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Review Article

The Diagnosis of Acute Calculus Cholecystitis: Narrative Review Article

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Abstract: Acute calculous cholecystitis (ACC) is a prevalent surgical emergency characterized by inflammation of the gallbladder, typically due to cystic duct obstruction by a gallstone. The diagnostic process relies on a combination of clinical assessment, blood investigations, and imaging modalities. Leukocytosis and elevated inflammatory markers like C.Reactive protein (CRP) are commonly seen in this condition, and ultrasound is the most common imaging modality used to diagnose acute calculus cholecystitis. The Tokyo Guidelines (TG) have served as a critical, internationally recognized framework for standardizing the diagnosis and severity grading of ACC, undergoing revisions in 2013 (TG13) and 2018 (TG18) to enhance specificity and accuracy. This review outlines the key diagnostic methods for acute calculus cholecystitis, focusing on the evolution of the Tokyo Guidelines criteria, the role of specific blood investigations, and the utility of various imaging modalities.

Keywords: Acute Calculus Cholecystitis, Blood Investigations, Diagnosis, Imaging, HIDA Scan, Ultrasound and Tokyo Guidelines.

INTRODUCTION

Acute cholecystitis is one of the most common complications of gallstone disease, and it is seen in 25% of patients who develop symptoms of gallstone disease. It is commonly seen in female patients, and it presents with symptoms of pain in the right hypochondrium along with symptoms of nausea and vomiting. On general examination, there may presence of fever, and abdominal examination may reveal a positive Murphy's sign or tenderness at the right hypochondrium(Schuld & Glanemann, 2015; Strasberg, 2008). Blood investigations like the presence of leukocytosis or elevated inflammatory markers like C.Reactive protein (CRP) are non-specific markers. Imaging modalities like ultrasound of the abdomen will reveal the presence of gallstones, inflammation of the gallbladder, and the presence of pericholecystic fluid around the gallbladder, is diagnostic of acute cholecystitis(Elwood, 2008; Gomes *et al*., 2017; Halpin, 2013). The management of acute cholecystitis can be divided into early and interval laparoscopic cholecystectomy according to its severity. Percutaneous cholecystostomy can be used as a bridging procedure to stabilize severe patients and perform a laparoscopic cholecystectomy later, once they are fit for surgery(Bagla *et al*., 2016; Indar & Beckingham,2002; Kuhlenschmidt *et al*., 2021; Yusoff *et al*., 2003).

The severity of acute calculus cholecystitis has been graded by the Tokyo Guidelines as mild, moderate, and severe. Mild disease is characterized by symptoms of acute cholecystitis; moderate disease is characterized by acute cholecystitis with local inflammation and leukocytosis, while severe acute cholecystitis is characterized by acute cholecystitis with systemic organ dysfunction(Costanzo *et al*., 2023).The 2016 World Society of Emergency Surgeons(WSES) guidelines on acute calculus cholecystitis have recommended a combination of history, clinical examination, and laboratory tests to establish the diagnosis of acute calculus cholecystitis(Ansaloni *et al*., 2016).The 2020 World Society of Emergency Surgeons(WSES) guidelines have recommended a combination of history taking, clinical examination, blood investigation, and imaging, with ultrasound being the initial imaging that is recommended to establish the diagnosis of acute calculus cholecystitis(Pisano *et al*., 2020).

This review article will look at the diagnosis of acute calculus cholecystitis, including the blood investigations that are used. We will also look at the various imaging modalities and how the Tokyo Guidelines are used to diagnose and assess the severity of acute calculus cholecystitis. We conducted a literature review using PUBMED, Cochrane database of clinical reviews, and Google Scholar, looking for clinical trials, observational studies, cohort studies, systematic reviews, and meta-analyses from 1990 to 2025. We used the following keywords: "Acute calculus cholecystitis", "blood investigations", "imaging", "ultrasound "," HIDA scan, "Tokyo Guidelines", and "diagnosis". All articles were in the English language only. Further articles were obtained by manually cross-referencing the literature. Case reports and studies with fewer than 10 patients and editorials were excluded. Adult male and female patients were included in this study.

DISCUSSION

The Tokyo Guidelines (TG) for the Diagnosis of Acute Calculus Cholecystitis

The Tokyo Guidelines of 2007 introduced diagnostic criteria for acute cholecystitis, which included local signs of inflammation (Murphy's sign or right upper quadrant mass), systemic signs of inflammation such as fever, leukocytosis, and elevated C-reactive protein (CRP), and imaging findings consistent with acute cholecystitis. A definitive diagnosis of acute calculus cholecystitis was obtained by using either the local signs or systemic signs of inflammation, but it must be confirmed by imaging findings (Hirota *et al*., 2007). The severity of acute cholecystitis was also graded into mild or grade 1, where there is mild inflammation of the gallbladder with no organ dysfunction. Moderate or Grade 2, where acute cholecystitis is associated with prolonged symptoms of 72 hours, a tender mass at the right iliac fossa, leukocytosis, and marked inflammation of the gallbladder. Severe or Grade 3, where there is acute cholecystitis with any one systemic dysfunction (cardiovascular, respiratory, neurological, hematological, renal, or hepatic)(Mayumi *et al*., 2007).

The Tokyo Guidelines 2013 revised the diagnostic criteria for acute cholecystitis, and a suspected diagnosis of acute cholecystitis should include either one clinical symptom, such as Murphy's sign or right upper quadrant tenderness, and one systemic sign of inflammation, such as fever, leukocytosis, or elevated C-reactive protein (CRP). A definitive diagnosis of acute cholecystitis should include one clinical symptom, one systemic sign of inflammation, and imaging confirmation of acute cholecystitis, with ultrasound being the most common imaging modality. The severity assessment of acute cholecystitis was adopted from the 2007 guidelines, with minor changes to cardiovascular dysfunction, with hypotension with the use of dopamine or norepinephrine being included under this category (Takada *et al*., 2013; Yokoe *et al*., 2013).

The Tokyo Guidelines 2018 diagnostic criteria and severity assessment of acute cholecystitis were adopted from the Tokyo Guidelines 2013, with no further changes, following validation studies deemed useful for the diagnosis of acute cholecystitis. The severity assessment of acute cholecystitis from the Tokyo Guidelines 2013 was validated and adopted by the Tokyo Guidelines 2018 with no changes (Okamoto *et al*., 2018; Yokoe *et al*., 2018).

Table Ⅰ

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 Ⅱ

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

Severity	Parameters
	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 >72hours 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 five-year retrospective study was conducted on the validity of the Tokyo Guidelines 2013 diagnostic criteria. A total of 169 patients were included in this study, and the sensitivity of the Tokyo Guidelines 2013 for the diagnosis of acute cholecystitis was at 83.1% and the specificity was at 37.5%(Naidu *et al*., 2016).Ambe *et al*., looked at the sensitivity of the Tokyo Guidelines in predicting the severity of acute cholecystitis. A total of 138 patients were included in this study, and the Tokyo Guidelines tend to underestimate the degree of severity in male patients with acute calculus cholecystitis (Ambe *et al*., 2015).

Blood Investigations in the Diagnosis of Acute Calculus Cholecystitis

Full blood count is one of the most common blood investigations that is used to diagnose acute calculus cholecystitis, which will reveal leukocytosis. C-reactive protein is the most common inflammatory marker that is used to aid in the diagnosis of acute calculus cholecystitis. Blood investigations are combined with clinical and imaging modalities to diagnose acute calculus cholecystitis(Chung & Duke, 2018). Uludag *et al*., looked at the role of serum inflammatory markers in predicting severe acute cholecystitis. A total of 250 patients were included in this study, and elevated leukocyte and C.reactive protein (CRP) were associated with a higher risk of severe acute calculus cholecystitis(Uludağ *et al*., 2022). A retrospective study evaluating the role of laboratory and radiological findings in the management of acute calculus cholecystitis was conducted by Turan *et al*., A total of 230 patients were included in this study, and there was a correlation between leukocytosis and gallbladder thickening in patients with acute calculus cholecystitis(Turan *et al*., 2025).

C. Reactive protein (CRP) has a better discriminative power than leukocytosis in the diagnosis of acute calculus cholecystitis, and this was assessed by Beliaev *et al.*, A total of 1843 patients were included in this study, and C. Reactive protein (CRP) was superior to white cell count in the diagnosis of mild, moderate, and severe acute calculus cholecystitis(Beliaev *et al*., 2015).A similar retrospective study by Yuzbasioglu *et al*., also found that C.reactive protein was better at assessing the severity of acute calculus cholecystitis(Yuzbasioglu *et al*., 2017.).

Imaging Modalities for the Diagnosis of Acute Calculus Cholecystitis

Ultrasound is the most common imaging modality that is used to diagnose acute cholecystitis. It can demonstrate the presence of gallstones, inflammation of the gallbladder wall, and the presence of pericholecystic fluid collection. It is the preferred first-line investigation that is performed to diagnose acute cholecystitis, but it is operator-dependent. Cholescintigraphy is reserved for patients where ultrasound has failed to diagnose acute cholecystitis, but the patient has high clinical suspicion. The disadvantage of cholescintigraphy is that it is not readily available, and it involves the ingestion of nuclear material. Computerized tomography is reserved for complications of acute cholecystitis, like emphysema and gangrenous cholecystitis(O'Connor & Maher, 2011; Patel *et al*., 2024; Pinto *et al*., 2013; Schuster *et al*., 2023).

Borzellino *et al*., retrospectively assessed the sonographic diagnosis of acute cholecystitis, with gallbladder distension, edema of the gallbladder wall and pericholecystic fluid collection being used as the signs to diagnose acute cholecystitis. The positive predictive value for patients with 2 or 3 signs were 78% and 100%, while the negative predictive value was 72.4% for the absence of any signs (Borzellino *et al*., 2016). Soiva *et al*., looked at the role of ultrasound in the diagnosis of acute cholecystitis in the emergency department. A total of 135 patients were included in this study, and the sensitivity and specificity of the diagnostic accuracy of ultrasound was 93% and 95%, respectively(Soiva *et al*., 1986). A systematic review and meta-analysis on the diagnostic performance of ultrasound in acute cholecystitis was conducted by Huang *et al*., A total of 40 studies with 8,652 patients were included in this study, yielding a pooled sensitivity of 71% and a specificity of 85% for ultrasound in the diagnosis of acute cholecystitis. There were no differences in the sensitivity and specificity of ultrasound performance among emergency physicians, surgeons, and radiologists. This study showed that ultrasound is a good imaging modality for the diagnosis of acute cholecystitis(Huang *et al*., 2023). A systematic review and meta-analysis on the performance of emergency physicians in using ultrasound to diagnose acute calculus cholecystitis was conducted by Wilson *et al*., A total of 7 studies with 1772 patients were included in this study, and the sensitivity was 70.9%, the specificity was 94.4%,

the positive likelihood ratio was 12.7, and the negative likelihood ratio was 0.31 for the diagnosis of acute calculus cholecystitis(Wilson *et al*., 2024).

Hepatobiliary scintigraphy is a nuclear scan that is used to diagnose acute calculus cholecystitis in patients where ultrasonography failed to diagnose acute calculus cholecystitis. This nuclear scan will reveal non-enhancement of the gallbladder due to obstruction of the cystic duct in patients with acute calculus cholecystitis. The sensitivity of Hepatobiliary scintigraphy ranges from 80% to 90%, and its specificity ranges from 85% to 90%. The disadvantages of Hepatobiliary scintigraphy include the use of nuclear material, it is time-consuming, and it is contraindicated in pregnant patients(Afzal *et al*., 2021; Tulchinsky *et al*., 2012; Ziessman, 2014).Kalimi *et al*., looked at the sensitivity of hepatobiliary scintigraphy and compared it with ultrasonography. A total of 126 patients were included in this study, and the patients with hepatobiliary scintigraphy had a higher sensitivity for diagnosing acute calculus cholecystitis(Kalimi *et al*., 2001).

Computerized Tomography is another imaging modality that can be used to diagnose acute cholecystitis. It can detect the typical changes that are seen in acute calculus cholecystitis, like wall thickening, pericholecystic fluid collection, and distension of the gallbladder. Computerized tomography is used to diagnose complications of acute cholecystitis, like empyema, emphysematous or gangrenous cholecystitis, and perforation of the gallbladder (Jeff *et al*., 1996.; Vignesh *et al*., 2020).Magnetic resonance imaging can be used for the diagnosis, but it is used for the diagnosis of complications of acute cholecystitis, like gangrene, emphysema, and perforation of the gallbladder. It is seldom used as the first investigation modality to diagnose acute calculus cholecystitis, as it is time-consuming and requires special expertise (Altun *et al*., 2007; Watanabe *et al*., 2007).

A systematic review and meta-analysis on the diagnostic performance of imaging in acute cholecystitis was conducted by Kiewiet *et al*., A total of 57 studies with 5859 patients were included in this study. The sensitivities of ultrasound, scintigraphy, and magnetic resonance imaging were 81%, 96%, and 95%, respectively. The specificity of ultrasound, scintigraphy, and magnetic resonance imaging were 83%, 90%, and 91%, respectively. Scintigraphy has the best sensitivity for diagnosing acute cholecystitis, followed by ultrasound. There is a lack of evidence on the role of computerized tomography and magnetic resonance imaging in the diagnosis of acute calculus cholecystitis due to limited studies (Kiewiet *et al*., 2012).

Table ⅠII

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

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

CONCLUSION

The diagnosis of acute calculous cholecystitis is strongly supported by clinical examination, laboratory, and imaging data. The Tokyo Guidelines (TG13/TG18) have provided an indispensable, validated, and globally accepted framework, requiring the presence of local signs, systemic signs of inflammation, and characteristic imaging findings for a definitive diagnosis of acute calculus cholecystitis. Abdominal ultrasonography remains the cornerstone of initial imaging, with Scintigraphy being reserved for patients with acute calculus cholecystitis where the ultrasound could not diagnose it. Blood investigations provide crucial evidence of systemic inflammation (Leukocytosis, elevated CRP). Integrating these clinical, laboratory, and imaging findings is essential for accurate, timely diagnosis and appropriate management, often leading to early cholecystectomy.

Conflict of Interest: There is no conflict of interest.

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