



## OVERVIEW OF CHOLECYSTITIS

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### Abstract

**Introduction:** A gallbladder is a small, pear-shaped organ located under the liver that stores bile produced by the liver. Cholecystitis is inflammation of the gallbladder. After the consumption of food, the gallbladder pumps bile to the small intestine to aid in the digestion of lipids. Bile is sent and received by bile ducts. Inflammation, discomfort, and swelling within the gallbladder can be caused by an infection or obstruction in the gallbladder or the bile ducts that attach to it. Cholecystitis is broadly classified into acute phase (sudden and require urgent care) and chronic phase (slow and longstanding). It can be calculous (related to gallbladder stone) or acalculous. Gallstones affect 15% of the population worldwide, and 20% of these individuals will experience cholecystitis due to developing gallstones. 95% of cases of cholecystitis are caused by gallstones. An inflammatory gallbladder may occur as a gradual reaction to a chronic condition or as an acute response to an immediate one. This is how acute and chronic cholecystitis differs from one another. The most common cause of both acute and chronic cholecystitis is gallstones. Therefore, most situations are "calculous." "Acalculous" is a term used by medical professionals to identify cholecystitis unrelated to gallstones.

**Aim of the study:** The purpose of the present review is to provide an overview of gallbladder inflammation, pathophysiology, manifestation, and management.

**Methodology:** The review is a comprehensive research of PUBMED from 1969 to 2023.

**Conclusion:** Most cases of acute and chronic cholecystitis appear to be caused by a mix of chemical irritants and gallstones, mucus, or inflammation obstructing the cystic duct. Early cholecystectomy is

typically advised once acute cholecystitis has been diagnosed. If deterioration is evident, an emergency procedure ought to be carried out. When acute cholecystitis is simple, surgery is urgently needed. The procedure for chronic cholecystitis can be planned around the patient's schedule, but only when the coexisting conditions have been managed and the patient's health has stabilized.

**Keywords:** Cholecystitis, gallbladder stone

### **Introduction**

A frequent gallbladder pathology called cholecystitis is characterized by inflammation of the gallbladder along with high white blood count, positive Murphy sign, and abdominal pain. One of the common etiology for cholecystitis is gallstones. Gallbladder disease most commonly manifests as gallstones, according to a reliable source. These small stones, which originate in the gallbladder, are composed of cholesterol and hardened bile. In industrialized nations, cholesterol is the main component of gallstones. The remaining substances are called pigment gallstones, and they are made up of calcium bilirubinate and other calcium salts. The tropics and Asia are home to the majority of pigmented stones. Approximately 20 million Americans suffer from gallstones. Gallstones affect 2% of the population annually, and 2% of those affected also experience symptoms. In the US, gallstones affect about 20 million individuals between the ages of 20 and 74. Fourteen million of these are female. Although gallstones can become lodged in a duct or aperture inside the gallbladder, symptoms are rarely present. This may cause acute pain in the abdomen, more precisely in the area directly below the right ribs, between the rib cage and the belly button. The shoulder blade or side may become affected by the pain.<sup>[1,2,3]</sup>

Cholecystitis is broadly classified as

1. Acute Cholecystitis
2. Chronic Cholecystitis

The progressive inflammation of the gallbladder known as acute cholecystitis is typically brought on by gallstones blocking the cystic duct. During the first two to four days of edematous cholecystitis, symptoms such as congestion and edema are noticeable. The 3-5 day stage of necrotizing cholecystitis is marked by bleeding and necrosis. The illness advances to its purulent phase, commonly referred to as suppurative cholecystitis, between 7 and 10 days. The condition develops into subacute cholecystitis and then becomes chronic cholecystitis if treatment is not continued at this stage. The management of cholecystitis may be affected by complications such as internal biliary fistula and peri-gallbladder abscess during the purulent phase, and gallbladder perforation (bile peritonitis) during the hemorrhagic and necrosis phase. <sup>[4]</sup>

### **Pathophysiology**

Two hypotheses have been place forth to explain the pathophysiology of acute cholecystitis:

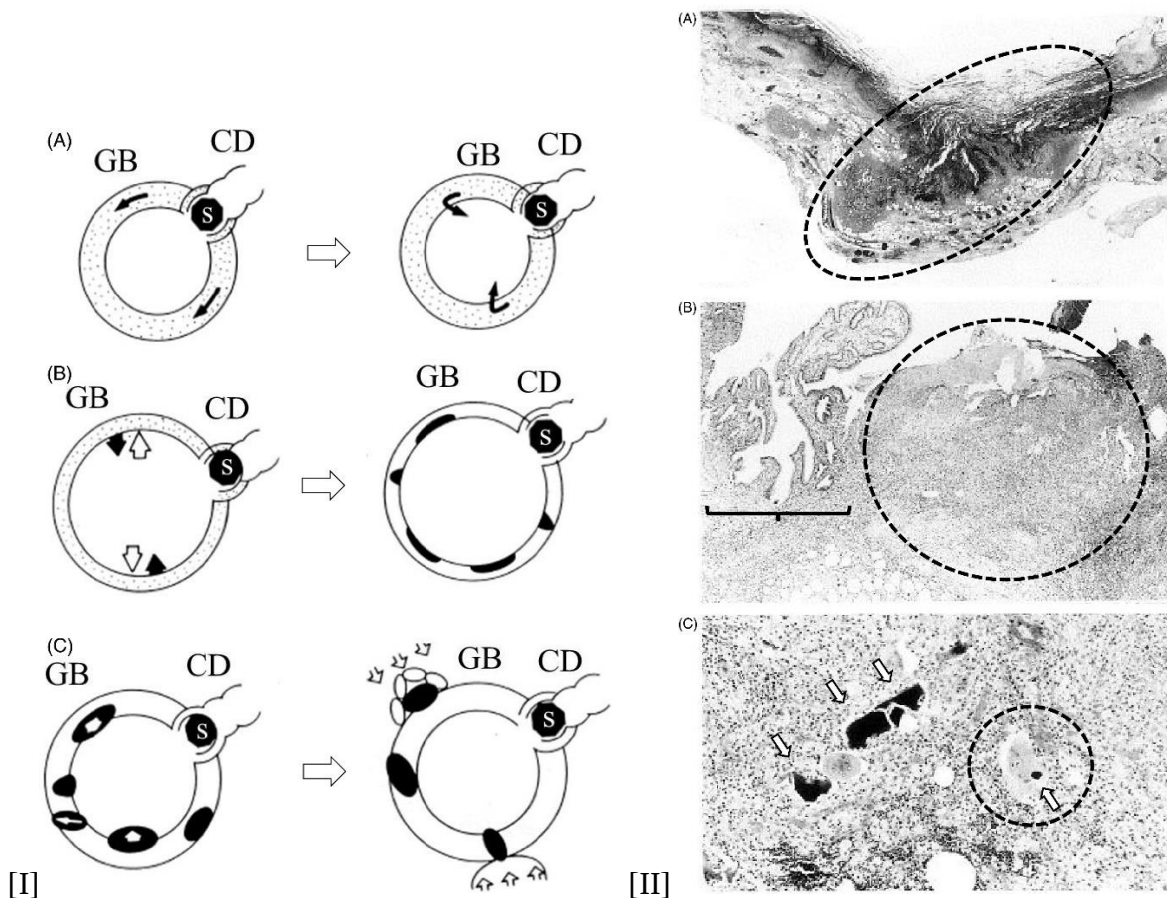
1. Occlusion of the gallbladder artery and blockage of the cystic duct.
2. Perpetual lithogenic bile and obstruction of the cystic duct.

Although the evidence for these theories comes from animal experiments, cystic duct obstruction is frequently seen in acute cholecystitis patients. However, not all cases of gallstone-related cystic duct obstruction result in cholecystitis; thus, an additional factor must be necessary in addition to cystic duct obstruction for the development of acute cholecystitis. Acute cholecystitis histologically observed exhibits arteriole blockage as a result of thrombus formation surrounding the dispersed necrotic lesions. Furthermore, because this lesion exhibits the characteristics of ischemic necrosis, it is most likely the result of a gallbladder artery branch becoming occluded. These results imply that obstruction of a gallbladder artery branch may also be the cause of acute obstructive cholecystitis, in addition to obstruction of the cystic duct.<sup>[5,6]</sup>

The progression of cholecystitis occurs when the cystic duct is obstructed by gallbladder stones. During the first two to four days, congestion and edema—also known as edematous cholecystitis—

are noticeable symptoms. Bleeding and necrosis are the hallmarks of necrotizing cholecystitis, which manifests in 3-5 days. The illness advances to its purulent phase, commonly referred to as suppurative cholecystitis, between 7 and 10 days. Cholecystitis' acute phase lasts anywhere from one week to ten days. Subacute cholecystitis develops into chronic cholecystitis after the purulent nest is replaced with granulation tissue, which occurs two to three weeks later. Below is a brief description of each phase's disease progression.<sup>[4]</sup>

**Congestive and edematous phase:** This stage of the circulatory disorder peaks two to four days after it starts. When a gallstone hits the cystic duct or gallbladder neck, it obstructs it. This presses against the blood vessels in the gallbladder wall surrounding the neck, leading to circulatory problems. The gallbladder fills with effusion as a result of the wall becoming edematous and clogged. On a macroscopic level, there is a distention of the gallbladder and edematous thickening of the gallbladder wall along with noticeable vessel dilation and edema. Histologically, however, the tissue of the gallbladder is preserved; the subserosa tissue exhibits significant edema as well as tiny blood vessels.<sup>[4,6]</sup>



**Fig.1** (A) Phase of congestion and edema. Gallbladder (GB), cystic duct (CD), and impacted stone (S). The flow of inflammatory effusion is indicated by the black arrow. Congestion with edematous change is indicated by dots in the gallbladder wall. (B) Phase of necrosis and hemorrhage.

Gallbladder (GB), cystic duct (CD), and impacted stone (S). The left figure displays a black arrow indicating the flow of inflammatory effusion and a white arrow indicating elevated luminal pressure. Spread necrosis is shown in the black area on the right figure. Phase of purulentness (C).

Gallbladder (GB), cystic duct (CD), and impacted stone (S).<sup>[4]</sup>

[II] Findings pathological in acute cholecystitis. (A) The mucosal surface is the upper portion. There is obvious whole layer necrosis (dotted area, HE  $\times$  25). (B) Normal mucosal tissue (curly bracket) and necrosis tissue (dotted area) are next to each other (HE  $\times$  50). (C) This image displays an abscess in its entirety. The white arrows point to the foreign body inside the abscess. The dotted area in the center-left of the screen shows an image of a polygonal giant cell phagocytosis phagocytizing the foreign body (HE  $\times$  100).<sup>[4]</sup>

**Hemorrhagic and necrosis phase:** Tissue necrosis and bleeding ensue when blood stasis and the circulatory disorder reach their peak. At this stage, which happens three to five days after the disease starts, gallbladder perforation and biliary peritonitis are also possible outcomes. As the disease progresses past the congestive edoema stage, the gallbladder wall becomes compressed due to an increase in internal pressure brought on by the buildup of inflammatory exudate in the gallbladder lumen. Histologically, there are mottled necrotic nests in every layer, but there are also scattered necrosis next to normal tissues and transmural necrosis, which are comparatively less common. In cases of cholecystitis, there appears to be less perforation in these distributions of necrotic lesions.<sup>[4,6]</sup>

**Purulent phase:** During this stage, suppuration starts and leukocyte infiltration takes place in the necrotic tissue. Additionally, pus builds up in the lumen, causing a wall abscess to develop. About five days after the disease's onset, this purulent phase starts and lasts for two to three weeks. Gallbladders that are dilated tend to contract during this phase, and inflammatory fibrosis causes the walls to become hypertrophic. The recovery from the inflammation is also rapid during this phase. Concentrated cholesterol and bile crystals can be found in the core of intramural abscesses, while relatively large, deep peri-cholecystic abscesses can be indicative of foreign body abscesses.<sup>[7,8]</sup>

More than 90% of cases of chronic cholecystitis have gallstones present. A common bile duct obstruction, such as that caused by strictures or neoplasms, can also cause bile flow stasis, which can result in gallstone formation and chronic cholecystitis. It has been suggested that hydrophobic bile salts from lithogenic bile increase the damage caused by free radicals. This leads to an ongoing inflammatory state, along with diminished mucosal protection from lower prostaglandin E2 levels. Affected smooth muscle cholecystokinin receptors impair gall bladder contraction, which exacerbates the permissive environment where lithogenic bile fuels inflammation and causes stasis.<sup>[9,10]</sup>

### **Manifestation**

Acute cholecystitis patients typically complain of vomiting, nausea, and upper quadrant abdominal pain when they first visit the doctor. The right infrascapular region is often the site of radiating pain. Fever, leukocytosis, tenderness, stiffness, and, oftentimes, a palpable mass in the right subcostal region accompany these symptoms. The right subcostal area becomes the localized site of pain and tenderness as the inflammatory process intensifies and irritates the visceral and parietal peritonea. Sudden movement, coughing, or deep inspiration aggravate the pain. The temperature is 99 to 101°F, which is somewhat high.<sup>[2]</sup>

Patients with chronic cholecystitis typically experience increasing stomach pain in the right upper quadrant along with bloating, increased gas, vomiting, and food intolerances, particularly to greasy and spicy foods. There may also be shoulder or midback pain. Years may pass before this pain is diagnosed. Patients who have chronic cholecystitis typically have dull upper abdominal pain that travels from the waist to the mid back or the tip of the right scapula. Although eating fatty foods may make the pain worse, acute cholecystitis' typical post-prandial pain is less frequent.<sup>[11]</sup>

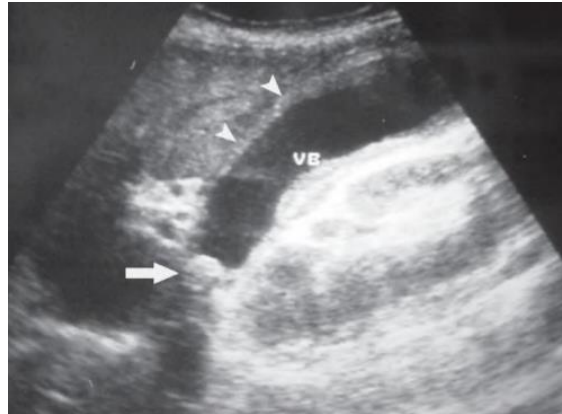
Upon physical examination, the right upper quadrant typically exhibits rigidity, voluntary and involuntary guarding, and localised rebound tenderness with a positive Murphy sign. A sharp, localised pain and inspiratory arrest occur when the patient inhales deeply and feels light pressure over the gallbladder area. This is a positive sign. Some patients have a palpable mass in the right subcostal area, which is typically a distended gallbladder. Omental adhesions and a localised gallbladder perforation with a contained abscess may also arise from the inflammation spreading through the gallbladder wall to the visceral peritoneum. While a palpable, tender gallbladder is indicative of acute cholecystitis, pancreatitis, abscess, and gallbladder, liver, or colon carcinoma can also cause a mass in this area.<sup>[12]</sup>

### **Investigations and Radiological Findings**

Cholecystitis diagnosis relies heavily on physical examination and thorough history taking. Additionally crucial are a comprehensive metabolic panel and a complete blood count (CBC). In instances of persistent cholecystitis, these outcomes might be typical. White blood cell count (WBC) may be elevated in cases of acute cholecystitis or severe illness. Liver enzyme levels could also be

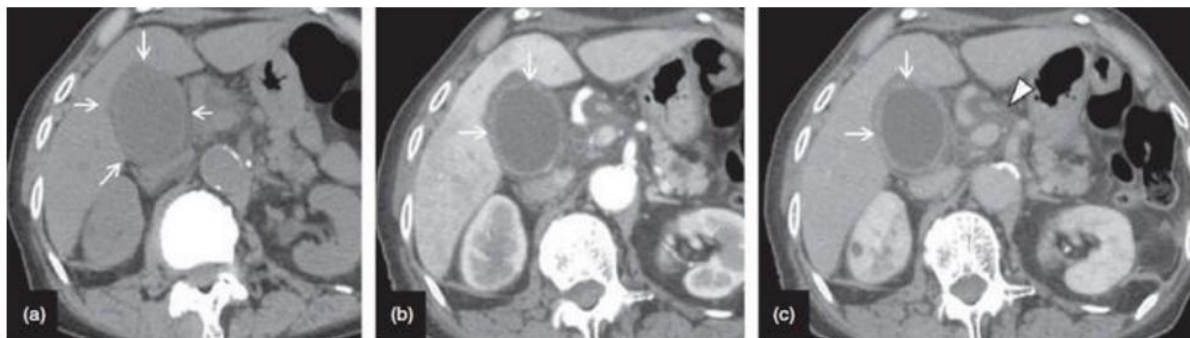
higher. Examine the possibility of a common bile duct stone if the elevated bilirubin level is greater than 2.<sup>[13,14]</sup>

Lab results may be normal when gallbladder disease is severe. To rule out pancreatitis, amylase and lipase levels also need to be examined. In the emergency room, a CT scan is frequently requested as the initial imaging test in the workup. This imaging frequently reveals gallstones and cholecystitis. The most effective test to first assess gallbladder disease is an ultrasound. Gallstones and a thickened gallbladder wall are typical symptoms of this disease. It is advised to perform a hepatobiliary (HIDA) scan in cases of acute cholecystitis. This scan will identify obstruction of the cystic duct or gallbladder function. In the absence of gallstones, cholecystokinin (CCK) may also be added to diagnose acalculous cholecystitis.<sup>[13,14]</sup>



**Fig. 2 Acute cholecystitis on Ultrasound** <sup>[15]</sup>

When the results of an ultrasound are unclear or the clinical picture points to the involvement of nearby organs (such as pancreatitis or duodenitis), computed tomography (CT) is a helpful modality. It is commonly known that CT has a low sensitivity for cholelithiasis, even though it nearly always shows gallbladder disease (BV) in patients who are fasting. It has been reported that magnetic resonance imaging (MRI) and computed tomography (CT) scanning can predict acute cholecystitis with a sensitivity and specificity of greater than 95%. <sup>[15]</sup>



**Fig. 3 CT with dynamic contrast (a. simple, b. initial phase, c. equilibrium phase, and so forth).** Plain CT scan results show gallbladder enlargement, gallbladder wall thickening, and edematous lesions beneath the gallbladder serosa (arrows). The hallmark appearance of gangrenous cholecystitis on contrast-enhanced CT (b, c) is the irregularity of the gallbladder wall and partial lack of contrast enhancement (arrows). Additionally visible are edematous alterations in the hepatoduodenal ligament (c. arrowhead) and transient early-phase staining of the liver parenchyma (b). These findings suggest widespread inflammation.<sup>[15]</sup>

Wall thickening (>4 mm), pericholecystic fluid, subserosal edema (in the absence of ascites), intramural gas, and sloughed mucosa are observations suggestive of acute cholecystitis. The potential exists for distinguishing between acute and chronic cholecystitis using diffusion-weighted (DW) MRI. Wang et al. found that elevated signal on high b-value images was highly sensitive and

somewhat specific for acute cholecystitis in a study involving 83 patients with abdominal pain. If the diagnosis is unclear, viewing the surrounding structures can also be beneficial from CT scanning and MRI.<sup>[16]</sup>

### Treatment and Management

Laparoscopic cholecystectomy is the most suitable course of treatment for cholecystitis. With a rapid recovery, there are minimal rates of morbidity and death. If the patient is not a good candidate for laparoscopy, this can also be done using an open technique. For patients who are deemed unsuitable for surgery, milder cases of chronic cholecystitis may be controlled with low-fat and low-spice diets. The outcomes of this therapy differ. There have also been isolated reports of sporadic success when using ursodiol for the medical treatment of gallstones.<sup>[17]</sup>

When choledocholithiasis is a concern, endoscopic retrograde cholangiopancreatography, or ERCP, is typically performed. Before having elective surgery, these patients typically have ERCP. It has been demonstrated that ursodeoxycholic acid (UDCA, also known as ursodiol) reduces the incidence of acute cholecystitis and biliary colic in patients with symptomatic cholelithiasis. On the other hand, there is little research on its function in chronic cholecystitis. Patient characteristics determine how to treat asymptomatic patients with chronic cholecystitis that was incidentally discovered. With follow-up imaging, asymptomatic patients who do not exhibit any radiological or clinical signs of malignancy can also be closely monitored.<sup>[18]</sup>

#### Laparoscopic Cholecystectomy (LC) Versus Open Cholecystectomy (OC):

Many relative contraindications, such as cirrhosis, pregnancy, and previous upper abdominal surgery, surfaced after LC was introduced. After that, it has been shown that LC is secure and feasible in all of these situations, if not more so. There aren't many reasons to choose an open operation now that technology has advanced and LC expertise has grown. These days, the main reason to perform an OC is when a laparoscopic approach fails to complete the procedure laparoscopically and needs to be converted. Surgeons who are asked questions about anatomy choose to take an open approach. Many conditions, such as the existence of severe inflammation, adhesions, anatomical abnormalities, bile duct injury, retained bile duct stones that are challenging to remove laparoscopically, and uncontrollable bleeding, are among the indications for conversion.<sup>[19]</sup>

The preferred anesthetic method for laparoscopic cholecystectomy (LC) is endotracheal general anesthesia (GA). As an alternative to GA for LC, regional anesthesia (spinal, epidural, or combined spinal-epidural) has also been reported to be the only method for performing LC.<sup>[20]</sup>

First, the abdomen is insufflated with carbon dioxide to a pressure of 15 mmHg after anesthesia is induced. Subsequently, four tiny abdominal incisions (supraumbilical x1, subxiphoid x1, and right subcostal x2) are made in order to place the trocar. The gallbladder is retracted over the liver using long instruments and a laparoscope camera. This makes the suggested hepatocystic triangle region visible. The critical view of safety is achieved through meticulous dissection. This view is characterized by the following three features: (1) the hepatocystic triangle's fibrous and fatty tissue has been cleared away; (2) there are only two tubular structures visible entering the gallbladder's base; and (3) the lower third of the gallbladder has separated from the liver to reveal the cystic plate.<sup>[21]</sup>

The operating surgeon isolates the cystic duct and cystic artery after obtaining this view to a sufficient degree. Both structures have been transected and clipped with precision. The gallbladder and liver bed are then totally separated using a harmonic scalpel or electrocautery. The abdomen should be allowed to deflate to 8 mmHg for two minutes in order to reach hemostasis. By using this method, one can prevent missing possible venous bleeding, which can be impeded by high intra-abdominal pressure (15 mmHg). The gallbladder is extracted and placed in a specimen pouch from the abdomen. Remove every trocar under direct visualization. In order to prevent incisional hernias during the recovery phase, this author suggests fascial closure of trocar sites larger than 5 mm. However, port site closure is surgeon-specific.<sup>[21]</sup>

General anesthesia and endotracheal intubation are typically required for open cholecystectomy (OC) in order to avoid aspiration and respiratory embarrassment. Avoiding anesthetics that impair mucociliary transport, providing postoperative pain relief sufficient to prevent deterioration of

respiratory mechanics, and facilitating ambulation as soon as feasible should be the objectives of anesthesia management for these patients. All of the aforementioned requirements are met by epidural anaesthesia, which also helps these patients recover from surgery quickly and painlessly.<sup>[22]</sup>

There are two approaches to OC:

1. retrograde (starting from the fundus downward)
2. anterograde (starting the dissection medially in the hepatoduodenal ligament).

Similar to LC, the antegrade approach begins with the peritoneum covering the Calot triangle being dissected in order to identify the cystic artery and duct, and it ends with the same critical view. After the artery and duct are divided and ligated, the gallbladder is released from the cystic plate in the subserosal plane (a cholangiogram is performed if necessary). Early cystic duct/artery dissection has the benefit of less blood loss during the removal of the gallbladder from the liver bed and easier identification in a bloodless field.<sup>[23]</sup>

Another OC method is the retrograde (top-down) technique, in which the dissection starts at the fundus and moves toward the hepatoduodenal ligament. This method allows for the precise identification of the cystic duct and artery since they are the only attachments left in place after the gallbladder is removed from the cystic plate.<sup>[23]</sup>

Most patients can be released the same day their gallbladder is removed. Over-the-counter analgesics can be used to manage mild pain. Due to retained CO<sub>2</sub> from laparoscopic insufflation, the patient may complain of excruciating shoulder pain. It is important to reassure them that this pain will subside as they move and the gas is gradually absorbed, which may take up to three days. Before being released from the hospital, the patient should be informed that bloating or diarrhea could be symptoms of possible greasy food intolerance. The reduced rate of fat emulsification brought on by the gallbladder's loss of stored bile may be transient or, to some extent, permanent. The majority of patients will experience a gradual improvement in their symptoms as their liver produces more bile. After surgery, there is a 3- to 4-week follow-up period.<sup>[23]</sup>

## Conclusion

Gallstones in the gallbladder or gallstones originating from the gallbladder obstructing the cystic duct (cholelithiasis) are the most common causes of cholecystitis, an inflammation of the gallbladder. The prognosis becomes less favorable if complications like perforation or gangrene develop. Most cases of simple cholecystitis result in a very good outcome. Supportive therapies can often alleviate symptoms. To avoid further complications, the majority of cases are treated with elective cholecystectomy. Despite the safety of surgery, bile duct injuries can occur and require close observation during the recovery phase. In situations where early surgery is not feasible, such as in elderly patients or those with serious conditions, gallbladder drainage can be used to achieve positive treatment outcomes before complications arise. It is crucial to take action to avoid complications from cholecystitis.

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