Long-Term Consequences of Intraoperative Spillage of Bile and Gallstones During Laparoscopic Cholecystectomy

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Laparoscopic cholecystectomy is associated with a higher incidence of iatrogenic perforation of the gallbladder than open cholecystectomy. The long-term consequences of spilled bile and gallstones are unknown. Data were collected prospectively from 1059 consecutive patients undergoing laparoscopic cholecystectomy over a 3-year period. Details of the operative procedures and postoperative course of patients in whom gallbladder perforation occurred were reviewed. Long-term follow-up (range 24 to 59 months) was available for 92% of patients. Intraoperative perforation of the gallbladder occurred in 306 patients (29%); it was more common in men and was associated with increasing age, body weight, and the presence of omental adhesions (each $P < 0.001$). There was no increased risk in patients with acute cholecystitis ($P = 0.13$). Postoperatively pyrexia was more common in patients with spillage of gallbladder contents (18% vs. 9%; $P < 0.001$). Of the patients with long-term follow-up, intra-abdominal abscess developed in 1 (0.6%) of 177 with spillage of only bile, and in 3 (2.9%) of 103 patients with spillage of both bile and gallstones, whereas no intra-abdominal abscesses occurred in the 697 patients in whom the gallbladder was removed intact ($P < 0.001$). Intraperitoneal spillage of gallbladder contents during laparoscopic cholecystectomy is associated with an increased risk of intra-abdominal abscess. Attempts should be made to irrigate the operative field to evacuate spilled bile and to retrieve all gallstones spilled during the operative procedure. (J GASTROINTEST SURG 1997;1:85-91.)

Laparoscopic cholecystectomy has become the "gold standard" for the surgical management of symptomatic cholelithiasis, and has replaced traditional open cholecystectomy. Although laparoscopic cholecystectomy is associated with a slightly higher incidence of iatrogenic injury to the biliary tract compared to open techniques, overall complication rates appear to be similar for the two procedures. We and others have noted that iatrogenic perforation of the gallbladder occurs more frequently during laparoscopic cholecystectomy, leading to intraperitoneal spillage of bile and gallstones.[1,2] Although some authors initially suggested that intraoperative perforation of the gallbladder should prompt conversion to an open procedure,[3] the current practice at most institutions is to retrieve as many stones as possible and to irrigate the peritoneal cavity to evacuate the spilled bile.

Although spillage of gallbladder contents is thought to be relatively innocuous, the long-term consequences of intraperitoneal spillage of bile and gallstones are undefined. Results of experimental studies in animals have been contradictory. Several studies showed a minimal fibrotic reaction to intraperitoneal stones,[2,4,5] whereas others demonstrated abscess formation.[6] Furthermore, there are numerous case reports of complications arising from spilled bile and gallstones.[7-15] The aim of this study was to determine the factors predisposing to intraoperative perforation of the gallbladder and the incidence and spectrum of adverse sequelae related to spillage of bile and gallstones.

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MATERIAL AND METHODS

Between July 1990 and August 1993, 1139 consecutive patients underwent attempted laparoscopic cholecystectomy for symptomatic cholelithiasis. Clinical, diagnostic, therapeutic, and follow-up data were collected prospectively. Excluded from analysis were 80 patients (7.0%) who were converted to open cholecystectomy because of the presence of dense adhesions (n = 26), severe inflammatory changes (n = 22), extensive spillage of bile or gallstones (n = 10), or for miscellaneous reasons (n = 22). Of the 1059 patients who underwent successful laparoscopic cholecystectomy, the gallbladder was removed intact in 753 (71%), whereas in 306 patients (29%) the gallbladder was perforated during the course of the operation. In these patients the specific details of the operative procedure were reviewed.

Short-term follow-up was based on a clinic visit 2 to 3 weeks postoperatively, and long-term follow-up was achieved by questionnaire or telephone conversation in 977 patients (92%) at a mean of 3.3 years (range 2.1 to 5 years). Of the 82 patients without satisfactory follow-up, 26 had died, nine were incarcerated (Federal Medical Center prisoners), eight no longer resided within the United States, and 39 declined to answer questionnaires. Hospital records of these patient subsets were carefully reviewed to exclude selection bias. The incidence of gallbladder perforation was similar between patients with and without satisfactory follow-up data (29% vs. 32%). No major early complications were identified in patients with intact gallbladders, but among those in whom intraoperative gallbladder perforation occurred, two developed perihepatic abscesses and two had superficial wound infections. The incidences of postoperative complications in the results to follow are based only on patients in whom long-term follow-up was completed.

Operative Technique

Laparoscopy was performed by either an attending surgeon or resident under direct staff supervision. Both elective and emergency cases were included in the study. A four-trocar technique with a 30-degree angled laparoscopic video camera was used.[16] Dissection of the gallbladder was performed using a combination of electrocautery and blunt dissection with fine graspers, and the cystic artery and cystic duct were ligated with titanium clips. The gallbladder was removed through either the umbilical or epigastric port. When perforation of the gallbladder occurred, attempts were made to retrieve all spilled stones, and the peritoneal cavity was irrigated with saline solution to evacuate the spilled bile. Patients typically received one preoperative and one postoperative dose of antibiotic, most commonly a cephalosporin. In patients with acute cholecystitis, especially when the bile culture was positive, broad-spectrum antibiotics were administered for a longer period depending on the clinical situation.

Statistical Analysis

Statistical comparisons of proportions were performed by means of either the chi-square test or Fisher's exact test, as appropriate. Continuous variables were compared by means of the Wilcoxon rank-sum test. P values <0.05 were considered statistically significant. Summary parameters within the text are expressed as mean ± standard deviation.

RESULTS

A total of 1059 patients underwent successful laparoscopic cholecystectomy between July 1990 and August 1993. Iatrogenic perforation of the gallbladder occurred in 306 patients (29%, with a 95% confidence interval ranging from 26% to 32%), of whom 191 (62%) had spillage of only bile detected, and 115 (38%) in whom spillage of both bile and gallstones was noted (Table I). There was a higher proportion of male patients in the perforated gallbladder group compared to the intact group (43% vs. 28%; $P < 0.001$). The mean age of the perforated gallbladder group was greater than that of the intact group (56 ± 15 years vs. 52 ± 16 years; $P < 0.001$), and patients in the perforated gallbladder group weighed more (81 ± 18 kg vs. 77 ± 17 kg; $P < 0.001$). A history of abdominal surgery was not associated with an increased incidence of intraoperative gallbladder perforation. Adhesions between the gallbladder and the omentum conferred a greater risk of gallbladder perforation (42% vs. 30%; $P < 0.001$). Although patients in the perforated group had a slightly higher incidence of acute cholecystitis compared to the intact group (11% vs. 8.5%), this difference was not statistically significant.

Iatrogenic perforation of the gallbladder was higher in the first year (1990) of our experience with laparoscopic cholecystectomy (40%), but the incidence decreased progressively each year thereafter to 24% in 1993. Perforation of the gallbladder occurred during dissection of the gallbladder from the liver in 47% of patients, during extraction through the abdominal wall in 21%, and as a result of intraoperative retraction in 14%. The operative time for patients in the perforated group was slightly longer (100 ± 38 minutes vs. 106 ± 38 minutes; $P < 0.01$) but of little clinical significance. Similar numbers of laparoscopic cholecystectomies were performed by surgical residents in both patient groups (26% vs. 24%; $P = 0.573$).

Postoperative Complications

There were no perioperative deaths and no bile duct injuries. Ten patients (1%) required reoperation for postoperative complications, including two patients in the intact group (0.3%) for closure of persistent cystic duct stump leaks, and eight in the perforated gallbladder group (3%), with three for drainage of intra-abdominal abscesses, two for decortication of empyema, two for repair of an iatrogenic cautery injury to the duodenum, and one for persistent postoperative hemorrhage.

No differences between groups were found in the incidence of postoperative wound infection, pulmonary complications, ileus, or bile leakage (Table II). Postoperative pyrexia occurred in 54 patients (18%) in the perforated gallbladder group and in 67 (9%) in the intact group ($P < 0.001$). There were no clinically significant differences in the preoperative white blood cell count, although the postoperative white blood cell count tended to be higher in the perforated gallbladder group (9800 ± 3200 vs. 9200 ± 3400; $P = 0.02$, a difference of no clinical relevance). Similarly there were no differences in the postoperative use of parenteral or oral analgesics administered to the two patient groups or in the need for an antiemetic. Mean hospital stay was longer in the perforated gallbladder group (2.1 ± 3.2 days vs. 1.6 ± 1.3 days; $P < 0.01$); however, there was no statistical difference in the mean time for each group to return to work (13.6 ± 10.7 days vs. 17.0 ± 31.8 days; $P = 0.3$). The majority of patients in both groups were satisfied with their operative procedures (92% vs. 96%; $P = 0.29$).

Among the 977 patients for whom long-term follow-up information was available, four (0.4%) developed intra-abdominal infections. All belonged to the perforated gallbladder group ($P = 0.001$). Two additional patients in the perforated gallbladder group, with no long-term follow-up, were identified as having developed intra-abdominal abscesses. One patient died of prostate cancer prior to the follow-up survey, and the other declined to complete the follow-up questionnaire. Of these six patients, four had spillage of both bile and gallstones and two had spillage of bile only. A perihepatic abscess occurred in three of the six patients, two of whom also had right-sided empyema. A subhepatic abscess developed in the other three patients.

Only one patient in whom an intra-abdominal ab-

Table I. Patient and operative characteristics

	Gallbladder status		
	Intact	Perforated	*P* value
Patients	753 (71%)	306 (29%)	
Bile only		191 (62%)	
Gallstones and bile		115 (38%)	
Sex			
Male	214 (28%)	132 (43%)	<0.001
Female	539 (72%)	174 (57%)	
Mean age (yr)	52 ± 16	56 ± 15	<0.001
Mean weight (kg)	77 ± 17	81 ± 18	<0.001
Acute cholecystitis	64 (8.5%)	35 (11%)	NS
Omental adhesions	226 (30%)	127 (42%)	<0.001
Mean surgical time (min)	100 ± 38	106 ± 38	0.008
Operation performed by surgical trainee	182 (24%)	79 (26%)	NS

Table II. Complications: Intact vs. perforated gallbladder (long-term follow-up)

Complication	Intact (%)	Perforated (%)	*P* value
Intra-abdominal infection	0 (0)	4 (1.4)	0.001
Ileus	9 (1.3)	4 (1.4)	NS
Pulmonary infection	1 (0.1)	2 (0.7)	NS
Bile leakage	2 (0.3)	1 (0.4)	NS
Hemorrhage	2 (0.3)	2 (0.7)	NS
Wound infection	17 (2.4)	3 (1.1)	NS
Residual gallstone symptoms	72 (10.9)	30 (11.1)	NS

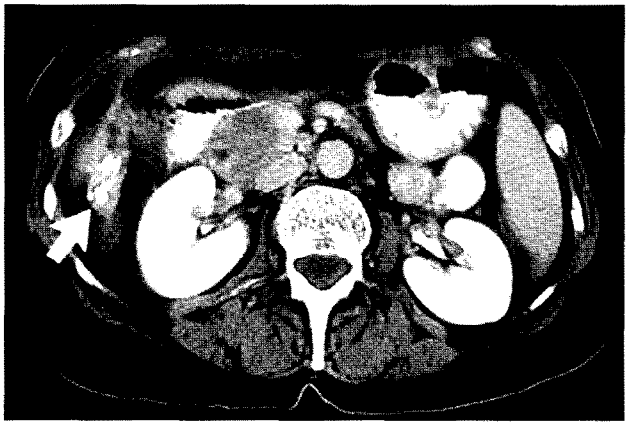
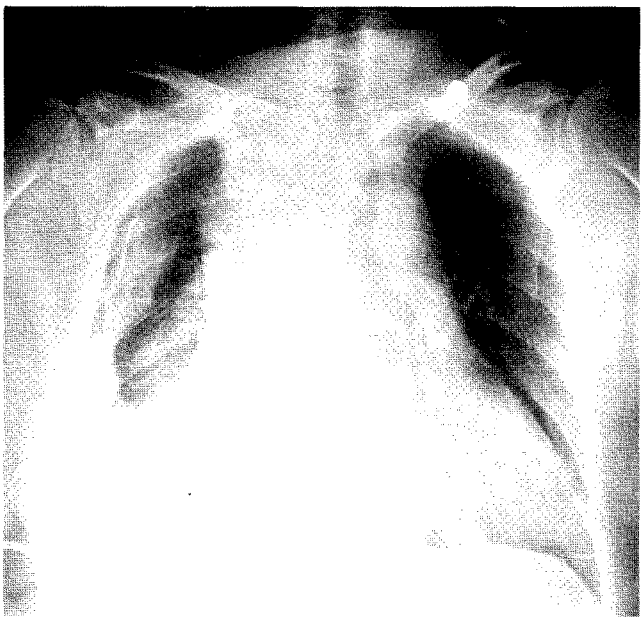


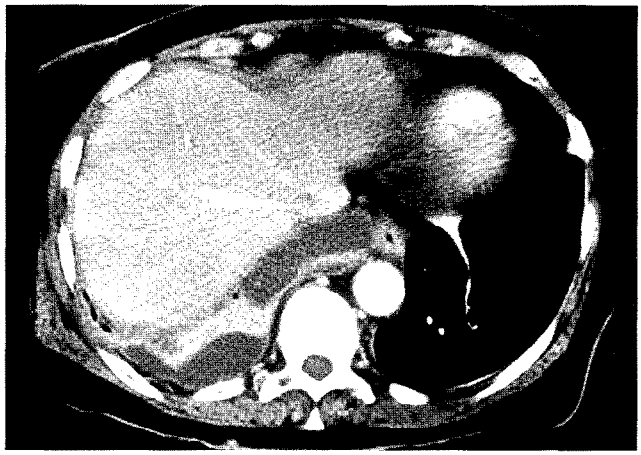
Fig 1. CT scan demonstrating intraperitoneal gallstones (arrow) with surrounding inflammatory reaction and fluid collection.

scess developed was known to have residual gallstones remaining at the completion of the procedure. These were not removed because of their inaccessibility laparoscopically. Signs of intra-abdominal infection occurred within 10 days of laparoscopic cholecystectomy in four patients; however, one patient presented with infection 28 days after the operation and another patient after 34 months.

Four patients had their intra-abdominal abscesses drained percutaneously under CT guidance, but three of them subsequently required operative intervention (Table III). In one patient symptoms resolved after CT drainage, but persistent right upper quadrant pain developed 6 months later and the patient underwent laparotomy. A small chronic subhepatic abscess was found, which contained three large, mixed stones (Fig. 1), and the symptoms resolved thereafter.

A





B

Fig. 2. A, Right-sided empyema secondary to perihepatic abscess resulting from retained gallstones. Thoracocentesis was performed, followed by right thoracotomy and decortication. **B,** CT scan of patient in *A*, showing subhepatic abscess, which required surgical drainage.

Table III. Major infective complications secondary to spilled bile and gallstones

Patient	Spillage	Site of infection	Percutaneous CT drainage	Operative intervention
1	Bile	Perihepatic	Successful	None
2	Bile	Perihepatic, right chest	Unsuccessful	Right thoracotomy and decortication of empyema, drainage of perihepatic abscess
3	Bile + gallstones	Subhepatic	Not attempted	Laparotomy, removal of intraperitoneal gallstones; postoperative pulmonary embolus
4	Bile + gallstones	Subhepatic	Unsuccessful	Laparotomy, drainage of abscess
5	Bile + gallstones	Subhepatic	Unsuccessful	Laparotomy, drainage of abscess
6	Bile + gallstones	Perihepatic, right chest	Not attempted	Right thoracotomy and decortication of empyema, removal of gallstones and drainage of perihepatic abscess

Laparotomy was performed in two other patients for drainage of an intra-abdominal abscess. Two patients required a transthoracic decortication for empyema secondary to perihepatic abscess formation (Fig. 2).

DISCUSSION

Since it was first reported in 1989, laparoscopic cholecystectomy has rapidly become the standard treatment for symptomatic cholelithiasis.[17] The procedure, however, is not without complications, most notably a higher incidence of biliary tract injuries compared to open cholecystectomy.[18-21] Nevertheless, 5 years of clinical experience and numerous prospective[22-25] and retrospective[26-28] trials have established laparoscopic cholecystectomy to be a safe procedure with a low incidence of major complications. Although a large number of studies have examined clinical outcomes of laparoscopic cholecystectomy, few have directly addressed the consequences of spillage of bile and gallstones within the peritoneal cavity, an event that occurs more frequently with laparoscopic than with open cholecystectomy.[1,2] There are case reports of gallstones lost at the time of surgery subsequently causing intra-abdominal abscesses,[7-10] empyema,[9] abdominal wall abscesses,[1,11,12] cutaneous sinus tracts,[13,14] and bladder fistulas.[15] Although these complications appear to be rare, their actual incidences are unknown.

Of 1059 patients who underwent laparoscopic cholecystectomy, 306 (29%) had spillage of bile alone or spillage of bile and gallstones into the peritoneal cavity. This incidence is similar to the 32% incidence of gallbladder perforation reported by Jones et al.[29] but is considerably greater than the perforation rate described in a Canadian multicenter study (9%).[30] Variables associated with greater risk of intraoperative gallbladder perforation were male sex, increasing age, and weight. Similar associations were noted by Jones et al. It is likely that a combination of factors makes the operation more technically challenging in heavier male patients, including the presence of increased abdominal wall adipose tissue, increased liver mass and friability (often fatty infiltration), which puts greater tension on the gallbladder during cephalad retraction, and a greater amount of fat around the cystic duct. In our study the most common timing of iatrogenic gallbladder perforation was during dissection of the gallbladder from the liver. All but 11 of our 1059 cholecystectomies were performed using electrocautery. Because only a few patients had the operation performed with laser dissection, we cannot draw any conclusions about the relative risk of perforation by other methods of dissection. The second most common time of iatrogenic gallbladder perforation was during removal of the gallbladder through the abdominal wall. To prevent bile and gallstone spillage when a large gallstone burden prevents ready extraction of the gallbladder through one of the ports, the gallbladder can be placed in a specimen bag before crushing or extracting stones with a stone forceps, or the fascial incision at the port site can be enlarged. These steps should minimize the incidence of gallbladder perforation and its subsequent infective complications.

It is noteworthy that the incidence of acute cholecystitis was similar in the intact and nonintact patient groups, a finding also reported by others.[2] Although an acutely inflamed gallbladder might be more friable superficially, the edematous and thickened gallbladder wall may also protect against inadvertent perforation during the different aspects of the operative procedure. In our early experience there was a low threshold for conversion to open cholecystectomy when the gallbladder was severely inflamed, which likely contributes to the low incidence of gallbladder perforation in these patients. As might be expected, there was a higher incidence of gallbladder perforation during the first year that laparoscopic cholecystectomy was performed at our institution; thereafter, however, the iatrogenic perforation rate stabilized at approximately 25%.

Despite the frequency of intraoperative perforation of the gallbladder, spillage of bile or gallstones did not lead to serious adverse sequelae in most patients. Surprisingly the incidence of wound infection was similar for both patients with an intact and perforated gallbladder. Even when spillage into the port site was analyzed separately, no significant correlation with subsequent wound problems was noted. Overall only six patients in the group with a perforated gallbladder had intra-abdominal abscesses; in two patients an empyema developed and required decortication. Empyema presumably developed from spilled gallstones that caused perihepatic abscess formation with subsequent erosion through the diaphragm into the right pleural cavity. This complication has been reported previously.[9] Although percutaneous CT-guided drainage was attempted in four patients, three still required surgical intervention because of inadequate drainage, probably because of the inability to remove the inciting gallstones.

Intraperitoneal gallstones plus bile have been shown to cause a predisposion to abscess formation in animal studies,[6] whereas sterile gallstones incite only a mild inflammatory reaction.[5] In our study, four of six patients who developed intra-abdominal abscesses had known spillage of both bile and gallstones. Brown pigmented stones theoretically may be more problematic when left within the abdomen because of their frequent association with bacterobilia.[31] Bile culture or stone analysis was not routinely performed; therefore no conclusions

can be drawn regarding the effects of spillage of infected bile or the type of gallstones spilled.

CONCLUSION

The overall risk of serious complications after intraoperative spillage of gallbladder contents during laparoscopic cholecystectomy is low. Intra-abdominal abscess formation after laparoscopic cholecystectomy occurred only in patients in whom bile and/or gallstones were spilled (1.4%). No intra-abdominal abscesses occurred in the 753 patients in whom gallbladder was removed intact. It therefore seems prudent to irrigate the peritoneal cavity with a large (>1 liter) quantity of saline solution if iatrogenic perforation of the gallbladder with spillage of bile or gallstones occurs. Whether topical antibiotics are important is unknown. If gallstones are knowingly spilled within the abdominal cavity, every attempt should be made to remove all gallstones. Because infective complications are rare following gallbladder perforation, conversion to laparotomy is not routinely indicated. However, conversion to an open procedure should be considered in patients in whom it is not possible to retrieve the majority of the gallstones laparoscopically, especially when bacterobilia is suspected or confirmed by Gram stain of the bile. Furthermore, if intra-abdominal abscess formation occurs, percutaneous drainage is likely to be ineffective unless the inciting gallstones can be removed.

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Discussion

Dr. L.W. Traverso (Seattle, Wash.). Since these data were not obtained prospectively, do you believe that the incidence of bile leakage is higher? Do you believe that the incidence of lost gallstones may also be higher? The incidence of bile leakage from the gallbladder at your institution was 29%, and you showed six patients in this group to have intra-abdominal abscesses giving an incidence for all patients of approximately 1.5% to 2%.

If you consider only the group that had bile leakage, or gallstone spillage, the incidence would be about 2%. If you just look at the subgroup in which gallstones were known to have contaminated the peritoneal cavity, the incidence of intra-abdominal abscess is approaching 4%.

Based on these data, I think you would have to inform your patients that there is an 11% chance that the gallbladder could be perforated and that stones could spill into the abdomen. Should this occur, the risk of intra-abdominal infection would be almost 4%. Have you examined the subgroup of patients for risk factors in this group that had only stone spillage? Were these stones spilled during retraction, during removal of the gallbladder from the abdomen, or during removal of the gallbladder from the gallbladder bed?

Dr. D.C. Rice. The clinical, therapeutic, and diagnostic follow-up data were collected in a prospective fashion in that the data base was prospectively generated in those patients who had spillage of gallbladder contents. We then went back and reviewed those patients' charts for further details of the intraoperative events such as the timing of gallbladder perforation. The overall perforation rate would remain 29%.

As was seen from the slides, bile spillage alone accounted for only two cases of intra-abdominal abscess. It is always difficult to know whether or not there may have been some small stones, or perhaps sludge that was not noted at the time of surgery, that could have accounted for a higher incidence or could have predisposed to abscess in those patients. I agree that gallstone spillage is significantly more likely to lead to abscess formation.

Dr. L. Way. (San Francisco, Calif.). Can you define the terms more precisely? What do you mean by spillage of bile? Do a few drops of bile suffice, or is there a specific threshold amount? In a retrospective study, can you obtain reliable information on the amount of bile and the number of stones, and can you get a sense of just how vigorous an effort was made to "tidy up" the peritoneal cavity?

Dr. Rice. It is difficult to quantify the amount of bile spillage. If the surgeon noted that there was light spillage of bile during cholangiography, we did not regard that as bile spillage. Only in cases where there was noted laceration or perforation of the gallbladder did we look on that as significant bile spillage.

Dr. N. Soper (St. Louis, Mo.). We too have examined our incidence of gallbladder perforation during laparoscopic cholecystectomy and it is remarkably similar at 30%. In our experience perforation did not lead to any untoward complications postoperatively, except for the fact that the operations took about 10 minutes longer because of the extra time needed to "clean up" the operative field. There was no increased incidence of abscess or other infectious complications. Do you proceed any differently once a perforation occurs? Do you culture the bile or administer a longer course of antibiotics? If in fact there was pus or an empyema of the gallbladder and you perforated it, would you recommend doing anything different at that time?

You stated that 10 patients were converted to open cholecystectomy because of perforation, yet your recommendation is that conversion is not required. What would cause you to convert to an open procedure at the time of surgery if a perforation of the gallbladder were to occur?

The other difference was that in the patients who suffered a perforation intraoperatively, the postoperative length of stay was longer than in those who did not, and I wonder why that was. Did it have to do with the patients who needed reoperation early on?

Would you make any other recommendations as to what should be done in the event of a perforation, such as placing the gallbladder in a bag? Do you think that because the initial incision is larger with an open entry there is less likelihood that the gallbladder will be perforated?

Dr. Rice. There was no difference in the amount of antibiotics given to patients who had perforation of the gallbladder and those who did not. Most patients did not develop intra-abdominal abscesses. Of those who did, four of the six presented within 10 days of surgery. They received a longer course of antibiotics.

The reason for the longer hospital stay could perhaps be attributed to the irritative effect of spillage of bile in the peritoneal cavity, which causes greater pain. Although when we analyzed narcotic pain medication used, comparing patients who suffered perforation with those who did not, we did not identify any difference. I am not quite sure why those patients stayed longer in the hospital.

Regarding prophylaxis in the case of a perforation, I think that sealing the perforation either with clips or with an Endoloop is something that should be done. Also, if the gallbladder is distended, prophylactic decompression can sometimes make it easier to manage.

If a large stone burden makes it difficult to remove the gallbladder through the fascial incision, we enlarge the fascial incision or use a stone crusher to try and break up the stones. Also, a laparoscopic specimen bag might be used if the gallbladder has been perforated.