REVIEW ARTICLE

Acute acalculous cholecystitis in the critically ill: risk factors and surgical strategies

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Abstract

Purpose Acute acalculous cholecystitis (AAC) is characterized by severe gallbladder inflammation without cystic duct obstruction. Critical illness and neurological deficits are often associated with AAC, and early radiologic imaging is necessary for the detection and timely treatment of AAC. In critically ill patients, effective surgical management is difficult. This review examines the three common surgical treatments for AAC (open cholecystectomy (OC), laparoscopic cholecystectomy (LC), or percutaneous cholecystostomy (PC)), their prevalence in current literature, and the perioperative outcomes of these different approaches using a large retrospective database.

Materials and methods This review examined literature gathered from PubMed and Google Scholar to select more than 50 sources with data pertinent to AAC; of which 20 are described in a summary table. Outcomes from our previous research and several updated results were obtained from the University HealthSystem Consortium (UHC) database.

Results LC has proven effective in treating AAC when the risks of general anesthesia and the chance for conversion to OC are low. In critically ill patients with multiple comorbidities, PC or OC may be the only available options. Data in the

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M. Goede e-mail: mgoede@unmc.edu literature and an examination of outcomes within a national database indicate that for severely ill patients, PC may be safer and met with better outcomes than OC for the healthier set of AAC patients.

Conclusions We suggest a three-pronged approach to surgical resolution of AAC. Patients that are healthy enough to tolerate LC should undergo LC early in the course of the disease. In critically ill patients, patients with multiple comorbidities, a high conversion risk, or who are poor surgical candidates, PC may be the safest and most successful intervention.

Keywords Acute acalculous cholecystitis · Open cholecystectomy · Laparoscopic cholecystectomy · Percutaneous cholecystostomy

Introduction

Acute acalculous cholecystitis (AAC) is a disease characterized by severe gallbladder inflammation without cystic duct obstruction due to gallstones. First recognized in 1844, AAC accounts for 2–15 % of acute cholecystitis cases [1–5]. AAC is associated with considerably higher patient morbidity as well as a mortality rate of up to 50 % [6–8] and typically has a worse prognosis than its calculous counterpart (ACC) [3, 9, 10].

Due to the severity of illness and nonspecific presentation, a high index of suspicion and early radiologic imaging are necessary to detect AAC [1, 2, 9, 11–14]. Critical illness and neurological deficits are frequently associated with AAC and may hinder an expedient diagnosis [3, 8]. AAC may be suspected with right upper quadrant pain and tenderness, an enlarged gallbladder, and a positive ultrasonographic Murphy's sign. Radiologic confirmation of a distended gallbladder, thickened wall, and pericholecystic fluid further suggest AAC [3, 11, 14, 15]. An absence of gallstones observed in imaging or laparoscopy confirms a diagnosis of AAC [11]. Complications of AAC are life-threatening and include gallbladder perforation, gangrene, empyema, and sepsis [4, 9, 11, 12, 16–18].

AAC occurs most frequently in critically ill patients, with incidence in this category ranging from 0.5 to 18 % [6]. AAC typically complicates surgery and can occur in conjunction with multiple organ failure, burn injury, or major trauma [1, 4, 7, 10, 13, 17, 19–21]. AAC also may coincide with congestive heart failure, diabetes mellitus, embolization of the cystic artery, immunosuppression, and abdominal vasculitis [14, 17, 22, 23]. In these patients, AAC often represents further progression of multiple systemic failure [2, 7]. This necessitates immediate action with the most appropriate and clinically successful surgical intervention possible. While some sources report that AAC is not limited to the critically ill [24–26], these cases remain outside the scope of this review.

AAC treatment options include open or laparoscopic cholecystectomy (OC and LC) or percutaneous cholecystostomy (PC). Open cholecystectomy originally served as the primary method of treatment [27], but the advent of minimally invasive techniques has enabled these operations to be performed laparoscopically [28]; some physicians instead opt for percutaneous drainage in cases of AAC [12]. In these critically ill patients, effective surgical management is difficult. Borzellino et al. notes the need for a comprehensive study of treatment modalities in the critically ill [29]. Discrepancies exists as to the preferred method of treatment [30, 31], and we believe that a large population-based study will help to determine the most successful intervention. In this review, we examine OC, LC, and PC and their clinical outcomes in the literature and using data from University HealthSystem Consortium (UHC).

Treatment options

Open cholecystectomy

OC is the traditional surgical intervention in cases of acute acalculous cholecystitis. Open removal of the gallbladder provides a definitive solution to cholecystitis, eliminating the possibility of recurrence [27, 32–36]. OC also allows easier surgical management of unclear anatomy, bleeding, and complications [27, 37]; when these complications manifest in LC and PC, the operation is typically converted to OC [15, 38]. Some surgeons perform only OC because they prefer immediate, aggressive action against AAC [34, 36]; they posit that OC improves cases of multiorgan failure, particularly restoring cardiovascular and respiratory function [34]. AAC complicated by gallbladder ischemia or a gangrenous wall also necessitates open cholecystectomy [34].

Current literature suggests several weaknesses of OC. The critically ill patient diagnosed with AAC is an unsafe candidate for surgery under general anesthesia [2, 32, 39–42]. In these patients, OC consistently results in high mortality and morbidity as compared to other methods [23, 30, 39, 40, 43]. Chung et al. cite 63–100 % morbidity and 31–57 % mortality as a result of emergent abdominal surgery in critically ill elderly patients and encountered 19 % mortality with OC as the primary treatment. OC elsewhere may be associated with up to 44–59 % mortality [2, 7, 41, 44]. Orlando et al. asserts that OC should be considered only in the case of severe gallbladder necrosis. Simorov et al. states that even in healthier patients, OC still met with worse outcomes than PC.

Laparoscopic cholecystectomy

LC serves as an effective substitute for open surgery. Less invasive than OC, LC is often preferred in cases indicating cholecystectomy. LC includes many advantages of OC, including definitive resolution and prevention of future gallbladder pathology [12, 45, 46]. LC carries distinct benefits from OC, such as decreased rate of infection, mortality, length of stay, and cost [4, 12, 15, 28, 38, 45, 47, 48]. Laparoscopy can be both diagnostic and therapeutic, which is useful in confirming a commonly elusive diagnosis such as AAC [6, 49–51]. Patient satisfaction with LC is relatively high [52, 53] as length of stay, recovery time, and cosmetic results are significantly improved when compared to the open procedure [15, 37, 52, 53]. Early LC is highly successful in treating AAC [15, 40, 54].

The disadvantages of laparoscopic cholecystectomy should be considered. First, a laparoscopic approach may not be possible for all surgeons. LC also requires general anesthesia, and this procedure is known to be of a higher risk in the critically ill [2, 32, 39–42, 55]. Additionally, converting to an open procedure poses a significant risk of complication in those with multiple comorbidities; literature suggests that conversion rates from LC to OC may be as high as 20– 35 %, with men and obese patients most susceptible to conversion [30, 38, 40, 46, 56–58]. Conversion to OC increases operative cost and complication rate in addition to losing the benefit of the laparoscopic approach [41]. LC is frequently performed only on the most fit AAC patients and may be unsuited for the severely ill.

Percutaneous cholecystostomy

PC has proven safe, rapid, and highly efficacious in treating acute acalculous cholecystitis. As a conservative treatment

option. PC can be performed at the bedside under local anesthesia. PC demonstrates a significant decrease in complication rate and consequent lower patient morbidity and mortality than OC and LC [30, 40, 59, 60]. The cholecystostomy tube is placed transhepatically with radiologic guidance, and drains the acutely inflamed gallbladder; it typically remains for 3 weeks or until subsequent cholecystectomy [12, 39, 40, 59, 61, 62]. Patient fitness for general anesthesia and surgery must be considered because AAC most commonly occurs in the critically ill. In patients too ill to undergo the open or laparoscopic procedure, minimally invasive management by therapeutic drainage serves as a potentially lifesaving treatment [1, 3, 6, 33, 41, 44, 63-66]. PC optimizes the patient's condition by normalizing local symptoms as well as reducing the overall inflammatory response [63, 64, 67]. Additionally, when PC is performed as a first response to AAC diagnosis, some patients may not require subsequent cholecystectomy. After drainage alone, patient improvement may be significant enough not to warrant further operation [6, 12, 39, 42, 44, 55, 59-61, 66, 68-73]. Chung et al. demonstrated a 93 % rate of symptom resolution in critically ill AAC patients.

It is also important to examine the weaknesses of percutaneous cholecystostomy. In many cases, it serves as only temporary relief until cholecystectomy may be safely performed. Even when PC successfully resolves symptoms, the gallbladder remains and is still susceptible to recurrence [32, 44]. Because cholecystostomy may not be a permanent resolution, many consider open or laparoscopic cholecystectomy the standard AAC treatment [32, 45, 49, 74]. Cholecystostomy is contraindicated in cases of gangrene or gallbladder perforation [6, 34], which may have an incidence from 37 to 81 % in AAC [4]. The cholecystostomy tube also inherently carries the risk of causing complication or infection, though this is quite rare [44]. In a large-scale population study, Anderson et al. posits that PC poses no significant benefit in cases of AAC, citing a higher mortality rate than no intervention at all [20, 75].

Materials and methods

Literature review of articles with data describing outcomes of OC, LC, and PC identified 50 sources containing information of interest. Searches were conducted using Google Scholar and PubMed. Of the 50 sources, 20 were selected based on their content specific to AAC for inclusion in the summary table included in this paper.

Recent data on AAC patients was gathered from the UHC database to determine if the findings presented previously by us and others are still supported in the overall population of patients receiving these procedures. UHC is an alliance of 100 academic medical centers and 250 of their affiliated

hospitals, representing 90 % of the nation's nonprofit academic medical centers. The information available through the UHC database includes that on the patient discharge, inpatient hospital stay, patient characteristics, length of stay (LOS), 30-day readmission rate, postoperative morbidity, risk-adjusted in-hospital mortality, and inpatient care costs [76, 77]. Patients were selected using the International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) diagnosis (575.0, 575.1) and procedure codes (OC: 51.22, LC: 51.23, PC: 51.01). Data on deaths occurring after discharge are not included in the UHC database. Readmission is defined as readmission for any reason within 30 days of discharge after the index procedure. LOS in the database is the period from the index procedure to the hospital discharge. This cost of patient care provided in the database is an estimated cost using a ratio of cost to charge.

Results

The literature

A systematic literature review yielded the results from a variety of studies on surgical interventions for AAC. These studies addressed the benefits and disadvantages of treatment, many of them explicitly comparing interventions. Table 1 summarizes the discrepancies between treatment options while illustrating a clear gap in current literature—the need for a large-scale, objective comparison of OC, LC, and PC (Table 1).

Our supplemental findings

Analysis conducted by our researchers in 2013 [40] concluded that PC was superior in its outcomes to LC and OC in severely ill patients. Similar relationships can be seen in updated analyses of all severity patient comparisons of PC vs OC from the same data source (Table 2). In the current results, morbidity occurred in 11.3 % of patients with PC compared to 14.2 % that received OC (p<0.05) while mortality was also lower in the PC group (11.3 % vs 14.2 %, p<0.05). Median length of stay was also a single day shorter in PC vs OC, similar to previous results. While readmission in our earlier study favored LC and OC, the current PC vs OC comparison demonstrates no significant difference in LOS between groups (Table 2).

Discussion

AAC in the critically ill patient presents significant difficulties in clinical management. Multiple surgical options exist, and the severity of AAC warrants an evidence-based recommendation.

Table 1 Studie	s on ac	ute acalci	ulous cholecystitis		
Source	Year	Ν	oc	IC	PC
Glenn [32]	1978	139	Successful management of AAC, eliminates future disease; many AAC patients are unfit for surgery	N/A	Preferred inpatients too ill for surgery; local anesthesia, minimal burden on patient
Orlando [2]	1982	6	Should be reserved for excessive gangrene/GB necrosis	N/A	Well suited to the critically ill patient, local anesthetic
Eggermont [59]	1985	9	Not indicated in most patients after PC, patients often too ill	Not indicated in most patients after PC, patients often too ill	Best option to overcome critical period; done at bedside, minimal burden to patient
Vauthey [60]	1993	10	N/A	N/A	High success rate, definitive, low complication rate
Frassinelli [53]	1998	30	N/A	Minimal morbidity, high patient satisfaction and symptom resolution	N/A
Davis [55]	1999	9	NA	Definitive treatment; unsafe for critical patients, general anesthesia	Effective, safe
Granlund [43]	2001	23	High mortality	N/A	Performed rapidly under local anesthetic at bedside, minimally invasive, highly successful
Welschbillig- Meunier [74]	2005	16	Definitive resolution; unacceptably high mortality in patients with septic shock or multisystem organ failure	Unacceptably high mortality in patients with septic shock or multisystem organ failure	Clinical improvement, few complications, safe in critically ill
Ferrarese [36]	2006	16	Low morbidity (18.7) and mortality; early OC nevents worsening	N/A	N/A
Laurila [34]	2006	24	Alters multiorgan dysfunction, especially cardiovascular and respiratory dysfunction	N/A	Possible complications in bleeding, biliary peritonitis, catheter dislodgement; contraindicated in gangrene and perforation
Koebrugge [39]	2010	16	High mortality risk in very ill	High mortality risk in very ill	Often definitive, low risk, and good alternative in unfit patients
Nasim [58]	2011	13	Performed under general anesthesia	Less complication and shorter LOS than OC; high conversion; general anesthesia	Often definitive, rapidly effective, low complication rate, local anesthesia
Melloul [30]	2011	12	Efficient in resolution; higher morbidity than PC	Efficient in resolution; not always possible/ indicated	Highly efficient, good bridge to operation, and lower morbidity; may not be definitive
Chung [44]	2012	57	May not be necessary, high morbidity/mortality	May not be necessary, high morbidity/mortality	Highly effective, good for patients unfit for surgery, and low morbidity/mortality
Nikfarjam [4]	2012	35	Definitive, required in significant number of patients, preferred unless contraindicated	Definitive, required in significant number of natients, meterred unless contraindicated	Safe for patients unfit for surgery
Anderson [75]	2013	58,518	Lower mortality, LOS, and cost than PC; higher complication rate than PC	Lower mortality, LOS, and cost than PC; higher complication rate than PC	Lower complication rate than OC/LC; higher mortality, LOS and cost than OC/LC
Simorov [40]	2013	1725	Definitive treatment; highest morbidity and mortality, risky in critical illness	Safe, shortens LOS, low morbidity and mortality; high conversion rate, risky in critical illness	Safe, successful, and cost-effective bridge treatment
Anderson [20]	2014	43,341	Low mortality	N/A	No survival benefits compared to no intervention in AAC cases involving sepsis/shock or unfit patients
Atar [71]	2014	10	N/A	N/A	High success rate, surgery may not be necessary but if so, PC makes them more successful
Gu [3]	2014	69	Recommended in patients who do not improve with antibiotics or progress to empyema	N/A	Potentially lifesaving in patients too ill for surgery

Table 2High severity patients [40]

	Procedure		p value
Simorov et al. [40], major/extreme SOI	PC	Lap and open	
Sample N	704	1021	-
Mortality	2.6 %	2.1 %	NS
Morbidity	5.0 %	8.0 %	< 0.05
ICU	28.1	34.6	< 0.05
LOS, median (IQ range)	7 (5, 10)	8 (5,12)	< 0.05
Cost, median (IQ range)	40,516	53,011	< 0.05
Readmission	29.0 %	16.1 %	< 0.05
UHC overview of all patients, 2011–2014	PC	OC	
Sample N	4655	1600	_
Mortality	11.3 %	14.2 %	< 0.05
Morbidity ^a	16.71 %	23.63 %	< 0.05
ICU	46.9 %	60.3 %	< 0.05
LOS, median (IQ range)	9 (5–18)	10 (6–20)	< 0.05
Readmission	9.4 %	9.1 %	NS

LOS length of stay in days, ICU intensive care unit, IQ range interquartile range, NS no statistical significance

^a Frequency of patients with any complication present as reported by UHC aggregate

In this review, we examined the three common AAC treatment methods, their prevalence in current literature, and their perioperative outcomes. As many studies indicate, LC has been proven effective in treating acute cholecystitis [4, 12, 28, 45, 46, 48, 56]. The high conversion rate, however, represents a significant increase in patient morbidity and mortality. In stable AAC patients, when the risks under general anesthesia and for conversion to OC are low, we agree that a laparoscopic approach should be the preferred surgical intervention. However, in critically ill patients with multiple comorbidities, only PC or OC may be available to surgeons [64, 65]. In these patients, our review indicates that PC is superior to OC and converted LC. Even in more severely ill patients, PC was safer and met with better outcomes than the outcomes observed in healthier OC patients [40]. As illness and liability of conversion increase, especially in critically ill patients unfit for laparoscopy, we strongly recommend PC as a bridging or definitive procedure.

Several studies indicate that PC may be a definitive treatment for AAC without requiring subsequent cholecystectomy [31, 37]. These patients improve significantly with PC alone, and further intervention may not be required after the removal of the cholecystostomy tube and resolution of the initial contributing condition.

With regard to our current findings, we suggest a threefold approach to surgical resolution of AAC. Patients healthy enough to tolerate it should undergo LC early in the course of illness [28, 48, 56]. In critically ill patients as well as patients with multiple comorbidities, high conversion risk, or poor surgical candidates, PC represents the safest and most successful intervention. These patients may later require cholecystectomy and should be evaluated for further treatment as their condition improves [31, 37, 46, 54, 64, 65]. Anderson et al. critique the role of PC with regard to OC, but largely analyze two different populations; their PC group had a sevenfold incidence of severe sepsis and shock as well as higher comorbidity compared to their OC patients. While they raise important questions regarding AAC care, we believe these factors to be significant.

Our previous study and updated figures are limited by factors inherent to any large, multicenter administrative database [40]. As a retrospective study, patient randomization was not possible. Aggregate data was collected and current database limitations inhibit patient-level outcomes including operative time, postoperative analgesia requirement, morbidity after the 30-day postoperative period, and quality-of-life assessments. These measures will likely be examined in the future and are important in evaluating clinical outcomes.

Conclusions

When examining the body of literature on the topic, we conclude that PC provides better outcomes with lower cost in AAC patients. Those at low risk for conversion and medically suited for the operation should be treated with LC. However, in highrisk patients unfit for surgery under general anesthesia, management by cholecystectomy poses a significant health threat. Even in sicker patients, PC has superior perioperative outcomes than OC. PC serves as a safe, highly successful, and costeffective treatment of AAC whether as definitive treatment or a bridge to further intervention. Our expanded reanalysis of PC and OC supports these findings, and we therefore recommend physicians consider PC in patients with AAC.

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Authors' contributions Dmitry Oleynikov, MD did the study conception and design. Charles Treinen, BS and Daniel Lomelin, MPH performed the acquisition of data and did the analysis and interpretation of data. Charles Treinen, BS; Daniel Lomelin, MPH; and Crystal Krause, PhD drafted the manuscript. Charles Treinen, BS; Daniel Lomelin, MPH; Crystal Krause, PhD; and Dmitry Oleynikov, MD critically revised the manuscript.

Ethics statement This study utilized the University HealthSystem Consortium database, which uses de-identified patient information, and as such does not require informed consent or IRB approval. The manuscript does not contain clinical studies or individual patient data.

Conflicts of interest None.

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