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A study of preoperative factors associated with a poor outcome following laparoscopic bile duct exploration

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Abstract
Background The aim of this study was to identify preoperative factors associated with poor outcome following laparoscopic bile duct exploration.
Methods Data regarding potential preoperative factors were collected prospectively and from a review of patient records of 436 patients who had undergone a laparoscopic bile duct exploration. A multivariate analysis was performed to identify significant predictors of five adverse outcomes: postoperative complication (stratified), conversion to open operation, prolonged hospital stay, bile leak following choledochotomy, and failure of surgical clearance of the duct.
Results The mean age was 57 years (range = 18–91) and 74% were female. No complications were experienced by 66.5% and 17% had a minor Clavien Grade I complication. There was one death. Clinically significant Clavien Grade II–V complications occurred more frequently in those of increasing age [OR = 1.03 (CI = 1.01–1.05), $p = 0.02$]. Increasing serum bilirubin [OR = 1.01 (CI = 1.00–1.01), $p = 0.01$] was associated with conversion to an open operation. Male sex [OR = 0.52 (CI = 0.27–0.99), $p = 0.05$], previous upper abdominal surgery [OR = 4.89 (CI = 1.10–21.74), $p = 0.04$], immunosuppressants [OR = 9.75 (CI = 1.06–89.93), $p = 0.05$], and a larger preoperative common bile duct diameter [OR = 1.16 (CI = 1.08–1.25), $p < 0.001$] were predictors of a prolonged hospital stay. No factors were identified as predictors of a controlled bile leak. Previous failed ERCP was not associated with adverse outcome.
Conclusion Laparoscopic exploration of the bile duct is safe but age, comorbidity, and degree of jaundice increase the risk slightly.

Keywords Common bile duct calculi · Gallstones · Laparoscopic surgical procedure · Complications · Postoperative · Outcome measures

There is growing acceptance that in experienced hands laparoscopic bile duct exploration is more efficient than, and at least as safe as, endoscopic sphincterotomy in patients with bile duct stones who are fit enough for general anaesthesia and cholecystectomy. A meta-analysis of five randomised clinical trials [1] and recent clinical guidelines [2] have endorsed this opinion. There are a good number of published series of more than 100 patients having undergone laparoscopic bile duct exploration [3–25]. Morbidity in these series is approximately 10% and mortality 1%. There is still concern, however, that in the elderly or those with comorbidity the potentially lengthy operation associated with laparoscopic bile duct exploration might result in a suboptimal outcome. Choledocholithiasis is particularly prevalent in these higher-risk groups [26] but there has been only one randomised study that has focused on these patients in particular [27].

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Assuming that laparoscopic bile duct exploration is the treatment of choice, in general it would be beneficial to identify a subset of patients who might fare less well after the laparoscopic approach. This might enable an alternative approach to be recommended in such patients.

There have been two published analyses performed specifically to try to identify factors relating to a poor outcome after open bile duct exploration. Neoptolemos et al. [28] performed a multivariate analysis of preoperative variables in 248 patients who underwent open bile duct exploration and found that serum bilirubin concentration, medical risk factors, and a previous attempt at endoscopic sphincterotomy were all significant predictors of postoperative complications. As a result, they suggested that jaundiced high-risk patients ought to be treated by sphincterotomy alone and that fit patients should be treated by open surgery alone without prior endoscopic sphincterotomy. In a smaller multivariate analysis of 158 patients, Larraz-Mora et al. [29] arrived at similar conclusions. They found that age, heart disease, and cholangitis were significant predictors of mortality after open operation. Furthermore, in that study those with cholangitis were eight times more likely to die than those without.

As yet there is no published analysis of predictors of adverse outcomes after laparoscopic bile duct exploration, hence the reason for this study.

Materials and methods

Four hundred thirty-six patients who underwent laparoscopic bile duct exploration during laparoscopic cholecystectomy between April 1994 and April 2005 by or under the direct supervision of two experienced laparoscopic biliary surgeons at Southmead Hospital were included in the analysis (those who were having a concomitant procedure were not included). The numbers of patients who underwent a transductal, transcystic, or "radiological" exploration (the flushing of small stones through the ampulla with the aid of hyoscine-N-butylbromide under cholangiographic or direct ultrasonic visualisation) were 293 (67%), 103 (24%), and 40 (9%), respectively. One patient required a transduodenal sphincteroplasty after a failed transcystic exploration and seven patients required biliary enteric drainage procedures after transductal explorations for the reasons shown in Table 1.

Seventy-three procedures were carried out in the first 5 years of the series and 363 in the latter 6 years. Ninety percent of the patients in the series had clinical or radiological evidence of bile duct stones preoperatively. Approximately 10% (44/436) of patients had presented with biliary colic or cholecystitis, a normal bile duct diameter, and normal reoperative liver function tests, meaning that their stones were found incidentally at operation.

Table 1 Reasons for biliary enteric drainage procedures in eight patients

Drainage procedure	Reason
Choledochoduodenostomy	Huge amount of sludge and small stones
Transduodenal sphincteroplasty	Impacted stone before availability of lithotripsy
Choledochojejunostomy	Impacted stone before availability of lithotripsy
Choledochojejunostomy	Mirizzi Type II
Choledochoduodenostomy	Numerous recurrent stones after previous endoscopic sphincterotomy
Choledochoduodenostomy	Numerous stones
Choledochoduodenostomy	Numerous stones
Choledochoduodenostomy	Numerous recurrent stones after previous endoscopic sphincterotomy

This study population represents an all-comers policy for the management of bile duct stones within the unit: patients fit enough for cholecystectomy were treated with laparoscopic bile duct exploration. Endoscopic sphincterotomy alone was used in the frail in whom the gallbladder was to remain in situ or in patients presenting with acute severe pancreatitis or severe cholangitis. A small group of 20 patients were the exception to this rule and were treated by endoscopic sphincterotomy and subsequent laparoscopic cholecystectomy after they were entered into the randomised clinical trial referred to earlier [27].

Operative technique

Laparoscopic bile duct exploration was performed with the patient under general anaesthesia. Patients were fitted with pneumatic calf compression devices. A carbon dioxide pneumoperitoneum was created via a 12-mm port inserted at the umbilicus using an open Hasson technique [30]. Views were obtained through a 10-mm 30° laparoscope and the pneumoperitoneum was maintained at a pressure of 10-mmHg. After insufflation the patient was positioned in a reverse Trendelenberg position tilted to the left. Three additional trocars were then positioned: a 10-mm port in the epigastrium and two 5-mm ports in the right hypochondrium. A wide local dissection of Calot's triangle was performed. Prior to division of the cystic duct and artery, the bile duct was imaged with laparoscopic ultrasound (7.5 MHz Aloka linear ultrasound probe, Key Med, Southend, UK) to confirm the presence of bile duct stones [31].

Once ductal stones had been confirmed the surgeon would then decide whether a transcystic or transductal approach was most appropriate. A larger bile duct diameter, larger stones, or multiple stones favoured a transductal approach. Choledochoscopy with a three-channel, 3- or 5-mm choledochoscope through a transverse incision in the cystic duct or a vertical incision in the common bile duct allowed direct visualisation of the bile ducts. Intermittent irrigation with normal saline was used to provide a clear field of view, allowing stones to be extracted using baskets, balloons, and electrohydraulic lithotripsy. Very small stones were flushed transcystically through the sphincter of Oddi under ultrasound visualisation with the aid of 20 mg of hyoscine-N-butylbromide given intravenously to relax the sphincter (termed a radiological exploration) without instrumentation of the duct with a choledochoscope. In the case of transcystic and transductal explorations, two passes up and down the duct with the choledochoscope confirmed duct clearance, which was then checked again with laparoscopic ultrasound. It should be noted that it was often not possible to pass the choledochoscope upwards into the common hepatic duct during a transcystic exploration. T-tube drainage of the bile duct was used very selectively in cases where multiple stones or fragments of stones had been removed or when the surgeon was not completely convinced of duct clearance. Biliary stents to protect the choledochotomy were not employed for two reasons. First, there is no scientific evidence to suggest a benefit in their use [32]. Second, instrumentation of the biliary sphincter during laparoscopic exploration of the bile duct appears to be associated with pancreatitis [33].

Cholecystectomy was then completed by diathermy dissection from the gallbladder bed after the cystic duct and artery had been clipped and divided. A drain was placed next to any choledochotomy. Antibiotic prophylaxis with 750 mg of intravenous cefuroxime was given if a choledochotomy was made or if there was spillage of gallbladder contents during dissection. Drains were left in place until the first postoperative morning or until bile was no longer present within the drainage bag.

The description detailed above represents the most recent operative technique used. There had been three developments to the technique over the preceding 11-year period to which the study relates: Early in the series the majority of choledochotomies were closed over a T tube, but from January 1998 they were used selectively if there was any doubt about duct clearance or after a particularly challenging procedure. Twenty-nine of 34 transductal explorations before 1998 utilised a T tube compared with 35/252 afterwards (7 who had a biliary enteric drainage procedure after transductal exploration were excluded). Second, transcholedochoscopic electrohydraulic lithotripsy was used for difficult impacted stones from March 1998 after the first 49 patients and was subsequently employed in 57/387 of the remainder of the series. Third, laparoscopic ultrasound was introduced in September 2000 after the first 127 patients; thereafter it was used to image the bile ducts routinely both pre- and post-exploration and eventually replaced operative cholangiography. For the first year of pre-exploratory laparoscopic ultrasound, pre-exploratory operative cholangiography was also performed to allow comparative study [34]. The methods of post-exploratory imaging of the bile duct to ensure duct clearance utilising choledochoscopy, cholangiography, and laparoscopic ultrasound also changed over the length of the series according to these technical developments.

Data regarding the following preoperative variables which were thought to influence outcome were collected for each patient: age, sex, ASA grade, weight, presentation (colic, pancreatitis, jaundice, cholangitis, or cholecystitis), previous failed ERCP, previous upper abdominal surgery, arrhythmia, hypertension, diabetes, ischaemic heart disease, respiratory disease, smoking, antiplatelet drugs, immunosuppressive drugs, β-blockers, plasma haemoglobin, white cell count, platelet count, serum bilirubin, alkaline phosphatase, alanine transferase albumin, urea, creatinine, and preoperative common bile duct (CBD) diameter.

The study variables were analysed with reference to the prediction of five adverse outcomes detailed below. Data were collected prospectively perioperatively according to standard protocol and from a review of case records.

The five adverse outcomes identified as being suitable for investigation were as follows:

(1) Morbidity: Postoperative complications were stratified using a validated classification system developed by Clavien et al. [35]. This system stratifies complications into five grades ranging from any deviation from the normal postoperative course (Grade I), those requiring certain pharmacological interventions (Grade II), those requiring surgical intervention (Grade III), life-threatening complications (Grade IV), to death (Grade V). In this study, predictors of relatively severe, Clavien Grade II–V, complications were sought.
(2) Conversion to an open operation.
(3) Prolonged postoperative hospital stay: The data collected regarding postoperative stay was dichotomised. Analysis was performed to identify predictors of a prolonged hospital stay which was defined as more than 3 postoperative days.
(4) Bile leak after primary closure of choledochotomy: Defined as bile within the drain the following morning after a transductal exploration without systemic upset.
(5) Failed surgical clearance: Defined as failure to clear the bile duct of stones at operation requiring subsequent intervention.

Potentially significant predictors of outcomes were identified by univariate analysis using logistic regression (SPSS v11.0). Individual predictors were then entered into a multivariate model. A significance level of $p \leq 0.10$ was used to identify factors on univariate analysis to enter into multivariate models. This was done to prevent the loss of potentially important clinical information as a consequence of relatively small numbers. On multivariate analysis, statistical significance was reported at $p \leq 0.05$.

Supplemental analysis performed to investigate whether the learning curve was associated with a poor outcome is also presented.

Results

The data set was 98.4% (15021/15260) complete. The data collected regarding patients' potential preoperative predictors and outcome measures are given in Table 2.

Predictors of Clavien Grade II–V complications

A summary of the complications encountered by the 436 patients is presented in Table 3. The types of complications occurring in different age groups are illustrated in Fig. 1. Patients over the age of 60 years were more likely to suffer respiratory [odds ratio (OR) = 3.65 (CI = 1.53–8.68), $p = 0.004$] and urinary [OR = 7.01 (CI = 2.04–24.06), $p = 0.002$] complications, whereas the occurrence of surgical/biliary complications was similar [OR = 0.91 (CI = 0.51–1.60), $p = 0.73$] when compared to those under 60 years of age. There was a strong trend toward cardiac complications in the older-age group but this was not statistically significant (OR = 5500.57, $p = 0.64$).

The complications were stratified as per the classification system described earlier and are shown in Fig. 2 (data were missing on 5 patients). Three hundred and sixty four of 431 (84.5%) patients suffered either no complication or a minor Clavien Grade I complication, and 67 (15.5%) suffered a more clinically significant Clavien grade II–V complication of which prediction was sought.

Age [OR = 1.04 (CI = 1.02–1.06), $p < 0.001$], antiplatelet drugs [OR = 1.84 (CI = 0.91–3.73), $p = 0.09$], and ASA grade (OR ASA I vs. II = 1.55 (CI = 0.69–3.49), OR ASA I vs. III + IV = 2.92 (CI = 1.12–7.65), $p = 0.03$] were found to be associated with a Clavien Grade II–V complication on univariate analysis and adjustment for age and sex. These predictors were then entered into a multivariate model which also included sex. On multivariate analysis, age (OR = 1.03 (CI = 1.01–1.05), $p = 0.02$] was the only factor that was statistically significant at the 5% level. A graphical representation of a multivariate model containing age and ASA grade for predicting the probability of a Clavien Grade II–V complication is shown in Fig. 3.

Table 2 Descriptive statistics for 436 patients who underwent laparoscopic bile duct exploration

Age (years)		59.0 (42.9–71.8)
	Missing data	*1*
Sex		
Female		323 (74.1)
Male		113 (25.9)
	Missing data	*0*
Presentation		
Colic		161 (36.9)
Jaundice		186 (42.7)
Pancreatitis		56 (12.8)
Cholangitis		15 (3.4)
Cholecystitis		18 (4.1)
	Missing data	*0*
Previous failed ERCP		69 (15.8)
	Missing data	*1*
Previous upper abdominal surgery		12 (2.8)
	Missing data	*1*
Medical risk factors		
Arrhythmia		23 (5.3)
	Missing data	*9*
Hypertension		115 (26.4)
	Missing data	*9*
Diabetes		21 (4.8)
	Missing data	*9*
Ischaemic heart disease		52 (11.9)
	Missing data	*9*
Respiratory disease		54 (12.4)
	Missing data	*9*
Smoking		170 (39.0)
	Missing data	*10*
Drugs		
Antiplatelet		54 (12.4)
	Missing data	*9*
Immunosuppressants		8 (1.8)
	Missing data	*9*
Beta blockers		54 (12.4)
	Missing data	*12*
Full blood count		
Plasma haemoglobin (g dL^{-1})		13.6 (12.8–14.4)
	Missing data	*12*
White cell count ($\times 10^3$ μL^{-1})		7.5 (6.0–9.2)
	Missing data	*12*
Platelet count ($\times 10^3$ μL^{-1})		276 (234–332)
	Missing data	*12*
Liver function		
Serum bilirubin (μmol L^{-1})		15 (9–40)
	Missing data	*2*
Serum alkaline phosphatase (IU L^{-1})		120 (78–252)
	Missing data	*2*

Table 2 continued

Serum alanine transferase (IU L^{-1})	43 (21–158)
Missing data	*2*
Serum albumin (g L^{-1})	40 (37–43)
Missing data	*12*
Renal function	
Serum urea (mmol L^{-1})	4.3 (3.2–5.4)
Missing data	*13*
Serum creatinine (mmol L^{-1})	87 (75–99)
Missing data	*12*
Preop CBD diameter (mm)	8 (6–11)
Missing data	*27*
ASA	
Grade I	135 (31)
Grade II	224 (51.4)
Grade III	63 (14.4)
Grade IV	1 (0.2)
Missing data	*13*
Weight (kg)	72 (62–83)
Missing data	*17*
Clavien Grade II–V complication	67 (15.5)
Missing data	*5*
Conversion	36 (8.3)
Missing data	*0*
Prolonged hospital stay (>3 nights)	155 (35.7)
Missing data	*2*
Bile leak	43 (10.0)
Missing data	*8*
Failed clearance	6 (1.4)
Missing data	*0*

Data are expressed as median (IQR) or *n* (%)

Predictors of conversion to an open operation

The conversion rate was 36/436 (8.3%). Conversion was associated with a less favourable outcome and an increased risk of a Clavien II–V complication [OR = 3.21 (CI = 1.36–7.54), $p = 0.01$] when entered into a multivariate model containing the other predictors of a Clavien II–V complication.

Cholangitis [OR = 4.48 (CI = 1.32–15.29), $p = 0.02$], previous upper abdominal surgery [OR = 4.72 (CI = 1.13–19.75), $p = 0.03$], plasma haemoglobin [OR = 0.77 (CI = 0.57–1.00), $p = 0.05$], serum bilirubin [OR = 1.01 (CI = 1.00–1.01), $p = 0.001$], serum alkaline phosphatase [OR = 1.00 (CI = 1.00–1.00), $p = 0.02$], preoperative CBD diameter [OR = 1.13 (CI = 1.03–1.23), $p = 0.01$], and weight [OR = 0.98 (CI = 0.95–1.00), $p = 0.10$] were found to be associated with conversion to an open operation on univariate analysis and adjustment for age and sex. These predictors were then entered into a multivariate

Table 3 Thirty-day postoperative complications in 436 patients undergoing LBDE

Complication type	*n* (%)
Death	1 (0.23)
Cardiac	
Atrial fibrillation/flutter	11 (2.52)
Complete heart block	1 (0.23)
Left ventricular failure	1 (0.23)
Myocardial infarction	2 (0.46)
Respiratory	
Atelectasis	11 (2.52)
Chest infection	19 (4.36)
Pleural effusion	1 (0.23)
Urinary	
Urinary tract infection	6 (1.38)
Urinary retention	16 (3.67)
Biliary	
Bile leak (controlled)	37 (8.49)
Bile leak requiring laparoscopy	6 (1.38)
T-tube complication	5 (1.15)
Postoperative endoscopic sphincterotomy	9 (2.06)
Acute pancreatitis (de novo)	4 (0.92)
Other	
Pulmonary embolus	1 (0.23)
Deep vein thrombosis	1 (0.23)
Wound infection	10 (2.29)
Intra-abdominal collection	4 (0.92)
Bleeding duodenal ulcer	2 (0.46)
Postoperative intra-abdominal bleeding	2 (0.46)
Noninfective diarrhoea	2 (0.46)
Clostridium difficile diarrhoea	4 (0.008)
Strangulated umbilical port site hernia	1 (0.23)
9th intercostal nerve neuropraxia	1 (0.23)

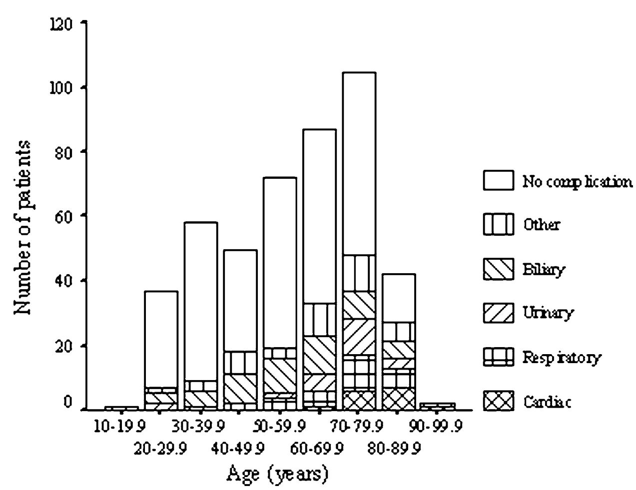

Fig. 1 Complication type versus age

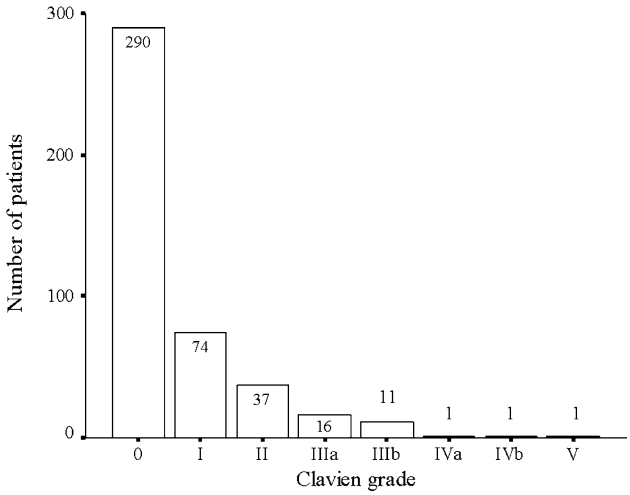

Fig. 2 Clavien Grade of 30-day postoperative complications

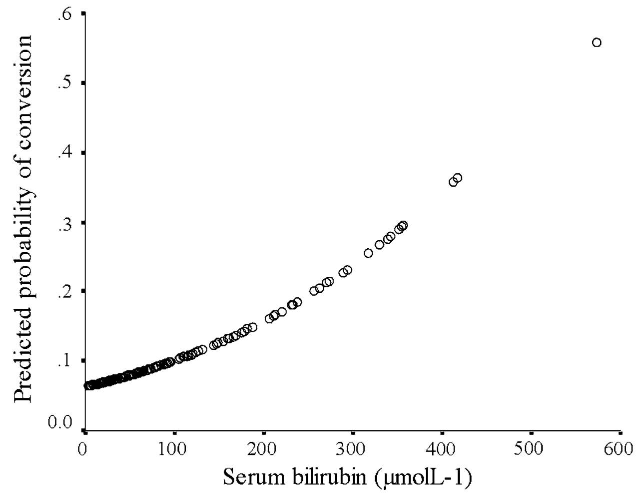

Fig. 4 Predictive model of serum bilirubin concentration for conversion to an open operation

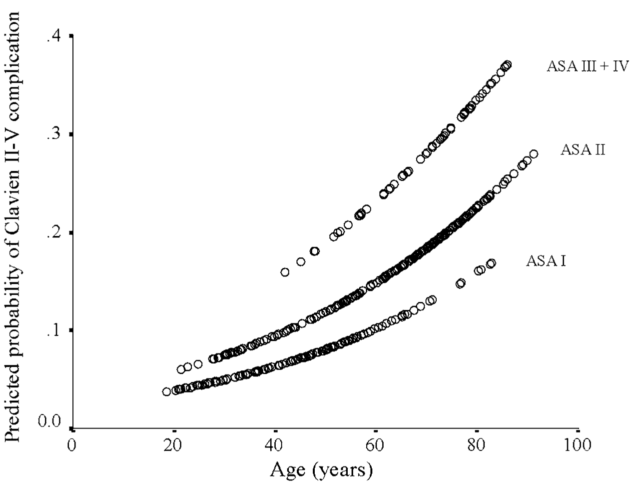

Fig. 3 Predictive model of age adjusted for ASA grade for a Clavien Grade II–V complication

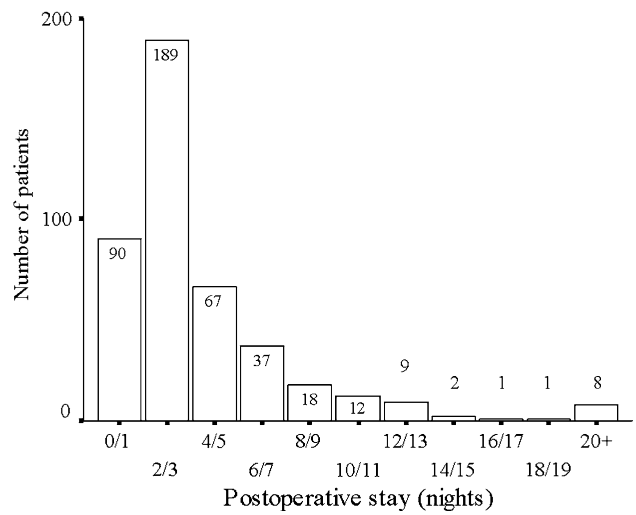

Fig. 5 Postoperative stay

model which also included age and sex. On multivariate analysis, only an increasing serum bilirubin [OR = 1.01 (CI = 1.00–1.01), $p = 0.01$] remained a significant predictor of conversion. A graphical representation of the model containing serum bilirubin for predicting the probability of conversion is shown in Fig. 4.

Predictors of a prolonged hospital stay

One hundred fifty-five of 434 (35.7%) patients had a prolonged hospital stay, defined as more than 3 postoperative days. The distribution of length of stay is represented in Fig. 5. Increasing age [OR = 1.03 (CI = 1.02–1.04), $p < 0.001$], cholangitis [OR = 4.36 (CI = 1.33–14.28), $p = 0.02$], previous upper abdominal surgery [OR = 4.27 (CI = 1.11–16.50), $p = 0.04$], ischaemic heart disease [OR = 2.22 (CI = 1.17–4.22), $p = 0.02$], immunosuppressants [OR = 10.69 (CI = 1.28–89.26), $p = 0.03$], plasma haemoglobin [OR = 0.84 (CI = 0.72–0.98), $p = 0.03$], serum bilirubin [OR = 1.01 (CI = 1.00–1.01), $p < 0.001$], serum alkaline phosphatase [OR = 1.00 (CI = 1.00–1.00), $p = 0.002$], serum albumin [OR = 0.95 (CI = 0.92–0.99), $p = 0.02$], preoperative CBD diameter [OR = 1.18 (CI = 1.11–1.26), $p < 0.001$], and ASA grade [OR ASA I vs. II = 1.56 (CI = 0.90–2.69), OR ASA I vs. III + IV = 3.73 (CI = 1.78–7.80), $p < 0.001$] were associated with a prolonged hospital stay after univariate analysis and adjustment for age and sex. These predictors were then entered into a multivariate model which also included sex. On multivariate analysis, male sex [OR = 0.52 (CI = 0.27–0.99), $p = 0.05$], previous upper abdominal surgery [OR = 4.89 (CI = 1.10–21.74), $p = 0.04$], immunosuppressants

[OR = 9.75 (CI = 1.06–89.93), $p = 0.05$], and a larger preoperative CBD diameter [OR = 1.16 (CI = 1.08–1.25), $p < 0.001$] remained significant predictors.

Predictors of bile leak after primary closure of the bile duct

The controlled bile leak rate in 229 patients who underwent transductal exploration with primary closure of the bile duct was 15.6% (35/225); data were missing on 4 patients. Bile leak was strongly associated with increased risk of a prolonged hospital stay [OR = 8.40 (CI = 3.16–22.32), $p < 0.001$] when entered into a multivariate model containing the other predictors of a prolonged hospital stay.

Colic [OR = 2.15 (CI = 1.02–4.55), $p = 0.04$] and plasma haemoglobin [OR = 1.31 (CI = 0.98–1.76), $p = 0.07$] were associated with a bile leak on univariate analysis and adjustment for age and sex. These predictors were then entered into a multivariate model which included age and sex. On multivariate analysis, no factors remained statistically significant.

Predictors of failed surgical clearance

Surgical clearance judged at the time of operation was achieved in 428/436 (98.2%) patients. Failed extraction was due to stone impaction before electrohydraulic lithotripsy was available in four patients, difficult access to the bile duct in three patients, and no particular reason was available for one patient. Due to the small numbers of patients who had a failed surgical treatment, it was statistically not possible to identify any predictors.

The influence of the learning curve

During the first 5 years of the series, the technique of laparoscopic bile duct exploration evolved as described earlier in the Methods section. Seventy-three procedures were carried out during this time and the remaining 363 were performed in the following 6 years. Regression analysis was performed to investigate whether this period, referred to as the learning curve, was associated with the poor postoperative outcomes investigated and whether it influenced the results of the previous analyses.

The learning-curve period was not associated with the occurrence of Clavien Grade II–V complications [OR = 0.74 (CI = 0.35–1.57), $p = 0.44$]. Clavien Grade II–V complications occurred in 12.5% (9/72) of patients in this period compared with 16.2% (58/359) afterwards. It had no significant influence on the multivariate analysis containing data for age, sex, antiplatelet drugs, and ASA grade for predicting a Clavien Grade II–V complication with age remaining the dominant factor.

This period was, however, associated with the need to convert to an open procedure on univariate analysis [OR = 4.21 (CI = 2.05–8.64), $p < 0.001$]. Conversion was necessary in 20.5% (15/73) in the learning-curve period compared to 5.8% (21/363) afterwards. This factor was then added into the multivariate analysis containing data for age, sex, cholangitis, previous upper abdominal surgery, haemoglobin, bilirubin, alkaline phosphatase, preoperative CBD diameter, and weight. Increasing serum bilirubin [OR = 1.01 (CI = 1.00–1.01), $p = 0.024$] still remained a significant predictor of conversion, but so did the learning-curve period [OR = 2.97 (CI = 1.22–7.24), $p = 0.017$].

A prolonged postoperative stay was also found to be influenced by the learning-curve period [OR = 1.98 (CI = 1.19–3.29), $p = 0.009$]. Thirty-six of 73 (49.3%) patients in this period had a prolonged hospital stay compared to 119/361 (32.0%) afterwards. This factor was then added into the multivariate analysis containing data for age, sex, cholangitis, previous upper abdominal surgery, ischaemic heart disease, immunosuppressants, haemoglobin, bilirubin, alkaline phosphatase, albumin, preoperative CBD diameter, and ASA grade. The learning-curve period remained significant in this analysis [OR = 2.24 (CI = 1.17–4.28), $p = 0.015$], but this had little effect on the other factors that were previously identified as being significant: male sex [OR = 0.53 (CI = 0.28–1.001), $p = 0.050$], previous upper abdominal surgery [OR = 4.06 (CI = 0.89–18.50), $p = 0.070$], immunosuppressants [OR = 9.52 (CI = 1.03–88.36), $p = 0.047$], a larger preoperative CBD diameter [OR = 1.15 (CI = 1.07–1.24), $p < 0.001$], and higher ASA grade [OR ASA I vs. II = 1.44 (CI = 0.77–2.68), OR ASA I vs. III + IV = 2.73 (CI = 1.07–6.97), $p = 0.042$].

The learning-curve period was not associated with the occurrence of bile leak after primary closure of a choledochotomy [OR = 0.60 (CI = 0.13–2.70), $p = 0.50$]. Bile leak occurred in 10.5% (2/19) of patients in this period compared with 16.5% (33/200) afterwards. It had no influence on the multivariate analysis containing data for age, sex, colic, and haemoglobin, with no significant predictor identified.

It was not possible to perform an analysis to predict failed surgical clearance because of small numbers, but the unavailability of electrohydraulic lithotripsy in the early part of the series (first 49 patients) was probably associated with inability to clear the duct [OR = 14.53 (CI = 3.36–62.85), $p < 0.001$]. Five of 49 (10.2%) patients operated on before the availability of lithotripsy had a failed clearance compared to 3/387 (0.7%) when it was available.

Discussion

The object of this study was to enable the clinician to identify patients at a higher risk of an adverse outcome after laparoscopic bile duct exploration with regard to preoperative patient indicators. This study has demonstrated that the only independently significant variables associated with a Clavien Grade II–V complication are increasing age and probably comorbidity, manifested by a trend towards complication in those with a higher ASA grade [OR ASA I vs. II = 1.52 (CI = 0.67–3.44), OR ASA I vs. III + IV = 2.59 (CI = 0.96–6.95), $p = 0.06$]. For example, in the model containing these variables, the probabilities of a 50-year-old ASA I patient and an 80-year-old ASA III patient having a clinically significant complication are approximately 7 and 33%, respectively. However, in contrast to the previously reported studies regarding open bile duct exploration [28, 29], jaundice was not found to be a predictor of complications despite a relatively large proportion (93/436) of this group of patients having a serum bilirubin of greater than 50 µmol L^{-1}. This may be because this series might have had a smaller proportion of patients with severe cholangitis, who would presumably have been at higher risk, compared to previous studies and would explain why the trend [OR = 2.20 (CI = 0.70–6.90)] in this study for those with cholangitis towards complication failed to become statistically significant. There was also a trend [OR = 2.51 (CI = 0.56–11.21)] towards those on immunosuppressant therapy to have complications but there were too few numbers in this group to provide proof.

It might be hypothesised that the laparoscopic approach to difficult bile duct stones in those patients in whom endoscopic therapy has failed might be associated with a poor outcome after a potentially more technically difficult operation. In this series these 69 patients fared no differently from the rest of the group. This supports other authors' claims [21, 36–38] that laparoscopic bile duct exploration after failed endoscopic treatment is not only possible but safe.

Conversion to an open procedure was found to be strongly associated with increasing serum bilirubin. Experience from this unit has previously described that conversion is usually required for dense gallbladder adhesions [3] rather than difficult access to the bile duct. An obstructed biliary tree is likely to be infected and as a consequence there will be a higher incidence of severe chronic cholecystitis found at operation necessitating conversion. Increasing patient weight [OR = 0.97 (CI = 0.95–1.00), $p = 0.09$] did not predict the need for conversion to an open procedure, rather the opposite may be true. However, this may be explained by a reluctance to convert larger patients. As one would expect, there was also a trend towards conversion in those who had undergone previous upper abdominal surgery [OR = 3.72 (CI = 0.79–21.77), $p = 0.15$].

The dominant predictor of a prolonged postoperative hospital stay of more than 3 days was the diameter of the bile duct measured preoperatively by transabdominal ultrasound. This simply reflected the need for choledochotomy in those patients, but other factors such as concurrent immunosuppression and previous upper abdominal surgery were also significant. There was also a trend of those with a higher ASA grade having a prolonged hospital stay but this was not statistically significant [OR ASA I vs. II = 1.33 (CI = 0.72–2.43), OR ASA I vs. III + IV = 2.30 (CI = 0.92–5.75), $p = 0.09$].

Whilst a controlled bile leak after primary closure of a choledochotomy is not a danger to the patient, it lengthens hospital stay to allow observation and increases treatment costs. Currently there is no evidence to suggest that the routine use of T tubes or biliary stents is advantageous [39, 40], and although the use of fibrin glue to seal the choledochotomy has been shown to be effective in animals [41, 42], no data on its use in humans in this situation is available, with stricturing being the main concern. Our analysis found no significant predictors of a bile leak but indicated that there may be an association with a clinical presentation of biliary colic, whereas bile duct diameter, which can influence the size of suture bite one is able to take at closure of the bile duct, had no influence. This association of bile leak with a presentation of biliary colic may be a spurious result, but increased inflammation in the tissues normally associated with other presentations of choledocholithiasis may be beneficial in sealing the bile duct.

Preoperative factors predicting failed surgical clearance of the duct were not able to be identified due to a 98.2% success rate. It should be reiterated that four of the failures were due to stone impaction in the distal bile duct prior to the use of electrohydraulic lithotripsy. Since the availability of lithotripsy, it has been found to be of benefit in approximately 15% of explorations in this series.

The influence of the learning curve during the development of the technique was investigated. It was found not to be associated with increased postoperative morbidity or a controlled bile leak after primary closure of a choledochotomy. However, it was found to be associated with the need for conversion to an open operation and a prolonged hospital stay. These findings may also be explained in part by the lack of availability of lithotripsy and the use of T tubes, respectively, early in the series.

In summary, laparoscopic bile duct exploration is well tolerated, with 83.5% of the patients in this series having only minor or no postoperative complications. It is safe and effective after failed endoscopic intervention. Increasing age, a higher ASA grade, and, to a lesser extent, jaundice were the dominant factors found to predict an adverse outcome. Whether patients in these circumstances would be better served by the alternative approach of endoscopic sphincterotomy and subsequent laparoscopic cholecystectomy needs further clarification.

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References

1. Martin DJ, Vernon, Toouli J (2006) Surgical versus endoscopic treatment of bile duct stones. Cochrane Database Syst Rev 2:CD003327
2. Williams EJ, Green J, Beckingham I, Parks R, Martin D, Lombard M (2008) Guidelines on the management of common bile duct stones (CBDS). Gut 57(7):1004–1021
3. Thompson M, Tranter S (2002) All-comers policy for laparoscopic exploration of the common bile duct. Br J Surg 89:1608–1612
4. Berci G, Morgenstern L (1994) Laparoscopic management of common bile duct stones. A multi-institutional SAGES study. Society of American Gastrointestinal Endoscopic Surgeons. Surg Endosc 8(10):1168–1174 (discussion 1174–1165)
5. DePaula AL, Hashiba K, Bafutto M (1994) Laparoscopic management of choledocholithiasis. Surg Endosc 8(12):1399–1403
6. Dorman JP, Franklin ME Jr, Glass JL (1998) Laparoscopic common bile duct exploration by choledochotomy. An effective and efficient method of treatment of choledocholithiasis. Surg Endosc 12(7):926–928
7. Drouard F, Passone-Szerzyna N, Berthou JC (1997) Laparoscopic treatment of common bile duct stones. Hepatogastroenterology 44(13):16–21
8. Keeling NJ, Menzies D, Motson RW (1999) Laparoscopic exploration of the common bile duct: beyond the learning curve. Surg Endosc 13(2):109–112
9. Lezoche E, Paganini AM, Carlei F, Feliciotti F, Lomanto D, Guerrieri M (1996) Laparoscopic treatment of gallbladder and common bile duct stones: a prospective study. World J Surg 20(5):535–541 (discussion 542)
10. Martin IJ, Bailey IS, Rhodes M, O'Rourke N, Nathanson L, Fielding G (1998) Towards T-tube free laparoscopic bile duct exploration: a methodologic evolution during 300 consecutive procedures. Ann Surg 228(1):29–34
11. Millat B, Atger J, Deleuze A, Briandet H, Fingerhut A, Guillon F, Marrel E, De Seguin C, Soulier P (1997) Laparoscopic treatment for choledocholithiasis: a prospective evaluation in 247 consecutive unselected patients. Hepatogastroenterology 44(13):28–34
12. Paganini AM, Lezoche E (1998) Follow-up of 161 unselected consecutive patients treated laparoscopically for common bile duct stones. Surg Endosc 12(1):23–29
13. Phillips EH, Liberman M, Carroll BJ, Fallas MJ, Rosenthal RJ, Hiatt JR (1995) Bile duct stones in the laparoscopic era. Is preoperative sphincterotomy necessary? Arch Surg 130(8):880–885 (discussion 885–886)
14. Phillips EH, Rosenthal RJ, Carroll BJ, Fallas MJ (1994) Laparoscopic trans-cystic-duct common-bile-duct exploration. Surg Endosc 8(12):1389–1393 (discussion 1393–1384)
15. Rhodes M, Nathanson L, O'Rourke N, Fielding G (1995) Laparoscopic exploration of the common bile duct: lessons learned from 129 consecutive cases. Br J Surg 82(5):666–668
16. Snow LL, Weinstein LS, Hannon JK, Lane DR (1999) Management of bile duct stones in 1572 patients undergoing laparoscopic cholecystectomy. Am Surg 65(6):530–545 (discussion 546–537)
17. Decker G, Borie F, Millat B, Berthou JC, Deleuze A, Drouard F, Guillon F, Rodier JG, Fingerhut A (2003) One hundred laparoscopic choledochotomies with primary closure of the common bile duct. Surg Endosc 17(1):12–18
18. Giurgiu DI, Margulies DR, Carroll BJ, Gabbay J, Iida A, Takagi S, Fallas MJ, Phillips EH (1999) Laparoscopic common bile duct exploration: long-term outcome. Arch Surg 134(8):839–843 (discussion 843–834)
19. Petelin JB (2003) Laparoscopic common bile duct exploration. Surg Endosc 17(11):1705–1715
20. Riciardi R, Islam S, Canete JJ, Arcand PL, Stoker ME (2003) Effectiveness and long-term results of laparoscopic common bile duct exploration. Surg Endosc 17(1):19–22
21. Tang CN, Tsui KK, Ha JP, Siu WT, Li MK (2006) Laparoscopic exploration of the common bile duct: 10-year experience of 174 patients from a single centre. Hong Kong Med J 12(3):191–196
22. Taylor CJ, Kong J, Ghusn M, White S, Crampton N, Layani L (2007) Laparoscopic bile duct exploration: results of 160 consecutive cases with 2-year follow up. ANZ J Surg 77(6):440–445
23. Tokumura H, Umezawa A, Cao H, Sakamoto N, Imaoka Y, Ouchi A, Yamamoto K (2002) Laparoscopic management of common bile duct stones: transcystic approach and choledochotomy. J Hepatobiliary Pancreat Surg 9(2):206–212
24. Topal B, Aerts R, Penninckx F (2007) Laparoscopic common bile duct stone clearance with flexible choledochoscopy. Surg Endosc 21(12):2317–2321
25. Berthou J, Dron B, Charbonneau P, Moussalier K, Pellissier L (2007) Evaluation of laparoscopic treatment of common bile duct stones in a prospective series of 505 patients: indications and results. Surg Endosc 21(11):1970–1974
26. Hermann RE (1989) The spectrum of biliary stone disease. Am J Surg 158(3):171–173
27. Noble H, Tranter S, Chesworth T, Norton S, Thompson M (2009) A randomised, clinical trial to compare endoscopic sphincterotomy and subsequent laparoscopic cholecystectomy with primary laparoscopic bile duct exploration during cholecystectomy in higher risk patients with choledocholithiasis. J Laparoendosc Adv Surg Tech A 19(6):713–720
28. Neoptolemos J, Shaw D, Carr-Locke D (1989) A multivariate analysis of preoperative risk factors in patients with common bile duct stones. Ann Surg 209:157–161
29. Larraz-Mora E, Mayol J, Martinez-Sarmiento J, Alvarez-Bartolom M, Larroque-Derlon M, Fernandez-Represa JA (1999) Open biliary tract surgery: multivariate analysis of factors affecting mortality. Dig Surg 16(3):204–208
30. Hasson HM (1984) Open laparoscopy. Biomed Bull 5(1):1–6
31. Tranter SE, Thompson MH (2001) Potential of laparoscopic ultrasonography as an alternative to operative cholangiography in the detection of bile duct stones. Br J Surg 88(1):65–69
32. Perez G, Escalona A, Jarufe N, Ibanez L, Viviani P, Garcia C, Benavides C, Salvado J (2005) Prospective randomized study of T-tube versus biliary stent for common bile duct decompression after open choledochotomy. World J Surg 29(7):869–872
33. Paganini AM, Guerrieri M, Sarnari J, De Sanctis A, D'Ambrosio G, Lezoche G, Perretta S, Lezoche E (2007) Thirteen years' experience with laparoscopic transcystic common bile duct exploration for stones. Effectiveness and long-term results. Surg Endosc 21(1):34–40
34. Tranter SE, Thompson MH (2003) A prospective single-blinded controlled study comparing laparoscopic ultrasound of the common bile duct with operative cholangiography. Surg Endosc 17(2):216–219

35. Dindo D, Demartines N, Clavien PA (2004) Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg 240(2):205–213
36. Karaliotas C, Sgourakis G, Goumas C, Papaioannou N, Lilis C, Leandros E (2007) Laparoscopic common bile duct exploration after failed endoscopic stone extraction. Surg Endosc 22(8):1826–1831
37. Tai CK, Tang CN, Ha JP, Chau CH, Siu WT, Li MK (2004) Laparoscopic exploration of common bile duct in difficult choledocholithiasis. Surg Endosc 18(6):910–914
38. Poole G, Waldron B, Shimi SM, Cuschieri A (1997) Laparoscopic common bile duct exploration after failed endoscopic stone extraction. Endoscopy 29(7):609–613
39. Gurusamy KS, Samraj K (2007) Primary closure versus T-tube drainage after open common bile duct exploration. Cochrane Database Syst Rev 1:CD005640
40. Gurusamy KS, Samraj K (2007) Primary closure versus T-tube drainage after laparoscopic common bile duct stone exploration. Cochrane Database Syst Rev 1:CD005641
41. Couto J, Kroczek B, Requena R, Lerner R (1987) Autologous fibrin glue as a sealant of the common bile duct. Surgery 101(3): 354–356
42. Kram HB, Garces MA, Klein SR, Shoemaker WC (1985) Common bile duct anastomosis using fibrin glue. Arch Surg 120(11): 1250–1256