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# Is inflammation a significant predictor of bile duct injury during laparoscopic cholecystectomy?

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**Abstract**
*Background* Bile duct injuries (BDI) have been reported to occur more frequently during laparoscopic cholecystectomy (LC) compared to open cholecystectomy (OC). Several studies have demonstrated various potential predisposing factors for BDI. However, there is a controversy as to whether gallbladder inflammation is a significant predictor for BDI. Therefore, out primary aim was to investigate the relationship between inflammation and BDI at LC, and secondarily to present the management and clinical outcome of BDI.
*Methods* We recorded all consecutive LC performed between 1993 and 2005 in our institution by nine staff surgeons. BDI were classified according to Strasberg's classification. Simple and multivariate logistic regression analysis was performed to evaluate the association between inflammation and BDI occurrence during LC.
*Results* There were 2,184 patients. Among those, 344 had inflammation (16%). The conversion rate was 5% and was higher among male, elder patients, and those with inflammation. The BDI incidence was 0.69% (0.14% for major and 0.55% for minor injuries) and it was significantly higher in those with inflammation compared to those without inflammation ($p = 0.01$). In particular, the risk for BDI was almost 3.5 times higher in those with inflammation (OR = 3.61, 95% CI 1.27–10.21). Inflammation remained an independent risk factor for BDI even after adjustment for potential confounders. Among patients sustaining injury, one died and two have recurrent cholangitis. No association was observed between clinical outcome and management of BDI, time of diagnosis, sex, and inflammation.
*Conclusion* We revealed that inflammation is an independent predictor of BDI occurrence during LC. Therefore, it would be advisable for surgeons to not hesitate to convert a LC to an OC in the presence of inflammation.

**Keywords** Cholecystectomy · CBD (common bile duct) · Complications

Open cholecystectomy (OC) was the gold standard for the treatment of symptomatic gallstones and acute cholecystitis (AC) for more than 100 years. However, since the introduction of laparoscopic cholecystectomy (LC) in the early 1990s, it has rapidly replaced OC and became the treatment of choice for symptomatic gallstones [1–3] and AC [4, 5]. Shorter hospital stay and faster recovery are the main benefits for patients who undergo LC compared to those undergoing OC. However, LC is associated with an increased incidence of bile duct injuries (BDI), which may result in increased patients' morbidity [6–8], mortality [9, 10], and impaired quality of life [11, 12] compared to OC. According to previous published series, the incidence of BDI ranged between 0.1% and 2% during LC [13–18] and between 0% and 0.7% during open cholecystectomy [19–21]. Several potential predisposing factors for BDI have been proposed in the past [17]. However, there is some controversy as to whether inflammation is an independent risk factor for BDI, since the previous findings are not consistent [7, 13, 16, 17]. Moreover, previous studies have examined the impact of inflammation on BDI occurrence without

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controlling for potential confounders. This implies that the increased incidence of BDI among those with inflammation, reported by several studies [13, 22], may be attributed to the presence of other risk factors (i.e., increased age, less laparoscopic experience of surgeons, and others).

Therefore, the primary aim of this study is to investigate whether inflammation is an independent predictor for BDI. Secondarily, we sought to estimate the incidence of BDI and to present the management and the clinical outcome of BDI after LC.

## Methods

### Patients and operations

LC was introduced at our department, the 3rd Surgical Department of "Evangelismos" General Hospital of Athens, Greece, in 1992. Between 1993 and 2005, 2,184 patients (35% men, 65% women) underwent LC carried out by nine surgeons. We retrospectively collected information regarding the aforementioned LC. In particular, we recorded demographic characteristics of patients (i.e., sex and age), experience of the surgeon (number of previous LC performed, LC performed by resident or not), conversion of LC to OC and the reason that led the surgeon to convert the LC to OC, concomitant gallbladder inflammation (acute/chronic cholecystitis), incidence of BDI occurrence, classification, timing of diagnosis (intraoperative/postoperative), type of management (immediate/delayed, conservative/operative), and the outcome after BDI occurrence (alive/dead/complications).

Since a proportion of bile duct injuries is revealed some time after the operation, particularly during the first year, follow-up ranged from 1–7 years (mean 3 years).

### Inflammation

Although inflammation is synonymous with cholecystitis the correlation between clinical cholecystitis and inflammation is not always straightforward. A patient with right upper quadrant pain, fever, and elevated white blood cells (WBC) with ultrasonographic findings of gallbladder inflammation is a patient with acute cholecystitis and usually the operative findings are corresponding. On the other hand, in a number of patients with gallbladder stones presenting with biliary colic or even vague symptoms the surgeon unexpectedly encounters gallbladder inflammation (and at times severe). In our study inflammation is recorded as present when the operative findings are suggestive of that, no matter what the clinical findings. Operative findings suggestive of inflammation include gallbladder adhesions, usually with the omentum but at times with transverse colon and duodenum, thickened gallbladder wall, and hard, difficult-to-dissect fibrotic tissue in Callot's triangle in various degrees. In the acute setting the aforementioned are accompanied by edema.

At our institution, calculus cholecystitis is preferentially treated with early laparoscopic cholecystectomy (during the first 72 h) unless hospital functional procedures make the operation impossible. In this situation interval laparoscopic cholecystectomy is performed (at least 2–3 months later).

### Bile duct injury classification

BDI were classified according to Strasberg's classification into types A–E (Table 1) [23]. For most authorities injuries of type E are considered major injuries, while the rest of types are regarded as minor injuries.

### Technique for LC

The four-trocar technique is employed at our institution for performing laparoscopic cholecystectomies. The surgeon is on the patient's right-hand side. The patient is then placed in a reverse Trendelemburg position and slightly rotated to the left (20°). Proper, inferior traction on Hartmann's pouch is applied to enable dissection in Callot's triangle. Dissection is kept in close proximity to the gallbladder. Dissection is continued until liver bed (hepatocystic triangle). When this is accomplished only two structures are left to ligate: the cystic duct and the cystic artery. These are ligated and transected and dissection is directed towards the gallbladder bed so as to remove the gallbladder. Although this is the preferred technique, inability to apply it did not restrain some surgeons from completing the operation without conversion to open.

**Table 1** Bile duct injuries classification according to Strasberg [23]

| Strasberg group | Definition |
|---|---|
| A | Bile leaks from minor ducts still in continuity with the common bile duct |
| B | Occlusion of part of the biliary tree |
| C | Transection of part of the biliary tree |
| D | Lateral injury to an extrahepatic bile duct |
| $E_1$ | Common bile duct stricture >2 cm distal to the hepatic duct confluence |
| $E_2$ | Common bile duct stricture <2 cm distal to the hepatic duct confluence |
| $E_3$ | Hilar stricture with no residual common bile duct but with hepatic duct confluence intact |
| $E_4$ | Destruction of hepatic duct confluence |
| $E_5$ | Strictures involving the right aberrant sectoral duct and the common bile duct |

Intraoperative cholangiography was not applied in any laparoscopic cholecystectomy.

### Statistical methods

Normally distributed continuous variables are summarized as mean values ± standard deviation. Skewed variables (i.e., duration of hospitalization) are summarized as median ($25^{th}$, $75^{th}$ interquartiles) and categorical variables as absolute and relative (percentage) frequencies. Association between continuous variables and categorical variables with two categories were evaluated using Student's *t*-test for normally distributed continuous variables and the Mann–Whitney test for skewed variables, while the association between categorical variables was evaluated through the chi-square test without the correction of continuity or with Fisher's exact test, if at least one cell had fewer than five observations. Incidence of BDI was calculated as the ratio of events (BDI) divided by the total number of LCs performed excluding those converted to open unless the reason for conversion was BDI. Simple and multivariate logistic regression analysis was performed to evaluate the association between inflammation and BDI occurrence during LC. Potential confounders entered in the model were age, sex, the laparoscopic experience of the surgeon, and whether the LC was performed by resident or not. The results are presented as odds ratio (OR) and 95% confidence interval (95% CI). A probability value of 5% was considered statistically significant. All statistical calculations were performed on SPSS version 12.0 software (SPSS Inc, Chicago, Il, USA).

## Results

### Patients and laparoscopic procedure characteristics

Among the 2,184 patients included in this study, 757 (35%) were men and 1,427 (65%) were women with age (mean ± SD) of 57.6 ± 14.5 years and 56.3 ± 14.5 years, respectively ($p = 0.004$). Inflammation was present in 344 (16%) patients. These were elder and their LC was more likely to be converted to OC and to be performed by residents compared to those without inflammation (Table 2).

Of the 2,184 LC performed, 110 (5%) converted to OC. The most common reason for conversion was the presence of inflammation (44%) following by adhesions due to previous laparotomy for other reason (28%) and inability to clarify the anatomy of the cholecystectomy triangle (10%). The remaining 17% of the converted operations was attributed to other reasons, such as unexpected other neoplasm, technical reasons, hemorrhage, CBD laceration, and biliary-enteric fistula. The conversion rate was higher in male (6.47% versus 4.27% in women, $p = 0.025$), in those with inflammation (14.83% versus 3.21% in those without, $p < 0.001$), in those with age over 65 years old (7.57% versus 4.11% and 2.71% in those <35 years old and 35–65 years old, respectively, $p = 0.001$) and in those where LC was performed by residents (6.70% versus 4.35% for LC performed by trainers, $p = 0.022$), while no significant difference was observed in conversion rate regarding the laparoscopic experience of surgeons ($p = 0.402$).

**Table 2** Patients and laparoscopic cholecystectomy characteristics for those with and without inflammation, separately

| Characteristics | With inflammation ($n = 344$) | Without inflammation ($n = 1{,}840$) | *p*-value |
|---|---|---|---|
| Gender | | | |
| Male | 121 (35 %) | 636 (35%) | 0.837 |
| Female | 223 (65%) | 1,202 (65%) | |
| Age (years) | 58.8 (14.7) | 56.4 (14.6) | 0.004 |
| Laparoscopic experience[a] | | | |
| <50 | 41 (12%) | 409 (22%) | <0.001 |
| 51–100 | 59 (17%) | 373 (20%) | |
| >100 | 244 (71%) | 1,058 (58%) | |
| LC performed by residents | 126 (37%) | 516 (28%) | 0.001 |
| Conversion rate | 51 (15%) | 59 (3%) | <0.001 |

[a] Experience of the surgeon in numbers of laparoscopic operations performed

### Inflammation, BDI, and postoperative adverse outcome rate

In 2,184 patients who underwent LC, 15 BDI occurred (0.69%). No statistically significant reduction in the incidence of BDI was observed during the period 1993–2005. In particular, the incidence of BDI has ranged between 0.44 in 2002 and 1.03 in 1993. Moreover, no difference was observed in the distribution of the gender, laparoscopic experience of the surgeons, age, and the performance of LC by residents between patients with BDI and those without (Table 3). However, incidence of BDI was significantly higher among those with inflammation (1.74%) compared to those without inflammation (0.49%, $p = 0.01$). The risk of BDI was almost 3.5 times higher among patients with inflammation compared to those without (unadjusted OR 3.61, 95% CI 1.27–10.21). Moreover, inflammation remained a significant predictor for BDI after controlling for potential confounders (adjusted OR 3.13, 95% CI 1.03–9.47).

Regarding postoperative adverse outcomes, one patient died (0.05%) and two had recurrent cholangitis (0.09%). These three patients had sustained a BDI during LC

**Table 3** Risk factors for BDIs

| Characteristics | With BDI ($n = 15$) | Without BDI ($n = 2,169$) | $p$-value |
|---|---|---|---|
| Gender (male) | 7 (47%) | 750 (35%) | 0.327 |
| Age (years) | 56 ± 16.8 | 57 ± 14.6 | 0.860 |
| Inflammation | 6 (40%) | 338 (16%) | 0.01 |
| Laparoscopic experience[a] | | | 0.408 |
| <50 | 3 (20%) | 447 (21%) | |
| 51–100 | 1 (7%) | 431 (20%) | |
| >100 | 11 (73%) | 1,291 (59%) | |
| LC performed by residents | 3 (20%) | 639 (29%) | 0.423 |

[a] Experience of the surgeon in numbers of laparoscopic operations performed

($p < 0.001$ for adverse outcome rate between those with BDI and those without) and they were older (>65 years). Moreover, the overall adverse outcome rate was marginally higher in patients with concomitant inflammation (0.58%) compared to those without inflammation (0.05%; $p = 0.066$).

BDI, their management, and clinical outcome

Three out of 15 BDI were major (0.14%) and 12 were minor (0.55%) injuries. According to Strasberg's classification, there were ten type A, one type C, D, and $E_2$, and two type $E_1$. Three injuries (one type $E_2$, one type $E_1$, and one type D) were diagnosed during LC (intraoperatively); LC was then converted to OC, in which BDI was verified and primary repair took place. Twelve injuries (80%; 1 major and 11 minor) were diagnosed postoperatively. Five of those diagnosed postoperatively (42%), were treated conservatively and the other seven (58%) necessitated surgical repair. Of the ten type A BDI, six required surgical intervention. Of these ten type A injuries, eight were due to leakage from the cystic stump due to either laceration of the cystic duct at a place lower to the clips applied (5) or due to clip failure (3), while two were attributed to leakage from a subvesical duct of Luschka. The decision to operate patients with type A injuries was solely clinical (sings of peritonitis either local or generalized) and the time interval from laparoscopic cholecystectomy to laparotomy ranged from 1–10 days (median 2 days). One patient required reoperation for abscess drainage. In patients treated conservatively as well as in two of the patients that required reoperation endoscopic retrograde cholangiopancreatography (ERCP) demonstrated the injury as well as contributed to the management of the injury. A type C injury developed peritonitis and multi-organ failure and despite vigorous operative and nonoperative management died. A type E1 injury (common bile duct stricture) was treated nonoperatively with ERCP and stent placement.

As mentioned above, adverse outcome (death or recurrent cholangitis) was observed in 3 out of 15 patients sustaining injuries (20%). One patient, who sustained minor injury, died, and the other two, who sustained major injuries, had recurrent cholangitis. No significant association was observed between adverse outcome and management of injury ($p = 0.999$), time of diagnosis ($p = 0.516$), gender ($p = 0.569$), or inflammation ($p = 0.525$), while the age of patients with an adverse outcome was marginally significantly higher compared to those without one ($p = 0.059$).

The median ($25^{th}$, $75^{th}$ interquartiles) duration of hospitalization postoperatively for patients sustaining an injury was 22 (10, 35) days with mean of almost 27 days. No difference was observed in duration regarding the type of injury—major or minor ($p = 0.772$) and the time of diagnosis of injury – intraoperatively or postoperatively ($p = 0.664$), while the duration of hospitalization was longer for patients whose injuries were treated surgically compared to those treated conservatively ($p = 0.002$).

## Discussion

In this work, we present the incidence of BDI and postoperative adverse outcome at LC, the association of inflammation with the risk of BDI occurrence, and the management and outcome of BDI, recorded in a single surgical department during the period 1993–2005, in Greece.

BDI were and remain the most serious complication of LC. With the exception of the early laparoscopic era where the BDI rate was unacceptably high ranging from 1.3% to 5.5% [8, 24] the subsequent period demonstrated lower BDI rates in the range of 0.4–1.2%. Although these rates are acceptable they are still higher than those demonstrated in the era of open cholecystectomy. Studies published later demonstrated even lower BDI rates in the range of the open era. Whether the BDI rate has declined or not since this time is a matter of debate. In our series, the BDI incidence was calculated to be 0.69%, which is almost consistent with the findings of recently published studies [13, 14, 22, 25]. Consistent with the literature is the finding that only three out of 15 BDI were recognized intraoperatively as well as the finding that type E BDI were more likely to be recognized intraoperatively compared to other types of BDI. Moreover the BDI rate in our series is constant over time.

Small discrepancies among the incidences reported by several series may be attributed to the different definition of injuries. Some studies have recorded only major injuries whereas other studies have collected both major and minor injuries. In our series, all BDI were included irrespective of

severity. Many authors classify injuries as minor or major. The purpose of this classification is to predict the outcome of these patients in the long term. In predicting early postoperative outcome the value of such a classification is a matter of debate. In our study, the type of injury (minor or major) does not influence early postoperative adverse outcome as far as death or hospital stay is concerned. In fact the only death recorded was for a type C injury where bile-induced peritonitis was followed by secondary bacterial peritonitis that resulted in multi-organ failure and death. For this reason characterizing an injury as minor or major so as to predict the early postoperative outcome is irrelevant. Early postoperative outcome is greatly influenced by the presence of bile-induced peritonitis and the presence of infection while biliary strictures are the cause of late morbidity in most of the patients with bile duct injury. In the setting of long-term morbidity and mortality we agree that discrimination of injuries into minor and major is justified and strongly influences outcome but the aforementioned discrimination is of no use in predicting short-term outcome. Thus, all BDI should be considered major as far as early postoperative management of the patient is concerned. In this view we find Strasberg's classification as more appropriate to describe BDI compared to earlier classifications [23].

Our results suggest an independent relationship between inflammation and BDI. Whether inflammation is a risk factor for BDI is a matter of debate. Although a number of studies attempted to clarify this issue, none of these adjusted for potential confounders [8, 24, 26, 27]. We revealed that the risk of BDI is almost three times higher in patients with concomitant inflammation compared to those without, after adjustment for demographics characteristics of patients, experience of surgeons, and other factors. This means that inflammation increases the risk for BDI and that no other risk factor studied can explain the association observed. Similar to our findings were the results of other studies where inflammation increased BDI rate two- to threefold [8, 27]. In contrast, others rejected the involvement of inflammation alone in increasing the rate of BDI [26].

From a pathogenetic standpoint, inflammation distorts anatomy of Callot's triangle and porta hepatis. Dissection under these circumstances can result in direct damage to the bile ducts or may compromise their delicate blood supply, resulting in strictures.

Anatomical variations of the biliary tree are of a wide range and can explain in part the occurrence of BDI in patients without inflammation. Recording variations in anatomy of every patient who is to undergo LC is certainly not possible and it is reasonably assumed that their occurrence is the same in both patients with or without inflammation. Whether the concomitant presence of an anatomical variation and inflammation would alter our results is not known, which is a limitation of the study. Since no studies to delineate hepatic anatomy preoperatively for the sake of an LC are conducted (and probably never will), the clinical implication of such a task is limited.

The technique of laparoscopic cholecystectomy is supposed to influence the rate of BDI to at least some extent. Safe technique implies that adequate and proper dissection of hepatocystic triangle is performed, resulting in two structures left to be ligated: the cystic duct and the cystic artery [23]. Through it is assumed that BDI of type E and possibly types C and D can be avoided. Avoiding type E injuries is certainly a step in the right direction but two aspects should be commented upon. The first is that safe technique is a method not applicable in all laparoscopic cholecystectomies for a number of reasons. It is a time consuming and at times technically challenging technique, especially in the presence of inflammation. If failure to employ safe technique would suggest conversion to open, then the conversion rate would probably rise. Surgical persistence in accomplishing a cholecystectomy through laparoscopy contrary to the aforementioned characteristics of the technique and an overestimated self-confidence derived mainly from personal experience makes surgeons unwilling to employ it in every case. This can explain the minor or even absent influence of surgical experience on the occurrence of a BDI, an observation made by others as well [28]. In our study (and in accordance with the aforementioned) performance of the operation by a resident surgeon does not seem to influence BDI rate. The second aspect that deserves comment is that BDI types A and D and perhaps B and D are possibly not avoidable irrespective of employing safe technique or not. And as we have shown the severity of BDI is not a predictor of outcome as far as the early postoperative period is concerned. The actual impact of the cholecystectomy technique on BDI is difficult to estimate since there is no measure for diversion from safe technique. It was our initial intention to evaluate this parameter but major disagreement among the study group as to what constitutes a diversion from safe technique and to what extent made this task unfeasible.

At our department, conversion rate in the presence of inflammation is 14% while in its absence the rate is 3.4%. Moreover, there is a tendency by some surgeons to proceed with open cholecystectomy without even laparoscopy in cases of expected severe inflammation. It is our belief that the aforementioned factors exert a "protective" role on the incidence of BDI in patients with inflammation. Without these factors it is logically assumed that the BDI rate would be higher. However, despite this selection bias, probably favouring reduction of BDI rate during LC for patients with inflammation, in our study inflammation is still an independent risk factor for BDI. Some would argue that

lowering the threshold for conversion to open in the presence of inflammation will lower the BDI rate. Although this argument seems sound, a profound question arises: what is the optimal conversion rate to lower a low BDI rate? However, in the minds of others strict adherence to the principles of safe technique might be a better solution. The way forward is difficult to determine.

## Conclusion

BDI is a dreadful and fearful complication of LC. The logistic regression analysis we performed clearly indicates that inflammation is an independent predictor of BDI occurrence during LC. According to our study, inflammation induces a threefold increase in BDI, an alarming finding that calls for attention. Therefore, careful dissection and adherence to the principles of safe technique is deemed necessary when inflammation is encountered. If this is not feasible, surgeons should not hesitate to convert a LC to an OC. in the presence of inflammation. As a rule of the thumb the threshold for converting a LC to open in the presence of inflammation must always be low.

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