

# ERCP endoscopic minimally invasive treatment of acute suppurative obstructive cholangitis: A study of 47 patients

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**Abstract.** The primary objective of the present study was to investigate the efficacy and safety of endoscopic therapy for acute obstructive suppurative cholangitis (AOSC) in patients with different underlying conditions. The present study comprised 47 patients diagnosed with AOSC, with a mean age of 70±14 years. Minimally invasive endoscopic treatments, including endoscopic duodenal papillary sphincterotomy, endoscopic duodenal nasobiliary drainage and/or placement of an endobiliary duct stent drainage tube, were performed. Variations in the levels of the white blood cell count, liver function, procalcitonin (PCT) and carbohydrate antigen-199 (CA199) were examined, compared and evaluated both prior to and following endoscopic retrograde cholangiopancreatography (ERCP). Among the 47 patients, 45 had a high fever, although their body temperature returned to normal after 7 days of ERCP treatment. The infection was difficult to control completely in two cases, including one case of biliary anastomosis secondary tumor with stenosis and AOSC and another case of an elderly patient with multiple choledocholithiasis complicated with sepsis. Within 7 days following treatment, the abdominal pain was resolved in 27 patients and jaundice subsided in 29 patients. On the 7th day after endoscopic treatment, the blood leukocyte, liver function, PCT and CA-199 parameters of all patients were significantly improved compared with those at admission. A total of 35 bile cultures yielded positive results, with *Escherichia coli* accounting for 11 cases (31.4%), *Klebsiella pneumoniae* accounting for 7 cases (20%), *Pseudomonas aeruginosa* accounting for 5 cases (14.3%), *Enterococcus faecus* accounting for 4 cases (11.4%) and other strains making up the remaining 17 cases. No

serious complications were encountered with these patients, such as perforation, bleeding, severe pancreatitis or mortality, following ERCP. In conclusion, ERCP has been shown to be a safe and effective minimally invasive treatment method for elderly patients with AOSC, yielding a high rate of success.

## Introduction

Acute obstructive suppurative cholangitis (AOSC) is a severe infectious disease characterized by acute suppurative infection and pus in the biliary system that is caused by biliary obstruction, which results in hepatobiliary system damage. This condition leads to the release of a large quantity of bacteria and toxins into the bloodstream, causing biliary hypertension and systemic damage to multiple organs. AOSC is considered to be a serious form of acute cholangitis (AC) (1). It is the predominant cause of mortality in patients with benign biliary disease. The clinical presentation of AOSC commonly includes abdominal pain, fever, jaundice and in severe cases it may be accompanied by septic shock characterized by shock and symptoms of nervous system suppression. AOSC can lead to multiple organ failure if not promptly detected and treated, resulting in a morbidity and mortality rate ranging from 13-88% (2). There are numerous factors associated with biliary tract infections, including bacterial infections, gallstones and trauma. When there are gallstones in the biliary tract, these can lead to biliary obstruction and, subsequently, enteric pathogens can retrogradely migrate into the bile duct, causing biliary tract infections. Systemic infections derived from bacteria in the bloodstream may also enter the bile duct. Moreover, in cases of severe trauma, burns or shock, the biliary system is prone to local vascular disturbances, which can also result in biliary tract infections (3).

In recent years, significant and rapid advances have been made in terms of the development of minimally invasive endoscopic intervention techniques. Endoscopic retrograde cholangiopancreatography (ERCP) is used more and more often in the clinic for the treatment of AOSC, due to its advantages of simple operation and high safety. Especially in Europe and the United States, with the development of endoscopic technology, the safety and effectiveness of ERCP have been widely studied and established in the treatment of biliary tract diseases (4,5). However, current clinical studies on ERCP in

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China mainly focus on patients with AC and there is still no conclusion on the efficacy and safety of ERCP in the treatment of AOSC patients, especially elderly patients (2,6). The present study therefore investigated an effective minimally invasive treatment approach that holds promise for improving treatment outcomes for patients with AOSC, with the goals of alleviating suffering and reducing complications, thereby offering a beneficial therapeutic option for both physicians and patients. These findings should prove to be beneficial for enhancing quality of life of patients and optimizing the utilization of medical resources.

## Materials and methods

**AOSC diagnosis.** The clinical data of 47 patients with AOSC treated in Hangzhou First People's Hospital between March 2021 and March 2022 were retrospectively analyzed. The diagnosis of AOSC met with the diagnostic criteria of the 2018 Tokyo Guidelines (TG 18) for severe cholangitis (grade III) (1). The inclusion criteria included the following: i) Age above 18 years; and ii) meeting the diagnosis of AOSC. The exclusion criteria included the following: i) Complicated blood system disease and severe renal failure; ii) cardiovascular system dysfunction, consciousness disorder, respiratory disorder, liver dysfunction, blood system dysfunction and renal dysfunction caused by non-AOSC; iii) non-AOSC septic shock; and iv) incomplete clinical data.

In accordance with TG 18, the diagnosis of AC was determined on the basis of systemic inflammation, cholestasis and imaging evidence, as shown in Table I. In addition, once the diagnosis was confirmed the AC was categorized further according to its grade, i.e., grade I represented mild AC, grade II was moderate AC, and grade III was severe AC, as shown in Table II. All patients in this group met the inclusion criteria for AC grade III.

Of the 47 included AOSC patients, 26 were males and 21 females. Their ages ranged from 31-93 years, with a mean age of  $70 \pm 14$  years. Among them, 14 patients had Charcot triad, shock and nervous central system inhibition, whereas the remaining 33 had 2-3 manifestations of Charcot triad. Among the 14 patients with Charcot triad, one patient developed coma, whereas 13 patients developed shock and were treated with vasoactive drugs [liver dysfunction: Prothrombin time-international normalized ratio (PT-INR)  $>1.5$  in nine cases; renal dysfunction: Oliguria, blood creatine (Cr)  $>2$  mg/dl in two cases; blood system dysfunction: Platelets (PLT)  $<100 \times 10^9/l$  in two cases (see Tables III and IV)]. Of the 47 patients with AOSC, 26 had common bile duct stones. A total of 43 patients had various underlying diseases, including five with bile duct malignant tumors, 13 with pancreatic malignant tumors, nine with sepsis, three with gastric malignant tumors and five with a personal history of subtotal gastrectomy (three were Billroth II, one was Billroth I and one was Roux-en-Y). There were a total of 16 patients diagnosed with hypertension, 17 patients diagnosed with hypoproteinemia, eight patients diagnosed with diabetes, six patients diagnosed with coronary heart disease, and two patients with a history of cerebral infarction. Additionally, there was one patient who was 16 weeks pregnant at the time of diagnosis. Further information is provided in Table V.

**Treatment.** All patients were given a comprehensive treatment, including control of inflammation and infection, improvement of microcirculation and rehydration capacity, maintenance of the internal environment stability and systemic support therapy. After admission, various antibiotics tailored to the patient's individual condition were empirically administered. The most commonly used antibiotic regimens were as follows: Piperacillin/Tazobactam administered intravenously at 4.5 g every 8 h for 7 days; Meropenem given intravenously at 1 g every 8 h for 7 days; Cefoperazone administered intravenously at 2 g every 12 h for 7 days; Vancomycin given intravenously at 1 g every 12 h for 7 days. Adjustments in dosage and timing were made under specific circumstances. Simultaneously, somatostatin was administered to prevent post-ERCP pancreatitis. The primary method involved a pre-ERCP intravenous injection of 250  $\mu$ g followed by a post-ERCP intravenous infusion of 250  $\mu$ g/h for at least 11 h. For patients with septic shock, isotonic balanced crystalloid fluids were administered for fluid resuscitation. In fasting patients, fluid supplementation was at 40 ml/kg, comprising daily physiological requirements of NaCl at 4.5 g, KCl at 3 g, along with necessary vitamins and trace elements to maintain water-electrolyte balance. Fluid replacement amounts were adjusted based on individual patient needs. Corticosteroids for anti-inflammatory effects, vasopressors for blood pressure elevation, oxygen therapy, gastric protection and other symptomatic supportive treatments were provided when necessary. ERCP treatment was performed for the patients within 24-48 h. The patients were routinely administered 10 mg nalbuphyl hydrochloride 40 mg drotaverine and 2 mg midazolam (injected intravenously via a needle), accompanied by electrocardiogram monitoring, inhalation of oxygen and adopted intensive care. The duodenal papilla is found at the descending part of the duodenum. The guide wire was inserted into the common bile duct using an incision knife. After performing cholangiography, the purulent bile and contrast agent were extracted in time to reduce the pressure of the biliary tract. Endoscopic sphincterotomy (EST), endoscopic nasobiliary drainage (ENBD) and/or endoscopic retrograde biliary drainage (ERBD) were performed according to the results of angiography. All patients were first treated with ENBD or EST + ENBD/ERBD to relieve biliary obstruction. EST plus basket removal was performed for patients with simple common bile duct stones, or stones with duodenal papilla and ampulla; alternatively, after having detected systemic symptoms for patients with large or multiple stones, who were unable to tolerate stone removal surgery for an extended period, mechanical lithotripsy and basket removal was performed; if neither of these treatments were feasible, stent implantation was performed instead for patients for whom stone removal was impossible, or who had bile duct cancer, including surgery or long-term drainage treatment of ERBD following remission (Table VI).

**Statistical analysis.** All the data were analyzed using SPSS26.0 statistical software (IBM Corp.). Measurement data are expressed as mean  $\pm$  standard deviation and a paired t-test was used for making comparisons before and after the various treatments.  $P < 0.05$  was considered to indicate a statistically significant difference.

Table I. Diagnostic criteria for AC.

Diagnostic criterion	Content
A. Systemic inflammation	1. T >38°C and/or chills
B. Cholestasis	2. WBC <4x10 <sup>9</sup> /l or >10x10 <sup>9</sup> /l, and CRP ≥1 mg/dl
	1. TB ≥34 μmol/l
C. Imaging evidence	2. ALP, GGT, AST, ALT >1.5x upper limit of normal
	1. Biliary dilation
	2. Imaging findings (stenosis, stones, stents)

For a suspected diagnosis, the patient needed to meet the following criteria: One of the terms of A, plus one of the terms of B or one of the terms of C. For an exact diagnosis, one term for each of A, B and C was required. T, Temperature; WBC, white blood cells; CRP, C-reactive protein; TB, total bilirubin; ALP, alkaline phosphatase; GGT, γ-glutamyltransferase; AST, aspartate aminotransferase; ALT, alanine aminotransferase.

Table II. Classification criteria of AC.

Grading standard	Content
Mild AC (grade I)	No diagnostic criteria for either grade II or grade III
Moderate AC (grade II; at least two items were met)	1. WBC >1.2x10 <sup>10</sup> /l or <4x10 <sup>9</sup> /l
	2. T ≥39°C
	3. Age ≥75 years old
	4. TB ≥5 mg/dl
	5. ALB <0.7x lower limit of normal
Severe grade (grade III; (at least one item)	1. Cardiovascular system dysfunction: The need for dopamine 5 μg/kg <sup>1</sup> min <sup>-1</sup> , or use of hypotension maintained by any dose of noradrenaline
	2. Nervous system dysfunction: A disorder of consciousness
	3. Respiratory system dysfunction: PaO <sub>2</sub> /FiO <sub>2</sub> <300 mmHg
	4. Liver dysfunction: PT-INR >1.5
	5. Renal dysfunction: Oliguria, blood Cr >2 mg/dl
	6. Hematological system dysfunction: PLT <100x10 <sup>9</sup> /l

AC, acute cholangitis; WBC, white blood cells; T, Temperature; TB, total bilirubin; ALB, albumin; PaO<sub>2</sub>, partial pressure of oxygen; FiO<sub>2</sub>, oxygen absorption concentration; PT-INR, prothrombin time-international normalized ratio; PLT, platelets.

## Results

Charcot's triad, shock and central nervous system depression were observed in 14 of 47 patients with AOSC. A total of 33 patients were found to have between two and four features of Charcot's pentalogy, including one patient with coma. After having performed clinical and endoscopic minimally invasive treatments, purulent bile outflow was observed in 47 patients with AOSC (Figs. 1 and 2), including 41 cases of common bile duct stones (Figs. 3 and 4). The end-stage tumors included bile duct malignancy in four cases and pancreatic cancer in two cases and the clinical symptoms were significantly improved. In this group, on day 7 after endoscopic treatment, blood inflammatory indexes and liver function were found to be significantly improved the most of the group compared with the measured values at admission: The level of PCT decreased from 8.95±15.26 to 0.42±0.37 ng/ml, the level of CA-199 was reduced from 635.04±907.76 to 164.68±475.78 kU/l and that of ALT was

decreased from 190.96±105.91 to 50.56±20.33 μmol/l. The value of the direct bilirubin test was decreased from 62.21±36.23 to 30.64±15.40 μmol/l and these differences were found to be statistically significant (P<0.05 or P<0.01), as shown in Table VII. Out of the total of 47 patients, 16 cases involved the use of ERCP and ENBD, 17 cases included the use of ERCP, EST and ENBD, 14 cases included the use of ERCP and ERBD, and 28 cases included the use of ERCP for stone extraction. During ERCP examination, purulent bile was discharged from the bile duct. A total of three patients underwent secondary ERCP (Table VI). Out of the total cases, 35 (74.5%) showed positive results in the bile culture. The predominant bacterium species identified were Gram-negative bacteria, with *Escherichia coli* being the most frequently observed in 11 instances (31.4%). *Klebsiella pneumoniae* was detected in seven instances, accounting for 20% of the cases. *Pseudomonas faecium* was identified in five cases (14.3%), *Enterococcus faecium* in four cases (11.4%), *Pseudomonas aeruginosa* in four cases

Table III. Organ or system dysfunction occurred in 47 patients with AOSC.

Organ or system dysfunction	n (%)
Cardiovascular system dysfunction	15 (31.9)
Nervous system dysfunction	21 (44.7)
Respiratory system dysfunction	14 (29.8)
Dysfunction of renal function	2 (4.3)
Hepatic dysfunction	9 (19.1)
Dysfunction of the blood system	2 (4.3)
AOSC, acute obstructive suppurative cholangitis.	

Table IV. Main clinical manifestations of 47 patients with AOSC.

Clinical manifestation	n (%)
Celialgia	31 (66.0)
Fever	32 (68.1)
Jaundice	29 (61.7)
A disorder of consciousness <sup>a</sup>	14 (29.8)
Shock	13 (27.7)
Charcot's triad	33 (70.2)
Renault's pentalogy	14 (29.8)

<sup>a</sup>The main neurological symptoms were apathy, lethargy, confusion and even coma; when combined with shock, it can also be manifested as agitation, delirium, etc., which are collectively referred to as disturbance of consciousness in the article. AOSC, acute obstructive suppurative cholangitis.

(11.4%), *Staphylococcus aureus* in three cases (8.6%) and *Enterococcus casseliflavus* in two cases (5.7%). There was one case of both *E. faecium* and *E. coli* (2.9%), two cases of *K. pneumoniae* and *Candida albicans* (5.7%), one case of *E. faecalis*, *K. pneumoniae* and *Enterococcus casseliflavus* (2.9%), one case of *Aeromonas hydrophila* (strain found in guinea pigs) and *E. faecalis* (2.9%), and two cases of *E. faecalis* and *E. coli* (5.7%). There were two cases of *Citrobacter freundii* and *Stenotrophomonas maltophilia*, accounting for 5.7% of the cases. Additionally, there was one case of *E. faecium* and *C. albicans*, which made up 2.9% of the cases. Within 1 to 7 days after treatment, the high fever of 45 of the patients disappeared and their body temperature returned to normal. It was difficult to completely control the infection in the remaining two patients after 7 days of ERCP treatment. One of these patients was an elderly patient ( $\geq 80$  years old) with a secondary tumor and stenosis of bilioenteric anastomosis complicated with AOSC. Even though the infection was not entirely treated while the patient was in the hospital, the family members requested that the patient be discharged. Another patient with multiple common bile duct stones complicated with sepsis underwent some improvements after a second line of ERCP was

Table V. Conditions and complications of the 47 patients.

Condition or characteristic	No. of patients (%, if applicable)
Sex	
Male	26 (55.3)
Female	21 (44.7)
Age (years)	70 $\pm$ 14
Cholelithiasis	26 (55.3)
History of bile duct malignancy	5 (10.6)
History of pancreatic malignancy	13 (27.7)
History of gastric malignancy	3 (6.4)
History of major gastrectomy	
Billroth II surgery	3 (6.4)
Billroth I surgery	1 (2.1)
Roux-en-Y surgery	1 (2.1)
Hypertension	16 (34)
Coronary heart disease	6 (12.8)
Diabetes mellitus	8 (17)
Hypoproteinemia	17 (36.2)
Sepsis	9 (19.1)
Cerebral infarction	2 (4.3)
Pregnant	1 (2.1)

Table VI. The different types of treatment for surgery performed in the present study.

Treatment operation	[Number/percentages of cases (%)]
ERCP + ENBD	11 (23.4)
ERCP + ERBD	3 (6.4)
ERCP + ENBD + ERBD	6 (12.8)
ERCP + EST + ENBD	18 (38.3)
ERCP + EST + ERBD	1 (2.1)
ERCP + EST + ERBD + ENBD	4 (8.5)
ERCP + EST + ERPD + ENBD	3 (6.4)
ERCP + EST + ERPD + ERBD	1 (2.1)
ERCP + stone removal	28 (59.6)
Secondary line of ERCP	3 (6.4)

ERCP, endoscopic retrograde cholangiopancreatography; ENBD, endoscopic nasobiliary drainage; EST, endoscopic sphincterotomy; ERBD, endoscopic retrograde biliary drainage.

performed and was discharged. Within 7 days of treatment, the abdominal pain of 27 patients, and jaundice experienced by 29 patients, were resolved. Hyperamylasemia or acute pancreatitis (mild) occurred in three patients following ERCP, which itself improved after conservative treatments. The average hospital stay per patient was 11.9 $\pm$ 4.6 days. Finally, no severe complications, including perforation, bleeding, severe pancreatitis or mortality, were identified for any of the patients.



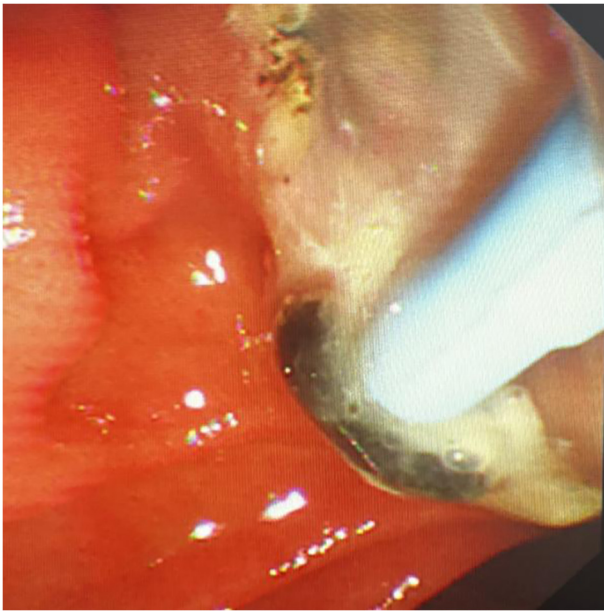


Figure 1. Purulent bile and black bile duct stones.

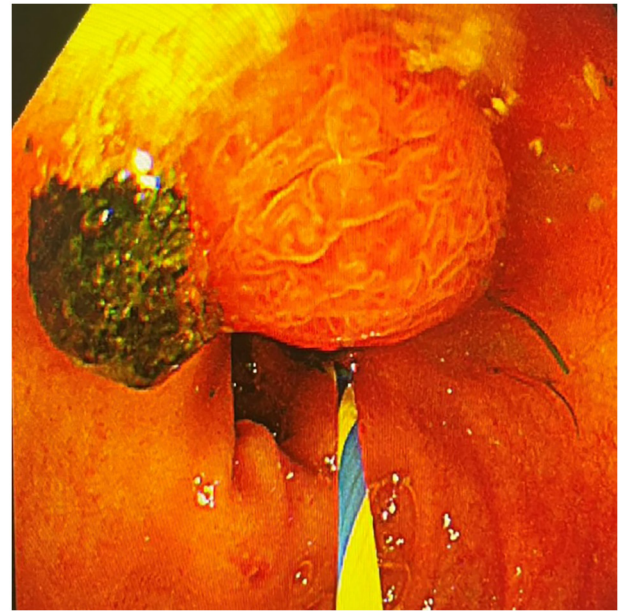


Figure 3. Stone impaction on duodenal papilla.

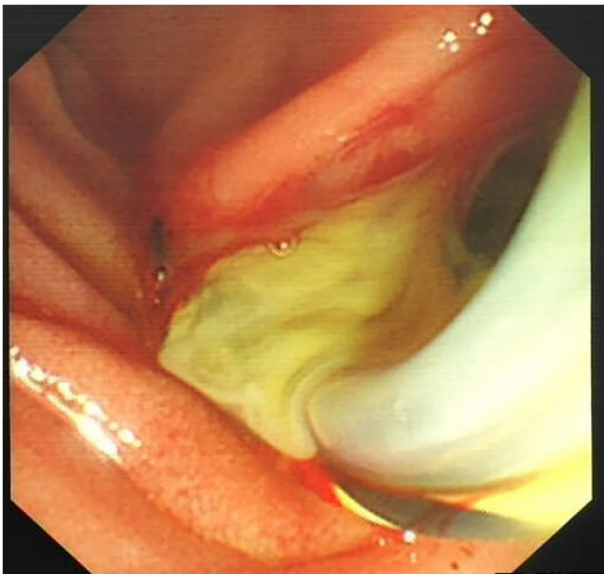


Figure 2. Large amount of purulent bile.

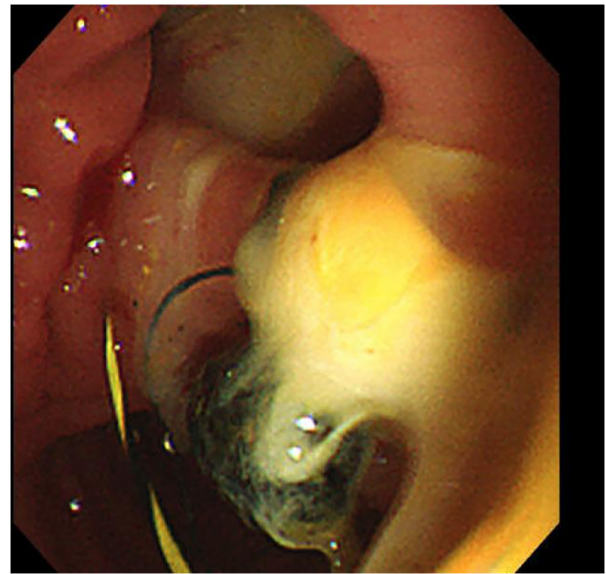


Figure 4. Removal of a black stone with a large gush of purulent bile.

## Discussion

AOSC is one of the most common biliary tract infections encountered in clinical practice and has the characteristics of rapid onset and rapid progress. If it is not diagnosed and treated in time, it may pose a serious threat to the lives of patients (7), especially those patients who have multiple comorbidities, including coronary heart disease, hypertension, diabetes, pulmonary heart disease, liver cirrhosis, renal insufficiency and a personal history of cerebral infarction. AOSC is characterized by severe biliary tract infection and empyema on the basis of biliary obstruction, resulting in biliary hypertension, the leakage of bacterial endotoxins into the blood and severe infectious diseases, including multiple organ damage. The initial clinical manifestations of AOSC

are mild. Subsequently, as the pressure in the bile duct increases, the septic substances in the bile duct flow back into the hepatic bloodstream, leading to hyperbilirubinemia and sepsis. This may result in symptoms such as chilliness, high fever, abdominal pain, jaundice, shock and mental changes (all symptoms of Reynolds pentalogy).

Biliary obstruction and bile infection are the two major factors leading to the onset of AC. There are numerous causes of biliary obstruction, the most common one being biliary stone obstruction, as mediated by bile duct stones and gallstones. Compression by malignant tumors of the biliary system, liver and pancreatic head can also cause biliary obstruction and, if accompanied by severe infection, this may also lead to cholangitis (7). In a healthy state, there are no bacteria present in the bile. The biliary tract, with its

Table VII. Comparative analyses of hemograms, blood biochemistry, PCT and CA199 results prior to and following ERCP (n=47; mean  $\pm$  standard deviation).

Time of assessment	Blood WBC (x10 <sup>9</sup> /l)	ALT ( $\mu$ mol/l)	AST ( $\mu$ mol/l)	TBil ( $\mu$ mol/l)	DBil ( $\mu$ mol/l)	ALP (U/l)	r-GT (U/l)	CA199 (kU/l)	PCT (ng/ml)
Before ERCP	16.47 $\pm$ 4.71	190.96 $\pm$ 105.91	135.35 $\pm$ 80.83	73.57 $\pm$ 39.13	62.21 $\pm$ 36.23	253.48 $\pm$ 150.77	312.32 $\pm$ 178.34	635.04 $\pm$ 907.76	8.95 $\pm$ 15.26
One week after ERCP	6.35 $\pm$ 2.94 <sup>a</sup>	50.56 $\pm$ 20.33 <sup>a</sup>	47.19 $\pm$ 16.11 <sup>b</sup>	32.85 $\pm$ 15.54 <sup>a</sup>	30.64 $\pm$ 15.40 <sup>b</sup>	183.10 $\pm$ 90.61 <sup>a</sup>	192.44 $\pm$ 91.36 <sup>b</sup>	164.68 $\pm$ 475.78 <sup>b</sup>	0.42 $\pm$ 0.37 <sup>a</sup>

Compared with those recorded at admission of the patients, the differences in the values were found to be significant (<sup>a</sup>P<0.01; <sup>b</sup>P<0.05). PCT, procalcitonin; CA199, carbohydrate antigen-199; ERCP, endoscopic retrograde cholangiopancreatography; WBC, white blood cells; ALT, alanine aminotransferase; AST, aspartate aminotransferase; TBil, total bilirubin; DBil, direct bilirubin; ALP, alkaline phosphatase; r-GT, glutamyltransferase.

tubular structure, is not conducive to bacterial presence. However, due to its anatomical location, structure and physiological characteristics, there is a high risk of infection when stone diseases such as choledocholithiasis, cholelithiasis and biliary ascariasis occur. These conditions can also disrupt the circulatory system of the body, affect bile excretion and lead to bacterial growth, resulting in infections (8). The biliary tract is connected to the intestinal tract, and retrograde infection from intestinal bacteria is the primary pathogenic cause of biliary tract infections. Therefore, the isolated pathogens from bile are generally consistent with the intestinal bacterial profile. The Gram-positive bacteria we identified to be present were mainly *Enterococcus*, whereas Gram-negative bacterial rods mainly included *Escherichia coli*, *Klebsiella pneumoniae* and *Pseudomonas aeruginosa*, findings that were in agreement with the those of a similar study (9). In some patients, the bacteria that remain in the gallbladder due to recurrent gallstone attacks are able to alter both the gallbladder's environment and the physicochemical properties of bile. This alteration makes it conducive for bacteria to proliferate within the biliary tract (10). Certain independent risk factors, including diabetes, lead to deficiencies in the mechanisms of immune defense in patients. In addition, high levels of blood sugar negatively affect the functions of neutrophils and T-lymphocytes, including their impaired migration, phagocytosis, intracellular killing and chemotaxis (11,12). This, in turn, leads to microvascular damage, compromising local biliary circulation, leading to a reduction in blood supply, worsening metabolic disorders and delaying the response to infections, allowing the infection to spread. Additionally, it causes autonomic nervous system dysregulation, resulting in dysfunction of the Oddi sphincter and gallbladder contraction and relaxation, leading to increased resting tension in the fasting state, the promotion of bile stasis, and increasing the risk of biliary tract infection (13). In recent years, some researchers have also proposed that the development of AC may be associated with an increase in vagal nerve excitability (11-13). However, due to the relatively limited research in this area, further investigations are required for an improved understanding of the role of the vagal nerve in AC.

Previous studies have also shown that the initial basic factor for its occurrence is bile duct obstruction, which, as explained above, causes an increase in intraluminal pressure, leads to retrograde bacteria from the biliary tract into the blood and biliary drainage disorders lead to infection. If there is no biliary obstruction, even simple injection of bacteria into the gallbladder or biliary tract will not cause biliary tract infection. Ligation of the cystic duct or common bile duct at the same time, resulting in cholestasis or obstruction of the blood supply of the biliary tract, will induce severe infection, and this has been borne out in the clinical results of a couple of previously published studies (14,15). In the present group of cases, the clinical manifestations of patients were not completely consistent with bile duct empyema (i.e., the most severe complication of acute cholangitis). Certain patients exhibited atypical clinical symptoms, although their blood tests revealed significantly elevated inflammatory markers, indicating the presence of severe sepsis. ERCP aspiration of bile revealed a large amount of pus in the bile duct, which is mainly associated with the delayed response of elderly patients. Collectively,

the results suggested that the culture of aspirated bile is helpful to guide clinical medication according to the drug-sensitivity test, and to promote the recovery of patients.

Elderly patients, especially, are subjected to weakened levels of immunity; moreover, they are often afflicted with multiple diseases, and their condition occasionally deteriorates rapidly, leading to mortality. Qin *et al* (16) found that advanced age is an independent risk factor for AOSC, and that the occurrence and development of sepsis was positively correlated with an advanced age. One of the explanations that may account for this is that early manifestations of patients are not typically identified, and Charcot's triad is rarely encountered in the early stage (17). It is often necessary to combine the patient's medical history, imaging examination and various laboratory indicators to evaluate the severity of AC in patients.

Previous studies have also demonstrated that early intervention with AOSC is crucial in terms of alleviating biliary obstruction and facilitating the drainage of infected bile within a 24-h timeframe. Failure to do so can result in the development of severe infections resulting from biliary obstruction and cholestasis. An elevated pressure in the bile duct can cause the contaminated bile to flow back into the bloodstream, leading to the onset of sepsis, shock, and even mortality (18,19). It has also been reported that hypoproteinemia is one of the factors that affects the poor prognosis of patients with sepsis (20). In severe infection, due to the increases in body catabolism and capillary permeability, the level of albumin (ALB) may be decreased. In addition, ischemia, hypoxia and oxidative damage may occur in severe infection and ALB is the main target of extracellular oxidative stress (21). Schneider *et al* (22) and Gravito-Soares *et al* (23) found that ALB at a concentration of 30 g/dl was an important risk predictor of in-hospital mortality in patients with AC. Cozma *et al* (13) showed that ALB is a protective factor for severe cholangitis, and the lower the level of ALB, the higher the incidence of severe cholangitis. There were 19 very elderly patients ( $\geq 80$  years old) in the present group of cases, and 15 patients had hypoproteinemia. Among the 15 patients with hypoproteinemia, nine patients developed sepsis and three patients exhibited poor therapeutic effects following the first ERCP, although their condition improved significantly after the second ERCP. The explanation for this was closely associated with obstruction drainage after ERCP. Therefore, the key to the treatment of AOSC is to relieve the biliary obstruction in a timely manner, effectively reducing the biliary pressure, and then to drain the purulent bile, block the liver-intestinal circulation of bilirubin so as to reduce the level of jaundice and relieve its injurious symptoms and gradually restore the function of the damaged bilirubin transporters and microvilli. Conjugated bilirubin in the blood is secreted into the biliary system and, as a consequence, the jaundice is gradually decreased and its symptoms are improved (24). Implementing this strategy should enable the body's recovery. In addition to the improvements in symptoms, the parameters of blood routine, TBil, PCT and CA199 were found to be significantly decreased at 3 days after operation. Previous studies (25,26) demonstrated that the success rate of ENBD treatment for AOSC was 97%, which marks a significant improvement compared with that of surgical drainage. ERCP minimally invasive endoscopic treatment can therefore be used as the first-choice treatment for AOSC (27-29).

PCT is a type of glycoprotein that lacks hormonal activity. In recent years, it has been found that PCT is closely associated with deep infections, such as liver abscess and sepsis. Bacterial infection can induce the production of inflammatory factors throughout the body, and initiate the body's neuro-endocrine cells, macrophages, monocytes and other cells to secrete PCT in large quantities, such that the serum PCT level is increased (30). In addition, a previous study found that PCT detection is not affected by steroid drugs or autoimmune status (including immune diseases, HIV and liver cirrhosis) and PCT is a specific indicator for the diagnosis of bacterial infection (30). An increased level of PCT detection is often indicative of a deep infection and it is also used to distinguish bacterial infection from viral infection in clinical practice. The results obtained in the present study showed that the serum PCT level in patients with AOSC was increased, although this was decreased significantly one week after ERCP in the majority of the patients. A previous study reported that the serum PCT level in patients with AOSC changed with the severity of cholangitis, although this tended to return to normal after the inflammation had been controlled (31). Following ERCP, the peripheral blood white blood cells, ALT, bilirubin and other indicators of the patients were found to be significantly decreased, the inflammatory reaction in the body was significantly controlled and so the liver function was restored and the PCT level was also significantly improved. These findings were consistent with those reported in a previous study (32). In that study, with patients with severe infection caused by bile duct obstruction, their levels of white blood cells, liver function indexes and PCT were often increased significantly, although the majority of these indexes improved significantly after the obstruction had been relieved.

CA199 is a carbohydrate antigen that has been confirmed to be associated with tumors. A previous study confirmed that CA199 is able to regulate the migration and adhesion of white blood cells in the inflammatory area, resulting in a leukocyte aggregation reaction (33). Although CA199 is a tumor marker, its expression is closely associated with biliopancreatic duct obstruction, which has also been confirmed by clinical observations. Zeng *et al* (34) found that the levels of CA199 and PCT were increased in patients with severe AC. Although abnormal changes in the level of CA199 do occur in malignant biliopancreatic tumors, Zhang *et al* (35) demonstrated that an increase in CA199 may be associated with biliopancreatic duct obstruction. When AC occurs, the serum concentration of CA199 is significantly increased, and this increase is positively correlated with the severity of cholangitis, which can therefore be used as a predictor of AC (35); a finding that was consistent with the results of the present study. It has also been shown that CA199 has certain reference value for the diagnosis of AC when it reaches a level of 52.50 kU/l (36). In the present study, there were two cases where the CA199 values were  $>12,000$  kU/l. Following examination, it was found that there were no tumor lesions, and the level of CA199 returned to normal after ERCP. It was recently reported by Chen *et al* (37) that CA199 is associated with calculous cholecystitis. The level of CA199 was found to be elevated in certain patients with calculous cholecystitis but without tumor disease, whereas the level of CA199 in these patients returned to normal following cholecystectomy. Therefore, an elevated



level of CA199 is not completely representative of neoplastic diseases, and it needs to be differentiated from other types of obstructive inflammatory disease.

In conclusion, the present study showed that, compared with traditional surgical drainage methods such as common bile duct incision, decompression and drainage of pus or cholecystostomy, endoscopic minimally invasive interventional therapy has a high success rate and a low incidence of postoperative bleeding, cholangitis and bile leakage (38). It can effectively relieve bile duct obstruction, reduce the difficulty of surgical clinical treatment to a certain extent, and improve the quality of life of patients. With the continuing development of endoscopic minimally invasive treatment technologies, as a treatment method, the endoscopic treatment of AOSC has the advantages of being rapid, effective, associated with lower levels of trauma, and it enables the rapid prognosis of patients, aspects that are in line with the developmental direction of modern medical therapies.

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### Availability of data and materials

The data generated in the present study may be requested from the corresponding author upon reasonable request.

### Authors' contributions

ZF and JL confirm the authenticity of all the raw data. ZF was the guarantor on the present study, and designed, planned and implemented the study. JL collected data, analyzed the data and interpreted patient data concerning AOSC, completed data statistics and was a major contributor to the manuscript. Both authors read and approved the final manuscript.

### Ethics approval and consent to participate

As a retrospective study, the present study was approved by the ethics committee of Hangzhou First People's Hospital (Hangzhou, China; approval no. 2021174-01). The study was performed in accordance with the 1964 Declaration of Helsinki and later amendments. Written informed consent was obtained from all the participants prior to their enrollment of the present study.

### Patient consent for publication

Not applicable.

### Competing interests

The authors declare that they have no competing interests.

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