

Management of Gallstones

CHARLES F. BELLOWS, M.D., and DAVID H. BERGER, M.D., *Baylor College of Medicine, Houston, Texas*
RICHARD A. CRASS, M.D., *University of Florida Health Science Center, Jacksonville, Florida*

Many patients with gallstones can be managed expectantly. Generally, only persons with symptoms related to the presence of gallstones (e.g., steady, nonparoxysmal pain lasting four to six hours located in the upper abdomen) or complications (such as acute cholecystitis or gallstone pancreatitis) warrant surgical intervention. Biliary pain is alleviated by cholecystectomy in the majority of cases. Laparoscopic cholecystectomy is considered the most cost-effective management strategy in the treatment of symptomatic gallstones. Medical management strategies are mostly palliative and are not widely supported. Patients with longer-lasting biliary pain, in combination with abdominal tenderness, fever, and/or leukocytosis, require an ultrasound evaluation to help establish a diagnosis of acute cholecystitis. Once a patient is diagnosed, having cholecystectomy early in the course of the disease can significantly reduce the hospital stay. (*Am Fam Physician* 2005;72:637-42. Copyright© 2005 American Academy of Family Physicians.)

Gallstone disease affects 12 percent of the population in the United States. Several factors are associated with an increased occurrence of gallstone formation (*Table 1*). In a multivariate analysis¹ of more than 900 patients, researchers identified a family history of cholecystectomy in a first-degree relative and obesity (defined as body mass index [BMI] greater than 30 kg per m²) as strong risk factors for symptomatic gallstone disease with a relative risk of 2.2 (95% confidence interval [CI], 1.5 to 3.0) and 3.7 (95% CI, 2.3 to 5.3), respectively.

Weight loss patterns also are associated with symptomatic gallstones. Weight loss

of more than 1.5 kg (3.3 lb) per week has been associated with a higher rate of gallstone formation compared with rates of less than 1.5 kg per week.² In a large cohort³ of middle-aged women, one or more cycles of weight loss and gain of 9 kg (20 lb) or more was a strong risk factor for cholecystectomy independent of BMI, with a relative risk approaching 2.0 (95% CI, 1.3 to 2.1). Interestingly, epidemiologic evidence suggests that increased physical activity is associated inversely with the risk of gallstone formation. In a prospective cohort study,⁴ symptomatic gallstone disease in men was reduced by approximately 20 percent in those who increased their physical activity by 25 metabolic equivalents per week (i.e., at least 30 minutes per day five times a week).

In the United States, cholesterol stones are the most common type of gallstone, with pigmented stones occurring less often. The formation of cholesterol stones is a result of cholesterol supersaturation, accelerated cholesterol crystal nucleation, and impaired gallbladder motility. The majority of asymptomatic patients with gallstones will remain asymptomatic for many years. According to a 1992 National Institutes of Health consensus conference on gallstones,⁵ 10 percent of patients with gallstones will develop symptoms in the first five years after diagnosis. In 1995, the Group for Epidemiology and Prevention of Cholelithiasis reported that

TABLE 1
Risk Factors Associated with Increased Occurrence of Gallstones

Body habitus: obesity,* rapid weight loss, cyclic weight loss
Childbearing
Drugs: ceftriaxone (Rocephin), postmenopausal estrogens, total parenteral nutrition
Ethnicity: Native American (Pima Indian), Scandinavian
Female gender
Heredity: first-degree relatives
Ileal disease, resection, or bypass
Increasing age

*—Obesity defined as body mass index greater than 30 kg per m².

SORT: KEY RECOMMENDATIONS FOR PRACTICE

<i>Clinical recommendation</i>	<i>Evidence rating</i>	<i>References</i>
Patients with suspected cholelithiasis should have an ultrasound examination. If the index of suspicion remains high, a test of biliary dyskinesia such as a hepatobiliary iminodiacetic acid scan should be obtained.	C	8, 9
Watchful waiting is indicated for most patients with asymptomatic gallstones.	C	5, 6
Patients with biliary pain should have laparoscopic cholecystectomy on first open operative day.	B	10
Oral dissolution therapy is recommended only for patients who are unable or unwilling to undergo surgery.	C	5
Patients with acute cholecystitis should have a laparoscopic cholecystectomy early in their management course. This reduces the hospital stay but does not reduce the complication rate compared with delayed surgery.	A	12
Patients with gallstone pancreatitis should have a laparoscopic cholecystectomy during the same hospitalization.	A	20, 21

A = consistent, good-quality patient-oriented evidence; B = inconsistent or limited-quality patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, see page 555 or <http://www.aafp.org/afpsort.xml>.

initially asymptomatic patients with gallstones had a 25.8 percent probability of developing symptoms within 10 years.⁶

Once symptoms begin, recurrent pain is common, and complications such as cholecystitis and pancreatitis are more likely to develop. In a randomized clinical study⁷ comparing surgery with observation for patients with symptomatic, noncomplicated gallstone disease, approximately 20 percent of patients in the observation group had recurrent biliary pain requiring hospital admission. Furthermore, with a median follow-up of 67 months, 4 percent of patients in the observation group developed complications, compared with 1 percent in the surgery group.⁷

Evaluating Suspected Gallstone Pain

Determining which abdominal symptoms are related to gallstones is often a diagnostic challenge. Gallstone pain typically arises in the right upper quadrant of the abdomen; however, pain in this area is not specific for gallstones. The physician must rely on the patient's description of the pain and on the results of laboratory testing and diagnostic imaging to make a correct diagnosis. The differential diagnosis of right upper quadrant pain is summarized in *Table 2*.

Patients with typical biliary pain should be evaluated promptly using ultrasonography. This scan is noninvasive and cost-effective, involves no ionizing radiation, and has a reported specificity of 99 percent

TABLE 2
Differential Diagnosis of Pain in the Right Upper Quadrant of the Abdomen

<i>Disease</i>	<i>Pain characteristics</i>	<i>Tests</i>
Biliary pain	Steady, nonparoxysmal pain, rapidly increases in intensity then plateaus, lasts four to six hours, occasionally radiates to the right subscapular area	Ultrasonography
Acute cholecystitis	Longer lasting (more than six hours) biliary pain with tenderness, fever, and/or leukocytosis	Ultrasonography and/or HIDA scan
Dyspepsia	Bloating, nausea, belching, intolerance to fatty foods	Upper endoscopy
Duodenal ulcer	Pain two hours after meals, relieved by taking food or antacids	Upper endoscopy
Hepatic abscess	Pain associated with fever and chills; palpable liver and subcostal tenderness	Chest radiography (pleural fluid on right side) Abdominal CT scan
Acute myocardial infarction	Right upper quadrant or epigastrium discomfort; may be similar to biliary pain	Electrocardiography (abnormal) AST/ALT: AST less than 150 U per L and no elevation in AST

HIDA = hepatobiliary iminodiacetic acid; CT = computed tomography; AST= aspartate transaminase; ALT= alanine transaminase.

for the detection of gallstones.⁸ In a small number of patients, no objective evidence of gallstones will be found despite the presence of classic biliary pain. If there is a high index of suspicion for gallbladder disease, patients should undergo testing to rule out biliary dyskinesia. In the majority (94 percent) of patients with dyskinesia, symptoms improve or the disease is cured after cholecystectomy.⁹ Dyskinesia was defined by a gallbladder ejection fraction of less than 50 percent using a cholecystokinin cholecystoscintigraphy (hepatobiliary iminodiacetic acid) scan in conjunction with typical clinical symptoms.⁹

Surgical Treatment of Gallstone Disease

Cholecystectomy remains the primary procedure for the management of symptomatic gallstone disease. It is safe, has the lowest risk of recurrence, and provides 92 percent of patients with complete relief of their biliary pain.¹⁰ Indications for cholecystectomy are listed in *Table 3*. Laparoscopic cholecystectomy continues to have numerous advantages compared with the open technique (*Table 4*), and the safety of the laparoscopic approach to the treatment of gallstone disease in various patient populations is gaining clinical acceptance (*Table 5*).

Between 5 and 26 percent of patients undergoing elective laparoscopic cholecystectomy will require conversion to an open procedure.^{11,12} A common reason for conversion is the inability to clearly identify the biliary anatomy. In a recent meta-analysis,¹¹ researchers compared the outcomes of laparoscopic cholecystectomy for more than 78,000 patients in 98 studies with the outcomes of open cholecystectomy for more than 12,000 patients in 28 studies. The researchers found a decreased mortality rate in patients undergoing laparoscopic cholecystectomy compared with those undergoing open cholecystectomy (8.6 to 16 deaths per 10,000 patients versus 66 to 74 deaths per 10,000 patients, respectively) but also noted a higher rate of common bile duct injury (36 to 47 injuries per 10,000 patients versus 19 to 29 injuries per 10,000 patients, respectively).¹¹ Common bile duct injuries associated with cholecystectomy can be extremely difficult to repair, and management at a tertiary care center with surgeons experienced in biliary injuries should be strongly considered.¹³

Nonsurgical Treatment of Gallstone Disease

Oral dissolution therapy using bile acids has successfully dissolved gallstones in an extremely limited patient population. The clinical efficacy of bile acid therapy was determined in patients with symptomatic radiolucent gallstones smaller than 15 mm within a functioning gallbladder. In this study,¹⁴ a 56 percent reduction in biliary pain was reported

TABLE 3
Indications for Cholecystectomy

<i>Conditions*</i>	<i>When to perform surgery</i>
Biliary pain	First open operative day
Biliary dyskinesia	First open operative day
Calcified gallbladder	First open operative day
Acute cholecystitis	Urgent (within 72 hours)
Choledocholithiasis	After the common bile duct is cleared
Gallstone pancreatitis	Before discharge but after pancreatitis resolves

*—Only patients who are fit for surgery.

TABLE 4
Benefits of Laparoscopy over Laparotomy

Better cosmesis	Less postoperative pain
Earlier return to work	Less tissue damage
Lower costs	Shorter or no hospital stay
Lower mortality	

TABLE 5
Vanishing Contraindications to Laparoscopic Cholecystectomy

Acute cholecystitis	Obesity
Advanced age	Pregnancy‡
Chronic obstructive pulmonary disease*	Previous abdominal surgery
Cirrhosis†	

*—Excluding patients with severe chronic obstructive pulmonary disease.

†—Child class A and B cirrhosis only; laparoscopic cholecystectomy not indicated for end-stage cirrhosis.

‡—No prospective clinical trials of laparoscopic cholecystectomy in pregnant women have been conducted.

after three months and a mean gallstone dissolution rate of 59 percent occurred after 12 months of treatment with 10 mg per kg per day of ursodeoxycholic acid. Gallstone recurrence is a disadvantage of this treatment; approximately 25 percent of patients develop recurrent gallstones within five years.¹⁵ Presently, bile acid therapy is indicated only for patients unfit or unwilling to undergo surgery.⁵

Management of Common Gallstone Complications

ACUTE CHOLECYSTITIS

Acute cholecystitis develops in up to 10 percent of patients with symptomatic gallstones and is caused by the com-

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plete obstruction of the cystic duct.¹⁶ Delayed diagnosis of acute cholecystitis can lead to gangrenous cholecystitis, gallbladder perforation,

and biliary peritonitis. Data abstracted from 17 studies identified no individual clinical or laboratory finding with sufficient diagnostic power to rule in or rule out the diagnosis of acute cholecystitis without additional testing.¹⁷ Therefore, the diagnosis of acute cholecystitis must be made using a combination of clinical acumen and diagnostic imaging such as ultrasonography and cholecystoscintigraphy (*Tables 2 and 6*), which have reported sensitivities of 88 and 97 percent, respectively.⁸

Historically, early surgery for acute cholecystitis was discouraged. Patients were treated medically with intravenous fluid, antibiotics, and analgesics until the inflammation in the gallbladder resolved, and then elective cholecystectomy (delayed surgery) was per-

formed. However, more than 20 percent of patients fail to respond to medical management or experience recurrent cholecystitis during the intervening period.¹² Consequently, 12 prospective randomized trials examined whether early cholecystectomy could improve outcomes for acute cholecystitis compared with delayed surgery. A meta-analysis¹² of these trials found that early cholecystectomy (up to 72 hours after admission) significantly reduced the total hospital stay but not the overall complication rate when compared with delayed surgery (72 hours to 12 weeks after the acute event). Based on these findings, once the diagnosis of acute cholecystitis is made, the patient should be resuscitated with intravenous fluids, concomitant medical problems should be stabilized, and cholecystectomy should be performed at the earliest available time.

Patients with acute cholecystitis who are critically ill or otherwise at very high risk for surgical complications should be managed medically with intravenous fluid, antibiotics, and analgesics; if this treatment fails, a percutaneous cholecystostomy should be considered. This procedure has been shown to achieve clinical improvement in 80 percent of patients within five days after placement.¹⁸

The Authors

CHARLES F. BELLOWES, M.D., is assistant professor of surgery in the Michael E. DeBakey Department of Surgery at Baylor College of Medicine, Houston, and chief of laparoscopic surgery at the Michael E. DeBakey Veterans Affairs Medical Center, Houston. Dr. Bellows received his medical degree from the Medical College of Pennsylvania, Philadelphia. He completed a general surgery residency at Tulane University School of Medicine, New Orleans.

DAVID H. BERGER, M.D., is associate professor and vice chairman of surgery in the Michael E. DeBakey Department of Surgery at Baylor College of Medicine. Dr. Berger is also chief of surgery and operative care line executive at the Michael E. DeBakey Veterans Affairs Medical Center. He received his medical degree from the State University of New York Health Science Center at Brooklyn College of Medicine, where he also completed a general surgery residency. He completed a surgical oncology fellowship at the University of Texas M.D. Anderson Cancer Center, Houston.

RICHARD A. CRASS, M.D., is professor and associate chair of surgery at the University of Florida Health Science Center, Jacksonville, and chief of surgery at Shands Jacksonville Medical Center. Dr. Crass received his medical degree from Temple University School of Medicine, Philadelphia. He completed a general surgery residency at the University of California, San Francisco, School of Medicine. He received his masters in business administration from the University of Oregon, Eugene.

Address correspondence to Charles F. Bellows, M.D., Dept. of Surgery, Michael E. DeBakey VAMC, M/C112, 2002 Holcombe Blvd., Houston, TX 77030 (e-mail: cbellows@bcm.tmc.edu). Reprints are not available from the authors.

CHOLEDOCHOLITHIASIS

Gallstones can migrate from their primary site of origin in the gallbladder through the cystic duct and into the common bile duct. Up to 15 percent of patients have common bile duct stones in combination with gallbladder stones, but the majority (73 percent) of these stones will pass spontaneously into the duodenum without significant sequelae.¹⁹ Patients with common bile duct stones will most likely present with biliary pain, cholecystitis, or pancreatitis in combination with bile duct dilation (exceeding 8 mm), and/or elevated liver function tests.¹⁹

Essential elements for treating choledocholithiasis involve gallbladder removal and clearance of retained common bile duct stones. Results of a multicenter, prospective, randomized trial²⁰ comparing single-stage laparoscopic cholecystectomy and laparoscopic stone extraction with preoperative endoscopic retrograde cholangiopancreatography (ERCP) followed by laparoscopic cholecystectomy demonstrated that the procedures were equally effective in the clearance of common bile duct stones. However, the single-stage strategy reduced the mean hospital stay by three days. In another study,²¹ researchers used decision modeling to examine the cost-effectiveness of the most popular strategies for managing common bile duct stones. Using a single case of residual common bile duct stones that was avoided as

a unit of effectiveness, researchers were able to show that laparoscopic common bile duct exploration was the most cost-effective method of managing common bile duct stones, followed by intraoperative cholangiography with selective postoperative ERCP.²¹

GALLSTONE PANCREATITIS

Gallstones can trigger an attack of acute pancreatitis by transiently impacting in the duodenal papilla as they migrate down the common bile duct. Once gallstone pancreatitis occurs, recurrence is common, with 61 percent of patients who are discharged before cholecystectomy requiring readmission for recurrent attacks of pancreatitis.²² In addition, significantly more complications (such as lung infections, wound infections, and myocardial infarction) have been reported in patients who had recurrent biliary pancreatitis and then underwent cholecystectomy (43 percent) compared with those who underwent cholecystectomy on first admission (11 percent) for gallstone pancreatitis.²² In the same study,²² hospital stays increased significantly in patients who had recurrent biliary pancreatitis and then underwent cholecystectomy, compared with those who underwent cholecystectomy on first admission (37 versus 15 days, respectively). The current recommendation is for cholecystectomy to be performed during the same hospital admission.²³ However, performing cholecystectomy too early in the course of severe gallstone pancreatitis is unwise, and the International Association of Pancreatology recommends waiting for resolution of the pancreatitis and clinical recovery before considering biliary surgery.²³ The role of ERCP in reducing the complications of gallstone pancreatitis has been investigated. Results of the most recent multicenter trial²⁴ demonstrated that ERCP performed within 72 hours did not statistically reduce the overall complication and mortality rates compared with conservative treatment. Importantly, this study²⁴ excluded patients with evidence of biliary obstruction. Today, it is generally agreed that ERCP is not indicated for all patients with gallstone pancreatitis but is beneficial in patients with obstructive jaundice and/or biliary sepsis.

Conditions that May Affect Treatment

PREGNANCY

In women who are pregnant, medical management of symptomatic gallstone disease with intravenous fluids and analgesics has successfully ameliorated biliary symptoms

TABLE 6

Characteristics of Acute Cholecystitis Found on Ultrasonography and Cholecystoscintigraphy

<i>Ultrasonography</i>	<i>Cholecystoscintigraphy (HIDA)</i>
Tenderness directly over the gallbladder (ultrasonic Murphy's sign)	Nonvisualization of the gallbladder (indicates that the cystic duct is occluded)
Pericholecystic fluid	
Thickened gallbladder wall	

HIDA = hepatobiliary iminodiacetic acid.

in 64 percent of patients.²⁵ Although some studies^{25,26} have shown successful maternal-fetal outcomes following cholecystectomy at different stages of pregnancy, no prospective trials comparing early cholecystectomy with medical management in pregnant patients have been published. Therefore, surgery generally is reserved for pregnant patients with recurrent or unrelenting biliary pain refractory to medical management or with complications related to gallstones.

When common bile duct stones are suspected during pregnancy, radiographic imaging of the bile duct can be performed safely and effectively as long as the mother's pelvis is shielded, the fetus is monitored, and the fetal dose of radiation is less than 5 radiation-absorbed doses.^{27,28} However, conclusions about the safety of radiographic imaging are limited to patients in their second and third trimesters.

CIRRHOSIS

Patients with cirrhosis and asymptomatic gallstones should be monitored closely; when biliary symptoms first become apparent, patients with compensated cirrhosis (i.e., Child's class A or B) should be considered for a cholecystectomy. In a meta-analysis²⁹ of six studies comparing outcomes after cholecystectomy in patients with and without cirrhosis, patients with cirrhosis had no significant difference in mortality rate. However, overall complications such as liver bleeding and new-onset ascites were higher in patients with cirrhosis compared with those without cirrhosis (21 versus 8 percent, respectively). Although the studies on cholecystectomy in patients with Child class C cirrhosis are not large enough

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to yield significant results, unacceptably high mortality rates have been reported. Therefore, it is generally agreed that a more conservative approach is warranted in patients with Child class C cirrhosis and symptomatic gallstone disease, directing treatment toward improving their liver function before cholecystectomy.

Members of various family medicine departments develop articles for "Problem-Oriented Diagnosis." This is one in a series from the Department of Family Medicine at the University of Florida, Gainesville. Coordinator of the series is R. Whit Curry, Jr., M.D.

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