REVIEW ARTICLE

Evidence-based Guidelines for the Management of Acute Cholecystitis

Bryce B Patin¹, Jacob M Welsch², Christopher S Davis³

Received on: 10 November 2022; Accepted on: 12 November 2022; Published on: 31 December 2022

ABSTRACT

Aim: This review aims to highlight the current evidence-based guidelines for acute cholecystitis.

Background: Laparoscopic cholecystectomy is the procedure of choice for acute cholecystitis. The severity of cholecystitis and the patient's clinical status is heterogeneous. Many guidelines have been established to guide the preoperative and intraoperative management of acute cholecystitis. We provide an up-to-date appraisal of these guidelines and expert consensus recommendations.

Review results: Many preoperative considerations exist, including patient health status/risk stratification, the severity of cholecystitis, choice of antibiotics, etiology of cholecystitis, considerations for gravid mothers, and utilization of cholecystostomy tubes. Intraoperative considerations are similarly paramount, including the surgical approach, adjuncts, and grading of the severity of cholecystitis once in the operating room.

Clinical significance: The management of acute cholecystitis should never be viewed as routine, particularly regarding the heterogeneity of the patient's clinical status and severity of the disease process. Adherence to up-to-date, evidence-based, and expert consensus practice is critical to optimal outcomes for these patients.

Keywords: Acute cholecystitis, Cholecystectomy, Evidence-based management, Literature review. Panamerican Journal of Trauma, Critical Care & Emergency Surgery (2022): 10.5005/jp-journals-10030-1398

BACKGROUND

Cholecystectomy is the most common procedure performed by general surgeons worldwide and is nearly always the treatment of choice for both calculus and acalculous cholecystitis. Several guidelines have been recently published or updated to guide surgical management for a safe and preferably laparoscopic cholecystectomy for acute cholecystitis. This review provides an up-to-date synthesis of these recommendations, as well as the most salient considerations of managing acute cholecystitis, given the heterogeneity of individual patient factors and the severity of gallbladder (GB) disease.

MATERIALS AND METHODS

A systematic literature search was conducted in the PubMed electronic database [(acute cholecystitis) or (cholecystectomy) and (management) or (treatment)] or [(The American Association for the Surgery of Trauma (AAST)] or (Parkland grading scale) or [Charlson comorbidity index (CCI)] or [The American Society of Anesthesiologists (ASA)] or [The National Surgical Quality Improvement Program (NSQIP)] or [Tokyo Guidelines 18 (TG18)] or (surgical approach) or (acalculous) or (Mirizzi) or (risk stratification) or (evidence-based) to identify all relevant articles written in English discussing or reporting evidence-based management of acute cholecystitis. Two reviewers (BBP and JMW) independently screened the titles and abstracts of the articles and selected the potentially relevant publications. The methodological quality of the eligible studies was evaluated by the first reviewer (BBP) and verified by the second (JMW). Additionally, the reviewers consulted the reference list of all retrieved articles for increased information. Discrepancies were resolved by discussion and consensus, and if a disagreement persisted, a third reviewer (CSD) was consulted to make the final decision. If two studies reported

^{1,2}Medical College of Wisconsin, Milwaukee, Wisconsin, United States
³Department of Surgery, Medical College of Wisconsin, Milwaukee, Wisconsin, United States

Corresponding Author: Christopher S Davis, Department of Surgery, Medical College of Wisconsin, Milwaukee, Wisconsin, United States, Phone: +1 4149551707, e-mail: davici07@gmail.com

How to cite this article: Patin BB, Welsch JM, Davis CS. Evidence-based Guidelines for the Management of Acute Cholecystitis. Panam J Trauma Crit Care Emerg Surg 2022;11(3):169–175.

Source of support: Nil Conflict of interest: None

the same information, the more recent of the two was used. The aforementioned third reviewer (CSD) actively oversaw and was involved in all aspects of this review. The preferred reporting items for systematic reviews and meta-analyses guidelines were followed for all the steps reported in the study.

REVIEW RESULTS

Preoperative Considerations

Patient Health Status/Risk Stratification

The ASA score preoperatively calculates a patient's preoperative anesthetic risk by assessing their overall physical health. The ASA score is based on a 1–5 scale, with a score of 1 being equivalent to a physically healthy patient and a score of 5 being equivalent to a patient with 24 hours to live, irrespective of if they receive surgery.¹ ASA scores are generally predictive of surgical complications, short-term and long-term prognosis, time spent in surgery, length of stay (LOS), blood loss, overall morbidity and mortality, and resource allocation.² In acute cholecystitis, increased patient ASA scores are associated with increased operation

© The Author(s). 2022 Open Access This article is distributed under the terms of the Creative Commons Attribution 4.0 International License (https://creativecommons. org/licenses/by-nc/4.0/), which permits unrestricted use, distribution, and non-commercial reproduction in any medium, provided you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons license, and indicate if changes were made. The Creative Commons Public Domain Dedication waiver (http://creativecommons.org/publicdomain/zero/1.0/) applies to the data made available in this article, unless otherwise stated. duration, hospital LOS, morbidity, and surgical difficulty. For acute cholecystitis patients with ASA scores of 1–3, laparoscopic cholecystectomy is the procedure of choice.³ However, the patient's age, gender, weight, pregnancy, comorbidities, the skill of the anesthetist or surgeon, and postoperative facilities available to the patient are not accounted for in this equation. Due to the subjective nature of ASA scores, they should not be utilized as the exclusive predictor for operative risk, as there is documented variation in patient ASA classifications in previous studies. Instead, ASA scores should only be used as an adjunct to assist surgeons and anesthesiologists in forecasting prospective complications and surgical outcomes for patients presenting with acute cholecystitis.

The CCI summates weighted scores based on a patient's comorbidities to provide an accurate risk assessment of the potential for morbidity and mortality following a procedure.⁴ For patients with acute cholecystitis, age-adjusted CCI is a beneficial tool that assists surgeons in selecting individualized treatment. A cutoff value of 5 for a patient's age-adjusted CCI is a predictive factor of inhospital complications, such as surgical conversion to open cholecystectomy, admission to the intensive care unit (ICU), postoperative complications, and mortality.⁵ Bergman et al. described increased patient age and CCI as factors correlated with decreased probability of surgery in elderly people with acute cholecystitis, and Alvino et al. illustrated lower patient CCI and ASA scores are associated with an increased likelihood of receiving a successful cholecystectomy for acute cholecystitis.^{6,7} For Tokyo grade I and grade II acute cholecystitis (discussed in greater detail below), CCI was an independent factor in predicting 30-day mortality. Age-adjusted CCI can be used as a complementary tool for surgeons and anesthesiologists when deciding upon management (surgical and conservative, or conservative and then surgical) for acute cholecystitis treatment in elderly and comorbid patients.⁵

The American College of Surgeons (ACS) NSQIP risk calculator estimates the likelihood of unfavorable outcomes, such as surgical complications or death, for a patient about to undergo surgery based on the surgical procedure combined with individualized patient factors, such as age, gender, mental status, medications, comorbidities, and personal history.⁸ When focusing specifically on cholecystectomy, ACS NSQIP can be imperfect when estimating complication rates, hospital LOS, conversion due to open surgery, etc. This is due to limitations in entering the reason and severity for the cholecystectomy. For example, the ACS NSQIP cannot differentiate between a cholecystectomy for severe acute cholecystitis with GB necrosis and perforation vs a mild form of acute cholecystitis. The ACS NSQIP is best used to calculate the general surgical risk for a patient but not the specific risks associated with the procedure.⁹

It should be emphasized that despite the availability of these and other risk assessment tools, none should be relied upon in isolation. This is supported by the 2020 World Society of Emergency Surgery guidelines, which indicate that no prognostic model can be suggested in the setting of acute cholecystitis, given the lack of high-quality studies for this purpose.¹⁰

Severity of Cholecystitis

Various guidelines have been established to aid surgeons in characterizing the severity of acute cholecystitis. AAST and the TG18 utilize multifactorial characteristics of a patient's acute cholecystitis to predict the severity, potential outcome, and optimal treatment plan for the patient. Diagnosis of acute cholecystitis with TG18 is based on the presence of local signs of inflammation,

signs of systemic inflammation, and confirmation of gallstone and GB inflammation upon intra-abdominal imaging.¹¹ According to TG18, the severity of acute cholecystitis is evaluated on a scale of grades I-III, based on preoperative factors to help guide the surgeon's decision behind electing for early or late laparoscopic cholecystectomy, or percutaneous GB drainage. Grade I acute cholecystitis is the mildest form. Grade II acute cholecystitis is associated with an elevated white blood cell (WBC) count, a palpable tender mass in the right upper quadrant (RUQ), and marked local inflammation. Grade III is the most severe form of acute cholecystitis that has the dysfunction of cardiovascular, neurological, hepatic, respiratory, or other organ systems.¹¹ In fact, the potential for a bile duct injury (BDI) progressively increases from Tokyo grade I (0.96%) to grade II (2.41%) and to grade III (8.43%). Mortality rates are also increased in grade III (5.4%) as compared to grade I (1.2%) acute cholecystitis.¹²

The TG recommends that patients with grade I cholecystitis undergo early laparoscopic cholecystectomy, while patients with grade III cholecystitis receive an initial round of antibiotic treatment with potential percutaneous cholecystostomy tube (PCT) placement prior to laparoscopic cholecystectomy. Management of grade II cholecystitis is dependent on the expertise of the surgeon in managing acute cholecystitis. Retrospective studies had validated these guidelines and have found that hospital LOS decreased when clinical decisions were compliant with the TG for cholecystitis severity grading.¹¹ With TG18, it is essential to consider patients' comorbidities and medical backgrounds when deciding upon the specific treatments for that patient. The TG focus on the severity of GB diseases without factoring the conditions of the patient into their treatment regimen. Using surgical risk stratification guidelines, such as the ASA physical status classification score combined with the TG, allows for analysis of the patient's risk for postoperative complications and mortality if submitted to surgery.

Additionally, the AAST guidelines provide anatomic grading for risk stratification and outcome adjustment in an acute care setting for acute cholecystitis. Severity is determined based on clinical status, imaging, operative, and pathologic indications, with the severity score being independently correlated with clinical outcomes for patients with acute cholecystitis. Unlike the TG system, the AAST incorporates anatomical characteristics of the disease process on a scale of I-V (Table 1). Increases in AAST grades are correlated with complication rates, ICU needs, hospital LOS, morbidity, and mortality. Compared to AAST grade I, patients with grade III acute cholecystitis were eight times as likely to spend time in the ICU and four times as likely to experience an adverse event (readmission or death).¹³ Due to the AAST grading being anatomically based, it is an attractive evaluation tool for acute cholecystitis, and it can be utilized to predict patient outcomes and patient-centered management practices.

Antibiotic Choice

It is recommended that all patients diagnosed with acute cholecystitis receive antibiotics to prevent progressive GB inflammation, development of secondary infection, or sepsis. Acute cholecystitis is primarily inflammatory, but infection can occur with cystic duct obstruction leading to bile stasis, potential infection, and sepsis.¹⁴ The antibiotic choice should cover common biliary pathogens, such as gram-negative rods, anaerobes, and bacteria in the Enterobacteriaceae family.¹⁵ The recommendations for antibiotic choice vary slightly according to the guideline. Generally speaking, for low-risk patients, piperacillin/tazobactam



AAST grade	Description	Clinical criteria	Imaging criteria (CT/US/ HIDA finding)	Operative criteria	Pathologic criteria
I	Acute cholecystitis	RUQ or epigastric pain with potential Murphy's sign and leukocytosis	Wall thickening, distention, gallstones, or sludge with pericholecystic fluid and non-visualization of the GB on the HIDA scan	GB inflammation with GB wall thickening, distention, and gallstones	Acute inflammation within the GB wall without necrosis or pus
II	GB empyema, gangrenous cholecystitis, or emphysematous cholecystitis	RUQ or epigastric pain with potential Murphy's sign and leukocytosis	Above, plus the air in GB lumen, wall, or in the biliary tree with focal mucosal defects without perforation	Distended GB with pus or hydrops and additional GB wall necrosis/gangrene with no perforation	Above, with pus in the GB lumen, GB wall necrosis, intramural abscess, epithelial sloughing, and no GB perforation
111	GB perforation with local contamination	Localized RUQ Peritonitis	HIDA with focal transmural defect, extraluminal fluid collection, or radiotracer (limited to RUQ)	Non-iatrogenic perforated GB wall with free bile limited to the RUQ	Necrosis with non- iatrogenic perforation of the GB
IV	GB perforation with pericholecystic abscess or gastrointestinal fistula	Multiple localized peritonitis, abdominal distension with symptoms of bowel obstruction	Abscess in RUQ outside the GB with potential bilio-enteric fistula or gallstone ileus	Pericholecystic abscess with bilioenteric fistula and gallstone ileus	Necrosis with non- iatrogenic perforation of the GB
V	GB perforation with generalized peritonitis	Generalized peritonitis at multiple locations, abdominal distension with symptoms of bowel obstruction	Free intraperitoneal bile	Above, with generalized peritonitis	Necrosis with non- iatrogenic perforation of the GB

Table 1. Adapted from AAST quidelines

AAST, American Association for the Surgery of Trauma; CT, computed tomography; GB, gallbladder; HIDA, hepatobiliary iminodiacetic scan; RUQ, right upper quadrant; US, ultrasound; Adapted from AAST guidelines

or a cephalosporin-based therapy with or without metronidazole is recommended, and in high-risk patients, such as those that are immunocompromised, elderly, or have had exposure to antibiotic-resistant organisms, piperacillin/tazobactam, ceftriaxone plus metronidazole, cefepime plus metronidazole, or a carbapenem can be used for management of acute cholecystitis. The duration of antibiotic treatment varies depending on case severity (e.g., sepsis) and should depend on clinical presentation and response to treatment.

Time since Onset of Symptoms

For the surgical management of diagnosed acute cholecystitis, the patient's underlying comorbidities (obesity, diabetes mellitus, pulmonary hypertension, cirrhosis, etc.) and medications (blood thinners, immunosuppressants, etc.) are what ultimately control the timing of surgery. According to TG18, patients with mild acute cholecystitis should undergo a laparoscopic cholecystectomy within 72 hours of symptom onset.¹¹ Patients who undergo cholecystectomy within 72 hours of symptom onset have fewer postoperative infections, a decreased risk of BDI, shorter LOS, shorter duration of antibiotic therapy, and less overall hospital cost compared to those >72 hours.^{16,17} In patients that present 72 hours after symptom onset, there is still evidence of improved outcomes

of performing a cholecystectomy within 72 hours of admission. However, there is no sufficient evidence to make a recommendation in patients with moderate to severe acute cholecystitis concerning the risk of BDI. If a patient is a poor surgical candidate, a 7-day course of antibiotics can be considered.¹⁸ However, in a study done by Brunt et al., 18.5% of patients managed nonoperatively with a planned cholecystectomy at a later date had to be seen again before their planned cholecystectomy, and about 10% of the patients needed emergency laparoscopic cholecystectomy earlier than planned.¹⁹

Acalculous vs Calculus Acute Cholecystitis

Acute cholecystitis occurs when the cystic duct is obstructed, most commonly by a gallstone, leading to inflammation of the GB, and it occurs more frequently in patients with symptomatic cholelithiasis. Common history includes ingestion of fatty food within an hour of symptom onset, which includes RUQ/epigastric pain. This pain may radiate to the right shoulder or back and usually lasts longer than 4-6 hours, commonly associated with nausea, vomiting, fever, and anorexia. On examination, patients are commonly ill-appearing, tachycardiac, and febrile with a positive Murphy's sign and true, local peritoneal tenderness. Upon lab testing, leukocytosis with a left shift is common. If patients have increased total bilirubin and alkaline phosphatase, there should be suspicion of biliary

obstruction. Although a positive Murphy's sign is supportive of the diagnosis, history, physical examination, and lab results should not be used alone to diagnose acute cholecystitis. Ultrasound (US) is the imaging of choice, as it is quick, accessible, inexpensive, and noninvasive with high sensitivity and specificity.²⁰ If the US is negative, but suspicion still exists for acute cholecystitis, then a hepatobiliary iminodiacetic acid (HIDA) scan can be obtained to evaluate for the absence of GB filling. Computed tomography (CT) and magnetic resonance cholangiopancreatography can also be used to look for acute cholecystitis, but they should be used to rule out other diagnoses or if the provider is considering other etiologies for the patient's presentation.

Less commonly, acute cholecystitis can arise without gallstones, which accounts for approximately 10% of all acute cholecystitis cases.²¹ Clinical presentation of acalculous cholecystitis varies greatly in each patient, depending on the severity of the illness. Patients may present with fever, sepsis, shock, and peritonitis with a palpable RUQ mass.²² Acalculous cholecystitis should be suspected in severely ill patients with unexplained jaundice. In patients with suspected acalculous cholecystitis, US imaging should be performed, followed by contrast-enhanced abdominal CT scans if the diagnosis is uncertain. Labs in patients with acalculous cholecystitis are nonspecific, with elevated leukocytes found in the majority of patients.²¹ Abnormal liver metabolites, including elevated alkaline phosphatases and serum aminotransferases, are common along with altered pancreatic enzymes and electrolytes.²³ Blood cultures should also be obtained from all patients with suspected acalculous cholecystitis to diagnose bacteremia and guide antibiotic selection. The likelihood of acalculous cholecystitis is increased in males and immunosuppressed patients due to opportunistic microsporidia. cryptosporidium, and cytomegalovirus infections.²⁴ Management of acalculous cholecystitis is necessary to prevent GB gangrene, rupture, and patient death.²⁵ In delayed treatment for acalculous cholecystitis, mortality can be as high as 75%, while rapid treatment can lower mortality to approximately 30%.²⁶ Treatment should include supportive care with intravenous fluids, antibiotics, and pain management with urgent laparoscopic cholecystectomy or GB drainage in patients who are poor surgical candidates.²⁷ If symptoms fail to resolve within 24 hours following GB drainage, rescue cholecystectomy is required.

Pregnancy

Cholelithiasis and cholecystectomies are more frequently encountered in pregnant women compared to nonpregnant patients. Increased estrogen and progesterone induce increased cholesterol and bile acid secretion in the biliary system, resulting in an increased predisposition to gallstone formation, along with progesterone slowing GB emptying.²⁸ In concordance with nonpregnant patients, acute cholecystitis is considered a complicated gallstone disease and increases the risk for maternal and neonatal morbidity.²⁹ Pregnant women with symptomatic gallstone disease will clinically present similar to nonpregnant patients.

Traditionally, surgery was avoided in the first and third trimesters to avoid spontaneous abortions or preterm delivery³⁰; however, this practice is not evidence-based. In pregnant patients with acute cholecystitis, laparoscopic cholecystectomy is generally indicated and can safely be performed during any trimester.³¹ In addition, compared to nonoperative management for acute cholecystitis, laparoscopic cholecystectomies result in lower rates of preterm delivery, labor, abortion, and decreased LOS.³² Additionally, for each day the laparoscopic cholecystectomy is delayed, there is an

increased risk of associated maternal-fetal complications.³³ Overall, performing laparoscopic cholecystectomies is not associated with a higher risk of maternal or fetal mortality compared to a nonoperative management approach to symptomatic gallstone diseases during pregnancy.³⁴ That said, cholecystectomies performed in the third trimester have been associated with higher rates of preterm delivery compared to patients who undergo surgery postpartum. If a patient is near-term, surgery can be deferred until after delivery, assuming the symptoms resolve with antibiotics and supportive care. The patient should be admitted to the hospital for monitoring. Delaying surgery to treat acute cholecystitis until after delivery increases the risk of complications, including emergency room visits, increased preterm labor, or fetal loss in pregnant patients.³³ Patients near-term should be explained the risks and benefits of later-term cholecystectomies compared to postpartum GB surgery for an informed decision to be made with the surgeons and obstetrician.

Pregnant patients will require laparoscopic cholecystectomy with alterations to the surgical techniques to protect the fetus and mother. First, the patient must be placed with their torso slightly elevated and tilted to the left to allow for the uterus to fall away from the inferior vena cava. Laparoscopic trocars can be placed in their regular positions until the third trimester. During the third trimester, the epigastric port should be moved into the upper left quadrant to provide an improved surgical window. Otherwise, the surgical technique follows the regular laparoscopic cholecystectomy protocol. For cholecystectomies, pregnancy is not a significant predictor of surgical complications, but pregnancy is an independent predictor of a longer LOS in the hospital compared to nonpregnant females.³⁴

Mirizzi Syndrome

Mirizzi syndrome is a condition frequently overlooked preoperatively in patients undergoing cholecystectomy due to similar symptoms expressed in cholecystitis. The syndrome is defined as an extrinsic impingement of the common hepatic duct elicited by an impacted gallstone within the cystic duct or infundibulum applying a compressive force on the common hepatic duct. Additionally, the lodged stone can cause local inflammation, cholangitis, and in rare cases, chronic inflammation that causes bile duct necrosis and erosion of the common bile duct, leading to a cholecystobiliary fistula. Preoperatively, patients with Mirizzi syndrome present with jaundice, fever, and pain localized to the RUQ. However, these symptoms can vary with each patient and are also commonly expressed in other diseases of the GB.³⁵ Mirizzi syndrome can lead to biliary injury and morbidity in patients undergoing laparoscopic surgery and is estimated to occur in 0.05–4% of patients undergoing surgery for cholelithiasis.³⁶

Diagnosis of Mirizzi syndrome requires abdominal imagining. US will show the presence of a stone impacted in the GB neck with dilation of the GB above the level of the stone with a drastic decrease in the width of the common duct below the level of the stone. US has a low sensitivity in diagnosing Mirizzi syndrome due to difficulties visualizing the common hepatic duct with proximity to the cystic duct. Endoscopic retrograde cholangiopancreatography (ERCP) or magnetic resonance cholangiopancreatography is used to confirm the diagnosis of Mirizzi syndrome and determine if a cholecystobiliary fistula is present. Diagnostic findings of Mirizzi syndrome are eccentric defects on the lateral wall of the common bile duct at the level of the cystic duct or GB neck. Cholecystobiliary fistulas can be visualized by ERCP with contrast material passing



from the proximal biliary channel into the GB.³⁷ Additionally, ERCP can provide therapeutic benefits to the patient as a temporary measure before surgery, as stenting allows for decompression of the common bile duct.³⁸

If Mirizzi syndrome is initially discovered during cholecystectomy, an intraoperative cholangiogram (IOC) should be performed prior to cholecystectomy to confirm the diagnosis and characterize the biliary anatomy, as the presence and characteristics of the cholecystobiliary fistula dictate the surgical approach during cholecystectomy. Exploration of the common duct should occur in patients with a cholecystobiliary fistula to identify potential choledocholithiasis.³⁹ Laparoscopic surgery for Mirizzi syndrome can be challenging due to the increased risk of biliary injury caused by dense adhesions and edematous inflammation of the tissue that can distort local anatomy. Often, conversion to an open surgery occurs in patients where Mirizzi syndrome is encountered intraoperatively.⁴⁰ In one retrospective study, conversion from laparoscopic to open cholecystectomy occurred in 67% of patients with Mirizzi syndrome.⁴¹

Cholecystostomy Tubes

Percutaneous cholecystostomy tube (PCT) placement is an available option for patients diagnosed with acute calculous or acalculous cholecystitis who are too high of a surgical or anesthesia risk (i.e., age-adjusted CCI >5) in the setting of antibiotic failure.⁵ PCT placement has been shown to resolve symptoms of acute cholecystitis without surgery successfully. One study found that PCT resulted in the resolution of symptoms in 91% of patients in patients with elevated CCI scores with a mortality rate of 9%. For complex acute cholecystitis cases where there are moderate to severe risks anticipated with laparoscopic cholecystectomy, PCT placement is a viable alternative to cholecystectomy that may provide resolution of acute cholecystitis with low mortality rates.' However, in some studies, PCTs have been shown to be associated with increased morbidity and mortality rates compared to laparoscopic cholecystectomy procedures.⁴² This may be partially attributed to patient selection bias, as patients that undergo PCTs are frequently older and have increased comorbidities or severity of illness. Yet, in a recent multicenter randomized controlled trial, laparoscopic cholecystectomy was found to be favorable compared to PCT in terms of fewer major complications (12 vs 65%; p < 0.001), reintervention (12 vs 66%; p< 0.001), recurrent biliary disease (5 vs 55%; *p* < 0.001), and median hospital LOS (5 vs 9 days; p < 0.001).⁴³

If chosen when truly a nonsurgical candidate, PCT should optimally be performed early, as it lowers procedure-related bleeding and LOS compared to late placement. In patients that are undergoing nonsurgical antibiotic treatment for acute cholecystitis and are not critically ill, PCTs should be placed after 1-3 days of antibiotic therapy if there is no improvement in clinical symptoms. If symptoms do not resolve in 3 days following tube placement and GB drainage, the patient is most likely experiencing GB gangrene, and a cholecystectomy should be considered regardless of surgical risk.⁴⁴ Finally, PCTs are not a definitive therapy for calculous cholecystitis, as antibiotic treatment or early laparoscopic cholecystectomy have similar efficacies; however, they may be a definitive treatment for patients with acalculous cholecystitis.⁴⁵ Following GB drainage, a patient's care plan depends on the resolution of clinical symptoms and individualized surgical plans. Patients who have become reasonable candidates for surgery can proceed with an elective cholecystectomy.

Intraoperative Considerations

Surgical Approach

Laparoscopic cholecystectomy is currently the procedure of choice for surgical management of acute cholecystitis due to the decrease in intraoperative complications (cardiac, pulmonary, wound, among others), reduced patient time spent in the hospital, and reduced time to baseline function. Several factors identified preoperatively have been shown to increase operative time and have higher rates of conversion to open cholecystectomy, such as body mass index, nonvisible GB on preoperative imaging, and cystic duct length. Additionally, advanced age, diabetes, male gender, GB wall thickening >4-5 mm, elevated bilirubin, elevated WBC count, and low albumin are risk factors for conversion to an open procedure.⁴⁶ However, the greatest concern with cholecystectomy is BDI. The rate of major BDI during laparoscopic cholecystectomy is between 0.15 and 0.36%, which equates to nearly 3,000 patients each year in the United States alone.¹⁹ BDIs can lead to an increased frequency of postoperative complications, re-interventions, hospitalization, and increased long-term morbidity and mortality; moreover, BDIs are one of the most common reasons for legal actions against general surgeons.^{47,48}

In terms of the surgical approach to cholecystectomy, recommendations should be considered to reduce the overall occurrence of BDIs. Standard multiport laparoscopic cholecystectomy is the preferred method, as it is associated with reduced numbers of BDIs and severe complications (Clavien-Dindo grade III or greater), as well as reduced operative time, reduced port site hernias, and reduced conversions to an open procedure.⁴⁹ The critical view of safety (CVS) is achievable in most cases, and evidence supports that obtaining the CVS should be standard practice when feasible. If the CVS cannot be obtained, then alternative methods of anatomical verification should be used to prevent BDI, such as IOC, laparoscopic US, or preoperative administration of indocyanine green. If a BDI is suspected, this can be confirmed with IOC, which has been shown to have a threefold increase in recognition of BDI, thus, not only increasing the recognition of BDI but also avoiding of potential worsening of the BDI.¹⁹

In the setting of marked acute local inflammation preventing obtaining CVS, surgeons should consider laparoscopic or open subtotal cholecystectomy (STC) based on the surgeon's experience and the patient's health status.⁵⁰ When the CVS cannot be obtained, and imaging cannot define biliary anatomy, surgeons should consider STC over fundus-first (top-down) total cholecystectomies, unless dissection of the hepatocystic triangle can be avoided, then either approach is feasible. Laparoscopic STC is preferred over open STC as there is decreased risk of infections, retained stones, reoperation, and mortality with the laparoscopic approach, and laparoscopic STC is an alternative procedure that is helpful in avoiding serious damage to the bile ducts or blood vessels.⁵¹ The fundus-first approach with STC is a reasonable alternative to avoiding BDI when there is severe inflammation of Calot's triangle. However, in patients with severe chronic inflammation, the fundus-first technique is associated with a greater risk of vasculobiliary injury.⁵² In cases where it is difficult to visualize the GB surface in Calot's triangle after various approaches or in severe fibrosis of Calot's triangle, then STC should be considered, and if this is not feasible, an open cholecystectomy should be considered.⁵³ Decompression via needle aspiration should be performed if the GB is so inflamed that it obstructs the view.

Based on prior meta-analyses, there is no significant difference in success rate, complication rate, and inhospital mortality of removing common bile duct stones *via* ERCP, followed by laparoscopic cholecystectomy, compared to laparoscopic common bile duct exploration at the time of laparoscopic cholecystectomy.⁵⁴ That said, patients prefer laparoscopic common bile duct exploration, as it only requires one procedure, resulting in a shorter LOS and hospital cost. The method that is used is ultimately dependent on the skill and preference of the surgeon.

With a previous history of acute calculous cholecystitis treated *via* cholecystostomy, patients should undergo cholecystectomy as long as the inflammation has subsided and they are appropriate surgical candidates. In patients that remain nonsurgical candidates, other nonsurgical approaches should be discussed. Patients have an increased risk of mortality after undergoing cholecystostomy, and patients who do not undergo interval cholecystectomy had increased rates of emergency room visits, need for emergency cholecystectomy, open cholecystectomy, and postoperative complications.⁵⁵

Parkland Grading Scale

The Parkland grading scale may be utilized intraoperatively to assess the level of severity for GB diseases into an I-V based grading system [grade I (no adhesions and normal GB), grade II (minor neck adhesions), grade III (distended GB with adhesions to the body with additional pericholecystic fluid), grade IV (adhesions to the majority of the GB with abnormal liver anatomy or impacted stone), and grade V (perforation, necrosis, and inability to visualize the GB due to adhesions)] based on the anatomy and inflammatory changes observed via intraoperative imaging during laparoscopic cholecystectomy.⁵⁶ Overall, the Parkland grading scale is a validated intraoperative grading scale that predicts the difficulty level of the laparoscopic procedure with an increase in grade that correlates with an increased risk for intraoperative complications, such as conversion to open cholecystectomy, worsened postoperative outcomes such as a biliary leak, length of operation, and overall case difficulty to allow for a more informed decision about the procedure for the specific case to be made by the surgeon.⁵⁷

DISCUSSION

Acute cholecystitis is one of the most common surgically treatable diseases worldwide. First performed in 1985, laparoscopic cholecystectomy was relatively slow to gain favor over the next decade for the management of acute cholecystitis. However, since the mid-1990s, laparoscopic cholecystectomy has been the gold standard for this disease, and over the course of the last 30 years, several guidelines have been published, such as to facilitate a safe cholecystectomy as well as to inform the patient of their surgical risk. Our review has highlighted the most up-to-date and pertinent of these guidelines with an emphasis on TG18, AAST, ACS NSQIP, the CHOCOLATE study, and multi-society practice guidelines. Ultimately, patients presenting with acute cholecystitis are heterogeneous in nature pertaining to comorbidities, gender, age, etc., as well as severity and duration of the inflammation/infection of the GB itself. Careful consideration of preoperative and intraoperative risk factors and consensus recommendations is crucial to the safety of cholecystectomy, as is keeping current with available literature and technology.

Clinical Significance

The management of acute cholecystitis should never be viewed as routine, particularly given the heterogeneity of the patient's clinical status and the severity of the disease process. Adherence to up-to-date, evidence-based, and expert consensus practice is critical to optimal outcomes for these patients.

REFERENCES

- 1. Dripps RD. New classification of physical status. Anesthesiology 1963;24:111.
- 2. Daabiss M. American society of anaesthesiologists physical status classification. Indian J Anaesth 2011;55(2):111–115. DOI: 10.4103/0019-5049.79879
- 3. Schuld J, Glanemann M. Acute cholecystitis. Viszeralmedizin 2015;31(3):163–165. DOI: 10.1159/000431275
- Charlson ME, Pompei P, Ales KL, et al. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis 1987;40(5):373–383. DOI: 10.1016/0021-9681(87)90171-8
- Bonaventura A, Leale I, Carbone F, et al. Pre-surgery age-adjusted charlson comorbidity index is associated with worse outcomes in acute cholecystitis. Dig Liver Dis 2019;51(6):858–863. DOI: 10.1016/j. dld.2018.10.002
- Bergman S, Sourial N, Vedel I, et al. Gallstone disease in the elderly: are older patients managed differently? Surg Endosc 2011;25(1):55–61. DOI: 10.1007/s00464-010-1128-5
- Alvino DM, Fong ZV, McCarthy CJ, et al. Long-term outcomes following percutaneous cholecystostomy tube placement for treatment of acute calculous cholecystitis. J Gastrointest Surg 2017;21(5):761–769. DOI: 10.1007/s11605-017-3375-4
- Bilimoria KY, Liu Y, Paruch JL, et al. Development and evaluation of the universal ACS NSQIP surgical risk calculator: a decision aid and informed consent tool for patients and surgeons. J Am Coll Surg 2013;217(5):833–842. DOI: 10.1016/j.jamcollsurg.2013.07.385
- Massoumi RL, Trevino CM, Webb TP. Postoperative complications of laparoscopic cholecystectomy for acute cholecystitis: a comparison to the ACS-NSQIP risk calculator and the Tokyo guidelines. World J Surg 2017;41(4):935–939. DOI: 10.1007/s00268-016-3816-3
- Pisano M, Allievi N, Gurusamy K, et al. 2020 World Society of Emergency Surgery updated guidelines for the diagnosis and treatment of acute calculus cholecystitis. World J Emerg Surg 2020;15(1):61. DOI: 10.1186/s13017-020-00336-x
- Yokoe M, Hata J, Takada T, et al. Tokyo Guidelines 2018: diagnostic criteria and severity grading of acute cholecystitis (with videos). J Hepatobiliary Pancreat Sci 2018;25(1):41–54. DOI: 10.1002/jhbp.515
- Törnqvist B, Waage A, Zheng Z, et al. Severity of acute cholecystitis and risk of iatrogenic bile duct injury during cholecystectomy, a population-based case-control study. World J Surg 2016;40(5):1060–1067. DOI: 10.1007/s00268-015-3365-1
- Vera K, Pei KY, Schuster KM, et al. Validation of a new American association for the surgery of trauma (AAST) anatomic severity grading system for acute cholecystitis. J Trauma Acute Care Surg 2018;84(4):650–654. DOI: 10.1097/TA.000000000001762
- Fuks D, Cossé C, Régimbeau JM. Antibiotic therapy in acute calculous cholecystitis. J Visc Surg 2013;150(1):3–8. DOI: 10.1016/j. jviscsurg.2013.01.004
- Strasberg SM. Acute calculous cholecystitis. N Engl J Med 2008;358(26):2804–2811. DOI: 10.1056/NEJMcp0800929
- Gurusamy K, Samraj K, Gluud C, et al. Meta-analysis of randomized controlled trials on the safety and effectiveness of early versus delayed laparoscopic cholecystectomy for acute cholecystitis. Br J Surg 2010;97(2):141–150. DOI: 10.1002/bjs.6870
- 17. Zafar SN, Obirieze A, Adesibikan B, et al. Optimal time for early laparoscopic cholecystectomy for acute cholecystitis. JAMA Surg 2015;150(2):129–136. DOI: 10.1001/jamasurg.2014.2339
- Overby DW, Apelgren KN, Richardson W, et al. SAGES guidelines for the clinical application of laparoscopic biliary tract surgery. Surg Endosc 2010;24(10):2368–2386. DOI: 10.1007/s00464-010-1268-7
- Brunt LM, Deziel DJ, Telem DA, et al. Safe cholecystectomy multi-society practice guideline and state-of-the-art consensus



conference on prevention of bile duct injury during cholecystectomy. Surg Endosc 2020;34(7):2827–2855. DOI: 10.1007/s00464-020-07568-7

- Shea JA, Berlin JA, Escarce JJ, et al. Revised estimates of diagnostic test sensitivity and specificity in suspected biliary tract disease. Arch Intern Med 1994;154(22):2573-2581. DOI: 10.1001/archinte.1994.00420220069008
- Huffman JL, Schenker S. Acute acalculous cholecystitis: a review. Clin Gastroenterol Hepatol 2010;8(1):15–22. DOI: 10.1016/j. cgh.2009.08.034
- 22. Barie PS, Eachempati SR. Acute acalculous cholecystitis. Curr Gastroenterol Rep 2003;5(4):302–309. DOI: 10.1007/s11894-003-0067-x
- 23. Owen CC, Jain R. Acute acalculous cholecystitis. Curr Treat Options Gastroenterol 2005;8(2):99–104. DOI: 10.1007/s11938-005-0001-4
- Wang AJ, Wang TE, Lin CC, et al. Clinical predictors of severe gallbladder complications in acute acalculous cholecystitis. World J Gastroenterol 2003;9(12):2821–2823. DOI: 10.3748/wjg.v9.i12.2821
- Kalliafas S, Ziegler DW, Flancbaum L, et al. Acute acalculous cholecystitis: incidence, risk factors, diagnosis, and outcome. Am Surg 1998;64(5):471–475. PMID: 9585788.
- DuPriest RW Jr, Khaneja SC, Cowley RA. Acute cholecystitis complicating trauma. Ann Surg 1979;189(1):84-89. DOI: 10.1097/00000658-197901000-00016
- Yang HK, Hodgson WJ. Laparoscopic cholecystostomy for acute acalculous cholecystitis. Surg Endosc 1996;10(6):673–675. DOI: 10.1007/BF00188528
- 28. Everson GT. Pregnancy and gallstones. Hepatology 1993;17(1):159–161. DOI: 10.1016/0270-9139(93)90206-3
- Maringhini A, Ciambra M, Baccelliere P, et al. Biliary sludge and gallstones in pregnancy: incidence, risk factors, and natural history. Ann Intern Med 1993;119(2):116–120. DOI: 10.7326/0003-4819-119-2-199307150-00004
- McKellar DP, Anderson CT, Boynton CJ, et al. Cholecystectomy during pregnancy without fetal loss. Surg Gynecol Obstet 1992;174(6):465–468. PMID: 1595022.
- Schwulst SJ, Son M. Management of gallstone disease during pregnancy. JAMA Surg 2020;155(12):1162–1163. DOI: 10.1001/jamasurg.2020.3683
- 32. Pearl J, Price R, Richardson W, et al. Guidelines for diagnosis, treatment, and use of laparoscopy for surgical problems during pregnancy. Surg Endosc 2011;25(11):3479–3492. DOI: 10.1007/s00464-011-1927-3
- Muench J, Albrink M, Serafini F, et al. Delay in treatment of biliary disease during pregnancy increases morbidity and can be avoided with safe laparoscopic cholecystectomy. Am Surg 2001;67(6):539–542. PMID: 11409801.
- Kuy S, Roman SA, Desai R, et al. Outcomes following cholecystectomy in pregnant and nonpregnant women. Surgery 2009;146(2):358–366. DOI: 10.1016/j.surg.2009.03.033
- Lai EC, Lau WY. Mirizzi syndrome: history, present and future development. ANZ J Surg 2006;76(4):251–257. DOI: 10.1111/j.1445-21 97.2006.03690.x
- Mishra MC, Vashishtha S, Tandon R. Biliobiliary fistula: preoperative diagnosis and management implications. Surgery 1990;108(5):835–839. DOI: 10.5555/uri:pii:003960609090278A
- Becker CD, Hassler H, Terrier F. Preoperative diagnosis of the Mirizzi syndrome: limitations of sonography and computed tomography. AJR Am J Roentgenol 1984;143(3):591–596. DOI: 10.2214/ajr.143.3.591
- Binmoeller KF, Thonke F, Soehendra N. Endoscopic treatment of Mirizzi's syndrome. Gastrointest Endosc 1993;39(4):532–536. DOI: 10.1016/s0016-5107(93)70165-0
- 39. Ibrarullah M, Mishra T, Das AP. Mirizzi syndrome. Indian J Surg 2008;70(6):281–287. DOI: 10.1007/s12262-008-0084-y
- 40. Yip AW, Chow WC, Chan J, et al. Mirizzi syndrome with cholecystocholedochal fistula: preoperative diagnosis and management. Surgery 1992;111(3):335–338. PMID: 1542859.

- Erben Y, Benavente-Chenhalls LA, Donohue JM, et al. Diagnosis and treatment of Mirizzi syndrome: 23-year mayo clinic experience. J Am Coll Surg 2011;213(1):114–119. DOI: 10.1016/j.jamcollsurg.2011.03.008
- 42. Smith TJ, Manske JG, Mathiason MA, et al. Changing trends and outcomes in the use of percutaneous cholecystostomy tubes for acute cholecystitis. Ann Surg 2013;257(6):1112–1115. DOI: 10.1097/SLA.0b013e318274779c
- 43. Loozen CS, van Santvoort HC, van Duijvendijk P, et al. Laparoscopic cholecystectomy versus percutaneous catheter drainage for acute cholecystitis in high risk patients (CHOCOLATE): multicentre randomized clinical trial. BMJ 2018;363:k3965. DOI: 10.1136/bmj.k3965
- Barak O, Elazary R, Appelbaum L, et al. Conservative treatment for acute cholecystitis: clinical and radiographic predictors of failure. Isr Med Assoc J 2009;11(12):739–743. PMID: 20166341.
- 45. Kirkegård J, Horn T, Christensen SD, et al. Percutaneous cholecystostomy is an effective definitive treatment option for acute acalculous cholecystitis. Scand J Surg 2015;104(4):238–243. DOI: 10.1177/1457496914564107
- 46. Philip Rothman J, Burcharth J, Pommergaard HC, et al. Preoperative risk factors for conversion of laparoscopic cholecystectomy to open surgery-a systematic review and meta-analysis of observational studies. Dig Surg 2016;33(5):414–423. DOI: 10.1159/000445505
- Mclean TR. Monetary lessons from litigation involving laparoscopic cholecystectomy. Am Surg 2005;71(7):606-612. DOI: 10.1177/000313480507100714
- Halbert C, Pagkratis S, Yang J, et al. Beyond the learning curve: incidence of bile duct injuries following laparoscopic cholecystectomy normalize to open in the modern era. Surg Endosc 2016;30(6):2239–2243. DOI: 10.1007/s00464-015-4485-2
- Arezzo A, Passera R, Forcignanò E, et al. Single-incision laparoscopic cholecystectomy is responsible for increased adverse events: results of a meta-analysis of randomized controlled trials. Surg Endosc 2018;32(9):3739–3753. DOI: 10.1007/s00464-018-6143-y
- Elshaer M, Gravante G, Thomas K, et al. Subtotal cholecystectomy for "difficult gallbladders": systematic review and meta-analysis. JAMA Surg 2015;150(2):159–168. DOI: 10.1001/jamasurg.2014.1219
- 51. Wakabayashi G, Iwashita Y, Hibi T, et al. Tokyo Guidelines 2018: surgical management of acute cholecystitis: safe steps in laparoscopic cholecystectomy for acute cholecystitis (with videos). J Hepatobiliary Pancreat Sci 2018;25(1):73–86. DOI: 10.1002/jhbp.517
- 52. Strasberg SM, Gouma DJ. 'Extreme' vasculobiliary injuries: association with fundus-down cholecystectomy in severely inflamed gallbladders. HPB (Oxford) 2012;14(1):1–8. DOI: 10.1111/j.1477-25 74.2011.00393.x
- Honda G, Hasegawa H, Umezawa A. Universal safe procedure of laparoscopic cholecystectomy standardized by exposing the inner layer of the subserosal layer (with video). J Hepatobiliary Pancreat Sci 2016;23(9):E14–E19. DOI: 10.1002/jhbp.382
- 54. Koc B, Karahan S, Adas G, et al. Comparison of laparoscopic common bile duct exploration and endoscopic retrograde cholangiopancreatography plus laparoscopic cholecystectomy for choledocholithiasis: a prospective randomized study. Am J Surg 2013;206(4):457–463. DOI: 10.1016/j.amjsurg.2013.02.004
- Winbladh A, Gullstrand P, Svanvik J, et al. Systematic review of cholecystostomy as a treatment option in acute cholecystitis. HPB (Oxford) 2009;11(3):183–193. DOI: 10.1111/j.1477-2574.2009.00052.x
- Madni TD, Leshikar DE, Minshall CT, et al. The Parkland grading scale for cholecystitis. Am J Surg 2018;215(4):625–630. DOI: 10.1016/j. amjsurg.2017.05.017
- Lee W, Jang JY, Cho JK, et al. Does surgical difficulty relate to severity of acute cholecystitis? Validation of the Parkland grading scale based on intraoperative findings. Am J Surg 2020;219(4):637–641. DOI: 10.1016/j.amjsurg.2018.12.005