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ORIGINAL ARTICLE

Can the timing of laparoscopic cholecystectomy after biliary pancreatitis change the conversion rate to open surgery?

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Summary *Background:* Biliary pancreatitis (BP) constitutes 30–55% of all cases of acute pancreatitis. Laparoscopic cholecystectomy (LC) has become the gold standard for the surgical treatment of gallbladder disease. We aimed to compare and evaluate the relation between the timing of LC and the rates and reasons of conversion to open surgery (OS) after BP.
Methods: Data were collected of patients who presented for the first time with acute BP and underwent LC. The patients were divided into two groups: early cholecystectomy (Group 1), patients who underwent cholecystectomy during the first pancreatitis attack upon admission and before discharge from hospital (1–3 days); and late cholecystectomy (Group 2), patients who received medical treatment during their first pancreatitis episode and underwent surgery after 4–10 weeks. Sex, Ranson scores, American Society of Anesthesiology scores, and conversion reasons were compared.
Results: Group 1 and Group 2 included 75 patients (20 men, 55 women) and 87 patients (25 men, 62 women), respectively. The mean age was 44.7 years (range, 21–82 years). Obscure anatomy with adhesions was detected in 16 patients (5 in Group 1, 11 in Group 2) as the leading cause of conversion to OS, but it was not statistically significant ($p = 0.054$). Acute inflammation with empyema and peripancreatic liquid collection was observed in 14 patients (12 in Group 1, 2 in Group 2), and conversion to OS was statistically significantly higher in Group 1 ($p = 0.016$).
Conclusion: Timing of LC does not influence the conversion rates to OS after BP.

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1. Introduction

Acute pancreatitis is the third most common gastrointestinal cause of acute hospital admission, with a mortality rate of 5%.[1,2] Biliary pancreatitis (BP) is caused by gallstones or sludge and constitutes approximately 30—55% of all cases.[3,4] The incidence of BP is increasing worldwide, possibly due to an increased risk of gallstone disease associated with nutritional and lifestyle change, and obesity.[5] The initial treatment of BP may either be medical or surgical. Recurrence is reported to range from 29% to 63% in patients with BP. Besides recurrence, gall stone-related complications in untreated BP such as acute pancreatitis, cholecystitis, cholangitis, or gallstone colics can also be seen. As such, surgery is highly recommended.[4,6—8] Over the past 2 decades, laparoscopic cholecystectomy (LC) has become the gold standard for the surgical treatment of gallbladder disease.[9]

The optimal time for performing cholecystectomy in acute BP is controversial. Nowadays, guidelines recommend performing early cholecystectomy (EC) after mild BP and advise delaying cholecystectomy (DC) until all signs of inflammation have resolved in severe pancreatitis. However, most surgeons may prefer DC several weeks after hospital discharge in routine practice due to the potential of high complications and mortality rates after EC.[10—12] Furthermore, there remains a strong potential for conversion to open surgery (OS) related with anatomic distortions of the perihepatic area due to acute inflammation. In this study, we aimed to compare and evaluate the relation between the timing of LC and the rates and reasons for conversion to OS after BP. In this respect, it is different from other studies in the literature.

2. Materials and methods

In this retrospective study, the data of patients with acute BP who presented for the first time to the Department of General Surgery at Goztepe Education and Research Hospital (Istanbul, Turkey) were collected during the period of January 2004 to December 2014. Among them, patients who were planned for LC were included. The study was approved by the ethics committee and written informed consent was obtained from each patient. The following parameters were evaluated: age, sex, current illness, medical history, vital signs, laboratory results, Ranson score (RS), American Society of Anesthesiology (ASA) score, and reasons for conversion from laparoscopy to laparotomy.

The diagnosis of acute BP was based on acute abdominal pain, tenderness, amylase, and lipase levels increased by up to three times the normal limit, and detection of gallstones on ultrasonography. Presentation of increased gallbladder wall thickness or presence of pericholecystic fluid in the investigations were accepted as concomitant acute cholecystitis. Severity of acute pancreatitis was assessed using the RS at the first hospitalization in both groups. The patients with RS $\leq$ 3 were named as mild and RS $>$ 3 (max 6) as moderate pancreatitis.

Patients were divided into two groups in accordance with resident surgeon's choice according to the time elapsed from the episode of acute BP to the operation. Group 1 included patients who underwent EC during the first pancreatitis attack upon admission and before discharge from the hospital (within 1—3 days). The RS is not adequate to estimate the severity of pancreatitis alone. Therefore, the surgical indication was approved in this group when clinical and laboratory improvements of abdominal pain, nausea, vomiting, decreasing course of aspartate transaminase, alanine transaminase, leukocyte, and amylase levels were observed. Group 2 included the patients who received medical treatment during their first pancreatitis episode and had an elective DC later with an interval between 4—10 weeks. All operations were performed by a total of 14 resident surgeons. Both groups were compared according to sex, RS, ASA, and conversion reasons. Patients in both groups who underwent conversion were also compared in terms of sex, RS, ASA, and conversion reasons.

Patients with jaundice, severe BP (RS $>$ 6), previous malignancy, any abdominal surgery history, concomitant choledocholithiasis and endoscopic sphincterotomy (ES), previous acute cholecystitis and pancreatitis attacks, and patients who were taking anticoagulant medications or had acalculous cholecystitis were excluded from the study. Unclear obscure anatomy, acute inflammation with empyema, common bile duct injury, friable edematous tissue around Calot's triangle, uncontrolled bleeding, spillage of gallstones, bowel injury, technical problems, and duodenal injury are reported causes for conversion to OS. The decision for either LC/OS or conversion during surgery was approved by the resident surgeon. The experience of the surgeons ranged between 2 years and 14 years.

Preoperatively, first-generation cephalosporin was administered intravenously within 1 hour of the incision time in all patients. The same open and laparoscopic surgical techniques were used in all operations, subcostal incision in open surgery, and a four-trocar (2×5 mm, 2×10 mm) technique in laparoscopic surgery with insufflation of the abdominal cavity at 12—15 mmHg. Following discharge, patient follow-up was conducted in the outpatient clinic or by the referring surgeon.

2.1. Statistical analysis

Number Cruncher Statistical System (2007; NCSS, Kaysville, Utah, USA) software was used for statistical analysis. Descriptive statistical methods (mean, standard deviation, frequency) as well as the Fisher—Freeman—Halton test, Fisher exact test, and Yates continuity correction test were used for the comparison of qualitative data between groups. Results were evaluated at a significance set at $p < 0.01$ and $p < 0.05$.

3. Results

In total, 162 patients (45 men, 117 women) were included in the study. The mean age was 44.7 years (range, 21—82 years). Group 1 included 75 patients (20 men, 55 women), and Group 2 included 87 patients (25 men, 62 women), respectively. The mean waiting time for surgery was 42 hours (range, 24—72 hours) in Group 1, and 6.4 weeks (range, 4—10 weeks) in Group 2. In terms of RS, 65 (86.7 %)

patients were RS < 3 in and 7 (13.3 %) patients were RS > 3 Group 1, and 72 (83.8%) patients were RS < 3 and 15 (16.2 %) patients were RS > 3 in Group 2.

In terms of ASA, 16 (21.3%) patients were ASA 1, 38 (50.7%) were ASA 2, 20 (26.7%) were ASA 3, and one (1.3%) patient was ASA 4 in Group 1. In Group 2, 18 (20.7%) patients were ASA 1, 42 (48.3%) were ASA 2, 26 (29.9%) were ASA 3, and one (1.1%) was ASA 4.

The requirement for conversion from laparoscopy to laparotomy in Groups 1 and 2 were as follows: 18 men and 12 women, RS < 3 ($n = 25$) and RS > 3 ($n = 5$); and 18 men and seven women, RS < 3 ($n = 10$) and RS > 3 ($n = 15$), respectively. In terms of ASA, 10 patients were ASA 1, six were ASA 2, 13 were ASA 3, and one patient was ASA 4 in Group 1. In Group 2, three patients were ASA 1, 10 were ASA 2, 11 were ASA 3, and one patient was ASA 4 (Table 1).

The reasons for the requirement of conversion from laparoscopy to laparotomy were analyzed. Unclear obscure anatomy with adhesions between omentum, gall bladder, peritoneum and surrounding tissues around Calot's triangle was found in five patients in Group 1, and 11 in Group 2. Acute inflammation with empyema was detected in 12 patients in Group 1 and two in Group 2. Common bile duct injury occurred in one patient in both groups. Friable edematous tissue around Calot's triangle was observed in six patients in Group 1 and three in Group 2. Uncontrolled excessive bleeding was seen in three patients in Group 1 and six in Group 2. Spillage of gallstones occurred in only one patient in Group 1. Bowel injury occurred in one patient in both groups. Technical problems (insuflator problems) occurred with one patient in Group 2 and duodenal injury occurred in one patient in Group 1 (Table 2).

There was no statistically significance between the sexes, RS, and ASA, and the timing of early and late-onset laparoscopy. In addition, the sex, RS, and ASA were not statistically significant in terms of conversion requirements of early and late-onset laparoscopy.

Among the reasons of conversion to OS, unclear obscure anatomy with adhesions was reported in 16 patients [Group 1 ($n = 5$), Group 2 ($n = 11$)]. The difference was large but not statistically significant ($p = 0.054$; $p > 0.05$). Acute inflammation with empyema and peripancreatic liquid collection was observed in 14 patients [Group 1 ($n = 12$), Group 2 ($n = 2$)] and conversion to OS was statistically significantly higher in Group 1 ($p = 0.016$). There was no mortality in our patients.

Postoperative complications were observed totally on seven converted patients; three seroma (two in the early and one in the delayed group), two hematoma (one in the

Table 2 Reasons for requirement of conversion from laparoscopy to laparotomy on early and delayed cholecystectomy groups.

	Total	Group 1	Group 2	p
	n (%)	n (%)	n (%)	
Unclear obscure anatomy[a]	16 (29.1)	5 (16.7)	11 (44)	0.054[b]
Acute inflammation with empyema	14 (25.5)	12 (40)	2 (8)	0.016[b,*]
Common bile duct injury	2 (3.6)	1 (3.3)	1 (4)	0.999[c]
Friable edematous tissue around Calot's triangle	9 (16.4)	6 (20)	3 (12)	0.487[c]
Uncontrolled bleeding	9 (16.4)	3 (10)	6 (24)	0.273[c]
Spillage of gallstones	1 (1.8)	1 (3.3)	0 (0)	0.999[c]
Bowel injury	2 (3.6)	1 (3.3)	1 (4)	0.999[c]
Technical problem[d]	1 (1.8)	0 (0)	1 (4)	0.455[c]
Duodenal injury	1 (1.8)	1 (3.3)	0 (0)	0.999[c]
Total	55	30	25	

[a] Adhesions between omentum, gall bladder, peritoneum, and surrounding tissues around Calot's triangle.
[b] Yates continuity correction test.
[c] Fisher exact test.
[d] Insuflator stopped working.
* $p < 0.05$.

Table 1 Patient's characteristics for each group and the number of converted patients to open surgery.

		Group 1	Group 2	p	Converted patients		p
					Group 1	Group 2	
		n=75 (%)	n=87 (%)		n=30 (%)	n=25 (%)	
Sex	Female	55 (73.3)	62 (71.3)	0.907[a]	12 (40)	7 (28)	0.518[a]
	Male	20 (26.7)	25 (28.7)		18 (60)	18 (72)	
RS	≤3	68 (90.7)	72 (83.8)	0.256[a]	25 (83.3)	10 (40)	0.002[a,*]
	>3	7 (9.3)	15 (16.2)		5 (16.7)	15 (60)	
ASA	1	16 (21.3)	18 (20.7)	0.957[b]	10 (33.3)	3 (12)	0.715[b]
	2	38 (50.7)	42 (48.3)		6 (20)	10 (40)	
	3	20 (26.7)	26 (29.9)		13 (43.3)	11 (44)	
	4	1 (1.3)	1 (1.1)		1 (3.3)	1 (4)	

Group 1: early cholecystectomy, Group 2: late cholecystectomy.
ASA = American Society of Anesthesiology score; RS = Ranson score.
[a] Yates continuity correction test.
[b] Fisher–Freeman–Halton test.
* $p < 0.01$.

early and one in the delayed group), and two surgical site infection (in the early group). Common bile duct, bowel and duodenal injuries that was caused on LC were improved without further complications.

4. Discussion

LC has been proposed for the treatment of mild and moderate acute BP, although conservative medical treatment modalities have priority.[7] The timing of cholecystectomy has already been mentioned with regards the guidelines, and there is consensus among surgeons that patients with gallstone pancreatitis should undergo cholecystectomy to prevent recurrence. However, the precise timing of cholecystectomy is not exactly clear. After mild BP, EC is recommended by most guidelines.[8,10,11] Also, DC is recommended in severe pancreatitis because of high complication and mortality rates of EC.[8,12] Nevertheless, there is no exact definition of *early*. Many studies have shown that LC is usually performed for mild BP around 6 weeks after discharge from hospital due to the fear of perioperative risks.[4,13–17] The British Society of Gastroenterology recommend LC within 2 weeks of discharge, whereas the International Association of Pancreatology and American Gastroenterological Association recommend that all patients with mild BP should undergo LC as soon as the patient has recovered from the attack.[7,8,11] In our study, we standardized Groups 1 and 2 as patients who underwent surgery within the first 72 hours of an acute attack, and those with an interval of 4–10 weeks of the pancreatitis attack, respectively.

DC after mild BP may result in readmission with recurrent biliary events, especially recurrent BP.[7,8] If gallstones are left untreated, the recurrence rate of BP is reported as 32–61%.[18] Therefore, EC during the first admission appears safe and recommended.[7,8] In a systematic review of nine studies including 998 patients, 18% of patients were readmitted because of recurrent biliary events. The median readmission time was 6 weeks after the first presentation for mild BP.[19] According to some guidelines, cholecystectomy should be delayed in case of peripancreatic collections until they either resolve or persist beyond 6 weeks. Cholecystectomy can be performed safely after that time.[4,8,11] In a study of 151 patients, Nealon et al[12] reported that an increased incidence of infected collections was found in patients who underwent EC after severe pancreatitis. In our study, acute inflammation with empyema was the cause of conversion in 14 (25.5%) patients.

There remains a high potential for conversion to OS. The rates of conversion in all LC surgeries has been reported in the literature, ranging from 0% to 27.7%.[9,20,21] Patient-related risks including male sex, older age, acute cholecystitis, and previous upper abdominal surgery are referred to in the literature as the predisposing factors of conversion, as well as the surgeon's experience.[22] Conversion rates are reported as 20–30% in cases of acute cholecystitis due to inflammatory change.[11,15,20,23] Acute BP *per se* is also a significant conversion factor. In a study by Shamiyeh et al,[24] 4505 patients who underwent LC were evaluated and 245 (5.4%) were converted to OS. In 178 (73%) of these patients, the reason for conversion was acute cholecystitis.[24] Ghnman et al[25] studied 240 patients in another report; 17 (5%) patients were converted to OC, and acute cholecystitis was the reason for conversion in 10 (58.8%) of these patients. In our study, we found a conversion rate of 33.9% (55 of 162). The ratio in our study was slightly higher than in the literature. When we analyzed early and delayed cholecystectomy groups according to RS, we observed that five of seven RS $>$ 3 patients in Group 1, and all 15 RS $>$ 3 patients in Group 2 were converted to OS. This was the main reason of the high conversion rate. Although statistically insignificant in RS $>$ 3 patients, cholecystectomy should be evaluated in a much more careful manner because of high conversion rates. We also suggest through these findings that EC or DC should be performed by experienced surgeons in patients who are RS $>$ 3 to avoid further morbidities. It is known that corrupted biliary tract anatomy by pericholecystic and peripancreatic inflammation makes dissection harder in BP.[26] This may also have been the cause of the high conversion rate in our study. Nevertheless, there was no statistically significant difference between the two groups with regards complications.

In most studies, male sex was found a to be significant factor for conversion to OC.[24,25,27] This association may be due to the increased severity of gallstone disease in men.[28] Sex of the patient, RS, and ASA were not found to be statistically significant in either Group 1 or Group 2 in the present study. These three parameters were also found not statistically significant in cases of conversion in the comparison of the groups (Table 1). In the literature, we could not found any reports about cholecystectomy in moderate BP (RS $>$ 3), whereas, according to our study, nonstatistically significant results were observed and we suggest that cholecystectomy can also be performed in the moderate group. There are some reports presented that high percentage of patients with mild BP underwent ES. Although some reports propose that EC is not necessary after ES in mild BP, a recent meta-analysis suggested that cholecystectomy should be performed even after ES to reduce complications and recurrent biliary events related with pancreatitis.[26,29] We excluded patients who underwent ES in this study.

Uncontrolled bleeding of cystic artery and friable gall bladder bed due to inflammation and recurrent attacks, bile duct injuries, spillage of gall stones and/or bile leakage due to perforated gall bladder, cholecystoduodenal fistula, adhesions due to previous operations and/or severe inflammation, suspicion of malignancy, and visceral injury of duodenum or colon, are all among the different reasons for conversion to OS in LC.[9,30] Previous cholecystitis or BP history are also other important reasons for conversion. The anatomy of Calot's triangle will change and laparoscopy becomes difficult to perform safely.[20,22] Previous abdominal surgery is not a contraindication for a safe LC. However, it is associated with an increased need for adhesiolysis and a higher conversion rate.[31] We excluded these patients in our study. The experience of the surgeon is also an important factor that enables the course of surgery in a good manner. All operations were performed by experienced surgeons in our study.

The main reason for conversion in our series was unclear obscure anatomy caused by dense and extensive adhesions. It creates unclear vision in Calot's triangle, which makes it

difficult to proceed with the dissection. A total of 16 patients [Group 1 ($n = 5$), Group 2 ($n = 11$)] were converted to OS for this reason. The rate of unclear anatomy due to dense and extensive adhesions was surprisingly higher in Group 2. However, this was not found to be statistically significant ($p > 0.05$). Guidelines recommend that it is enough to wait 6 week for delayed cholecystectomy. However, we observed in our study that conversion rates were high in patients with RS > 3 BP both in the EC and DC group, despite waiting for 6 weeks. Therefore, DC can be delayed for more than 6 weeks. In addition, conversion rates probably will decrease with more experienced surgeons in both RS > 3 EC and RS > 3 DC. Further studies are required to clarify these issues.

Other underlying causes of conversion were acute inflammation with empyema, common bile duct injury, friable edematous tissue around the Calot's triangle, uncontrolled bleeding, spillage of gallstones, bowel injury, technical problems with insuflator, and duodenal injury, respectively. Among these only acute inflammation with empyema was found to be statistically significantly higher ($p = 0.016$) in Group 1. In total, 14 patients [Group 1 ($n = 12$), Group 2 ($n = 2$)] were converted to OS due to acute inflammation and empyema. There was no significant relation between other conversion reasons and groups. We could not find any studies in the literature comparing the timing of LC and conversion rates and reasons after BP.

5. Conclusion

Cholecystectomy can be safely performed after the resolution of an acute attack in mild and moderate pancreatitis. The timing of LC has no significant influence on conversion rates to OS after BP. EC in BP could also remove the need of prior ES and will prevent patients from possible recurrent attacks and complications. However, we suggest that cholecystectomy should be performed by experienced surgeons in patients with RS > 3 moderate BP because of the high conversion rates in this group.

Conflicts of interest

All authors have no conflicts of interest to declare.

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