

Original Research Article

Early recognition and management of gangrenous cholecystitis: a single-center experience and a comprehensive review of risk factors and imaging findings

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ABSTRACT

Background: Annually, approximately 200,000 acute cholecystitis (AC) cases are diagnosed in the U.S., with gangrenous cholecystitis (GC) occurring in 2-20% of AC cases. GC, characterized by ischemic necrosis of the gallbladder, is often associated with delayed diagnosis, leading to increased complications, longer hospital stays, and mortality rates ranging from 15-50%. This study presents a series of GC cases treated at our institution.

Methods: A retrospective review was conducted at a community hospital on patients from October 2012 to December 2022 with GC confirmed by pathology. Data collected included demographics, clinical parameters, lab values, imaging, operative findings, management, and outcomes, aiming to identify risk factors, treatment approaches, and associated outcomes.

Results: Out of 5,746 cholecystectomy patients, 67 (1.16%) had GC. The average age was 56, with a male predominance (64%). Incidence was highest among Hispanic (37%) and Asian (28%) populations. Common comorbidities included hypertension (48%), obesity (36%), and diabetes (33%). Clinical presentations included right upper quadrant pain (64%) and epigastric pain (46%). Computed tomography (CT) findings showed gallbladder distention (43%), fat stranding (22%), and perforation (3%). Surgical approaches were laparoscopic cholecystectomy (75%), converted-to-open cholecystectomy (19%), and open cholecystectomy (3%). Complications included bile leak (7%), wound infection (4%), hematoma (3%), and wound dehiscence (1%), with a 1.4% mortality rate.

Conclusions: GC is a severe AC complication linked to delayed presentation, with higher complication and mortality rates. Recognizing risk factors such as age, gender, and imaging/laboratory findings can facilitate early diagnosis and timely surgical intervention, improving patient outcomes.

Keywords: Gangrenous cholecystitis, Gallbladder necrosis, Cholecystectomy

INTRODUCTION

Each year, approximately 200,000 cases of acute cholecystitis (AC) are diagnosed in the United States. Gangrenous cholecystitis (GC), a condition involving ischemic necrosis of the gallbladder, develops in about 2% to 20% of AC cases, with mortality rates around 15-50%.¹⁻

³ At our institution in Queens, New York, a total of 5,746 patients underwent surgical intervention for AC between 2012 and 2022, of which only 1.1% (n=67) met histopathological criteria for GC. This observational study examines the characteristics and outcomes of patients treated for GC at our institution in Queens, NY, aiming to

identify potential risk factors, treatment strategies, and associated clinical outcomes for GC.

METHODS

This study is a retrospective observational analysis conducted at Flushing Hospital Medical Center in Queens, New York, covering the period from October 2012 to December 2022. The study included patients who underwent cholecystectomy and were diagnosed with GC, confirmed by pathological examination of the cholecystectomy specimens. Patients were included if they had a confirmed histopathological diagnosis of GC following surgery for AC. Exclusion criteria included patients who did not undergo cholecystectomy or those who had insufficient clinical data for analysis. Data collection involved a comprehensive chart review, gathering information on patient demographics, clinical presentation, laboratory values, imaging studies, operative findings, treatment approaches, and outcomes. Imaging studies reviewed included ultrasound and computed tomography (CT) scans to identify findings associated with GC, such as gallbladder wall thickening, pericholecystic fluid, and fat stranding. Operative details included the type of surgery performed—laparoscopic cholecystectomy (LC), conversion to open cholecystectomy (LC-O), or open cholecystectomy (OC)—and any intraoperative findings. Postoperative outcomes, including complications and mortality, were documented to assess factors influencing patient prognosis. The study was approved by the institutional review board (IRB) at Flushing Hospital Medical Center, ensuring compliance with ethical standards for retrospective research. Descriptive statistics were calculated for patient demographics, comorbid conditions, clinical presentations, imaging findings, surgical methods, and outcomes. Continuous variables were reported as means with standard deviations, and categorical variables as frequencies with percentages. Analyses were conducted to identify potential risk factors for GC and to evaluate treatment outcomes. Statistical significance was determined with a p value threshold of <0.05.

RESULTS

Among 5,746 patients who underwent cholecystectomy between 2012 and 2022, 1.16% met the criteria for gangrenous cholecystitis based on the histopathology evaluation. A total of 67 patients were diagnosed as GC. The average age was 56 (SD=16.5) and 64% were male. Incidence was highest in Hispanic (37%) and Asian (28%) populations (Table 1). Associated comorbid conditions included hypertension (48%), obesity, defined as BMI >30 (36%), and diabetes (33%). On physical assessment, 64% presented with right upper quadrant pain and 46% with epigastric pain. CT imaging findings included gallbladder distention (43%), fat stranding (22%), and perforation (3%) (Table 2). Treatments consisted of laparoscopic cholecystectomy (LC; 75%), laparoscopic converted-to-open cholecystectomy (LC-O; 19%), and open

cholecystectomy (OC; 3%). Complications included bile leak (7%), wound infection (4%), hematoma (3%), and wound dehiscence (1%). Our overall mortality rate was 1.4% (Table 3).

Table 1: Demographic data of gangrenous cholecystitis patients.

Demographic factors	N	Percentage
Total patients	5746.0	100.0
Gangrenous cholecystitis patients	67.0	1.16
Age		
Mean age (years)	56.0	nan
Standard deviation	16.5	nan
Gender		
Male	43.0	64.0
Female	24.0	36.0
Ethnicity		
Hispanic	25.0	37.0
Asian	19.0	28.0
Others	23.0	35.0

Table 2: Clinical characteristics of gangrenous cholecystitis patients.

Clinical characteristics	N	Percentage
Comorbidities		
Hypertension	32.0	48.0
Obesity (BMI >30)	24.0	36.0
Diabetes	22.0	33.0
Presenting symptoms		
Right upper quadrant pain	43.0	64.0
Epigastric pain	31.0	46.0
Gallbladder distention	29.0	43.0
Imaging findings		
Fat stranding	15.0	22.0
Perforation	2.0	3.0

Table 3: Treatment outcomes and complications in gangrenous cholecystitis patients.

Outcomes	N	Percentage
Surgical treatments		
Laparoscopic cholecystectomy (LC)	50.0	75.0
Laparoscopic converted-to-open (LC-O)	13.0	19.0
Open cholecystectomy (OC)	2.0	3.0
Complications		
Bile leak	5.0	7.0
Wound infection	3.0	4.0
Hematoma	2.0	3.0
Wound dehiscence	1.0	1.0
Mortality		
Overall mortality rate	nan	1.4

DISCUSSION

Annually, 200,000 AC cases are diagnosed in the U.S. GC occurs in 2%-20% of AC.¹ GC is often associated with a delay in diagnosis, leading to increased complications and mortality. Mortality rates for GC range from 15% to 50%.² In a large study of 5,812 patients undergoing cholecystectomy over 11 years at Saint Agnes Hospital Center in Baltimore, 2,219 had AC, and 351 had GC (6%). Among all 351 patients with GC, only 9% (32) were diagnosed preoperatively.¹ Different variables have been described as either risk factors or associated factors for GC, including age above 45 years by Wu et al or above 69 years by Nikfajam et al, male gender, diabetes, temperature >38, tachycardia >90, gallbladder wall thickening ≥ 4 mm, fluid around the gallbladder on ultrasound, white blood cell >13000, elevated C-reactive protein, and American Society of Anesthesiology (ASA).¹⁻⁴

Other cited concerning lab values are hyperuricemia and elevated creatinine by Nikfarjam et al, hyponatremia (Na <135 mEq) by Falor et al, and hypoalbuminemia and a CRP value of more than 20 mg/dl predicting gangrenous cholecystitis with 100% sensitivity and 87.9% specificity.^{3,5,6} In addition, Menendez et al reported that there was an 8.8% increase in risk for GC with each CRP unit increase. There was also an 8.5% increased risk for GC when there was an increase in leukocyte levels. Sensitivity was 70.8% and specificity was 69.3% with a CRP value of 10.73 mg/dl.⁷

In considering imaging studies, ultrasound (US) findings pointing towards GC include decreased focal wall perfusion on color doppler, irregular mucosal outline, gallbladder wall thickening and delamination, gas within the gallbladder wall, and large pericholecystic collections. In addition, GC is less likely to have an impacted gallstone compared to acute or chronic cholecystitis.⁸

The US findings in our study included: positive for gallstone in 86%, gallbladder wall thickening in 46%, and pericholecystic fluid in 19% of all patients.

CT findings that support the diagnosis of GC include markedly distended gallbladder greater than 4 cm, decreased mural enhancement, gas in the wall or lumen, intraluminal membranes, irregular or absent wall, abscess, and relaxed gallbladder with dense content along with perihepatic effusion.⁸⁻¹⁰ The association of gallbladder distention greater than 4.0 cm, mural striation, and fat stranding can independently predict gangrenous cholecystitis.¹⁰ HIDA may demonstrate what is known as the "hot sign," a peripherally enhanced rim with an encompassing tracer-deficient gallbladder.¹¹

In our sample, CT imaging of GC included gallbladder distension (43%), fat stranding (22%), and gallbladder perforation (3%).

In 2010, Yacoub et al created a scoring system stratifying groups into a low, intermediate, or high probability of having GC. Variables included age, HR, male gender, WBC >13,000, and US observed gallbladder wall thickening. Points were assigned as 1 for age >45, HR >90, and GWBT >4.5 mm; 1.5 for WBC >13,000; and 2 for male gender. Overall scores were interpreted as 0-2 (low probability=13%), 2-4.5 (intermediate=33%), and >4.5 (high=87%). The results helped determine which patients may need prompt cholecystectomy.¹²

In addition, it is important to note that GC presenting in COVID-19 patients is believed to be multifactorial, including an increased risk of vascular microthrombi, biliary stasis, distension of the gallbladder, SIRS, immunosuppression, opportunistic infections, hypercoagulable state, and ischemia to the gallbladder.^{9,13}

The outcomes of GC, a serious sequela of AC, include longer hospital stays, increased complication rates, and higher mortality. Common complications included increased bile leak with a range between 2.6 to as high as 24%, hemorrhage, surgical site infections, and intra-abdominal abscesses.^{3,14} Onder et al. found 36 complications after cholecystectomy in 29 patients with GC, with surgical site infection being the most common, in 12 (33.3%).²

Bile duct injury (BDI) has been found in one study six-fold higher (1.1%) after cholecystectomy for GC, compared with non-GC cases (1.1% versus 0.18%, making it the costliest complication). Surgery for GC is associated with increased estimated blood loss and more frequent open cholecystectomies.² While acute cholecystitis occurs in 2-30% of patients with a mortality rate of 0.2-0.5%, in patients with GC, it increases to 15%-20% with mean time delay to hospital admission of 21 hours compared with 54 hours in those in whom mortality occurred.^{2,6} In our sample, complications included bile leak (7%), wound infection (4%), hematoma (3%), and wound dehiscence (1%). Our overall mortality rate was 1.4%.

The role of nonsurgical management with percutaneous tube placement has been discussed; however, since GC by definition is a perforated or impending perforation of the gallbladder, the weak gallbladder wall would not be able to hold the tube. In addition, placing a percutaneous tube would not address the underlying pathology. It causes delays in definitive treatment and would not be as beneficial as it is in acalculous cholecystitis in critically ill patients.^{8,15} Surgical management includes LC with conversion rates to open cholecystectomy (OC) reported as 21% for GC compared to 3.4% for non-GC.¹

In our institution, nongangrenous AC was managed by laparoscopic cholecystectomy (LC) 92.8%, robotic (RC) (5.8%), and conversion to open cholecystectomy (OC) (1.4%). Considering our data showed the conversion rate in GC is pretty similar to previous published data (19% conversion rate and 3% upfront OC) it seems despite

significant progress in LC regarding techniques and equipment, the conversion rate is still the same as described by Wu et al in 2015. Similar to other studies, the conversion to OC is explained by the limitation to completely visualize the biliary anatomy to safely complete the gallbladder dissection or in case of uncontrollable hemorrhage.¹

Pathology findings in specimens of GC can show atrophic gallbladder mucosa, vasculitis of the gallbladder with the inflammatory changes, and endoluminal obliteration of vessels associated with wall breakthrough, hemorrhagic infarction.¹⁰ Immunohistochemistry findings include an endothelial overexpression of medium-size vessels (anti-CD31), CD 20, CD 38, along with significant macrophage activity (anti-CD68) and T helper lymphocytes (anti-CD4) against the gallbladder wall and vessels.^{10,16}

Limitations

This is a single-center retrospective study; it did not include patients who may have undergone percutaneous cholecystostomy for GC.

CONCLUSION

Gangrenous cholecystitis is a serious complication of acute cholecystitis, associated with delayed presentation and a higher complication and mortality rate. A high index of suspicion based on key factors such as age, gender, and certain laboratory values and imaging findings can lead to prompt diagnosis, and early surgical management to improve outcomes.

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