

# Evaluation of Acalculous Cholecystitis, Diagnosis, and Management

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## Abstract

**Background:** Around 10% of all cases of cholecystitis are related to the acalculous disease. Acalculous cholecystitis is traditionally known to occur in patients with critical illness and the symptoms may also be vague and intermittent. Therefore, diagnosing and treating such cases can be very difficult and challenging. **Objective:** In this review, we aimed to assess the published literature that discussed acalculous cholecystitis diagnosis and management. **Method:** PubMed database was used for articles selection, and the following keys were used in the MeSH ("Acalculous Cholecystitis "[Mesh]) AND ("Acalculous Cholecystitis management"[Mesh])). A total of 30 papers were reviewed and included in the review. **Conclusion:** An appropriate history, clinical findings, and laboratory data along with high suspicion index are factors needed in order to reach a correct and rapid diagnosis. These factors should be completed by imaging such as computed tomography and ultrasound. The initial step in treating acalculous cholecystitis should be antibiotics and source control. Then, cholecystectomy or drainage by percutaneous cholecystostomy can be done. Percutaneous cholecystostomy has shown a high success rate in controlling the cases of acalculous cholecystitis.

**Keywords:** Acalculous Cholecystitis, Management, Diagnosis

## INTRODUCTION

Obstruction of the biliary tract from stones is mostly the leading cause of acute cholecystitis <sup>[1]</sup>. Acute calculous cholecystitis is the second source of complicated intra-abdominal infection with a percentage of 18.5% <sup>[2, 3]</sup>. Nevertheless, around 10% of all cases of cholecystitis are related to acalculous disease <sup>[2, 4]</sup>. In this paper, we are going to review the literature that discussed acute acalculous cholecystitis.

## METHODOLOGY

PubMed database was used for articles selection, and the following keys were used in the MeSH ("Acalculous Cholecystitis "[Mesh]) AND ("Acalculous Cholecystitis management"[Mesh])). A total of 30 papers was reviewed and included in the review.

Inclusion criteria: the articles were selected according to the relevance to the project, which should include Acalculous Cholecystitis Management.

Exclusion criteria: all other articles that had no related aspect to the Acalculous Cholecystitis management as their primary endpoint or repeated studies.

## DISCUSSION

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Acute acalculous cholecystitis is the inflammation of the gallbladder without the presence of gallstone<sup>[5, 6]</sup>. Acalculous cholecystitis is prevalent mostly in critically ill patients, after cardiac surgery, severe trauma, abdominal vascular surgery, sepsis or burns<sup>[5, 7, 8]</sup>. Other causes of increasing the incidence of acalculous cholecystitis can be long periods of fasting, total parenteral nutrition, and drastic weight loss. Typically, acalculous cholecystitis affects older men more than females, which have predominance in calculous cholecystitis<sup>[8]</sup>.

The main pathophysiology of the disease is the hypo-motility of the gallbladder. This stasis of the gallbladder is caused by the lack of the stimulation of gallbladder resulting in the concentration of the bile salts. Then, the intraluminal pressure within the gallbladder will rise up leading to progressive ischemia and pressure necrosis. Eventually, gangrenous changes and perforation can result from progressive ischemia and they subsequently may lead to sepsis and shock<sup>[9]</sup>.

Cases of chronic acalculous cholecystitis have more insidious presentations. Symptoms are more prolonged and may be less severe. Symptoms may also be vaguer and more intermittent, despite patients can present with signs of acute biliary colic<sup>[10, 11]</sup>.

Moreover, because of this static condition, enteric pathogens will grow, for example, *Escherichia coli*, *Klebsiella*, *Bacteroides*, *Proteus*, *Pseudomonas*, and *Enterococcus faecalis*. This colonization of bacteria will also contribute to the inflammatory response. The exact cause of chronic acalculous cholecystitis is unknown but hypokinetic biliary dyskinesia results from decreased gallbladder emptying function among chronic patients. Several other factors can cause this condition, for example, hormonal changes, vasculitis, and decreased nerve innervation as a complication caused by conditions, such as diabetes<sup>[12, 13]</sup>.

Gastrointestinal disorders and cardiac events are strictly correlated. They often coexist and the differential diagnosis can be very difficult<sup>[14]</sup>. There are some cardiovascular disorders that can be associated with a hypovolemic state, such as acute myocardial infarction or acute heart failure. As mentioned earlier, this hypovolemic state can lead to ischemic damage to the gallbladder and its inflammation. Cases of aortic dissection have been reported that coexisted with acute acalculous cholecystitis. They suggested that the triad of stasis, ischemia, and sepsis was the pathophysiology behind these cases<sup>[15]</sup>.

The presentation of acalculous cholecystitis is similar to calculous cholecystitis. There are right upper quadrant pain, fever, and a positive murphy's sign<sup>[16]</sup>. Nevertheless, in critically ill patients, the diagnosis can be more difficult than in ambulatory patients because it may have non-specific symptoms, such as symptoms of sepsis, change in mental status, and overall worsening of the clinical course<sup>[17]</sup>. In

addition, the patient sometimes cannot express his abdominal discomfort.

There can be mild elevations in the liver function tests. However, jaundice is not usually caused directly by the disease at least not in the early stages<sup>[16]</sup>. The fulminant course of this disease is mostly associated with empyema, perforation, and gangrene and also significantly higher mortality and morbidity<sup>[5, 18]</sup>. As mentioned earlier, complicated diabetes as well as major cardiovascular disorders, autoimmune disease and AIDS are common predisposing factors<sup>[4, 19, 20]</sup>.

Patients are often asymptomatic. Clinical status and examination cannot be conclusive. Moreover, laboratory data may be entirely negative, not helpful or mild positive and nonspecific especially in late stages of the disease. The diagnosis of acute acalculous cholecystitis is difficult due to the overlapping with concomitant disorders, such as cardiovascular disorders. Early diagnosis and treatment can be useful, or, in certain cases, lifesaving<sup>[15]</sup>.

As mentioned earlier, acute acalculous cholecystitis arises in 0.2–0.4% of all critically ill patients and its mortality rate is 30 %. Delayed diagnosis directly increases mortality<sup>[21]</sup>. Early detection and early intervention will result in clinical improvement and better outcomes. Ultrasound is considered a useful tool in diagnosing cholecystitis in the emergency room. It is not only useful for acute gallbladder disease, but also for other conditions causing abdominal pain, becoming fundamental in the clinical practice. Ultrasound plays a key role in the acalculous cholecystitis diagnosis. It is simple, cost-saving, safe, radiation-free and rapid<sup>[15]</sup>. To confirm the diagnosis, ultrasound imaging can be combined with cholescintigraphy plus cholecystokinin (HIDA-CCK). Nevertheless, the diagnosis can be made if the ultrasound showed a distended gallbladder with inflammation and a thickened wall even without the presence of stones<sup>[16]</sup>. A highly thickened wall or the presence of fluid around the gallbladder in the ultrasound increases the specificity of the diagnosis. Abnormal ultrasound findings can be seen in critically ill patients without having acalculous cholecystitis. Therefore, ultrasound specificity might be low in such patients<sup>[22, 23]</sup>. On the other hand, CT detects gallbladder abnormalities more accurate than ultrasound particularly in critically ill patients despite CT's lack of specificity. There are many similarities between ultrasound and CT regarding the abnormal gallbladder findings. Pneumobilia is considered a highly specific finding for diagnosing acalculous cholecystitis. It is defined as the presence of gas in the gallbladder. However, if there are no abnormal gallbladder features detected in the imaging, it is associated with a high negative predictive value that mostly will rule out the diagnosis of acalculous cholecystitis<sup>[16, 24]</sup>.

A high suspicion index, along with an appropriate history, clinical findings, and laboratory data are needed to achieve a

correct and rapid diagnosis. However, they should be completed by ultrasound imaging. Proper diagnosis allows early treatment of acute acalculous cholecystitis, which reduces the risk of mortality and complications rate [16].

## Management

The initial step in treating acalculous cholecystitis should be similar to treating other infections, i.e. antibiotics and source control. Then, cholecystectomy or drainage by percutaneous cholecystostomy should be done [16].

Intravenous antibiotics administration early plays a critical role in fighting the infection and achieving source control. There are several recommended antibiotic agents for the initial empiric treatment of acalculous cholecystitis [25]. In mild to moderate infection, ceftriaxone, cefuroxime, and cefazolin are sound options. In severe infection or high-risk factors, such as end-organ disease, immunocompromise, and advanced age, cefepime, levofloxacin, piperacillin/tazobactam, ciprofloxacin, or carbapenems, each in combination with metronidazole are the recommended options. Carbapenems or piperacillin/tazobactam, each in combination with metronidazole are the advised options in patients with extended-spectrum beta-lactamase (ESBL)-producing organisms. The duration of antibiotic therapy is related to the control of the source and can be stopped 4-5 days after source control is achieved [25, 26].

Cholecystectomy was the historic treatment of acalculous cholecystitis because of the need to resect or debride the gallbladder in cases of gangrene or perforation [27-29]. However, minimally invasive alternatives, such as percutaneous cholecystostomy are now the recommended approach, especially for unstable patients [27, 30, 31].

The percutaneous cholecystostomy tube should be placed by the interventional radiologist to secure the drainage of the gallbladder [16]. Compared to open cholecystectomy, percutaneous cholecystostomy has shown lower morbidity, fewer admissions in the intensive-care unit, decreased length of stays, and lower costs [32]. Percutaneous cholecystostomy controls acalculous cholecystitis in more than 85% of the patients [33-35]. Moreover, the overall rate of complications of percutaneous cholecystostomy is approximately 2%, which is considered low especially that it is mostly used in critically ill patients [36, 37]. In percutaneous cholecystostomy, the gallbladder is usually intubated under laparoscopic or sonographic control by an anterolateral or anterior trans-hepatic approach to minimize bile leakage. A trans-peritoneal puncture can also be used. If percutaneous cholecystostomy is successful, rapid improvement is expected [27]. In addition, the percutaneous drain might be removed eventually in improved patients, which helps these patients to live comfortably without the burden of the drain and its care [16].

## CONCLUSION

An appropriate history, clinical findings, and laboratory data along with high suspicion index are factors needed in order to reach a correct and rapid diagnosis. These factors should be completed by imaging such as computed tomography and ultrasound.

The initial step in treating acalculous cholecystitis should be antibiotics and source control. Then, cholecystectomy or drainage by percutaneous cholecystostomy can be done. Percutaneous cholecystostomy has shown a high success rate in controlling cases of acalculous cholecystitis. Successful percutaneous cholecystostomy is associated with very good outcomes and rapid improvement.

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