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Review Article

Acute Calculus Cholecystitis: An Update: Review Article

Kumar, H. R. MBBS, MS[1*], Somanathan, M. FRCS[2]

[1]Department of Surgery, Taylors University School of Medicine and Health Science, 47500 Selangor, Malaysia
[2]Taylor's University School of Medicine Clinical Campus, 47500 Sg Buloh, Selangor, Malaysia

***Corresponding Author:** Kumar, H. R
Department of Surgery, Taylors University School of Medicine and Health Science, 47500 Selangor, Malaysia

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Abstract: The management of acute calculus cholecystitis has evolved from conservative treatment with intra-venous antibiotics and analgesics to early cholecystectomy. Cholecystectomy is considered the definitive management of acute calculus cholecystitis and laparoscopic cholecystectomy is the gold standard in the management of acute calculus cholecystitis. The management of acute calculus cholecystitis can be divided into early laparoscopic cholecystectomy and delayed laparoscopic cholecystectomy. The current trend in the management of acute calculus cholecystitis is early laparoscopic cholecystectomy. The grey areas in the management of acute calculus cholecystitis include the timing of early laparoscopic cholecystectomy and the role of percutaneous cholecystostomy in high-risk patients. We have conducted this review article to look at the role of conservative treatment, the time for performing an early laparoscopic cholecystectomy and the role of percutaneous cholecystostomy.

Keywords: Acute calculus cholecystitis, laparoscopic cholecystectomy, early cholecystectomy, percutaneous cholecystostomy, conservative management.

INTRODUCTION

Acute calculus cholecystitis is a complication of gallstone disease that is characterized by inflammation of the gallbladder secondary to obstruction of the cystic duct by gallstones. Its clinical presentation includes symptoms of upper abdominal pain and on examination of the abdomen, Murphy's sign is usually positive. Laboratory investigations may reveal leukocytosis, raised C-reactive protein and imaging with an ultrasound abdomen which will reveal thickening of the gallbladder and presence of gallstones. This condition is more common in women and is seen in 20% of cases of biliary colic (Halpin, 2013; Indar & Beckingham, n.d.; Strasberg, 2008; Yusoff *et al.*, 2003).

Acute calculus cholecystitis is characterized by bacterial infection of the gallbladder with the more common bacteria being the gram-negative organisms like Escherichia coli, klebsiella and anaerobes like Bacteroides'. The treatment often includes keeping the patient fasted, starting intra-venous antibiotics and analgesics. Antibiotic therapy often includes using third generation cephalosporins like ceftriaxone or amoxycillin clavulanic acid or piperacillin/tazobactam. The definitive treatment of acute calculus cholecystitis is cholecystectomy which can be performed as an open or laparoscopic method (Elwood, 2008; Kuhlenschmidt *et al.*, 2021; Saverio, n.d.).

The severity of acute calculus cholecystitis can be graded according to the Tokyo Guidelines (TG)18/13 into Grade1 which is a mild acute cholecystitis with no organ dysfunction, Grade 2 which is acute cholecystitis with symptoms of more than 72hrs, marked leukocytosis, a tender mass in the right hypochondrium with marked local inflammation. Grade 3 is acute cholecystitis with dysfunction of any of the following systems, cardiovascular, respiratory, renal, hepatic, neurological or hematological. The severity grading is used to stratify the management of patients with acute calculus cholecystitis with grade 1 being managed with elective cholecystectomy, grade 2 with early laparoscopic cholecystectomy and grade 3 are managed with percutaneous cholecystostomy and followed by delayed laparoscopic cholecystectomy (Okamoto *et al.*, 2018; Yokoe *et al.*, 2013, 2018).

The World Society of Emergency Surgeons (WSES) in their guidelines have recommended that the definitive, first line management of acute calculus cholecystitis is laparoscopic cholecystectomy. The timing of laparoscopic cholecystectomy can be divided into early laparoscopic which is performed within 7 days of admission or 10 days from the onset of symptoms. Delayed laparoscopic cholecystectomy can be performed after 6 weeks from the onset of symptoms. Percutaneous cholecystostomy is reserved for high-risk patients who are not fit for laparoscopic cholecystectomy, and it is used as a bridging procedure to stabilize them and perform a delayed laparoscopic cholecystectomy (Ansaloni *et al*., 2016; Campanile *et al*., 2014; Pisano *et al*., 2020).

Severity	Criteria
Grade 1-mild	Acute cholecystitis with mild inflammation of the gallbladder
Grade 2-moderate	Acute cholecystitis with any of the following features-Leukocytosis, duration of symptoms of more than 72hrs, and marked local inflammation
Grade 3-severe	Acute cholecystitis with dysfunction of any one of the following systems-Cardiovascular, respiratory, renal, hepatic, hematological.

Table showing the Tokyo Guideline severity grading for acute cholecystitis.

As there is no current consensus in the management of acute cholecystitis with regards to the role of conservative treatment, the time of performing laparoscopic cholecystectomy and if it should be performed as an early or delayed procedure. The definition of early laparoscopic cholecystectomy has also not been defined. The indication of percutaneous cholecystostomy has been defined but the time of removal of the tube has also not been defined and the time for performing a cholecystectomy has not been standardized. We have conducted this review article looking for answers for all these factors in the management of acute cholecystitis. We conducted a literature review using PUBMED, the Cochrane database of systemic reviews, Google scholar and semantic scholar looking for randomized control trials, non-randomized trials, observational and cohort studies, clinical reviews, systemic reviews, and meta-analysis from 1990 to 2023.The following keywords were used, “acute calculus cholecystitis”, “early cholecystectomy”, “laparoscopic cholecystectomy”, “percutaneous cholecystostomy “and “conservative management”. All articles were in English, and all articles were assessed by manual cross referencing of the literature. Commentaries, case reports and editorials were excluded from this review. Adult male and female patients were included in this study and pediatric patients were excluded.

DISCUSSION

Conservative treatment of acute calculus cholecystitis

All patients who are admitted to the ward for management of acute calculus cholecystitis are managed with conservative treatment. Conservative treatment involves the use of intravenous antibiotics, intravenous fluids, and analgesics to treat this condition. This is done to prepare the patient for surgery and empirical antibiotics are started without obtaining cultures of bile from the gallbladder. The Tokyo Guidelines often requires a specimen of bile from the gallbladder to be sent for culture and sensitivity before starting intravenous antibiotics, but this is not always done in clinical practice. The antibiotics that are prescribed should be able to penetrate the bile in the gallbladder, with coverage against gram negative and anaerobes. The common first line antibiotics that are prescribed include third generation cephalosporins like ceftriaxone, Piperacillin/tazobactam with the quinolones being used as second line antibiotics. There is no consensus on the duration of therapy with the standard therapy being for 5 days (Costanzo *et al*., 2023; Fuks *et al*., 2013; Janssen *et al*., 2020; Kanafani *et al*., 2005).

A systemic review of antibiotic treatment for acute calculus cholecystitis was conducted by van Dijk *et al*., 5830 patients were included in this study of which 2997 had early cholecystectomy, 2791 received initial antibiotics and 42 were treated conservatively. The recurrence rate was 20% and this study concluded that antibiotics are not indicated in the management of acute calculus cholecystitis, but this study only included one randomized trial that compared antibiotic versus non antibiotic treatment and there were substantial heterogenicity in most of the studies. This study highlights the need for further randomized control trials to be conducted to assess if antibiotics are required in the management of acute cholecystitis... (Van Dijk *et al*., 2016).

For high-risk patients or patients with positive bile cultures who present with acute calculus cholecystitis, adequate empirical antibiotic therapy is essential to prevent complications from occurring and to reduce mortality. The common antibiotics that are prescribed include piperacillin/tazobactam which has excellent coverage for the common organisms that cause acute calculus cholecystitis. The other choices of antibiotics include the third generation cephalosporins like cefoperaxone, ceftriaxone and ceftazidime. The recommendation is for short term therapy with antimicrobial therapy and for de-escalation therapy once the organism is isolated (de Miguel-Palacio *et al*., 2023).

The timing of laparoscopic cholecystectomy for acute calculus cholecystitis

The introduction of laparoscopic cholecystectomy has seen a trend from delayed to early laparoscopic cholecystectomy. As our experience in laparoscopic surgery improved, surgeons now are confidently attempting early laparoscopic cholecystectomy as this is associated with reduced cost and reduced hospital stay. Early laparoscopic cholecystectomy means performing the surgery during the index admission (Schuld & Glanemann, 2015; Tzovaras *et al*., 2006).

The time of performing early laparoscopic cholecystectomy for acute calculus cholecystitis is from 24 hours to 7 days from the onset of symptoms. The Tokyo guidelines and the World Society of Emergency Surgeons (WSES) both recommend performing early laparoscopic cholecystectomy within 72hrs of admission for acute calculus cholecystitis (Knab *et al*., 2014; Koti *et al*., 2015).

Several studies have compared early versus delayed laparoscopic cholecystectomy in the management of acute calculous cholecystitis. The conclusions from these studies were that early laparoscopic cholecystectomy was safe, effective, and associated with reduced hospital stay and cost (Agrawal *et al*., 2015; Budişcă *et al*., 2024; Bundgaard *et al*., 2021).

A meta-analysis of randomized control trials on early versus delayed laparoscopic cholecystectomy for acute cholecystitis was conducted by Siddiqui *et al*., 375 patients were included in this study and the early laparoscopic cholecystectomy group was associated with reduced operative time and hospital stay when compared to the delayed laparoscopic cholecystectomy group. A similar meta-analysis of randomized control trials by Lyu *et al*., and Gurusamy *et al.*, also reported the same conclusions (Gurusamy *et al*., 2010; Lyu *et al*., 2018; Siddiqui *et al*., 2008).

A meta-analysis on the timing of cholecystectomy for acute calculous cholecystitis was conducted by Papi *et al*., 1255 patients were enrolled in this study and the complication rates were similar between both groups, but early cholecystectomy was associated with reduced operative time and hospital stay. This was also confirmed by a similar meta-analysis by Cao *et al*., (Cao *et al*., 2016; Papi *et al*., 2004)

The Acute cholecystitis early versus delayed cholecystectomy (ACDC) multi-center randomized control trial was conducted by Gutt *et al*., 618 patients were randomized to 304 patients who underwent early laparoscopic cholecystectomy and 314 patients who underwent delayed laparoscopic cholecystectomy. The morbidity rate, length of hospital stays, and cost were lower in the early laparoscopic cholecystectomy group and this study highlighted that early laparoscopic cholecystectomy can be safely performed in acute calculus cholecystitis (Gutt *et al*., 2013).

A systemic review and meta-analysis on early cholecystectomy for acute cholecystitis in the elderly population was conducted by Loozen *et al*., 592 patients were included in this study, and the morbidity rate was 23% and the mortality rate was 3.5%. This study showed that early laparoscopic cholecystectomy was feasible in the treatment of acute calculous cholecystitis in elderly patients (Loozen *et al*., 2017).

The conclusion from all of these studies was that early laparoscopic cholecystectomy was safe and feasible.

Percutaneous cholecystostomy in acute cholecystitis

This is an interventional radiological procedure to drain the gallbladder in patients who are present with severe acute cholecystitis. It is usually used in patients who present with grade 3 Tokyo Guidelines (TG) severity or in elderly patients with co-morbidities who are not fit for surgery. The procedure can be done via a transhepatic or a transperitoneal approach and it is commonly used as a bridging procedure to stabilize a patient and perform a delayed cholecystectomy once the patient is stable (Gulaya *et al*., 2016; Howard *et al*., 2009; Stanek *et al*., 2018).

A systemic review and meta-analysis on the management of acute cholecystitis in high-risk patients where percutaneous cholecystostomy as a definitive treatment was compared to emergency cholecystectomy by Cirocchi *et al*., 17 studies were included, and the emergency cholecystectomy group had a mortality rate of 2.37% when compared to the percutaneous cholecystostomy group which was 13.78%. The length of hospital stay and readmission rate were lower in the emergency cholecystectomy group. A similar systemic review and meta-analysis on the outcomes of percutaneous cholecystostomy in elderly patients also came with the same conclusion. That emergency cholecystectomy was associated with better outcomes when compared to percutaneous cholecystostomy (Cirocchi *et al*., 2023; Markopoulos *et al*., 2021).

A multi-center randomized control trial on laparoscopic cholecystectomy versus percutaneous cholecystostomy in high-risk patients with acute cholecystitis was conducted by Loozen *et al*., 142 patients with acute cholecystitis were randomized to 66 who underwent laparoscopic cholecystectomy and 68 who underwent percutaneous gallbladder drainage. The major complication rates were 12% in the cholecystectomy group and 65% in the percutaneous drainage group. The

recurrence rate and length of hospital stay was higher in the percutaneous drainage group. This study concluded that cholecystectomy was associated with better outcome in high-risk patients with acute cholecystitis (Loozen *et al*., 2018).

The time of removal of the percutaneous cholecystostomy tube is an area of concern, with the tube being kept in situ for a minimum of 21 days to prevent recurrence of symptoms and readmission to the hospital. A tube cholangiography should also be performed to see if there is free flow of contrast to the duodenum as obstruction of the cystic duct will often lead to recurrence of symptoms (Kayaoglu & Tilki, 2022; Søreide *et al*., 2020).

CONCLUSION

The management of acute cholecystitis has seen a trend towards early laparoscopic cholecystectomy and with better surgical training the risk of conversion to open cholecystectomy can be reduced. Conservative treatment is used to initiate treatment of acute calculous cholecystitis and prepare them for surgery. Percutaneous cholecystostomy does have a role in the initial management of acute calculus cholecystitis in high-risk patients where it may serve as a bridging procedure to perform a delayed laparoscopic cholecystectomy.

The move towards early laparoscopic cholecystectomy can only be implemented in most general surgical units if the general surgeons are willing to treat them as an emergency. Most units continue to treat them with conservative treatment followed by a delayed laparoscopic cholecystectomy.

Early laparoscopic cholecystectomy for acute calculus cholecystitis should be encouraged as it can help reduce cost and the length of stay in the hospital. It can eliminate the need for a delayed laparoscopic cholecystectomy.

Conflict of Interest: There is no conflict of interest.

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