DOI:10.1111/j.1477-2574.2008.00002.x HPB

ORIGINAL ARTICLE

Timing of referral impacts surgical outcomes in patients undergoing repair of bile duct injuries

Craig P. Fischer, Bridget N. Fahy, Tom A. Aloia, Barbara L. Bass, A. Osama Gaber & R. Mark Ghobrial

Department of Surgery, Weill Cornell Medical College, The Methodist Hospital Department of Surgery, Houston, TX, USA

Abstract

Bile duct injury (BDI) after laparoscopic cholecystectomy (LC) remains a significant surgical challenge. Despite claims to the contrary, the incidence of bile duct injury has remained elevated since the introduction of LC. Several issues regarding the surgical management of BDI are controversial, including: (i) identification of the surgeon and centre most capable of managing the injury, (ii) timing of surgical repair, (iii) incidence and significance of associated vascular injury and (iv) identification of patient factors which significantly impact outcome after repair. Variability in timing of referral of BDI to tertiary centres has been noted in the literature. The impact of timing of referral upon post-operative outcomes after definitive surgery has yet to be clearly investigated. We report our experience with 44 patients who required reconstructive surgery after BDI. In contrast to the many studies available in the literature, patients in the current study were classified according to a modern injury classification system. Additionally, we examined the impact of delayed referral to our centre on short- and long-term outcomes after surgical repair of BDI.

Keywords

bile duct injury, outcomes, timing of referral

Received 10 May 2008; accepted 30 August 2008

Correspondence

Craig P. Fischer, Department of Surgery, The Methodist Hospital, Weill Cornell Medical College, Smith 1661, 6550 Fannin, Houston, TX 77030, USA. Tel: +1 713 441 5175. Fax: +1 713 790 6472. E-mail: cpfischer@tmhs.org

Introduction

Bile duct injury (BDI) after laparoscopic cholecystectomy (LC) remains a significant surgical challenge. Despite claims to the contrary, the incidence of BDI has remained elevated since the introduction of LC.[1] Over 750 000 cholecystectomies are performed in the United States annually.[2,3] The estimated incidence of BDI is between 300 and 500 per 100 000 operations performed; conservatively yielding approximately 4000 bile duct injuries occurring each year.[1,2,4–6]

Even with improved critical care for patients and expanding numbers of specialized centres with expertise in management of this complex complication, a significant number of BDIs continue to be managed by the surgeon responsible for the injury. A series reported from Connecticut indicated that 89% of injuries in that state are repaired in the same institution where the injury occurred.[7] Other reports indicate that in the United States, 58–75% of BDIs are repaired by the injuring surgeon.[2,6] Flum and colleagues reported increased mortality when the repairing surgeon was the same as the injuring surgeon.[2]

In this setting, several issues regarding the surgical management of BDI remain controversial, including: (i) identification of the surgeon and centre most capable of successfully managing the injury, (ii) timing of surgical repair, (iii) incidence and significance of associated vascular injury and (iv) identification of patient factors which significantly impact outcome after repair.

Variability in timing of referral of BDI to tertiary centres has been noted in the literature.[8–10] Cameron and colleagues noted a median time to referral of 3 weeks.[11] Although informative, this series included patients with biliary stricture and did not define biliary injury according to a common injury classification schema that allows for identification of the subset of patients who lack biliary enteric continuity, and thus may require earlier repair. The

Presented at the 2008 American Hepato-Pancreato-Biliary Association Congress, March 23-30, 2008, Fort Lauderdale, Florida.

impact of timing of surgery and subsequent post-operative outcomes have been studied by Gouma *et al.* who reported a negative effect of early repair upon surgical outcomes after reconstructive surgery for BDI.[10] The impact of timing of referral upon post-operative outcomes after definitive surgery has yet to be clearly investigated.

In the current study, we report our experience with 44 patients who required reconstructive surgery after BDI. In contrast to previous studies available in the literature, patients in the current study were classified according to a modern injury classification system. Additionally, we examined the impact of delayed referral for surgical management on short- and long-term outcomes after surgical repair of BDI.

Material and methods

Data collection

A prospective database for Hepato-Pancreatico-Biliary (HPB) surgery patients was maintained in accordance with our institutional review board. Data collected included demographics, indication for LC, use of cholangiography, time from injury to diagnosis and time to referral to our institution, diagnostic and therapeutic studies performed prior to and after referral, operative details of the cholecystectomy, peri-operative complications after BDI repair and clinical follow-up.

Injuries to the biliary tree were classified according to the Hanover system and the Bismuth classification[12–14] to allow specific characterization of the type and level of injury at the time of diagnosis. From 2001–2007, 72 patients were referred for management of BDI; 44 of whom underwent operative repair and are the subject of this report. The remaining 28 patients underwent endobiliary stent therapy without need for surgical intervention. Patients with bile duct strictures from trauma, malignancy and inflammatory processes were excluded. Additionally, for the purposes of this report, patients with Hanover class A injuries (cystic duct stump leaks and gallbladder fossa leaks) and Hanover class E injuries (stricture of the main bile duct) were also excluded from analysis. In this study, early referral was defined as within 72 h of recognition of the injury and delayed referral as greater than 72 h after recognition of injury. After definitive surgical repair, a post-operative biliary leak was defined as bile in a surgical drain at any time in the post-operative period or a leak demonstrated by cholangiography. Biliary stricture was defined as a narrowing of the biliary-enteric anastomosis requiring percutaneous dilation, stenting or external drainage. When patients were referred within 7 days of injury and no concomitant intra-abdominal infection was present, immediate surgical repair was considered. In the majority of patients, to allow portal inflammation to subside and to determine the level of biliary ischaemia, BDI repair was delayed for a period of 6 weeks. During this interval, bilomas were percutaneously drained and patients underwent biliary drainage with percutaneous transhepatic biliary drains, when appropriate. Definitive establishment of bilioenteric continuity was accomplished with hepaticojejunostomy to the common hepatic duct or via a Hepp-Couinaud[15] approach when appropriate.

Statistical analysis

Comparison between groups was performed with the χ^2-test, Fisher's exact test and Student's *t*-test using In Stat 3.0 (GraphPad Software, San Diego, CA, USA). Using overall complications as the dependent variable, a separate univariate Cox proportional hazards regression analysis was performed. Covariates that affected overall complications at the $P = 0.05$ level of significance were included in a multivariate Cox proportional hazards model (GraphPad Software). Results are reported as mean $\pm$ SD and Odds Ratio (OR) [95% Confidence Interval (CI) and *P*-value]. Statistical significance was accepted at the 5% level.

Results

From 2001–2007, 72 patients were referred to our institution for management of BDI; 44 of whom underwent operative repair. Patient demographics, clinical factors at presentation, type of index operation (initial type of cholecystectomy) and classification of injury are summarized in Table 1. The mean age of all patients was 44.6 $\pm$ 15.4 years (range: 14–84 years). Seventy-five per cent of patients referred were women. Cholangitis was present upon arrival to our institution in 40%, jaundice was present in 60% (defined as total bilirubin >3.0) and biloma was detected in 83% of patients (10% sterile, 73% infected). Thirty-two per cent of patients met diagnostic criteria for either systemic inflammatory response syndrome (SIRS) or multiple organ failure (MOF) at the time of initial presentation.

Of the 44 patients operated, 42 of the BDIs occurred at an outside hospital and 2 injuries occurred at our institution. The initial operation was LC without cholangiogram in 84% of patients ($n = 37$). None of the patients in this series underwent LC with cholangiogram as the index operation. LC converted to open cholecystectomy was performed in 5% of patients ($n = 2$) and 11% ($n = 5$) underwent LC converted to open cholecystectomy with primary repair of the BDI. In the latter group, all five patients presented with continued biliary fistula after a failed primary repair (primary anastamosis in two patients, choledochoduodenostomy in one patient and hepaticojejunostomy in two patients). Overall, only 30% of injuries were recognized by the primary operating surgeon at the time of LC.

Complete radiographic visualization of the biliary tree was obtained after referral to our institution in all patients. Eleven per cent of patients were found to have a clip placed on the extrahepatic biliary tree (Hanover class B). Tangential injury extrahepatic biliary tree without a clip was noted in 7% of cases (Hanover class C). Eighty-two per cent of patients ($n = 36$) had complete transection of the extrahepatic biliary tree (Hanover class D). Based upon the Bismuth classification for level of injury, 73% of patients were classified as level I–III, whereas 27% were level IV–V.

Table 1 Demographics and clinical factors

Demographics/clinical factors	Number	%
Total patients	44	
Age (years)		
Mean	44.6 ± 15.2	
Range	14–84	
Gender		
Male	11	25
Female	33	75
Clinical factors at presentation		
Cholangitis	13	40
Jaundice	50	60
Biloma-sterile	25	10
Biloma-infected	32	73
SIRS	15	25
MOF	3	7
Type of index operation	Number	%
Initial operation		
Outside institution	42	95
Our institution	2	5
Type of initial operation		
Laparoscopic cholecystectomy	37	84
Laparoscopic cholecystectomy with cholangiogram	0	0
Laparoscopic converted to open cholecystectomy	2	5
Laparoscopic converted to open with repair	5	11
Recognition of injury by laparoscopic surgeon at time of surgery	13	30
Type and level of injury		
Hanover classification, type of injury		
B, clip on bile duct	5	11
C, tangential or partial injury.	3	7
D, transection of main biliary tree, any level	36	82
Bismuth level of injury		
Levels I–III	32	73
Levels IV–V	12	27

Hanover class A and E excluded. SIRS, systemic inflammatory response syndrome; MOF, multiple organ failure.

The post-repair complications and clinical outcomes of patients based upon timing of referral after recognition of BDI are summarized in Table 2. Thirty-four per cent of patients were referred early ($n = 15$) whereas 66% had a delayed referral after 72 h ($n = 29$). There were no differences between the early and delayed referral groups with regard to gender, Hanover classification of injury or Bismuth classification of level of injury.

After definitive surgical repair at our facility, no significant differences were noted between the early and late referral groups with regard to rates of anastomotic leak, need for reoperation, post-operative bleeding (defined as transfusion of two more units of blood post-operatively), superficial wound infection or biliary stricture. In contrast, intra-abdominal abscess and need for intensive care unit (ICU) stay >7 days were more frequently observed in patients referred after 72 h ($P < 0.05$). There was one death in our series yielding a post-operative mortality rate of 2.3%; this death occurred in the early referral group. The patient was an 84 year-old woman with a Hanover class D injury, who presented with MOF and was found to have a right hepatic artery and portal vein injury.

Table 3 summarizes the time and place of BDI diagnosis (in hospital versus after discharge), and interventions directed at diagnosis or treatment of the injury prior to referral to our unit. There were no differences between the early and delayed referral groups with regard to time or place of BDI diagnosis. Pre-referral percutaneous drainage of biloma was performed significantly more often in the delayed referral group (30 drainages in 29 patients) compared with the early referral group (9 drainages in 15 patients, $P < 0.001$). No differences were noted in the use of diagnosistic endoscopic retrograde cholangiopancreatography (ERCP) between the groups, although patients in the delayed referral group were more likely to have received ERCP with stent placement compared with patients in the early referral group (2/15 vs. 14/29, $P < 0.05$). When the total number of interventions performed prior to referral was analysed, patients in the delayed referral group underwent significantly more interventions compared with patients in the early referral group (1.04 ± 0.34 vs. 2.4 ± 0.65 interventions per patient, $P < 0.001$). The mean time from recognition of injury to referral was 2.8 days in the early referral group versus 8.2 days in the delayed referral group. The mean time from creation of injury to referral was 5.6 days in the early referral group and 13.1 days in the delayed referral group.

Study covariates associated with overall complications at the $P = 0.05$ univariate level of significance were included in a multivariate Cox proportional hazards model (Table 4). Backwards stepwise regression analysis determined that Hanover class D, high Bismuth level, delayed referral and the number of pre-referral interventions were correlated to total complications (OR 2.57, $P = 0.004$, OR 1.32, $P = 0.04$, OR 1.68, $P = 0.07$, OR 1.25, $P = 0.06$, respectively). In univariate analysis, age >45 years was associated with increased overall major complication rates (OR 1.37; 95% CI: 0.11–0.45, $P = 0.034$), but was not significant in the multivariate analysis (OR 0.38, 95% CI: 0.14–0.44, $P = 0.06$).

Discussion

We report our experience with 44 patients who required reconstructive surgery after BDI with a specific focus on the timing of referral and impact upon post-operative and long-term outcomes after definitive repair. Patients who were referred after 72 h of recognition of BDI were more likely to have an intra-abominal abscess and prolonged ICU stay after definitive repair, when compared with patients referred within 72 h. Delayed referral patients had similar types and levels of BDI, yet were more likely to undergo significant interventions at the outside hospital. A

Table 2 Timing of referral, injury type and surgical complications

	Early referral *n* = 15 (%)	Delayed referral *n* = 29 (%)	*P*-value
Age	43	45	
Gender			
Male	3 (20)	7 (24)	ns
Female	12 (80)	22 (76)	ns
Injury type			ns
Hanover Class B	1 (7)	2 (7)	ns
Hanover Class C	0 (0)	5 (17)	ns
Hanover Class D	14 (93)	22 (76)	ns
Level of injury, bismuth			
I–III	11 (73)	21 (72)	ns
IV–V	4 (27)	8 (28)	ns
Surgical complications			
Anastomotic leak	3 (20)	2 (7)	ns
Need for reoperation	0 (0)	1 (3)	ns
Post-operative bleeding	4 (27)	6 (21)	ns
Superficial wound infection	2 (13)	5 (17)	ns
Biliary stricture	0 (0)	2 (7)	ns
Mortality, 30 day	1 (7)	0 (0)	ns
ICU stay >7 days	1 (7)	8 (28)	$P < 0.05$
Intra-abdominal abscess	1 (7)	9 (31)	$P < 0.05$

ICU, intensive care unit.

Table 3 Time of diagnosis of injury, interventions prior to transfer and timing of referral

Time of diagnosis and outside interventions	Early referral *n* = 15 (%)	Delayed referral *n* = 29 (%)	*P*-value
Timing of diagnosis of bile duct injury			
During initial cholecystectomy	1 (7)	7 (24)	ns
In-hospital	4 (27)	13 (45)	ns
After discharge	10 (67)	9 (31)	ns
Interventions prior to referral[a]			
None	5 (33)	1 (35)	ns
Relaparotomy without repair	0 (0)	3 (10)	ns
Relaparotomy with repair	0 (0)	5 (17)	ns
Percutaneous drainage of biloma	9 (60)	30[a]	$P < 0.001$
Percutaneous transhepatic cholangiogram	0 (0)	1 (3)	ns
ERCP	5 (33)	16 (55)	ns
ERCP + stent placement	2 (13)	14 (48)	$P < 0.05$
Total interventions at OSH (mean interventions/patient)	1.04 ± 0.34[a]	2.4 ± 0.65[a]	$P < 0.001$
Time from recognition of injury to referral (days, mean)	2.8	8.2	$P < 0.05$
Time from injury to referral (days, mean)	5.6	13.1	$P < 0.05$

ERCP, endoscopic retrograde cholangiopancreatography; OSH, outside hospital.
[a]Patients may have undergone more than one intervention.

number of these interventions were of limited value – 49% of patients underwent therapeutic ERCP with stent placement, yet lacked biliary enteric continuity (Hanover Class B and D). All five patients who underwent relaparotomy and attempt at repair at the outside facility failed, requiring revisional surgery at our facility.

The impact of pre-referral interventions on complication rates after reconstructive surgery for BDI has received little attention in the surgical literature. In their review of 500 patients referred to the Academic Medical Center in Amsterdam, De Reuver, determined that post-operative complications after definitive repair

Table 4 Univariate and multivariate analysis of major complications

Variable	Major complications [No. (%)]	Univariate analysis odds ratio (95%CI)	*P*	Multivariate analysis odds ratio (95%CI)	*P*
Age >45	12 (27)	1.37 (0.11–0.45)	0.034	0.38 (0.14–0.44)	0.06
Age <45	33 (75)	–		–	
BDI type D					
Yes	32 (71)	2.54 (1.44–4.54)	0.004	2.57 (1.46–4.58)	0.004
No	4 (9)	–		–	
BDI level IV–V					
Yes	11 (24)	1.32 (0.12–0.79)	0.03	0.34 (0.013–0.81)	0.04
No	1 (2)	–		–	
Delayed referral					
Yes	28 (62)	1.63 (1.35–1.86)	0.02	1.68 (1.39–2.12)	0.07
No	2 (4)	–		–	
Any pre-referral intervention					
Yes	35 (78)	1.20 (0.98–1.74)	0.04	1.25 (1.10–1.83)	0.06
No	3 (7)	–		–	

BDI, bile duct injury.

were more likely in patients who underwent interventions at an outside facility prior to referral.[10] Other than this report, few other studies have examined this potentially important variable. Our data suggest that delayed referral and interventions performed at outside facilities both conspire to increase the risk of definitive repair.

It is estimated that the majority of bile duct injuries that occur in the United States are managed at the facility where the injury occurred and that definitive biliary repair is frequently performed by the surgeon responsible for the injury.[2,4,5,7,16] Carroll *et al.* reported a success rate of only 27% for repairs carried out by the surgeon who performed the cholecystectomy,[4] whereas Stewart *et al.* noted that only 17% of primary repairs and 0% of secondary repairs were successful.[17] Even more concerning, Flum and colleagues demonstrated in a large cohort of Medicare beneficiaries, that the risk of death was elevated by 11% if the repairing surgeon was the same as the injuring surgeon. In the present series, five out of five primary repairs performed before referrals were unsuccessful and required revision. Mercado *et al.* showed that patients with an anastomosis fashioned below the biliary confluence were more likely to require revisional surgery than those with an anastomosis at the biliary confluence.[18] None of the previously operated patients in our series underwent the 'gold standard' operation for a complete transection or ligation of the biliary tree – i.e. hepaticojejunostomy to the confluence of the biliary tree or the left hepatic duct.[8,15,19,20]

In summary, this analysis indicates that pre-referral interventions and delay in referral adversely impact outcomes after definitive repair. These data support an open policy of early referral to tertiary biliary surgery centres. Minimization of the number and invasive nature of pre-referral procedures to only those that ensure the safety of transfer is recommended. Subsequent large cohort series should focus on the details of pre-referral procedures to more precisely determine the optimal treatment algorithm for these patients.

Conflicts of interest

None declared.

References

1. Adamsen S, Hansen OH, Funch-Jensen P, Schulze S, Stage JG, Wara P. (1997) Bile duct injury during laparoscopic cholecystectomy: a prospective nationwide series. *J Am Coll Surg* 184:571–578.
2. Flum DR, Cheadle A, Prela C, Dellinger EP, Chan L. (2003) Bile duct injury during cholecystectomy and survival in medicare beneficiaries. *JAMA* 290:2168–2173.
3. Archer SB, Brown DW, Smith CD, Branum GD, Hunter JG. (2001) Bile duct injury during laparoscopic cholecystectomy: results of a national survey. *Ann Surg* 234:549–558; discussion 558–559.
4. Carroll BJ, Birth M, Phillips EH (1998) Common bile duct injuries during laparoscopic cholecystectomy that result in litigation. *Surg Endosc* 12:310–313; discussion 314.
5. Deziel DJ, Millikan KW, Economou SG, Doolas A, Ko ST, Airan MC. (1993) Complications of laparoscopic cholecystectomy: a national survey of 4,292 hospitals and an analysis of 77,604 cases. *Am J Surg* 165:9–14.
6. Francoeur JR, Wiseman K, Buczkowski AK, Chung SW, Scudamore CH. (2003) Surgeons' anonymous response after bile duct injury during cholecystectomy. *Am J Surg* 185:468–475.
7. Russell JC, Walsh SJ, Mattie AS, Lynch JT. (1996) Bile duct injuries, 1989–1993. A statewide experience. Connecticut Laparoscopic Cholecystectomy Registry. *Arch Surg* 131:382–388.
8. Thomson BN, Parks RW, Madhavan KK, Wigmore SJ, Garden OJ. (2006) Early specialist repair of biliary injury. *Br J Surg* 93:216–220.
9. Mercado MA (2006) Early versus late repair of bile duct injuries. *Surg Endosc* 20:1644–1647.

10. de Reuver PR, Grossmann I, Busch OR, Obertop H, van Gulik TM, Gouma DJ. (2007) Referral pattern and timing of repair are risk factors for complications after reconstructive surgery for bile duct injury. *Ann Surg* 245:763–770.

11. Sicklick JK, Camp MS, Lillemoe KD, Melton GB, Yeo CJ, Campbell KA *et al.* (2005) Surgical management of bile duct injuries sustained during laparoscopic cholecystectomy: perioperative results in 200 patients. *Ann Surg* 241:786–792; discussion 793–795.

12. Bektas H, Schrem H, Winny M, Klempnauer J. (2007) Surgical treatment and outcome of iatrogenic bile duct lesions after cholecystectomy and the impact of different clinical classification systems. *Br J Surg* 94:1119–1127.

13. Hepp J, Moreaux J, Bismuth H (1964) [Ruptures of the common bile duct in closed abdominal injuries.] *Ann Chir* 18:953–960.

14. Bismuth H (2003) Surgical management of bile duct stricture following laparoscopic cholecystectomy. *Acta Chir Belg* 103:140–142.

15. Hepp J, Couinaud C (1956) [Approach to and use of the left hepatic duct in reparation of the common bile duct.]. *Presse Med* 64:947–948.

16. Gigot J, Etienne J, Aerts R, Wibin E, Dallemagne B, Deweer F *et al.* (1997) The dramatic reality of biliary tract injury during laparoscopic cholecystectomy. An anonymous multicenter Belgian survey of 65 patients. *Surg Endosc* 11:1171–1178.

17. Stewart L, Way LW (1995) Bile duct injuries during laparoscopic cholecystectomy. Factors that influence the results of treatment. *Arch Surg* 130:1123–1128; discussion 1129.

18. Mercado MA, Chan C, Orozco H, Tielve M, Hinojosa CA. (2003) Acute bile duct injury. The need for a high repair. *Surg Endosc* 17:1351–1355.

19. McDonald ML, Farnell MB, Nayorney DM, Ilstrup DM, Kutch JM. (1995) Benign biliary strictures: repair and outcome with a contemporary approach. *Surg* 118:582–590; discussion 590–591.

20. Alves A, Farges O, Nicolet J, Watrin T, Sauvanet A, Belghiti J. (2003) Incidence and consequence of an hepatic artery injury in patients with postcholecystectomy bile duct strictures. *Ann Surg* 238:93–96.