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**SURGICAL TREATMENT FOR BENIGN BILIARY STRICTURES:
SINGLE-CENTER EXPERIENCE ON 64 CASES**

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ABSTRACT

Objectives: In order to describe treatment options for postoperative benign biliary strictures and find a proper approach for treatment, we describe the presentation and management of postoperative biliary stricture in 64 patients.

Methods: Demographical and clinical data from 64 patients undergoing surgical reconstructions by retrospective methods during the past 6 years were analyzed. Clinical features of Grade I and II group versus Grade III and IV group and bile duct plasty versus biliojejunostomy were compared.

Results: Of the 64 patients, 21 received bile duct plasty and the other 43 underwent biliojejunostomy. Patients with bigger bile duct dilatation had better outcomes than those with smaller one, $P=0.0372$. Hepaticojejunostomy was correlated to better outcomes than other surgical procedures, $P=0.0483$. Bile duct plasty was related to Bismuth classification Type I, $P=0.0001$. But biliojejunostomy was related to Bismuth classification Type II, $P=0.0001$ and Type III, $P=0.0059$. Patients with bigger bile duct dilatation had more biliojejunostomy than those with smaller one, $P=0.0001$.

Conclusion: Both biliojejunostomy and bile duct plasty had good treatment outcomes. Bile duct plasty should be confined to patients with a degree of bile duct dilatation less than 1.5 cm and Bismuth classification (Type I). The degree of dilatation, hepaticojejunostomy and postoperative morbidity were factors statistically correlated to long term outcomes.

Keywords: benign biliary strictures, biliojejunostomy, bile duct plasty, long term outcome

INTRODUCTION

Benign stricture of the bile duct is a serious complication of upper abdominal surgery that leads to repeated cholangitis, biliary cirrhosis, hepatic failure, and death. Biliary injury and stricture are mainly caused by biliary operation, especially occurring after open or laparoscopic cholecystectomy. In recent years, with the popularity of laparoscopic cholecystectomy, the rate of biliary injury was reported to be significantly

higher than in previous investigations concerning open cholecystectomy (Chapman et al., 1995; Tocchi et al., 1996; Lillemoe et al., 1997; MacFadyen et al., 1998; Fletcher et al., 1999). Numerous reports have demonstrated that the incidence of bile duct injuries has risen from 0.1 %-0.2 % to 0.4 %-0.7 % from the era of open cholecystectomy to the era of laparoscopic cholecystectomy (Flum et al., 2003; Lai and Lau, 2006). Several factors have been proposed to account for the different outcomes of

these patients, including level of the stricture and degree of dilatation, the type of operation performed and the type of sutures used, the use and length of postoperative stenting, and the length of follow-up (Csendes et al., 1992; Lillemoe et al., 1992; Ross et al. 1989; Bismuth et al., 1978; Schweizer et al., 1991; Innes et al., 1988).

In order to be more aware of the presence of postoperative benign biliary strictures and find a better approach for treatment, we herein analyze the outcome of surgical treatment of 64 patients by using Bismuth classification. The present study mainly evaluated clinical factors which were related to the long-term outcome and surgical treatment of benign biliary strictures.

METHODS

Patients

64 patients with benign biliary strictures after bile duct injury were included in this study and underwent operation from January 2004 through January 2010 in Tianjin Nankai Hospital. Patients with strictures that developed after operation were included in this study. Patients with stricture due to lithiasis, sclerosing cholangitis, choledochal cyst, chronic pancreatitis or ampullary disease were excluded. Demographic details, presenting symptoms and signs, investigations, operative details, salvage procedures, complications and follow-up were evaluated. The study was performed after the approval was granted by the Ethics Committee of Tianjin Nankai Hospital. The written informed consent for participation was obtained from participants in the study.

The degree of bile duct dilatation

The degree of common bile duct dilatation was classified as follows: A, width above the stricture is less than 1.5 cm; B, width is from 1.5 to 3.0 cm; and C, width is more than 3.0 cm.

The level of biliary stricture

The level of biliary obstruction was classified according to Bismuth classification (Lau et al., 2010).

- Type I: Low common hepatic duct (CHD) stricture, with a length of CHD stump of > 2 cm.
- Type II: Proximal CHD stricture, with a length of CHD stump of < 2 cm.
- Type III: Hilar stricture, no residual CHD, but the hepatic ductal confluence is preserved.
- Type IV: Hilar stricture, with involvement of confluence and loss of communication between right and left hepatic duct.
- Type V: Involvement of aberrant right sectorial hepatic duct alone or with concomitant stricture of the CHD.

Surgical treatment

The types of biliary reconstruction were Roux-en-Y biliojejunostomy (hepaticojejunostomy, choledochojejunostomy, intrahepatic cholangiojejunostomy) and bile duct plasty (end-to-end bile duct anastomosis and bile duct repair).

Patient follow-up

All patients were seen in the outpatient department within 3 months of initial operation and every other 6 months thereafter. The presence of symptoms, weight loss or gain, and food intolerance were asked and patients were clinically examined, and liver function tests and ultrasound study were evaluated for each follow-up visit. Long-term results were assessed with the following clinical grading according to Terblanche et al. (1990). The rate of restenosis was also determined.

- Grade I: No biliary symptoms
- Grade II: Transitory symptoms, currently no symptoms
- Grade III: Clearly related symptoms requiring medical therapy
- Grade IV: Recurrent stricture requiring correction or related death.

Grades I and II constituted excellent or good results, grade III fair, and grade IV poor.

Statistical analysis

Data were analyzed by using SPSS 16 (version 20.0.0). The Chi-square test, Fisher's exact test and Student's t-test were used to compare differences of the data. Multivariable logistic regression analysis by binary logistic regression was used to evaluate factors that favored the outcome of Grade I and II and features for bile duct plasty. A p-value less than 0.05 indicated statistically significant.

RESULTS

Clinical characteristics of patients

Clinical characteristics of patients were listed in Table 1. The average age of the 64 patients was 48 years, range: 23–66 years. There were 30 males and 34 females. In 8 patients, the biliary lesion occurred in our institution whereas 56 patients were referred from other hospitals. 60 patients had upper abdominal pain. 50 patients presented with cholangitis and 41 of them had jaundice. And 11 patients presented with stones and 3 patients had biliary fistula. As for former operations, laparoscopic cholecystectomy was performed for 33 patients, open cholecystectomy was performed for 23 patients, cholecystectomy and CBD exploration were performed for 6 patients, and partial liver resection was performed for 2 patients. The indications for cholecystectomy and CBD exploration were cholecystitis and cholelithiasis. In patients with postoperative stricture, the interval between the injury and referral ranged from 4 to 36 weeks (median, 12 weeks). Of these 64 patients, 8 patients experienced more than 2 biliary operations and others only had 1 biliary operation before this admission. Total bilirubin and ALT Patients were elevated in these patients and they were $82 \pm 58 \mu\text{mol/L}$ and $128 \pm 68 \text{ U/L}$, respectively.

Table 1: Clinical data of patients undergoing treatment for benign biliary stricture

Item	No. of patients
Patient characteristics	
Age, median, range, y	48, 23-66
Sex, F/M	30/34
Symptoms and signs, n (%)	
Pain	60 (93.7)
Cholangitis	50 (78.1)
Jaundice	41 (64.1)
Stone	11 (17.2)
Biliary fistula	3 (4.7)
Cause, n (%)	
Open cholecystectomy	23 (35.9)
Laparoscopic cholecystectomy	33 (51.6)
Cholecystectomy and CBD exploration	6 (9.4)
Partial liver resection	2 (3.1)
Biliary operation history before this admission, n (%)	
1	56 (87.5)
≥ 2	8 (12.5)
Interval between trauma and referral, median, range, w	
	12, 4-36
Laboratory findings, mean ± SD	
Bilirubin, $\mu\text{mol/L}$	82 ± 58
ALT, U/L	128 ± 68
Bismuth classification, n (%)	
I	26 (40.6)
II	20 (31.2)
III	12 (18.8)
IV	6 (9.4)
V	0
Dilatation of bile duct above stricture, n (%)	
A (< 1.5 cm)	25 (39.1)
B (1.5-3.0 cm)	32 (50)
C (> 3.0 cm)	7 (10.9)
Surgical treatment, n (%)	
Bile duct plasty	21 (32.8)
Intrahepaticojejunostomy	6 (9.4)
Hepaticojejunostomy	28 (43.8)
Choledochojejunostomy	9 (14.0)
Hospital stay after final surgical intervention, median, range, d	
	21, 14–62
Morbidity, n (%)	
Bile leakage	2
Abdominal abscess	5
Intestinal obstruction	2
Wound infection	6
Mortality	
	0
follow-up, n	
Length of follow-up, median, range, m	38, 13–67
Lost number of follow-up	11
Stenosis	3
Lithiasis	2
Cholangitis	3
Clinical grading, n (%)	
Grade I	39 (60.9)
Grade II	14 (21.9)
Grade III	6 (9.4)
Grade IV	5 (7.8)

Radiological examinations (Ultrasonography, CT, MRCP, ERCP, PTC and T tube imaging) showed dilated intrahepatic bile duct, discontinued extrahepatic bile duct and invisible common bile duct. They were helpful to reveal obstructive plane at different levels of biliary duct system. The preoperative visualization of biliary tree was obtained by perfusional cholangiography in 9 cases, endoscopic retrograde cholangiography in 49 cases, and percutaneous transhepatic cholangiography in 6 patients. In our study, 26 patients were reported as type I, 20 as type II, 12 as type III, 6 as type IV, and 0 as type V. Dilatation of bile duct above stricture were less than 1.5 cm in 25 patients, from 1.5 to 3.0 cm in 32 patients, and more than 3.0 cm in 7 patients.

Of the 64 patients, 21 received bile duct plasty and the other 43 underwent biliojejunostomy. In bilioenteric anastomosis patients, restoration of biliary enteric continuity was achieved with a Roux-en-Y jejunal loop by means of either intrahepatic cholangiojejunostomy, hepaticojejunostomy or choledochojejunostomy. Bismuth IV strictures were managed by separately anastomosing the right and left hepatic ducts to a Roux-en-Y limb, which was considered as intrahepatic cholangiojejunostomy. The right and left hepatic ducts were exposed by excising the liver tissue. In almost all cases, anastomosis was performed by a single layer of interrupted silk stitches to obtain a mucosa-to-mucosa approximation. In non-bilioenteric anastomosis patients, we restored the biliary continuity by using bile duct repair and end-to-end bile duct anastomosis. Transanastomotic stents were used where appropriate.

The median hospital stay after final surgical intervention was 21, range: 14–62 days in this institution. The 30-day operative mortality rate was 0. Complications occurred in 15 (23.4 %) patients. One patient required reoperation because of intestinal obstruction in the early postoperative course.

Mean follow-up was 38, range: 12–67 months. Excellent or good results were achieved in 53 patients, whereas the remaining 11 patients experienced fair or poor results. 2 patients with recurrent cholangitis without evidence of anastomotic stricture had a favorable outcome with simple medical treatment. 1 patient with recurrent cholangitis with anastomotic stricture had a biliary enteric reanastomosis. Stones in bile duct of 2 patients were extracted by endoscopic method. Restrictures requiring further treatment occurred in 3 patients within 3 years and biliary enteric reanastomosis was successfully performed in these patients.

Comparison of patient clinical data between different outcomes for benign biliary strictures

In order to find the factors related to long term outcome, we compared the differences of clinical data between Grade I and II group and Grade III and IV group. Patients with biliary stones before final operation more often presented with bad outcomes than those without biliary stones, $P=0.0162$. The degree of bile duct dilatation was associated with outcomes of surgical treatment. Patients with bigger bile duct dilatation had better outcomes than those with smaller one, $P=0.0372$. Hepaticojejunostomy was correlated to better outcomes than other surgical procedures, $P=0.0483$. Other factors such as hospital stay after final surgical intervention and morbidity were also related to outcomes of surgical treatment. However, we didn't find there was a correlation between level of biliary stricture or biliary operation history before this admission and outcomes of surgical treatment. Detailed results were listed in Table 2. Multivariable logistic analysis for the outcome of Grade I and II revealed that dilatation of bile duct (> 1.5 cm), hepaticojejunostomy, morbidity were the independent variables related to the outcome (Table 3).

Table 2: Comparison of clinical data between different surgical treatment outcomes for benign biliary strictures

Item	Grade I and II	Grade III and IV	P value
No. of patients	53	11	-
Symptoms and signs, n			
Pain	50	10	0.5391
Cholangitis	41	9	1.0000
Jaundice	32	9	0.3012
Stone	6	5	0.0162
Biliary fistula	1	2	0.0739
Cause, n			
Open cholecystectomy	19	4	1.0000
Laparoscopic cholecystectomy	28	5	0.7412
Cholecystectomy and CBD exploration	5	1	1.0000
Partial liver resection	1	1	0.3165
Biliary operation history before this admission, n			0.1421
1	46	8	-
≥ 2	5	3	-
Interval between trauma and referral, mean ± SD, w	19 ± 7.3	23 ± 4.4	0.1332
Laboratory findings, mean ± SD			
Bilirubin, µmol/L	77 ± 54	87 ± 65	0.1035
ALT, U/L	158 ± 67	164 ± 54	0.5879
Bismuth classification, n			
I	24	2	0.1757
II	16	4	0.7283
III	10	2	1.0000
IV	5	1	1.0000
V	0	0	-
Dilatation of bile duct above stricture, n			0.0372
A (< 1.5 cm)	17	8	-
B (1.5-3.0 cm)	30	2	-
C (> 3.0 cm)	6	1	-
Surgical treatment, n			
Bile duct plasty	15	6	0.1552
Intrahepaticojejunostomy	4	2	0.2111
Hepaticojejunostomy	30	2	0.0433
Choledochojejunostomy	8	1	1.0000
Hospital stay after final surgical intervention, mean ± SD, d	18 ± 11	32 ± 14	0.0358
Morbidity, n	8	7	0.0020
Bile leakage	1	1	-
Abdominal abscess	1	4	-
Intestinal obstruction	1	1	-
Wound infection	5	1	-

Table 3: Multivariate logistic regression analysis for clinical features in patients with Grade I and II

Item	Odds ratio	95% CI
Dilatation of bile duct (> 1.5 cm)	5.647	1.328 to 23.998
Hepaticojejunostomy	5.869	1.155 to 29.827
Morbidity	0.101	0.024 to 0.429

Comparison of patient clinical data between bile duct plasty and biliojejunostomy for benign biliary strictures

In order to find the factors related to different surgical procedures, we compared the differences of clinical data between bile duct plasty group and biliojejunostomy group. Patients with more than 2 biliary operations before this admission more often performed by biliojejunostomy for treatment, P=0.0450. Patients with bigger bile duct dilatation had more biliojejunostomy than those with smaller one, P=0.0001. Bile duct plasty was related to Bismuth classification

Type I, P=0.0001. But Biliojejunostomy was related to Bismuth classification Type II, P=0.0001 and Type III, P=0.0059. Other factors such as cholangitis, interval between trauma and referral and elevated bilirubin were also related to different surgical procedures. However, we didn't find there was a correlation between restenosis and different surgical procedures. Detailed results were shown in Table 4. Multivariable logistic analysis revealed that dilatation of bile duct (< 1.5 cm) and Bismuth classification (Type I) were the independent variables related to bile duct plasty (Table 5).

Table 4: Comparison of patient clinical data between bile duct plasty and biliojejunostomy for benign biliary strictures

Item	Bile duct plasty	Biliojejunostomy	P value
No. of patients	21	43	-
Symptoms and signs, n			
Pain	21	39	0.2937
Cholangitis	10	40	0.0001
Jaundice	12	29	0.5858
Stone	2	9	0.3144
Biliary fistula	0	3	0.5449
Cause, n			
Open cholecystectomy	10	13	0.2669
Laparoscopic cholecystectomy	9	24	0.4265
Cholecystectomy and CBD exploration	2	4	1.0000
Partial liver resection	0	2	1.0000
Biliary operation history before this admission, n			0.0450
1	21	35	-
≥ 2	0	8	-
Interval between trauma and referral, mean ± SD, w	11 ± 6.3	18 ± 4.2	0.0355
Laboratory findings, mean ± SD			
Bilirubin, µmol/L	50 ± 34	95 ± 66	0.0473
ALT, U/L	145 ± 66	166 ± 78	0.1220
Bismuth classification, n			
I	19	7	0.0001
II	2	18	0.0100
III	0	12	0.0059
IV	0	6	0.1658
V	0	0	-
Dilatation of bile duct above stricture, n			0.0001
A (< 1.5 cm)	20	5	-
B (1.5-3.0 cm)	1	31	-
C (> 3.0 cm)	0	7	-
Hospital stay after final surgical intervention, mean ± SD, d	18 ± 8.9	26 ± 15	0.0439
Morbidity, n			
Bile leakage	1	1	-
Abdominal abscess	1	4	-
Intestinal obstruction	0	2	-
Wound infection	4	2	-

Table 4 (cont.): Comparison of patient clinical data between bile duct plasty and biliojejunostomy for benign biliary strictures

Item	Bile duct plasty	Biliojejunostomy	P value
<i>Follow-up, n</i>	2	6	1.0000
Stenosis	1	2	-
Lithiasis	1	1	-
Cholangitis	0	3	-
<i>Clinical grading, n</i>			
Grade I	12	27	0.7863
Grade II	5	9	1.0000
Grade III	2	4	1.0000
Grade IV	2	3	1.0000

Table 5: Multivariate logistic regression analysis for clinical features in patients with bile duct plasty

Item	Odds ratio	95%CI
Dilatation of bile duct (< 1.5 cm)	152	16.603 to 1391.550
Bismuth classification (Type I)	48.8571	9.225 to 258.729

DISCUSSION

The goal of treatment for a bile duct stricture is long-term absence of symptoms and free from further hospitalization. The surgical therapy is to establish a bile flow within the proximal gastrointestinal tract in a manner that prevents cholestasis, cholangitis, sludge or stone formation and restriction. The critical surgical principle is to suture healthy tissues with a tension-free anastomosis. Until now there is a number of open surgical procedures including mucosal grafting, end-to-end repair, choledochoduodenostomy and Roux-en-Y choledochojejunostomy or hepaticojejunostomy (Innes et al., 1988; Malik et al., 2012; Aust et al., 1967; Wexler and Smith, 1975). Excision of the stricture and end-to-end anastomosis establish the repair with a normal anatomic status and drainage through an intact sphincter of Oddi. But end-to-end bile duct anastomosis can only repair some selected damaged duct because of invariable loss of duct length caused by fibrosis associated with injury. Previous reports have suggested hepaticojejunostomy as the best treatment for benign biliary stenosis (Nealon and Urrutia, 1996; Tocchi et al., 2000; Kozicki et al., 1994). In this study, our surgical procedures consisted of Roux-en-Y

biliojejunostomy and bile duct plasty including resection of the stricture and end-to-end anastomosis of the bile duct with a defect less than 0.5 cm.

Our analysis was focused on patients with long-term follow-up. Univariate analysis showed the degree of dilatation, hepaticojejunostomy, hospital stay after final surgical intervention and morbidity as factors statistically correlated to long-term good outcomes. The results indicated hepaticojejunostomy as the effective therapeutic option for 67.1 % of patients of biliary tract stricture. In our series, the degree of common bile duct dilatation was a factor found to significantly affect the outcome. Dilatation provides not only a wide anastomosis, but also an easy and effectual long term stenting of the biliary tree. In the multivariate analysis, the degree of bile duct dilatation (> 1.5 cm), hepaticojejunostomy and postoperative complications proved to be significant independent predictors of outcome.

Our results confirmed that more than 80 % of patients were treated successfully with bile duct plasty or biliojejunostomy procedures and there was no significant difference for long-term outcome between bile duct plasty and biliojejunostomy. The long-

term outcome in our series was as good as that of other reports. In order to evaluate bile duct plasty and biliojejunostomy in the treatment for benign biliary stricture, we analyzed the clinical factors in both bile duct plasty and biliojejunostomy group. Biliary operations history before this admission, degree of bile duct dilatation, Bismuth classification, and interval between trauma and referral were related to different surgical procedures. In the multivariate analysis, dilatation of bile duct (< 1.5 cm) and Bismuth classification (Type I) proved to be significant independent predictors for bile duct plasty. Our results indicated that for patients with only one biliary operation before this admission, bile duct dilatation less than 1.5 cm, Bismuth classification type I and enough duct length for repair, bile duct plasty was preferred. For other cases, a biliary jejunostomy constructed to a Roux-en-Y jejunal limb was the preferable procedure.

In conclusion, our results revealed that both biliojejunostomy and bile duct plasty were effective surgical procedures for the treatment of benign biliary stricture. Bile duct plasty should be confined to patients with a degree of bile duct dilatation less than 1.5 cm and Bismuth classification (Type I). The degree of dilatation, hepaticojejunostomy and postoperative morbidity were factors statistically correlated to long term outcomes.

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