculous cholecystitis. The pathogenesis of acute acalculous cholecystitis is believed to relate to the biochemical changes that occur in bile during periods of bile stasis. The authors note that lysocephatidylcholine and β-glucuronidase, substances that increase in concentration in static bile, have produced changes in the gallbladders of experimental animals that closely resemble the pathological changes seen in acute acalculous cholecystitis. Bile stasis is observed in patients receiving mechanical ventilation, especially when positive end-expiratory pressure is used. This situation leads to increased portal pressure and increased hepatic venous pressure, which may contribute to bile stasis. Stimulation of gallbladder emptying has not been effective in preventing acalculous cholecystitis. Bile stasis, bacterial superinfection, and low flow states contribute to produce ischemia of the gallbladder wall.

The hypothesis that gallbladder ischemia is the critical event in producing acute acalculous cholecystitis is supported by the frequent observation of gallbladder necrosis in patients with this condition. Postcholecystectomy arterial injection studies cited by Barie and Eachampati document the presence of multiple occlusions in the gallbladder microcirculation. Multiple inflammatory mediators also contribute to the microcirculatory insufficiency commonly observed. Microscopic analysis of excised gallbladder tissue from patients with acute acalculous cholecystitis show leucocyte margination, lymphatic dilation, and infiltration of bile pigment into the gallbladder wall tissues consistent with a microcirculatory response to inflammatory mediators, according to data cited by Huffman and Schenker.68

Diagnosis of acute acalculous cholecystitis requires a high index of suspicion. Signs of sepsis are common in critically ill patients. Patients who are sedated and on mechanical ventilation cannot communicate the presence of pain and/or tenderness. Leucocytosis and elevated levels of serum bilirubin are common in acute acalculous cholecystitis and in many other conditions that complicate critical illness. All of these clinical indices are nonspecific.

Abdominal ultrasound is the most valuable initial imaging modality. Thickening of the gallbladder wall > 3.5 mm is highly suggestive as is a transverse diameter of the gallbladder exceeding 5 cm. Intramural gas and pericholecystic fluid are also helpful signs. False positive examinations can occur in patients with ascites and the presence of sludge in the gallbladder. Huffman and Schenker68 cite data from several studies that indicate sensitivities of abdominal ultrasound ranging from 29%–92%. Specificity of abdominal ultrasound ranged from 89%–100%. Hepatobiliary scintigraphy may be helpful in making the diagnosis. Nonvisualization of the gallbladder one hour after administration of the radioisotope (especially if intravenous morphine sulfate is administered (0.04–0.05 mg/kg) 45 minutes after administration of the radioactive tracer) is considered to be diagnostic for acalculous cholecystitis. The disadvantages of radioscintigraphy are the need to transport the patient to the scanning facility and the need for the patient to remain in the scanning area for two hours.

Huffman and Schenker review several reports assessing the accuracy of radioisotope studies for the diagnosis of acute acalculous cholecystitis. Sensitivity and specificity percentages for radioisotope scintigraphy range from 67%–100% and 38%–100%, respectively. Computerized tomography scanning is reported to be as accurate as ultrasound for making the diagnosis. Limited data comparing CT scanning to ultrasound examination are reviewed by Barie and Eachampati.70 They conclude that ultrasound is the better initial imaging study because of lower cost and availability at the bedside in the intensive care unit. Cholecystectomy has traditionally been the preferred treatment for acute acalculous cholecystitis. Laparoscopic cholecystectomy can be performed at the bedside in the intensive care unit using local anesthesia and sedation but this is a cumbersome and expensive approach. Percutaneous cholecystostomy is currently the pre-
ferred initial management for suspected acute acalculous cholecystitis, with laparoscopic cholecystectomy offered to patients whose conditions do not improve. Huffman and Schenker recommend image-guided percutaneous cholecystostomy whenever acute acalculous cholecystitis is suspected.

Biliary dyskinesia

Pain that mimics that of symptomatic cholelithiasis accompanied by an abnormal radioisotope scan of the gallbladder are two features that support the diagnosis of biliary dyskinesia. Clinical management of patients with suspected biliary dyskinesia is reviewed in this section.

Cholecystectomy for biliary dyskinesia is increasingly used for young patients. This topic is the focus of two articles reviewed at this time. The first is by Bielefeldt in *Alimentary Pharmacology and Therapeutics*, 2013. The author reviewed a group of 200 patients who underwent cholecystectomy for biliary dyskinesia to find the most common ICD-9 diagnostic codes associated with this condition. He then reviewed data from a large administrative database and determined that between 1997 and 2013, the rate of cholecystectomy for the diagnosis code most often used in patients with biliary dyskinesia had tripled. Cholecystectomy was most frequently used for young, privately insured patients.

The second article is by Lacher and coauthors in *Journal of Pediatric Surgery*, 2013. The authors reviewed a single-center experience including 82 patients. Mean age of the group was 13.5 years and the mean BMI was 25. All patients had symptoms compatible with gallbladder disease and 74 patients had low gallbladder ejection fraction on radioisotopic cholescintigraphy. After cholecystectomy, less than half the patients had resolution of symptoms and the only factor associated with a good outcome was normal BMI. The authors concluded that cholecystectomy is likely useful in patients with typical symptoms, a gallbladder ejection fraction of 15% or less, and a normal BMI. Other patients should be evaluated for other diagnoses (such as irritable bowel disease).

A meta-analysis of the literature relevant to the diagnosis, management, and outcomes of treatment is discussed. The meta-analysis is by Mahid and coauthors in *Archives of Surgery*, 2009. The article opens with an explanation of a “positive” radioisotope gallbladder scan. The scan is determined to be positive (impaired emptying of the gallbladder) when the fraction of the radioisotope emptied from the gallbladder is less than 50% (range 40–65% depending on the report cited) over one hour after administration of the radioisotope followed by stimulation of gallbladder contraction with cholecystokinin administered as a bolus or as a continuous infusion. These authors gathered relevant articles reported in the medical literature. Included patients were required to have typical biliary pain according to standard definitions. Gallstones were proven to be absent using standard tests, and the main endpoint was the frequency with which biliary symptoms were resolved. Ten studies involving more than 600 patients were selected. The data show that patients with typical biliary pain, no other evident diagnosis, and a “positive” radioisotope scan of the gallbladder were 15 times more likely to have a significant degree of pain relief following cholecystectomy than after nonoperative management. These results were consistently maintained over the course of more than five years of follow-up. Patients were eight times more likely to experience complete relief of symptoms after cholecystectomy.

In the discussion section of the report, the authors cite data indicating a prevalence of biliary pain without gallstones in the general population of 2.4%. The majority of these patients are women. Analyses of surgical practice data suggest that up to one-third of cholecystectomies are done for gallbladders without stones. The authors note that decreased gallbladder ejection fraction can be present in patients with normal gallbladders and this fact complicates the diagnostic process. Opiate drugs and calcium channel blockers can contribute to impaired gallbladder emptying. Additional data cited in this report indicate that biliary dyskinesia may not be a disease exclusively of the gallbladder but may include dysfunction of the sphincter of Oddi (see related discussion of pancreas divisum later in the overview) or of the cystic duct. The authors review data on the management of patients with biliary-like pain and a normal gallbladder ejection fraction. These patients seem to do as well or better with nonoperative management. Based on the review of the available data, the authors recommend thorough evaluation of the patient with biliary pain without gallstones. The evaluation includes a careful search for other condi-
Gallstone ileus

Gallstone ileus is an uncommon cause of small bowel obstruction occurring in 1%–4% of patients with diagnosed small intestine obstruction. It was first described by Bartholin in 1654. Recent data have suggested an increasing frequency of diagnosis of gallstone ileus. The condition is caused by a biliary-duodenal fistula formation with migration of a gallstone into the intestinal lumen. The stone later becomes impacted (usually but not always in the distal ileum) and intestinal obstruction is the result. Gallstone ileus clusters in elderly patients.

The first article reviewed is by Halabi and coauthors in *Annals of Surgery*, 2014. This article is supplied as a full-text reprint accompanying some formats of SRGS. The authors reviewed data from the National Inpatient Sample database. Of more than three million patients treated for intestinal obstruction over a four-year interval, 0.95% were diagnosed with gallstone ileus. The most common patient group diagnosed with gallstone ileus was elderly (>70 years of age) women. The frequency of gallstone ileus was stable over the study interval; this finding was surprising given the increasing proportion of elderly patients in the population. Procedures performed included enterotomy with stone extraction, bowel resection, and stone extraction with fistula closure. A significantly lower mortality rate (5.8% versus 8%–14%) was observed for enterotomy with stone extraction compared with fistula closure or bowel resection. The higher mortality for bowel resection may represent a group of patients with more complicated bowel obstruction with higher rates of bowel necrosis. The authors stress that enterotomy with stone extraction is probably the preferred approach for this condition. They further emphasize the importance of thorough examination of the entire length of the bowel because up to 25% of patients have multiple intraluminal stones.

Another article on this topic is by Ayantunde and Agrawal in *World Journal of Surgery*, 2007. The authors open the discussion by noting that the classical triad of clinical findings of gallstone ileus (pneumobilia, ectopic gallstone, and small bowel obstruction) is documented in less than half of patients ultimately found to have the condition. This observation may be due to the insensitivity of plain abdominal radiographs as the main diagnostic imaging approach. Newer diagnostic modalities such as abdominal ultrasound and CT scanning have improved the accuracy and efficiency of diagnosis.

Controversy has continued about the appropriate management of gallstone ileus. One of the traditional approaches is entero-lithotomy and suture closure of the bowel to relieve the obstruction, with operative management of the biliary disease done later, if clinical indications exist. Data cited by Ayantunde and Agrawal indicate that more recent publications have suggested one-stage procedures consisting of entero-lithotomy, takedown of the biliary enteric fistula, and cholecystectomy. The use of this more extensive procedure in patients who are likely to be older, higher risk patients has been criticized as “overtreatment” of the condition. These authors sought to examine their experience using a retrospective medical record review of 22 patients seen over an eight-year interval. The mean age of the patient group was 77 years and
86% of patients had ASA scores of 3 or higher, indicating a high surgical risk group of patients. Computerized tomography was the most effective diagnostic imaging study. Diagnostic delay was common because most episodes of symptoms suggestive of intestinal obstruction were transient due to the “tumbling” phenomenon, a term applied to the natural history of the enteric stones. These stones intermittently lodge in narrowed portions of the intestine causing symptoms. The stone is then dislodged and symptoms are relieved. Many stones never cause persistent intestinal obstruction and are passed into the distal bowel. Twenty of the 22 patients underwent enterolithotomy alone. Single stones were recovered in 18 patients and four had multiple stones. Most stones were recovered from the ileum, but stones were found in the jejunum in five patients. The site of the biliary enteric fistula was documented in 20 patients. Nineteen patients had a cholecystoduodenal fistula and one had a cholecystogastric fistula. Five patients (22.7%) died peripherative and five additional patients died after discharge over a follow-up interval of 10 months.

The authors stress that the perioperative and postdischarge mortality rates are consistent with the aged and high-risk nature of the patient group. Ayantunde and Agrawal note that the one-stage complete reconstruction procedure supported in several reports is defended based on the perception that recurrent biliary symptoms are common. These authors note that recurrent biliary symptoms are encountered in only 5% of patients and, of this group, only 10% will require reoperation. The authors use their experience and cited data to support their approach, which includes careful diagnostic evaluation using CT, establishment of surgical risk, and enterolithotomy alone for most patients with the one-stage complete reconstruction used for patients with recurrent symptoms or for good-risk patients.

Acute pancreatitis

Acute pancreatitis imposes a significant health burden in the U.S. Most cases are not severe and resolve with a modest investment of supportive care. Severe forms of acute pancreatitis will require input from surgeons, gastroenterologists, radiologists, and critical care specialists to ensure optimum outcomes. In this section of the overview, we discuss the epidemiology, etiologies, clinical presentation, pathogenesis and expected outcomes for this condition. In subsequent sections, detailed information about specific types of acute pancreatitis is provided. Separate sections are devoted to the diagnosis and management of severe acute pancreatitis, and complications of pancreatitis. Chronic pancreatitis will be discussed in the next issue of SRGS.

Pathogenesis and pathophysiology

Information about the health burden and epidemiology of acute pancreatitis is found in an article by Wu and Banks in Gastroenterology, 2013. This article is supplied as a full-text reprint accompanying some formats of SRGS. The authors note that hospital admissions for acute pancreatitis exceed 280,000 annually in the U.S. The average hospital length of stay for an admission for acute pancreatitis is five days. The authors list several etiologies for acute pancreatitis including gallstone migration into the bile duct, alcoholic pancreatitis, pancreatitis from hypercalcemia and hypertriglyceridemia, and pancreatitis from autoimmune disease. Ischemic pancreatitis is a complication of visceral vascular occlusive disease. Pancreatitis can also occur as a complication of medical interventions, such as ERCP.

Additional information on the epidemiology of pancreatitis is presented by Talukdar and Vege in Clinics in Gastroenterology, 2009. These authors note that the frequency of acute pancreatitis is rising in many countries. In the past 20 years, there has been a 100% increase in hospital admissions for pancreatitis in the U.S. Acute pancreatitis is the third most common gastrointestinal diagnosis in patients discharged from hospitals in the U.S. Similar, significant increases have been observed in the Netherlands, the United Kingdom (U.K.), and in Sweden. In the U.K., the age-standardized incidence of acute pancreatitis was highest in elderly patients. There was a significant association noted between the risk for diagnosis of acute pancreatitis and living in economically deprived areas.

Data supporting a meaningful association of poverty and the risk for developing pancreatitis are supplied in an article by Ellis and coauthors in the British Journal of
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Surgery, 2008. Admissions to 18 hospitals with the main diagnosis of acute pancreatitis, defined by elevated levels of pancreatic enzymes, were tracked over the course of six months. Medical records of 963 patients were reviewed and age-specific incidence, mortality risk, and geographic location of patient residence according to economic status were assessed. The data disclosed that the age-specific incidence of acute pancreatitis was 56.5/100,000 population; this figure was twice the previously reported incidence in the U.K. As noted previously, incidence among the elderly rose significantly. There was a strong correlation of pancreatitis risk and poverty with the risk more than doubled in economically deprived areas. The increased risk in these areas seemed mostly from increased frequency of alcoholic pancreatitis. Talukdar and Vege\textsuperscript{79} cite data that indicate a higher risk of pancreatitis among current smokers. They also cite data showing an increased risk of pancreatitis among older women with biliary microlithiasis.

Mortality rates for acute pancreatitis vary according to illness severity; mortality is 3% for interstitial (edematous) pancreatitis and rises to 15% for patients who develop pancreatic necrosis. Information presented in a review by Baron\textsuperscript{81} confirms that pancreatitis is an inflammatory condition that is, in a small proportion of patients, complicated by necrosis of the pancreas and peripancreatic fat (evidence cited by the authors indicates that excess peripancreatic fat, as might be found in obese patients, is associated with increased risks for morbidity and mortality). Pancreatitis that progresses to necrosis might be complicated by infection that occurs because of translocation of enteric bacteria from the colon, stomach, or duodenum into the necrotic tissue and/or from a direct fistulous connection with the lumen of the intestine. Wu and Banks\textsuperscript{78} as well as Baron\textsuperscript{81} stress the importance of early diagnosis of inflammation and quantification of risk of progression because effective early fluid resuscitation and supportive care may prevent progression to pancreatic necrosis. Features of effective fluid resuscitation and use of scoring systems for determining illness severity and estimating risk of progression is discussed later.

Additional features of the pathophysiology of acute pancreatitis include damage to pancreatic parenchymal cells due to ductal obstruction with increased ductal pressure. Activation of trypsinogen, with conversion to trypsin within the pancreatic parenchyma, and small ducts then occur. Inadequate elimination of trypsin due to duct obstruction leads to severe inflammation of the pancreas. This inflammatory process can cause tissue destruction in the retroperitoneum surrounding the pancreas as well, and the process serves to activate mediators of systemic inflammation. The relationship between activation of pancreatic enzymes and damage to the pancreatic parenchyma and surrounding tissues as well as damage causing dysfunction of distant organs is emphasized in an article by Waldthaler\textsuperscript{82} in Digestive Disease, 2010. Waldthaler notes that animal models of acute pancreatitis provide inconsistent information about pathogenesis. Noteworthy is the fact that administration of alcohol alone is not sufficient to cause pancreatitis in experimental animals. As an aside, the article also noted that there is no clear explanation of why acute pancreatitis develops in only a small proportion of heavy alcohol users. Direct infusion of agents that damage the endothelium, ductal infusion of bile or intestinal content, and occlusion of the pancreatic arterial supply are all means of producing severe pancreatitis in experimental animals. The data provided by these experiments is limited because producing an identical degree of injury in all animals is not possible and the responses of individual animals vary significantly.

The author emphasizes that the main abnormality that permits the accumulation of trypsin within pancreatic cells, with subsequent cellular necrosis, is disruption of the orderly accumulation of trypsinogen in granules that are concentrated at the apex of the acinar cell. Trypsinogen, which accumulates at the apex of the cell, can be expelled in an orderly sequence into the duct. As the cellular damage of pancreatitis progresses, trypsinogen-containing granules accumulate in the basal regions of the acinar cells leading to pathological exocytosis. Release of trypsinogen and activated trypsin from the basal areas of the acinar cells into the pancreatic interstitium is where the inflammatory process starts and perpetuates. The author provides valuable illustrations of this process in the article. The presence of activated trypsin in the pancreatic parenchyma serves to activate trypsinogen in cells located close by. Local inflammation spreads due to washout of activated enzymes and this leads to extensive local and systemic damage.
The inflammatory changes are accelerated and augmented by necrotic cell death in the pancreatic parenchyma. Mechanisms available to limit the spread of inflammation include autophagy and cellular autodigestion, apoptosis of damaged parenchymal cells, and intrinsic inhibitors of trypsin. The trypsin inhibitors include chymotrypsin and pancreatic secretory trypsin inhibitor–1 (SPINK-1). The effectiveness of these limiting mechanisms is related, in part, to intracellular calcium levels. Cellular hypercalcemia along with systemic hypercalcemia (a known etiology of acute pancreatitis) inhibits the mediators of apoptosis and autophagy. Apoptosis has been shown to limit the severity of experimental pancreatitis. Apoptosis of pancreatic cells prevents necrotic cell death. Autophagy and autodigestion of damaged pancreatic cells also prevents necrosis and can limit the severity of pancreatitis. Waldthaler presents a diagram illustrating these relationships. The diagram is reproduced as Figure 8. Local tissue necrosis is mediated by lipase and phospholipase. Distant organ dysfunction is consistently associated with increased vascular permeability facilitated by multiple inflammatory mediators.

**Practice guidelines**

Practice guidelines for the management of acute pancreatitis have been promulgated by several organizations such as the Society for Surgery of the Alimentary tract (available free at www.ssat.org), the American College of Gastroenterology (available free at www.gi.org), and the International Association of Pancreatology/American Pancreatic Association (available free at www.internationalpancreatology.org). Evidence-based recommendations from these guidelines documents are used in the discussions of diagnosis and management of acute pancreatitis in subsequent sections of the overview. The guidelines note that abdominal ultrasound is useful in diagnosing biliary pancreatitis and has the advantage of portability so that the examination can be performed in a critically ill patient. The test does not have excellent sensitivity, however. Computerized tomography imaging, once the patient is hemodynamically stable, is preferred to document the presence of pancreatitis as well as the absence of other conditions.

The guidelines provide some useful comments about the management of pancreatitis. The guidelines stress that the use of certain pharmacologic interventions, such as the intravenous administration of protease inhibitors to reduce the severity pancreatitis, has been evaluated only in research studies from Japan and, as such, this intervention is not recommended outside of a research protocol. The guidelines also emphasize the controversy surrounding the use of preventive antibiotics in patients with pancreatitis (see later discussion). They further present the opinion that early ERCP with sphincterotomy, followed by cholecystectomy as soon as feasible, represents an optimum (although controversial) approach for biliary pancreatitis. This topic is discussed in more detail later.
The guidelines stress that the selection of surgical or percutaneous interventions for management of infected pancreatic necrosis depends on local availability of resources and the condition of the patient. For example, patients with extensive necrosis without localized fluid collections and ongoing sepsis and/or organ failure would probably be better served by an open approach as opposed to percutaneous drainage. The guidelines close with a discussion of the management of pseudocysts and the multiple open, minimally invasive, and endoscopic approaches to these. Open and percutaneous management of pancreatic necrosis and the management of pseudocysts is discussed later.

Data on rates of adherence to clinical practice guidelines for patients with acute pancreatitis are presented by Vlada and coauthors in HPB (Oxford), 2013. The authors reviewed medical record data on 67 patients with clinically severe acute pancreatitis transferred to a tertiary care facility after initial management in an outside institution. Review of records from the transferring hospital showed that more than half of the patients underwent CT imaging within 24 hours of the clinical diagnosis of pancreatitis, but the imaging techniques used were not those recommended in available clinical practice guidelines. Antibiotics were initiated in 53% of patients even though there was no site of infection identified. The authors concluded that adherence to available clinical practice guidelines was poor in this group of severely ill patients.

### Diagnosis

Wu and Banks and Baron emphasize the importance of early diagnosis of pancreatitis and early detection of signs of systemic inflammatory response syndrome so that effective resuscitation can be instituted. The clinical diagnosis of pancreatitis requires fulfillment of two of the following three criteria: typical upper abdominal pain that is usually accompanied by nausea and vomiting, serum levels of amylase or lipase that are ≥ 3 times the upper limit of normal, and confirmation of inflammatory changes in the pancreas by cross-sectional imaging. Both reviews stress that serum enzyme levels are variably sensitive but very specific. The serum lipase level might be a more dependable measure than serum amylase since amylase levels tend to decline at an earlier time point. Additional laboratory studies to document the presence of pancreatitis include measurement of serum calcium (hypercalcemia with elevated enzyme levels is predic-
tive of pancreatitis). Elevated alanine aminotransferase levels are observed in patients with biliary pancreatitis. Hypertriglyceridemia is associated with pancreatitis as well. Serum levels of trypsinogen activation peptide and trypsinogen-2 may also be helpful in confirming the diagnosis, but these are not as widely available. Baron\textsuperscript{81} cites data indicating that urinary trypsinogen-2 levels > 50 ng/ml may assist in the diagnosis of pancreatitis. Baron and Wu and Banks\textsuperscript{78} emphasize that early imaging is usually not helpful unless the clinical diagnosis is uncertain and other serious or life-threatening abdominal conditions (intestinal ischemia, perforated viscus) need to be ruled out. Abdominal tenderness is typically present but signs of peritoneal irritation (localized guarding) are not usually present except in patients with severe pancreatitis, where findings of an acute abdomen with distention may be present.

Baron notes that signs of systemic inflammatory response syndrome include tachycardia (heart rate > 90 beats/minute), fever > 38 deg C or < 36 deg C, white blood cell count of > 12,000 mm\textsuperscript{3} or < 4,000 mm\textsuperscript{3}, and respiratory rate > 20 breaths/minute. Because pancreatitis is associated with inflammation and increased capillary permeability, clinical evidence of fluid extravasation in the retroperitoneum and peritoneal cavity, with increased abdominal pressure and pleural effusion visible on chest radiographs, may be present.

Scoring systems for determining severity

Several scoring systems are available for predicting the course and outcomes of acute pancreatitis. The most commonly used scoring systems based on clinical and laboratory criteria are the Ranson criteria\textsuperscript{86} (Figure 9), the Imrie-Glasgow scoring system\textsuperscript{87} (Figure 10), the Apache II score\textsuperscript{89} (Figure 11), the Atlanta criteria\textsuperscript{88} and the revised Atlanta criteria,\textsuperscript{89} and the Bedside Index of Severe Pancreatitis (BISAP) score\textsuperscript{91} (Figure 12). The presence of three or more of Ranson’s criteria, the presence of three or more factors in the Imrie-Glasgow score, an Apache II score of 8 or more and/or a BISAP score greater than 3 indicates severe pancreatitis. In the Atlanta criteria, the diagnosis of organ failure and the presence of local complications such as pancreatic necrosis, pancreatic abscess, or pseudocyst are used as adjunctive factors leading to a diagnosis of severe pancreatitis. Because of its reasonable accuracy, its simplicity, and the fact that it uses data that are readily acquired, Baron\textsuperscript{81} recommends that clinicians caring for patients with acute pancreatitis use the BISAP score.

Pancreatitis severity scores were compared by Papa-christou and coauthors\textsuperscript{91} in the American Journal of Gastroenterology, 2010. These authors compared the predictive value of all available scores, except the Imrie-Glasgow score. Predictive accuracy was determined by the area under the receiver-operation characteristic curve (AUC). There was no significant difference in the predictive accuracy of the scores, but the Ranson score was the only scoring system with an AUC > 0.9. The authors concluded that the BISAP score was accurate and easy to use for predictive scoring within 24 hours of hospital admission. They emphasize, however, that each of the scoring systems has shortcomings and the limitations of clinical and radiologic scoring systems suggest that new approaches to predicting severity of acute pancreatitis are needed.

The use of a combination of imaging findings and clinical evidence to determine pancreatitis severity is the focus of an article by Dellinger and coauthors\textsuperscript{92} in Annals of Surgery, 2012. This article is supplied as a full-text reprint accompanying some formats of SRGS. The authors sought opinions from an international group of experts in
medical and surgical management of pancreatitis. Based on the opinions, the authors developed a scoring system that used imaging evidence of pancreatic necrosis and a clinical diagnosis of the presence of and persistence of organ failure as a means of determining pancreatitis severity. A useful diagram of the scoring system is reproduced as Figure 13. The severity scoring system described has not yet been confirmed in high-quality prospective studies.

**Editorial comment:** Scoring systems are valuable for alerting clinicians to the possibility of severe disease but they are not a substitute for careful sequential clinical assessment at the bedside. Patient variability limits the usefulness of scoring systems as a means of decision support for the care of individual patients. Scoring systems are very valuable, however, for categorizing patients in the course of producing scientific studies of disease processes like pancreatitis.
Initial management

Baron stresses the importance of initial management of patients with acute pancreatitis. The main objective of early management is the prevention (or at least containment) of progressive organ failure by providing supportive care to maintain oxygenation, organ perfusion, and adequate nutrition. Baron notes that a key feature of early management is fluid resuscitation. Lactated Ringer’s solution is the fluid of choice; an initial fluid bolus of 20 ml/kg followed by an initial infusion of 3 ml/kg/hr has been shown to be an effective initial approach, according to data cited by Wu and Banks.

Interval assessments are performed at least every six hours and more frequently in settings where critical care support of the patient is required. Failure of vital signs, urine output, and BUN levels to respond may indicate worsening pancreatitis or the onset of organ failure due to peripancreatic infection. The authors note that clinical improvement (decreasing BUN level, increasing urine output) should trigger a reduction of the fluid infusion rate to 1.5 ml/kg/hr. Detailed discussions of critical care of surgical patients can be found in SRGS, Volume 39, Numbers 5 and 6.

An analysis of the strength of evidence supporting recommendations for fluid therapy for patients with acute pancreatitis is by Haydock and coauthors in Annals of Surgery, 2013. The authors conducted a systematic review of available evidence relevant to the early fluid management of patients with acute pancreatitis. Fifteen studies of acceptable quality were identified. Only two of these were randomized prospective trials. Studies comparing aggressive versus nonaggressive fluid therapy protocols (n = nine studies) produced conflicting results. Half of the studies supported a nonaggressive approach while the remainder supported aggressive fluid therapy. Similarly, studies of goal-directed fluid therapy were inconclusive; the authors note, however, that most available clinical practice guidelines support a goal-directed approach to fluid therapy. Similarly, data in support of bedside or laboratory measures to serve as goals of fluid therapy are inconclusive. The authors cite data in support of bedside goals such as heart rate and urine output. Cited studies of laboratory values support the use of declining BUN as a therapeutic goal. Available data note that a high admission hematocrit (> 47%) is associated with need for aggressive fluid therapy, but other studies show that a rapid decline in hematocrit during early fluid therapy was associated with an increased risk of sepsis and organ failure. The authors concluded that high-quality data to support one approach to fluid management over another were not currently available.

Abdominal compartment syndrome is a potential complication of acute pancreatitis because of increased capillary permeability induced by the severe inflammatory process. The association of increased intraabdominal pressure and outcomes of acute pancreatitis is the focus of an article by Aitken and coauthors in Surgery, 2014. The authors estimated intraabdominal pressure using intravesical pressure measurements obtained prospectively in more than 200 patients admitted to a single center with a diagnosis of acute pancreatitis. They found that an early elevation of intraabdominal pressure to levels > 12 mmHg was predictive of organ failure and death. Late onset abdominal hypertension occurred in 3% of patients and mortality was highest in this group (50%). The data suggest that a threshold of abdominal pressure of 9 mmHg is potentially useful as a trigger for efforts to control abdominal hypertension and prevent abdominal compartment syndrome.
Additional data on the management of abdominal compartment syndrome in patients with pancreatitis are presented by van Brunschot and coauthors\textsuperscript{95} in JAMA, 2014. The authors conducted a systematic review of available literature. The quality of the identified studies was rated moderate-to-low. Based on their analysis the authors suggest that abdominal compartment syndrome is associated with an increased mortality for pancreatitis (approaching 50%). They suggest monitoring intravesical pressure is an effective means of diagnosing abdominal hypertension. Initial approaches to control of intraabdominal pressure recommended by Baron\textsuperscript{81} include sedation (and possible paralysis) of the patient, use of a peritoneal dialysis catheter to remove intraabdominal fluid, decompression of the gastrointestinal tract with nasogastric and rectal tubes, and decompressive laparotomy as a last resort. The article by van Brunschot and coauthors\textsuperscript{97} recommends use of negative pressure wound care and early fascial closure in patients who require decompressive laparotomy.

Nutritional support using enteral formulas is an important feature of the early care of patients with severe acute pancreatitis. Wu and Banks\textsuperscript{78} and Baron\textsuperscript{81} recommend the use of a low-fat diet in patients who can tolerate normal feeding and early nasogastric or nasoenteric enteral nutrition if patients cannot tolerate normal feedings. The use of immune-enhancing enteral nutrition is not recommended. A randomized, prospective trial comparing enteral nutrition with a nasogastric tube until oral feedings were tolerated with no nutritional support until oral feedings were tolerated in a group of patients with mild-to-moderate acute pancreatitis is by Petrov and coauthors\textsuperscript{96} in Clinical Nutrition, 2013. The analysis showed that pain scores were significantly lower in patients receiving nasogastric feedings. The need for opiate drugs was significantly less in the group fed via nasogastric tube and rates of oral food intolerance were lower. The authors conclude that nasogastric tube feeding may be valuable in patients with mild-to-moderate pancreatitis similar to patients with severe pancreatitis requiring critical care. They urge caution in interpreting their results because of the small sample size. Of note is the fact that a recent randomized prospective trial by Harvey and coauthors\textsuperscript{97} showed equivalent results for patients treated with early enteral versus early parenteral nutrition. Thus, there was no advantage for the use of early parenteral nutrition in critically ill patients. A detailed discussion of nutritional support of surgical patients is presented in SRGS, Volume 39, Number 7.

Use of diagnostic imaging

Findings on plain chest radiographs and plain abdominal films are nonspecific. Pleural effusion may be present with pancreatitis and the abdominal film may disclose midabdominal dilated small bowel loops (sentinel loop sign). Clinical practice guidelines recommend the use of abdominal ultrasound in patients with acute pancreatitis as a means of detecting gallstones.\textsuperscript{83} Computerized tomography imaging and MRI are useful for detecting choledocholithiasis and to demonstrate peripancreatic inflammation. Computerized tomography imaging is useful for predicting severity of pancreatitis and CT imaging scoring systems are discussed in a subsequent section. Computerized tomography imaging with contrast is most useful later in the course of the disease to document the presence of pancreatic necrosis, according to data cited by Wu and Banks\textsuperscript{78} and Baron.\textsuperscript{81}

The use of imaging to detect pancreatic necrosis is discussed by Dellinger and coauthors.\textsuperscript{92} The analysis of the opinions surveyed showed that there was agreement that CT imaging was the best means of documenting pancreatic necrosis, but there was no uniform agreement on the proportion of pancreatic and peripancreatic tissue with imaging evidence of necrosis (nonenhancement) necessary to support a diagnosis of pancreatic necrosis. Because of the lack of agreement, the authors decided that any evidence of pancreatic or peripancreatic necrosis observed on CT images would be recommended as a definition of pancreatic necrosis. The expert opinions gathered in the survey were in agreement that the presence of gas bubbles within areas of pancreatic necrosis defined the presence of infection. The authors note that serum levels of procalcitonin have shown promise for diagnosing infected pancreatic necrosis especially in patients with evidence of organ failure, but the accuracy of this assay is insufficient to support a recommendation for its use.

A review of the use of imaging for the diagnosis of pancreatitis is by Kim and Pickhardt\textsuperscript{98} in Surgical Clinics of North America, 2007. This article has a clear discussion of imaging strategies for acute as well as chronic pan-
Acute pancreatitis and contains several clear and helpful imaging photographs. These authors note that initial CT imaging of patients suspected of having pancreatitis can delineate the presence of pancreatic abnormalities and also assist in excluding other processes that may present with similar clinical findings. As the severity of pancreatitis progresses, edema of the pancreas causes loss of normal architecture of the pancreas on CT imaging. The borders of the gland become indistinct. Hazy, soft tissue stranding may be present and, as severity increases, stranding may extend from the pancreas into adjacent retroperitoneal tissues. Necrosis of the pancreas and adjacent tissue produces zones of low attenuation due to nonenhancing parenchymal tissue. The presence of gas bubbles within the pancreatic parenchyma suggests infection and should stimulate additional interventions for diagnosis and treatment. These alternatives are discussed in later sections of the overview dealing with infected pancreatic necrosis.

Computerized tomography is helpful for the evaluation of acute peripancreatic fluid collections. The images will demonstrate the characteristics of the tissue surrounding the fluid collection and document the changes in these tissues that indicate the formation of a mature wall around a pseudocyst. Computerized tomography imaging has a therapeutic arm as well since CT-guided needle aspiration of pancreatic fluid with microbial cultures can be used to document the presence of infection and CT-guided drainage can be used to drain pancreatic abscesses. These issues are discussed in more detail later when the management of severe pancreatitis and its complications are reviewed. Kim and Pickhardt\(^8\) close their discussion of the use of imaging for acute pancreatitis by noting that angiography can be used to diagnose erosion of the inflammatory process into an adjacent artery and angiographic embolization can be a valuable adjunctive treatment for acute bleeding from these complications.

Additional data about imaging of acute pancreatitis is found in an article by Koo and coauthors\(^9\) in the British Journal of Radiology, 2010. This article provides a useful discussion of a widely used CT scoring system for pancreatitis (Balthazar score). Five grades of changes observed on CT images of the pancreas are delineated grades A–E. Grade A is a normal gland, grade B denotes pancreatic enlargement, grade C pancreatic inflammation and/or peripancreatic fat necrosis, grade D is defined as a single peripancreatic fluid collection, and grade E is defined as two or more fluid collections and/or the presence of retroperitoneal air. Points are assigned to each category with 0 points for grade A to 4 points for grade E. Koo and colleagues provide a detailed description of CT-guided interventions for the management of pancreatic infected necrosis. They note that use of these procedures can provide drainage and irrigation of areas of suspected infected necrosis. In many situations, these procedures can substitute for open debridement of infected pancreatic necrosis. This topic is discussed in more detail later in the overview.

**Impact of infection on severity and mortality**

Local and systemic inflammation is a central pathologic feature of acute pancreatitis. Extensive pancreatic and peripancreatic necrosis can occur and remain stable, but Baron\(^8\) notes that the risk of infection increases with increasing extent of necrosis. Patients with necrosis of 30% or less of the pancreas have a 22.5% chance of developing infection within the necrotic tissue and this risk approaches 50% if more than half of the pancreatic mass is involved with necrosis. Although necrosis can exist without increasing patient mortality risk, the factor that is most closely associated with the risk for multiple organ dysfunction, systemic sepsis, and mortality is infection of the local inflammatory process, infection in another site (pneumonia), and bacteremia.

The influence of infection on outcomes for acute pancreatitis is the focus of an article by Besselink and coauthors\(^10\) in the British Journal of Surgery, 2009. This analysis was a medical record review of 711 patients with acute pancreatitis. Specific diagnostic criteria were established for the diagnosis of bacteremia (two or more positive blood cultures disclosing the same organism). Diagnostic criteria were established for infected pancreatic necrosis (positive cultures of peripancreatic fluid concomitant with systemic signs of infection). Pneumonia was defined as a positive sputum culture along with an infiltrate present on chest radiograph or lowered oxygen saturation, cough, and/or dyspnea. Bacteremia and pneumonia were diagnosed usually within the first 10 days after admission. Infected pancreatic necrosis was diagnosed at a median
of 26 days. Organisms recovered represented a variety of gram-positive and gram-negative organisms typical of those recovered from critically ill patients. An infection was diagnosed in 171 patients. Sixty-one patients died and 80% of these had a history of at least one infection. Bacteremia was significantly associated with the risk for infected pancreatic necrosis. Overall mortality was 16%; if bacteremia occurred along with infected pancreatic necrosis, the risk of death increased to 40%. On multivariate analysis, factors predictive of death were older age, bacteremia, and persistent organ failure. Based on these data, the authors recommend early efforts to prevent infection, especially bacteremia. Readily available interventions include resuscitation and reoxygenation along with early enteral nutrition. Given ongoing concerns about the emergence of resistant organisms, preemptive antibiotic therapy should be used selectively and with culture and sensitivity guidance, if possible.

Additional data confirming the importance of infection and subsequent organ failure as drivers of adverse outcomes in patients with pancreatitis are found in an article by Petrov and coauthors in *Gastroenterology*, 2010. These authors conducted a systematic review of available literature to determine whether infection or organ failure is the main determinant of mortality and morbidity in patients with severe pancreatitis. The authors identified 14 studies involving nearly 1,500 patients. The analysis disclosed that both organ failure and infection were associated with mortality rates in excess of 30%. There was no difference discovered when patients with infection without organ failure or organ failure without infection were compared. Notably, patients with both organ failure and infection had a significantly higher mortality risk (43%). The authors concluded that the presence of infection and organ failure should prompt aggressive management of both conditions, including percutaneous and open approaches for drainage and debridement.

Because infection, especially bacteremia, is an important apparent driver of outcomes in pancreatitis, it raises the question of the potential value of preventive antibiotic therapy. Three systematic reviews of the literature have examined this question. The first is by Bai and coauthors in *The American Journal of Gastroenterology*, 2008. These authors evaluated seven trials involving 467 patients. All trials were randomized and compared intravenous antibiotics to either placebo or no therapy. The data disclose no significant reduction in the frequency of infected pancreatic necrosis. Mortality rates decreased in groups treated with antibiotics but this reduction was not significant. The second systematic review is by Jafri and coauthors in the *American Journal of Surgery*, 2009. These authors reviewed articles in all languages and identified eight acceptable studies involving 502 patients. All included studies were placebo controlled. The analysis disclosed no protective effect on mortality or the risk of infected pancreatic necrosis. The authors stress that the persistent reports of the emergence of resistant strains of bacteria, especially involving infections in the critically ill, suggest that preventive antibiotics should not be used in patients with pancreatitis.

The final systematic review is by Wittau and coauthors in the *Scandinavian Journal of Gastroenterology*, 2010. These authors included 14 trials that enrolled 841 patients. This analysis did not disclose a significant benefit of preventive antibiotics in terms of mortality or the risk of infected pancreatic necrosis. Wittau and colleagues stress that they could not guarantee that early drug therapy occurred in all their trials but the overwhelming majority of the studies indicated that preventive drug therapy was instituted within five days. The authors conclude that there is no convincing evidence of benefit from preventive antibiotic therapy in patients with acute pancreatitis even when the drugs are administered early in the course of pancreatitis.

As mentioned previously, observation of gas bubbles within areas of pancreatic necrosis is highly suggestive of infection within the area of necrosis. If the clinical status of the patient suggests the presence of infection (fever, leucocytosis, presence of systemic inflammatory response syndrome, persistent or worsening organ failure), but imaging does not provide confirmation of the diagnosis of infected pancreatic necrosis, CT-guided fine-needle aspiration of the area of pancreatic necrosis is recommended in the article by Baron. If clinical evidence of infection does not improve with systemic antibiotic therapy, percutaneous or open drainage of the area of pancreatic necrosis is indicated.

Recent data have confirmed the safety and effectiveness of endoscopic transgastric drainage of infected pancreatic necrosis. These data are the focus of an ar-
article by Bakker and coauthors\textsuperscript{105} in \textit{JAMA}, 2012. The authors present results of a randomized, prospective trial comparing endoscopic transgastric drainage of infected pancreatic necrosis with open debridement and drainage. The authors note that the main disadvantage to surgical necrosectomy and drainage for patients with suspected infected pancreatic necrosis is the frequent worsening of the inflammatory response and progression of organ failure that follows the procedure. They note that a variant of natural orifice transluminal endoscopic surgery (NOTES) is endoscopic transgastric drainage of the area of infected pancreatic necrosis. Data were available on 20 patients. The primary endpoint was the post-procedure inflammatory response as indicated by serum levels of interleukin-6. The secondary endpoint was a composite of new major complications or mortality. The analysis showed that the inflammatory response was significantly less in the patients treated endoscopically and the secondary endpoint occurred significantly less often in this patient group. The authors acknowledge an important limitation of their study in that the surgical patients were subjected to one or more attempts at percutaneous drainage that failed to result in improvement before they underwent open necrosectomy. This fact could have contributed to the increased inflammatory response that followed the open procedures. Nonetheless, the results strongly suggest, that the less invasive approach is safer than the open surgical approach and just as effective.

\textbf{Biliary pancreatitis}

Duncan and Riall\textsuperscript{1} note that gallstone pancreatitis is mild in most patients and that common bile duct stones pass into the duodenum spontaneously in most patients. Thus, for patients with mild pancreatitis and gallstones, ERCP is not recommended, but early cholecystectomy is an effective and safe approach in patients who are acceptable operative risks. The authors supply a useful treatment algorithm for patients with gallstone pancreatitis. This algorithm is reproduced as Figure 14. In high-risk patients who are not operative candidates, ERCP with sphincterotomy reduces, but does not eliminate, the risk of recurrent pancreatitis and hospital admission for gallstone-related complications. Wu and Banks\textsuperscript{78} emphasize that patients with severe gallstone pancreatitis who have clinical evidence of bile duct obstruction and/or cholangitis should undergo ERCP and sphincterotomy within 24 hours of the diagnosis of severe pancreatitis or biliary obstruction/cholangitis.

The clinical presentation of gallstone pancreatitis is identical to other forms of acute pancreatitis (as discussed earlier). Transabdominal ultrasound is used to identify gallstones or dilation of the common bile duct. Endoscopic ultrasound is useful as a minimally invasive method to detect gallstones and guide the decision process for use of ERCP and laparoscopic cholecystectomy. Data pertinent to the decision process for choosing early endoscopic intervention versus conservative therapy for patients with biliary pancreatitis are found in two articles discussed here. The first article is by Oria and coauthors\textsuperscript{106} in \textit{Annals of Surgery}, 2007. In this article, patients with acute pancreatitis and signs of biliary obstruction as judged by bile duct dilation on imaging and elevated liver chemistries were randomized to receive either early (within 48 hours of admission) ERCP with sphincterotomy (51 patients) or conservative therapy (52 patients). All patients underwent laparoscopic cholecystectomy with intraoperative cholangiography were performed during the same hospital. When the groups were compared, there were no differences in severity assessment for pancreatitis (17 patients in the early endoscopy group and 21 patients in the delayed group had severe pancreatitis according to CT image scoring). The analysis disclosed biliary stones in 72% of patients undergoing early ERCP and 40% of patients in the group that did not undergo ERCP had stones documented at the time of laparoscopic cholecystectomy. There was no difference in the frequency of local complications (necrosis, abscess, pseudocyst) in the two groups. No ERCP complications were encountered. There were no significant changes in organ failure scores in the two groups over the first 5–7 days of hospitalization. The authors stress that they excluded patients with signs of cholangitis, and, therefore, the patient group studied included patients that many clinicians would choose for early, conservative therapy. The authors concluded, based on these data from relatively good-risk patients, that early endoscopy offers no advantage in the management of biliary pancreatitis.
Additional data relevant to the early management of patients with biliary pancreatitis are found in a systematic review of the literature by Petrov and coauthors\textsuperscript{107} in *Annals of Surgery*, 2008. These authors reviewed available trials with sufficient quality to determine the value of early ERCP in patients with acute biliary pancreatitis without clinical evidence of cholangitis. They were able to identify seven randomized trials involving 450 patients and the patients were equally divided between the early endoscopy and conservative therapy arms. The data analysis disclosed that there was no significant advantage to the use of early ERCP. This conclusion did not change when patients were stratified according to severity of pancreatitis. The authors concluded that patients with biliary pancreatitis without evidence of cholangitis can be successfully managed with early supportive care without ERCP.

The timing of cholecystectomy in patients with biliary pancreatitis is the focus of a systematic review of the literature by an article by van Baal and coauthors\textsuperscript{108} in *Annals of Surgery*, 2012. The authors identified nine studies with acceptable quality (one prospective randomized trial) involving more than 900 patients. The data analysis showed that readmission for gallstone-related problems within the first four months after the diagnosis of pancreatitis was observed in 18% of patients who had interval cholecystectomy compared with none of the patients who underwent cholecystectomy during the index admission. Perioperative mortality was zero in both groups and there was no difference in morbidity rates. The authors concluded that cholecystectomy was safe and effective during the index admission and that this strategy lowered the risk of early gallstone-related disease recurrence.

Additional data on this topic are presented by Aboulian and coauthors\textsuperscript{109} in *Annals of Surgery*, 2010. These authors report a consecutive case series of patients with mild pancreatitis as defined by Ranson scores on admission of <3 who were randomized to early cholecystectomy (within 48 hours of admission) or nonoperative management. The analysis stopped at an interim point because patients randomized to early cholecystectomy had median hospital lengths of stay of three days compared to median length of hospital stay of four days in the nonoperative group. The authors concluded that patients who are acceptable operative risks and who have mild biliary pancreatitis can be successfully managed with early cholecystectomy.

**Pancreatitis during pregnancy**

Pancreatitis is an unusual complication of pregnancy. Pancreatitis in the pregnant patient is challenging because a significant proportion of these patients emerge during the first trimester of pregnancy and distinguishing mild pancreatitis from hyperemesis gravidarum can be a challenge. A single review article dealing with this problem is by Pitchumoni and Yegneswaran\textsuperscript{110} in the *World Journal of Gastroenterology*, 2009. The authors note that reports of the prevalence of pancreatitis during pregnancy vary widely. Recent data from the U.S. cited by these authors noted 1/3,300 live births in one study and 1/1,500 live births in another study. Given data supporting the fact
that the frequency of acute pancreatitis is rising in the U.S., an increase in cases of pancreatitis associated with pregnancy is expected. The authors note that pancreatitis in pregnancy is most often related to biliary stone disease and that the management approach to these patients can be chosen based on the severity of pancreatitis. Endoscopic ultrasound is an accurate diagnostic tool for documenting the presence of bile duct stones without the need for radiation. The important questions facing the clinician caring for a pregnant patient with pancreatitis are to establish the diagnosis, determine whether biliary stone disease is present, estimate the severity of the pancreatitis, and select a management approach appropriate for the trimester of pregnancy. Patients seen in the first trimester of pregnancy are managed with supportive care. If endoscopic ultrasound shows choledocholithiasis and there is severe pancreatitis with persistent bile duct obstruction, ERCP or laparoscopic exploration of the biliary ductal system may be unavoidable. Supportive therapy with intravenous fluids and enteral nutrition are employed to attempt to postpone direct intervention until the second trimester. Pancreatitis not due to biliary tract disease is managed supportively as noted above. Data cited by these authors indicate that optimal management is associated with no mortality in the mother and a fetal loss of less than 5%, based on current literature.

**Alcoholic pancreatitis**

Alcoholic pancreatitis as a clinical entity presents along a continuum of symptom severity similar to other forms of pancreatitis. Whitcomb in a review article in the *New England Journal of Medicine*, 2006, notes that a key issue in patients with alcoholic pancreatitis is to institute a program to control habitual and binge drinking. Both patterns of alcohol use lead to an increased risk of pancreatitis. Successful clinical management of a severe case of alcoholic pancreatitis may require critical care management of alcohol withdrawal along with measures to manage pancreatitis. Intervention to document the importance of alcohol as a cause of the pancreatitis and institution of inpatient efforts to educate the patient about the likelihood of alcohol use as a cause of the disease are important. Detailed discharge planning is essential to make sure that the intervention to prevent continued alcohol use continues after discharge from the hospital.

**Ischemic pancreatitis**

Ischemic pancreatitis is a highly lethal complication of low-flow states or mesenteric ischemia. A case series reviewing this entity is by Hackert and coauthors in the *American Journal of Surgery*, 2009. These authors present a retrospective medical record review of 11 patients seen over a four-year interval. The diagnosis of ischemic pancreatitis involved 8% of all patients diagnosed with pancreatitis in the authors’ institution during the same interval. Hypotension leading to ischemic pancreatitis followed an episode of severe postpartum hemorrhage and it was seen in several patients following cardiopulmonary bypass. Four of their patients had ischemic pancreatitis due to occlusion of a major mesenteric vessel. The authors note that diagnosis is often difficult because of inability to document abdominal pain and tenderness in a sedated patient. They stress the value of CT imaging as a means of detecting the pathologic changes in the pancreas. Six of the 11 patients died despite maximum critical care and aggressive surgical approaches to the management of pancreatic necrosis. Observation of the high mortality rate supports the fact that these patients were compromised due to multisystem critical illness. The authors conclude by emphasizing the need for a high index of suspicion in patients with abdominal pain and elevated pancreatic enzymes in the setting of mesenteric ischemia and a low-flow state.
Management of severe pancreatitis

Severe pancreatitis is defined according to clinical and imaging scoring systems. This variant of pancreatitis is complicated by pancreatic necrosis and infection leading to critical illness, organ failure, sepsis, and a reported mortality risk ranging from 20%–40%. The traditional approach to pancreatic necrosis in patients with critical illness and organ failure is open debridement of the necrotic peripancreatic tissue, placement of drainage/irrigation catheters, and an open abdomen managed with dressings or, more recently, vacuum-assisted temporary closure. The main indication for an open debridement approach is suspicion of peripancreatic infection (gas bubbles in the area of pancreatic necrosis seen on CT scan and/or positive cultures recovered on needle aspiration of peripancreatic fluid) that is unresponsive to antibiotic therapy and percutaneous drainage attempts. The open approach is frequently complicated by bleeding and worsening organ failure. There is a need for repeated operation leading to prolonged hospital stay and the complications of an open abdomen. These observations have led some clinicians to question whether the open debridement approach is needed in all patients with pancreatic necrosis and suspected infection or persistent organ failure. Good results gained from studies of minimally invasive and percutaneous drainage procedures have supported the use of a graded approach to this set of problems. Several articles dealing with this subject are reviewed in this section of the overview.

Pancreatic necrosis and pancreatic abscess

The current approach to management of pancreatic necrosis and infected pancreatic necrosis grades patients according to the severity of illness. Patients are treated with aggressive supportive therapy consisting of fluid resuscitation, support of organ function, enteral nutrition, and assessment of the extent of pancreatic necrosis by CT imaging. Baron recommends the use of endoscopic or percutaneous drainage of pancreatic necrosis that is persistent, associated with organ failure, or the cause of symptoms such as gastric outlet syndrome.

A metaanalysis of available data on the use of endoscopic transmural debridement of pancreatic necrosis is by Puli and coauthors in the Canadian Journal of Gastroenterology and Hepatology, 2014. The authors identified eight studies involving 233 patients. The mean number of endoscopic debridement procedures necessary to control the pancreatic necrosis was four; mean length of hospital stay was 32 days. Recurrence of necrosis was observed in 11% of patients and open surgical debridement was ultimately required in 13% of patients. Complications were observed in 22% of patients and some of the more severe complications included bleeding, perforated viscus, and sepsis. These were reflective of the high-risk patients included in the analyzed studies. Overall, the endoscopic approach was successful in 81% of patients. The authors concluded that the endoscopic approach to pancreatic necrosis was safer and more effective than open approaches.

An important study analyzing the value of a graded, minimally invasive approach to pancreatic necrosis is by van Santvoort and coauthors in the New England Journal of Medicine, 2010. An editorial by Warshaw accompanies this article. Van Santvoort and colleagues conducted a randomized prospective trial that assigned patients with pancreatic necrosis and suspected or confirmed infection of the necrotic tissue to management with open necrosectomy or a “step-up” approach consisting of percutaneous drainage or retroperitoneal minimally invasive debridement and drainage. The authors note that open necrosectomy is the traditional approach to infected pancreatic necrosis. They note that this approach has been described in several articles that report mortality rates varying from 11%–40%. Complications such as bleeding, enterocutaneous fistula, and long-term pancreatic insufficiency have also been reported, according to data cited by these authors. In this study, infection was defined as a positive needle aspiration of peripancreatic fluid, positive culture of debrided pancreatic tissue, or the presence of gas in peripancreatic tissue on CT imaging. Suspected infection was defined as persistent sepsis or progressive clinical deterioration despite maximum supportive care. Patients with chronic pancreatitis or a prior drainage operation were excluded from the analysis. Patients undergoing open
necrosectomy had a standard anterior transperitoneal approach. Patients treated with the step-up approach had, first, percutaneous drainage via the left retroperitoneal approach with catheters placed for drainage and irrigation. If no improvement occurred over the subsequent 72 hours, a minimally invasive, video-assisted left retroperitoneal debridement was performed. The laparoscope was inserted along the tract of the previously placed, left retroperitoneal drain and loosely adherent necrotic tissue was debrided with irrigation assistance. Eighty-eight patients were randomized, 45 to the open necrosectomy group and 43 to the step-up approach. There was no significant difference between the groups with regard to age, gender, etiology of pancreatitis, body mass index, ASA score, or indices of pancreatitis severity or extent of necrosis. Critical illness scores were similar in both groups.

The authors chose a composite endpoint that combined mortality and major complications. They found that when mortality was examined in isolation, there was no difference between the groups. Open necrosectomy was associated with a significant increase in complications so this led to a statistical advantage, in terms of the composite endpoint, for the step-up approach. The authors noted a reduction in the frequency of new-onset organ failure in the step-up group.

In the editorial that accompanies this article, Warshaw\textsuperscript{115} emphasizes that stable patients with pancreatic necrosis, even if it is extensive, do not require debridement. Furthermore, the best results from debridement are realized in patients where operation can be delayed until 4–6 weeks after the acute episode of pancreatitis. In reviewing the article by van Santvoort and colleagues, he notes 19 institutions gathered 88 patients who were randomized from a group of 378 patients initially considered eligible for enrollment. He stresses further that the primary benefit of the step-up approach was realized from a reduction in complications. More than one-third of the randomized patients required only the initial percutaneous drainage procedure. Warshaw notes that these limitations to the study should not detract from the fact that the study confirms the value of a graded approach to patients with severe pancreatitis and suspected infection.

The article by van Santvoort and associates stimulated two letters to the editor of the New England Journal of Medicine that I have selected for additional discussion. In the first letter, de Waele\textsuperscript{116} stresses that identification of patients who will not respond to percutaneous drainage/debridement is an important clinical task. Tailoring the intervention to the needs of the individual patient may be preferable to the sequential step-up approach. In the second letter, Steinberg\textsuperscript{117} notes that the failure to reduce mortality is disappointing. In addition, he notes that there were significant complications (bleeding, enterocutaneous fistula) in the minimally invasive group even though seen less often than in the open necrosectomy group. In their reply to these letters, van Santvoort and coauthors note that the mortality reported is similar to mortality rates found in other reports. They note that the approach they used is applicable to 98% of patients with severe pancreatitis, pancreatic necrosis, and suspected infection.

Recent articles have tended to confirm the findings in the van Santvoort study that a graded approach emphasizing minimally invasive techniques is safe and effective in the management of patients with suspected infected pancreatic necrosis. A systematic review of the literature by van Baal and coauthors\textsuperscript{118} was reported in the British Journal of Surgery, 2011. This analysis identified 11 studies involving 384 patients. Organ failure was present in more than two-thirds of the patients included in the analysis. The authors noted that percutaneous drainage was the only intervention necessary for 56% of patients. In patients treated with percutaneous drainage techniques, the mortality ranged from 15%–17%.

When localized collections of potentially infected peripancreatic fluid (pancreatic abscess) can be identified, minimally invasive measures are also valuable. An article dealing with the use of endoscopic ultrasound as a means of identifying these collections is by Seewald and coauthors\textsuperscript{119} in Digestive Endoscopy, 2009. These authors reviewed available literature and determined that the success rate of endoscopic ultrasound-guided transgastric or transduodenal endoscopic drainage of localized pancreatic abscesses was 92%. The authors stress that the abscess should have a mature wall and be located within 1 cm of the gastric wall. Similar success rates are reported in an article by Vitale and coauthors\textsuperscript{120} in Surgical Endoscopy, 2008. In this article transgastric, transduodenal, or combined transluminal and transpapillary endoscopic drainage approaches were successful in 80% of a group of 35 patients with pancreatic abscesses.
One of the main limitations of the graded, minimally invasive approaches to pancreatic necrosis and infected pancreatic necrosis is the need for multiple procedures. A potentially valuable alternative approach is described in an article by Worhunsky and coauthors in the *Journal of the American College of Surgeons, 2014*. This article is supplied as a full-text reprint accompanying some formats of SRGS. The authors report a single-center experience with 21 patients who had significant symptomatic pancreatic necrosis located in the retrogastric region. The authors approached the area of necrosis using a laparoscopic transgastric technique. Ports were placed into the gastric lumen using openings placed in the anterior wall of the stomach. These openings were made laparoscopically with inflation of the stomach accomplished endoscopically. An opening in the dorsal gastric wall was made using the intragastric ports and debridement of the necrotic area was carried out. The authors note that successful debridement resulting in resolution of the necrosis symptoms occurred in 19 of the 21 patients. There was one postoperative death. Severe complications occurred in six patients; the most significant of these was postoperative bleeding requiring angiembolization. Mild complications occurred in 15 patients. All surviving patients were discharged by 14 days postoperatively. Over a follow-up interval of almost one year there were no instances of pancreatic fistula or wound complications observed. The authors concluded that the laparoscopic transgastric approach has potential value as a means of achieving debridement of symptomatic or infected pancreatic necrosis.

**Mesenteric venous thrombosis associated with acute pancreatitis**

A specific complication of acute pancreatitis with necrosis is mesenteric venous thrombosis that occurs as a complication of the inflammatory process. This complication can result in the formation of gastric varices that have been considered a risk for bleeding complications over long-term followup. An article presenting data on the clinical course of this complication is by Easler and coauthors in *Clinical Gastroenterology and Hepatology, 2014*. The authors present a retrospective medical record review of outcomes in 22 patients from a group of 122 patients admitted with a diagnosis of acute pancreatitis. All patients had undergone CT imaging and venous thrombosis was discovered in this way. Mesenteric venous thrombosis was in the splenic vein in more than 80% of patients. The superior mesenteric vein and portal vein were involved in 36% and 27%, respectively. Gastric varices were frequently seen on endoscopy, but no bleeding complications occurred over long-term followup. Repeat imaging studies during followup showed that thromboses did not recanalize.

A literature review relevant to this complication is by Nadkarni and coauthors in *Pancreas, 2013*. The review notes that mesenteric venous thrombosis is reported in 1%-24% of patients with acute pancreatitis and in 5%-37% of patients with chronic pancreatitis. The authors note that variceal bleeding was reported to be a frequent complication of mesenteric venous thrombosis in articles published before 1990, and recent articles have shown a risk for variceal bleeding in the range of 12%. The authors recommend the use of endoscopic ultrasound to determine the patency of mesenteric vessels and the use of CT or MRI for documentation of thrombosis and formation of collateral channels. If thrombosis is detected prior to the formation of collateral channels, anticoagulation may be helpful. The authors recommend the use of endoscopic ligation if variceal bleeding occurs and, given the low risk of variceal bleeding, preemptive splenectomy is not recommended.

**Pancreatic pseudocyst**

Peripancreatic fluid collections are common in patients with pancreatitis. When these are present during the acute phase of pancreatitis, no specific intervention is required so long as the fluid collections are asymptomatic and there is no suspicion of infection. Later in the course of the illness, mature walls may form around fluid collections and when this occurs, these collections are termed mature pseudocysts. Mature pseudocysts frequently communicate with the pancreatic duct indicating that ductal leakage is a significant contributor to the development of pseudo-
cysts. Intervention to drain a mature pseudocyst is usually indicated for mature pseudocysts that are symptomatic. Symptoms of mature pseudocysts include pain and signs of gastric or duodenal obstruction due to pressure from the pseudocyst on adjacent structures. Pseudocysts that are adjacent to major visceral arteries may become symptomatic due to erosion of the pseudocyst into the artery with hemorrhage into the cyst. A pseudocyst located in the splenic hilum may represent a high-risk setting for hemorrhage into the pseudocyst. In this section of the overview, we discuss the evaluation and management of acute and chronic peripancreatic fluid collections and pseudocysts.

**Acute peripancreatic fluid collections and pseudocysts**

Peripancreatic fluid collections can occur during the clinical course of acute pancreatitis. Most of these will resolve as the clinical condition improves. Pancreatic pseudocysts occur as a result of fluid collections that do not resolve but develop a fibrous wall surrounding the fluid collection. Pseudocysts also occur as a result of pancreatic ductal disruption with one or more walled off collections of ductal secretions. Ductal disruption that connects to an area of drainage of pancreatic necrosis or infection may result in external pancreatic fistula. Symptoms of fluid collections and pseudocysts are mainly from pressure of the fluid collection or pseudocyst on adjacent visceral structures. Pain, nausea, and vomiting can occur because of obstruction of the gastric outlet, duodenum, or colon due to a large fluid collection or pseudocyst.

An article examining risk factors for development of acute peripancreatic fluid collections is by Cui and coauthors in *Digestive Disease and Sciences*, 2014. The authors report data from a prospective, multicenter study involving 302 patients admitted with a diagnosis of acute pancreatitis. Acute peripancreatic fluid collections occurred in 43% of patients and pancreatic pseudocyst occurred in 6.3% of patients. All patients who developed pseudocysts had peripancreatic fluid collections diagnosed during the course of the episode of acute pancreatitis. Fluid collections resolved in 70% of patients and pseudocysts reduced in size over the course of followup in more than 80% of patients. Acute intervention was required for infection, bleeding, or obstructive symptoms in 10% of patients. Fluid collections and pseudocysts were more likely to occur in patients with alcoholic pancreatitis and in patients with elevated markers for systemic inflammatory response syndrome. The authors concluded that fluid collections and pseudocysts do not often require interventional therapy and resolve over time in most patients.

Another article dealing with acute fluid collections and pseudocysts is by Ocampo and coauthors in the *Journal of Gastrointestinal Surgery*, 2007. These authors defined an acute pseudocyst as one developing within four weeks of the acute pancreatitis episode. A treatment algorithm was developed for the management of patients who developed complications, such as bleeding, infection or perforation. The authors evaluated 43 patients with suspected complicated acute pseudocyst. The most common complication was infection of the pseudocyst. Perforation and bleeding occurred in 21% and 4.6% of patients, respectively. The overall mortality for a complicated pseudocyst was 19%. Percutaneous drainage was used to delay operation and permit stabilization of patients, and was successful in 11 of 13 patients. The authors conclude that an algorithm approach to acute complicated pseudocysts is safe and effective.

**Management of mature pseudocysts**

For symptomatic pancreatic pseudocysts adjacent to the stomach, open cystgastrostomy has been the traditional treatment approach. Recent data have confirmed the efficacy and safety of laparoscopic cystgastrostomy and endoscopic transmural cystgastrostomy. An article presenting data on the laparoscopic approach is by Khaled and coauthors in the *Journal of Hepato-Biliary-Pancreatic Sciences*, 2014. The authors report data from a retrospective case-matched, medical record review comparing outcomes in 30 patients who underwent laparoscopic cystgastrostomy with 10 patients matched for age, comorbid conditions, pseudocyst location and size, and etiology of pancreatitis. The data analysis showed that the laparoscopic approach was associated with shorter operative times and more rapid return to full function compared with the open approach. There was one postoperative death in the open group. Overall complications were significantly less in the laparoscopic group.
Another article describing laparoscopic techniques for management of symptomatic pancreatic pseudocysts is by Hamza and Ammori in the *Journal of Gastrointestinal Surgery*, 2009.\(^{127}\) The authors reviewed 30 patients treated with laparoscopic cyst enterostomy. The locations of the cysts and the laparoscopic techniques are clearly described. The approaches pertinent to cysts in various locations, particularly the splenic hilum, are illustrated. The authors observed successful cyst decompression in all patients. Two patients (7.1%) recurred at a mean followup of 15 months. Readers are encouraged to review the technical descriptions included in this article.

Outcomes of endoscopic cystgastrostomy are reported by Varadarajulu and coauthors\(^{128}\) in *Gastroenterology*, 2013. These authors compared outcomes of endoscopic transgastric cystgastrostomy with open cystgastrostomy in a randomized prospective clinical trial involving 40 patients randomized to receive open or endoscopic cystgastrostomy. The data showed that recurrence rates were not significantly different when the groups were compared. Hospital lengths of stay were shorter and overall costs were lower in the endoscopic group. At 24 months of followup, quality of life scores were significantly better in the endoscopic group.

An examination of the evidence supporting the approach to diagnosis and management of mature pancreatic pseudocysts is presented in an article by Cannon and coauthors\(^{129}\) in the *Journal of the American College of Surgeons*, 2009. The authors note that most pancreatic pseudocysts result from episodes of alcoholic pancreatitis with gallstone pancreatitis as the second most common preceding condition. The authors stress, however, that pancreatitis due to any cause can result in pseudocyst formation. The main factor contributing to the formation of pancreatic pseudocyst is ductal disruption. The authors emphasize that acute fluid collections are common during the initial four weeks following an episode of acute pancreatitis. Approximately 85% of these collections will resolve spontaneously with 5%–15% of collections forming symptomatic mature pseudocysts. Pseudocysts larger than 6 cm in diameter that persist for more than six weeks have been recommended for surgical therapy in older studies. More recent work has shown that asymptomatic pseudocysts of any size do not require intervention. The authors stress that when imaging studies disclose septations, or irregularities in the cyst wall, a cystic neoplasm should be suspected. Cystic neoplasms are discussed in the next issue of SRGS (Volume 41, Number 1).

The authors recommend that in patients with symptomatic pseudocysts, a definitive open or endoscopic intervention should be considered. Usually, ERCP is used to define the ductal anatomy immediately prior to the chosen intervention. Where communication of the pseudocyst with the duct system is demonstrated, transpapillary drainage may be successful. For pseudocysts adjacent to the stomach or duodenum, endoscopic transluminal drainage is feasible and effective. Laparoscopic cystenterostomy is also feasible and effective. The authors note that endoscopic drainage is used when there is a definable bulge noted endoscopically in the wall of the stomach or duodenum. Endoscopic entry into the cyst with placement of catheters to maintain an open communication is used.

A study by Cavallini and coauthors\(^{130}\) in *Surgical Endoscopy*, 2010, evaluated 55 patients with pseudocysts due to pancreatitis or complication of peripancreatic surgical procedure. Successful cure of the pseudocyst was achieved in 78% of patients. Complications, mainly superinfection of the cyst or bleeding, occurred in 16% of patients. One patient died following drainage. Recurrence of the pseudocyst was observed in 14% of patients and recurrence more commonly occurred in pseudocysts related to pancreatitis. The authors conclude that endoscopic therapy of pancreatic pseudocyst is feasible but significant complications and recurrences limit the wide application of this approach.

Cannon and coauthors\(^{129}\) note that percutaneous drainage may be useful for high risk patients, but laparoscopic or open cystenterostomy are the preferred approaches because external drainage is associated with persistent drainage and catheter complications.

An article comparing surgical with nonsurgical drainage of pseudocysts is by Johnson and coauthors\(^{131}\) in the *Journal of Clinical Gastroenterology*, 2009. The report reviews the medical records of 61 patients who had symptomatic pseudocysts. Thirty patients had surgical drainage and the remainder had endoscopic or percutaneous external drainage. Open surgical and endoscopic drainage procedures were equally effective (93% and 88% pseudo-
cyst resolution, respectively). The authors concluded that endoscopic and open procedures were equally effective for the management of symptomatic pancreatic pseudocysts.

Additional data regarding endoscopic drainage of symptomatic pseudocysts are found in an article by Guimaste and Aron\textsuperscript{132} in the Journal of Clinical Gastroenterology, 2010. These authors reviewed available literature and noted that transpapillary drainage of pseudocyst may be useful when a documented communication between the main pancreatic duct and the pseudocyst is present. This approach is feasible in only 30\%-60\% of pseudocysts. When used appropriately, the complication rate is low (10\%-20\%) and recurrence of the pseudocyst is observed in 10\%-20\% of patients. Endoscopic transluminal decompression is effective in more than 80\% of patients. Bleeding, infection, and retroperitoneal perforation are seen in up to 20\% of patients. The authors note that minimally invasive (laparoscopic) cyst enterostomy is associated with successful treatment of the pseudocyst in 97\% of patients. In patients who are acceptable operative risks, laparoscopic cystenterostomy is the most effective approach.

**Disconnected pancreatic duct**

Disconnected pancreatic duct is a challenging complication of pancreatitis. Pancreatic necrosis can cause disruption of the duct system because of collection of pancreatic fluid internally or the formation of an external fistula. When ductal disruption is detected, approaches to treatment vary depending on whether the disruption is detected acutely during and immediately after an episode of acute pancreatitis or detected later as a pseudocyst or pancreatic fistula. An article presenting a retrospective clinical experience with this entity is by Fischer and coauthors\textsuperscript{133} in the Journal of the American College of Surgeons, 2014. The authors present a useful clinical classification based on their experience. They note that ductal disruption that occurs during the late stages of pancreatic necrosis is an indication for necrosectomy. CT and MRI facilitate diagnosis in this patient group. Bleeding during necrosectomy may be reduced by preoperative splenic artery embolization. Patients with disconnected pancreatic ducts who present later during long-term followup with a pseudocyst or a fistula will benefit from cystenterostomy or distal pancreatectomy. Bleeding is a risk from distal pancreatectomy that can be reduced using preoperative splenic artery embolization. Disconnected pancreatic duct that complicates chronic pancreatitis can be treated with lateral pancreaticojejunostomy.

Pancreatic ductal disruption with fistula formation encountered as an acute complication of pancreatic necrosis has been treated with innovative endoscopic techniques. These techniques are described in an article by Irani and coauthors\textsuperscript{134} in Gastrointestinal Endoscopy, 2012. Interested readers are encouraged to review the content of this article.

**Sphincter of Oddi dysfunction and pancreas divisum**

One subset of idiopathic pancreatitis can be caused by ductal obstruction due to sphincter of Oddi (SOD) dysfunction. In this setting it is important to document obstruction with endoscopic sphincter of Oddi manometry. In patients where sphincter of Oddi hypertension is documented, sphincterotomy is effective treatment. A more challenging problem is pancreas divisum, which can cause ductal obstruction in the residual dorsal pancreatic duct and produce obstructive pancreatitis. This condition can occur in children and adults. A review of the use of ERCP in patients with acute pancreatitis includes a discussion of pancreas divisum. The article is by Canlas and coauthors\textsuperscript{135} in the World Journal of Gastroenterology, 2007. Canlas and colleagues note that SOD is a controversial condition because of the lack of concrete pathological findings that define the condition. The authors provide a description of three types of SOD. Type I is defined as typical biliary/pancreatic pain associated with pancreatic duct dilation and delayed emptying of the pancreatic and common bile duct. Type II consists of biliary pain, with one or two of the associated abnormalities noted above, and Type III is defined as pain without objective anatomic or physiologic findings. The patient group at highest risk of SOD is young women with biliary/pancreatic pain.
Patients with suspected SOD are managed initially with pharmacologic interventions such as antidepressant drugs, calcium channel blockers, anticholinergics, and analgesics. If persistent symptoms occur, endoscopy is indicated. The authors suggest that patients without imaging evidence of gallstones undergo endoscopy with endoscopic ultrasound. If no bile duct stones are identified, ERCP with bile sampling for microlithiasis is performed. If microlithiasis is not present, sphincter of Oddi manometry is performed. If a hypertensive sphincter is documented, sphincterotomy of both the pancreatic and bile ducts is performed.

Endoscopic sphincterotomy is a very effective intervention if high sphincter of Oddi pressure can be confirmed, especially in SOD Type I and II patients. If sphincter pressure is normal or if the patient has Type III SOD results are not as good. Sphincterotomy is further limited by settings in which the papilla is not accessible, such as following gastric resection with Billroth II reconstruction or after operation for morbid obesity. Although endoscopic and laparoscopic transgastric access to the papilla have been described for patients needing ERCP and sphincterotomy after obesity surgery,136-138 patients with difficult access to the papilla or with recurrent symptoms after endoscopic sphincterotomy are frequently referred for surgical management.

An article discussing outcomes of treatment for recurrent pain or difficult access is by Morgan and coauthors139 in the *Journal of the American College of Surgeons*, 2008. These authors present a retrospective medical record review with long-term followup assessed by a standard quality-of-life questionnaire in 68 patients seen over a 4-year interval in a single institution. Of the 68 patients, 51 had previously undergone endoscopic sphincterotomy. Seventeen patients could not have the papilla accessed because of previous gastric surgery. Open transduodenal sphincterotomy was done in all patients. There was no operative mortality; morbidity was observed in 10% of patients. The overall response rate for long-term followup was 66% and the mean followup interval was nearly 4 years. Forty-four patients had SOD and the remainder had pancreas divisum. Overall, 62% of the patients who had long-term data available had favorable responses with sustained improvement in pain. Ninety percent of the patients with prior gastric surgery had improvement, while 54% of the patients who had previously undergone endoscopic sphincterotomy responded. Good outcomes were more frequently observed in older patients. Improvement was observed in 90%–99% of patients who were over 50 years of age. The overall quality-of-life scores in the patients analyzed were slightly, but not significantly, lower than scores for healthy, age-matched controls.

Despite the overall good quality of life, 40% of patients reported that they required narcotic analgesics daily. Seventy percent of patients had returned to work. When patient data were analyzed by multivariate analytic techniques, younger age and the presence of chronic pancreatitis were both associated with worse outcomes. In the discussion that followed the presentation of the paper at the 2007 meeting of the Southern Surgical Association, the authors acknowledged that outcomes assessment was limited by the fact that data on 40% of the patients were missing. There were no data available on possible histologic differences in the sphincters of older versus younger patients.

In the next issue of *SRGS* (February 2015), we will review the evaluation and management of chronic pancreatitis, choledochal cyst, and neoplastic disease of the biliary tract and pancreas.


References | BILIARY TRACT & PANCREAS, PART I

References

References | BILIARY TRACT & PANCREAS, PART I


The posttest should be completed AFTER taking the pretest and reading the overview. Both tests must be completed online. See new log-in procedures for completing this CME test on page viii.

1. The number of cholecystectomies performed annually in the United States is which of the following?
   a) 750,000
   b) 2 million
   c) 100,000
   d) 450,000
   e) 5 million

2. Each of the following is associated with gallbladder stasis and an increased risk for gallstone formation except which one?
   a) Vagotomy
   b) Rapid weight loss
   c) Age < 30 years
   d) Prolonged total parenteral nutrition
   e) Somatostatin administration

3. Which of the following increases the risk of noncholesterol biliary stone formation?
   a) Male gender
   b) Obesity
   c) Pregnancy
   d) Age < 25 years
   e) Cirrhosis

4. Which of the following is the most common clinical manifestation of cholesterol gallstones?
   a) Acute cholecystitis
   b) Obstructive jaundice
   c) Abdominal pain
   d) Gallstone ileus
   e) Biliary pancreatitis

5. Sensitivity and specificity of abdominal ultrasonography for diagnosis of cholelithiasis is which of the following?
   a) 35%
   b) 95%
   c) 50%
   d) 65%
   e) None of the above

6. A 33-year-old woman is seen in the emergency department for right-sided abdominal pain. Abdominal ultrasound examination confirms the diagnosis of cholecystitis. Analgesics are prescribed and the patient is discharged. She returns with similar symptoms five weeks later. If cholecystectomy is not performed, which of the following is the risk for recurrence of symptoms?
   a) 15%
   b) 30%
   c) 45%
   d) 70%
   e) 100%
7. Laparoscopic cholecystectomy results in cure of gallstone symptoms in which proportion of patients?
   a) 40%
   b) 95%
   c) 76%
   d) 33%
   e) 52%

8. According to data published by Fry and coauthors, the overall 90-day mortality risk for Medicare patients undergoing elective cholecystectomy is which of the following?
   a) 0.5%
   b) 0.2%
   c) 4%
   d) 2%
   e) 7.5%

9. According to data published by Parmar and coauthors, each of the following is associated with increased risk for the development of complications of cholelithiasis in elderly patients except which one?
   a) Age > 75 years
   b) Female gender
   c) Initial presentation to an emergency department
   d) Initial presentation with complications of cholelithiasis
   e) Male gender

10. According to Strasberg, the “critical view” in laparoscopic cholecystectomy is defined as?
    a) Routinely obtaining intraoperative cholangiography
    b) Routine use of a 30-degree laparoscope
    c) Not dividing any structure until the cystic duct and cystic artery entry points into the gallbladder are clearly visible
    d) Perform routine preoperative endoscopic retrograde cholangiopancreatography (ERCP)
    e) Obtain routine preoperative isotope radioscintigraphy

11. Data published by Joseph and coauthors indicates that the rate of bile duct injury associated with single-incision laparoscopic cholecystectomy is which of the following?
    a) 15%
    b) 0.1%
    c) 4%
    d) 1.8%
    e) 0.7%

12. According to data from the case series reported by Pitt and coauthors, bile leaks were diagnosed in 45% of their patients. Endoscopic management was successful in which proportion of this patient group?
    a) 28%
    b) 96%
    c) 12%
    d) 65%
    e) 50%

13. Data from the report by Marks and coauthors indicate that single-incision laparoscopic cholecystectomy is associated with which of the following?
    a) Increased length of hospital stay
    b) Increased rate of postoperative pneumonia
    c) Increased rate of incisional hernia
    d) Similar rates of wound infection compared with multiple-incision laparoscopic cholecystectomy
    e) Increased need for postoperative analgesia

14. Data published by de Mestral and coauthors indicate that recurrence of biliary symptoms is observed in which percentage of patients diagnosed with acute cholecystitis who do not undergo cholecystectomy?
    a) 29%
    b) 2.5%
    c) 55%
    d) 11%
    e) 70%
15. The report by Duzsak and Behrman indicates that the region of the United States with the highest rate of use of percutaneous cholecystostomy is which of the following?

a) Southeastern region
b) Southwestern region
c) Pacific Northwest
d) Northeastern region
e) Rocky Mountain region

16. Data from the report by Petrov and Savides indicate that endoscopic ultrasound permitted omission of ERCP examination in what percentage of patients with suspected choledocholithiasis?

a) 10%
b) 34%
c) 6%
d) 67%
e) 21%

17. Data from the report by Rogers and coauthors indicate that the main advantage of one-stage laparoscopic cholecystectomy and common bile duct exploration compared with ERCP followed by laparoscopic cholecystectomy is which of the following?

a) Shorter hospital length of stay and lower overall cost
b) Decreased risk of postoperative myocardial infarction
c) Lower overall mortality
d) Reduced risk of postoperative pneumonia
e) Reduced risk of wound infection

18. Data from the report by Papachristou and coauthors indicate that the BISAP pancreatitis score is preferred because of which of the following?

a) Higher accuracy rate
b) Ease of use
c) Extensive use of CT results
d) Most valuable for patients less than 40 years of age
e) Accurate prediction of pseudocyst formation

19. The pancreatitis severity score described in the article by Dellinger and coauthors uses which of the following to determine pancreatitis severity?

a) Renal function and arterial blood gas analysis
b) Urinary lipase levels
c) Fever and leukocytosis
d) CT evidence of necrosis and persistent organ failure
e) Glasgow-Imrie score and Ranson criteria

20. Data from the report by Aitken and coauthors suggest which bladder pressure value as a useful threshold for initiating efforts to control intraabdominal pressure?

a) 25 mmHg
b) 4 mmHg
c) 16 mmHg
d) 3 mmHg
e) 9 mmHg

The following four questions are required by the American College of Surgeons for accreditation purposes. You must complete these four questions before submitting your answers.

21. This issue met the stated learning objectives.

a) Strongly agree
b) Agree
c) Neutral
d) Disagree
e) Strongly disagree

22. The content was relevant to my educational needs and practice environment.

a) Strongly agree
b) Agree
c) Neutral
d) Disagree
e) Strongly disagree
23. There are potential barriers to incorporating what I have learned from this issue into my practice.
   a) Strongly agree
   b) Agree
   c) Neutral
   d) Disagree
   e) Strongly disagree

24. The content was fair, objective, and unbiased.
   a) Strongly agree
   b) Agree
   c) Neutral
   d) Disagree
   e) Strongly disagree

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Lewis Flint, MD, FACS, Editor-in-Chief
Phone: 312-202-5224
E-mail: lflint@facs.org

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Lynanne Feilen, Managing Editor
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E-mail: srgs@facs.org

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