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Comparison of Sensitivity and Specificity between B.I.L.E. Criteria and Tokyo Guidelines 2018 (TG18) for Diagnosing Acute Cholangitis

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Abstract

Acute cholangitis is an inflammatory condition of the biliary system due to bacterial infection associated with biliary stasis or obstruction. Diagnosis is made using the Tokyo Guidelines 2018 (TG18) criteria. The biliary imaging abnormality, inflammatory test abnormality, liver test abnormality, and exclusion of cholecystitis/pancreatitis (B.I.L.E.) criteria are relatively new, with limited studies evaluating their sensitivity, specificity, and validation. This study aimed to compare the sensitivity and specificity of B.I.L.E. and TG18 criteria for the diagnosis of acute cholangitis. This is an observational analytic study with prospective cohort design during May 2023–May 2024. Data were obtained from patients who came to the Emergency Department of Dr. Hasan Sadikin General Hospital Bandung, Indonesia, with clinical symptoms of fever and jaundice, suspected of acute cholangitis. There were 95 subjects in this study. Based on B.I.L.E. criteria, 57 (60%) patients were categorized as high probability and 38 (40%) patients were categorized as unlikely acute cholangitis, while the TG18 criteria resulted in 61 (64.2%) patients classified as definite and 34 (35.8%) patients classified as suspected acute cholangitis. The sensitivity of the B.I.L.E. criteria was 92.1%, with a specificity of 94.73%. Positive Predictive Value (PPV) and Negative Predictive Value (NPV) of B.I.L.E. criteria were 92.1% and 94.73%, respectively. In contrast, the sensitivity and specificity of TG18 criteria in this study were 82.35% and 83.6%, respectively. The PPV of TG18 reached 73.68% while the NPV of TG18 reached 89.47%. In conclusion, B.I.L.E. criteria have higher sensitivity and specificity than TG18 criteria in diagnosing acute cholangitis patients.

Keywords: Acute Cholangitis, B.I.L.E. Criteria, Diagnostic, TG18 Criteria

Introduction

Acute cholangitis is a severe condition caused by obstruction of the bile ducts, resulting in bile stasis and subsequent infection. The causes of bile duct obstruction vary, ranging from benign conditions such as choledocholithiasis to malignant causes. Obstruction in the bile ducts increases pressure within the biliary system, which in turn leads to reflux into the venous and lymphatic systems due to the absence of a basal membrane between the sinusoids and the small bile ducts. Microorganisms or endotoxins from infected bile can then enter systemic circulation, triggering systemic inflammation that, if untreated, may progress to septic shock and death. Accurate diagnosis and timely intervention are therefore critical to improving outcomes.[1]

Asymptomatic gallstones affect approximately 1–2% of the population, and 1–3% may experience mild symptoms.[2] These cases may progress to serious complications, including acute cholangitis, acute cholecystitis, severe jaundice, or pancreatitis. Without prompt antibiotic therapy and biliary drainage, acute cholangitis carries a high mortality rate. Endoscopic retrograde cholangiopancreatography (ERCP) is the most common method of biliary drainage and decompression, and meta-analyses indicate that early intervention reduces mortality. However, ERCP carries a complication rate of about 10%, with mortality between 0.33% and 1%. Early complications include acute pancreatitis, bleeding, sepsis, and perforation, while later complications may involve recurrent pain and jaundice. [3,4]

Charcot's triad has historicallybeen used for diagnosise but it exhibits low sensitivity, ranging from 21.2% to 70%. Recognizing

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these limitations, the Tokyo Guidelines 2007 (TG07) were introduced as a global standard for diagnosing and grading the severity of acute cholangitis. However, subsequent revisions, including the Tokyo Guidelines 2013 (TG13), aimed at improving sensitivity but failed to enhance specificity. The definitions in the Tokyo Guidelines 2018 (TG18) are similar to TG13, focusing on diagnosing cholangitis based on biliary infection, with less emphasis on non-infectious causes. This gap in specificity poses a significant concern, as a highly specific diagnostic tool is essential to avoid unnecessary interventions like ERCP, which carries a risk of complications such as pancreatitis, bleeding, and perforation.[5]

In 2021, the American Society for Gastrointestinal Endoscopy (ASGE) introduced the biliary imaging abnormality, inflammatory test abnormality, liver test abnormality, and exclusion of cholecystitis/pancreatitis (B.I.L.E.) criteria to improve diagnostic accuracy. Four criteria biliary abnormalities or intervention, raised inflammatory markers, abnormal liver function tests, and exclusion of cholecystitis and acute pancreatitis are used to identify people who have a high risk of developing acute cholangitis. Studies assessing the B.I.L.E. criteria's sensitivity, specificity, and general validity are still few, nonetheless. Additionally, the B.I.L.E. criteria had a higher sensitivity in identifying acute cholangitis, fewer needless ERCP treatments, and less post-ERCP sequelae than TG18, while requiring more sophisticated diagnostic tests.[6] The limited evidence base for the B.I.L.E. criteria create uncertainty regarding which diagnostic tool provides greater accuracy and reliability for clinical decision-making. In particular, evidence is needed to clarify whether the B.I.L.E. criteria can truly outperform TG18 in balancing sensitivity and specificity while minimizing unnecessary invasive interventions. To address this gap, this study aims to compare the diagnostic performance of the B.I.L.E. and TG18 criteria in patients with suspected acute cholangitis at Dr. Hasan Sadikin General Hospital, Bandung.

Methods

This research uses a prospective cohort design and observational analysis. Patients with fever and jaundice who were suspected of having acute cholangitis and who visited the emergency room at Dr. Hasan Sadikin General Hospital Bandung, Indonesia between May 2023 and May 2024 provided the study's data.

The inclusion criteria were: (1) patients presenting with clinical symptoms suggestive of acute cholangitis, which may be caused by factors such as stones or tumors; (2) patients who underwent relevant diagnostic evaluations; (3) patients with post-hepatic jaundice accompanied by clinical symptoms of fever; and (4) patients aged 18 years and older. The exclusion criteria were: (1) patients diagnosed with cholecystitis and/or acute pancreatitis; (2) patients whose diagnostic tests did not meet the criteria set by the B.I.L.E. or Tokyo Guidelines 2018; and (3) patients with pre-hepatic or intra-hepatic jaundice. The sample size for this study was calculated using the sample size formula for diagnostic test research, resulting in a total of 95 study subjects. The sampling method used was consecutive sampling, in which subjects were selected consecutively based on the order in which they met the inclusion criteria until the predetermined minimum sample size was achieved.

Descriptive analysis was used to present categorical data such as age, gender, symptoms of fever, jaundice, lab results, and imaging findings. The study focused on determining the sensitivity and specificity of the B.I.L.E. and TG18 criteria for diagnosing acute cholangitis, with statistical analysis conducted using contingency coefficient computations. The r-value was used to categorize correlation strength, with a $p<0.05$ signifying significant findings. The correlations ranged from extremely strong to very weak. The ROC curve was used to examine sensitivity and specificity at various cutoff points in order to forecast the diagnosis of acute cholangitis.

The accuracy of the diagnostic criteria was assessed by testing the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV). The Health Research Ethics Committee of Universitas Padjadjaran granted ethical permission for the research under registration number DP.04.03/D.XIV.6.5/266/2024.

Results

A total of 95 subjects met the inclusion criteria and did not meet the exclusion criteria, with the data presented in Table 1.

This table provides a summary of characteristics for a sample size of 95 individuals, divided into different categories along with their

Table 1 Characteristics of Subjects

Characteristics	n=95	%
Age (years)		
18–21	0	0
21–30	0	0
31–40	0	0
41–50	30	31.5
51–60	53	55.8
61–70	12	12.7
Sex		
Male	54	56.8
Female	41	43.2
Diagnosis of Acute Cholangitis		
Yes	57	60.0
No	38	40.0
ERCP		
Yes	17	17.9
No	78	82.1
B.I.L.E. Criteria		
Unlikely	38	40.0
High probability	57	60.0
TG18 Criteria		
Suspected: 1 item A + 1 item B/C	34	35.8
Definite: 1 item A, 1 item B, and 1 item C	61	64.2

respective counts (n) and percentages (%). Each category summarizes patient demographics and diagnostic criteria. The sample includes slightly more males (56.8%) than females (43.2%). There were no subjects aged over 18 and under 40 years, nor those aged over 70 years. This age distribution suggests that acute cholangitis or the need for diagnosis likely occurs more commonly in older adults, particularly those aged 50 and above. The majority of patients (55.8%) are in the 51–60 age group, followed by 31.5% in the 41–50 age group, and 12.7% in the 61–70 age group. About 60% of the patients are diagnosed with acute cholangitis, while 40% are not. The TG18 criteria further classify patients into suspected" 35.8% and "definite" 64.2%. Based on the B.I.L.E. criteria, 40% of patients are deemed "unlikely while 60% are considered to have a "high probability" of having acute cholangitis. Approximately, only 17.9% of the patients underwent an ERCP.

According to the B.I.L.E. criteria (Table 2), the majority of patients had biliary imaging abnormalities (81.1%), abnormal inflammatory markers (78.9%), and abnormal liver tests (100%). Cholecystitis or pancreatitis was excluded in 92.6% of patients. Based on TG18 criteria (Table 3), most patients presented with inflammatory evidence (90.5%), jaundice (96.8%), and abnormal liver function tests (100%). Imaging findings were also common, with 77.9% showing bile duct dilatation and 92.6% showing other imaging evidence such as

Table 2 Characteristics based on B.I.L.E. criteria

B.I.L.E. Criteria	n=95	%
Biliary imaging abnormalities (duct dilation >6 mm, strictures, choledocholithiasis) and/or interventions within the past 30 days (ERCP, percutaneous biliary drainage, or biliary surgical procedures).		
Yes	77	81.1
No	18	18.9
Abnormal inflammatory test results, such as body temperature >100.4°F (38°C), leukocytosis (WBC >12), leukopenia (WBC <4), or bandemia (>10% bands).		
Yes	75	78.9
No	20	21.1
Abnormal liver tests (total bilirubin above normal, aspartate aminotransferase, alanine aminotransferase, or alkaline phosphatase).		
Yes	95	100
No	0	0
Exclusion of cholecystitis and acute pancreatitis		
Yes	88	92.6
No	7	7.4

Table 3 Characteristics based on TG18 Criteria

TG18 Criteria	n=95	%
A-1 Fever > 38°C		
Yes	9	9.5
No	86	90.5
A-2 Inflammatory evidence - WBC <4,000 or > 10,000 /uL - CRP ≥1 mg/dL		
Yes	86	90.5
No	9	9.5
B-1 Jaundice - T-Bil ≥2 (mg/dL)		
Yes	92	96.8
No	3	3.2
B-2 Abnormal liver function test - AST/ALT, ALP/GGT > 1.5 x STD		
Yes	95	100
No	0	0
C-1 Dilatation of bile system		
Yes	74	77.9
No	21	22.1
C-2 Other imaging evidence (stricture, stone, stenosis, etc)		
Yes	88	92.6
No	7	7.4

strictures or stones. The diagnostic performance of both criteria was assessed (Table 4). TG18 showed a significant association with the diagnosis of acute cholangitis ($p<0.001$), with a strong correlation ($r=0.868$). Similarly, the B.I.L.E. criteria demonstrated a significant association ($p<0.001$) and a good correlation ($r=0.645$).

The ROC curve analysis (Figure 1, Table 5) demonstrated excellent diagnostic performance for both scoring systems. The B.I.L.E. criteria showed a higher AUROC (0.934, 95% CI: 0.874–0.994) compared to TG18 (0.830, 95% CI: 0.738–0.992), indicating superior accuracy in diagnosing acute cholangitis.

Further analysis of diagnostic performance (Table 6) revealed that the B.I.L.E. criteria had higher sensitivity (92.1%) and specificity (94.7%) compared to TG18 (sensitivity 82.4%, specificity 83.6%). The positive and negative predictive values were also superior for the B.I.L.E. criteria (92.1% and 94.7%, respectively).

Discussion

This study found that the B.I.L.E. criteria demonstrated higher sensitivity (92.1%) and specificity (94.7%) compared to the Tokyo Guidelines 2018 (TG18), which showed sensitivity of 82.3% and specificity of 83.6%. These results indicate that the B.I.L.E. criteria may serve as a more accurate diagnostic tool for acute cholangitis in clinical practice.

The superior performance of the B.I.L.E.

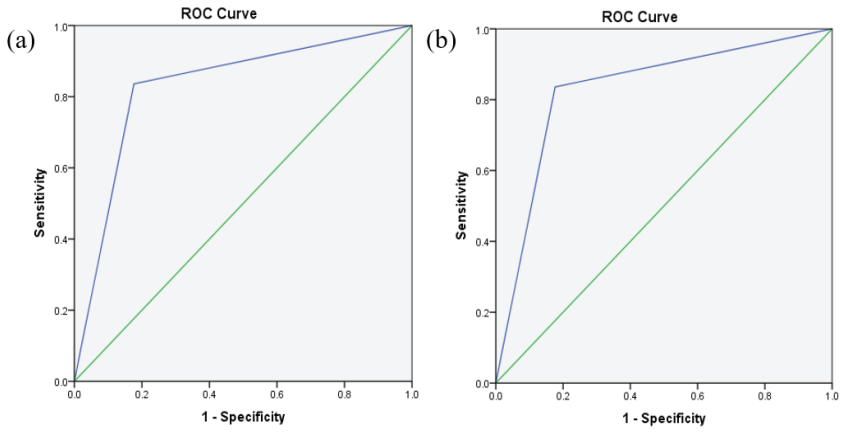

Figure 1 ROC Curve Analysis Of Acute Cholangitis from (a) B.I.L.E. criteria and (b) TG18

Table 4 TG18 and B.I.L.E Criteria in Diagnosing Acute Cholangitis

Diagnosis	B.I.L.E. Criteria		p-value	r
	Not Acute Cholangitis	Acute Cholangitis		
TG 18 criteria				
Suspected	28 (29.5%)	6 (6.3%)	<0.001	0.645
Definite	10 (10.5%)	51 (53.7%)		
B.I.L.E criteria				
Unlikely	35 (36.8%)	3 (3.2%)	<0.001	0.868
High Probability	3 (3.2 %)	54 (56.8%)		

Table 5 Results of the Area Under the ROC Curve of Binary Logistic Regression

Diagnostic Criteria	AUROC	p-value	95%CI	
			Lower bound	*Upper bound*
B.I.L.E.	0.934	0.000	0.874	0.994
TG18	0.830	0.000	0.738	0.992

*AUROC: Area under the Receiver Operating Characteristic (ROC) curve; 95% CI (Confidence Interval); TG18: Tokyo Guidelines 18

Table 6 Sensitivity, specificity, PPV, and NPV

Diagnostic Criteria	Sensitivity	Specificity	PPV	NPV
B.I.L.E. (High probability)	92.10	94.73	92.10	94.73
TG18 (*Definite: 1 item A, 1 item B,* dan *1 item C*)	82.35	83.60	73.68	89.47

*95% CI (Confidence Interval); PPV: Positive Predictive Value; NPV: Negative Predictive Value; TG18: Tokyo Guidelines 18

criteria may be explained by its comprehensive approach, which incorporates biliary imaging abnormalities, inflammatory markers, and liver function tests, while also excluding differential diagnoses such as acute cholecystitis and pancreatitis. This multimodal assessment increases diagnostic precision and helps reduce false positives, thereby lowering the likelihood of unnecessary ERCP procedures. In contrast, TG18 relies more heavily on clinical and laboratory features that are less specific for cholangitis, which may account for its lower diagnostic accuracy.

This study findings are consistent with prior studies. Buxbaum et al.[13] reported that the B.I.L.E. criteria could reduce unnecessary ERCPs and post-ERCP complications. Similarly, Gravito-Soares et al.[11] highlighted variability in the diagnostic accuracy of TG18, while Sperna Weiland et al. reported lower specificity, supporting the need for improved criteria. Hudgi et al.[2] also demonstrated inconsistencies in TG18 performance across different populations. These differences suggest that although TG18 remains widely adopted, its diagnostic reliability may vary depending on patient characteristics and clinical settings.

From a clinical perspective, the use of B.I.L.E. criteria have important implications. More accurate diagnosis allows physicians to promptly identify true cases of acute cholangitis, initiate appropriate treatment, and avoid invasive procedures in patients who do not require them. This is particularly significant given the risks associated with ERCP, including pancreatitis, bleeding, sepsis, and perforation. By minimizing unnecessary interventions, the B.I.L.E. criteria have the potential to improve both patient outcomes and healthcare resource efficiency.

Despite these promising findings, this study has several limitations. First, the research was conducted at a single center with a relatively small sample size, which may limit generalizability. Second, the study focused only on diagnostic accuracy and did not assess the severity grading of cholangitis or patient outcomes, both of which

are essential for comprehensive management. Third, as the B.I.L.E. criteria are still relatively new, further multicenter validation with larger cohorts is needed to strengthen the evidence for their use in daily clinical practice.

In conclusion, this study demonstrates that the B.I.L.E. criteria outperform TG18 in sensitivity and specificity for diagnosing acute cholangitis. While our findings support the potential of B.I.L.E. as a more reliable diagnostic tool, further research is required to confirm its validity across different clinical contexts and to explore its impact on patient outcomes.

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