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A focus on acute cholecystitis and acute cholangitis

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ABSTRACT

Biliary infections are very common intra-abdominal infections. Laparoscopic cholecystectomy for acute cholecystitis and endoscopic retrograde management of acute cholangitis play important roles in the treatment of biliary infections. Also antimicrobial therapy is nevertheless important in the overall management of biliary infections. A multidisciplinary team of physicians, including surgeons trained in laparoscopic techniques, interventional gastroenterologists, and interventional radiologists may improve outcomes of patients with biliary infections. This review focuses the clinical presentation, diagnosis, and state of the art management of acute cholecystitis and acute cholangitis.

1. Introduction

Gallbladder stones are an extremely common disorder and are usually asymptomatic, but they may cause insidious infections.

Acute cholecystitis is a bacterial infection caused by an obstruction of the cystic duct with gallstones. The obstruction results in gallbladder distention, wall edema, ischemia and bacteria infection. The wall of the gallbladder may undergo necrosis and gangrene and ultimately perforate, with the development of an abscess or generalized peritonitis. The obstruction is usually caused by gallstones (>90%), but acute cholecystitis may infrequently be acalculous or caused by sludge[1-2].

Acute cholangitis is a bacterial infection caused by an obstruction of the biliary tree most commonly from gallstones.

The biliary tract obstruction results in elevated intraluminal pressure, and infection of bile.

2. Acute cholecystitis

2.1 Diagnosis

No single clinical finding or symptom carries have sufficient weight to establish or exclude acute cholecystitis without further testing. Clinical symptoms of acute cholecystitis may include severe abdominal pain (right upper abdominal pain), nausea, vomiting and fever.

Clinical findings of acute cholecystitis may include tenderness in the right upper abdomen and palpable gallbladder and Murphy's sign[3-4].

Ultrasound is the imaging examination of first choice in acute cholecystitis.

The sensitivity of sonography for this condition ranges from 80% to 100% and specificity ranges from 60% to 100%. Ultrasound imaging findings may include Cholelithiasis, gallbladder wall thickening (>4-5 mm), enlarged gallbladder (long axis diameter >8 cm, short axis diameter >4 cm), pericholecystic fluid, presence of a positive sonographic Murphy sign, abnormally increased gallbladder distention and echogenic bile (sludge)[5-7].

The combination of ultrasonography and measurement of C reactive protein concentration may be helpful in the routine investigation of all patients with suspected acute cholecystitis[8].

In 1992 an interesting prospective clinical study was published in order to assess the value of ultrasonography together with C reactive protein concentration in predicting which patients with acute cholecystitis require immediate operation. Ultrasonography correctly classified 79% with acute cholecystitis. When the findings were combined with those of increased concentrations of C reactive protein the accuracy rose to 97%.

CT is commonly used in the evaluation of abdominal pain when other diagnoses in addition to acute cholecystitis are

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being considered.

CT Imaging findings may include gallbladder wall thickening (>3–5 mm), mural or mucosal, hyperenhancement, pericholecystic fluid, adjacent soft-tissue inflammatory stranding abnormally increased, gallbladder distention and cholelithiasis that may be observed on CT in the setting of acute cholecystitis[9-10].

MRI is playing an increasing role in the evaluation of acute right upper abdominal pain, particularly for pediatric and pregnant patients. MRI has sensitivity of 95% and specificity of 69% for the detection of acute cholecystitis, it allow to investigate common bile duct stones.

Imaging MRI findings for acute cholecystitis may include pericholecystic high signal, enlarged gallbladder and Thickened gallbladder wall[11-13].

2.2 Surgical management

Although acute cholecystitis had initially been considered a contraindication to laparoscopic cholecystectomy because of the higher incidence of complications than in non-acute cholecystitis, many evidences showed that laparoscopic cholecystectomy is an effective treatment for acute cholecystitis[14-19].

Common bile injuries during laparoscopic cholecystectomy for acute cholecystitis remain the most serious complication associated to this procedure. Especially in the beginning of the laparoscopic area, several studies reported much higher rates of common bile duct injuries but it decreased significantly as the laparoscopic experience of the surgeon increased[20,21].

The most important innovation in the surgical treatment of acute gallstone cholecystitis (AGC) concerns timing.

Acute cholecystitis may be treated by both early laparoscopic cholecystectomy (early operation and antimicrobial prophylaxis) and delayed laparoscopic cholecystectomy (delayed operation and antimicrobial therapy).

Many evidences showed that early laparoscopic cholecystectomy during acute cholecystitis appears safe and shortens the total hospital stay when it is compared with delayed laparoscopic cholecystectomy[22-25].

Some reports (case-series studies) have examined the effectiveness and safety of percutaneous transhepatic gallbladder drainage as the treatment of first choice for acute cholecystitis in elderly patients, particularly in those with comorbid conditions, and they indicate its usefulness.

There are no controlled studies evaluating the outcome of percutaneous cholecystostomy *vs.* cholecystectomy. It is not possible to make definitive recommendations regarding treatment by PC or cholecystectomy in elderly or critically ill patients with acute cholecystitis. Low mortality rates after cholecystectomy in elderly patients with acute cholecystitis have been reported in recent years[26].

Gallbladder perforation is an unusual initial presentation of gallbladder disease. Early diagnosis of gallbladder perforation and immediate surgical intervention are of prime importance in decreasing morbidity and mortality associated with this condition. It is rarely diagnosed preoperatively. Late operative intervention is associated with increased morbidity, mortality, number of ICU admissions, and long postoperative hospital stays. An early cholecystectomy strategy may lead to improved outcomes but may be difficult to implement and may not be cost-effective[27-31].

3. Acute cholangitis

3.1 Diagnosis

Clinical findings associated with acute cholangitis include abdominal pain, jaundice, fever (Charcot's triad), and rigor [32,33].

The diagnosis of acute cholangitis requires, white blood cell count, measurement of the C-reactive protein level and liver and biliary function tests[34].

Recently in order to identify common clinical, biochemical, and etiologic variables that can be used to predict mortality and the need for early biliary drainage in patients with acute cholangitis, a retrospective study of patients with acute cholangitis was published. Total bilirubin ($P<0.01$), partial prothrombin time ($P<0.01$), and presence of a liver abscess ($P<0.01$) were found to be significant in predicting mortality. Alanine aminotransferase ($P<0.01$) and white blood cell count ($P<0.01$) were determined to be predictive of a need for early biliary drainage[35].

3.2 Biliary Drainage

The goals of therapy for choledocholithiasis are to remove the stones from the biliary tree and to decompress the biliary tree urgently if bacterial cholangitis is present.

Biliary drainage takes the most important part in the treatment of acute cholangitis.

Biliary drainage can be achieved by endoscopic, percutaneous transhepatic or open drainage

Literature showed that endoscopic drainage is the effective method to drainage biliary tree.

In 1992 a randomized controlled trial was conducted to compare endoscopic and open drainage in 82 patients with severe acute cholangitis with hypotension and disturbed consciousness. This study demonstrated that the morbidity and mortality of endoscopic nasobiliary drainage endoscopic sphincterotomy were significantly lower than those of T-tube drainage under laparotomy. The Authors concluded that morbidity and mortality of endoscopic nasobiliary drainage + endoscopic sphincterotomy were lower than those of T-tube drainage under laparotomy[36].

Also the usefulness of percutaneous transhepatic drainage has been widely investigated[37,38]. However, even if there is no randomized study comparing endoscopic and percutaneous drainage, endoscopic drainage currently is the method of first choice because of a lower risk of complication than percutaneous procedures. Considering the lower occurrence of serious complications such as intraperitoneal hemorrhage and biliary peritonitis, and the shorter duration of hospitalization, endoscopic drainage is the preferred method[39,40].

Open drainage should only be used in patients for whom endoscopic or percutaneous transhepatic drainage is contraindicated or those in whom it has been unsuccessfully performed.

Gallbladder management after biliary drainage. Some studied showed that the incidence of cholecystitis in patients whose gallbladders have been left with stones after endoscopic sphincterotomy for choledocholithiasis is not significantly different from the incidence of cholecystitis in patients with asymptomatic cholecystolithiasis[41-44].

However in 2002 a randomized control trial assessed the clinical value of prophylactic laparoscopic cholecystectomy in patients whose choledocholithiasis was successfully treated with endoscopic sphinterectmy (all patients had gallbladder stones). Symptoms related to cholecystitis

appeared in 46% of patients who had not undergone prophylactic laparoscopic cholecystectomy. The authors concluded that prophylactic cholecystectomy was of clinical value[45].

3.3 Cholecysto-choledocholithiasis

Combining endoscopic stone extraction during endoscopic retrograde colangiography with laparoscopic cholecystectomy has been found to be a useful means of treating patients with cholecysto-choledocholithiasis.

There were several reports of combinations of endoscopic stone extraction and laparoscopic cholecystectomy, and in most of them, the interval between the two procedures was a few days. Length of time between endoscopic sphincterotomy and laparoscopic cholecystectomy do not affect the latter procedure in terms of complications or conversion to open surgery[46-50].

Laparoscopic common bile duct exploration is well accepted by patients because treatment is obtained during the same operation. Recently a prospective trial that compared laparoscopic cholecystectomy (LC) plus laparoscopic common bile duct exploration (LCBDE) versus endoscopic retrograde cholangiopancreatography sphincterotomy (ERCP) plus laparoscopic cholecystectomy (LC), was published[51]. Both ERCP/S+LC and LC+LCBDE were highly effective in detecting and removing common bile duct stones and were equivalent in overall cost and patient acceptance.

The development of endoscopic techniques changed surgical approach in many regards. Recently the alternative procedure of combined laparoscopic cholecystectomy with intraoperative ERCP and andoscopic sphintectomy is emerging in an attempt to manage cholecysto-choledocholithiasis in a single-step procedure. Some studies[52] suggested that laparoscopic cholecystectomy plus intraoperative ERCP for the management of cholecysto-choledocholithiasis is a safe technique. It offers an alternative for surgeons especially those who do not practice laparoscopic common bile duct exploration to treat patients in a single step procedure.

Antimicrobial therapy for biliary infections. The most important factors for antimicrobial drug selection in biliary infections are antimicrobial activity against causative bacteria, the clinical condition of the patient in question, and the biliary levels of the antimicrobial agents.

The microorganisms that are most often isolated in biliary infections are the gram-negative aerobes, Escherichia coli and *Klebsiella pneumoniae*, and several anaerobes, especially *Bacteroides fragilis*. Activity against enterococci is not typically required[53,54] unless a biliary-enteric anastomosis is present[55].

Even if there are there are no clinical or experimental data to strongly support the recommendation of antimicrobials with excellent biliary penetration for these patients, the efficacy of antibiotics in treating biliary infections depends on the drugs' resulting biliary concentrations.

Tables 1-4 are summarized antimicrobial regimens for antimicrobial therapy in biliary community-acquired intra-abdominal infections, recommended by WSES guidelines[56].

In no critically ill patient and in absence of risk factors for ESBL, Amoxicillin/clavulanate or Ciprofloxacin plus metronidazolo are recommended.

In no critically ill patient and in presence of risk factors for ESBL, Tigecycline is recommended.

In critically ill patient and in absence of risk factors for ESBL, Piperacillin/tazobactam is recommended.

In critically ill patient and in presence of risk factors for ESBL, Tygecycline plus Piperacillin, plus Fluconazole (in presence of risk factors for Candida) are recommended.

Table 1.
Antimicrobial regimens for biliary IAI in no critically patient and in absence of risk factors for ESBL.

Community-acquired biliary IAI	No critically ill patient Absence of risk factors for ESBL
Amoxicillin/clavulanate	Daily schedula: 2.2 g every 6 h (Infusion time 2 h) OR (Allergy to beta-lactams)
Ciprofloxacin	Daily schedula: 400 mg every 8 h (Infusion time 30 min)+
Metronidazole	Daily schedula: 500 mg every 6 h (Infusion time 1 h)

Table 2.
Antimicrobial regimens for biliary IAI in no critically patient and in presence of risk factors for ESBL.

Community-acquired biliary IAI	No critically ill patient Presence of risk factors for ESBL
Tigecycline	Daily schedula: 100 mg LD then 50 mg every 12 h (Infusion time 2 h)

Table 3.
Antimicrobial regimens for biliary IAI in critically patient and in absence of risk factors for ESBL.

Community-acquired biliary IAI	Critically ill patient (> SEVERE SEPSIS) Absence of risk factors for ESBL
Piperacillin/tazobactam	Daily schedula: 8/2 g LD then 16/2 g/die by continuous infusion or 4.5 g every 6 h (infusion time 4 h)

Table 4.
Antimicrobial regimens for biliary IAI in critically patient and in presence of risk factors for ESBL

Community-acquired biliary IAI	Critically ill patient (SEVERE SEPSIS) Presence of risk factors for ESBL
Piperacillin	Daily schedula: 8 g by LD then 16 g by continuous infusion or 4 g every 6 h (Infusion time 4 h)+
Tigecycline	Daily schedula: 100 mg LD then 50 mg every 12 h (Infusion time 2 h)+/-
Fluconazole	Daily schedula: 600 mg LD then 400 mg every 24 h (Infusion time 2 h)

4. Conclusions

Acute cholecystitis and acute cholangitis are very common intra-abdominal infections.

When it is possible, acute cholecystitis should be treated with early laparoscopic treatment. In critically ill patients treatment may be with percutaneous cholecystostomy. Endoscopic drainage is the preferred form of biliary drainage in acute cholangitis and these patients should subsequently undergo elective laparoscopic cholecyctectomy.

Effective management of acute cholecystitis and acute

cholangitis relies on close cooperation between surgeons, gastroenterologists, and radiologists.

Conflict of interest statement

The authors declare that there is no conflict of interest.

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