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Chapter 7

An Update on the Diagnosis of Acute Calculus Cholecystitis: Review

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Abstract

Acute calculous cholecystitis (ACC) represents a common surgical emergency, characterized by inflammation of the gallbladder, typically resulting from cystic duct obstruction by a gallstone. The diagnostic process involves a combination of clinical evaluation, blood tests, and imaging techniques. Leukocytosis and elevated inflammatory markers, such as C-reactive protein (CRP), are frequently observed in this condition, with ultrasound being the most employed imaging modality for diagnosing acute calculous cholecystitis. The Tokyo Guidelines (TG) have provided a crucial, internationally recognized framework for standardizing the diagnosis and severity grading of ACC, with revisions in 2013 (TG13) and 2018 (TG18) aimed at enhancing specificity and accuracy. This review delineates the principal diagnostic methods for acute calculous cholecystitis, emphasizing the evolution of the Tokyo Guidelines criteria, the role of specific blood tests, and the utility of various imaging modalities..

Keywords: Acute calculus cholecystitis, Blood investigations, Diagnosis, Imaging, HIDA scan, Ultrasound, and Tokyo Guidelines.

1. Introduction

Acute cholecystitis is a prevalent complication of gallstone disease, occurring in approximately 25% of patients who exhibit symptoms of this condition. It is more frequently observed in female patients and is characterized by pain in the right hypochondrium, accompanied by nausea and vomiting. Upon general examination, fever may be present, and abdominal assessment may reveal a positive Murphy's sign or tenderness in the right hypochondrium [1, 2]. Blood tests indicating leukocytosis or elevated inflammatory markers, such as C-reactive protein (CRP), serve as non-specific indicators. Diagnostic imaging, particularly abdominal ultrasound, can confirm the presence of gallstones, gallbladder inflammation, and pericholecystic fluid, which are indicative of acute cholecystitis [3–5]. Management strategies for acute cholecystitis are categorized into early and interval laparoscopic cholecystectomy, depending on the severity of the condition. In severe cases, percutaneous cholecystostomy may be employed as a temporary measure to stabilize patients, allowing for subsequent laparoscopic cholecystectomy once the patient is deemed fit for surgery [6–9].

The Tokyo Guidelines classify the severity of acute calculus cholecystitis into three categories: mild, moderate, and severe. Mild disease is identified by the presence of acute cholecystitis symptoms; moderate disease is characterized by acute cholecystitis accompanied by local inflammation and leukocytosis; and severe acute cholecystitis is defined by the presence of systemic organ dysfunction [10]. The 2016 guidelines from the World Society of Emergency Surgeons (WSES) recommend utilizing a combination of patient history, clinical examination, and laboratory tests to diagnose acute calculus cholecystitis [11]. The 2020 WSES guidelines further suggest incorporating history taking, clinical examination, blood investigations, and imaging, with ultrasound being the preferred initial imaging modality, to establish the diagnosis of acute calculus cholecystitis [12].

This chapter examines the diagnostic approach to acute calculus cholecystitis, with a particular focus on the relevant blood investigations. Additionally, it explores the various imaging modalities employed and the application of the Tokyo Guidelines in diagnosing and assessing the severity of acute calculus cholecystitis. A comprehensive literature review was conducted utilizing PUBMED, the Cochrane Database of Clinical Reviews, and Google Scholar, targeting clinical trials, observational studies, cohort studies, systematic reviews, and meta-analyses published between 1990 and 2025. The search employed the following keywords: "Acute calculus cholecystitis," "blood investigations,"

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"imaging," "ultrasound," "HIDA scan," "Tokyo Guidelines," and "diagnosis." Only articles published in English were considered. Additional articles were identified through manual cross-referencing of the literature. Exclusion criteria included case reports, studies with fewer than 10 patients, and editorials. The study population comprised adult male and female patients.

2. Discussion

The Tokyo Guidelines (TG) for the diagnosis of acute calculus cholecystitis

The Tokyo Guidelines of 2007 established diagnostic criteria for acute cholecystitis, encompassing local signs of inflammation, such as Murphy's sign or a right upper quadrant mass, systemic signs of inflammation, including fever, leukocytosis, and elevated C-reactive protein (CRP), as well as imaging findings indicative of acute cholecystitis. A definitive diagnosis of acute calculus cholecystitis necessitates the presence of either local or systemic signs of inflammation, which must be corroborated by imaging findings [13]. The severity of acute cholecystitis is categorized into three grades: mild or Grade 1, characterized by mild inflammation of the gallbladder without organ dysfunction; moderate or Grade 2, where acute cholecystitis is associated with prolonged symptoms lasting 72 hours, a tender mass in the right iliac fossa, leukocytosis, and marked inflammation of the gallbladder; and severe or Grade 3, where acute cholecystitis is accompanied by dysfunction in any one of the systemic systems, including cardiovascular, respiratory, neurological, hematological, renal, or hepatic [14].

The Tokyo Guidelines 2013 revised the diagnostic criteria for acute cholecystitis. A suspected diagnosis of acute cholecystitis should include at least one clinical symptom, such as Murphy's sign or tenderness in the right upper quadrant, along with one systemic sign of inflammation, such as fever, leukocytosis, or elevated C-reactive protein (CRP). A definitive diagnosis requires the presence of one clinical symptom, one systemic sign of inflammation, and imaging confirmation of acute cholecystitis, with ultrasound being the most commonly employed imaging modality. The severity assessment of acute cholecystitis, originally established in the 2007 guidelines, underwent minor modifications, particularly in the category of cardiovascular dysfunction, where hypotension requiring the use of dopamine or norepinephrine was included [15, 16].

The diagnostic criteria and severity assessment for acute cholecystitis outlined in the Tokyo Guidelines 2018 were directly adopted from the Tokyo Guidelines 2013, without any modifications. This decision followed validation studies that confirmed the utility of the 2013 guidelines for diagnosing acute cholecystitis. Consequently, the severity assessment criteria from the Tokyo Guidelines 2013 were validated and incorporated into the 2018 guidelines unchanged [17, 18].

Table 1: Tokyo Guidelines 13/18 diagnostic criteria for acute calculus cholecystitis

Criteria Category	TG07 Diagnostic Criteria	TG13/TG18 Diagnostic Criteria
A. Local Signs	Murphy's sign, Right Upper Quadrant (RUQ) mass/pain/tenderness	Murphy's sign, RUQ mass/pain/tenderness
B. Systemic Signs	Fever, Elevated White Blood Cell count (WBC), Elevated C-reactive protein (CRP)	Fever, Elevated WBC count, Elevated CRP
C. Imaging Findings	Imaging findings characteristic of acute cholecystitis (e.g., gallbladder distension, wall thickening, pericholecystic fluid, gallstones)	Imaging findings characteristic of acute cholecystitis
Definitive Diagnosis	1 item in A + 1 item in B + Imaging findings in C	**Suspected Diagnosis:** 1 item in A + 1 item in B. **Definitive Diagnosis:** 1 item in A + 1 item in B + Imaging findings in C.

Table showing the Tokyo Guidelines 13/18 diagnostic criteria for acute calculus cholecystitis.

Table 2: Tokyo Guidelines 13/18 severity grading for acute cholecystitis

Severity	Parameters
Grade 3(severe) Acute Cholecystitis	1. Cardiovascular Dysfunction-Hypotension being treated with dopamine or norepinephrine. 2. Neurological dysfunction: decreased consciousness. 3. Respiratory dysfunction 4. Renal dysfunction 5. Hepatic dysfunction 6. Hematological dysfunction (Grade 3 acute cholecystitis is associated with any one of the following parameters)
Grade 2(Moderate) Acute Cholecystitis	Elevated white cell count ($> 17,000$) Palpable mass in the right upper quadrant Duration of symptoms > 72 hours Marked local inflammation (gangrenous or emphysematous cholecystitis)
Grade 1(Mild) Acute Cholecystitis	Acute cholecystitis with mild inflammation and no organ dysfunction.

Table showing the Tokyo Guidelines 13/18 severity grading for acute cholecystitis

A retrospective study spanning five years was conducted to evaluate the validity of the Tokyo Guidelines 2013 diagnostic criteria. This study included a total of 169 patients, revealing a sensitivity of 83.1% and a specificity of 37.5% for the diagnosis of acute cholecystitis according to the Tokyo Guidelines 2013 [19]. In a separate investigation, Ambe et al. examined the sensitivity of the Tokyo Guidelines in predicting the severity of acute cholecystitis. This study involved 138 patients and indicated that the Tokyo Guidelines tend to underestimate the severity of acute calculus cholecystitis in male patients [20].

Blood investigations in the diagnosis of acute calculus cholecystitis

A complete blood count is a frequently utilized diagnostic tool for identifying acute calculous cholecystitis, often revealing leukocytosis. C-reactive protein serves as a prevalent inflammatory marker to assist in diagnosing this condition. The integration of blood tests with clinical assessments and imaging techniques is essential for the accurate diagnosis of acute calculous cholecystitis [21]. Uludag et al. investigated the predictive value of serum inflammatory markers for severe acute cholecystitis. Their study included 250 patients and found that elevated leukocyte counts, and C-reactive protein (CRP) levels were associated with an increased risk of severe acute calculous cholecystitis.[22]. Additionally, Turan et al. conducted a retrospective study examining the role of laboratory and radiological findings in managing acute calculous cholecystitis. This study, which included 230 patients, identified a correlation between leukocytosis and gallbladder wall thickening in individuals with acute calculous cholecystitis [23].

In the study conducted by Beliaev et al., C-reactive protein (CRP) demonstrated superior discriminative power compared to leukocytosis in diagnosing acute calculus cholecystitis. The study encompassed a total of 1843 patients, revealing that CRP outperformed white cell count in diagnosing mild, moderate, and severe forms of acute calculus cholecystitis [24]. Similarly, a retrospective study by Yuzbasioglu et al. corroborated these findings, indicating that CRP was more effective in assessing the severity of acute calculus cholecystitis [25].

Imaging modalities for the diagnosis of acute calculus cholecystitis

Ultrasound is the most frequently utilized imaging modality for diagnosing acute cholecystitis. It effectively identifies the presence of gallstones, inflammation of the gallbladder wall, and pericholecystic fluid accumulation. As the preferred initial diagnostic tool for acute cholecystitis, ultrasound is, however, dependent on the operator's expertise. Cholescintigraphy is employed in cases where ultrasound fails to confirm acute cholecystitis, yet there remains a high clinical suspicion. The limitations of cholescintigraphy include its limited availability and the requirement for the ingestion of radioactive material. Computed tomography is reserved for identifying complications of acute cholecystitis, such as emphysematous and gangrenous cholecystitis [26–29].

Borzellino et al. conducted a retrospective evaluation of the sonographic diagnosis of acute cholecystitis, utilizing gallbladder distension, edema of the gallbladder wall, and pericholecystic fluid collection as diagnostic indicators. The positive predictive values for patients exhibiting two or three of these signs were 78% and 100%, respectively, while the negative predictive value was 72.4% in the absence of any signs [30]. Soiva et al. investigated the role of ultrasound in diagnosing acute cholecystitis within the emergency department. This study included 135 patients and reported a diagnostic sensitivity and specificity of ultrasound at 93% and 95%, respectively [31]. Huang et al. conducted a systematic review and meta-analysis on the diagnostic performance of ultrasound in acute cholecystitis, incorporating 40 studies with a total of 8,652 patients. The analysis yielded a pooled sensitivity of 71% and a specificity of 85% for ultrasound in diagnosing acute cholecystitis, with no significant differences in sensitivity and specificity among emergency physicians, surgeons, and radiologists. This study affirmed that ultrasound is an effective imaging modality for diagnosing acute cholecystiti [32]. Wilson et al. performed a systematic review and meta-analysis on the performance of emergency physicians using ultrasound to diagnose acute calculus cholecystitis. This study included seven studies with 1,772 patients, reporting a sensitivity of 70.9%, a specificity of 94.4%, a positive likelihood ratio of 12.7, and a negative likelihood ratio of 0.31 for diagnosing acute calculus cholecystitis [33].

Hepatobiliary scintigraphy is a nuclear imaging technique employed to diagnose acute calculus cholecystitis in cases where ultrasonography has proven inadequate. This procedure identifies the non-visualization of the gallbladder, indicative of cystic duct obstruction in patients with acute calculus cholecystitis. The sensitivity of hepatobiliary scintigraphy ranges from 80% to 90%, while its specificity is between 85% and 90%. However, the method has certain limitations, including the use of radioactive materials, its time-intensive nature, and contraindications for pregnant patients [34–36]. Kalimi et al. conducted a study comparing the sensitivity of hepatobiliary scintigraphy with that of ultrasonography, involving 126 participants. The findings demonstrated that hepatobiliary scintigraphy exhibited higher sensitivity in diagnosing acute calculus cholecystitis [37].

Computed tomography (CT) is an imaging modality employed in the diagnosis of acute cholecystitis. It is capable of identifying characteristic changes associated with acute calculous cholecystitis, such as gallbladder wall thickening, pericholecystic fluid accumulation, and gallbladder distension. CT is also utilized to diagnose complications arising from acute cholecystitis, including empyema, emphysematous or gangrenous cholecystitis, and gallbladder perforation [38]. While magnetic resonance imaging (MRI) can be used for diagnostic purposes, it is primarily applied in identifying complications of acute cholecystitis, such as gangrene, emphysema, and gallbladder perforation. MRI is infrequently employed as the initial investigative modality for diagnosing acute calculous cholecystitis due to its time-consuming nature and the requirement for specialized expertise [39, 40].

Kiewiet et al. conducted a systematic review and meta-analysis to evaluate the diagnostic performance of imaging modalities in acute cholecystitis. This study incorporated 57 studies encompassing a total of 5,859 patients. The sensitivities of ultrasound, scintigraphy, and magnetic resonance imaging were found to be 81%, 96%, and 95%, respectively. The specificities for these imaging techniques were 83% for ultrasound, 90% for scintigraphy, and 91% for magnetic resonance imaging. Scintigraphy demonstrated the highest sensitivity for diagnosing acute cholecystitis, followed by ultrasound. However, there is a paucity of evidence regarding the role of computerized tomography and magnetic resonance imaging in diagnosing acute calculus cholecystitis, attributed to the limited number of studies available [41].

Table showing the sensitivity and specificity of ultrasound, scintigraphy, and magnetic resonance imaging in the diagnosis of acute cholecystitis by Kiewiet et al.

Imaging	Sensitivity	Specificity
Ultrasound	81%	83%
Scintigraphy	96%	90%
Magnetic Resonance Imaging	95%	91%

3. Conclusion

The diagnosis of acute calculous cholecystitis is robustly supported by clinical examination, laboratory assessments, and imaging data. The Tokyo Guidelines (TG13/TG18) offer an essential, validated, and internationally recognized framework, necessitating the presence of local signs, systemic signs of inflammation, and characteristic imaging findings for a definitive diagnosis of acute calculous cholecystitis. Abdominal ultrasonography remains the primary modality for initial imaging, while scintigraphy is reserved for cases where ultrasound fails to provide a diagnosis. Blood investigations yield critical evidence of systemic inflammation, such as leukocytosis and elevated C-reactive protein (CRP) levels. The integration of these clinical, laboratory, and imaging findings is crucial for an accurate and timely diagnosis, facilitating appropriate management, which often involves early cholecystectomy.

Article Information

Conflict of interest: There is no conflict of interest.

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