

# Gallbladder perforation during elective laparoscopic cholecystectomy: Incidence, risk factors, and outcomes

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# ABSTRACT

**OBJECTIVE:** This study aimed to reveal the risk factors and outcomes of gallbladder perforation (GP) during laparoscopic cholecystectomy.

**METHODS:** Videotapes of all patients who underwent an elective cholecystectomy at our department were retrospectively analyzed, and the patients were divided into two groups based on the presence of GP. The possible risk factors and early outcomes were analyzed.

**RESULTS:** In total, 664 patients [524 (78.9%) females,  $49.7\pm13.4$  years of age] were observed, and GP occurred in 240 (36.1%) patients, mostly while dissecting the gallbladder from its bed (n=197, 82.1%). GP was not recorded in the operation notes in 177 (73.8%) cases. Among the studied parameters, there was no significant risk factor for GP, except preoperatively elevated alanine transaminase level (p=0.005), but the sensitivity and specificity of this measure in predicting GP were 14.2% and 7.4%, respectively. The two groups had similar outcomes, but the operation time (35.4±17.5 vs 41.4±18.7 min, p=0.000) and incidence of drain use (25% vs 45.8%, p=0.000) increased in the GP group.

**CONCLUSION:** The present study reveals that GP occurs in 36.1% of patients who undergo laparoscopic elective cholecystectomy, but it may not be recorded in most cases. We did not find any reliable risk factor that increases the possibility of GP. GP causes an increase in the operation time and incidence of drain use; however, the other outcomes were found to be similar in patients with GP and those without.

Keywords: Alanine transaminase; gallbladder perforation; laparoscopic cholecystectomy.

In general surgery practice, cholecystectomy is the second most commonly performed abdominal operation [1, 2]. Laparoscopic cholecystectomy has some advantages over the conventional technique, including better cosmetic results, lesser postoperative pain, a shorter hospital stay, and early return to daily activities [3]. Besides, cholecystectomy is not a risk-free procedure and may cause severe complications, including bile duct injury, bleeding, abscess, and pancreatitis. Gallbladder perforation (GP), which is a common intraoperative complication during cholecystectomy, has been reported to occur with a high incidence of 10%-33% [4]. The risk factors and consequences of GP have also been studied [4-9]. It has been advocated that male sex, a history of acute cholecystitis or previous laparotomies, the use of a laser, an inflamed or nonvisualized gallbladder, and a difficult operation increase the risk of GP [5-7]. In addition, bile and stone spillage have rarely



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been reported to lead to severe problems [10-15]. GP does not worsen the outcomes of the procedure, but it has been stated that lost stones after GP may infrequently cause secondary complications, including pain, fever, or intraabdominal abscesses, because they are a potential nidus of infection and bile spillage may lead to chemical peritonitis [4, 10-16]. However, most of the information present in the literature may be misleading because the data is mostly based on retrospective information, and it is probable that GPs were not recorded in the operation documents because GP is generally believed to be harmless, with no adverse consequences in most instances. Thus, to understand the incidence, risk factors, and consequences of GP, we aimed to analyze compact disc videos of the operations.

# MATERIALS AND METHODS

The Institutional Review Board approved the design and content of the study (Reference number: B104ISM4340029/1009/20). All the patients who underwent an elective cholecystectomy between March 2011 and March 2015 at our department were retrospectively reviewed. The procedures were performed or supervised by one of six surgeons at our department and were performed using a four-trocar technique as described previously [17]. In case of GP during the operation, the management was generally alike: free bile was aspirated, the soiled areas were irrigated with physiological saline until clear, and spilled stones were retrieved whenever possible. These patients continued to receive intravenous and peroral antibiotics for 1 week in most instances. The placement of a drain and conversion to open surgery were decided by the operating surgeon. The patients were generally discharged from the hospital on the next day, but longer hospitalization was sometimes necessary.

The primary aims of the present study were to reveal the incidence and risk factors for and outcomes after intraoperative GP during elective laparoscopic surgery. The patients for whom conversion to open surgery was undertaken were excluded from further analyses, but the reasons for conversion were stated. An experienced surgeon (YEA) blinded to the patients, operators, and outcomes of the procedures watched the operation videos taped on compact discs (CD) of all the included patients. The patients were classified into two groups based on the presence of GP at the time of the operation (Perforation or No perforation groups). The patients were excluded if the operation CDs were not available or defective. During this inspection, the degree of difficulty was calculated according to Cuschieri's scale, which defines the complexity of the procedure in four grades [18]. Grade 1 refers to an easy cholecystectomy without any further problems. Grade 2 refers to the presence of light pericholecystitis or adherences or fatty tissue masking the cystic pedicle or mucocele. According to this scale, grade 3 defines severely difficult cholecystectomies in patients with gangrenous cholecystitis; shrunken fibrotic gallbladder; intense pericholecystitis; subhepatic abscesses; or advanced hepatic diseases, such as cirrhosis or portal hypertension. In those patients, the dissections of the cystic pedicle or the body gallbladder from the hepatic bed are hard or sometimes impossible because of the accompanying problem or adherence of Hartman's pouch over the common bile duct. Patients with grade 4 difficulties were excluded because it refers to conversion to open surgery [18].

The timing of perforation was noted as follows: during traction of the gallbladder, during the dissection of adhesions and bands, during the dissection of Callot's triangle prior to cystic duct clipsing, during the further dissection of Callot's triangle after cystic duct clipsing, during the dissection of the gallbladder from the hepatic fossa, and during the extraction of the gallbladder from the abdominal cavity. A chart review was completed for all patients, and computer-based data were scanned for the following information as risk factors for and outcomes of intraoperative GP: demographics; body mass index; the presence/absence of previous hospitalization for acute cholecystitis, biliary pancreatitis, or choloangitis; the American Society of Anesthesiology score; laboratory findings [alanine transaminase (ALT), aspartate transaminase (AST), gamma-glutamyl transaminase (GGT), albumin, white blood cell (WBC), hemoglobin, total bilirubin, and amylase]; the necessity and findings of magnetic resonance imaging cholangiography (MRCP) and/or endoscopic retrograde cholangiography (ERCP); ultrasound findings; the presence/absence of previous laparotomy [regional (midline or right subcostal incisions) or others (McBurney or Pfannenstiel)]; previous operations (operations of the gallbladder or gastroduodenal region; or others, including appendectomy, section, or gynecological); the experience of the operator (staff or resident); the degree of difficulty of the operation as described by Cuschieri; operation time; the presence or omission of drain placement; hospitalization period; complications; and re-hospitalization and its causes,

mortality, and pathological findings. Finally, the operation notes were also scanned by two investigators (EG and MH) who were blinded to the patients' information and operation CDs, and whether or not the perforation was stated in the operation notes was assessed.

The patients with a previous hospitalization related to gallbladder stones received an interval cholecystectomy from 6 to 8 weeks after the initial presentation. In our routine practice, if the operation and hospitalization period are uneventful, the patients are seen at day 7 postoperatively. In case of having no complaints, further follow-up is not offered.

#### **Statistical Analysis**

Data were analyzed using SPSS 17.0 for Windows (SPSS Inc., Chicago, IL, USA). Results were given as percentages, mean and standard deviations, or median and ranges. Quantitative and qualitative variables were compared using Student's t-test and chi-square (Pearson's or Fischer's exact) test, respectively. A Mann–Whitney U test was preferred when there was an abnormal distribution of the samples confirmed by the Kolmogorov– Smirnov test. A p value <0.05 was accepted to be significant.

# RESULTS

In total, 737 patients [575 (78.0%) females with a mean (SD) age of  $49.1\pm13.3$  years] underwent an elective cholecystectomy at our department during the study period. However, the operation CDs were not available or defective in 60 (8.1%) cases, leaving 677 cases for further analyses. Of these, 13 (1.9%) necessitated conversion to open surgery due to severe adhesions (n=9, 1.3%) not identifying anatomical structures (n=2, 0.3%), severe bleeding (n=1, 0.1%), and injury to the transverse colon (n=1, 0.1%). Thus, current data include a total number of 664 cases [524 (78.9%) females with a mean (SD) age of  $49.7\pm13.4$  years].

Of 664 patients, an intraoperative GP was observed in 240 (36.1%) patients (Perforation group) during traction of the gallbladder (n=15, 6.3%), the dissection of adhesions and bands (n=2, 0.8%), the dissection of Callot's triangle prior to cystic duct clipsing (n=9, 3.8%), the further dissection of Callot's triangle after cystic duct clipsing (n=6, 2.5%), the dissection of the gallbladder from its bed (n=197, 82.1%), and the extraction of the gallbladder from the abdominal cavity (n=11, 4.6%). The remaining patients (n=424) were present in the No perforation group. Of 240 patients, GP was not stated in the operation records in 177 (73.8%) cases.

The present study evaluated the risk factors; however, almost none of the analyzed parameters were found increase intraoperative GP during elective laparoscopic cholecystectomy, including patient-related aspects, preoperative laboratory or other diagnostic findings, and operative features (Table 1). The only risk factor that increased the risk of GP was preoperative ALT level (p <0.05). Of the 63 patients with elevated ALT levels, 33 (52.4%) had GP, but the sensitivity and specificity of elevated ALT in predicting GP were 14.2% and 7.4%, respectively. There were no differences between the blood tests, apart from ALP. Although some patients required MRCP or ERCP due to elevated bilirubin levels or choledocholithiasis, there were no patients who were in need of intraoperative cholangiography, exploration of the common bile duct, or laparoscopic ultrasonography in the current study.

The outcomes after the operations were also analyzed. The results showed no statistically significant differences between the groups regarding postoperative hospitalization period, complications, and re-hospitalizations (Table 2). In addition to the median (range) operation time [32 (10-120) vs 36.5 (11-120)], the rate of drain use was significantly increased in patients with GP (p <0.001 for both). No patients required reoperation as a consequence of the complications. However, the pathological evaluations revealed gallbladder cancer in two patients (0.8%), both in the Perforation group. Subsequent procedures were required for both the patients, and they remained alive 5 and 9 months after the operations without any evident tumor recurrence.

### DISCUSSION

Cholecystectomy is one of the most common indications for surgery worldwide [1]. Besides, GP frequently occurs during laparoscopic cholecystectomy. A recent review on 18.280 patients has revealed that the incidence of GP is 18.3% [19]. In another analysis, the rate of GP in 1059 consecutive laparoscopic cholecystectomies was 29% [20]. However, it is possible that even this higher rate may not be the actual incidence of GP because prospective information has shown that the frequency of GP during laparoscopic cholecystectomy reaches up to 33% [9]. Consequently, it may be more reasonable to consider the highest reported rates in the literature because

	No perforation (n=424)	Perforation (n=240)	р
Demographics			
Age	49.8±13.2	49.7±13.8	0.914
Gender			0.143
Females	342 (80.7)	182 (75.8)	
Males	82 (19.3)	58 (24.2)	
Body mass index	28.5±5.1	29.6±5.5	0.053
Previous hospitalization for	18 (4.2)	8 (3.3)	0.561
Acute cholecystitis	8 (1.9)	2 (0.8)	0.343
Biliary pancreatitis	7 (1.7)	5 (2.1)	0.764
Cholangitis	3 (0.7)	1 (0.4)	0.999
ASA score			
Ι	83 (20.2)	62 (26.7)	
II	262 (63.9)	129 (55.6)	0.104
III	63 (15.4)	41 (17.7)	
IV	2 (0.5)	0	
Laboratory Findings			
ALT	20 (6-548)	18 (7-671)	
	(n=408)	(n=232)	0.176
Elevated ALT	30 (7.4)	33 (14.2)	0.005
MRCP findings	(n=25)	(n=12)	
Cholelithiasis	21 (84.0)	11 (91.7)	0.999
+ Choledocolithiasis	4 (16.0)	1 (8.3)	
ERCP findings	(n=14)	(n=4)	
Sphincterotomy only	9 (64.3)	2 (50.0)	
+ stone extraction $\pm$ stent application	5 (35.7)	2 (50.0)	0.999
USG findings	n=338	n=207	
Stone	322 (95.3)	200 (96.6)	
Polyp	8 (2.4)	4 (1.9)	0.930
Sludge	7 (2.1)	3 (1.4)	
Residue gallbladder	1 (0.3)	0	
Stone size (>1 cm/ < 1cm)	153/169 (63.2/60.4)	89/111 (36.8/39.6)	0.502
Single/multiple	86/236 (62.8/61.3)	51/149 (37.2/38.7)	0.760
Previous operation/laparotomy			
Operations to gallbladder or gastroduodenal region	4 (0.9)	3 (1.3)	0.708
Regional laparotomy	5 (1.2)	5 (2.1)	0.508
Overall laparotomy	41 (9.7)	31 (12.9)	0.196
Experience of the Surgeon			
Staff/Resident	42 (58.3) / 382 (64.5)	30 (41.7) / 210 (35.5)	0.302
Degree of difficulty <sup>+</sup>			0.136
Ι	321 (75.7)	165 (68.8)	
II	57 (13.4)	39 (16.3)	
III	46 (10.8)	36 (15.0)	

TABLE 1. The risk factors for gallbladder perforation during elective cholecystectomy

(Data are presented as either median [range] or mean [±standard deviation]. Information in the parentheses indicates the percentages).

\*The levels of Hgb are presented separately in male and female patients; †: Data are presented according to Cuschieri's scale, which defines the complexity of the procedure in 4 grades; however patients with grade 4 difficulties were excluded since it refers to conversion to open surgery [18].

ASA: American Society of Anesthesiology score; AST: Alanine transaminase; ALT: Aspartate transaminase; GGT: Gamma-glutamyl transaminase; WBC: White blood cell; Hbg: Hemoglobin; MRCP: Magnetic resonance imaging cholangiography; ERCP: Endoscopic retrograde cholangiography; USG: Ultrasonography.

	No perforation (n=424)	Perforation (n=240)	р
Operation time (minutes)	35.4±17.5	41.4±18.7	0.000
Drain use	106 (25.0)	110 (45.8)	0.000
Hospitalization period (days)	) 1.3±1.0	1.3±0.9	0.664
Complications			
Bile drainage	0	2 (0.8)	0.130
Evisceration	0	1 (0.4)	0.361
Abscess	3 (0.7)	3 (1.3)	0.673
Cholangitis	4 (0.9)	1 (0.4)	0.659
Respiratory	2 (0.5)	0	0.538
Overall	9 (2.1)	7 (2.9)	0.522
Re-hospitalization	6 (1.4)	5 (2.1)	0.538

TABLE 2. Outcomes after gallbladder perforation

most perforations may not be documented in operation records. The controversy probably arises from the fact that some surgeons do not report GP in the operation records, which are the data sources of retrospective studies. A recent analysis on operative notes has revealed that GP with or without bile and stone spillage was not documented in some instances [21]. Thus, we believe that the rate of GP presented in the present study is more realistic because the data were obtained from operation videos. Accordingly, our data shows that GP may be more common than expected and occurs in at least one third of all patients undergoing laparoscopic cholecystectomy. In addition, the present study has also shown that GP is not noted in almost three-fourth of the operation records probably because most surgeons do not consider this problem a major complication in most instances and believe that GP is harmless and thus do not report it.

Several studies have evaluated the potential risk factors for GP during laparoscopic cholecystectomy. A multivariant logistic regression analysis has revealed male sex, a history of acute cholecystitic, the use of a laser, and the presence of a grossly inflamed gallbladder as individually significant risk factors for GP [5]. Other studies have underlined some other parameters influencing the frequency of GP, for example, age; preoperative ultrasound findings, including a thickened gallbladder wall and hydrops; the presence of a previous laparotomy; the nature of the stone (pigment stones); and the surgeon's experience [5, 7, 9, 22]. However, these studies may be criticized to include both groups of patients who underwent emergent and elective procedures, which are probably different types of operations. Thus, the patients who underwent emergent cholecystectomies were excluded in the present study. In addition, the patients for whom conversion to open surgery was undertaken were also excluded because it was generally impossible to determine whether the adverse consequences in these cases were due to GP or the conversion itself. Thus, the present study focuses on a more specific condition that only includes elective non-problematic laparoscopic cholecystectomy, which is actually the case in most instances.

Although the present study has revealed that a preoperatively elevated ALT level may be an indicator for a possible GP at the time of the operation, we are not sure whether it is a significant factor or an incidental finding because the risk for GP was only 52.4% in patients with elevated ALT levels, which was <two-fold of that with normal ALT levels. Consequently, because the sensitivity and specificity were unacceptably low, in our opinion, the preoperative ALT level cannot be considered a predictive factor for GP. Interestingly, a correlation between GP and the difficulty scale of the cholecystectomy was not attained within the framework of the present data. Although the statistical analysis revealed no difference, the p value of 0.136 may suggest a trend. Our data did not reveal any other risk factor that increased the possibility of GP. Thus, we believe that GP may be unpredictable in the case of an elective cholecystectomy.

In a recent study, it has been mentioned that 69 of 131 GPs (52.7%) occurred while dissecting the gallbladder from the hepatic fossa [6]. Because we had the same result, we can conclude that the separation of the gallbladder from its bed is probably the most risky stage of cholecystectomy for a possible GP. We believe that this information is significant, and it may warn surgeons about this particular threat. In addition, the above-mentioned point should be emphasized during the training period of surgeons.

The consequences of GP have been extensively evaluated previously. In animal models, it has been generally shown that GP and the consequent spillage of bile and/ or stones are harmless and do not cause any infection or mortality during the follow-up period [23, 24]. In contrast, the data derived from human studies remain controversial. Although, at least theoretically, GP leads to the contamination of the peritoneal cavity with bile, calculi, and bacteria, some believe that that the adverse consequences of spillage after GP during laparoscopic cholecystectomy may be minimized by the prompt retrieval of as many of the spilled stones as possible, abundant irrigation of the peritoneal cavity, and adequate antibiotic therapy [6]. It has been shown in most studies that GP does not increase the complication risk, reoperations, or hospital stay [6, 25]. A recent prospective study has also advocated that GP and retained gallstones do not adversely affect respiratory mechanics or alter postoperative pain [9]. Besides, other studies have reported adverse consequences of bile spillage due to GP because bile is frequently contaminated in the presence of gallstones [26]. In an analysis of 1059 consecutive laparoscopic cholecystectomies, increased incidences of fever and intraabdominal abscesses have been reported if GP had happened at the time of the operation [20]. In addition, some case reports have advocated that retained gallstones and bile spillage cause infection or abscesses, fibrosis, adhesions, cutaneous sinuses, small-bowel obstructions, or generalized septicemia [27, 28]. Finally, even conversion to open surgery has been recommended in a study in patients with a loss of numerous or large pigment stones that cannot be retrieved by laparoscopy [4]. However, we believe that the adverse consequences of spillage after GP during laparoscopic cholecystectomy may be minimized by the prompt retrieval of as many of the spilled stones as possible, abundant irrigation of the peritoneal cavity, and adequate prophylactic antibiotic therapy [6], as mentioned above. With this approach, we have found that GP and consequent intraabdominal contamination does not increase the risk of complications or alter the outcomes during the early postoperative period. Consequently, the present study reveals that GP increases the incidence of drain use and lengthens the operation time, both of which are probably the consequences of GP because the retrieval of stones and peritoneal irrigation are required in these cases. However, the present study found no other adverse consequence of GP in patients who underwent laparoscopic cholecystectomy. In contrast, similar short-term complications may be related to the treatment strategy followed in patients with GP. In addition, many of the documented complications from split gallstones are long-term, and they often happen after 1 year. Therefore, based on the results of the present study, we cannot comment on any long-term complications. Thus, we believe that GP is something that may be avoided whenever possible, but in the case of GP, the outcomes do not alter if certain rules for limiting the contamination are followed.

Finally, it is necessary to detail the outcomes in two patients with gallbladder cancer in the present study. These patients received further operations, including partial hepatic resections and lymph node dissection in the hepatic hilum, because their pathological results denied early T1 tumors. However, the spillage of bile has led to tumor implants over the anterior wall of the stomach in one patient; this patient required a distal gastrectomy. We believe that tumor spillage is the most significant adverse consequence of GP, but it also is a very exceptional problem because incidental gallbladder cancer is rare in patients undergoing elective cholecystectomy.

The present study has some limitations mostly due to its retrospective nature. Missing information, namely, the lack of operation CDs of 60 patients, limits the value of the present data. In addition, the findings of the study may be criticized in some standpoints. First, although the difference was statistically significant, we do not know whether a 6-min increase in the operation time reflects an importance in daily practice. In addition, the increased incidence of drain use in the Perforation group may be because there was no clear-cut criteria about the indications to put a drain. This may stem from the retrospective nature of the study. Furthermore, the increase in the operation time and the necessity of drain use may not be caused by GP, but all the three endpoints occurred due to the difficulty of the operation. The present study data may be criticized regarding the experiences of the surgeons because all staff surgeons do not have the same expertise. In addition, because the surgeons know they are being recorded, their performance may be more meticulous, which may have an impact on our results.

In conclusion, the present study reveals that GP occurs in 36.1% of the patients undergoing laparoscopic elective cholecystectomy but is less commonly reported in the operation notes. GP is unpredictable because there are probably no risk factors that increase the risk of GP, except a preoperatively assessed elevated ALT level; however, the sensitivity and specificity of this measure are low. The early postoperative outcomes are similar in patients with GP and those without, but the operation time lengthens and the incidence of drain use increases in patients with GP.

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