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Original Article

Treatment of acute cholangitis of severe type with different modes of biliary drainage under X-ray-free endoscopy: a single center, retrospective study

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Abstract: To compare the efficacy of X-ray-free endoscopic internal biliary drainage with external biliary drainage for treatment of acute cholangitis of severe type (ACST). Sixty elderly patients with ACST were retrospectively analyzed. Patients were divided into an internal group, who underwent endoscopic retrograde biliary drainage (ERBD) with a plastic stent and an external group, who received nasobiliary drainage. Improvements in symptoms including abdominal pain, fever, and shock and changes in liver function, white blood cell counts, procalcitonin, blood urea nitrogen and Systemic Inflammatory Response Syndrome scores before and after the operation were analyzed. Complications and operation times were compared. After the operation, the symptoms were significantly improved and each biochemical index was significantly decreased in the two groups, with statistically significant differences observed compared to the pre-operation conditions. In the internal and external drainage groups after the operation, the symptoms were significantly alleviated in 86.7% (26/30) and 90.0% (27/30) of cases, respectively and there were no significant differences in biochemical indexes between the two groups. However, the operation time was significantly shorter in the internal drainage group (P = 0.001 vs. external drainage group) and no endoscopy-related severe complications occurred in either group. Both the internal and external drainage methods relieve biliary obstruction, and quickly alleviate the symptoms. Both methods are suitable for critically ill patients who are not transportable; however, the internal drainage method is characterized by practical simplicity, short duration and high success rate of first-time indwelling, which is more acceptable to patients.

Keywords: Plastic stent, nasobiliary drainage, acute cholangitis of severe type, endoscopy, treatment

Introduction

Acute cholangitis of severe type (ACST), which is a common critical illness treated by hepatobiliary surgery, is characterized by acute onset, severity and rapid progress, and is often accompanied by septic shock. Severe complications may be encountered if timely treatment is not applied. Elderly patients often have weakened immunity and are often combined with diabetes, and other disorders of the heart, brain, lung, liver and kidney. Consequently, ACST often progresses rapidly, leading to early occurrence of toxemia and septicemia. Such patients are prone to septic stock and multiple organ failure, leading to high mortality rates (20%-50%) [1]. For patients with obstruction of the bile duct, the positive rate of bile bacterial cultures is between 75% and 90%, and targeting the infected lesion by intravenous injection of antibiotics is very difficult; therefore, the only effective method is emergency biliary drainage [2]. Treatment methods and intervention timing are important considerations in the diagnosis and treatment of the ACST. Elderly patients have poor physical conditions and complex disorders and the traditional open biliary decompression drainage method carries a higher risk and is associated with more complications, leading to high perioperative mortality. Furthermore, the majority of elderly patients are not tolerant to general anesthesia.

In recent years, the development of the endoscopic retrograde cholangiopancreatography (ERCP) technique has highlighted advantages

beyond the traditional conservative treatment and surgery for ACST. Emergency ERCP + endoscopic nasobiliary drainage (ENBD) is safe and has become the first choice for treatment of ACST [3, 4]. It is used mainly for short-term drainage of bile, and rapidly alleviates the symptoms, with advantages of practical simplicity and absence of the risks of anesthesia and surgery. Furthermore, this simple and convenient drainage method saves time for both patients and physicians, thus providing the opportunity to improve the patients' physical condition to allow thorough treatment with endoscopy or surgery.

For critically ill patients who require urgent treatment or are not transportable, conventional ERCP + ENBD, which is performed under X-ray fluoroscopy, cannot be successfully implemented. Therefore, X-ray-free endoscopic external ENBD drainage at the bedside has been developed. Due to the absence of X-ray guidance, the selective intubation procedure must be conducted by endoscopists with ERCP experience. However, this method is advantageous in that the intrahepatic pressure is significantly increased in ACST patients, which may enlarge the bile duct opening in the ampulla, leading to significantly improved success rate of selective bile duct intubation and easier withdrawal of bile for collection.

Our center has achieved satisfactory decompression efficacy using bedside X-ray-free external ENBD for ACST. This technique has comparable efficacy with the conventional methods, while avoiding the risk of transportation. Based on these advantages, we attempted to apply internal drainage with a plastic stent for the treatment of ACST, and also obtained satisfactory results with rapid alleviation of the condition.

In this study, we conducted a retrospective comparison of the data of patients with ACST treated by X-ray-free external nasobiliary drainage and those treated by internal drainage with a plastic stent in our center to evaluate the efficacy of these two surgical methods.

Materials and methods

Clinical data

A total of 65 ACST patients aged ≥ 75 years old admitted to the Intensive Care Unit for hepatobiliary surgery at the First Affiliated Hospital of Xi'an Jiaotong University between January 2012 and December 2014 were included. These patients accorded with the diagnostic criteria of ACST based on the acute cholangitis Charcot triad as follows: the patients had systolic blood pressure at septic shock of ≤ 70 mmHg or any two of the following characteristics: 1) inhibition of central nervous system; 2) body temperature ≥ 39°C or ≤ 36°C; 3) pulse rate ≥ 120 beats/min; 4) WBC ≥ 20×10^9. Among these patients, 60 underwent emergency bedside X-ray-free endoscopic internal biliary decompression drainage, while the other five patients did not receive this treatment due to endoscopic contraindication or history of gastroenterostomy. Among the 60 patients undergoing biliary drainage, 30 received external nasobiliary drainage (ENBD) and 30 received ERBD with a plastic stent. After admission, patients were scored for Systemic Inflammatory Response Syndrome (SIRS) based on the criteria proposed by Malone et al. [5] to assess the presence of characteristics such fever or hypothermia, sychnosphygmia, shortness of breath, increased WBC count, where each characteristic was awarded one point. The SIRS severity was rated from 0 to 4 points.

Endoscopic equipment

Duodenoscope (Olympus TJF-160R), arcuate knife (Olympus CleverCut 3V KD-V411M725), Zebra guide wire (Boston-Scientific, Jagwire 0.035 inch M00556581), plastic stent (Cook CLSO-7-7/8/9/10) and nasobiliary drain (Cook ENBD-7-NAG-C).

Treatment method

Patients received emergency treatment after admission. Venous transfusion was established, followed by fluid infusion, anti-infection and symptomatic treatment. Meanwhile, combined with hormones, noninvasive or invasive mechanical ventilation was applied if necessary. Routine endoscopic preparation procedures were then conducted. To minimize the impact on breathing, the patients were placed in the left lateral or supine position, received oral tetracaine hydrochloride mucilage (5 g/bottle, LijunJinghua Pharmaceutical Co., Ltd. Xi'an, China) for throat lubrication and topical anesthesia, and propofol (DIPRIVAN 50 mL: 500 mg CordenPharma S.P.A. Italy) for sedation. The duodenoscopy was performed at the bedside under electrocardiogram monitoring. After the papilla was identified, the lens body was straightened, the papilla was adjusted,

Table 1. Comparison of general information between the internal and external drainage groups

	Internal drainage	External drainage	*P* value
Sex			λ = 1.07, P=0.30
Male	12	16	
Female	18	14	
Age (years)	80.2 (75-91)	81.0 (75-88)	P = 0.75
First attack	19	20	λ = 0.07, P = 0.79
Second or multiple attack	11	10	
Charcot triad positive	24	23	λ = 0.098, P = 0.75
Complications			
Hypotension	7	4	λ = 1.00, P = 0.32
Gallstone pancreatitis	5	8	λ = 0.88, P = 0.35
Acute renal insufficiency	6	2	λ = 2.31, P = 0.13
Concomitant disease			
Hypertension	24	22	λ = 0.37, P = 0.54
Chronic emphysema	5	0	λ = 5.46, P = 0.02
Cirrhosis	6	0	λ = 6.67, P = 0.01
Type 2 diabetes	10	8	λ = 0.32, P = 0.57
Coronary disease	13	15	λ = 0.27, P = 0.61
Cerebral hemiplegia	1	0	-
History of biliary tract surgery	18	14	λ = 1.07, P = 0.30
Disease etiology			λ = 1.07, P = 0.30
Choledocholithiasis	22	20	λ = 0.32, P = 0.58
Tumor	5	6	λ = 0.11, P = 0.74
Benign cholangiostenosis	3	4	λ = 0.16, P = 0.69

and a catheter was inserted along the papillar portion of the common bile duct using a slitter combining with a guide wire. After successful intubation, the guide wire was withdrawn, and bile was withdrawn using a hollow needle along the channel of the guide wire until brown infected bile was observed to confirm that the duodenoscope was successfully inserted into the bile duct. The collected bile was used for bacterial cultures and drug-sensitivity testing. A guide wire was then re-inserted and a plastic stent (7-10 cm, 7F Cook) was inserted in the internal drainage group, while a nasobiliary tube was guided into position in the external drainage group. Due to the absence of X-ray monitoring, extreme care should be taken when inserting the stent to prevent its complete entry into the bile duct and also when withdrawing to prevent stent shedding. Drainage clearance was observed after successful insertion. For cases with difficulties in intubation or papilla stone impaction, intubation could be performed after opening the papilla with a slitter or needle knife. After the operation, patents fasted for longer than 48 h, and received anti-infection treatment, acid suppression and enzyme inhibition therapy.

Observational index

The observational indexes included SIRS scores before and after treatment. Clinical symptoms included addominal pain, fever, and increased blood pressure and heart rate. The laboratory examinations included WBC counts, blood platelet counts and total bilirubin, measurement of calcitonin, blood urea nitrogen and lactic acid by arterial blood gas analysis before and after the operation. The complications included duodenoscope-related perforation, bleeding and pancreatitis.

Statistical analysis

Statistical analyses were performed using SPSS13.0 software. Measurement data were expressed as mean ± standard deviation(s). Intra-group comparisons were performed using analysis of variance (ANOVA), and inter-group comparisons were conducted using independent sample *t*-tests. Intra- or inter-group comparisons were conducted using Chi-square test for enumeration data. A difference of $P < 0.05$ was considered statistically significant.

Results

General information

A total of 60 patients with ACST were enrolled, with 30 cases in each of the internal and external drainage groups (**Table 1**).

Extrahepatic bile duct obstruction was confirmed by preoperative abdominal B-ultrasound, computed tomography or magnetic resonance cholangiopancreatography (MRCP) imaging. Preoperative WBC and bilirubin (direct acting bilirubin dominated) were significantly incre-

Table 2. Changes in symptoms of patients

		Before operation	1 d after operation	3 d after operation	Intra-group P	Inter-group P
Abdominal pain	I	26	3	1	λ = 57.9, P = 0.00	λ = 0.35, P = 0.84
	E	27	4	2	λ = 54.4, P = 0.00	
Fever	I	24	5	2	λ = 42.0, P = 0.00	λ = 1.49, P = 0.48
	E	23	2	1	λ = 50.0, P = 0.00	
Pulse rate ≥ 120 beats/min	I	24	3	0	λ = 54.2, P = 0.00	λ = 0.05, P = 0.82
	E	20	2	0	λ = 43.8, P = 0.00	
Symptoms of nervous system	I	4	0	0	λ = 8.4, P = 0.015	λ = 0.74, P = 0.39
	E	5	1	0	λ = 7.5, P = 0.024	

I, internal drainage group; E, external drainage group.

ased in all the patients. The operations were conducted within 24 h after admission.

Comparison of efficacy between the internal drainage and external drainage groups

Comparison of effectiveness: In the internal drainage group, the postoperative symptoms were significantly alleviated in 26 patients, with an effective alleviation rate of 86.7%. In the other 4 patients with unsatisfactory efficacy, two patients were due to obstruction by full type bile duct stones, 1 patient suffered from poorly controlled infection caused by poor drainage due to biliary duct bleeding, 1 patient experienced relapse due to early stent shedding and achieved alleviation after secondary indwelling. In the external drainage group, symptoms were significantly alleviated in 27 patients, with an effective alleviation rate of 90.0%. In the other 3 patients with unsatisfactory efficacy, 2 patients underwent emergency percutaneous transhepaticcholangial drainage (PTCD) due to poor drainage caused by combination with intrahepatic bile duct obstruction, 1 patient underwent secondary indwelling due to nasobiliary shedding. There was no significant difference in the effective alleviation rate between the two groups (P = 0.104). It should be noted that the first-time indwelling rate in the internal drainage group was 100%, while that in the external drainage group was 86.7%, with reoperations conducted in 4 patients in this group due to nose biliary shedding during intraoperative endoscopic withdrawal.

Comparison of symptom improvement: Symptoms such as abdominal pain, fever, rapid heartbeat and symptoms of nervous system were improved after drainage in both groups, as shown in **Table 2**.

Comparison of improvement in biochemical indicators: Results of laboratory tests are shown in **Table 3**. There were significant differences in the preoperative and postoperative biochemical indicators within the groups ($P < 0.05$), but not between the groups ($P > 0.05$).

Comparison of postoperative complications

After the endoscopic treatment, acute pancreatitis occurred in 2 patients in the internal drainage group and one patient in the external drainage group. Transient elevation of blood amylase occurred in 11 patients in the internal drainage group and 10 patients in the external drainage group; normal levels were restored after acid suppression and enzyme inhibition treatment. One patient in the internal drainage group was identified with a tumor of the biliary tract, with extensive blood clotting found in the bile duct in the secondary laparotomy due to preoperative biliary tumor bleeding. No endoscopy-related severe complications (perforation of the digestive tract, bleeding, severe acute pancreatitis, death, etc.) occurred in either of the groups. Infection was controlled at 72 h after the operation in all patients. Subsequently, underwent endoscopic sphincterotomy or laparotomy, and achieved good recovery.

*Comparison of SIRS score (**Table 4**)*

Comparison of operation time: The mean operation time was significantly shorter in the internal drainage group compared to that in and external drainage groups (20.2±4.8 min

Table 3. Changes in laboratory examination results

Clinical index		Before operation	1 d after operation	3 d after operation	F	Intra-group *P*
TBIL	I	98.3±18.1	78.2±14.2	40.7±8.8	34.76	0.000
	E	101.4±16.4	80.0±10.2	43.4±4.7	27.3	0.000
	Inter-group *P*	0.325	0.402	0.545		
Leukocytes	I	26.5±8.0	12.4±2.6	8.4±1.8	24.5	0.000
	E	28.0±6.3	10.4±4.6	6.4±0.8	55.56	0.000
	Inter-group *P*	0.263	0.812	0.200		
Blood platelets	I	30.0±24.4	82.4±18.8	160.6±80.5	18.0	0.000
	E	46.8±28.0	90.2±14.8	150.4±76.8	24.4	0.000
	Inter-group *P*	0.362	0.547	0.422		
Arterial blood lactate (mmol/L)	I	4.2±1.8	3.2±1.1	1.9±0.6	27.38	0.000
	E	5.0±2.4	2.8±1.5	2.1±0.4	21.5	0.000
	Inter-group *P*	0.572	0.222	0.065		
Procalcitonin (ng/mL)	I	25.7±6.8	6.2±3.6	2.2±0.2	82.3	0.000
	E	18.8±7.6	7.2±3.8	2.1±0.4	107.9	0.000
	Inter-group *P*	0.707	0.761	0.668		
Blood urea nitrogen (mmol/L)	I	18.7±6.8	11.2±4.6	8.1±3.6	28.93	0.000
	E	15.6±7.2	13.2±3.8	7.6±3.2	12.12	0.000
	Inter-group *P*	0.094	0.165	0.431		

I, internal drainage group; E, external drainage group.

Table 4. Changes and comparison of SIRS scores of the internal drainage and external drainage groups

SIRS score		Before operation	1 d after operation	3 d after operation	Intra-group P	Inter-group P
0-1	I	0	15	26	λ = 45.8, P = 0.00	λ = 0.05, P = 0.82
	E	0	16	25	λ = 43.1, P = 0.00	
2	I	2	8	1	λ = 8.9, P = 0.012	λ = 73, P = 0.70
	E	1	10	2	λ = 13.1, P = 0.01	
3	I	4	3	2	λ = 0.74, P = 0.69	λ = 0.14, P = 0.93
	E	4	2	2	λ = 1.1, P = 0.58	
4	I	24	4	1	λ = 47.7, P = 0.00	λ = 0.16, P = 0.92
	E	25	3	1	λ = 54.1, P = 0.00	

vs. 30.6±5.4 min, respectively; P = 0.001) (**Figure 1**).

Discussion

Quick and effective biliary decompression drainage is the most effective treatment for ACST [6]. Studies have shown that the mortality rate associated with endoscopy for ACST is approximately 10%, which is significantly lower than that associated with surgery biliary drainage group (approximately 30%) [7, 8]. ERCP + ENBD/ERBD have basically replaced traditional laparotomy due to the effectiveness of this method. Emergency X-ray-free endoscopy at the bedside for the treatment of ASCT avoids the risks associated with transportation of the patient and allows continuous life supporting therapy, especially for patients in shock, elderly patients and patients requiring mechanical ventilation.

Emergency X-ray free endoscopic ENBD at the bedside has been widely implemented in clinics. Lin et al. [9] reported successful ENBD in a total of six patients in their emergency care unit. However, because of the absence of X-ray monitoring, the drainage tube is likely to fall off in withdrawal and the operation is time-consuming. To address this issue, we attempted to replace ENBD with endoscopic retrograde biliary drainage using a plastic stent for treatment of ACST and compared the advantages and disadvantages of these two drainage methods. Our results indicate that the efficacy of these two drainage methods used in an emergency is consistent with that of conventional ERCP; the

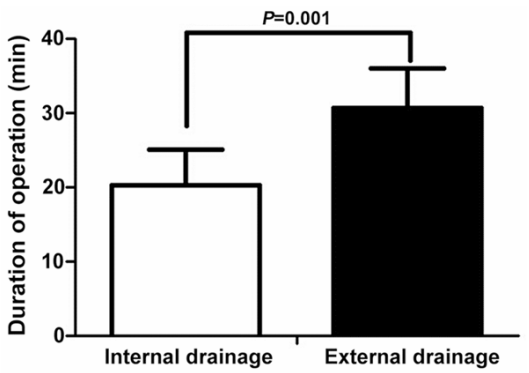

Figure 1. Comparison of operation time between the internal and external drainage groups, where the operation time in the internal drainage group was significantly shorter than that in the external drainage group (P = 0.001).

symptoms were significantly alleviated, each laboratory index was improved and SIRS scores were significantly decreased in the patients. No severe complications were observed in the two groups, with the exception of three cases of pancreatitis and transient blood amylase elevation in some patients. Therefore, our retrospective analysis indicates that bedside X-ray-free therapy is preferable for the treatment of critically ill patients with ACST who are not suitable for transportation.

Our experience is to withdraw as much bile as possible after confirmation of papillar intubation of the bile duct by withdrawing bile, and successful drainage tube indwelling has been achieved after full biliary decompression. ENBD is conducive to monitoring the amount and traits of the bile, and repeated bile culture. However, this procedure is complicated, especially for inexperienced endoscopists, by the propensity of the nasobiliary tube to fall off in the bile duct during the operation. Furthermore, postoperative nasobiliary nursing is necessary. Internal drainage with an indwelling stent is characterized by practical simplicity and a high first-time success rate, avoids the risk of shedding of the drainage shedding in withdrawal, and facilitates collection of the infected bile for bacterial culture. Furthermore, the internal drainage method is more acceptable to patients because it avoids the discomfort and stress associated with the placement of the nasobiliary tube. For some patients with stone ampulla obstruction and difficulty in positioning the indwelling stent, this can be facilitated by opening the papilla with a needle knife, allowing direct discharge of the stones and reducing the possibility of damaging the posterior wall of bile duct and pancreas port, thus reducing the risk of pancreatitis [10]. To ensure the effective drainage, monitoring can be performed at the bedside by abdominal plain film imaging. Second indwelling can be performed in patients with unsatisfactory drainage based on the disease conditions and tolerance.

Elderly patients with ACST are often accompanied by septic shock and reduced oxygen partial pressure, while some patients require intermittent invasive ventilation or even endotracheal intubation, and are therefore unsuitable for transportation. Thus, the risks may be dramatically increased if these patients are transferred from routine units to endoscopy centers. In such cases, bedside X-ray-free endoscopy represents a feasible and safer option. In addition to a requirement for experienced endoscopists to improve the success rate of selective intubation, the X-ray-free method performed at the bedside also requires the cooperation of nurses, who are required to ensure timely clearing of vomit and respiratory secretions to prevent choking since the patients' head is required to be in the left lateral position throughout most of the operation.

Due to the absence of X-ray monitoring, it is not possible to locate the internal drainage stent or ENBD tube accurately. Consequently, the efficacy of drainage may be affected by shedding or displacement of the drainage tube or because the stent or drainage tube may not cross the stone obstruction. First-time indwelling was successful in all the patients in the internal drainage group, while reoperation was conducted in four patients in the external drainage group due to shedding of the nasobiliary tube during withdrawal. Therefore, external drainage is not suitable for routine application, and is only applicable for critically ill patients who are not suitable for transportation.

Extensive blood clotting was also found in the bile duct in one patient in the internal drainage group during secondary laparotomy. Since the primary disease was distal bile duct cancer, the patient was speculated to have biliary tumor bleeding at admission. For patients with hematobilia, it is difficult to achieve accurate diagnosis in the short time before the emergency

operation. If patients exhibit intraoperative bleeding in the bile, ENBD is preferable for observation and treatment, because the internal stent drainage is prone to clot obstruction, leading to inefficient drainage and this approach is not conducive to determining disease changes.

The limitation of this study is that we selected a 7F plastic stent with the same diameter as the nasobiliary duct, and further studies are required to compare the efficacy of nasobiliary drainage using stents with different diameters. Furthermore, the sample size in this study is limited; thus further large-scale studies are needed to verify the results.

Conclusion

X-ray-free endoscopic internal and external biliary drainage methods are effective for treatment of ACST; both approaches can be used to achieve rapid and effective alleviation of the symptoms and signs of the disease and are of important clinical value for early emergency treatment. However, the internal drainage method is characterized by practical simplicity, short duration and high success rate of first-time indwelling.

Disclosure of conflict of interest

None.

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