Acute Cholangitis: An Update in Management Based on Severity Assessment

Robert Christeven, Frandy**, Andersen****

[*]Department of Emergency, Pemangkat Regional General Hospital, Sambas
[**]Department of Emergency, St Vincentius Hospital, Singkawang
[***] Department of Emergency, Kartika Husada Army Hospital, Kubu Raya

Corresponding author:
Robert Christeven. Department of Emergency, Pemangkat Regional General Hospital, Jl. Abdul Kadir Kasim No 20 Sambas Indonesia. Phone/facsimile: +62-562-241203. E-mail: rchristeven.rc@gmail.com

ABSTRACT

Acute cholangitis (AC) is a biliary tract emergency which causes significant morbidity and mortality. The direct cause of death in AC is sepsis that leads to irreversible shock and multiple organ failure. The most common predisposition are bile duct stones and previous invasive manipulation of the biliary tree. Biliary infection and biliary obstruction are the two main factors in pathophysiology of AC. Gram-negative bacteria are isolated frequently from bile and blood culture in cholangitis. The most common cause of biliary obstruction is gallstone.

The Charcot's triad which commonly has been used to diagnose AC is severely limited and the clinical presentation of the disease has wide spectrum ranging from mild symptoms to severe life-threatening disease. Thus, the use of the most updated Tokyo Guidelines (TG18) is imperative to diagnose the disease and to assess the severity. The TG18 diagnostic criteria is based on the presence of systemic inflammmation, cholestasis, and evidence on imaging studies of biliary tract. The prompt treatment is tailored according to severity assessed by TG18. Initial treatment includes sufficient fluid replacement, hemodynamic control, electrolyte compensation, intravenous antibiotic administration, and intravenous analgesic administration. The definitive treatment which related to the pathophysiology of the disease are biliary drainage and antibiotic administration.

Keywords: *acute cholangitis, Tokyo guidelines, biliary tract, biliary obstruction, gallstone, Charcot's triad*

ABSTRAK

Kolangitis akut (KA) adalah suatu kegawatan traktus biliar yang menyebabkan kesakitan dan kematian yang bermakna. Penyebab kematian langsung pada kolangitis akut adalah sepsis yang berkembang menjadi syok yang ireversibel dan kegagalan multi organ. Faktor predisposisi tersering adalah batu empedu dan riwayat manipulasi traktus biliaris. Infeksi bilier dan obstruksi bilier adalah dua patofisiologi utama kolangitis akut. Bakteri gram negatif sering ditemukan pada kultur cairan empedu dan darah. Penyebab utama obstruksi bilier adalah batu empedu.

Trias Charcot yang sering digunakan untuk mendiagnosis kolangitis akut memiliki banyak keterbatasan dan gejala klinis dari penyakit memiliki gambaran yang luas yang berkisar dari gejala ringan sampai penyakit berat yang mengancam nyawa. Oleh karena itu, penggunaan Panduan Tokyo yang terbaru (TG18) penting digunakan untuk mendiagnosis penyakit dan menilai keparahan. Kriteria diagnostik TG18 berdasarkan adanya inflamasi sistemik, kolestasis, dan bukti dari pemeriksaan pencitraan terhadap traktus bilier. Terapi yang dini disesuaikan berdasarkan derajat keparahan yang ternilai dengan TG18. Terapi awal terdiri dari penggantian cairan yang adekuat, pengendalian hemodinamik, kompensasi elektrolit, pemberian antibiotik

intravena, dan pemberian anti nyeri intravena. Terapi definitif yang berhubungan dengan patofisiologi penyakit adalah drainase bilier dan pemberian antibiotik

Kata kunci: *kolangtis akut, Panduan Tokyo, traktus biliaris, obstruksi biliar, batu empedu, trias Charcot's*

INTRODUCTION

Acute cholangitis (AC) is one of the biliary tract emergencies in the spectrum of acute biliary infection with high morbidity and mortality rates; thus, it needs straightforward diagnostic evaluation and immediate treatment initiation. Acute cholangitis is an acute condition with inflammation and infection of the biliary tract.[1,2] Clinical presentation of AC ranges from mild symptoms to severe life-threatening with septic shock conducting rapidly to death.[2] In 1877, Charcot first described the Charcot's triad – a clinical pattern with intermittent fever accompanied by chills and rigor, right upper abdominal pain and jaundice. About 50-70% of the patients with acute cholangitis present with Charcot's triad. Later, in 1959, Reynolds and Dragan described a syndrome consisting of fever, jaundice, abdominal pain, altered mental status (confusion or lethargy), and shock. They called it Reynold's pentad with the underlying pathology of acute obstructive cholangitis.[1-4] Longmire described these two conditions as acute suppurative cholangitis and acute obstructive suppurative cholangitis. They are associated with increased morbidity and mortality.[1]

The most common cause of acute cholangitis is common bile duct stone (choledocholithiasis).[2] Other causes of AC are malignancy, benign strictures, and interventions to the biliary ducts that cause biliary obstruction.[3] Mortality rate in severe cholangitis remains significant without appropriate management. Advances in intensive care, antibiotic regimens and biliary drainage techniques have dramatically improved the mortality rate of more than 50% prior to the 1970s to less than 10% in the 1980s.[2]

There is a wide spectrum of disease courses in acute bacterial cholangitis,[4] 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 As a therapeutic procedure for severe cases or to prevent increased severity, decompression of the biliary tract (i.e., biliary tract drainage) is necessary.[5] 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 cholangitis. However, it remains a life-threatening disease if the timing of biliary tract drainage has been missed.[3,5] Therefore, immediate and precise judgment of severity is of the utmost importance. The most well-known diagnostic criteria and severity assessment that has been used for years is Tokyo Guidelines (TG) with their most updated Tokyo Guidelines 2018 (TG18).

Epidemiology

The incidence of acute cholangitis ranges from 0.3 to 1.6% with a proportion of severe cholangitis that reaches 12.3%.[2] The most common characteristics that predispose patients to the development of cholangitis are bile duct stones and previous manipulation of the biliary tree, including stenting and biliary surgery resulting in stricture. Incidence of cholangitis is associated with prevalence of cholelithiasis.[6] Gallstones are found in 10% to 15% of the white population in the United States. It is much more prevalent in native Americans (60%-70%) and Hispanics but less common in Asians and African Americans. Many patients get admitted to the hospital with gallstone disease and 6% to 9% of them are diagnosed with acute cholangitis.[7] Gallstones are estimated to be responsible for approximately 65% of cholangitis cases, followed by 24% as a result of malignant stenosis, 4% caused by benign stenosis, 3% a result of sclerosing cholangitis, and 1% caused by other or unknown factors. Of those with asymptomatic gallbladder stones, approximately 0.6%–1.3% will go on to develop cholangitis over a 10-year period.[6] Males and females are equally affected. The average age of patients presenting with acute cholangitis is 50 to 60 years. Less than 200.000 cases of cholangitis occur per year in the United States.[7] There is no report about acute cholangitis incidence in Indonesia.

The proportion of cases diagnosed as severe (grade III) according to the Tokyo Guidelines 07 (TG07) severity assessment criteria was 12.3 %.[2] In a large, multicenter case series study on patients with Acute Cholangitis conducted in Japan and Taiwan, application of the TG13 severity grading criteria to the case series yielded 1,521 patients with Grade III

(25.1%), 2,019 patients with Grade II (33.3%), and 2,523 patients with Grade I (41.6%).[8]

Pathophysiology

Acute cholangitis is characterized by acute inflammation and infection of the bile duct system with increased bacterial loads (biliary infection) and high intraductal pressure levels (biliary obstruction) favoring bacterial and endotoxin translocation into the vascular and lymphatic drainage (concept of cholangiovenous and cholangiolymphatic reflux, respectively).[4]

Bacteria primarily enter the biliary system by ascending from the duodenum into the common hepatopancreatic duct (hence the terms ascending and suppurative cholangitis).[6,9] The portal venous system and the periportal lymphatic system are also potential routes of entry, which is thought to occur less frequently. The mere presence of bacteria in the biliary system, termed bacterobilia, is not sufficient to elicit cholangitis symptoms without coexistent obstruction due to effective antibacterial mechanical effects of bile flow and biliary immunoglobulin (Ig) A secretion protecting Kupffer cell function and integrity of biliary tight junctions.[4]

Intracholedochal (intrabiliary) pressure is the most important factor.[3] The critical threshold of intrabiliary pressure has been determined to be >20 cm H2O (normal value: 7–14 cm H2O).[4] If the pressure exceeds 25 cm H2O, which is the critical value, hepatic defence mechanisms against infection are disrupted and infection spreads into the intrahepatic canalicules, and cholangiovenous reflux ensues, followed by the access to the hepatic veins and lymphatics, resulting in bacteriemia and endotoxinemia.[3,7]

Besides this, systemic release of inflammatory mediators like tumor necrosis factor (TNF), soluble TNF receptors, interleukin (IL)-1, IL-6 and IL-10 leads to profound hemodynamic compromise. In conjunction with an increased permeability of the acutely inflamed biliary epithelium, the stage is set for potentially fatal complications such as biliary sepsis and hepatic abscess.[4] Sepsis is common in the case of suppurative infections.

Clinical Presentation

Classically, patients present with high fever persisting for more than 24 h, abdominal pain and jaundice (Charcot's triad or hepatic fever). The right upper quadrant abdominal pain is generally mild.[7] Additionally, these three signs plus findings of hypotension and altered mental status (Reynold's pentad) are seen in only 5%–7% of cases, but typically represent more severe disease when present.[6,7]

Charcot's triad has low sensitivity (26.4%) and high specificity (95.9%). Although the presence of Charcot's triad is suggestive of acute cholangitis, it is not diagnostic. However, some patients may not manifest all the symptoms and signs.

Imaging Findings

Imaging evaluation of the hepatobiliary system has the primary role in diagnostic modalities, staging and management for cholangitis.[9] However, even though new technologies and knowledge are steadily accumulating, there is no way to directly diagnose Acute Cholangitis based on imaging findings.[8] Diagnostic imaging is considered as a method to directly identify biliary stenosis/blockage that can cause Acute Cholangitis or to describe cholangiectasis that can be used as an indirect finding in support of a diagnosis. Imaging modalities capable of yielding such findings include abdominal ultrasound, computed tomography (CT), and magnetic resonance imaging (MRI)/magnetic resonance cholangiopancreatography (MRCP), whereas simple X-rays are not suited to diagnose. Endoscopic retrograde cholangiopancreatography is performed for the purposes of treatment (drainage), but is not suitable as first choice for diagnostic purposes.[8]

Diagnosis

Acute cholangitis (AC) has been diagnosed on the basis of Charcot's triad, which depends on clinical signs. To compensate for the low sensitivity of Charcot's triad, the Tokyo Guideline 2007 (TG07) diagnostic criteria were based on Charcot's triad with the addition of blood test and imaging findings; however, this still did not provide good sensitivity. In the updated TG13 guidelines, the Tokyo Guidelines Revision Committee conducted joint research at multiple sites which had exhibited good sensitivity (95.1%) but poor specificity (66.3%) due to the high rate (38.8%) of false positives for acute cholecystitis. The TG13 diagnostic criteria is being used again in recently updated TG18 (Figure 1).[8]

Severity Assessment

Severity assessment and risk stratification is needed because there is a wide spectrum of disease in acute cholangitis, ranging from self-limiting to life-threatening with the need to tailor treatment accordingly.

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 Creactive protein levels, and other changes indicating inflammation B-2: Increased serum ALP, r-GTP (GGT), AST, and ALT levels. Other factors which are helpful in diagnosis of acute cholangitis include abdominal pain (right upper quadrant 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 count (91,000/lL) <4 or >10 CRP (mg/dL) ≥1 B-1 Jaundice T-Bil ≥2 (mg/dL) B-2 Abnormal liver	function tests ALP (IU) >1.5 9 STDa cGTP (IU) >1.5 9 STDa AST (IU) >1.5 9 STDa ALT (IU) >1.5 9 STDa

Figure 1. TG18/TG13 diagnostic criteria for acute cholangitis[8]

Grade III (severe) acute cholangitis "Grade III" acute cholangitis is defined as acute cholangitis that is associated with the onset of dysfunction at least in any one of the following organs/systems: 1. Cardiovascular dysfunction: hypotension requiring dopamine ≥5 μg/kg per min, or any dose of norepinephrine 2. Neurological dysfunction: disturbance of consciousness 3. Respiratory dysfunction: PaO2/FiO2 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/mm3 Grade II (moderate) acute cholangitis "Grade II" acute cholangitis is associated with any two of the following conditions: 1. Abnormal WBC count (>12,000/mm3, <4,000/mm3) 2. High fever (≥39°C) 3. Age (≥75 years old) 4. Hyperbilirubinemia (total bilirubin ≥5 mg/dl) 5. Hypoalbuminemia (<STDa90.7) **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.	Early diagnosis, early biliary drainage and/or treatment for etiology, and antimicrobial administration are fundamental treatment for acute cholangitis classified not only "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 figure 1).

Figure 2. TG18/TG13 severity assessment criteria for acute cholangitis[8]

The TG13 severity grading criteria are recommended to be used as the TG18 criteria because patients whose prognosis can potentially be improved by early biliary drainage can be identified by using these criteria (Figure 2).[8]

The most recent study has demonstrated that procalcitonin predicts severe acute cholangitis with better accuracy than conventional biomarkers (WBC and CRP), regardless of the cause. The optimal cut off value for procalcitonin for prediction of severe acute cholangitis was 2.2 ng/ ml. The study suggested potential usefulness of procalcitonin-based risk stratification of acute cholangitis to facilitate timely identification of patients in whom biliary drainage is indicated.[10]

Treatment

Patients with cholangitis should be managed at the hospital, as this is considered as an emergent condition. Patients should be resuscitated first. As cholangitis is due to infection and obstruction of the biliary system, we have to treat both aspects.[7]

Initial Treatment

For all patients with early recognition of cholangitis, initial treatment including the infusion of sufficient fluid replacement, electrolyte compensation, intravenous administration of analgesics and full-dose antimicrobial agents is started, with careful monitoring of blood pressure, heart rate, and urine volume.[6,7,11,12] Analgesics should be administered proactively at an early stage. Opioid analgesics such as morphine hydrochloride and other similar types of drug (such as non-opioid analgesics and pentazocine) cause the sphincter of Oddi to contract, which may elevate biliary pressure, and must therefore be administered with caution.[11]

In the case of serious deterioration, such as the appearance of shock (hypotension), disturbance of consciousness, acute dyspnea, acute renal dysfunction, hepatic dysfunction, or disseminated intravascular coagulation (DIC) (reduced platelet count), emergency biliary drainage should be considered alongside appropriate organ support and respiratory/circulatory management (such as artificial ventilation, tracheal intubation, and the use of hypertensive agents).[11]

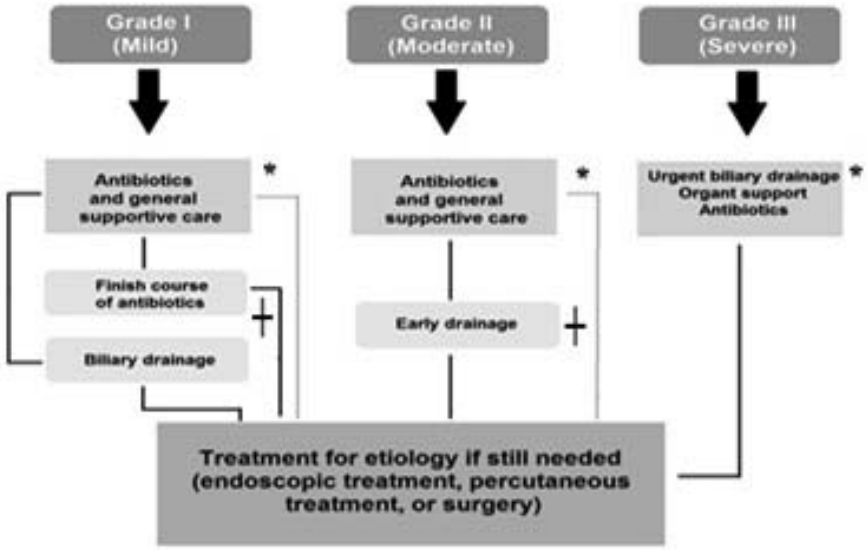
Antibiotic

Once the microorganism culture and sensitivity testing results are available, initial broad-spectrum antimicrobial therapy is revised to a more targeted narrow spectrum therapy.[1] For patients with septic shock, appropriate antimicrobial therapy should be administered within an hour. For less acute ill patients, therapy should be administered within 6 h of diagnosis.[6,7,13] The roles of antimicrobial therapy for acute cholangitis is to allow patients to have elective drainage procedures other than emergency.[13]

Antimicrobial agents appropriate for use as empirical therapy for community-acquired and healthcare-associated infections are provided in table 3, table 4, and table 5. In the TG18, the duration of therapy for patients with acute cholangitis is for 4 to 7 days once the source of infection is controlled by integrating the above studies and expert opinion. When bacteremia with Gram-positive bacteria such as Enterococcus spp. and Streptococcus spp. is present, it is prudent to offer antimicrobial therapy for 2 weeks since these organisms are well-known to cause infective endocarditis.[13] Once susceptibility testing results of causative microorganisms are available, specific therapy (or definitive therapy) should be offered. This process is called de-escalation[13]

Algorithm for the Management of Acute Cholangitis

After severity has been assessed and the patient's general status has been evaluated, a treatment strategy should be decided on the basis of the flowchart (figure 3) for the management of acute cholangitis or acute, and treatment should immediately be provided.[11] Acute cholangitis should be treated in accordance with its severity. The two key pillars of the treatment of acute cholangitis are antibiotics and biliary drainage. If blood culture has not been performed as part of the initial response, it should be carried out before antibiotic administration. If biliary drainage is performed, bile samples must always be sent for culture.



Treatment according to grade, response, and according to need for addional theraphy

* Performance of a blood culture shuold be taken into consideration befeore initiation of administration of antibiotics. A bile culture should be performed during biliary drainage.

┼ Principle of treatment for acute cholangitis consists of antimicrobial administration and biliary drainage including treatment for etiology. For patient with choledocholithiasis, treatment for etiology might be performed stimultaneously, if possible, with biliary drainage.

Figure 3. TG18 flowchart for the management of acute cholangitis[11]

Grade I (mild acute cholangitis)

Grade I or mild acute cholangitis is defined as cholangitis which does not meet the TG18 severity assessment criteria for moderate or severe cholangitis. In most cases initial treatment including antibiotics is sufficient, and most patients do not require biliary drainage. However, biliary drainage should be considered immediately if a patient does not respond to initial treatment within 24 hours.[11-12] Endoscopic sphincterotomy (EST) and subsequent choledocholithotomy may be performed at the same time as biliary drainage. Postoperative cholangitis usually improves with antibiotic treatment alone, and biliary drainage is not usually required.[11]

Table 1. Antimicrobial recommendations for grade I (mild) acute cholangitis[13]

Antimicrobial class	Antimicrobial agents
Penicillin-based therapy	Ampicillin/sulbactam* is not recommended if > 20% resistance rate
Cephalosporin-based therapy	Cefazolin** or Cefotiam** or Cefuroxime**, or Ceftriaxone, or Cefotaxime** ±Metronidazole*** Cefmetazole**, Cefoxitin**, Flomoxef**, Cefoperazone/ sulbactam
Carbapenem-based therapy	ertapenem
Fluoroquinolone-based therapy	Ciprofloxacin, Levofloxacin, Pazufloxacin ± Metronidazole*** Moxifloxacin

*Ampicillin/sulbactam has little activity left against Escherichia coli. It is removed from the North American guidelines

**Local antimicrobial susceptibility patterns (antibiogram) should be considered for use

***Anti-anaerobic therapy, including use of metronidazole, tinidazole, or clindamycin, is warranted if a biliary-enteric anastomosis is present. The carbapenems, piperacillin/tazobactam, ampicilli n/ sulbactam, cefmetazole, cefoxitin, flomoxef, and cefoperazone/sulbactam have sufficient anti-anaerobic activity for this situation

Grade II (moderate acute cholangitis)

Moderate acute cholangitis requires early biliary drainage. In the TG18 severity assessment criteria, moderate cholangitis is assessed if at least two of the following five criteria are met: WBC ≥ 12,000 or < 4,000, temperature ≥ 39°C, age ≥ 75 years, total bilirubin ≥ 5 mg/dL, or albumin < (lower limit of normal value 9 0.73 g/dL). Early endoscopic or percutaneous transhepatic biliary drainage is indicated.[12] If early drainage cannot be performed because of a lack of facilities or skilled personnel, consider transferring the patient.[12]

If the underlying etiology requires treatment, this should be provided after the patient's general condition has improved, and EST and subsequent. choledocholithotomy may be performed together with biliary drainage. Cholecystectomy should be performed for cholecystolithiasis after the acute cholangitis has resolved.[11]

Table 2. Antimicrobial recommendations for grade II (moderate) acute cholangitis[13]

Antimicrobial class	Antimicrobial agents
Penicillin-based therapy	Piperacillin/tazobactam
Cephalosporin-based therapy	Ceftriaxone, or Cefotaxime, or Cefepime, or Cefozopran, or Ceftazidime ±Metronidazole* Cefoperazone/sulbactam
Carbapenem-based therapy	ertapenem
Fluoroquinolone-based therapy	Ciprofloxacin, Levofloxacin, Pazufloxacin ± Metronidazole* Moxifloxacin

*Anti-anaerobic therapy, including use of metronidazole, tinidazole, or clindamycin, is warranted if a biliary-enteric anastomosis is present. The carbapenems, piperacillin/tazobactam, ampicillin/sulbactam, cefmetazole, cefoxitin, flomoxef, and cefoperazone/sulbactam have sufficient anti-anaerobic activity for this situation

Grade III (severe acute cholangitis)

Severe acute cholangitis is cholangitis with sepsis-induced organ damage. In the TG18 severity assessment criteria, severe cholangitis is assessed if any one of the following criteria is met: cardiovascular dysfunction (requiring the use of dopamine ≥ 5 μg/kg per min or noradrenaline), neurological dysfunction (disturbance of consciousness), respiratory dysfunction (PaO2/ FiO2 ratio < 300), renal dysfunction (oliguria or serum creatinine > 2.0 mg/dL), hepatic dysfunction (PT-INR >1.5), or coagulation disorder (platelet count < 104.000 mm^3). As the patient's condition may deteriorate rapidly, a swift response is essential including appropriate respiratory/circulatory management (tracheal intubation followed by artificial ventilation

Table 3. Antimicrobial recommendations for grade III (severe) acute cholangitis and healthcare-associated cholangitis[13]

Antimicrobial class	Antimicrobial agents
Penicillin-based therapy	Piperacillin/tazobactam
Cephalosporin-based therapy	Cefepime, or Ceftazidime, or Cefozopran ± Metronidazole*
Carbapenem-based therapy	Imipenem/cilastatin, Meropenem, Doripenem, Ertapenem
Monobactam-based therapy	Aztreonam Metronidazole

*Anti-anaerobic therapy, including use of metronidazole, tinidazole, or clindamycin, is warranted if a biliary-enteric anastomosis is present. The carbapenems, piperacillin/tazobactam, ampicillin/sulbactam, cefmetazole, cefoxitin, flomoxef, and cefoperazone/sulbactam have sufficient anti-anaerobic activity for this situation

and the use of hypertensive agents). Endoscopic or percutaneous transhepatic biliary drainage should be performed as soon as possible after the patient's condition has been improved by initial treatment and respiratory/ circulatory management. If treatment for the underlying etiology is required, this should be provided after the patient's general status has improved.[11]

Indications and Techniques of Biliary Drainage

In the recently updated TG18, biliary drainage is recommended for acute cholangitis regardless of the degree of severity except in some cases of mild acute cholangitis in which antibiotics and general supportive care are effective.[13]

Endoscopic Transpapillary biliary Drainage (ETBD)

Endoscopic transpapillary biliary drainage should be considered as the first-line drainage procedure because of its less invasiveness and lower risk of adverse events than other drainage techniques despite the risk of post-endoscopic retrograde cholangiopancreatography (ERCP) pancreatitis.[14,15] This technique is gold standard treatment for acute cholangitis irrespective of the benign or malignant nature of the primary disease[14]. Endoscopic transpapillary biliary drainage is divided into two types: endoscopic nasobiliary drainage (ENBD) for external drainage and endoscopic biliary stenting (EBS) for internal drainage. Basically, both types of endoscopic biliary drainage can be performed in all forms of acute cholangitis. In the case of biliary drainage for acute cholangitis therapy, a precise endoscopic technique is mandatory because long and unsuccessful procedures may lead to serious complications in critically ill patients.

In the updated TG18, we suggest that either ENBD or EBS may be considered for biliary drainage by procedure according to the cause of the cholangitis, bile property, and patient's preference.

Endoscopic Nasobiliary Drainage

Endoscopic nasobiliary drainage procedures are described in detail in TG07. In brief, after selective biliary cannulation, a 5-Fr to 7-Fr nasobiliary tube is placed in the bile duct as an external drainage over the guidewire.

Endoscopic Biliary Stenting

The EBS procedure is also described in detail in the previous clinical practice guidelines. In brief, after selective biliary cannulation, a 7-Fr to 10-Fr plastic stent is placed in the bile duct as an internal drainage over the guidewire.[14] There are two different stent shapes, a straight type and a double pigtail type. The straight type has a single flap with a side hole (Amsterdam type) or radial flaps without a side hole (Tannenbaum type) on both sides. The double pigtail type prevents inward and outward stent migration. To our knowledge, there is currently no comparative study between the straight type and pigtail type stents. Therefore, either stent can be selected according to the endoscopist's preference.

The internal drainage by endoscopic transpapillary biliary drainage produces less pain after the procedures than that of the external drainage by percutaneous transhepatic biliary drainage (PTBD), also known as percutaneous transhepatic cholangial drainage (PTCD).[14] PTCD places more burden on cosmetic problems, skin inflammation, and bile leakage, affecting the patient's quality of life. A single treatment session for a bile duct stone is possible with the endoscopic transpapillary approach, making shorter length of hospitalization.

Percutaneous Transhepatic Cholangial Drainage (PTCD)

PTCD is a useful alternative drainage procedure to endoscopic transpapillary biliary drainage approach and being indicated to the patients with an inaccessible papilla due to upper gastrointestinal tract obstruction, or when skilled pancreaticobiliary endoscopists are not available in the institution.[14] Furthermore, PTCD can be used as a salvage therapy when conventional endoscopic transpapillary drainage has failed owing to difficult selective biliary cannulation. Recently, endoscopic ultrasound-guided biliary drainage (EUS-BD) has been developed and reported as a novel useful alternative drainage technique when standard endoscopic transpapillary drainage has failed.[14]

PTCD is performed with ultrasonography-guided transhepatic puncture of the intrahepatic bile duct is initially performed using an 18-G to 22-G needle. After confirming the backflow of bile, a guidewire is advanced into the bile duct. Finally, a 7-Fr to 10-Fr catheter is placed in the bile duct under fluoroscopic control over the guidewire. Puncture using a small-gauge (22-G) needle is safer in patients without biliary dilation than in patients with biliary dilation.[14,15]

Surgical Drainage

Open drainage for decompression of the bile duct is performed as a surgical intervention. When surgical drainage in critically ill patients with bile duct stones is performed, prolonged operations should be avoided and simple procedures, such as T-tube placement without choledocholithotomy, are recommended. At present, surgical drainage is extremely rare because of the widespread use of endoscopic drainage or PTCD for acute cholangitis therapy.[14]

Prognosis

The prognosis depends on the timing of biliary drainage, administration of antibiotics and comorbidities of the patient. Early biliary drainage leads to rapid clinical improvement. But, if biliary drainage is delayed, patients can deteriorate quickly and die. The overall mortality acute cholangitis is less than 10% after biliary drainage. Poor prognostic factors in the setting of acute cholangitis include old age, high fever, leukocytosis, hyperbilirubinemia and hypoalbuminemia. Patients with comorbidities like cirrhosis, malignancy, liver abscess and coagulopathy also carry poor prognosis.

CONCLUSION

Prompt clinical recognition, accurate diagnostic workup and severity assessment including adequate laboratory assessment and etiology oriented imaging are critical steps in the management of acute cholangitis. Treatment is directed at the two major interrelated pathophysiologic components, i.e. bacterial infection (immediate antimicrobial therapy) and bile duct obstruction (biliary drainage).

REFERENCES

1. Liau KH, The C, Serrablo A. Management of acute cholecystitis and acute cholangitis in emergency setting. Cent. Eur J Med 2014;9:357-69.
2. Tringali A. Endoscopic management of acute cholangitis. Gastroenterol Hepatol Open Access 2016;5:1-8.
3. Buyukasik K, Toros AB, Bektas H, Ari A, Deniz MM. Diagnostic and therapeutic value of ERCP in acute cholangitis. ISRN Gastroenterol 2013;2013:191729.
4. Zimmer V, Lammert F. Acute bacterial cholangitis. Viszeralmedizin 2015;31:166-72.
5. Kiriyama S, Takada T, Strasberg SM, Solomkin JS, Mayumi T, Pitt HA, et al. TG13 guidelines for diagnosis and severity grading of acute cholangitis (with videos). J Hepatobiliary Pancreat Sci 2013;20:24–34.
6. Ely R, Long B, Koyfman A. The emergency medicine focused review of cholangitis. The Journal of Emergency Medicine 2018;54:64–72.
7. Ahmed M. Acute cholangitis - an update. World J Gastrointest Pathophysiol 2018;9:1-7
8. Kiriyama S, Kozaka K, Takada T, Strasberg SM, Pitt HA, Gabata T, et al. Tokyo guidelines 2018: diagnostic criteria and severity grading of acute cholangitis (with videos). J Hepatobiliary Pancreat Sci 2018;25:17–30.
9. Alizadeh AHM. Cholangitis: diagnosis, treatment and prognosis. J Clin Transl Hepatol 2017;5:404-13.
10. Umefune G, Kogure H, Hamada T, Isayama H, Ishigaki K, Takagi K, et al. Procalcitonin is a useful biomarker to predict severe acute cholangitis: a single-center prospective study. J Gastroenterol 2017;52:734-45.
11. Miura F, Okamoto K, Takada T, Strasberg SM, Asbun HJ, Pitt HA. Tokyo guidelines 2018: initial management of acute biliary infection and flowchart for acute cholangitis. J Hepatobiliary Pancreat Sci 2018;25:31-40.
12. Mayumi T, Okamoto K, Takada T, Strasberg SM, Solomkin JS, Schlossberg D,et al. Tokyo guidelines 2018: management bundles for acute cholangitis and cholecystitis. J Hepatobiliary Pancreat Sci 2018;25:96-100.
13. Gomi H , Solomkin JS, Schlossberg D, Okamoto K, Takada T, Strasberg SM, et al.. Tokyo guidelines: antimicrobial therapy for acute cholangitis and cholecystitis. J Hepatobiliary Pancreat Sci 2018;25:3-16.
14. Mukai S, Itoi T, Baron T, Takada T, et al. Indications and techniques of biliary drainage for acute cholangitis in updated Tokyo Guidelines 2018. J Hepatobiliary Pancreat Sci 2018;25:3–16. J Hepatobiliary Pancreat Sci 2017;24:537-49.
15. Tsuchiya T, Sofuni A, Tsuji S, Mukai S, Matsunami Y, Nagakawa Y, et al. Endoscopic management of acute cholangitis according to the TG13. Dig Endosc 2017;29:94–9.