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ACUTE CHOLECYSTITIS – A NARRATIVE REVIEW FOR PRACTICAL APPROACH

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Acute calculous cholecystitis is a significant medical condition characterized by inflammation of the gallbladder due to the obstruction of bile duct by gallstones. The objective of this review is to clear out the current understanding of pathophysiology, clinical presentation, diagnostic techniques, and management strategies of acute calculous cholecystitis.

The discussion begins with an examination of the epidemiology of cholecystitis, highlighting pertinent risk factors and clinical manifestations. Furthermore, diagnostic modalities, particularly ultrasound and computed tomography, are evaluated.

This review also addresses both surgical and non-surgical treatment options, placing particular emphasis on laparoscopic cholecystectomy as the gold standard while considering alternative therapies for patients at high risk.

Through a thorough analysis of recent literature, this article aims to provide valuable insights into best practices and future directions for managing acute calculous cholecystitis, ultimately improving patient outcomes and reducing the morbidity associated with this prevalent condition.

Keywords: *acute cholecystitis, laparoscopic cholecystectomy, choledocolithiasis, cholecystostomy, conservative management.*

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Introduction

Acute cholecystitis (AC), a common surgical emergency, is characterized by inflammation of the gallbladder, most frequently caused by gallstone obstruction of the cystic duct [1]. It accounts for a significant proportion of hospital admissions for abdominal pain, with an estimated prevalence of 5-10% among patients presenting with acute abdominal conditions [2]. The pathophysiology of AC involves a complex interplay of mechanical obstruction, inflammation, and bacterial infection. Gallstones, present in approximately 90% of cases, lead to bile stasis and increased intraluminal pressure, triggering an inflammatory cascade [3]. If left untreated, complications such as gallbladder perforation, abscess formation, or sepsis can arise, underscoring the importance of timely diagnosis and intervention [4]. Recent advancements in diagnostic imaging, including ultrasound and computed tomography (CT), have improved the accuracy of early detection, while evolving treatment strategies, such as laparoscopic cholecystectomy, have set new standards for management [5]. However, challenges remain in managing high-risk patients, such as the elderly or those with significant comorbidities, necessitating a tailored approach to care [6].

This narrative review aims to provide a comprehensive update on AC, by integrating recent literature and clinical guidelines, seek to offer practical insights for clinicians and highlight future directions in the management of this prevalent condition.

Material and methods

The authors undertook a comprehensive literature review to address specific research questions and relevant keywords. They meticulously coordinated various tasks, including the development of the review protocol, the establishment of inclusion and exclusion criteria, the selection of suitable search strategies, and the assurance of data quality throughout the process. Utilizing databases such as PubMed, Science Direct, and Springer Link, the authors employed several keywords to identify relevant articles. These keywords included “Acute cholecystitis,” “Laparoscopic Cholecystectomy,” “Choledocolithiasis,” “Cholecystostomy,” and “Conservative Management.” The final article inclusion was approved by all the authors.

1. Epidemiology and pathophysiology

AC is a prevalent condition, most commonly caused by gallstones, with 90-95% of cases classified as acute calculous cholecystitis (ACC) accounting for approximately 3-10% of all patients presenting with abdominal pain [1, 2]. The incidence of gallstone-related cholecystitis increases with age, particularly in individuals over 50 years, and is more common in women due to hormonal influences such as estrogen, which promotes cholesterol saturation in bile [7]. Other risk factors include obesity, rapid weight loss, diabetes, and a sedentary lifestyle [8]. Geographic and ethnic variations also play a role, with higher prevalence rates observed in Western populations compared to Asian and African populations.

The pathophysiology of AC is primarily driven by gallstone obstruction of the cystic duct, leading to bile stasis, increased intraluminal pressure, and subsequent inflammation of the gallbladder wall [3]. This obstruction prevents bile outflow, causing distension and ischemia of the gallbladder mucosa, which triggers an inflammatory response mediated by prostaglandins and cytokines, which further exacerbate the condition [9]. Secondary bacterial infection, often involving organisms such

as Escherichia coli, Klebsiella, and Enterococcus, can lead to suppurative process and lead to complications like empyema or gangrene [11]. In rare cases, acute acalculous cholecystitis (AAC) occurs without gallstones, typically in critically ill patients due to factors such as ischemia, sepsis, or prolonged fasting [12].

2. Methods of diagnosis

The diagnosis of ACC relies on a combination of clinical, laboratory, and imaging findings.

2.1 Diagnosis based on clinical manifestations and laboratory analysis

Its clinical manifestations typically develop over a timeframe ranging from several hours to a few days. The hallmark symptom of this condition is a severe and persistent pain localized to the right upper quadrant of the abdomen. This pain may radiate to the right shoulder or back, a phenomenon known as referred pain [2]. This occurs due to the shared nerve pathways of the diaphragm and gallbladder, which are both innervated by the phrenic nerve, leading to discomfort in seemingly unrelated areas.

A critical clinical sign associated with AC is Murphy's sign. This sign is elicited during physical examination when the examiner applies pressure to the right upper quadrant while the patient inhales. A positive Murphy's sign is indicated by a notable increase in pain, reflecting the inflammation in the gallbladder.

In addition to abdominal pain, patients often report significant and persistent nausea and vomiting, which can further complicate their clinical picture. Fever is another common symptom, usually starting as low-grade but potentially increasing as the disease progresses. The development of a high fever accompanied by chills may suggest a bacterial infection and raise concerns for the progression to suppurative cholecystitis [11].

Jaundice can occasionally be observed in patients, particularly if the inflammatory process extends to the common bile duct or if there is a presence of choledocholithiasis, where gallstones are lodged in the bile duct. It is worth noting that jaundice is not typical in cases of uncomplicated ACC, emphasizing the importance of differential diagnosis [1]. Upon physical examination, patients often present in acute distress. Vital signs may indicate tachycardia and tachypnea, especially in instances of severe inflammation or systemic involvement. An abdominal examination will usually reveal tenderness and guarding in the right upper quadrant, indicating irritation of the peritoneum.

It is crucial to understand that the clinical presentation of ACC can vary significantly among different populations, particularly in elderly patients or individuals with diabetes mellitus. These groups may exhibit atypical symptoms or, in some cases, remain relatively asymptomatic [6]. This atypical presentation can lead to a delayed diagnosis, significantly increasing the risk of complications such as perforation or the development of abscesses. Therefore, healthcare providers must maintain a high level of suspicion for AC in these high-risk populations and ensure prompt diagnostic imaging.

Laboratory findings in AC often reflect inflammation and infection. Common abnormalities are leukocytosis (>10,000/μL) is a hallmark of inflammation and infection [9]. Liver function tests (LFTs): Mild elevations in bilirubin, alkaline phosphatase (ALP), and transaminases (ALT/AST) may occur due to bile duct obstruction or secondary cholangitis [3]. Elevated C-reactive protein (CRP): CRP levels are often increased, indicating systemic inflammation [4].

2.2 Instrumental findings

Imaging plays a pivotal role in the diagnosis of AC, providing both confirmation of the condition and assessment of complications. Ultrasound is the first-line imaging modality due to its accessibility, non-invasiveness, and high sensitivity (85-90%) for detecting AC [2]. Key findings include gallstones or sludge present in 90-95% of cases of ACC [1], sonographic murphy's sign, pain elicited by transducer pressure over the gallbladder, with a specificity of 79-96% [4], gallbladder wall thickening (>4 mm), a hallmark sign of inflammation, pericholecystic fluid, indicative of localized inflammation or abscess formation [11]. CT is less sensitive than ultrasound for diagnosing AC but is useful in evaluating complications or atypical presentations. Findings may include abscess formation or perforation indicated by localized fluid collections or free air [9]. Gallbladder wall thickening and pericholecystic fluid, and air in the gallbladder wall (emphysematous cholecystitis) are rare but severe complications [3].

Magnetic Resonance Imaging (MRI) and Magnetic Resonance Cholangiopancreatography (MRCP) MRI/MRCP is reserved for complex cases or when bile duct obstruction is suspected. It provides detailed visualization of bile duct stones or dilation, gallbladder wall inflammation and pericholecystic fluid. Hepatobiliary Scintigraphy (HIDA Scan) is highly specific (90-97%) for AC, particularly in cases where ultrasound findings are equivocal [12].

3. Treatment modalities

3.1 Surgical interventions

Laparoscopic Cholecystectomy, the gold standard for treating AC is laparoscopic cholecystectomy [1], preferably performed within 72 hours of symptom onset (early cholecystectomy). This approach is associated with shorter hospital stays, reduced complications, and lower costs compared to delayed surgery. A timeframe of 7 to 10 days following the clinical onset of AC is now regarded as acceptable for the performance of early laparoscopic cholecystectomy (ELC) [2]. Expert guidelines advocate for the execution of this procedure within 72 hours of symptom onset (very early) or within 7 to 10 days (early), despite the lack of high-quality definitive evidence supporting this practice [10]. In instances where ELC is not feasible, a delayed laparoscopic cholecystectomy (DLC) may be considered. However, it is essential to note that laparoscopic cholecystectomy is typically advised against within 1 to 6 weeks following the onset of AC due to an increased likelihood of serious

adverse events during this interval [15]. Therefore, for patients unable to undergo ELC within the specified 7 or 10 days from symptom onset, it is recommended that surgery be postponed beyond 6 weeks to mitigate the associated risks [6].

For patients who cannot have surgery or have serious health issues, there are alternative treatments available. One option is percutaneous cholecystostomy (PC). This is a minimally invasive procedure where doctors insert a drainage catheter into the gallbladder using imaging guidance. This allows the infected bile to be drained, relieving pressure in the gallbladder. PC can be a temporary solution until surgery can be performed or, in some cases, it can be the final treatment. Recent studies show that some hospitals use PC as the first option for elderly or critically ill patients [16].

Endoscopic methods are also gaining popularity for treating ACC, especially when there are common bile duct stones present. Doctors can perform endoscopic retrograde cholangiopancreatography (ERCP) to remove stones and drain bile before doing cholecystectomy. New techniques, like endoscopic ultrasound-guided gallbladder drainage (EUS-GBD), offer alternatives to PC for high-risk patients. EUS-GBD creates a connection between the gallbladder and the digestive tract for internal drainage of infected bile [17].

Another method is percutaneous trans-hepatic gallbladder decompression (PTGBD). This also uses imaging to help decompress the gallbladder. It is particularly useful for patients with high risk of laparoscopic or open surgery [9]. PTGBD is less invasive than surgery and can help stabilize patients with AC until they are strong enough to have surgery later [10]. However, it can have complications like bleeding, bile leakage, infection, pneumothorax, and catheter dislodgement. PTGBD is not a permanent solution and does not fix the underlying problem, so patients often need surgery later.

Advancements in surgical techniques have improved how doctors treat ACC. Single-incision laparoscopic cholecystectomy (SILC) and natural orifice transluminal endoscopic surgery (NOTES) are being studied as less invasive options to traditional laparoscopic surgery [18]. These methods aim to reduce trauma, enhance cosmetic results, and speed up recovery. However, they are not widely used yet due to technical difficulties and the need for specialized training.

3.2 Conservative management

Conservative management of AC is typically reserved for patients who are not immediate candidates for surgical intervention due to high surgical risk, significant comorbidities, or patient preference [2]. This approach involves medical therapy to control inflammation, infection, and symptoms, with the goal of stabilizing the patient for potential delayed surgical intervention or as a definitive treatment in select cases components of conservative management NPO, patients should be kept NPO to reduce gallbladder stimulation and allow the inflamed gallbladder to rest [1]. Gradual reintroduction of oral intake can be considered once symptoms improve. Intravenous Fluids, Maintain hydration and correct electrolyte imbalances with intravenous fluids (e.g., normal saline or lactated Ringer's solution) [11]. Monitor urine output and hemodynamic status closely. Analgesia, Pain management is essential and can be achieved with Opioids, intravenous morphine or fentanyl for severe pain, NSAIDs, Ketorolac or diclofenac for mild to moderate pain [9]. Antibiotic Therapy Empirical antibiotic therapy is initiated to cover common pathogens, including gram-negative bacteria (e.g., Escherichia coli, Klebsiella) and anaerobes [13]. Recommended regimens include monotherapy, Piperacillin-tazobactam or carbapenems (e.g., meropenem). combination therapy, third-generation cephalosporins (e.g., ceftriaxone) plus metronidazole [14]. Antibiotics should be tailored based on culture results and local resistance patterns. Duration of therapy is typically 4–7 days, depending on clinical response [12].

3.3 Use of Cytokines in the Treatment of AC: Current Evidence and Future Directions

Cytokines are signaling molecules that play a critical role in inflammation and immune responses [9] In AC, the inflammatory process is driven by the release of pro-inflammatory cytokines such as interleukin-6 (IL-6), interleukin-1β (IL-1β), and tumor necrosis factor-alpha (TNF-α). Cytokine Inhibition as an adjunct to antibiotics combining cytokine inhibitors with antibiotics may enhance the resolution of inflammation and infection, particularly in severe or complicated cases [19]. While the primary treatment for AC remains surgical (e.g., cholecystectomy) and medical (e.g., antibiotics, analgesia), there is growing interest in the potential use of cytokine modulation as an adjunctive therapy. Anti-IL-6 agents, Tocilizumab, an IL-6 receptor antagonist, has been used in other inflammatory conditions could be explored for AC [20]. Anti-TNF-α agents, like Infliximab or etanercept, which inhibit TNF-α, have shown efficacy in inflammatory diseases but have not been studied in AC [21]. IL-1 receptor antagonists, Anakinra, an IL-1 receptor antagonist, could potentially mitigate inflammation in AC [22]. Current evidence animal studies preclinical studies have demonstrated that cytokine inhibition reduces gallbladder inflammation and improves outcomes in animal models of AC [23]. Challenges and limitations risk of immunosuppression cytokine inhibitors may increase the risk of infections, which is a concern in AC, where bacterial infection is a key component [24]. Lack of clinical trials there are no large-scale randomized controlled trials (RCTs) evaluating the safety and efficacy of cytokine-based therapies in AC. Future directions clinical trials well-designed RCTs are needed to evaluate the role of cytokine inhibitors in AC, particularly in high-risk or refractory cases.

4. Conclusion

In conclusion, ACC remains a significant clinical challenge requiring prompt diagnosis and effective management to reduce morbidity and mortality. While current diagnostic tools like ultrasound and CT imaging have improved detection, gaps in early

diagnosis, especially in high-risk populations, persist. Future research should aim to refine diagnostic criteria and explore novel imaging techniques, such as MRCP and advanced ultrasound, to enhance accuracy. Surgical intervention is the gold standard for treatment, but conservative management strategies for high-risk patients need further investigation, including standardized protocols for antibiotics, pain management, and cytokine modulation. The efficacy of minimally invasive techniques like single-incision laparoscopic cholecystectomy also warrants more study. A multidisciplinary approach incorporating advancements in diagnostics and treatment is essential for effectively managing ACC. Collaborative efforts among clinicians, researchers, and policymakers can lead to improved outcomes. The exploration of cytokines in treating elderly patients with ACC shows promise, and targeted research is necessary to optimize these therapeutic strategies and fill existing knowledge gaps.

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ОСТРЫЙ ХОЛЕЦИСТИТ – НАРРАТИВНЫЙ ОБЗОР ДЛЯ ПРАКТИЧЕСКОГО ПРИМЕНЕНИЯ

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Острый калькулезный холецистит является серьезным медицинским состоянием, характеризующимся воспалением желчного пузыря вследствие закупорки пузырного протока желчным камнем. Данный обзор стремится прояснить современное понимание его патогенеза, клинической картины, диагностических методов и стратегий лечения.

Обсуждение начинается с рассмотрения эпидемиологии холецистита, выделяя соответствующие факторы риска, а также детально анализируются клинические проявления. Кроме того, оцениваются диагностические методы, в частности ультразвуковое исследование и компьютерная томография.

Рассматриваются как хирургические, так и нехирургические варианты лечения с особым акцентом на лапароскопическую холецистэктомию как золотой стандарт, при этом учитываются альтернативные методы терапии для пациентов с высоким риском.

Благодаря тщательному анализу последних научных публикаций, данная работа направлена на предоставление сведений о лучших практиках и будущих направлениях в лечении острого калькулезного холецистита, что в конечном итоге способствует улучшению результатов лечения пациентов и снижению заболеваемости, связанной с этим распространенным состоянием.

Ключевые слова: *острый холецистит, лапароскопическая холецистэктомия, холедохолитиаз, холецистостомия, консервативное лечение*

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