Ascending cholangitis is an infectious syndrome of the biliary tree that can pose significant morbidity to affected patients if not recognized and treated appropriately. Accurate diagnosis and assessment of disease severity is essential to guide selection of antimicrobials, timing of biliary decompression, and selection of a decompression technique. This article reviews the current literature related to ascending cholangitis management, in conjunction with current international guidelines.

INTRODUCTION

Ascending cholangitis (AC) is an infection of the biliary tract. The normal biliary tree is near-sterile secondary to constant drainage, bacteriostatic bile salts, and mucosal immune mechanisms. Biliary obstruction disrupts these processes and causes elevated intraductal pressure with increased bile duct permeability, which permits endotoxin and bacterial translocation into lymphatic and portosystemic circulation. Biliary obstruction is most frequently caused by biliary stones, though there are many causes including mass effect of malignancy, benign and malignant strictures, parasites (e.g., Ascaris), and iatrogenic causes (e.g., biliary stenting, surgery).

The organisms implicated in AC originate from enteric flora, and cultures are usually polymicrobial. The most frequently isolated Gram-negative organisms are *E. coli* and *K. pneumoniae*, with *Enterococcus* species being the most common Gram-positive organism. Anaerobes, primarily *Bacteroides* and *Clostridium*, are relatively infrequently isolated. Accurate diagnosis and assessment of severity are fundamental to guide appropriate therapy. In addition to clinical support and resuscitation, antibiotic administration and biliary decompression represent the central components of AC management. This article presents current data pertinent to these areas.

Diagnosis of Ascending Cholangitis

The classic clinical characteristics of AC are fever, right-upper-quadrant (RUQ) abdominal pain, and jaundice (Charcot’s triad). More severe cases may present with hypotension and altered mental status (Reynold’s pentad). However, because few cases present with all of these features, standardized
dysfunction. Organ dysfunction is defined as the presence of cardiovascular dysfunction requiring intravenous dopamine >5µg/kg/min or any dose of norepinephrine, neurologic dysfunction (i.e., disturbance of consciousness), respiratory dysfunction (PaO₂/FiO₂ <300), renal dysfunction (oliguria or serum creatinine >2mg/dL), hepatic dysfunction (INR >1.5), or hematologic dysfunction (platelet count <100,000/µL). Grade II (moderate) cholangitis is defined by the presence of high fever (>39°C), leukocyte count <4,000/µL or >12,000/µL, advanced age (>75 years), or hypoalbuminemia (<70% lower limit of normal). Grade I (mild) cholangitis lacks the aforementioned criteria. A large study that stratified patients by severity grade found 5.1%, 2.6%, and 1.2% 30-day mortality in patients with Grade III, II, and I disease, respectively.

Antibiotics
Initiation of antibiotics should occur within one hour in cases of sepsis, or within six hours for all other cases. Prescribing adequate empiric coverage is becoming increasingly difficult due to antibiotic resistance patterns. Appropriate selection of empiric coverage is also made with consideration given to comorbidity, allergy, or other factors.

General recommendations for empiric coverage include intravenous treatment with a third-generation cephalosporin or a penicillin derivative/beta-lactamase inhibitor combination. TG18 and the Surgical Infection Society/Infectious Disease Society of America (SIS/IDSA) guidelines recommend to consult local antibiograms and administer alternative medications if community pathogen resistance exceeds 10-20%. Ampicillin-sulbactam and fluoroquinolones are not recommended for empiric use due to widespread E. coli resistance, but are frequently used in clinical practice. Antipseudomonal agents can be reserved for severe cases and healthcare-associated infection. Coverage of Enterococcus species with vancomycin is recommended in severe or healthcare-associated disease, or in immunocompromised patients. Anaerobic coverage with metronidazole is recommended in patients with a surgical history of biliary enteric

Severity Grading of Ascending Cholangitis
TG18 includes a severity grading system that has prognostic value and may help to guide appropriate intervention timing. Grade III (severe) cholangitis is manifested by evidence of organ dysfunction. Organ dysfunction is defined as the presence of cardiovascular dysfunction requiring intravenous dopamine >5µg/kg/min or any dose of norepinephrine, neurologic dysfunction (i.e., disturbance of consciousness), respiratory dysfunction (PaO₂/FiO₂ <300), renal dysfunction (oliguria or serum creatinine >2mg/dL), hepatic dysfunction (INR >1.5), or hematologic dysfunction (platelet count <100,000/µL). Grade II (moderate) cholangitis is defined by the presence of high fever (>39°C), leukocyte count <4,000/µL or >12,000/µL, advanced age (>75 years), or hypoalbuminemia (<70% lower limit of normal). Grade I (mild) cholangitis lacks the aforementioned criteria. A large study that stratified patients by severity grade found 5.1%, 2.6%, and 1.2% 30-day mortality in patients with Grade III, II, and I disease, respectively.

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Figure 1. Ascending Cholangitis Treated via ERCP

**Figure 1a.** Ampulla with purulent material visible at orifice

**Figure 1b.** Cannulation of the bile duct with a sphincterotome

**Figure 1c.** After cannulation, copious pus starts to drain spontaneously

**Figure 1d.** After sphincterotomy a large stone is extracted from the duct with a balloon catheter.

**Figure 1e.** A biliary stent is placed to further promote drainage of purulent contents. This stent was removed 2 weeks later.

**Figure 2.** Placement of a metal stent via ERCP in a patient with pancreatic cancer who developed cholangitis. Note purulent drainage.

(continued on page 36)
anastomosis or for general prophylaxis.\textsuperscript{4,10} This is due to a relative scarcity of anaerobe isolation in AC, and reports that anaerobic coverage for other indications does not improve outcomes.\textsuperscript{2,3,11,12,13}

Antibiotic treatment can be adjusted based on patient response and pathogen susceptibility data. TG18 and SIS/IDSA guidelines recommend a total of 4-7 days of therapy after source control is obtained, obstruction removed, and assuming absence of local complications (e.g., liver abscess).\textsuperscript{4,10} In the presence of Gram-positive bacteremia, 2 weeks of therapy is recommended.\textsuperscript{4}

### Timing of Biliary Decompression

Several studies, mostly related to ERCP, have assessed clinical outcomes in AC patients with regards to time-to-intervention but a clear consensus has not been well defined. Based on findings of improved mortality in patients with Grade II (moderate) disease that received biliary drainage within 48 hours, TG18 generally recommends decompression within 48 hours in patients.\textsuperscript{5,7} In practice, however, sometimes patients are too unstable to undergo a drainage procedure and require more time before biliary decompression. The recommendation for 48 hours as a general cutoff is supported by investigators who found worse outcomes (persistent organ failure, longer hospitalization, relapse, or mortality) in patients with further delayed decompression.\textsuperscript{14, 15, 16, 17, 18}

In contrast, other studies favor decompression within 24 hours, mostly on the basis of shorter hospitalization.\textsuperscript{16,17,19,20,21} A recent study describes outpatient management of AC after endoscopic drainage, suggesting that early intervention in mild to moderate disease can prevent hospitalization altogether.\textsuperscript{22} Patients with septic shock or critical illness appear to warrant early decompression after appropriate resuscitation, with significantly improved mortality reported when decompressed before 12 or 24 hours, respectively.\textsuperscript{23, 24}

### Biliary Drainage Techniques

Biliary drainage is recommended for all cases of AC, irrespective of severity.\textsuperscript{25} Techniques for biliary decompression are broadly categorized into endoscopic, percutaneous, and surgical.

#### Endoscopic Biliary Drainage

ERCP biliary decompression by direct cannulation of the major duodenal papilla is the gold standard for acute cholangitis.\textsuperscript{25,26} This is due to high success rates, minimally invasive nature, and fewer adverse events compared to percutaneous or surgical procedures.\textsuperscript{26,27,28,29} Disadvantages, however, include need for sedation.\textsuperscript{30} Endoscopic duct clearance by sphincterotomy, balloon extraction, and/or endoscopic stenting for strictures is performed as needed. Patients in whom stone extraction cannot be performed can simply undergo stent placement. An additional adjunctive technique is direct cholangioscopy with lithotripsy. Nasobiliary drains are rarely used in modern practice.\textsuperscript{26,27,31} Balloon-assisted enteroscopy ERCP (BE-ERCP) is recommended in cases of altered postoperative anatomy.\textsuperscript{25}

Endoscopic ultrasound biliary drainage (EUS-BD) is a relatively new and developing technique, though current data are largely related to obstructive jaundice generally, and not specific to cholangitis. Several studies indicate that EUS-BD, in the hands of experienced endoscopists, is an effective alternative after failed ERCP and may outperform percutaneous drainage.\textsuperscript{32,33,34,35,36,37,38} EUS-BD may also represent a feasible approach in patients with surgically altered anatomy.\textsuperscript{39} Research into the optimal tools and techniques to perform EUS-BD is ongoing.

#### Percutaneous Biliary Drainage

Percutaneous techniques include percutaneous transhepatic biliary drainage (PTBD) and percutaneous cholecystostomy (PC). PTBD is currently the recommended alternative to traditional ERCP drainage and may be required when endoscopy is unavailable or contraindicated (e.g., unusual anatomy) or after failed ERCP.\textsuperscript{25} PTBD usually involves local anesthesia, puncture of an intrahepatic duct with a fine needle under US or fluoroscopy, and placement of a drain. Successful needle placement requires ample intrahepatic ductal dilatation.\textsuperscript{40} PTBD is second-line to ERCP due to invasiveness, common requirement for additional procedures, and higher rate of adverse events.\textsuperscript{25,29,37} PTBD is primarily used to provide biliary drainage, whereas stone
removal is much less commonly performed via this route. Patients with stones and AC often require ERCP at a later time to remove the stones from the biliary tree, usually via sphincterotomy and balloon/basket extraction. PC, though rarely used for this indication, can be a useful alternative to PTBD, especially if intrahepatic duct dilation is insufficient to allow a successful transhepatic approach.41,42

**Surgical Biliary Drainage**

Surgical drainage of the biliary ducts is generally thought of as the last option after unsuccessful endoscopic or percutaneous intervention.25 This is primarily due to high success rates of less invasive techniques and observations of higher mortality compared to other less invasive methods.1,2,5,28

**CONCLUSION**

Ascending cholangitis is a treatable illness with practice guidelines in place to assist in guiding diagnosis, severity grading, antibiotic selection, and therapeutic intervention. Use of the diagnostic and severity grading criteria reliably identifies patients and provides prognostic information. Antimicrobial selection is based on community isolate resistance patterns. ERCP remains the most common procedure selected for biliary drainage. PTBD is an acceptable alternative, with EUS-BD gaining acceptance as experience broadens.

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