

## TG13 guidelines for diagnosis and severity grading of acute cholangitis (with videos)

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**Abstract** Since the publication of the Tokyo Guidelines for the management of acute cholangitis and cholecystitis (TG07), diagnostic criteria and severity assessment criteria for acute cholangitis have been presented and extensively used as the primary standard all over the world. However, it has been found that there are crucial limitations in these criteria. The diagnostic criteria of TG07 do not have enough sensitivity and specificity, and its severity assessment criteria are unsuitable for clinical use. A working

team for the revision of TG07 was organized in June, 2010, and these criteria have been updated through clinical implementation and its assessment by means of multi-center analysis. The diagnostic criteria of acute cholangitis have been revised as criteria to establish the diagnosis where cholestasis and inflammation demonstrated by clinical signs or blood test in addition to biliary manifestations demonstrated by imaging are present. The diagnostic criteria of the updated Tokyo Guidelines (TG13) have high sensitivity (87.6 %) and high specificity (77.7 %). TG13 has better diagnostic capacity than TG07. Severity assessment is classified as follows: Grade III: associated with organ failure; Grade II: early biliary drainage should

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be conducted; Grade I: others. As for the severity assessment criteria of TG07, separating Grade II and Grade I at the time of diagnosis was impossible, so they were unsuitable for clinical practice. Therefore, the severity assessment criteria of TG13 have been revised so as not to lose the timing of biliary drainage or treatment for etiology. Based on evidence, five predictive factors for poor prognosis in acute cholangitis—hyperbilirubinemia, high fever, leukocytosis, elderly patient and hypoalbuminemia—have been extracted. Grade II can be diagnosed if two of these five factors are present.

Free full-text articles and a mobile application of TG13 are available via <http://www.jshbps.jp/en/guideline/tg13.html>.

**Keywords** Acute cholangitis · Diagnostic criteria · Severity assessment · Diagnostic imaging guidelines

## Introduction

Patients with acute cholangitis are at risk of developing severe and potentially lethal infections such as sepsis unless appropriate medical care is provided promptly. As a therapeutic procedure for severe cases or to prevent increased severity, decompression of the biliary tract (i.e., biliary tract drainage) is necessary. Recent advances in and diffusion of endoscopic biliary tract drainage along with the administration of antimicrobial agents have contributed to the decrease in the number of deaths due to acute cho-

langitis. However, it remains a life-threatening disease if the timing of biliary tract drainage has been missed. Therefore, immediate and precise judgment of severity is of the utmost importance.

Since Charcot reported a patient with severe acute cholangitis as a case of “hepatic fever” in 1877, Charcot’s triad has been widely used as one of the most important diagnostic criteria [1–5]. However, Charcot’s triad has extremely low sensitivity despite its high specificity. In 2006, we conducted a systematic review of references and sponsored the International Consensus Meeting of Tokyo Guidelines, which resulted in the introduction of new diagnostic criteria and severity assessment criteria in the Tokyo Guidelines for the management of acute cholangitis and cholecystitis (TG07) [6].

Diagnostic criteria and severity assessment criteria should be reconsidered and updated according to their implementation in clinical settings and their assessment. In TG07, there are impractical aspects and discrepancies between the diagnostic criteria and severity assessment criteria of acute cholangitis and the actual clinical settings [7]. Therefore, in order to make the updated Tokyo Guidelines (TG13), the working team carried out a retrospective observational study in multiple tertiary care centers in Japan. This study found limitations in the diagnostic criteria and severity assessment criteria of TG07. The problems which were made clear by the implementation and assessment of TG07 were then corrected, and new updated diagnostic criteria and severity assessment criteria were presented [8]. TG13 provides more accurate and

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reliable diagnostic criteria and severity assessment criteria for acute cholangitis to enable us to perform biliary drainage or other procedures without delay as compared with TG07.

## Diagnostic criteria for acute cholangitis

### Background

#### *Charcot's triad*

#### **Q1. What is the role of Charcot's triad in the diagnostic criteria for acute cholangitis?**

Charcot's triad shows very high specificity. The presence of any one sign of Charcot's triad strongly suggests the presence of acute cholangitis. However, due to the low sensitivity, it is not applicable in using as diagnosis criteria for acute cholangitis (level B).

A diagnosis of acute cholangitis has traditionally been made according to the presence of Charcot's triad, that is, a clinical sign. Charcot's triad has high specificity [9] but low sensitivity. According to several reports, cases presenting all the symptoms of Charcot's triad accounted for 26.4–72 % [2, 3, 8–14].

The previous definition of acute cholangitis was not clear and varied in different references. Therefore, in the analysis of cases of biliary tract diseases collected from

multiple facilities, we defined the “gold standard” for acute cholangitis, that one of the three following conditions was present: (1) Purulent bile was observed. (2) Clinical remission followed bile duct drainage. (3) Remission was achieved by antibacterial therapy alone, in patients in whom the only site of infection was the biliary tree. So it showed low sensitivity (26.4 %) when Charcot's triad was adopted as a diagnostic criterion for acute cholangitis. On the other hand, the specificity was very favorable (95.9 %), but it was positive (11.9 %) for acute cholecystitis. The presence of Charcot's triad supports the diagnosis of acute cholangitis. However, judging from the low sensitivity, Charcot's triad as a diagnostic criterion for acute cholangitis is doubtful [8].

#### *TG07 diagnostic criteria for acute cholangitis*

#### **Q2. How are the diagnostic criteria for acute cholangitis in TG07 appraised?**

Although the sensitivity has been improved compared a with Charcot's triad, TG07 have limitations and their validity is insufficient for using them to make a diagnosis of life-threatening acute cholangitis without a rapid clinical suspicion and appropriate treatment (level B).

As has already been mentioned, there were limitations in Charcot's triad due to its low diagnostic sensitivity; however, there was no alternative diagnostic criterion. Under these circumstances, the International Consensus Meeting was held in Tokyo in 2006 so that an international

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agreement could be reached on diagnostic criteria and severity assessment criteria. At that meeting, diagnostic criteria were presented combining blood tests and diagnostic imaging together with Charcot's triad [15]. Diagnostic criteria were then established in TG07.

However, there has been a report showing that, even in TG07, the sensitivity is low (63.9 %) for making a definite diagnosis of acute cholangitis [7]. We carried out a multi-center analysis and found that the sensitivity was 82.6 % and the specificity was 79.8 % [8]. The diagnostic criteria for acute cholangitis in TG07 were found to be insufficient for making a diagnosis of life-threatening acute cholangitis without a rapid diagnosis and appropriate treatment.

#### *Revision of TG07 diagnostic criteria for acute cholangitis*

Due to the inappropriate combination of such items as clinical context and manifestations, laboratory data and imaging findings, TG07 failed to associate them with three types of morbid conditions of acute cholangitis. We then performed an analysis of each of the items of the diagnostic criteria in TG07, which can be classified as the following three morbidities: (1) fever and/or evidence of inflammatory response such as inflammation, (2) jaundice and abnormal liver function test results such as cholestasis, and (3) a history of biliary diseases, abnormal pain and biliary dilatation, or evidence of etiology such as biliary manifestations. It was considered that those cases meeting these 3 categories can be diagnosed as acute cholangitis. However, a history of biliary diseases and abdominal pain is not specific to biliary manifestations, thus making the differentiation from acute cholecystitis or acute hepatitis impossible. Consequently, abdominal pain and a history of biliary diseases were excluded. To make up for the reduced sensitivity due to the exclusion of abdominal pain, "suspected diagnosis" in which inflammatory findings are dispensable was added. By establishing "suspected diagnosis," early biliary drainage or source control of infection among patients with acute cholangitis can be provided without waiting for the definitive diagnosis [8].

#### TG13 diagnostic criteria for acute cholangitis

The revised diagnostic criteria for acute cholangitis are shown in Table 1. The morbidity of acute cholangitis is associated with the occurrence of cholangiovenous and cholangiolymphatic reflux along with elevated pressure in the biliary ducts and bile infections due to bile duct obstruction induced by stones and tumors. TG13 Diagnostic Criteria of Acute Cholangitis are criteria to establish the diagnosis when cholestasis and inflammation based on

clinical signs or blood test in addition to biliary manifestations based on imaging are present.

### **Q3. How are TG13 diagnostic criteria for acute cholangitis appraised?**

**TG13 diagnostic criteria for acute cholangitis is more accurate and reliable diagnostic capacity than TG07 (recommendation 1, level B).**

A multi-center analysis assessing TG13 found that the sensitivity was 91.8 % and the specificity was 77.7 %. TG13 showed similar specificity to TG07 but showed markedly increased sensitivity and further improvement in diagnostic ability (Table 2). The specificity of Charcot's triad was the highest. The presence of Charcot's triad strongly suggested the presence of acute vasculitis [8].

#### *Systemic inflammation*

Acute cholangitis is accompanied by the findings of systemic inflammation due to fever or an increased inflammatory response such as an increased white blood cell count and high levels of C-reactive protein (CRP). While an increase in the white blood cell count is observed in 82 %, a decrease may be observed in severe vasculitis [5].

#### *Cholestasis*

Many reports show that jaundice is observed in 60–70 % of cases of acute cholangitis (Table 2). A blood test shows an increase in the levels of ALP,  $\gamma$ GTP, LAP and transaminases (AST, ALT). The threshold in liver function tests is particularly important in differentiating from acute cholecystitis when making a diagnosis of acute cholangitis according to the present diagnostic criteria. The thresholds of the tests needed to be established. However, the normal range of liver function tests differs from facility to facility. A fixed threshold is, therefore, not practical. From the results of multi-center analysis, it is appropriate and practical that the threshold is set at 1.5 times the normal upper limit for the liver function test [8].

#### *Imaging findings*

There were no direct imaging findings which showed evidence of bile infection. Recently, it has been reported that acute cholangitis can directly be depicted by computed tomography (CT) of the abdomen with contrast (Figs. 1, 2).

However, in clinical practice, imaging modalities usually support the diagnosis of acute cholangitis by showing indirect findings, which are biliary dilatation or evidence of

**Table 1** TG13 diagnostic criteria for acute cholangitis

A. Systemic inflammation
A-1. Fever and/or shaking chills
A-2. Laboratory data: evidence of inflammatory response
B. Cholestasis
B-1. Jaundice
B-2. Laboratory data: abnormal liver function tests
C. Imaging
C-1. Biliary dilatation
C-2. Evidence of the etiology on imaging (stricture, stone, stent etc.)
Suspected diagnosis: One item in A + one item in either B or C
Definite diagnosis: One item in A, one item in B and one item in C

## Note:

A-2: Abnormal white blood cell counts, increase of serum C-reactive protein levels, and other changes indicating inflammation

B-2: Increased serum ALP,  $\gamma$ GTP (GGT), AST and ALT levels.

Other factors which are helpful in diagnosis of acute cholangitis include abdominal pain [right upper quadrant (RUQ) or upper abdominal] and a history of biliary disease such as gallstones, previous biliary procedures, and placement of a biliary stent.

In acute hepatitis, marked systematic inflammatory response is observed infrequently. Virological and serological tests are required when differential diagnosis is difficult.

## Thresholds

A-1	Fever		BT $>38$ °C
A-2	Evidence of inflammatory response	WBC ( $\times 1000/\mu\text{L}$ )	$<4$ , or $>10$
		CRP (mg/dl)	$\geq 1$
B-1	Jaundice		T-Bil $\geq 2$ (mg/dL)
B-2	Abnormal liver function tests	ALP (IU)	$>1.5 \times \text{STD}$
		$\gamma$ GTP (IU)	$>1.5 \times \text{STD}$
		AST (IU)	$>1.5 \times \text{STD}$
		ALT (IU)	$>1.5 \times \text{STD}$

Cited from the Ref. [8]

STD upper limit of normal value, ALP alkaline phosphatase,  $\gamma$ GTP (GGT)  $\gamma$ -glutamyltransferase, AST aspartate aminotransferase, ALT alanine aminotransferase

**Table 2** Retrospective comparison of various diagnostic criteria of acute cholangitis in a multi-center study in Japan

	Charcot's triad (%)	TG07 (%)	The first draft criteria (with abdominal pain and history of biliary disease) (%)	TG13 (%)
Sensitivity	26.4	82.6	95.1	91.8
Specificity	95.9	79.8	66.3	77.7
[Positive rate]				
Acute cholecystitis	11.9	15.5	38.8	5.9

Cited from Ref. [8]

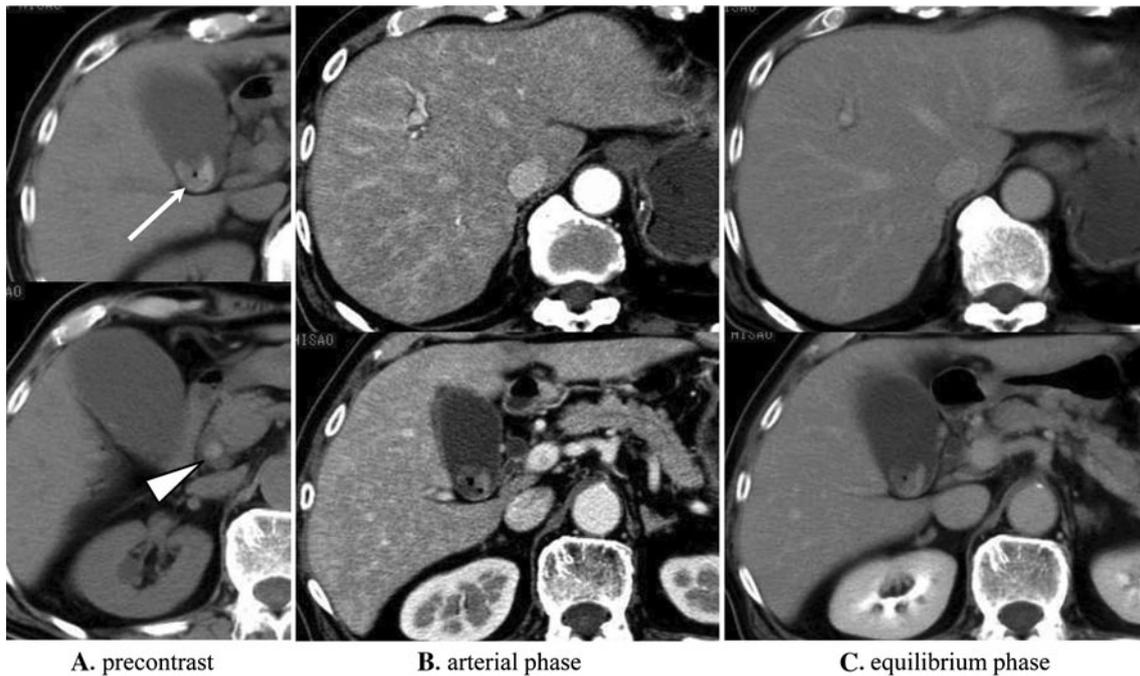
its etiology. A diagnosis of acute cholangitis requires that the presence of stones, tumors or stents inducing bile duct dilatation or cholangitis is confirmed with ultrasonography (US) of the abdomen (Supplementary Figures 1, 2, Supplementary Movie), CT of the abdomen with contrast

(Figs. 1, 2; Supplementary Figure 3) and magnetic resonance cholangiopancreatography (MRCP) (Supplementary Figure 6).

#### Q4. Is it possible to diagnose acute cholangitis by computed tomography (CT) of the abdomen?

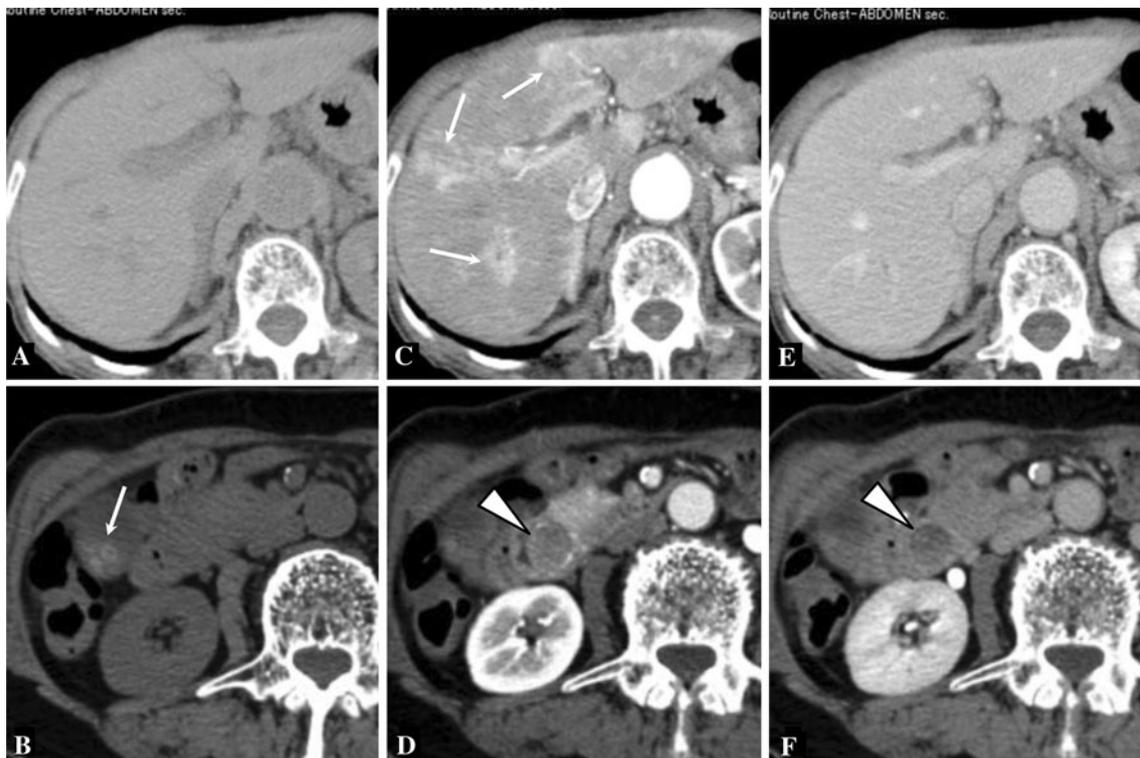
We suggested that dynamic CT of the abdomen with contrast enables making the diagnosis of acute cholangitis (recommendation 2, level D).

Radiological examinations such as ultrasonography, CT and magnetic resonance imaging (MRI) are carried out for evaluation of the site and cause of biliary obstruction and degree of biliary dilatation. However, CT of the abdomen with contrast has limitations in the diagnosis and evaluation of acute cholangitis [16]. Because helical CT is clinically available, the whole of the upper abdominal organs



**Fig. 1** CT demonstrating acute cholangitis with gallstone and common bile duct stone (74-year-old female). Precontrast CT (a) shows gallstone (arrow) and common bile duct stone (arrowhead). The arterial phase of contrast-enhanced dynamic CT (b) shows

diffuse inhomogeneous enhancement of the liver. In the equilibrium phase of dynamic CT (c), the inhomogeneous enhancement disappears



**Fig. 2** CT demonstrating acute cholangitis with gallstone and papillary tumor of the duodenum (77-year-old female). a, b Precontrast CT, c, d arterial phase of dynamic CT, e, f equilibrium phase. Precontrast CT shows gallstones (b arrow). Arterial phase of dynamic

CT shows enhanced papillary tumor of the duodenum (d arrowhead). The liver parenchyma shows inhomogeneous enhancement surrounding the bile ducts, indicating acute cholangitis. In the equilibrium phase, inhomogeneous enhancement disappears

can be assessed by contrast-enhanced dynamic CT. Pre- and postcontrast CT can depict biliary stones, pneumobilia, bile duct dilatation, bile duct wall thickening, and bile duct stenosis or occlusion. However, such CT findings do not necessarily suggest the presence of acute cholangitis.

Hepatic parenchymal changes seen at imaging in acute cholangitis are likely to be related to the extension of the inflammatory process into the periportal tissues [17–20]. In acute cholangitis, the inflammatory process of the peripheral bile duct spreading as far as the periportal areas (Glisson's sheath) causes a decreased portal blood flow and an increased arterial blood flow. On the arterial phase of dynamic CT, inhomogeneous hepatic parenchymal enhancement (nodular, patchy, wedge-shaped or geographic) is frequently seen in patients with acute cholangitis [16, 17] (Figs. 1, 2). This inhomogeneous hepatic enhancement of contrast-enhanced dynamic CT appears in the arterial phase only, and disappears in the portal and equilibrium phases. Follow-up dynamic CT performed after treatment for acute cholangitis showed decreased or no inhomogeneous enhancement, according to the improvement of biliary inflammation (Supplementary Figure 4).

In conclusion, contrast-enhanced dynamic CT is recommended for making a prompt diagnosis of clinically suspected acute cholangitis.

#### **Q5. Can CT make a diagnosis of the etiology and complications of acute cholangitis?**

**CT is suggested as the most effective imaging method for the diagnosis of etiology and complication of acute cholangitis (recommendation 2, level D).**

CT scan is a useful imaging modality for exploring the etiology of acute cholangitis such as biliary stones (cholelithiasis, choledocholithiasis, hepatolithiasis) and pancreaticobiliary malignancies (extrahepatic bile duct carcinoma, gallbladder carcinoma, pancreatic head carcinoma). Because non-calcified biliary stones cannot be detected by CT, ultrasonography and/or MRI (MRCP) is also recommended (Supplementary Figure 5).

Hepatic abscesses sometimes occur in patients with acute cholangitis. It is important to differentiate abscesses from malignant hepatic tumors such as liver metastasis or intrahepatic cholangiocarcinoma. Characteristic imaging findings of hepatic abscesses have also been reported in dynamic CT as well as acute cholangitis [21–24] (Supplementary Figure 6). Hepatic abscess shows a double target sign with a transient segmental enhancement in the arterial phase of dynamic CT. The segmental enhancement

disappears in the equilibrium phase. This transient segmental enhancement in dynamic CT reflects a decrease in segmental portal blood flow and an increase in compensatory hepatic arterial blood flow due to periportal inflammation within the Glisson's sheath adjacent to the hepatic abscess [24, 25].

#### **Q6. What are the indication and significance of MRI (MRCP) for acute cholangitis?**

**MRI (MRCP) is suggested for the etiologic diagnosis of acute cholangitis (recommendation 2, level D).**

Magnetic resonance cholangiopancreatography (MRCP) has a high sensitivity for detecting biliary calculi and malignant biliary obstruction [25–27] (Supplementary Figure 7). Inhomogeneous enhancement in dynamic MRI as well as dynamic CT is also able to depict acute cholangitis [28].

#### *Other factors which are helpful in diagnosis of acute cholangitis*

A past history of gallbladder diseases is found in many reports of acute cholangitis [2, 3, 10–14], and it is referred to as 'the past history of surgery for the diseases of the biliary system', supposedly cholecystectomy for gallbladder stones in particular [3, 10–13].

The importance of 'the past history of biliary diseases' in a diagnosis of acute cholangitis was recognized at the International Consensus Meeting in 2006. The presence of bile stones and the placement of stents in the biliary tract were also considered to be contributing factors in making a diagnosis of acute cholangitis.

Abdominal pain is reported to be observed in 80 % or more cases (Table 3). However, it is not a symptom specific to cholangitis. It was excluded from the diagnostic criteria for acute cholangitis for the reason that its presence reduced the specificity and complicated the differentiation from acute cholecystitis [8].

#### **Severity assessment criteria for acute cholangitis**

##### **Background**

Patients with acute cholangitis may present with any severity ranging from self-limiting to severe and/or potentially life-threatening diseases. Most cases respond to initial medical treatment consisting of general supportive therapy and intravenous antimicrobial therapy.

**Table 3** Incidence of clinical manifestations of acute cholangitis

	Disease	N	Charcot's triad (%)	Fever (%)	Jaundice (%)	Abdominal pain (%)	Reynolds' pentad (%)	Shock (%)	Disturbed consciousness (%)	History of biliary diseases
Welch [2]	ASC	5	50	80	60			0	20	100
	AOSC	15	50	88	67			33	27	46.7
Boey [3]	AC	99	69.7	93.9	78.8	87.9	5.1	16.2	16.2	75
	SC	14					7	57	28	
	NonSC	72					4	8	12	
Csendes [9]	ASC	512	22	38.7	65.4	92.2		7	7.2	
Thompson [10]	AC	66	About 60	100	66	59		7	9	66
Gigot [11]	AC	412	72				3.5	7.8	7	61
O'Connor [12]	AC	65	60				7.7	32	14	21.5
	SC	19	53				5	47	11	
	NonSC	46	63				9	26	15	
Lai [13]	Severe AC	86	56	66	93	90		64		27.9
Hauptert [14]	ASC	13	15.4	100	61.5	100	7.7	23.1	7.7	53.8

AC acute cholangitis, SC suppurative cholangitis, AOSC acute obstructive suppurative cholangitis

It has been reported in the United States that approximately 70 % of patients with acute cholangitis are able to achieve improvement with medical therapy alone [29]. Some cases do not respond to medical treatment and the clinical manifestations and laboratory data do not improve. Such cases may progress to sepsis with or without organ dysfunction and require appropriate management that includes intensive care, organ-supportive care, and urgent biliary drainage, in addition to medical treatment. There is also a report showing approximately a 10 % mortality rate due to acute cholangitis despite the occurrence of responses to antimicrobial therapy and biliary drainage [30, 31].

#### TG07 severity assessment criteria for acute cholangitis

TG07 established the world's first severity assessment criteria for acute cholangitis at the International Consensus Meeting in Tokyo in 2006 [6] and classified those conditions with organ dysfunction as 'severe' (Grade III), those showing no responses to the initial treatment as 'moderate' (Grade II), and those responding to the initial treatment as 'mild' (Grade I).

However, the use of TG07 severity assessment criteria in actual situations has shown that it is impossible to distinguish moderate cases (Grade II) and mild cases (Grade I) as soon as the initial diagnosis has been made. In TG07, Grades II and I were only assessed after observation of the treatment courses. In this treatment strategy, urgent biliary drainage can be indicated for cases assessed as severe, but

provision of early biliary drainage is impossible. Acute cholangitis can progress rapidly to sepsis and disseminated intravascular coagulation (DIC) and the "observation strategy" in TG07 may induce increased severity during the initial treatment. In Japan, many cases (46.8 %, 258 of 551 cases) of Grades II or I underwent urgent biliary drainage in the same manner as Grade III. In these cases, differentiation between Grade II and Grade I was impossible, because the definition of Grade II in TG07 was ambiguous [8].

#### Revision of TG07 severity assessment criteria for acute cholangitis

Given these inconveniences of TG07 in clinical practice, revision was made to improve severity assessment strategies upon diagnosis to allow provision of immediate source control of infection among patients with acute cholangitis.

To begin with, we examined the items reported as predictive factors of poor prognosis among patients with acute cholangitis and those who required urgent biliary drainage. Furthermore, factors endoscopic gastroenterologists value in determining the timing of biliary drainage were integrated, except for the factors that define Grade III cases (severe cases). Factors which were inappropriate for use as items of severity assessment were excluded. Consequently, five factors—hypoalbuminemia, elderly patients, high fever, leukocytosis and hyperbilirubinemia—were extracted [8, 32]. Cases with two of these five factors present were classified as Grade II (moderate) [8].

**Table 4** TG13 severity assessment criteria for acute cholangitis

## Grade III (Severe) acute cholangitis

“Grade III” acute cholangitis is defined as acute cholangitis that is associated with the onset of dysfunction in at least one of any of the following organs/systems:

- |                               |  |
|-------------------------------|--|
| 1. Cardiovascular dysfunction | Hypotension requiring dopamine $\geq 5$ $\mu\text{g}/\text{kg}$ per min, or any dose of norepinephrine |
| 2. Neurological dysfunction   | Disturbance of consciousness   |
| 3. Respiratory dysfunction    | $\text{PaO}_2/\text{FiO}_2$ ratio $< 300$  |
| 4. Renal dysfunction          | Oliguria, serum creatinine $> 2.0$ mg/dl   |
| 5. Hepatic dysfunction        | PT-INR $> 1.5$   |
| 6. Hematological dysfunction  | Platelet count $< 100,000/\text{mm}^3$   |

## Grade II (moderate) acute cholangitis

“Grade II” acute cholangitis is associated with any two of the following conditions:

1. Abnormal WBC count ( $> 12,000/\text{mm}^3$ ,  $< 4,000/\text{mm}^3$ )
2. High fever ( $\geq 39$  °C)
3. Age ( $\geq 75$  years old)
4. Hyperbilirubinemia (total bilirubin  $\geq 5$  mg/dL)
5. Hypoalbuminemia ( $< \text{STD} \times 0.7$ )

## Grade I (mild) acute cholangitis

“Grade I” acute cholangitis does not meet the criteria of “Grade III (severe)” or “Grade II (moderate)” acute cholangitis at initial diagnosis.

## Notes

Early diagnosis, early biliary drainage and/or treatment for etiology, and antimicrobial administration are fundamental treatments for acute cholangitis classified not only as Grade III (severe) and Grade II (moderate) but also Grade I (mild).

Therefore, it is recommended that patients with acute cholangitis who do not respond to the initial medical treatment (general supportive care and antimicrobial therapy) undergo early biliary drainage or treatment for etiology (see flowchart).

Cited from Ref. [8]

*STD* lower limit of normal value

## TG13 severity assessment criteria for acute cholangitis

The revised assessment criteria for acute cholangitis are shown in Table 4.

The severity of acute cholangitis is classified as follows;

Grade III (severe): presence of organ dysfunction.

Grade II (moderate): risk of increased severity without early biliary drainage.

Grade I (mild).

The severity assessment criteria are very important for determining the treatment strategy for acute cholangitis, especially for Grade II cases which may progress to Grade III without immediate intervention. Treatment of acute cholangitis requires “treatment for causes” for cases with any severity, along with the administration of antimicrobial agents and biliary drainage.

**Q7. What morbid conditions are referred to as ‘Grade III (severe)’ in assessing severity for acute cholangitis?**

‘Severe’ is referred to as a condition that gives rise to organ dysfunction due to acute cholangitis requiring intensive care such as respiratory and circulatory support.

Organ dysfunction is the most common predictor of poor outcome. On the other hand, based on the pathophysiology, “severe” acute cholangitis can also be defined as that which accompanies organ dysfunction caused by sepsis. Thus, “the presence of organ dysfunction” is an important factor in the definition of Grade III (severe) acute cholangitis [6].

**Q8. What morbid conditions are referred to as ‘moderate’ in assessing severity for acute cholangitis?**

‘Grade II (moderate)’ is referred to as a condition suggesting cholangitis requiring emergent or early biliary drainage without presence of organ dysfunction, but with risks of progression to Grade III.

**Q9. How are TG13 Severity Assessment Criteria for acute cholangitis appraised?**

TG13 Severity Assessment Criteria for Acute Cholangitis is more suitable and practical for clinical use than TG07, because of enabling us to identify Grade II which requires early biliary drainage at the time of initial diagnosis (recommendation 1, level B).

According to TG13 severity assessment criteria, the number of cases for which biliary drainage was carried out within 48 h included 50 Grade III cases (69.4 %), 129 Grade II cases (59.7 %), and 181 Grade I cases (54.0 %). However, many of the Grade I cases that had undergone biliary drainage within 48 h were accounted for as the treatment of etiology such as bile stones. Grade I cases that had undergone biliary drainage as an urgent treatment were very few in number [8].

#### Q10. Are the acute cholangitis cases that meet Charcot's triad considered as severe cases?

The presence or absence of Charcot's triad does not reflect severity. So, cases that meet Charcot's triad are not necessarily assessed as severe (level B).

In the multi-center analysis, of the 110 cases of acute cholangitis that showed Charcot's triad, only 13 cases (11.8 %) were classified as Grade III. Compared with the cases that did not show Charcot's triad, there were no differences in terms of severity. Furthermore, many (approximately 80 %) of the Grade III cases in TG13 failed to satisfy Charcot's triad [8]. The presence or absence of conformity with Charcot's triad was not associated with severity. Cases that meet Charcot's criteria are not necessarily classified as severe cases.

**Conflict of interest** None.

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