

2) Moderate and severe cases (refer to Manuscript 8) ¹⁵

For moderate cases, wide-spectrum penicillins, second-generation cepheims and oxacephems are empirically recommended as the drug of first choice. **For severe cases**, which are often infected by polymicrobials and/or resistant organisms (level 2b-3b) ¹⁷⁻¹⁹, 3rd- and 4th- generation cepheims with a wide antimicrobial spectrum are recommended as the drug of first choice. When the drug of first choice is ineffective, intravenous administration of new-quinolones and carbapenems are used as the drug of second choice. It should not be ignored that inappropriate overuse of 3rd- and 4th-generation cepheims and carbapenems have resulted in the emergence of resistant bacteria.

< Examples of uses >

First options for moderate cases

Wide spectrum penicillin/ β -lactamase inhibitor

Piperacillin/tazobactam, Ampicillin/sulbactam

2nd-generation cepheims

Cefmetazole, Cefotiam

Oxacephem

Flomoxef

First options for severe cases

3rd- and 4th- generation cepheims

Cefoperazon/sulbactam, Ceftriaxone, Ceftazidime,

Cefozopran

Monobactams

Aztreonam

Second options for severe cases

New quinolones

Ciprofloxacin, Pazufloxacin

+ metronidazole (when anaerobic bacteria are detected or are expected to co-exist)

Carbapenems

Meropenem, Impenem/cilastatin,

Panipenem/betamipron

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Interventional Techniques for Gallbladder drainage: Tokyo Guideline for the Management of Acute Cholangitis and Cholecystitis

Running title: Drainage Methods for Acute Cholecystitis

Abstract

A principal management of acute cholecystitis is early cholecystectomy. Indications of biliary drainage are medium or severe acute cholecystitis cases who cannot undergo surgery for some reasons. Percutaneous biliary drainage is an indispensable procedure for the patients with high-risk acute cholecystitis, especially acalculous cholecystitis, though its clear superiority over conservative treatment has yet to be proven. Percutaneous transhepatic gallbladder aspiration (PTGBA) is a simple drainage method with fewer complications, though its clinical usefulness is endorsed only by case series studies. Indications and clinical effects of PTGBA should be clarified, considering its advantages such as simpler procedure and less damage to patients' activity of daily living (ADL), though its drainage effect is inferior to that of general percutaneous transhepatic gallbladder drainage (PTGBD).

Key words:

Percutaneous cholecystostomy, percutaneous transhepatic gallbladder drainage (PTGBD), percutaneous transhepatic gallbladder aspiration (PTGBA), acalculous cholecystitis, endoscopic transpapillary gallbladder drainage

Clinical Questions

Q1. What procedure should be chosen when the performance of biliary drainage is required in acute cholecystitis?

Introduction

Biliary drainage used to be a procedure for surgical external biliary fistulation under local anesthesia, and was called “percutaneous cholecystostomy”. With the popularization of ultrasonography, percutaneous transhepatic gallbladder drainage (PTGBD), which is an interventional method, has become a standard method. The usefulness of PTGBD as a drainage method for high-risk patients is endorsed by many case series studies¹⁻⁸, but its superiority over conventional treatment has not been proven by randomized controlled trials (RCT) based on the highest level of evidence. Percutaneous transhepatic gallbladder aspiration (PTGBA), another biliary drainage method in which gallbladder content is puncture-aspirated without placing a drainage catheter. The usefulness of PTGBA has been reported only in case-series studies⁹⁻¹⁰. This paper discusses the clinical significance, indications and results of biliary drainage in acute cholecystitis.

1. Clinical significance

A basic treatment policy for acute cholecystitis is early cholecystectomy. Indications of biliary drainage are those who are assessed as medium or severe acute cholecystitis cases, according to the severity assessment criteria (refer to Manuscript 8) and satisfy the criteria: (1) no surgery is applicable due to high surgical risk, (2) early surgery is not applicable for the reason of medical institution and (3) surgery is rejected by patients. In other words, biliary drainage is a useful therapy for the medium or severe cases who cannot undergo early surgery for some reasons¹⁻¹⁰.

PTGBD, a method performed under local anesthesia, is considered as a useful non-invasive therapy applicable to the surgery-intolerant cases and ICU patients. In RCT¹¹ comparing with conservative treatment, PTGBD was not more useful for improving symptoms and mortality. However, in view of the fact that this RCT has several problems including (1) more ICU patients are included in the drainage group and half of them died and (2) drainage protocol was changed in the middle of the trial, due to fatal complication (biliary peritonitis) from transperitoneal to percutaneous transhepatic puncture, the usefulness of PTGBD needs to be verified by further RCTs (Table 1).

Acalculous cholecystitis is known to occur in elderly or high-risk patients with poor systemic conditions, and it could be treated by biliary drainage alone^{1,2,13,14}. Because of less post-operative recurrence, PTGBD may be an alternative to surgical cholecystectomy

Table 2. RCT comparing PTGBD and conservative treatment for high-risk acute cholecystitis (PTGBD)
(Adapted from reference 11)

	n (ICU*)	Symptom improvement	Mortality
PTGBD group	63 (6)	86%	17.5%
Conservative treatment	60 (2)	87%	13%

] p > 0.05

* No. of patients in ICU (intensive care unit)

2. Timing of drainage

Severe cases should undergo drainage immediately, while medium cases can wait until they are found to be progressing to severe cases based on their response to the primary care. Mild cases are subjected to drainage only when they do not respond to primary care 12-24 hours later.

3. Procedures

1) Percutaneous transhepatic gallbladder drainage (PTGBD)

After ultrasound-guided transhepatic gallbladder puncture with an 18G needle, a 6-10Fr pig-tail catheter is placed in the gallbladder using a guide wire under fluoroscopy (Seldinger technique. Figure 1). This is established as a gallbladder drainage method because of its easiness in bile aspiration and lavage, but it has disadvantages that a drainage tube cannot be extracted until fistulation (7-10 days), restricted patients' activity of daily living (ADL) and the displacement of the tube.

2) Percutaneous transhepatic gallbladder aspiration (PTGBA)

This is a method to aspirate bile from the gallbladder with a small-gauge needle under sonographic guidance (Figure 2), and is easy and low-cost bedside-applicable procedure requiring no X-ray fluoroscopy and causing fewer complications. It has various advantages as compared with PTGBD, such as the absence of complications including those caused by tube displacement as it requires no drainage tube management³ and less restriction of patients' ADL, but RCT¹² indicates that the drainage is less effective (Table 3). However, as it is known that the effect of drainage is enhanced when PTGBA is performed 2 times or more^{9, 11}, RCT should be performed to verify the effect of PTGBA by simply comparing not only with those of PTGBD but also other outcome including complications and patients' ADL.

Considering a potential leakage of bile into the peritoneal cavity, a transhepatic puncture route is chosen, and the content of the gallbladder should be completely aspirated until the gallbladder collapses with ultrasound-guided checking of a needle tip (Figure 2).

The use of a large-gauged 18G needle is convenient for aspirating highly viscous bile containing inflammatory products and biliary sand, but the leakage of bile after removing the needle should be

carefully prevented. While a small-gauge 21G needle has a lower risk of leakage after removal, aspirating highly viscous bile is difficult and should be conducted while washing with saline containing antibiotics. Many of the reports^{9, 11, 12} use 21G needles.

3) Endoscopic naso-gallbladder drainage (ENGBD)

ENGBD is an external drainage procedure by placing a 5-7Fr tube with a guide wire technique after the selective cannulation into the gallbladder. ENGBD can be used for the patients with severe comorbid conditions, especially end-stage liver disease, in whom the percutaneous approach is difficult to be performed. However, because it requires difficult endoscopic technique, and the relevant case-series studies have been conducted only in a limited number of institutions¹⁵⁻¹⁸, ENGBD has not been established as a standard method (Fig. 3)¹⁹.

The Guidelines established the following grades of recommendation for the gallbladder drainage based on the currently available evidence.

Q1. What procedure should be chosen when biliary drainage is required in acute cholecystitis?

PTGBD: Recommendation grade B (particularly for high-risk cases)
 PTGBA: Recommendation grade C
 ENGBD: Recommendation grade C

Table 3. Comparison of results between PTGBA and PTGBD

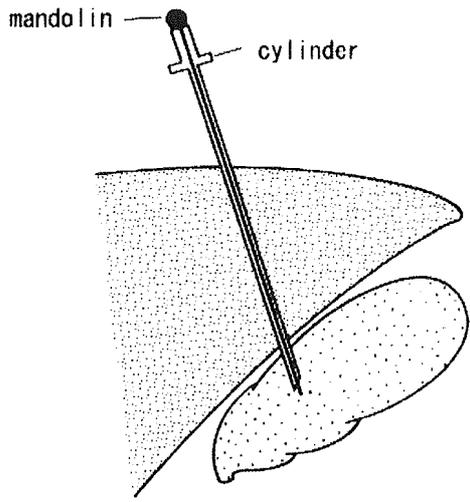
Authors		n	Technical success	Clinical	
				Responses	Complications
Ito ¹² (2004)	PTGBA	28	82%	61%	0.4%
	PTGBD	30	100%	90%	0.3%
Kutsumi ⁹ (2004)	PTGBA	94	100%	83%(91%**)	1.1%
	PTGBD	13	100%	-	23.1%
Chopra ³ (2001)	PTGBA	31	97%	74%	0
	PTGBD	22	97%	86%	12%
Mizumoto ¹⁰ (1992)	PTGBA	58	98%	81%(94%**)	2.5%

*: p<0.05

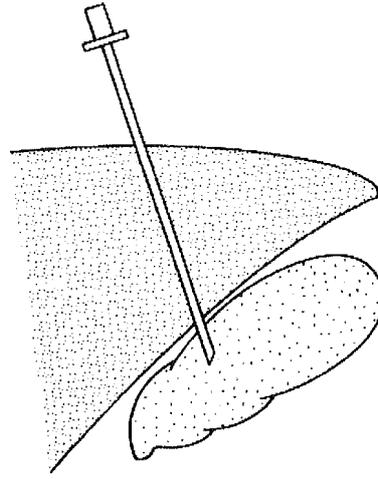
** : Rate of remission after 2 or more PTGBA applications

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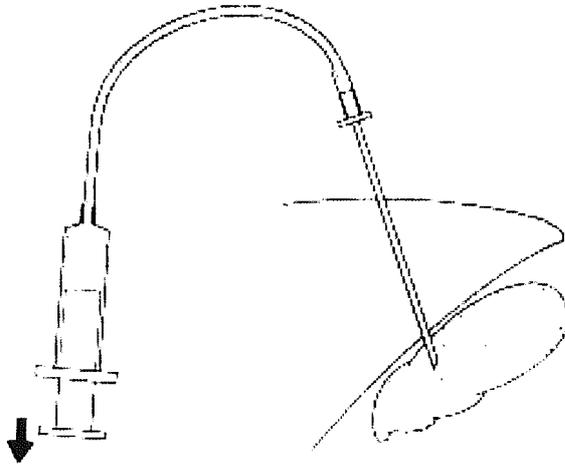
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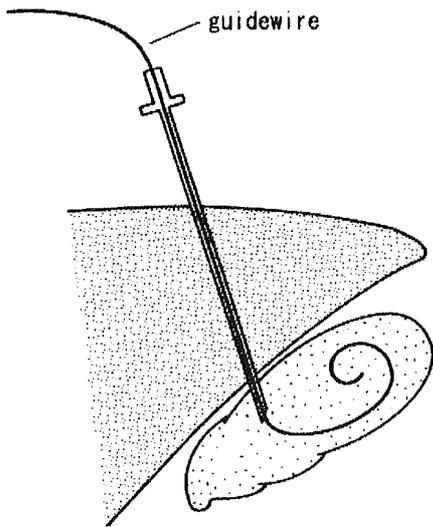
(a)



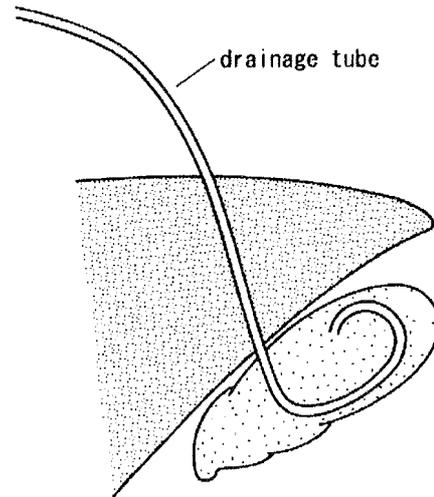
(b)



(c)



(d)



(e)

Fig. 1. Percutaneous transhepatic gallbladder drainage (PTGBD) procedure.

- (a) A hollow needle (a mandolin with a cylinder) is inserted into the gallbladder.
- (b) Only the mandolin is removed and the cylinder is stayed.
- (c) Backward bile flow is confirmed.
- (d) A guidewire is inserted into the gallbladder.
- (e) A drainage tube is passed over the guidewire into the gallbladder. The guidewire is then withdrawn, and the external end of the tube is fixed to the skin surface.

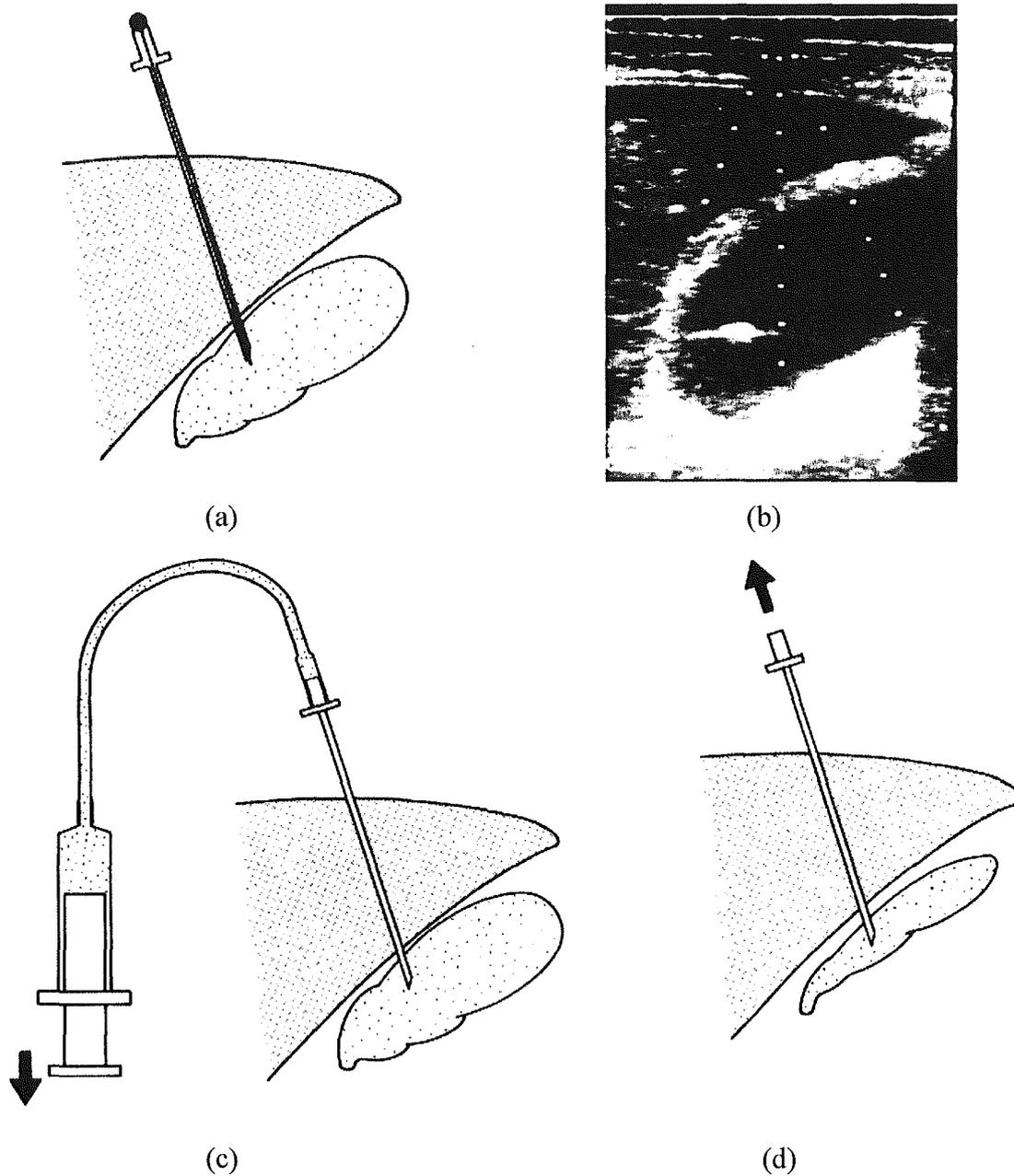


Fig. 2. Percutaneous transhepatic gallbladder aspiration (PTGBA) procedure.

- (a) Under ultrasound guidance, the mandolin with the cap is transhepatically inserted into the gallbladder. The mandolin is then removed.
- (b) Real-time ultrasound image. The three dotted lines represent insertion guide routes. The gallbladder is differentiated from the bottom of the liver by low-intensity echo. The high-intensity echo spot within the gallbladder depicts the area around the tip of the inserted needle.
- (c) The mandolin is removed, and bile is aspirated.
- (d) After sufficient aspiration of bile, the needle is withdrawn.

Fig 3A

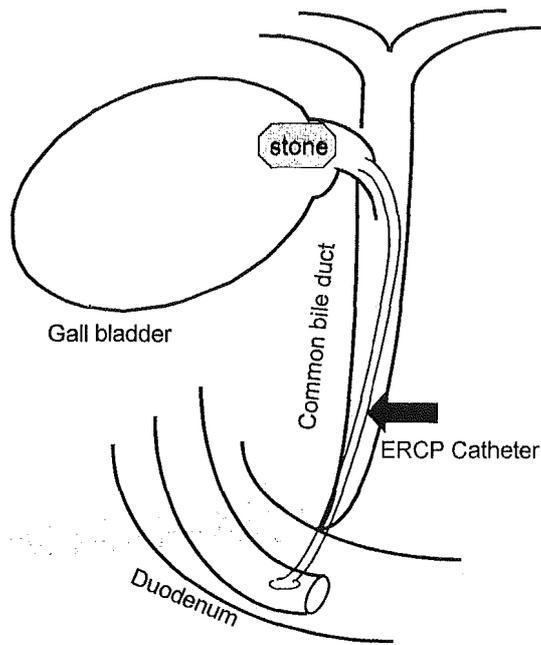


Fig 3B

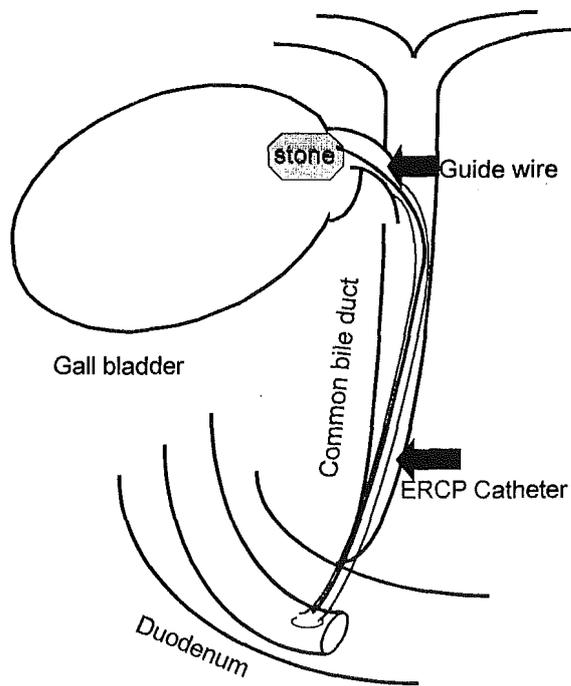


Fig.3A: ERCP catheter was inserted in the cystic duct, but the gallbladder was not visualized because of a stone impacted in the neck of the gallbladder.

Fig.3B: Through the ERCP catheter, a radiofocus guidewire was passed beyond the obstruction.

Fig 4A

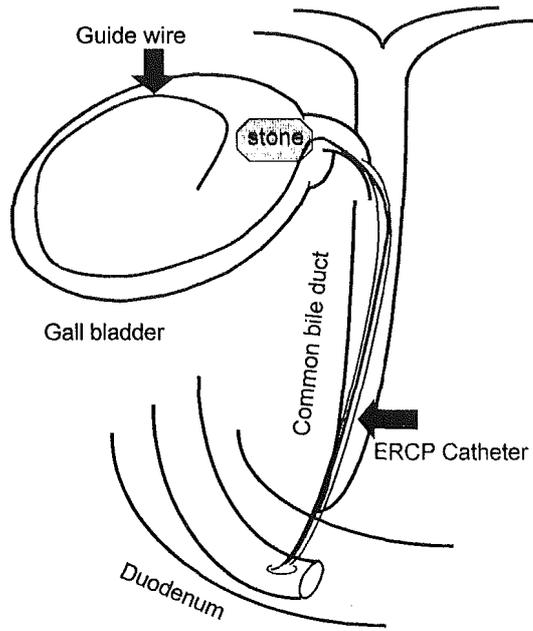


Fig 4B

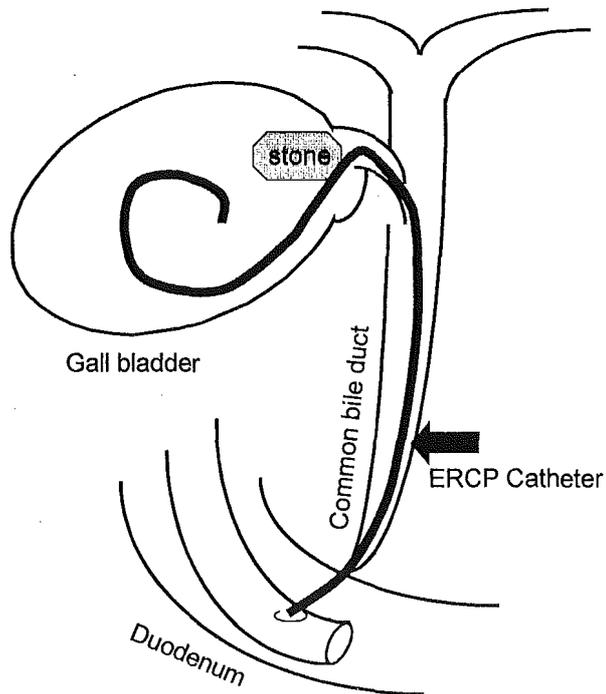


Fig.4A: The radiofocus guidewire was inserted into the gallbladder

Fig.4B: The ENGBD catheter was inserted into the gallbladder for drainage.

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Surgical Treatment for the Patients with Acute Cholecystitis

Running title: Surgical treatment for acute cholecystitis

Abstract

Cholecystectomy has been widely performed in the treatment of acute cholecystitis. Laparoscopic cholecystitis is being adopted to acute cholecystitis for last 10 years. Despite the well-accepted success of laparoscopic cholecystectomy in elective treatment of symptomatic gallstones, acute cholecystitis had been considered to be a contraindication of laparoscopic cholecystectomy in the beginnings of laparoscopic cholecystectomy. The reasons for contraindication were a technical difficulty in acute cholecystitis and occurrence of complications such as bile duct injury, bowel injury, and hepatic injury. However, laparoscopic cholecystectomy is now accepted as safe for acute cholecystitis when expert surgeons at laparoscopic technique performed it. Laparoscopic cholecystectomy for acute cholecystitis is recognized to be superior to open cholecystectomy in an incidence of complications, post-operative length of hospitalization, recuperation, and earlier return to work. However, laparoscopic cholecystectomy for acute cholecystitis has not pervaded because the timing and approach to the surgical management in patients with acute cholecystitis is still unsettled. This paper indicates the timing of and an optimal surgical treatment for acute cholecystitis in a question-and-answer format.

Key words: Acute cholecystitis, cholecystectomy, laparoscopic cholecystectomy, open surgery, cholecystostomy

Introduction

Cholecystectomy has been widely accepted as an effective treatment for acute cholecystitis. Several studies conducted in the open cholecystectomy era demonstrated the advantages of early cholecystectomy for patients with acute cholecystitis because of safety, cost effectiveness, and quick return to normal activity.¹⁻³⁾ Though acute cholecystitis had been considered to be a contraindication of laparoscopic cholecystectomy in the beginnings of laparoscopic cholecystectomy because of higher incidence of complications comparing with non-acute cholecystitis.⁴⁾ With development of technical skill and laparoscopic instruments, laparoscopic cholecystectomy is now accepted as safe when expert surgeons at laparoscopic technique perform it. Some recent randomized clinical trials⁵⁻⁹⁾ have addressed the timing and surgical approach to cholecystectomy in patients with acute cholecystitis, and indicated that laparoscopic cholecystectomy was associated with a shorter hospital stay, quick recovery, and a reduction in the overall cost of a treatment, and that early laparoscopic cholecystectomy is sufficiently safe.

On the other hand, urgent or early laparoscopic cholecystectomy for acute cholecystitis seems to remain an unpopular practice at present^{10,11)}. The reasons for this unpopularity included a lack of availability of experienced surgeons and the limited availability of surgical operation theater space.^{10,11)}

The critically ill patients with acute cholecystitis often present a difficult therapeutic dilemma. Although those patients require emergency surgical intervention, many patients with this disorder complicating another serious medical or surgical problem may be too ill to undergo an open or laparoscopic cholecystectomy under general anesthesia. Cholecystostomy offers a distinct advantage in those critically ill patients by avoiding the risks of cholecystectomy. However, the optimal timing of subsequent surgery has not been examined following this drainage. This paper indicates the timing and an optimal surgical treatment for acute cholecystitis in a question-and-answer format.

1. Surgical treatment

Q1. Which surgical procedure should be adopted, laparoscopic cholecystectomy or open cholecystectomy?

A surgeon should adopted his experienced procedure of cholecystectomy: Recommendation grade. Laparoscopic cholecystectomy is preferable, as far as possible: Recommendation grade A

Cholecystectomy has been widely performed in the treatment of acute cholecystitis. laparoscopic cholecystectomy is being adopted to acute cholecystitis for the last 10 years. At the beginning period of laparoscopic cholecystectomy era, several reports of complications associated with it's practice caused transient wane of enthusiasm for early cholecystectomy.¹²⁻¹⁵⁾ These concerns have been allayed by an evidence indicating that early laparoscopic cholecystectomy is safe, effective, and short hospitalization for patients with AC.^{6,9,16-19)} Thus, increased experience with this condition has led to laparoscopic