16 Gallstone Disease and the Timing of Cholecystectomy for Acute Cholecystitis and Gallstone Pancreatitis

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Background

Prevalence and Incidence

The prevalence of gallstone disease varies dramatically. In the United States, the third National Health and Nutrition Examination Survey published in 1999 reported that more than 20 million persons have gallbladder disease with approximately one million new cases diagnosed per year. The prevalence was demonstrated to differ according to sex and ethnicity with non-Hispanic black men having the lowest prevalence (5.3%) and Mexican American women having the highest (26.7%). From 1890 to 1980, various autopsy and oral cholecystography studies determined the prevalence of cholelithiasis to range from extremely low rates in Africa (1%) and Asia (<7%) to much higher rates in Europe (up to 18.5%). This was similar in the Americas with reported rates by autopsy of 9.1%, 14.3%, 19.4%, and 26.6% in Chicago, USA; Mexico; São Paulo, Brazil; and Chile, respectively. The highest recorded prevalence in a single population was 48.6% in a sample of 596 Pima Indians in Phoenix, Arizona. The advent of ultrasound in the early 1980s allowed larger population-based studies to be conducted due to its less-invasive nature. These studies reported similar rates ranging between 5 and 30% depending on the study population. Factors that affect the prevalence and incidence of gallstone disease include *age*, *sex*, *obesity and rapid weight loss*, ethnicity, diet, physical inactivity, genetics, and medical comorbidities.

Cholecystectomy rates in the United States are three times higher in patients 65 years and older compared to the 15–44 age range and twice as high in females versus males (except in the age range 60–74). Obesity; high-calorie, low-fiber, high-fat diets; dyslipidemia; insulin resistance; rapid weight loss; and physical inactivity have all been demonstrated to cause hepatic secretion of supersaturated bile, hypersecretion of biliary mucin, gallbladder stasis, intestinal hypomotility, and faster cholesterol crystallization and solid crystal precipitation. Genetic factors are thought to be responsible for at least 30% of symptomatic gallstone disease. The incidence of gallstones in patients with affected first-degree relatives appears to be two or three times higher compared to patients without family history. Twin studies support the role of genetics in gallstone pathogenesis. The cited studies included only patients with symptomatic disease, and thus the actual role of genetics is likely even higher if asymptomatic gallstone disease is included.

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Natural History

Despite being common in the general population relatively few patients will progress to symptomatic cholelithiasis. Approximately two-thirds of gallstones are asymptomatic. Only about 2–3% per year, 10% in 5 years, or 15–25% of patients over 10–20 years with asymptomatic gallstones will progress to symptomatic gallstone disease. This occurs when a gallstone obstructs the cystic or common bile duct and is inaccurately referred to as biliary colic. Even fewer (1–3%) will progress to complications of gallstone disease, of which acute cholecystitis is the most common. Symptomatic patients are more likely than asymptomatic patients to develop complications. Other complications include chronic cholecystitis, choledocholithiasis with or without cholangitis, gallstone pancreatitis, fistulas of the biliary tract and digestive system, and gallbladder carcinoma. Almost all patients will experience symptoms before developing complications.

Behind endoscopy of the small and large intestine, cholecystectomy is the most performed digestive system operation with a rate of 13.4 per 10,000 population per year. However, not all patients with gallstones will require cholecystectomy. There is wide agreement that surgical treatment is indicated for symptomatic patients and primarily only for those who remain symptomatic despite medical management over a sustained period of time unless acute complication develops. Even the onset of biliary colic does not portend inevitable surgery as the symptoms are known to self-abate without surgical intervention frequently. In a population-based cohort study involving 580 asymptomatic patients with gallstones, 453 remained asymptomatic; 127 patients went on to develop mild or severe symptoms. Approximately half of those that became symptomatic experienced resolution without operative intervention. Therefore, expectant management is the best approach for asymptomatic patients, and medical management is advisable for symptomatic patients prior to undergoing surgery, excepting complications or special circumstances (e.g., porcelain gallbladder, hemolytic anemia, large gallstones, bariatric surgery, patients who have received a transplant).

Presentation

In order to discuss the appropriate timing of operative intervention for acute cholecystitis and gallstone pancreatitis, it is required to understand their presentation.

Acute Cholecystitis

Cholelithiasis with cholecystitis is the second most common gastrointestinal admission diagnosis in the United States and is associated with an aggregate cost of 4.4 billion dollars per year. Acute cholecystitis is secondary to gallstones >90% of the time and is the most common complication occurring in patients with cholelithiasis (see section "Natural History"). Acalculous cholecystitis accounts for the remaining 5–10%. Certain patients, such as critically ill patients in intensive care units or those with extensive burns, receiving parenteral nutrition, sepsis, trauma, or multi-organ disease are at higher risk for acalculous cholecystitis. Cystic duct obstruction by a tumor is a very rare cause of acute cholecystitis.

The majority of patients with acute cholecystitis will present with a history of chronic cholecystitis. This history consists of recurrent attacks of pain, referred to as biliary colic, and is caused most commonly by a gallstone attempting to pass the cystic duct. The pain is constant and steadily increasing in severity for the first 30–45 minutes. It will last anywhere from 1 to 6 hours and is typically located in the right hypochondrium or midline epigastrium. Referred pain to the inferior angle of the right scapula, acromion, or clavicle may also be felt. These attacks are traditionally taught to be worse at night or after eating fatty foods; however, studies have demonstrated biliary colic and referred pain to be the only symptoms consistently related to gallstones.

Biliary colic is a misnomer because the pain is not typically paroxysmal but is constant and steadily increasing. It can last up to 4–6 hours. It is not colicky in nature because the muscle wall of the gallbladder and bile ducts is scant (a

distinct muscle layer is not present in the human common bile duct). Any episode of biliary colic can progress to acute cholecystitis, but it is impossible to predict which. This occurs when obstruction of the cystic duct persists and leads to gallbladder distension, inflammation, edema, and eventually necrosis and supervening bacterial infection. After experiencing the symptoms described above, a pain-free interval with subsequent return of pain in the right hypochondrium is often described. This pain is usually felt to be worse or of a different character and often exacerbated by movement, deep breathing, or coughing due to irritation of the parietal peritoneum. Fever, anorexia, nausea, and vomiting may accompany the pain. An arrest of inspiration with palpation of the right subcostal area may be elicited, famously known as Murphy's sign. The reported positive likelihood ratio of Murphy's sign varies dramatically between studies from 0.8 to 8.6. Trowbridge et al. report a summary positive likelihood ratio of 2.8, the highest for any single physical exam or laboratory finding.

A mild or moderate leukocytosis (>10,000 cells/mm^3) is often present but not necessary. A severe leukocytosis suggests a worsening complication, such as gallbladder necrosis or rupture. Jaundice and hyperbilirubinemia are typically absent unless the gallstone has impacted in the common bile duct or impaction of the stone in Hartmann's pouch compresses the common hepatic duct (Mirrizzi syndrome). Serum liver enzymes are typically normal or mildly elevated.

Gallstone Pancreatitis

Acute pancreatitis is the third most common gastrointestinal admission diagnosis in the United States and is associated with an aggregate cost of 2.6 billion dollars per year. Gallstones and alcohol account as the cause for the vast majority of cases. The ratio of gallstone-induced pancreatitis to alcohol-induced pancreatitis varies regionally, but gallstones appear to be the casual factor in women and the elderly more than other demographic groups.

Impaction of the common bile duct, pancreatic duct, or the ampulla of Vater is associated with acute pancreatitis. The exact pathophysiology is not clearly defined. Multiple hypotheses have been proposed to include reflux of bile into the pancreatic duct; duodenal fluid reflux into the pancreatic duct due to stenting open of the ampulla by a gallstone; or ductal hypertension leading to ductal disruption and extravasation of pancreatic juices and enzymes caused by pancreatic duct obstruction. These hypotheses have not been reproduced in experimental models.

The clinical presentation is similar to acute pancreatitis of other etiologies. This includes persistent, gnawing epigastric pain that often radiates to the back. Nausea and vomiting, hypotension, tachycardia, and abdominal distension may be present. Though rare, blue discoloration of the flank or umbilicus (Grey Turner's sign and Cullen's sign, respectively) can be appreciated in cases of hemorrhagic pancreatitis. When gallstones are causative, signs and symptoms of biliary obstruction such as right upper quadrant pain, jaundice, and fever will likely be present. Gallstone pancreatitis will typically be associated with elevated serum liver tests. Elevation of alanine aminotransferase (ALT) to a value three times greater than normal has been found to have a positive predictive value of 95% for gallstone pancreatitis. Definitively differentiating gallstone pancreatitis from other causes of acute pancreatitis requires imaging. Ultrasound is the modality of choice and boasts a high sensitivity and specificity of 95% and 90%, respectively. Pancreatitis-induced ileus can sometimes limit an ultrasonographical study due to the presence of overlying bowel gas. Furthermore, if gallstone pancreatitis is caused by microlithiasis, it is often impossible to detect the causative gallstone by ultrasound. Gallstones can be retrospectively determined to have caused an episode of acute pancreatitis when a gallstone is retrieved from feces within 10 days of the attack. The term gallbladder sludge is sometimes used to describe findings on an ultrasound. This should be considered gallstone disease, and symptomatic patients or patients who present with gallstone pancreatitis should be referred for a cholecystectomy.

Cholecystectomy

For patients suffering from symptomatic gallstone disease, surgical intervention in the form of an elective laparoscopic cholecystectomy is the most frequently recommended treatment. A cholecystectomy is the most common major abdominal procedure performed in Western countries, and there are few absolute contraindications.

Acute Cholecystitis

Laparoscopic cholecystectomy is the treatment of choice for symptomatic gallstone disease to include acute cholecystitis. This disease process accounts for 14% to 30% of cholecystectomies around the world. There are only two absolute contraindications – uncontrolled coagulopathy and end-stage liver disease. In a patient with severe refractory gallstone disease, even the latter of the absolute contraindications can be surmounted by a cholecystectomy with concurrent liver transplantation. Patients with severe obstructive pulmonary disease or congestive heart failure are at risk of increased morbidity and mortality due to decreased tolerance of the required pneumoperitoneum; however, these comorbidities are only relative contraindications.

Although consensus exists that laparoscopic cholecystectomy is correctly indicated for acute cholecystitis, the timing of operative intervention has been hotly debated. Proponents of early intervention advocate the "golden 72-hour rule," while proponents of delayed intervention advocate a "cooling off period."

The recommendation for early intervention is predicated on evidence that suggests complication rates, conversion to open cholecystectomy, length of hospital stay, and readmission rates are non-inferior or superior to patients in which intervention is delayed beyond a variably defined window. Delay is believed to unnecessarily expose patients to the risk of recurrent gallstone complications in the interval period and allow for fibrosis and adhesive disease to anatomically complicate the eventual definitive surgery. Some authors define "early" as within 24 hours, while others extend the definition to 1 week.

Advocates of delayed intervention believe that laparoscopic cholecystectomy is more technically challenging during the acute window due to active inflammation. This is primarily due to fears that early operation increases the rates of bile duct injury, a potentially life-threating condition which requires difficult and urgent corrective surgery. Even with successful repair, bile duct injury can be severely detrimental to a patient's quality of life. A perception also exists that early operation is associated with an increased risk of conversion to open cholecystectomy.

The body of evidence available since the 1970s–1980s overwhelmingly suggests that early cholecystectomy is either non-inferior or superior to delayed cholecystectomy (see Table 16.1). However, surveys worldwide still demonstrate that the number of surgeons performing early laparoscopic cholecystectomy for acute cholecystitis varies dramatically, reaching as low as

Table 16.1 Meta-analyses concerning early vs. delayed laparoscopic cholecystectomy for acute cholecystitis

Name	Year	No. patients	No. studies	Recommended timing
Papi[a, b]	2004	1255	12[c]	Early
Siddiqui[a]	2008	375	4	Early
Gurusamy[a]	2013	488	6	Early
Zhou[a]	2014	1106	7	Equivocal
Cao[a]	2015	1608	14	Early
Menahem[a]	2015	617	9	Early
Wu[a]	2015	1625	15	Equivocal
Cao[d]	2016	40,910	77	Early

[a]Randomized controlled trials
[b]Included open and laparoscopic cholecystectomy
[c]Only 3 of 12 studied laparoscopic cholecystectomy
[d]Case-control studies

11% in British general surgeons in 2004 and 33% of Japanese general surgeons in 2007.

Early Versus Delayed Laparoscopic Cholecystectomy for Acute Cholecystitis

Papi et al. were the first to summarize findings through 2004 regarding the timing of cholecystectomy for acute calculous cholecystectomy. The majority of included studies defined delayed operation as ≥8 weeks and early operation as within 7 days of onset. There was no significant difference in the rate differences of operative or perioperative complications between early and delayed cholecystectomy (open and laparoscopic); however, the laparoscopic subgroup analysis was underpowered to avoid a type 2 error due to the low complication rate. A trend toward lower rates of conversion to open cholecystectomy is reported in early versus delayed laparoscopic cholecystectomy, but the rate difference was ultimately nonsignificant. The study emphasizes that 20% of patients initially randomized to delayed surgery failed to respond to medical management and more than 50% underwent unplanned urgent surgery. Hospital stay was significantly reduced in the early versus delayed *open* cholecystectomy group and nonsignificantly reduced in the early versus delayed *laparoscopic* cholecystectomy group. For these reasons, the meta-analysis concludes by stating:

> Considering all these features, there is no argument to support delayed operation: early surgery should be considered the preferred approach for patients with uncomplicated lithiasic cholecystitis.

The most recent meta-analysis by Cao et al., published in 2016, is a meta-analysis of 77 case-control studies comprising 40,910 patients. The majority of the studies were retrospective. The results demonstrate a clear and significant benefit of early laparoscopic cholecystectomy for acute cholecystitis. Statistically significant reductions in mortality, total complication rate, bile duct leaks and injuries, wound infections, conversion to open cholecystectomy, length of hospital stay, and blood loss were associated with early laparoscopic cholecystectomy. Previous meta-analyses including only randomized controlled trials had difficulty demonstrating statistical significance in any outcome measure other than total length of hospital stay. This was likely due to the low sample sizes of randomized controlled trials and the rarity of complication events. A large sample size is the obvious benefit of case-controlled studies. This benefit comes at this increased risk of selection bias inherent in case-controlled studies. Interestingly, Cao et al. reported nonsignificant differences in length of operation time between the early and delayed group with a trend toward shorter operating times favoring early intervention. This is contrary to all previous meta-analyses in which shorter operating times were typically the only reported statistically significant benefit in favor of delayed intervention. The study also reports a 16% failure rate in the delayed intervention group requiring urgent laparoscopic cholecystectomy. Cao et al. conclude by declaring early laparoscopic cholecystectomy to be:

> clearly superior to delayed laparoscopic cholecystectomy in the management of patients presenting with acute cholecystitis and [should] now be considered to be the standard of care in the management of acute cholecystitis.

The authors recommend targeting a goal window of within 72 hours of symptom onset.

Song et al. conducted a summary of meta-analyses in 2016 and determined that – across seven meta-analyses – early laparoscopic cholecystectomy lowers the risk of wound infection; shortens hospital stay; and increases cost-effectiveness, patient satisfaction, and quality of life. It is also associated with an increase in operation time. There was no significant difference in the incidence of mortality, bile duct injury, bile leakage, overall complications, or conversion to open cholecystectomy. Using Jadad selection criteria, Cao et al. [1] and Wu et al. were determined to be the most appropriate meta-analyses with which to generate treatment recommendations on timing of laparoscopic cholecystectomy in acute cholecystitis. Song et al. summarize nearly five decades of randomized controlled trials comparing early versus late laparoscopic cholecystectomy for acute cholecystitis:

> With the best available evidence, we recommend ELC [early laparoscopic cholecystectomy] to be

the standard treatment option in treating acute cholecystitis.

Song et al. do not recommend a definition for what constitutes "early," but the majority of included randomized controlled trials define it as between 3 and 7 days of symptom onset. Therefore, it is appropriate to assume this definition. Further clarification of optimal timing is still required; however, as even studies comparing the definition of early laparoscopic cholecystectomy between as soon as possible and within 7 days have reported higher mortality and costs when delayed.

Gallstone Pancreatitis

Cholecystectomy is essential to prevent recurrence of gallstone pancreatitis. The timing of cholecystectomy is important and still debated. A laparoscopic *index cholecystectomy* – a cholecystectomy that occurs in the same admission and prior to discharge – is usually safe. An *interval cholecystectomy* – a cholecystectomy occurring after an appropriate time interval – is recommended in certain patients.

The controversy regarding timing of intervention is evident in the literature at least as early as 50 years ago. Traditionally, allowing recovery from acute pancreatitis with follow-up elective cholecystectomy 6–12 weeks later was advised. This recommendation was predicated on the fear that early operation would encounter excessive peripancreatic inflammation and result in higher rates of surgical complication. With the revelation that nearly all patients with gallstones and acute pancreatitis had demonstrable migration of stones through the common bile duct, the traditional approach was challenged. Surgeons hypothesized that the benefits of early removal of the obstructing gallstone during the index admission may outweigh the potential risk of operating around an inflamed and edematous pancreas by preventing a potentially fatal reoccurrence of pancreatitis before delayed cholecystectomy could occur. The recurrence rate of acute pancreatitis after discharge without surgical intervention ranges from 29% to 63%. In 1978, Acosta published results comparing 86 patients who underwent delayed elective biliary tract surgery to 46 patients who underwent biliary tract surgery on admission (average, 28 hours from onset of crisis). The mortality rates were 16% and 2%, respectively. Acosta et al. suggested early relief of the obstruction is critical to patient recovery.

There still remained a question about timing of the operation within the first admission. Immediate and delayed index admission cholecystectomies were, until then, found to be equivocal in terms of mortality (6–8%). Immediate cholecystectomy allowed simultaneous exploration and removal of common bile duct stones. The advent of endoscopic sphincterotomy allowed the surgeon to separate removing the gallstones and removing the gallbladder into two discrete steps; thus, the question of immediate versus delayed cholecystectomy achieved greater import.

There was early evidence that operative timing should be predicated on pancreatitis severity. In 1979, Ranson et al. conducted a retrospective study in which early (days 0–7) definitive biliary surgery was undertaken in 11 patients with "mild" pancreatitis, with 1 death (9%), and in 6 patients with "severe" pancreatitis, with 4 deaths (67%). This suggested that early correction of associated biliary disease may be undertaken safely in patients with mild acute pancreatitis but should be deferred in severe pancreatitis until pancreatitis has subsided (but still during the index admission). In 1988, Kelly et al. reported that in patients with three or fewer positive Ranson's signs, the time of surgery appeared to have little effect on the outcome. In patients with more than three positive signs, early surgery resulted in a significant increase in rates of morbidity and mortality. By the early 1990s, the consensus on the management of gallstone pancreatitis settled on allowing the acute pancreatitis to resolve with delayed cholecystectomy during the index admission and cholangiography before or during cholecystectomy to allow extraction of impacted gallstones.

The following decade of research supported this consensus and further clarified the role of grading pancreatitis severity in determining operative timing. A retrospective case series

involving 142 patients and a prospective study involving 77 patients suggested that laparoscopic cholecystectomy is safe in patients recovering from gallstone pancreatitis and early operation (within 1 week) can safely be recommended in patients with mild pancreatitis. Patients with severe pancreatitis should undergo surgery 3 weeks after admission or face increased risk of operative complications, conversion to open, and longer postoperative stays.

Most evidence arises from retrospective studies and non-randomized prospective studies; little evidence is generated from randomized controlled trials. To date, no large high-quality RCT regarding timing of intervention in severe acute pancreatitis has been published. The PONCHO study, a randomized controlled trial published, included 266 inpatients from 23 hospitals in the Netherlands recovering from mild gallstone pancreatitis. These patients were randomized to either interval cholecystectomy (25–30 days after randomization and discharge) or index admission cholecystectomy (within 3 days of randomization). The results predictably echoed earlier retrospective studies:

> Compared with interval cholecystectomy, same-admission cholecystectomy reduced the rate of recurrent gallstone-related complications in patients with mild gallstone pancreatitis, with a very low risk of cholecystectomy-related complications.

Operative Technique

Critical View of Safety

Regardless of the approach (open, laparoscopic, robotic, single-port, reduced-port, etc.), the critical view of safety must be obtained during cholecystic pedicle dissection. This is particularly important in laparoscopic compared to open cholecystectomy given that the laparoscopic procedure relies more heavily on visual identification of critical structures without the benefit of manual palpation. Visual perceptual illusion is the primary cause of error in 97% of laparoscopic bile duct injuries. Faulty technical skills are present in only 3% of injuries which likely explains why, despite improving equipment and increasing laparoscopic experience, the incidence of bile duct injury has not decreased over time (≤1.5%). This illusion can be so convincing that surgeons fail to recognize duct misidentification and erroneous transection of the duct even after it has occurred. One study reports that in 42 cases of bile duct injury, the injury was unrecognized in 70% of patients; delay of recognition even persisted into the postoperative period in 57%.

Per the original author, Strasberg et al., the critical view of safety has three requirements:

1. The triangle of Calot must be cleared of fat and fibrous tissue. The common bile duct does *not* need to be exposed.
2. The lowest part of the gallbladder must be separated from the cystic plate (liver bed of the gallbladder).
3. Two structures, and only two structures, should be seen to enter the gallbladder (cystic duct and artery).

Once these three criteria are fulfilled, the critical view of safety has been attained.

The importance of obtaining this view is demonstrated by multiple studies. If 97% of bile duct injury is due to misidentification, then it serves that the critical view of safety – if properly achieved – should significantly reduce the number of bile duct injuries in laparoscopic cholecystectomies. A study of 3042 patients undergoing laparoscopic cholecystectomy and using the critical view of safety for structural identification between 2002 and 2006 reported only one bile duct injury in an 80-year-old patient. The injury was incurred prior to achieving the view. This reported rate of injury was an order of magnitude lower than the expected 2–4 per 1000 cholecystectomies. A prospective study conducted between 2002 and 2004 involving consecutive laparoscopic cholecystectomies in which the critical view of safety was photodocumented in 97 of 100 patients reported a single postoperative cystic duct stump leak. Kaya et al. reported in 2017 that 0 of 120 patients in whom the critical view of safety was achieved suffered intraoperative or postoperative biliary complications.

Despite the well-demonstrated efficacy of the critical view of safety, a study involving ten surgeons of variable training and experience across six hospitals in North Carolina found that only two surgeons (20%) satisfactorily achieved the critical view of safety during laparoscopic cholecystectomy. Although this is an isolated study with a small sample size, it serves to remind all readers to clearly and purposefully obtain the critical view of safety.

Laparoscopic Partial Cholecystectomy and Damage Control

Performing a cholecystectomy in the acute setting can be technically challenging, and the anatomy difficult to discern. The feasibility and safety of a laparoscopic partial cholecystectomy in cases of difficult laparoscopic cholecystectomy is emerging as an alternative to open conversion. Traditionally, when the critical view of safety could not be obtained due to acute inflammation, unfamiliar anatomic variants, or any other reason, conversion to open cholecystectomy was advised. However, some surgeons may feel more comfortable operating laparoscopically. This is becoming more applicable to younger generations of surgeons who perform relatively few, if any, open procedures. There is also evidence that conversion of laparoscopic to open cholecystectomies is at increased risk of major complications compared to a planned open cholecystectomy. Therefore, conversion may no longer be the best alternative when positive identification of biliary anatomy cannot be obtained.

The first open partial cholecystectomy for management of difficult gallbladders was described in 1985 by Bornman and Terblanche. Since 1993, laparoscopic partial cholecystectomies have also been performed. The technique was developed as an alternative to conversion to open cholecystectomy in situations where injury to biliary structures or the cystic artery was at increased risk. There are different techniques described but primarily revolve around either removal or non-removal of the posterior wall and closure or non-closure of the cystic duct and gallbladder stump. The most basic definition of a partial cholecystectomy requires "some portion of the gallbladder left in continuity with the cystic duct and not resected." No parallel randomized controlled studies directly comparing techniques exist.

A systematic review conducted in 2013 reported on 625 patients and 4 different operative techniques. The review included primarily retrospective consecutive studies, but four prospective consecutive studies were also included. Of the 625 patients included, 90% of patients undergoing difficult resection safely underwent laparoscopic partial cholecystectomy. Only 10.4% of patients required conversion to open procedure. One case of major bile duct injury occurred. The most frequent complication was bile leakage from an inadequately or not closed cystic duct. Gallstone formation in the gallbladder remnant pouch is often cited as a concern in regard to partial cholecystectomy. Symptomatic gallstone disease was found to be present in only 4 of 184 patients (2.2%) who underwent partial cholecystectomy.

The authors of this systematic review suggest that:

> LPC seems to be feasible and may be a good alternative to conversion for a difficult gallbladder at LC.

However, they make no firm recommendations in regard to the method of partial cholecystectomy, but they do recommend closure of the remnant gallbladder pouch, cystic duct, or both to minimize the risk of a postoperative bile leak; this was higher in a series that did not close the gallbladder stump.

A 2015 meta-analysis – which included many of the same studies – similarly concluded that subtotal cholecystectomy, when necessary, is associated with morbidity rates in difficult gallbladders comparable to rates reported for total cholecystectomy. The authors state that:

> ...treatment in patients with complex conditions undergoing SC is managed as safely as in patient with simple conditions undergoing TC.

The authors' results suggest that laparoscopic subtotal cholecystectomy produces less risk of

subhepatic collections, retained stones, wound infections, reoperations, and mortality but more bile leaks compared with open subtotal cholecystectomy. They failed to demonstrate any significant difference between different subtotal cholecystectomy techniques and therefore make no recommendations.

Readers should note that many of the studies included in the two publications discussed above were retrospective studies with small sample sizes and of poor quality. Furthermore, the exact surgical techniques utilized varied between studies and made pooling of data difficult. Continued high-quality research is necessary.

Summary of Recommendations

Gallstone disease is more common in the elderly, women, obese, and those with poor dietary patterns. Two-thirds of patients with gallstones are asymptomatic, and only 2–3% per year of patients with asymptomatic gallstones will progress to symptomatic gallstone disease. Early laparoscopic cholecystectomy should be the standard procedure of choice for patients with acute cholecystitis. Early laparoscopic cholecystectomy during the index admission is suggested for patients presenting with mild acute gallstone pancreatitis. There is limited evidence to suggest performing laparoscopic cholecystectomy 1–3 weeks after presentation in patients with severe pancreatitis. Obtaining the critical view of safety is critical to safely performing a laparoscopic cholecystectomy. A laparoscopic partial cholecystectomy is a feasible alternative to conversion to open cholecystectomy when managing a difficult gallbladder.

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