

TG13 diagnostic criteria and severity grading of acute cholecystitis (with videos)

Masamichi Yokoe · Tadahiro Takada · Steven M. Strasberg · Joseph S. Solomkin · Toshihiko Mayumi · Harumi Gomi · Henry A. Pitt · O. James Garden · Seiki Kiriyaama · Jiro Hata · Toshifumi Gabata · Masahiro Yoshida · Fumihiko Miura · Kohji Okamoto · Toshio Tsuyuguchi · Takao Itoi · Yuichi Yamashita · Christos Dervenis · Angus C. W. Chan · Wan-Yee Lau · Avinash N. Supe · Giulio Belli · Serafin C. Hilvano · Kui-Hin Liao · Myung-Hwan Kim · Sun-Whe Kim · Chen-Guo Ker

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Abstract Since its publication in 2007, the Tokyo Guidelines for the management of acute cholangitis and cholecystitis (TG07) have been widely adopted. The validation of TG07 conducted in terms of clinical practice has shown that the diagnostic criteria for acute cholecystitis are highly reliable but that the definition of definite diagnosis is ambiguous. Discussion by the Tokyo Guidelines Revision Committee concluded that acute cholecystitis should be suspected when Murphy's sign, local inflammatory findings in the gallbladder such as right upper quadrant

abdominal pain and tenderness, and fever and systemic inflammatory reaction findings detected by blood tests are present but that definite diagnosis of acute cholecystitis can be made only on the basis of the imaging of ultrasonography, computed tomography or scintigraphy (HIDA scan). These proposed diagnostic criteria provided better specificity and accuracy rates than the TG07 diagnostic criteria. As for the severity assessment criteria in TG07, there is evidence that TG07 resulted in clarification of the concept of severe acute cholecystitis. Furthermore, there is evidence that severity assessment in TG07 has led to a reduction in the mean duration of hospital stay. As for the factors used to establish a moderate grade of acute cholecystitis, such as leukocytosis, ALP, old age, diabetes, being

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M. Yokoe (✉)
General Internal Medicine, Nagoya Daini Red Cross Hospital,
2-9 Myoken-cho, Showa-ku, Nagoya, Aichi 466-8650, Japan
e-mail: yokoe@nagoya2.jrc.or.jp

T. Takada · F. Miura
Department of Surgery, Teikyo University School of Medicine,
Tokyo, Japan

S. M. Strasberg
Section of Hepatobiliary and Pancreatic Surgery,
Washington University in Saint Louis School of Medicine,
Saint Louis, MO, USA

J. S. Solomkin
Department of Surgery, University of Cincinnati College
of Medicine, Cincinnati, OH, USA

T. Mayumi
Department of Emergency and Critical Care Medicine,
Ichinomiya Municipal Hospital, Ichinomiya, Japan

H. Gomi
Center for Clinical Infectious Diseases, Jichi Medical University,
Tochigi, Japan

H. A. Pitt
Department of Surgery, Indiana University School of Medicine,
Indianapolis, IN, USA

O. J. Garden
Clinical Surgery, The University of Edinburgh, Edinburgh, UK

S. Kiriyaama
Department of Gastroenterology, Ogaki Municipal Hospital,
Ogaki, Japan

J. Hata
Department of Endoscopy and Ultrasound, Kawasaki Medical
School, Okayama, Japan

T. Gabata
Department of Radiology, Kanazawa University Graduate
School of Medical Science, Kanazawa, Japan

M. Yoshida
Clinical Research Center Kaken Hospital, International
University of Health and Welfare, Ichikawa, Japan

male, and delay in admission, no new strong evidence has been detected indicating that a change in the criteria used in TG07 is needed. Therefore, it was judged that the severity assessment criteria of TG07 could be applied in the updated Tokyo Guidelines (TG13) with minor changes. TG13 presents new standards for the diagnosis, severity grading and management of acute cholecystitis.

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

Keywords Acute cholecystitis · Diagnostic criteria · Severity grading · Diagnostic imaging · Guidelines

Introduction

Acute cholecystitis is a disease frequently encountered in daily practice presenting with right hypochondrial pain as the main symptom [1–4]. However, there were no diagnostic criteria and severity assessment criteria for this commonplace disease before the publication in 2007 of the Tokyo Guidelines for the management of acute cholangitis and cholecystitis (TG07) in the *Journal of Hepato-Biliary-Pancreatic Surgery* (vol. 14.1:1–121, 2007). There is a treatise in TG07 released with the expectation that it will present international guidelines for improvement in the diagnosis and treatment of acute cholecystitis [5].

The diagnostic criteria in TG07 were set at high sensitivity to provide medical care suitable for a larger number of cases and the sensitivity has been reported as 84.9 % on

the basis of the test results for TG07 diagnostic criteria [6]. TG07 guidelines have already been recognized as the diagnostic criteria to be recommended in today's medical care for acute cholecystitis [1]; however, guidelines should achieve further evolution. In view of the current situation where diagnostic imaging such as ultrasonography (US), CT and scintigraphy (HIDA scan) are frequently used for the definite diagnosis of acute cholecystitis, integration of such diagnostic modalities in guidelines is the main theme in the present revision.

Acute cholecystitis sometimes requires emergency treatment for morbidities such as gangrenous cholecystitis, emphysematous cholecystitis and gallbladder torsion. An indication that it may require high-level skills is given by its other name, “difficult gallbladder” [7, 8]. In making a diagnosis of acalculous cholecystitis, challenges may be encountered. There may be cases with a poor prognosis [9, 10]. The severity assessment criteria in TG07 defined severe acute cholecystitis as acute cholecystitis accompanying organ dysfunction directly related to vital prognosis. Actually, the overall mortality rate of acute cholecystitis is approximately 0.6 % [11, 12], and that of severe cases was reported in TG07 as 6.0 % [13]. Acute cholecystitis is essentially not a disease with a high mortality rate. However, it was thought that guidelines should make it clear that appropriate management with appropriate use of severity assessment criteria does lead to improved vital prognosis.

K. Okamoto
Department of Surgery, Kitakyushu Municipal Yahata Hospital,
Kitakyushu, Japan

T. Tsuyuguchi
Department of Medicine and Clinical Oncology, Graduate
School of Medicine Chiba University, Chiba, Japan

T. Itoi
Department of Gastroenterology and Hepatology, Tokyo
Medical University, Tokyo, Japan

Y. Yamashita
Department of Gastroenterological Surgery, Fukuoka University
School of Medicine, Fukuoka, Japan

C. Dervenis
First Department of Surgery, Agia Olga Hospital, Athens,
Greece

A. C. W. Chan
Department of Surgery, Surgery Centre, Hong Kong Sanatorium
and Hospital, Hong Kong, Hong Kong

W.-Y. Lau
Faculty of Medicine, The Chinese University of Hong Kong,
Hong Kong, Hong Kong

A. N. Supe
Department of Surgical Gastroenterology, Seth G S Medical
College and K E M Hospital, Mumbai, India

G. Belli
General and HPB Surgery, Loreto Nuovo Hospital, Naples, Italy

S. C. Hilvano
Department of Surgery, College of Medicine-Philippine General
Hospital, University of the Philippines, Manila, Philippines

K.-H. Liao
Hepatobiliary and Pancreatic Surgery, Nexus Surgical
Associates, Mount Elizabeth Hospital, Singapore, Singapore

M.-H. Kim
Department of Internal Medicine, Asan Medical Center,
University of Ulsan, Seoul, Korea

S.-W. Kim
Department of Surgery, Seoul National University College of
Medicine, Seoul, Korea

C.-G. Ker
Yuan's General Hospital, Kaohsiung, Taiwan

Six years have passed since the publication of TG07 and the Tokyo Guidelines Revision Committee has been charged with examining the results of the validation that has been conducted so far, involving problems such as inconvenience of their use in actual clinical settings [6, 13–15]. Considering the progress of diagnostic technology and detection of new evidence, diagnostic criteria and severity grading revised as the updated Tokyo Guidelines (TG13) are presented in accordance with actual clinical settings [16].

Diagnostic criteria for acute cholecystitis; TG13

Background

Murphy's sign

Q1. How large is the diagnostic capacity of Murphy's sign for acute cholecystitis?

Murphy's sign shows high specificity, however the sensitivity has been reported low. It is not applicable in making a diagnosis of acute cholecystitis due to the low sensitivity (level D).

Murphy's sign refers to where the patient stops breathing due to pain when an examiner touches the inflammatory gallbladder of the patient. In 1903, Murphy [17] described the condition as a sign of cholelithiasis. Murphy's sign has also been widely known as a diagnostic factor of acute cholecystitis. Substantial numbers of clinicians throughout the world providing treatment for acute cholecystitis refer to Murphy's sign. It has been reported in previous studies to have a sensitivity of 50–65 % and a high specificity of 79 % [18] or 96 % [2] for the diagnosis of acute cholecystitis although the sensitivity was once reported to be as low as 20.5 %, while the specificity was 87.5 % [6]. It has a weak point in that an accurate diagnosis of cholecystitis can be made when Murphy's sign is present, while its absence does not necessarily mean the absence of cholecystitis.

TG07 diagnostic criteria for acute cholecystitis

Q2. How are the diagnostic criteria for acute cholecystitis in TG07 appraised?

Although the sensitivity had been improved compared with Murphy's sign, TG07 diagnostic criteria have limitations and their validity is insufficient for using them to make a definite diagnosis (level D).

At an international consensus meeting held in Tokyo in 2007, the world's first diagnostic criteria were presented in the Tokyo Guidelines for the management of acute cholangitis and cholecystitis; these are international clinical practice guidelines. According to a review referring to these diagnostic criteria, a definite diagnosis of acute cholecystitis can be made when a local sign or symptom and a systemic sign are present, and test imaging provides confirmation [1]. There is a report of cases for which favorable sensitivity (84.9 %) and specificity (50.0 %) have been achieved when using TG07 diagnostic criteria in clinical practice [6]. Multicenter analysis by the Tokyo Guidelines Revision Committee showed that the sensitivity was 92.1 % and the specificity was 93.3 % in TG07 [16].

Revision of TG07 diagnostic criteria for acute cholecystitis

The most important problem in TG07 was that the criteria for definite diagnosis were ambiguous and difficult to use. In TG07, there were two categories determining the definite diagnosis of acute cholecystitis. "Definite diagnosis 1": To obtain a definite diagnosis one item in A and one item in B had to be positive. "Definite diagnosis 2": Imaging findings (criterion C) confirmed the diagnosis when acute cholecystitis was suspected clinically.

The Tokyo Guidelines Revision Committee concluded that the term "definite diagnosis" could not be supported in current practice without positive diagnostic imaging studies. We have now changed the expressions: "suspected" diagnosis is achieved when one item from section A and one item from section B are present. "Definite" diagnosis is achieved when imaging findings characteristic of acute cholecystitis (item C) are also present (one item in A + one item in B + C) [16].

TG13 diagnostic criteria for acute cholecystitis

The revised diagnostic criteria for acute cholecystitis are shown in Table 1.

A diagnosis of acute cholecystitis is made as follows according to diagnostic criteria. When acute cholecystitis is suspected from clinical signs and results of blood tests, a definite diagnosis is made after it has been confirmed by diagnostic imaging.

Q3. How are the diagnostic criteria for acute cholecystitis in TG13 appraised?

TG13 diagnostic criteria of acute cholecystitis have a high sensitivity and a high specificity (recommendation 1, level B).

Table 1 TG13 diagnostic criteria for acute cholecystitis

A. Local signs of inflammation etc.
(1) Murphy's sign, (2) RUQ mass/pain/tenderness
B. Systemic signs of inflammation etc.
(1) Fever, (2) elevated CRP, (3) elevated WBC count
C. Imaging findings
Imaging findings characteristic of acute cholecystitis
Suspected diagnosis: One item in A + one item in B
Definite diagnosis: One item in A + one item in B + C
Acute hepatitis, other acute abdominal diseases, and chronic cholecystitis should be excluded
RUQ right upper abdominal quadrant, CRP C-reactive protein, WBC white blood cell

An assessment by multicenter analysis of TG13 diagnostic criteria shows that sensitivity (91.2 %) and specificity (96.9 %) are favorable and that diagnostic capacity is almost the same as that in TG07 [16]. It is pointed out that the diagnostic criteria for acute cholecystitis in TG07 have limitations in that patients with few systemic symptoms tends to be underdiagnosed [1]. There is also a report showing that neither fever nor an elevated white cell count were observed in 16 % of cases with gangrenous cholecystitis or in 28 % of cases with non-gangrenous cholecystitis [8]. It is important that the diagnosis is confirmed repeatedly for cases with suspected cholecystitis.

Clinical context and manifestations

Q4. What is the most important physical manifestation for making a diagnosis of acute cholecystitis?

The most typical clinical sign of acute cholecystitis is abdominal pain.

The main symptom of uncomplicated cholelithiasis is biliary colic caused by the obstruction of the gall-bladder neck by stones [1]. The proportion of patients with right hypochondrial pain and epigastric pain combined is 72–93 %. This is followed in frequency by nausea and vomiting. Note that the proportion of patients with fever is not high; that of fever exceeding 38 (°C) is low (about 30 %). Muscular defense is observed in about half of cases; palpable tumors are rare in the right hypochondrial region. Rebound tenderness and stiffness are also rare (Tables 2, 3) [2–4, 19–23].

Laboratory data

What is the most important blood test for making a diagnosis of acute cholecystitis?

There are no specific blood tests for making a diagnosis of acute cholecystitis. So, the diagnosis can be made if the following findings are present: general inflammatory findings (abnormal white blood cell count, elevated CRP level), an increase in blood cell count of more than 10000 mm³/dl, an increase in CRP level of more than 3 mg/dl, and a mild increase of serum enzymes in the hepato-biliary-pancreatic system and bilirubin.

The bilirubin level may rise to 4 mg/dl (68 μmol/dl) in the absence of complications [1]. When ultrasonography shows findings that suggest acute cholecystitis and a CRP level exceeding 3 mg/dl, a diagnosis of acute cholecystitis can be made with 97 % sensitivity, 76 % specificity, and 95 % positive predictive value [24].

Table 2 Incidence of clinical symptoms of acute cholecystitis

	<i>n</i>	RUQ pain (%)	Epigastralgia (%)	Nausea (%)	Emesis (%)	Fever (%)	Rebound (%)	Guarding (%)	Rigidity (%)	Mass (%)	Murphy's sign (%)
Eskelinen [2]	124	56	25	31	60	62 (≥37.1 °C)	48	30	66	16	62
Brewer [19]	26				77	30 (≥38 °C)	35	58	3.9		
Schofield [20]	64				83	31 (>37.5 °C)				14	
Staniland [21]	100	38	34	About 80	About 70		About 30	About 45	About 10	About 25	
Halasz [3]	191	93								23	
Johnson [4]	37	70	11	73	62	24					62
Singer [22]	40					10 (>38.0 °C)					65
Adedeji [23]	62										48

RUQ right upper abdominal quadrant

Imaging findings

Ultrasonography (US)

Q5. Which type of diagnostic imaging method should be used, first of all, for making a diagnosis of acute cholecystitis?

Ultrasonography should be performed at the initial consultation for all cases for which acute cholecystitis is suspected (recommendation 1, level A).

Ultrasonography is the test that should be performed first of all for every case of suspected acute cholecystitis. Even emergency physicians who are not specialists in ultrasonography are able to make a satisfactory diagnosis [25, 26].

In view of its convenience and lack of invasiveness, ultrasonography should be considered the first option among morphological tests for this morbidity.

Q6. How large is the diagnostic capacity of ultrasonography for acute cholecystitis?

Ultrasonography shows 50–88 % sensitivity and 80–88 % specificity.

A report by Chatziioannou et al. [27] discussing 107 cases of acute cholecystitis in terms of the diagnostic capacity of ultrasonography has found that sensitivity is 50 %, specificity 88 %, PPV 64 %, NPV 80 %, and accuracy 77 %.

On the basis of a meta-analysis of five treatises involving a total of 532 cases, Shea et al. show that the diagnostic capability of ultrasonography for acute cholecystitis: sensitivity 88 % (95 % CI 0.74–1.00) and specificity 80 % (95 % CI 0.62–0.98) [28]. The diagnostic capacity of ultrasonography for acute cholecystitis is generally thought to be good.

Q7. What are the ultrasonographic imaging findings characteristic of acute cholecystitis?

They are mainly enlarged gallbladder, thickening of the gallbladder wall, gallbladder stones, and debris echo.

A diagnosis of acute calculous cholecystitis can be made radiologically when the following findings are present at the same time: thickening of the gallbladder wall (5 mm or greater), pericholecystic fluid, or direct tenderness when the probe is pushed against the gallbladder (ultrasonographic Murphy's sign) [1]. Other ultrasonographic findings may include gallbladder enlargement, gallbladder stones, debris echo and gas imaging (Fig. 1).

However, due to differences among reports in the frequency of the occurrence of individual findings, sensitivity, and specificity, diagnosis should be made after a comprehensive judgment has been made of individual findings [29, 30] (Supplement Table 1).

There are many diagnostic modalities enabling depiction of stones. However, there is a report showing that bile stones could be depicted by ultrasonography in only 13 % of cases (1 of 7 cases). Therefore, the use of other

Table 3 Diagnostic capability of clinical symptoms for acute cholecystitis

	No. of studies	No. of patients	Summary LR (95 % CI)		Sensitivity (95 % CI)	Specificity (95 % CI)
			Positive	Negative		
Anorexia	2	1135	1.1–1.7	0.5–0.9	0.65 (0.57–0.73)	0.50 (0.49–0.51)
Emesis	4	1338	1.5 (1.1–2.1)	0.6 (0.3–0.9)	0.71 (0.65–0.76)	0.53 (0.52–0.55)
Fever	8	1292	1.5 (1.0–2.3)	0.9 (0.8–1.0)	0.35 (0.31–0.38)	0.80 (0.78–0.82)
Guarding	2	1170	1.1–2.8	0.5–1.0	0.45 (0.37–0.54)	0.70 (0.69–0.71)
Murphy's sign	3	565	2.8 (0.8–8.6)	0.5 (0.2–1.0)	0.65 (0.58–0.71)	0.87 (0.85–0.89)
Nausea	2	669	1.0–1.2	0.6–1.0	0.77 (0.69–0.83)	0.36 (0.34–0.38)
Rebound	4	1381	1.0 (0.6–1.7)	1.0 (0.8–1.4)	0.30 (0.23–0.37)	0.68 (0.67–0.69)
Rectal tenderness	2	1170	0.3–0.7	1.0–1.3	0.08 (0.04–0.14)	0.82 (0.81–0.83)
Rigidity	2	1140	0.50–2.32	1.0–1.2	0.11 (0.06–0.18)	0.87 (0.86–0.87)
RUQ mass	4	408	0.8 (0.5–1.2)	1.0 (0.9–1.1)	0.21 (0.18–0.23)	0.80 (0.75–0.85)
RUQ pain	5	949	1.5 (0.9–2.5)	0.7 (0.3–1.6)	0.81 (0.78–0.85)	0.67 (0.65–0.69)
RUQ tenderness	4	1001	1.6 (1.0–2.5)	0.4 (0.2–1.1)	0.77 (0.73–0.81)	0.54 (0.52–0.56)

Cited from Ref. [18]

RUQ right upper abdominal quadrant, LR likelihood ratio, CI confidence interval

techniques, such as MR cholangiography (MRCP), should be considered depending on conditions [31].

According to a report by Cohan et al. [32] who examined 51 cases that had developed thickening of the gallbladder wall, including 13 cases of acute cholecystitis, a so-called sonolucent layer (hypoechoic layer), referred to as a low-echo zone, within the gallbladder wall showed 8 % sensitivity (95 % CI 0–22.1) and 71.0 % specificity (95 % CI 56.6–85.5). Therefore, it cannot be considered a

good diagnostic measure for acute cholecystitis. The presence of a low-echoic area with an irregular multiple structure showing 62 % sensitivity (95 % CI 35.1–88.0) and 100 % specificity (95 % CI 100–100) has a higher diagnostic value [32] (Supplement Fig. 1; Supplement Movie 1).

Q8. What findings are to be noted when ultrasonography is conducted for cases for which acute cholecystitis is suspected?

Ultrasonographic Murphy's sign shows high specificity and it is useful for making a diagnosis.

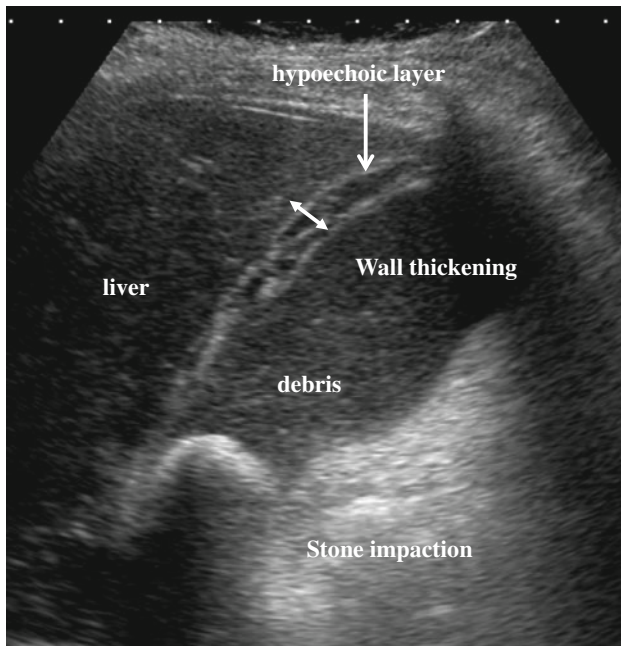
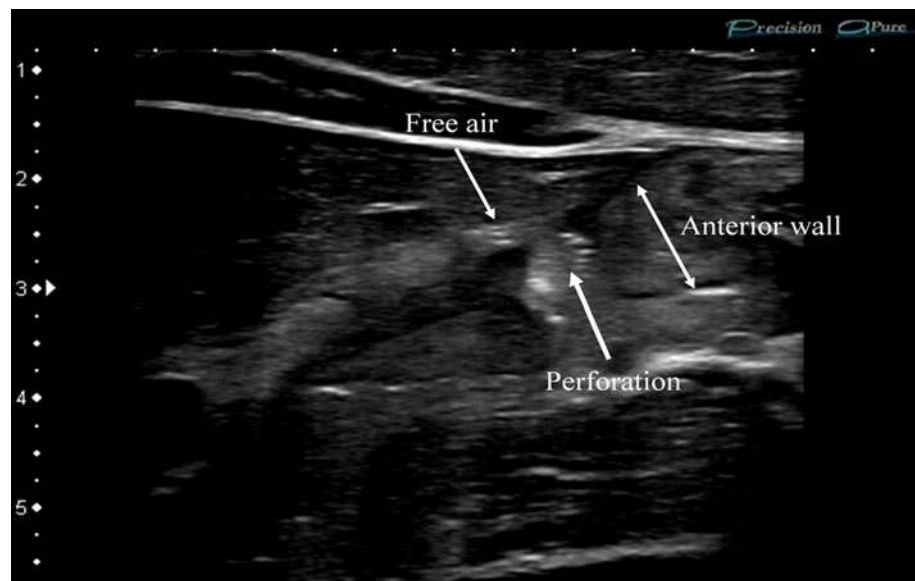


Fig. 1 US images of acute cholecystitis. Gallbladder swelling, wall thickening with hypoechoic layer, massive debris, and stone impaction are demonstrated

Fig. 2 US images of perforated duodenal ulcer case with positive Murphy's sign (non-ultrasonographic), increased white blood cell count and elevated C-reactive protein. Wall thickening of the anterior wall of the duodenal bulb as well as a large wall defect accompanied with extramural air is clearly demonstrated by US



positive due to other diseases and for diagnosis of the causative disease, such as duodenal ulcer (Fig. 2).

Q9. Is color or power Doppler imaging useful for making a diagnosis of acute cholecystitis?

The findings of power Doppler imaging are useful for making a diagnosis of acute cholecystitis (recommendation 2, level C).

Soyer et al. examined 129 cases complaining of acute pain in the upper right quadrant abdomen and reported that the diagnostic capacity for acute cholecystitis on the basis of Doppler sonographic findings were: sensitivity 95 %, specificity 100 %, accuracy 99 %, PPV 100 %, and NPV 99 %, exceeding that of the B-mode Doppler sonography (sensitivity 86 %, specificity 99 %, accuracy 92 %, PPV 92 %, and NPV 87 %) [35] (Supplement Table 2).

On the other hand, Tessler et al. [36] who examined a small number of cases have found that intramural Doppler signals are also observed in normal cases and that signal depiction becomes more remarkable after food intake. Furthermore, Jeffrey et al. carried out detailed discussion of 54 cases undergoing surgery for cholecystitis and 115 normal controls including the area of depiction and have found that the presence or absence of signal depiction alone is not a finding specific to cholecystitis. They looked at the presence of a blood flow signal extending over more than half of the anterior wall (26 % occurrence rate compared with 2 % for normal cases), and discovered that the signal depicted on the bottom is a more specific finding (the frequency of occurrence being 0 % for normal cases and 19 % for cholecystitis cases) [37].

On the basis of the above observations, it may be possible to make a diagnosis of cholecystitis by means of color or power Doppler sonography. However, the detective capacity of Doppler signals is influenced by the performance and settings of the instruments used and, and the physique of subjects. Careful judgment should be made when using Doppler sonographic findings as the only reference findings including B-mode findings (Supplement Fig. 2).

CT

Q10. What are the characteristic contrast enhanced CT findings of acute cholecystitis?

CT findings of acute cholecystitis are gallbladder distention, pericholecystic fat stranding, gallbladder wall thickening, subserosal edema, mucosal enhancement, transient focal enhancement of the liver adjacent to the gallbladder, pericholecystic fluid collection, pericholecystic abscess, gas collection within gallbladder.

CT findings of acute cholecystitis were reported as: GB distention (41 %), gallbladder wall thickening (59 %), pericholecystic fat density (52 %), pericholecystic fluid collection (31 %), subserosal edema (31 %), and high-attenuation gallbladder bile (24 %) (Fig. 3; Supplement Fig. 3) [38].

Anatomically, a part of the cholecystic vein directly drains into the liver parenchyma surrounding the gallbladder fossa. In patients with acute cholecystitis, venous blood flow from the gallbladder wall into the liver increases. So, the arterial phase of dynamic CT shows transient focal enhancement of the liver adjacent to the inflamed gallbladder (Fig. 3; Supplement Fig. 3) [39–42]. This enhancement disappears during the portal and equilibrium phase.

In mild acute cholecystitis, gallbladder distention without wall thickening or edema are the only signs on CT. Because gallbladder size is variable depending on the individual, gallbladder distention is difficult to evaluate on diagnostic imaging (such as ultrasonography or non-contrast CT) of acute cholecystitis. Dynamic CT, especially during the arterial phase, is very useful in mild cholecystitis because of the high sensitivity of transient focal enhancement of the liver adjacent to the gallbladder [41].

Tc-HIDA scans

Hepatobiliary scintigraphy involves intravenous injection of technetium-labeled analogues of iminodiacetic acid, which are excreted into the bile. The failure of the gallbladder to fill within 60 min after administration of the tracer indicates that the cystic duct is obstructed and has a sensitivity of 80–90 % for acute cholecystitis. The false positive rate of 10–20 % is largely explained by cystic duct obstruction induced by chronic inflammation, although in some cases normal gallbladders do not fill due to insufficient resistance at the sphincter of Oddi. When the cystic duct is patent (i.e., no cholecystitis), the gallbladder is normally visualized within 30 min. The “rim sign” is a blush of increased pericholecystic radioactivity, which is present in about 30 % of patients with acute cholecystitis and in about 60 % with acute gangrenous cholecystitis [1]. In patients with suspected acute cholecystitis, hepatobiliary scintigraphy has significantly higher specificity [27] and higher accuracy [43] than ultrasonography. Nevertheless, ultrasonography is usually preferred as the first test because of its immediate availability, easy access, a lack of interference by elevated serum bilirubin levels (since cholestasis interferes with biliary excretion of the agents used for scintigraphy), the absence of ionizing radiation, and the

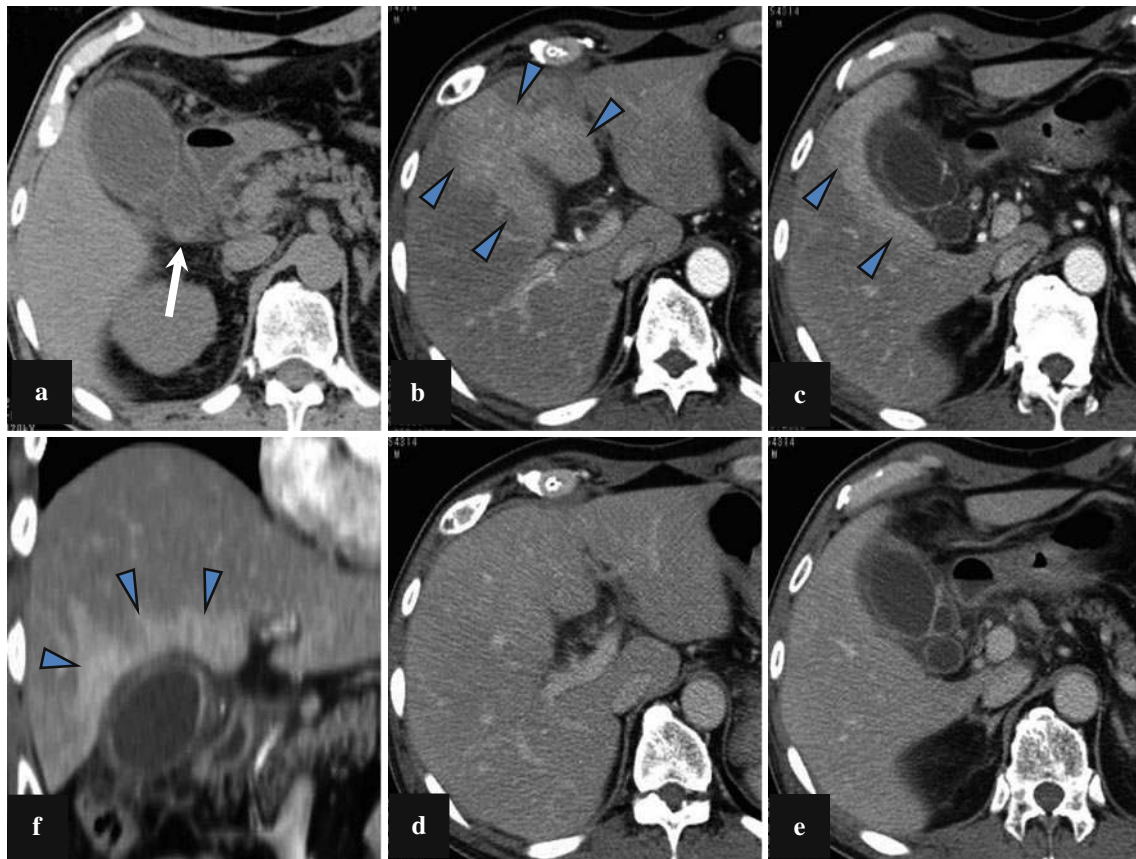


Fig. 3 Acute cholecystolithiasis (62-year-old male). Non-contrast CT (a) shows gallbladder distention, wall thickening, and gallstone (arrow). The arterial phase of contrast-enhanced dynamic CT (b, c,

f) shows gallbladder wall edema (asterisk) and focal hepatic enhancement adjacent to the gallbladder (arrowheads). Hepatic enhancement disappears on the equilibrium phase of CT (d, e)

ability to provide information regarding the presence of stones [1].

Severity assessment criteria for acute cholecystitis; TG13

Background

Patients with acute cholecystitis may present a spectrum of disease stages ranging from a mild, self-limited illness to a fulminant and potentially life-threatening disease. In fact, the overall mortality rate of acute cholecystitis is approximately 0.6 % [11, 12]. There were no severity assessment criteria for this common disease until 2007 [16].

TG07 severity assessment criteria for acute cholecystitis

The severity assessment criteria were first presented throughout the world in TG07 [5], where the severity

grading of acute cholecystitis was classified into the following 3 categories: “mild (Grade I)”, “moderate (Grade II)” and “severe (Grade III)”. Severe (Grade III) acute cholecystitis was defined as acute cholecystitis associated with organ dysfunction.

Moderate (Grade II) acute cholecystitis was defined as acute cholecystitis in which the degree of acute inflammation is likely to be associated with increased operative difficulty in performing cholecystectomy [44–49].

Mild (Grade I) acute cholecystitis was defined as occurring in a patient who has no findings of organ dysfunction and mild disease in the gallbladder, enabling cholecystectomy as a safe and low risk procedure. These patients do not have a severity index that meets the criteria for “moderate (Grade II)” and “severe (Grade III)” acute cholecystitis in TG07.

There are reports that discussed and appraised the TG07 severity assessment criteria. According to those papers, the distribution varies as follows: 39.3–68.5 % of the cases were classified as Grade I, 25.5–59.5 % as Grade II, and 1.2–6 % as Grade III [14, 15]. In addition, there is a report

suggesting that the assessment criteria have contributed to a decrease in the period of hospital stay [13]. This demonstrates that TG07 severity assessment criteria have received good appraisal; there has so far been no treatise or report that has pointed out matters to be improved and weak points of TG07.

Revision of severity grading for acute cholecystitis; TG07

There are reports on poor prognostic factors of acute cholecystitis and those enabling the estimation of emergency surgery. Factors reported after 2000 include leukocytosis [13, 15, 50–55], ALP [50, 56, 57], old age [53, 54, 58], diabetes [51, 52], male sex [51, 53], and admission delay [55]. There are also reports of imaging findings such as ultrasonographic findings of gallbladder wall thickening [53] and common bile duct distention [57]. To date there has been a small number of new reports of AST, ALT, LDH, BUN, and creatinine. The severity assessment criteria were reconsidered by the Tokyo Guidelines Revision Committee with new information, evidence, and evaluations of TG07. Consequently, the TG07 severity assessment criteria did not have significant problems that required major revision of the definitions or structures [16]. However, minor changes were made to the description of Grade III severity: dopamine and norepinephrine were both considered as evidence of cardiovascular dysfunction consistent with the SOFA scoring system [59].

TG13 severity assessment criteria for acute cholecystitis

The revised severity grading for acute cholecystitis is shown in Table 4.

TG07 severity assessment criteria have been adopted in TG13 with minor changes [16].

Q11. What morbid conditions are referred to as severe in assessing severity for acute cholecystitis?

“Severe” is referred to as a condition that has developed organ dysfunction as circulatory failure, consciousness disturbance, respiratory failure, renal failure, hepatic failure or blood coagulation disorder. Intensive care with respiratory and circulatory management should be performed.

Acute cholecystitis has a better outcome/prognosis than acute cholangitis but requires prompt treatment when gangrenous cholecystitis, emphysematous cholecystitis, or torsion of the gallbladder are present. The progression of acute cholecystitis from the mild/moderate to the severe form means the development of multiple organ dysfunction syndrome (MODS). Organ dysfunction scores, such as Marshall’s multiple organ dysfunction (MOD) score and the sequential organ failure assessment (SOFA) score [60], are sometimes used to evaluate organ dysfunction in critically ill patients. The six factors involved in organ dysfunction have therefore been adopted in TG07 as factors that enable severity assessment.

Table 4 TG13 severity grading for acute cholecystitis

Grade III (severe) acute cholecystitis

Associated with dysfunction of any one of the following organs/systems:

- | | |
|-------------------------------|--|
| 1. Cardiovascular dysfunction | Hypotension requiring treatment with dopamine ≥ 5 $\mu\text{g/kg}$ per min, or any dose of norepinephrine |
| 2. Neurological dysfunction | Decreased level of consciousness |
| 3. Respiratory dysfunction | $\text{PaO}_2/\text{FiO}_2$ ratio <300 |
| 4. Renal dysfunction | Oliguria, 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 cholecystitis

Associated with any one of the following conditions:

1. Elevated white blood cell count ($>18,000/\text{mm}^3$)
2. Palpable tender mass in the right upper abdominal quadrant
3. Duration of complaints >72 h
4. Marked local inflammation (gangrenous cholecystitis, pericholecystic abscess, hepatic abscess, biliary peritonitis, emphysematous cholecystitis)

Grade I (mild) acute cholecystitis

Does not meet the criteria of “Grade III” or “Grade II” acute cholecystitis. Grade I can also be defined as acute cholecystitis in a healthy patient with no organ dysfunction and mild inflammatory changes in the gallbladder, making cholecystectomy a safe and low-risk operative procedure

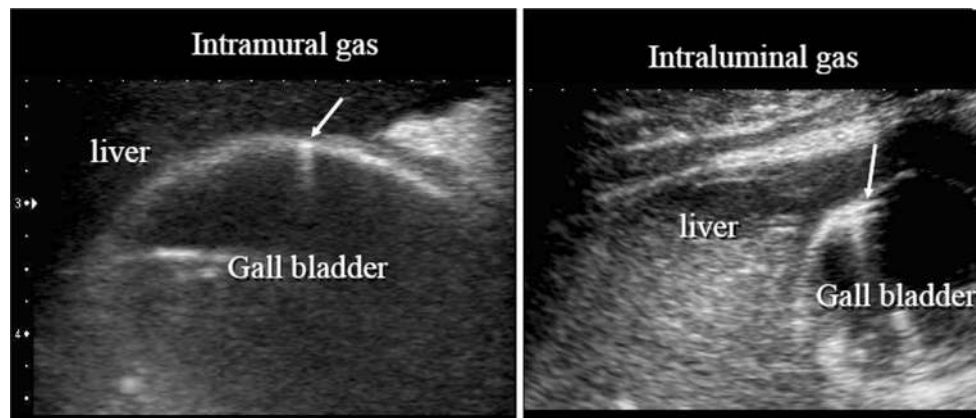


Fig. 4 Emphysematous cholecystitis. The presence of intramural/intraluminal gas indicates emphysematous cholecystitis. The echo from small gas bubbles shows multiple reverberation

Q12. What morbid conditions are referred to as moderate in assessing severity for acute cholecystitis?

“Moderate” is referred to as a condition of acute cholecystitis without organ dysfunction but with its risk, accompanying serious local complication, and for which cholecystectomy and biliary drainage are to be carried out immediately.

Q13. In making a diagnosis of acute cholecystitis, what are the factors that enable the assessment of moderate cases?

The presence of leucocytosis, palpable right upper quadrant abdominal pain, persistence of symptoms for more than 72 hours after onset or severe inflammation findings.

TG07 included findings such as an elevated level of WBC and imaging findings in assessment items specifically applied in moderate (Grade II) acute cholecystitis. Included in these items is evidence such as leukocytosis ($>18,000 \text{ mm}^3$) detected at the time of hospitalization, prognostic factors that contribute to the change of surgical techniques from laparoscopic surgery to open surgery, and the time of symptom persistence (of more than 72 h) from the onset of symptoms [44, 61]. The criteria for Grade II (moderate) acute cholecystitis can be defined as acute cholecystitis associated with local inflammatory conditions that make cholecystectomy difficult.

As for the factor “old age”, the following statement had been adopted to call attention in TG07; however the statement is useful for the revised edition, too. “Elderly” per se is not a criterion for severity itself but indicates a propensity to progress to the severe form, and thus is not included in the criteria for severity assessment [5].

When acute cholecystitis is accompanied by acute cholangitis, the criteria for the severity assessment of acute cholangitis should also be taken into account [62, 63].

Q14. What are the findings to be noted when the assessment of gangrenous cholecystitis and emphysematous cholecystitis is carried out by means of ultrasonography?

Irregular thickening of the gallbladder wall and imaging of the ruptured gallbladder wall should be noted.

Through the discussion of 19 cases of gangrenous cholecystitis, Jeffrey et al. [7] found that the membranous structure of the lumen within the gallbladder is observed in 31.6 % (6 cases), irregular thickening of the gallbladder wall in 47.4 % (9 cases), both of these findings in 21.1 % (4 cases), and either of these findings in 57.9 % (11 cases). Regarding perforation, Forsberg et al. [64] also reported on the basis of the discussion involving 24 cases of perforation and 21 cases of acute cholecystitis without perforation that no specific findings were observed, although a slightly thickened wall was observed (3–20 mm, mean 7 mm, for cases with perforation; 2–13 mm, mean 5.3 mm, for cases without perforation). On the other hand, according to Sood et al. [65] depiction of the ruptured wall as a direct finding of gallbladder perforation was able to be made with ultrasonography in 70 % (16 of 23 cases) and with CT in 78 % (14 of 18 cases). Depending on the performance of the instrument used, it can be assumed that the diagnosis can be made for considerable numbers of cases (Fig. 4; Supplement Movie 2).

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