ORIGINAL RESEARCH

Comparison of Efficacy of ERCP+LC and LC+LCBDE on Cholecysto-Choledocholithiasis and Analysis of Risk Factors for Recurrence of Choledocholithiasis

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ABSTRACT

Objective • Laparoscopic cholecystectomy (LC) combined with laparoscopic common bile duct exploration (LCBDE) and endoscopic retrograde cholangiopancreatography (ERCP) or endoscopic sphincterotomy (EST) combined with LC are the two primary treatment modalities for common bile duct stones (CCL) at present. The aim of this study is to compare the efficacy and safety of the two surgical approaches in treating CCL and analyze the risk factors for the recurrence of common bile duct stones.

Methods • The clinical data of 148 CCL patients treated in the hospital from March 2014 to March 2016 were retrospectively analyzed. ERCP+LC was performed for 74 patients (ERCP+LC group), while the remaining 74 patients underwent LC+LCBDE (LC+LCBDE group). The success rate of lithotomy, operation time, total hospital stay time, postoperative hospital stay time, clinical symptoms, incidence rate of complications, and hospitalization expenses were compared between the two groups. The patients were followed up, the recurrence of choledocholithiasis was recorded, and the risk factors for recurrence were analyzed.

Results • The success rate of lithotomy was 97.3% in the LC+LCBDE group and 94.6% in the ERCP+LC group. In the ERCP+LC group and LC+LCBDE group, the average operation time was (125.7±20.3) min and (106.5±25.4) min, the postoperative anal ventilation time was (20.8±3.5) d and (18.7±3.7) d, and the postoperative hospital stay time was (9.3±3.1) d and (7.7±3.3) d, respectively. It can be seen that the above three indexes were all significantly shorter in the LC+LCBDE group than those in ERCP+LC group ($P < .001$, $P < .001$, $P = .003$). The hospitalization expenses in the LC+LCBDE group [(19±1) thousand yuan] were obviously lower than those in the ERCP+LC group [(26±2) thousand yuan] ($P < .001$). The postoperative symptoms included fever, vomiting, abdominal pain and abdominal distension. The incidence rate of abdominal pain in the LC+LCBDE group was far higher than that in the ERCP+LC group ($P = .025$), and that of the remaining symptoms had no statistically significant difference between the two groups ($P > .05$). The postoperative complications mainly included incision infection, bile duct bleeding, biliary fistula, abdominal infection, bile duct pneumatosis, cholangitis and acute pancreatitis. Hyperamylasemia occurred in 8 cases after operation in the ERCP+LC group, greatly more than that in the LC+LCBDE group (1 case) ($P = .016$), while the incidence of other complications had no statistically significant difference between the two groups ($P > .05$). The patients were followed up for 3-5 years, and it was found that the recurrence rate of choledocholithiasis was 17.6% and 13.5%, and the mean postoperative recurrence time was 13.7 months and 13.9 months, respectively, in ERCP+LC group and LC+LCBDE group. The results of multivariable logistic regression analysis revealed that the level of cholesterol >572 mm/L (OR=5.108, 95%CI: 1.263-11.472, $P = .038$), choledochectasia (OR=2.165, 95%CI: 1.019-8.418, $P = .034$) and parapapillary diverticulum (OR=6.761, 95%CI: 1.334-15.613, $P = .039$) were independent risk factors for postoperative recurrence of choledocholithiasis.

Conclusions • In our study, we found that ERCP+LC and LC+LCBDE have definite efficacy in the treatment of CCL. Patients treated with LC+LCBDE need short hospital stay time and low treatment expenses and have relatively few long-term complications. (*Altern Ther Health Med.* 2024;30(7):103-107).

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INTRODUCTION

It is reported in the literature that 10-20% of patients with symptomatic cholecystolithiasis are complicated with choledocholithiasis, and the risk of cholecysto-choledocholithiasis (CCL) increases with age.[1] CCL can lead to a variety of complications. Smaller stones may be embedded in Oddi's sphincter, thereby causing distal obstruction and acute pancreatitis. Larger stones often result in proximal biliary obstruction, often accompanied by such complications as obstructive jaundice and cholangitis.[2,3] Laparoscopic cholecystectomy (LC) combined with laparoscopic common bile duct exploration (LCBDE) and endoscopic retrograde cholangiopancreatography (ERCP) or endoscopic sphincterotomy (EST) combined with LC are the two primary treatment modalities for common bile duct stones (CCL) at present. According to a large amount of literature, the effectiveness of these two methods is similar, but which

method should be chosen in clinical practice remains controversial. For example, the study conducted by Qian et al. revealed that LC + ERCP + EST treatment for gallbladder stones combined with common bile duct stones had significant advantages in reducing hospitalization duration and lowering the risk of pulmonary infections.[4] However, Pan et al. argue that LCBDE+LC is superior to EST+LC in terms of perioperative safety and short- and long-term postoperative efficacy. They suggest it should be considered the optimal treatment choice for gallbladder stones combined with common bile duct stones.[5] Therefore, choosing a reasonable treatment method and standardized technical means based on the condition of the disease has become a top priority.[6]

In this study, the efficacy and safety of ERCP+LC and LC+LCBDE in the treatment of CCL patients were retrospectively analyzed, and the risk factors for the recurrence of choledocholithiasis were also analyzed to provide a basis for the selection of clinical therapeutic regimen and prognostic analysis of such patients.

Table 1. Demographics and general clinical data of all studied patients

Parameters	ERCP group (n = 74)	LCBDE group (n = 74)	*P* value
Gender (Male/Female)	41/33	38/36	.742
Age (years)	53.54±9.41	52.18±9.17	.375
BMI (kg/m^2)	24.05±2.53	23.79±2.64	.542
Serum cholesterol level			.553
Normal	57 (77.0%)	53 (71.6%)	
Elevated	17 (23.0%)	21 (28.4%)	
Common bile duct stones property			.647
Pigment gallstone	37 (50.0%)	34 (45.9%)	
Cholesterol gallstone	9 (12.2%)	13 (17.6%)	
Mixed gallstone	28 (37.8%)	27 (36.5%)	
Number of common bile duct stones			.496
1	61 (82.4%)	64 (86.5%)	
≥2	13 (17.6%)	10 (13.5%)	
Largest stone diameter (mm)			.630
<10	19 (25.7%)	21 (28.4%)	
10-20	53 (71.6%)	49 (66.2%)	
≥20	2 (2.7%)	4 (54.1%)	
Common bile duct diameter (mm)			.605
<10	15 (20.3%)	18 (24.3%)	
10-20	56 (75.7%)	51 (68.9%)	
≥20	3 (4.1%)	5 (6.8%)	
Total bilirubin (μmol/L)	73.82±34.63	71.94±36.50	.748
Serum glutamic oxaloacetic transaminase (μ/L)	175.64±90.57	169.76±97.83	.705
Serum glutamic pyruvic transaminase (μ/L)	180.34±106.48	167.52±102.75	.457

Abbreviations: ERCP, Endoscopic Retrograde Cholangiopancreatography; LCBDE, Laparoscopic common bile duct exploration; BMI, Body Mass Index.

MATERIALS AND METHODS

General data

A total of 148 CCL patients treated in our hospital from March 2014 to March 2016 were enrolled, including 79 males and 69 females aged 37-77 years old, with a median of 53.1 years old. Inclusion criteria were as follows: 1) patients diagnosed with CCL *via* preoperative imaging examinations, such as abdominal B ultrasound, abdominal CT or abdominal MRCP, 2) those not accompanied by hepatolithiasis and biliary stricture, and 3) those who had no dysfunction of important organs, had normal blood routine results, hepatic-renal function and cardiac function, and could tolerate surgery. Exclusion criteria included: 1) patients with contraindications for treatment, such as malignant biliary diseases or severe lesions of important organs, or 2) those with severe complications, such as obvious bleeding, perforation, biliary fistula or acute pancreatitis. ERCP+LC was performed for 74 patients (ERCP+LC group), while the remaining 74 patients underwent LC+LCBDE (LC+LCBDE group). The baseline characteristics of general conditions in both groups before treatment were shown in Table 1, and the differences were not statistically significant ($P > .05$). The Ethics Committee of our hospital approved this study. All patients were informed of this study in accordance with the *Declaration of Helsinki* and signed the informed consent.

Therapeutic regimens

In the ERCP+LC group, a duodenoscope was inserted under general anesthesia into the descending part of the duodenum through the mouth, esophagus, gastric cardia, and pylorus. The duodenal papilla was found and selectively intubated till the common bile duct under the guidance of a guide wire. Then, the contrast agent was injected through the incision knife for ERCP. For patients whose stones could be removed through the mouth, EST was performed using the knife-retraction method along the 11 o'clock direction of the duodenal papilla, and papillary balloon dilation was also conducted as needed. According to the location, size, number and hardness of stones, the appropriate methods of lithotomy and lithotripsy were selected. After lithotomy, whether there were residual stones was confirmed using cholangiography, and if so, duodenoscopic lithotomy needed performing again. After endoscopic lithotomy, a nasobiliary drainage tube was routinely indwelled for bile duct irrigation and bile drainage. After the operation, patients' blood, urine amylase, and clinical signs were closely monitored. LC could be performed if there were no abnormalities in the blood and urine amylase, and no obvious positive signs according to clinical observation at 24 h. At 1-2 d after LC, the nasociliary drainage tube was withdrawn if no abnormalities were found in naso-cholangiography.

In the LC+ LCBDE group, patients underwent LC under general anesthesia. The common bile duct was confirmed through puncture and bile withdrawal. A longitudinal incision (about 1 cm long) was made on the anterior wall of the common bile duct near its mid-upper end, the internal and external bile ducts were explored using a choledochoscope, and the stones in the common bile duct were removed using the stone basket. After it was confirmed by choledochoscope that there were no residual stones in the intrahepatic bile duct and common bile duct, and the stone basket could smoothly pass through the duodenal papilla, the anterior wall of the common bile duct was subjected to phase I continuous full-thickness suture using Quill absorbable surgical sutures. After the operation, patients' blood, urine amylase, clinical signs and peritoneal drainage were closely monitored. The next day, the patients could take food orally.

Observation indexes

The operation conditions (success rate of operation, operation time, and intraoperative bleeding) and postoperative

conditions (postoperative complications, anal ventilation time, postoperative hospital stay time, and total hospitalization expenses) were compared between the two groups.

The patients were followed up after the operation, and received blood biochemistry and B ultrasound examinations. They should receive hepatic function and B ultrasound examinations promptly during jaundice and abdominal pain. Patients with confirmed choledocholithiasis through abdominal ultrasound, abdominal CT, MRCP, or other imaging studies underwent repeat ERCP for stone retrieval. The detection of choledocholithiasis 6 months post-surgery indicated a recurrence.

Statistical analysis

Statistic Package for Social Science (SPSS) 22.0 software (IBM, Armonk, NY, USA) was used for statistical analysis. Measurement data were expressed as mean ± standard deviation ($\bar{x} \pm s$), and *t* test was performed for the intergroup comparison. Enumeration data were expressed as a rate (%), and χ^2 test was performed for the intergroup comparison. The possible influencing factors for recurrence of choledocholithiasis were subjected to multivariable logistic regression analysis and expressed as OR value (95%CI). $P < .05$ was considered to be statistically significant.

RESULTS

Comparison of operation conditions and success rate of lithotomy between the two groups

There were no cases of laparotomy and deaths in both groups. In the LC+LCBDE group, the stones failed to be completely removed in 2 cases due to severe cholangitis and many stones, so a T tube was placed during operation, and the success rate of lithotomy was 97.3%. In the ERCP+LC group, one-time lithotomy was successful in 70 cases, 2 cases suffered from difficult intubation due to duodenal papilla located in the duodenal diverticulum, and the bile duct stones were too large to be removed smoothly in 2 cases, so LCBDE was conducted, with a success rate of lithotomy of 94.6% (Table 2). There was no statistically significant difference in the success rate of lithotomy between the two groups ($P = .681$).

In the ERCP+LC group and LC+LCBDE group, the average operation time was (125.7±20.3) min and (106.5±25.4) min, and the postoperative anal ventilation time was (20.8±3.5) d and (18.7±3.7) d, and the postoperative hospital stay time was (9.3±3.1) d and (7.7±3.3) d, respectively (Table 2). It can be seen that the above three indexes were all significantly shorter in the LC+LCBDE group than those in ERCP+LC group ($P < .001$, $P < .001$, $P = .003$). The intraoperative blood loss had no statistically significant difference between the two groups [(57.6±10.8) mL *vs.* (54.3±13.9) mL] ($P = .109$). The hospitalization expenses in the LC+LCBDE group [(19±1) thousand yuan] were obviously lower than those in the ERCP+LC group [(26±2) thousand yuan] ($P < .001$). In ERCP+LC group, there were 4 cases (5.4%) of fever, 10 cases (13.5%) of vomiting, 3 cases (4.1%) of abdominal pain, and 15 cases (20.3%) of abdominal distension. In the LC+LCBDE group, there were 6 cases (8.1%) of fever, 14 cases (18.9%) of vomiting, 11 cases (14.9%) of abdominal pain, and 22 cases (29.7%) of abdominal distension (Table 2). The incidence rate of abdominal pain in the LC+LCBDE group was far higher than that in the ERCP+LC group ($P = .025$), and that of fever, vomiting, and abdominal distension had no statistically significant difference between the two groups ($P > .05$).

Table 2. Comparison of surgery parameters and postoperative symptoms of patients in the two studied groups

Complications	ERCP group (n = 74)	LCBDE group (n = 74)	*P* value
Operation time (min)	125.7±20.3	106.5±25.4	.001
Blood loss (ml)	57.6±10.8	54.3±13.9	.109
Postoperative anal ventilation time (d)	20.8±3.5	18.7±3.7	.001
Postoperative hospital stay time (day)	9.3±3.1	7.7±3.3	.003
Hospitalization expenses (thousand yuan)	26±2.0	19±1.0	.001
Postoperative symptoms			
Fever	4 (5.4%)	6 (8.1%)	.513
Vomiting	10 (13.5%)	14 (18.9%)	.372
Abdominal pain	3 (4.1%)	11 (14.9%)	.025
Abdominal distention	15 (20.3%)	22 (29.7%)	.184

Abbreviations: ERCP, Endoscopic Retrograde Cholangiopancreatography; LCBDE, Laparoscopic common bile duct exploration.

Table 3. Comparison of postoperative complications of patients in the two studied groups

Complications	ERCP group (n = 74)	LCBDE group (n = 74)	*P* value
Incision infection	1 (1.4%)	2 (2.7%)	.560
Bile duct bleeding	1 (1.4%)	0 (0%)	.316
Biliary fistula	1 (1.4%)	3 (4.1%)	.311
Abdominal infection	1 (1.4%)	0 (0%)	.316
Bile duct pneumatosis	6 (8.1%)	4 (5.4%)	.513
Cholangitis	7 (9.5%)	5 (6.8%)	.547
Hyperamylasemia	8 (10.8%)	1 (1.4%)	.016
Acute pancreatitis	4 (5.4%)	1 (1.4%)	.301

Abbreviations: ERCP, Endoscopic Retrograde Cholangiopancreatography; LCBDE, Laparoscopic common bile duct exploration.

Table 4. Multivariable logistic Regression analysis of predictors for choledocholithiasis recurrence of cholecysto-choledocholithiasis patients

Parameters	OR value	95% CI	*P* value
Gender	1.535	0.728-3.162	.518
Age	1.406	0.816-2.430	.435
BMI (kg/m^2)	1.239	0.728-5.741	.539
Elevated cholesterol level	5.108	1.263-11.472	.038
Common bile duct stones property	1.718	0.659-5.601	.321
Number of common bile duct stones	0.557	0.679-1.850	.446
Largest stone diameter	1.742	0.885-6.206	.291
Common bile duct diameter	2.165	1.019-8.418	.034
Total bilirubin	1.437	0.866-1.743	.336
Serum glutamic oxaloacetic transaminase	2.093	0.969-3.096	.313
Serum glutamic pyruvic transaminase	1.949	0.886-2.347	.439
Para-papillary diverticulum	6.761	1.334-15.613	.039

Abbreviations: OR, Odds ratio; CI, Confidence interval; BMI, Body Mass Index.

Comparison of postoperative complications between the two groups

In the ERCP+LC group, the patients underwent duodenoscopic lithotomy first and then LC. Bleeding occurred in 1 case after duodenoscopic lithotomy, and it was stopped by conservative treatment. Then LC was performed after no abnormalities were observed for 2 d. Moreover, 1 case had an

abdominal infection due to gallbladder bed effusion after LC, and treated with puncture, catheterization, and drainage. Acute pancreatitis occurred in 4 cases. In the LC+LCBDE group, after LC and phase I suture of the common bile duct, there were 3 cases of bile leakage and 1 case of acute pancreatitis with obvious abdominal pain. Then conservative treatment was performed, the indwelling time of the drainage tube in the abdominal cavity was extended, and the drainage tube was withdrawn when the drainage fluid was markedly reduced. Hyperamylasemia occurred in 8 cases after operation in the ERCP+LC group, greatly more than that in the LC+LCBDE group (1 case) (P = .016), while the incidence of other complications had no statistically significant difference between the two groups (P > .05) (Table 3).

Recurrence of choledocholithiasis

The patients were followed up for 3-5 years, and it was found during follow-up that the recurrence rate of choledocholithiasis was 17.6% (13 cases) and 13.5% (10 cases), and the mean postoperative recurrence time was 13.7 months and 13.9 months, respectively, in ERCP+LC group and LC+LCBDE group (Table 3). There were 5 cases and 4 cases of recurrence within 12 months after the operation, 5 cases and 3 cases of recurrence within 12-24 months, and 3 cases and 3 cases of recurrence after 2 years, respectively, in the two groups (Table 3). It can be seen that recurrence was found mainly within 2 years after operation (76.9%, 10/13, 70%, 7/10).

Analysis of risk factors for recurrence of choledocholithiasis

Gender, age, BMI, elevated level of cholesterol, nature of choledocholithiasis, number of stones, size of stones, diameter of common bile duct, total bilirubin level, blood glutamic-pyruvic transaminase level, and blood glutamic-oxalacetic transaminase level were incorporated into logistic regression analysis (Table 4). The results showed that the level of cholesterol >572 mm/L (OR=5.108, 95%CI: 1.263-11.472, P = .038), choledochectasia (OR=2.165, 95%CI: 1.019-8.418, P = .034) and parapapillary diverticulum (OR=6.761, 95%CI: 1.334-15.613, P = .039) were independent risk factors for postoperative recurrence of choledocholithiasis.

DISCUSSION

With the development of laparoscopic, choledochoscopic, and duodenoscopic techniques, extrahepatic bile duct calculus treatment has changed from traditional laparotomy to minimally-invasive surgery.[7] Currently, ERCP+LC and LC+LCBDE are two major minimally-invasive surgical methods for CCL, which have been widely performed and exhibited obvious advantages over traditional laparotomy.[8] However, the two methods have their own characteristics, advantages, and disadvantages.

LCBDE, characterized by minimal invasion, a clear surgical field, rapid recovery of gastrointestinal function, mild abdominal adhesion, and no damage to Oddi's sphincter, was reported by Phillip for the first time in 1991, and patients undergoing LCBDE need shorter hospital stay time and lower expenses than those treated with ERCP/EST+LC.[9] The results of a meta-analysis of Zhu *et al* revealed that the stone clearance rate of LC+LCBDE is higher than that of ERCP/EST+LC (90.2% *vs.* 85.7%) on the basis of no statistically significant differences in the incidence rate of complications and perioperative mortality.[10] Through LCBDE, the papillary sphincter is not damaged, the normal opening-closing function of the biliary tract is retained, and the food reflux into the common bile duct and recurrence of choledocholithiasis is reduced. Moreover, the patients have less pain after phase I operation, and the expenses are lower, Therefore, this surgical approach is more likely to be accepted by patients with limited financial resources. [11] It is needed to quickly relieve biliary obstruction in patients complicated with acute suppurative cholangitis and unstable vital signs. In such cases, ERCP should be the first-choice surgical approach because it can be completed under analgesia with diazepam, which has a smaller impact on the vital signs of patients..[12] Patients complicated with biliary pancreatitis often have severe intra-abdominal inflammation, in which case it is difficult to perform LCBDE, and biliary tract injury may occur. However, controlling inflammation may also be difficult if biliary obstruction is not relieved. Therefore, ERCP for such patients can quickly relieve biliary and pancreatic duct obstruction, and then phase II LC can be conducted.[13,14] Besides, it is hard to perform LCBDE in simple choledocholithiasis patients with a history of upper abdominal surgery, but ERCP is a perfect choice.[15]

In Chinese guidelines and Tokyo Guidelines 2013, EST and endoscopic nasobiliary drainage are recommended as the preferred treatment for CCL complicated with acute cholangitis, but laparoscopic surgery is not explicitly recommended, and LC-LCBDE can be done for younger mild-moderate acute cholangitis patients with normal cardiopulmonary function. Phase II ERCP+LC is more suitable for the elderly emergency severe patients without choledochectasia and with small and few stones. However, LC needs to be performed after ERCP at an interval of 48-72 h, so that the hospital stay time, operation time, and expenses are all increased. As a result, the mental stress of patients will be enhanced significantly due to two operations during one-time hospitalization. Moreover, Oddi's sphincter is damaged, pancreatitis is induced easily, and long-term complications of the biliary system are increased, so ERCP+LC should be selected with caution for young patients.[16] Choledocholithiasis is prone to recurrence. The recurrence of choledocholithiasis has not been uniformly defined in academic circles. It is reported in the literature that the duration between complete clearance of primary stones and recurrence of lithiasis is at least 6 months, and the recurrence rate is 4-24%.[17,18] Studies have revealed that infection of the biliary tract, parapapillary duodenal diverticulum, choledochectasia, history of biliary tract surgery, number and size of stones, age, obesity, and hypercholesterolemia are all related to the recurrence of choledocholithiasis. According to some studies, cholecystectomy is associated with postoperative recurrence of

choledocholithiasis.[19,20] Through the normal excretory function of gallbladder, the bile duct can be effectively washed, and the deposits in the bile duct can be reduced, thereby preventing the recurrence of lithiasis. In addition, the gallbladder can effectively control the pressure of Oddi's sphincter. After cholecystectomy, the basal pressure of Oddi's sphincter declines, so the incidence rate of retrograde infection of the biliary tract will rise.[21] In this study, the patients were followed up for 3-5 years. The recurrence rate of choledocholithiasis was 17.6% and 13.5%, respectively, in the ERCP+LC group and LC+LCBDE group. The level of cholesterol >572 mm/L, choledochectasia, and parapapillary diverticulum were independent risk factors for postoperative recurrence of choledocholithiasis.

Similar to the above guidelines, we found that the success rate of lithotomy was 97.3% in the LC+LCBDE group and 94.6% in the ERCP+LC group. LC+LCBDE group had significantly shorter operation time, postoperative anal ventilation time, and postoperative hospital stay time, and obviously lower hospitalization expenses than ERCP+LC group. Hyperamylasemia occurred in 8 cases after operation in the ERCP+LC group, greatly more than that in the LC+LCBDE group (1 case) ($P = .016$), while the incidence of other complications had no statistically significant difference between the two groups ($P > .05$). Therefore, when suffering from Cholecysto-Choledocholithiasis, the preferred surgical approach should be LC+LCBDE rather than ERCP+LC.

However, this study also has some limitations. Firstly, being a single-center study, the number of cases included in this research is relatively small, and the follow-up period is only 3-5 years, which is relatively short. Secondly, the proficiency of surgeons in performing the surgery can also introduce bias into the results. Therefore, we plan to conduct a multicenter study to overcome the factors that may affect the results mentioned above.

CONCLUSION

ERCP+LC and LC+LCBDE have definite efficacy in the treatment of CCL. Patients treated with LC+LCBDE need short hospital stay time and low treatment expenses and have relatively few long-term complications. Therefore, when encountering patients with cholecysto-choledocholithiasis (CCL) requiring surgical treatment, LC+LCBDE should be the first-choice surgical approach. Hypercholesterolemia, choledochectasia, and parapapillary diverticulum are independent risk factors for postoperative recurrence of choledocholithiasis, When encountering CCL patients with the above-mentioned risk factors, caution should be exercised regarding the recurrence of the disease.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

AUTHOR CONTRIBUTIONS

WS and JL designed the study and performed the experiments, JF and QD collected the data, AH and CL analyzed the data, WS prepared the manuscript. All authors read and approved the final manuscript.

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This study did not receive any funding in any form.

ETHICAL COMPLIANCE

This study was approved by the ethics committee of the First People's Hospital of Dali City. Signed written informed consents were obtained from the patients and/or guardians.

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