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ORIGINAL ARTICLE

Risk Factors and Predictors of Poor Outcome Following Hepaticojejunostomy for Postcholecystecomy Bile Duct Injury

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Abstract

Bilio-enteric anastomosis is the main line of treatment of bile duct injury (BDI). This study aims at exploring factors related to poor outcome after surgical reconstruction especially operative factors. Special emphasis on Hepp-Couinaud technique, theoretically, ensuring larger stoma and better blood supply. Between January 1992 and July 2015, 321 cases of postcholecystectomy BDI underwent hepaticojejunostomy. Retrospective analysis of demographics, perioperative data and management, and outcome according to Terblanche et al. Development of anastomotic strictures (AS) was evaluated. The mean follow-up time was 84.7 ± 61.9 months. Women represented 76% of all cases with a mean age of 40.1 ± 12.8. ERCP was performed in 105 (32.7%) patients. E2 and E3 strictures accounted for 76% of cases. One hundred thirty-seven (42.7%) patients underwent an end-to-side HJ. Abdominal collection or biloma was the commonest complication. Anastomotic stricture occurred in 16 (5.2%) patients after a mean time of 45 ± 31.3 months. Excellent or good outcome was detected in 281 (91.8%) patients, while fair or poor outcome was proved in 25 (8.2%) patients. On multivariate analysis, the only significant factors that predict a poor outcome were post-ERCP pancreatitis ($p = 0.008$), the design of HJ as end to side ($p = 0.033$), and postoperative biloma or abdominal collection ($p = 0.021$). On multivariate analysis, the only factor that was found to significantly affect the development of AS was postoperative development of collection or biloma ($p = 0.032$). HJ has very good results in specialized centers. Careful operative technique with sound wide stoma improves the outcome. ERCP should be used selectively and with caution for diagnosis of biliary strictures.

Keywords Bile duct injury · Cholecystectomy · Hepaticojejunostomy · ERCP · Biliary reconstruction

Introduction

Bile duct injury (BDI) is the most feared complication of cholecystectomy either open or laparoscopic [1, 2]. Minor or major bile duct injuries with or without biliary leakage may occur, as well as concomitant vascular injuries, making patients' evaluation and the choice of the best therapeutic modality difficult in some cases and multidisciplinary teams are usually involved [2, 3].

Endoscopic treatment is widely used to treat some BDIs where the biliary tract continuity is maintained, especially with bile leakage or fistula [1, 4–6]. However, surgery is still the main line of treatment in the difficult situations where the biliary tract continuity is lost [7, 8]. Biliary enteric reconstruction in the form of hepaticojejunostomy (HJ) is the main method of reconstruction. Choledochoduodenostmy and direct duct to duct repair may be used, also. Several modifications of the surgical technique were described including the use of stents, access loops. The most important modification was the routine use of high biliary anastomosis with extension of the incision to the left hepatic duct or "Hepp-Couinaud technique." This technique, theoretically, ensures a larger stoma and better blood supply [8].

The outcome of HJ is excellent in most series with a success rate of more than 85% [9]. Long-term follow-up is recommended as anastomotic stricture may develop years after surgical reconstruction and may lead to biliary cirrhosis

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[10–12]. A prospective controlled trial is very difficult to conduct in such a complex situation and limited numbers [9].

This large retrospective study aims to evaluate both the short-term and long-term results of HJ for the reconstruction of major BDI and explore the factor-related poor outcome, with special emphasis on the surgical technique.

Patients and Methods

Data Collection

In the period between January 1992 and July 2015, 321 cases of postcholecystectomy bile duct injuries (BDI) underwent hepaticojejunostomy (HJ) as a method for biliary reconstruction. All these cases are included in this study. BDI due to other causes or those managed endoscopically were not included. The data were obtained from the medical records and a prospective data base maintained after the year 2005. The follow-up was completed through office visits or by telephone. This case series study was approved by local ethical committee of Mansoura Faculty of Medicine, code number: R/16.10.09. All patients gave informed written consent for surgery, possible consequences, and the use of data for scientific purposes. The study is registered in Research Registry under UIN researchregistry3031. This research work has been reported in line with the PROCESS criteria [13].

Our center is the referral center for the Egyptian Delta area and serves more than 5 million capita. We manage patients referred from private practices, governmental district, and university hospitals. The management is multidisciplinary including surgeons who are well trained on ERCP, radiologists, and interventional radiologists. All surgeons who performed the biliary reconstruction were well qualified professors and consultants hepatobiliary surgeons. Minimal inter-surgeon quality difference is assured.

Data analyzed included demographics, referring surgeon management, our interventions prior to definitive surgery, the details of operative management with special emphasis on the surgical reconstruction, postoperative course including hospital mortality, follow-up data with special concern for development of anastomotic strictures (AS), readmissions, and further interventions.

The Bismuth-Strasberg classification of biliary injury was utilized to describe the level of injury [14]. All patients were of class E injuries based on preoperative and intraoperative assessment. The operative management differed according to the preference of the surgeon.

End-to-side HJ is defined as division of the encircled proximal biliary stump followed by anastomosis to the side of the jejunal loop. A side-to-side HJ is defined as an anastomosis, without encircling the proximal stump, to the transversely or longitudinally incised anterior wall of the common hepatic duct (CHD) without extension to the left hepatic duct. Hepp-Couinaud technique is a modification of the side-to-side anastomosis with extension to the left hepatic duct (LHD) [15].

Definition of Complications

Anastomotic stricture (AS) was defined as documented stricture by radiology in the presence of symptoms or deranged liver function tests, regardless of the management. Cholangitis was defined in patients without AS who required antibiotic therapy for right upper quadrant abdominal pain, fever, or leukocytosis with cholestatic liver function tests [14].

Short-term complications were defined as those occurring within 30 days of definitive surgery. During follow-up, when the clinical signs and/or abdominal sonography suggest the presence of AS, magnetic resonance cholangiography (MRCP) was ordered.

Outcomes

The primary outcome was the success of the biliary reconstruction, based on the classification suggested by Terblanche et al. [16]. For comparison reasons, we grouped the first two categories together as *good outcome*, the last two categories together as *poor outcome*. Secondary outcomes are the risk factors for *poor outcome* and *anastomotic stricture*.

Statistical Analysis

Numerical data were presented as means and standard deviations. Categorical and ordinal variables were presented as proportions. Continuous variables were compared with the two-tailed Student's *t* test, whereas categorical variables were compared with the chi-square test. Logistic regression was used to detect independent factors affecting the outcome. Kaplan-Meier and log rank tests were used to detect risk factors for the occurrence of AS. Cox regression test was used to examine significant risk factors to identify independent predictors of AS. $P < 0.05$ was considered statistically significant. All statistical analyses were performed using IBM SPSS v.21 software.

Results

Demographics

In the period between January 1992 and July 2015, 321 patients underwent HJ for biliary reconstruction following major postcholecystectomy BDI. Women represented 76% of all cases. The mean age was 40.1 ± 12.8. Laparoscopic cholecystectomy (LC) accounted for 14.4% of the offending

cholecystectomies. Eight (2.5%) cases were performed in our center (Table 1).

Presentation and Preoperative Management (Table 2)

Jaundice was the commonest presentation. Cholangitis was absent in patients who were referred within the first 10 days and significantly more in patients referred after 1 month from the index cholecystectomy ($p = 0.003$). Intraoperative recognition of BDI occurred in 11 (3.4%) patients including three patients who were operated in our center, out of eight BDIs that occurred in this time period (37.5%).

Twenty-one (6.5%) patients had previous attempts of repair, 8 of them underwent HJ and 13 had a direct duct to duct anastomoses. Two patients, out of 21, underwent duct to duct anastomosis in our center. One patient required HJ after 62 months for recurrent stricture that was not possible to correct endoscopically. The other had a duodenal perforation during ERCP that urged a definitive HJ with repair of the duodenum 8 months after OC.

All ERCPs and interventional radiology procedures were performed in our center. ERCP was performed in 105 (32.7%) patients and identified 73 (69.5%) patients with complete ligation of the CBD that is impassable to the guidewire and 32 (30.5%) patients with significant biliary strictures who were treated with stent placement and or balloon dilation but did not succeed. Twelve (11.4%) patients experienced post-ERCP pancreatitis that was managed conservatively. Two patients had bleeding that was controlled endoscopically and one patient had a duodenal perforation and was explored immediately with repair and definitive HJ.

Table 1 Demographic data and details of the index cholecystectomy

	Number (%)
1. Age	
Mean (± SD)	40.1 (± 12.8)
Range (min–max)	72 (3–75)
2. Gender	
Male	77 (24%)
Female	244 (76%)
3. Approach of cholecystectomy	
Open	275 (85.6%)
Laparoscopic	40 (12.5%)
Converted lap	6 (1.9%)
4. Place	
Outside GISC*	313 (97.5%)
Private sector	212 (66%)
General hospitals	88 (27.5%)
University hospitals	13 (4%)
Inside GISC	8 (2.5%)
Total number	321

GISC Gastrointestinal Surgical Center

Intraoperative Details (Table 3)

One hundred thirty-seven (42.7%) patients underwent an end-to-side HJ, whereas 184 (57.3%) patients had either a side to side or Hepp-Couinaud HJ. The procedure did not include access loop in any patient.

Early Postoperative Data (Table 4)

Hospital mortality occurred in 6 (1.9%) patients. Four patients died of sepsis related to biliary leakage. Two of them had right hepatectomy in association with biliary reconstruction and were re-explored for control of biliary leakage. Two patients developed cholangitis, they had liver cirrhosis on exploration, their serum bilirubin level did not improve, and died of sepsis associated with liver failure.

The mean hospital stay was 6.4 ± 4.1 days. One hundred five (32.7%) patients developed one or more complications. Reoperation during the first 90 days was required in 11 (3.4%) patients.

Long-Term Follow-up Data

The long-term follow-up was available for 306 (95.3%), out of 321, patients. Fifteen patients of the original cohort were excluded; 6 died in hospital and 9 patients missed follow-up and did not respond to our communications. The mean follow-up time was 84.7 ± 61.9 months.

Forty (13.1%) patients developed one or more late complications. Sixteen (5.2%) patients developed anastomotic stricture, after a mean period of 45 ± 31.3, range (4–204) months. Five patients underwent successful refashioning of the HJ, one of them underwent balloon dilation for AS, 24 months later. Percutaneous transhepatic anastomotic dilation was successful in one patient. One patient underwent percutaneous transhepatic tube drainage, after failed dilation. Because of advanced liver cirrhosis, poor liver functions, and portal hypertension, six patients were managed non-surgically. Three patients with AS and mild disturbance of liver enzymes were managed conservatively and followed up. These nine patients were managed with antibiotics and supportive medical treatment.

Excellent or good outcome was apparent in 281 (91.8%) patients, while fair or poor outcome was detected in 25 (8.2%) patients. Three patients with documented AS on follow-up did not show significant symptoms. Late mortality occurred in 11 patients. One patient died of sepsis related to anastomotic stricture that was managed conservatively. Ten patients died of causes not related to the biliary injury.

Table 2 Pre-reconstruction management in relation to time of recognition of injury

Time of recognition of injury	Nr (%)	Attempted surgical repair	Nr	Interventional radiology			Trial ERCP and findings		
				USTD	PTD	Both	Nr	Ligated	Stricture
Intraoperative	11 (3.4%)	Repair over stent	3				3	1	2
		HJ	2			1			
		No attempt		2		1	1		1
Early postoperative (less than 2 weeks)	229 (72.8%)	Repair over stent	7				3	1	2
		HJ	5	1	1	1			
		Abdominal toilet and drainage	17	3	1	1	10	7	3
		No attempt		21	5	1	58	46	12
Intermediate (2–6 weeks)	42 (13.1%)	Repair over stent	2				1	1	
		HJ	1			1	1		1
		Abdominal toilet and drainage	5	1	2		4	4	
		No attempt		3	4		10	7	3
Late postoperative (more than 6 weeks)	39 (10.7%)	Repair over stent	1				1	1	
		No attempt			1		13	5	8
Total	321		43	31	14	6	105	73	32

USTD ultrasound-guided tube drainage, *PTD* percutaneous transhepatic tube drainage

Factors Affecting the Outcome

Many variables were analyzed for their effect on the outcome, as shown in Table 5. On multivariate analysis, the only significant factors that predicted a poor outcome, Terblanche grade 3 or 4, were post-ERCP pancreatitis ($p = 0.008$), the design of HJ as end to side ($p = 0.033$), and postoperative biloma or abdominal collection ($p = 0.021$).

Factors Affecting the Development of Anastomotic Stricture

On univariate analysis using Kaplan-Meier test for the effect of previous factors on the development of AS, the following factors were found to be significant: post-ERCP pancreatitis ($p = 0.038$), interval to referral between 10 days and 3 months ($p = 0.045$), intraoperative finding of internal biliary fistula ($p = 0.049$), postoperative biloma or collection ($p = 0.002$). On multivariate analysis, the only factor that was found to significantly affect the development of AS was postoperative development of collection or biloma ($p = 0.032$).

Discussion

Multidisciplinary management is crucial in the decision as regards preoperative evaluation, preparation, and the proper intervention. Surgical management gives the best results with specialized teams. This ensures excellent knowledge of the hilar biliary anatomy [9]. Preoperative awareness of associated vascular injuries is also important [17].

Surgical reconstruction involves creating as wide bilioenteric anastomosis as possible, not under tension and well perfused. This is best done when the tissues are not significantly inflamed, either within 48 h of BDI or after 4–6 weeks [9, 18]. HJ can be created as end to side, side to side, or by the Hepp-Couinaud technique [9, 19]. In this series, we assessed the use of end-to-side technique in comparison to the other two techniques because the end to side appears to be technically more difficult, may aggravate ischemia, endanger the portal vein, and it is difficult to be extended. Routine use of Hepp-Couinaud technique is reported to give better results [20, 21]. Even in cases of E1 or E2 strictures, we tend to create a long stoma more than 25 mm by longitudinally incising the anterior wall of the duct and extension to the left hepatic duct as required.

HJ for repair of bile duct is reported by many authors to be safe with good preoperative patient optimization. Hospital mortality rate ranging from 0 to 1.5% are reported with early complications of 3 to 33.3%. Bile leakage and intra-abdominal collections are the most significant complications [7, 12, 14, 22]. These figures are similar to ours. These patients are usually in their 4th or 5th decade with good life expectancy after surgery. This emphasizes the importance of long-term outcome [12]. Being the only center in our locality performing such major hepatobiliary surgery, we follow our patients carefully and persuade them to contact us any upon any related symptom. Seventy-seven percent of our patients were followed up for more than 2 years.

The long-term results are reported according to recurrence of anastomotic stricture [10, 14] or outcome classifications such as Terblanche et al. [16] or McDonald et al. [7, 12, 23].

Table 3 Intraoperative data

	Number (%)
Liver cirrhosis	43 (13.4%)
Biloma	65 (20.2%)
Internal biliary fistula	42 (13.1%)
Right hepatic artery injury	13 (4%)
Level of injury	
E1	49 (15.3%)
E2	180 (56.1%)
E3	64 (19.9%)
E4	24 (7.5%)
E5	4 (1.2%)
Number of anastomosis	
Single	293 (91.3%)
Double	8 (2.5%)
Ductoplasty (2 or more)	20 (6.2%)
Technique of anastomosis	
End-to-side	137 (42.7%)
Side-to-side	18 (5.6%)
Hepp-Couinad	166 (51.7%)
Stoma size (mm) Mean (±SD)	18 ± 6
Stent use	22 (6.8%)
Operative time (min) Mean (±SD)	184 ± 53
Blood loss (mL)	
Mean (±SD)	196 ± 355
Range	50–2800
Intraoperative complications	
Vascular injury	9 (2.8%)
Intestinal injury	3 (0.9%)

We believe that AS is important factor for the outcome, but still some cases show mild AS that is not symptomatic nor interfering with the patient daily activities. In this study, the long-term success rate (grades 1 and 2) was 91.8% while the failure rate was 8.2%. These figures are similar to most figures reported in the literature recently [7, 12, 22].

Post-ERCP pancreatitis can lead to more difficult situation during surgical reconstruction as the endoscopic maneuver not only maintains the inflammatory response related to the original injury but also potentiates it around the pancreas and the biliary system. This leads to thickening of the ducts and development of dense adhesions increasing the difficulty of the repair. Such factor was not previously reported except in another study from our center on a smaller number of patients [10]. However, a recent study by Kirks et al. found ERCP trials to be correlated with increased risk of readmission after surgical repair [24].

Hepp-Couinaud technique facilitates the creation of a wide stoma giving good results on the long term [8, 12]. This technique is practiced in our center by one group while the other group believes in the end to side reconstruction. This series proved that an end-to-side anastomosis is inferior to Hepp-Couinaud technique. This may be attributed to the wider stoma and better vascularity.

Postoperative biloma or collection was found to significantly affect the outcome and the development of AS. Abdominal sepsis in the vicinity of the anastomosis is expected to produce intense inflammatory reaction and progressive fibrosis that subsequently leads to stenosis. Pottakkat et al. [7] reported that external or internal biliary fistula found during the repair may lead to failure of HJ. They pointed to persistent inflammation and non-dilated duct system. We did not find a significant effect of biliary fistula on the outcome. This may be related to our practice to delay the repair until the cessation of fistula.

Higher level of injury, E3 and E4, is commonly related to failure of HJ [14, 25]. This series showed that patients with E4 and E3 injuries had higher failure rate but not statistically significant. Similar result was reported by Lubikowski et al. [22]. Previous attempt of repair was found to promote failure of the HJ by some authors [7, 26]. In this series, 9 patients underwent high repair in the form of HJ. Only one patient had a recurrent anastomotic stricture (11.1%), with no significant

Table 4 Early postoperative complications and their management

	Number (%) $N = 321$	Management			
Early complications	105 (32.7%)	Conservative	Surgical Toilet and drainage	Refashioning of HJ	Radiological (USTD)
1. Bile leakage	47 (14.6%)	32 (10%)	3 (0.9%)	1 (0.3%)	11 (3.4%)
2. Biloma/Collection	73 (22.7%)	54 (16.8%)	1 (0.3%)	0	18 (5.6%)
3. Internal hemorrhage	6 (1.9%)	0	6 (1.9%)	0	0
4. Persistent hyperbilirubinemia	14 (4.4%)	14 (4.4%)	0	0	0
5. Wound infection	16 (5%)	16 (5%)	0	0	0
6. UTI/renal impairment	4 (1.2)				
7. Chest infection	9 (2.8)				

Table 5 Factors affecting the outcome of hepaticojejunostomy in 306 patients

	Good outcome	Poor outcome	*p* value
Type of cholecystectomy			
Open	238 (91.5%)	22 (8.5%)	0.831
Lap	43 (93.5%)	3 (6.5%)	
Timing of recognition of injury			
Intraoperative	9 (82%)	2 (18%)	0.53
Less than 2 weeks	200 (92%)	17 (8%)	
2–6 weeks	35 (90%)	4 (10%)	
More than 6 weeks	37 (95%)	2 (5%)	
Pre-reconstruction corrective surgery			
Yes	265 (92%)	22 (8%)	0.211
No	16(84%)	3(16%)	
Pre-reconstruction ERCP			
Yes	86 (89%)	11 (11%)	0.168
No	195 (93%)	14 (6.7%)	
Post-ERCP pancreatitis			
Yes	7 (64%)	4 (63%)	0.005
No	79 (92%)	7 (8%)	
Interval to referral			
Less than 10 days	11 (85%)	2 (15%)	0.008
10 days to 3 months	188 (95%)	9 (5%)	
More than 3 months	82 (85%)	14 (15%)	
Interval to repair			
Intraoperative	0	1 (100%)	< 0.001
Less than 3 days	1 (50%)	1 (50%)	
3 days to 6 weeks	121 (96%)	5 (4%)	
> 6 weeks	159 (90%)	18 (10%)	
Preoperative AST			
Mean (SD)	111 (85)	85 (39)	0.039
Preoperative ALT			
Mean (SD)	126 (110)	84 (46)	0.004
Operation past 2002			
Up to 2002	66 (87%)	10 (13%)	0.067
Post 2002	215 (93%)	15 (7%)	
Liver cirrhosis			
Yes	36 (12.8%)	2 (8%)	0.485
No	245 (87.2)	23 (92%)	
Internal biliary fistula			
Yes	37 (13.2%)	5 (20%)	0.341
No	244 (86.8%)	20 (80%)	
Associated RHA injury			
Yes	11 (3.9%)	1 (4%)	0.983
No	270 (96.1%)	24 (96%)	
Intraoperative level of BDI			
E1	46 (98%)	1 (2%)	0.474
E2	153 (91%)	15 (9%)	
E3	57 (91%)	6 (9%)	
E4	21 (88%)	3 (12%)	
E5	4 (100%)	0	
Design of anastomosis			
End to side	112 (86%)	18 (14%)	0.002
Hepp-Couinaud or side to side	169 (96%)	7 (4%)	
Number of anastomoses			
Single	256 (92%)	22 (8%)	0.855
Ductoplasty	7 (87.5%)	1 (2.5%)	
Two anastomoses	18 (90%)	2 (10%)	
Technique of suturing			
Interrupted	118 (93%)	9 (7%)	0.366
Continuous	47 (87%)	7 (13%)	
Mixed	116 (93%)	9 (7)	
Operative time (min)			
Mean (SD)	181 (50)	220 (66)	0.009
Postoperative bile leak or collection			
Yes	71 (84%)	14 (16%)	0.001
No	210 (95%)	11 (5%)	

RHA right hepatic artery

difference from those who did not undergo such repair. This may be related to the fact that in our center, the difficult cases are allocated to the surgeons with the vast experience. Other factors that may influence the outcome include associated vascular injury, the presence of external or internal biliary fistula, and the presence of portal hypertension [7, 12, 24]. These factors were not found to be statistically significant in this study. Associated vascular injury is gaining importance in recent literature as a significant risk factor for failure of surgical reconstruction and it is estimated to occur in up to 39–47% of cases [22]. Major vascular injuries including the right portal vein may be catastrophic and require liver transplantation [24]. Our results may be not entirely accurate, as we did not routinely investigate for associated vascular injuries. Our results can be explained by the delayed repair adopted by us in most of the cases. This allows time the formation of collateral circulation and restoration of good blood supply to the hilar structures.

This study is limited by its retrospective nature, its spread over long period and involvement of many surgeons. A prospective controlled study is very difficult to implement with the small number of cases referred annually to us and by their complex nature. Also, we did not include minor bile duct injuries that were treated endoscopically, Strasberg class A and D. Further studies will be needed in the future, especially with the advent of laparoscopic and robotic biliary reconstruction.

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Compliance with Ethical Standards

This case series study was approved by local ethical committee of Mansoura Faculty of Medicine, code number: R/16.10.09.

Conflict of Interest The authors declare that they have no conflicts of interest.

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