ACUTE CHOLECYSTITIS

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ABSTRACT

Acute cholecystitis is the inflammation of the gall bladder. The most common cause is the presence of gall stones. It accounts for 3%−10% of all patients with acute abdominal pain, being higher in patients >50 years than in younger patients. More than 80% of patients with cholelithiasis are unaware of their disease and are asymptomatic. Therefore less than 20% of these patients become symptomatic with attacks of biliary colic. Only 20% of these symptomatic patients develop ACC.

KEYWORDS: Acute cholecystitis, Gall stones, Acute acalculous cholecystitis.

INTRODUCTION

Acute cholecystitis (AC) is an acute inflammation that involves the wall of the gallbladder with various degrees of severity.[1] It may be calculous or acalculous.

Acute calculous cholecystitis (ACC)

Gallstones (cholelithiasis) account for 90%−95% of all cases of AC.[2-5] It accounts for 3%−10% of all patients with acute abdominal pain, being higher in patients >50 years than in younger patients.[6,7] Its incidence is estimated to be approximately 1-4% every year.[8] More than 80% of patients with cholelithiasis are unaware of their disease and are asymptomatic. Therefore less than 20% of these patients become symptomatic with attacks of biliary colic.[9,10] Only 20% of these symptomatic patients develop ACC.[11]

Pathologically

ACC begins by impaction of a stone in the cystic duct.[12] Obstruction of the cystic duct increases the pressure inside the gallbladder leading to its dilatation, biliary stasis and proliferation of microorganisms, congestion of capillaries and lymphatics in the wall, with subsequent subserosal edema and wall thickness. This stage lasts for 2-4 days. If not detected and treated in this stage, areas of hemorrhage and necrosis begin to appear in the gallbladder wall due to vascular thrombosis. The necrotic areas are superficial and does not involve the full thickness of the gallbladder wall. If not treated in this stage the gallbladder wall becomes inflamed with neutrophils infiltration and areas of suppuration involving the entire thickness of the gallbladder wall with pericholecystic abscess formation.[13]

Clinically

Typically, the patient presents with acute constant pain localized in the right upper abdomen which may radiate to the epigastrium, posterior right scapula or right shoulder area. The pain is usually precipitated by ingestion of a fatty meal and associated with nausea and vomiting.[13] This acute presentation is usually preceded by several attacks of biliary colic. The typical patient is usually an obese fair female, in the fourth decade of life. There may be a history of multiple pregnancies or taking birth control pills or history of rapid weight loss.[14-18] Family history of gallstones may be present.[19]

Tachycardia and elevated temperature are characteristic vital signs in AC.

Abdominal examination reveals tenderness in the right upper quadrant with positive Murphy's sign (Inspiratory arrest with manual pressure below the gallbladder).[20] A palpable gallbladder may be elicited.

Diagnosis: White blood cell count (WBC) is a critical laboratory investigation to diagnose the presence and severity of AC. Typically 12000-15000/mm^3 is diagnostic for the presence of acute inflammation of the gallbladder. A WBC count >20000/mm^3 should suggest further complications of AC such as the formation of pericholecystic abscess. Liver function tests including serum bilirubin and alkaline phosphatase may be abnormal.[21]

Abdominal ultrasound (AUS) remains the best diagnostic test for ACC as it can diagnose the presence of gallstones as well as the assessment of the degree of inflammation of the gallbladder wall. It is safe, cheap, rapid, not

invasive and accessible in emergency department. US findings include the presence of an obstructing gallstone, wall thickening, pericholecystic fluid or abscess. US provides additional information about the size of the common bile duct CBC and the presence of CBD stones or hepatic ducts dilatation. A stone < 1.5 mm may not be detected by US. Its sensitivity and specificity ranges between 90-95%.[12]

Computed tomography (CT) scan occasionally is performed in evaluating the patient with abdominal pain and acute illness. It may demonstrate evidence of ACC, including gallbladder wall thickening, pericholecystic fluid and edema and gallstones, although it is less sensitive in these than US.[22]

Hepatobiliary iminodiacetic acid (HIDA) scan occasionally is needed to provide additional information in cases that are not well defined by US. It enables visualization of the biliary system. Concentration of the radionuclide in the bile by the liver allows a demonstration of bile flow from the liver into the common hepatic duct, filling or non-filling of the gallbladder, and emptying of the gallbladder and biliary tree in the duodenum. Non filling of the gallbladder is an evidence of the presence of ACC.[23]

After confirmation of the diagnosis, the disease severity should be classified. Although there are a lot of options for severity assessment, the revised Tokyo consensus guidelines (TG13) represent the best parameters for directing diagnosis and treatment of AC.[24,25] According to TG13, AC can be classified into grade I; mild, grade II; moderate and grade III; severe.[25] **(Table 1).**

Table. 1: Severity assessment criteria for acute cholecystitis.

Grade	Definition
I (mild)	Acute cholecystitis does not meet the criteria of "Grade III" or "Grade II" It can also be defined as acute cholecystitis in a healthy patient with no organ dysfunction and mild inflammatory changes in the gallbladder, making cholecystectomy a safe and low-risk operative procedure
II (moderate)	Acute cholecystitis is associated with any one of the following conditions: 1. Elevated white blood cell count (>18,000/mm3) 2. Palpable tender mass in the right upper abdominal quadrant 3. Duration of complaints > 72 hours 4. Marked local inflammation (gangrenous cholecystitis, pericholecystic abscess, hepatic abscess, biliary peritonitis, emphysematous cholecystitis).
III (severe)	Acute cholecystitis is associated with dysfunction of any one of the following organs/systems 1. Cardiovascular dysfunction defined as hypotension requiring treatment with dopamine ≥ 5 μg/kg per min, or any dose of norepinephrine 2. Neurological dysfunction defined as decreased level of consciousness 3. Respiratory dysfunction defined as a PaO2/FiO2 ratio < 300 4. Renal dysfunction defined as oliguria, creatinine > 2.0 mg/dl 5. Hepatic dysfunction defined as PT-INR > 1.5 6. Hematological dysfunction defined as platelet count < 100,000/mm^3

From "Yokoe M, et al.[26]

Management of ACC
Initial management includes hospital admission, no further intake by mouth, intravenous hydration and systemic antibiotics. The antibiotic regimen should be appropriate for typical bowel flora (gram negative rods and anaerobes). Regimens include: third generation cephalosporin with anaerobic coverage or third generation cephalosporin with metronidazole or aminoglycoside with metronidazole.[12]

This systemic treatment must be reassessed frequently and should include: monitoring of the patient as regards temperature curve, physical examination and laboratory values. In most patients, AC will resolve with conservative systemic treatment.

Patients in whom conservative treatment was successful (about 90%) should have laparoscopic cholecystectomy either early (24-72 hours of onset) or delayed (6-12 weeks later).[27] The most recent prospective multicenter trial comparing early and delayed cholecystectomy confirmed that early cholecystectomy was associated with significantly lower morbidity, hospital stay and hospital cost.[28] These results suggest that early cholecystectomy should be considered the treatment of choice.[29,30]

From 9-13% of patients do not show improvement or even deteriorate[31,32], then alterations in the treatment must be made; either change in the systemic antibiotics being administered or moving the patient to operation either cholecystectomy or cholecystostomy.

Types of cholecystectomy
Laparoscopic cholecystectomy (LC) is the gold standard treatment of ACC.[33] The advantages of LC made it attractive to patients, surgeons and hospitals. Advantages include less scarring, shortened hospital

stays and earlier returns to usual activities.[34] Increased surgical experience and technical innovations have extended the indications for the laparoscopic approach to patients with complicated disease processes. LC has certain limitations, such as two-dimensional imaging, restricted range of motion of the instruments and poor ergonomic positioning of the surgeon.[35]

Open cholecystectomy (OC): Still, there are a number of patients who require conversion to OC for the safe completion of the surgical procedure.[36] Conversion rates of 2.6% to 14% had been described in literature.[36-39] Reasons for conversion of LC to OC include difficult dissection due to dense adhesions, severe inflammation, obscure anatomy and retraction difficulty, common bile duct (CBD) problems such as abnormal laparoscopic intraoperative cholangiography (IOC), failed attempt at laparoscopic CBD exploration and failed attempt at IOC, bleeding, duodenal injury, cystic duct avulsion, respiratory acidosis, and miscellaneous factors which includes enterobiliary fistula, inability to secure cystic duct, equipment problems and unsuspected pathology.[39]

Robotic cholecystectomy: In recent years, robotic-assisted surgery has gained popularity in general and gastrointestinal surgery.[40] Advantages of robotic technology include the three-dimensional view, improved ergonomics, the ability to articulate instruments and the more natural feel of open surgery.[41] In select surgical procedures, robotic surgery has improved outcomes over laparoscopic and open surgery.[42] Early experience has shown robotic cholecystectomy (RC) to be safe with a low rate of major injury.[43] The cost and utilization of robotic surgery has been well elucidated[44]; however, the cost utility or cost-effectiveness factoring in outcome benefits compared to LC has yet to be determined.

Cholecystectomy in cirrhotic patients: The major difficulties encountered during LC in cirrhotic patients include, adhesions with increased neo-vascularity, difficult retraction of the liver, inadequate exposure of Calot triangle, a high-risk gallbladder bed and a high risk hilum.[45,46] Conversion to open surgery is always an option if laparoscopic dissection proves difficult. Operative time, conversion and morbidity rate were significantly higher in cirrhotic patients. Conversion is meant to prevent more serious complications which include significant bleeding or biliary tract injury, leading to deterioration of liver function and sepsis.[47-49] Mortality rates as high as 76% have been reported in patients diagnosed with class C cirrhosis.[50,51] The most important predictors of mortality are severity of liver disease reflected by the model for end-stage liver disease (MELD) score, age, and comorbid conditions as determined by the American Society of Anesthesiologists (ASA) physical status classification.[52]

Subtotal cholecystectomy (SC): This is a rescue procedure in cases of technically difficult total cholecystectomy.[53] SC involves piecemeal excision of the gallbladder, starting at the Hartmann pouch and leaving a rim of the posterior wall attached to the liver. The mucosa of this remnant is coagulated or left intact, and the cystic duct is closed from within the gallbladder with a purse-string suture. This technique was adopted by numerous surgeons with minor modifications.[54-57] With the introduction of laparoscopic cholecystectomy, laparoscopic SC is considered in cases of difficult cholecystectomy.[58]

SC is indicated in severe cholecystitis, inflammation, and fibrosis at the Calot triangle which made the dissection of the cystic duct and artery difficult and potentially dangerous.[59-61] It is also indicated in cases of cholelithiasis in liver cirrhosis and portal hypertension[56,62,63], gangrene, empyema, or perforated gallbladder.[55,64,65]

Postoperative subhepatic collections and bile leaks were more frequent postoperative outcomes following SC.[34,66,67] It is possible that stones were missed in the gallbladder remnant or slipped from the gallbladder into the CBD during difficult dissections.[68,69] Similarly, postoperative ERCPs were more frequent following SC.[66] Reoperation rates and mortality rates were higher following SC.[34,66,67,70] This finding could reflect the greater technical difficulty of patients undergoing SC.

Percutaneous cholecystostomy (PC): Although cholecystectomy is generally safe, the mortality rate of cholecystectomy in patients at high risk for surgery from comorbid conditions ranges between 14% and 30%.[71,72] Factors contributing to the high surgical mortality in this setting include the presence of sepsis, poor general condition of the patient, immunosuppression and diminished liver function. As a temporizing measure, high-risk patients are treated with a regimen consisting of decompression of the gallbladder combined with broad-spectrum antibiotics.

Bile is sent for gram staining, culture and cell count. Bed rest (for 2 - 4 hours) with regular monitoring of vital signs, provision of adequate analgesia is routinely indicated in the first few hours following the procedure. Catheter is flushed and aspirated regularly with saline (6 to 8 hourly). A cholecystogram is performed when the patient is stable, to help establish satisfactory catheter position and the state of the gallbladder. Complication rate is around 10% and includes bile leaks, bleeding requiring transfusion and drain migration.[73]

Specific forms of ACC
ACC with pregnancy: Pregnancy carries a higher risk of developing ACC than non-pregnant patients.[74,75] ACC is the second most common cause of acute abdomen in pregnant women Routine US detect cholelithiasis in 3.5% of pregnant women.[76] Approximately 30% eventually require surgery during their pregnancy because recurrence of symptoms occur

in most symptomatic patients treated with nonoperative therapy. If possible, surgery should be avoided during the first trimester to avoid abortion and third trimester to avoid premature delivery.[77] There is no evidence that LC increases the maternal or fetal risks.[78]

ACC in children: Hemolytic diseases are responsible for 20%-30% of cholelithiasis in children. Ileal disease, ileal resection and total parenteral nutrition are responsible for 40%-50% of cases.[79-81] In these children, regular screening with ultrasound (US) is recommended to detect the presence of gallstones.[82] In the presence of gall stones, cholecystectomy is recommended even it is asymptomatic.[83] About 30% to 40% of gallstones in children are idiopathic.[79-81]

ACC with jaundice: The presence of jaundice with ACC should be evaluated with caution because it reflects a wide spectrum of potentially benign and malignant conditions. Although US continues to be the diagnostic gold standard for detecting choledocholithiasis (especially within the distal CBD), MR cholangiography (MRC) may also be useful to define the etiology.[84] The goals of the treatment includes treatment of concurrent sepsis, evacuation of the CBD, and prevention of future recurrences. ERCP and laparoscopic cholecystectomy represent the 2 dominant therapies.[85,86] Laparoscopic CBD exploration (transcystic or transductal) is also a viable option and has the added benefit of being performed as a single procedure.[87,88]

ACC and drugs: Drugs promoting the formation of stones are indirectly associated with a risk of ACC.[89] It is reported that women taking oral conceptives have a higher risk of having gallbladder disease.[90] Fibrate used for the treatment of hyperlipidemia is shown to be associated with gallstone diseases.[91] One report suggests that thiazides induce ACC.[92] The administration of a large dose of ceftriaxone, a third-generation cephalosporin antimicrobial, in infants, precipitates calcium salt in bile and forms a sludge in 25%–45% of them, but these effects disappear when the medication is discontinued.[89] It is reported that the long-term administration of octreotide causes cholestasis, and that administration for a year causes cholelithiasis in 50% of patients.[89]

ACC and Ascaris: Complications in the biliary tract include cholelithiasis with the ascarid as a nidus for stone formation and ACC.[93] Biliary tract disease is caused by the obstruction of the hepatic and biliary tracts by the entry of ascarids from the duodenum through the papilla. Ascarids entering the biliary tract usually return to the duodenum in a week, but if they stay over 10 days there, they will die and form a nidus for stone formation. Ascarid-associated biliary diseases occur more frequently in women (male/female ratio 1: 3) and less frequently in infants. The risk of biliary complications is higher in pregnant than in non-pregnant women.[93] In epidemic regions such as China and Southeast Asia, ascariasis is a frequent cause of cholelithiasis.[93]

ACC in cirrhotic patients: Cholelithiasis is very common in cirrhotic patients (15-30%), occurring 1 to 3 times more often than in general population. Gallstones are usually small and friable due to diminished gallbladder contractility and increased bile flow and rarely migrate thus making them frequently asymptomatic. When symptoms do occur, they are similar to those accounted in general population: biliary colic, acute cholecystitis, cholangitis. Septic complications can cause cirrhosis decompensation and thus dominating the clinical picture. The presence of cirrhosis, hepatocellular failure and/or portal hypertension increases the risk of postoperative complications in any type of surgery, especially on the biliary tree. In case of cirrhosis, the indication of cholecystectomy should be particularly weighted.[50,94]

Acute Acalculous Cholecystitis (AAC)
Five to 10% of AC are acalculous.[95] Presence of an inflamed gallbladder in the absence of an obstructed cystic duct. Aetiology is thought to have ischemic basis in the form of atherosclerosis or thrombosis of the cystic artery. Therefore, inflammation of the wall of the gallbladder in presence of ischemia may result in gangrene, perforation, peritonitis and septic shock with high mortality rate.[96]

Emphysematous cholecystitis (EC): is an uncommon variant of AAC.[97] EC frequently affects elderly men and diabetics. The causative organisms are gas-forming bacteria (anaerobes) including Clostridium perfringens.[96]

Typically AAC occurs in the setting of a critically ill patient (e.g., severe burns, multiple traumas, lengthy postoperative care, and prolonged intensive care) and in patients known to have immunosuppressive conditions[98], or under immunosuppressive therapy.[95]

Symptoms of AAC are usually very vague and may adopt different forms from minimal pain to septic shock[99], therefore, it should be suspected in these types of patients. Early diagnosis can be achieved by US. In cases with EC, it shows air in the gallbladder lumen; in the wall, or in the adjacent tissues and elsewhere in the biliary ducts.[96] When US examination is positive, it should be followed by computed tomography (CT) because it is the most sensitive modality for the detection of the intraluminal or intramural gallbladder gas[100], and it can also demonstrate local complications, such as pericholecystic inflammatory changes, abscess formation, or perforation.[101]

The treatment proposed is cholecystectomy, either conventional or laparoscopic. As an alternative technique percutaneous cholecystostomy may be used, if the

patient's situation is not good enough for surgical treatment.[102]

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