Original Article

Timing of Laparoscopic Cholecystectomy in Acute Cholecystitis

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Abstract

Background: Timing of laparoscopic cholecystectomy (LC) in acute cholecystitis (AC) is still debated. **Aims:** The aim of this study was to investigate the effect of timing on operative results; from the first appearance of symptoms to the operation. **Methods:** The study included 57 sequential patients operated laparoscopically for AC. Patients operated within the first 3 days of admission (Group 1), those operated between 4th and 7th days (Group 2) and those operated after 7th day (Group 3) were evaluated and compared with respect to demographics, time from admission to operation, duration of operation, adhesion score, complications, conversion rates, duration of hospital stay, morbidity and mortality rates, bile culture results, and histopathological evaluation. **Results:** A total of 63% of the patients were female and 21 (37%) were male. The mean age was 48 years (range, 21–74). There was no significant difference among the groups with respect to demographics ($P > 0.05$, for each). The duration of operation was significantly shorter in Group 1 than both Groups 2 and 3 ($P < 0.05$ and $P < 0.001$, respectively). Duration of operation was also significantly shorter in Group 2 than Group 3 ($P < 0.001$). Group 1 had significantly fewer adhesions compared to Group 2 and Group 3 ($P < 0.05$ and $P < 0.001$, respectively), and no significant difference was found between Group 2 and Group 3 ($P > 0.05$). Duration of hospital stay was significantly shorter in Group 1 compared to Group 2 and Group 3 ($P < 0.001$) and also was significantly shorter in Group 2 than Group 3 ($P < 0.05$). Group 1 had significantly lower rate of culture proliferation than Group 3 ($P < 0.001$), whereas no significant differences were evident in other inter-group analyses ($P > 0.05$, for each). **Conclusion:** LC can safely be performed within 7 days of admission in cases of AC.

Keywords: *Acute cholecystitis, cholecystectomy, conversion, laparoscopy, timing of surgery*

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Introduction

Cholelithiasis constitute a significant health problem in developing or developed societies, affecting 10% to 15% of the adult population.[1] A total of 15–26% of these patients present to emergency department with acute cholecystitis (AC).[2] Laparoscopic cholecystectomy (LC) is considered gold standard in the treatment of symptomatic gallstone disease.[3,4] However, LC and its timing in AC is still a controversial issue. Although some centers have reported that early laparoscopic surgery is a safe procedure, some others have recommended an interval LC approach.[5,6] In the latter approach, 15% of cases still require an inevitable urgent surgical intervention during the interval period, whereas another 25% are hospitalized for recurrent attacks.[7]

Early cholecystectomy (EC) is defined as an operation performed within 72 hours of admission, whereas intermediate cholecystectomy (IC) as an operation performed between 4th and 7th days. Late

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cholecystectomy (LC) is performed after the 7th day. On the contrary, interval cholecystectomy (INT-C), on the other hand, is defined as cholecystectomy performed 6-8 weeks after symptomatic medical treatment.[8]

The aim of the present study was to investigate the effects of time duration, from the first appearance of symptoms to the surgery, in patients diagnosed with AC.

Materials and Methods

Patients who diagnosed with AC were prospectively enrolled between January 2007 and October 2009. Exclusion criteria were as follows: ASA (American Society of Anaesthesiologists) score > IV patients, signs of diffuse peritonitis, denial of surgical therapy and pregnancy. AC was diagnosed by clinical, laboratory, and radiological data. Clinical criteria were as follows: pain in the right upper quadrant, local tenderness, and axillary body temperature above 37.5°C. Laboratory criteria were defined as a white blood cell count above 10.000 K/UL or an increased C-reactive protein (CRP) level above 5 mg/L. Radiological criteria were gallbladder distention, an increase in wall thickness, pericholecystic fluid, and a positive ultrasonographic Murphy's sign. The patients were divided into three groups with respect to time from symptom onset to operation. Group 1 was formed by patients operated within 3 days after the first appearance of symptoms; Group 2 patients were operated between 4th and 7th days after the symptom-onset; and Group 3 patients were patients who were not taken to operation room until the 7th day. In the laparoscopic technique, the abdominal cavity was entered from the umbilicus with open technique using Hasson trocar. Gallbladder was decompressed with needle and a sample was taken for culture antibiogram. The duration of operation was defined as time from skin incision to skin closure. The gallbladders perforated during operation were externalized by means of an endoscopic bag and the intact ones were removed directly through the umbilical port. Fasciae at umbilical and epigastric trocar entry points were closed at the end of the procedure. Duration of hospital stay was determined as the time from the operation to discharge.

Operative findings were recorded and an adhesion scoring was performed as described by Noir *et al*.[9] [Table 1]. Sakuramoto classification[10] was used to evaluate histopathological results [Table 2].

Patients in each group were compared with respect to demographics, time from admission to operation, indications, duration of operation, adhesion score, gallbladder perforation, bleeding, bile duct injury, conversion rates, duration of hospital stay, morbidity (bile fistula, intraabdominal abscess, and/or sepsis, wound site infection), and mortality rates. Bile culture results and histopathological evaluation parameters were also recorded and compared.

Statistical analyses were performed using Kruskal–Wallis and Mann–Whitney U tests, and the results were assessed with confidence interval (CI) of 95%. A *P* value less than 0.05 was considered statistically significant.

Results

A total of 78 patients with a diagnosis of AC were evaluated. A total of 5 patients with accompanying acute cholangitis, 13 patients with an ASA score of 4, and 3 patients who refused the operation were excluded, and the remaining 57 patients were enrolled. Thirty-six (63%) of the patients were female and 21 (37%) were male. The mean age was 48 years (21-74 years). Group 1 included 22 (39%) patients, Group 2; 24 (44%) patients, and Group 3; 11 (17%) patients. The mean time from symptom onset to operation was 33 hours in Group 1 (first 3 days), 98 hours in Group 2 (between 4th and 7th days), and 220 hours in Group 3 (after 7th day). There was no significant difference among the groups with respect to demographics ($P > 0.05$, for each).

Mean duration of operation was 50 min (range, 30-70) in Group 1, 74 min (range, 40–135) in Group 2, and 132 min (range, 100–165) in Group 3. Comparison of the groups revealed that the duration of operation was significantly shorter in Group 1 than both Groups 2 and 3 ($P < 0.05$ and $P < 0.001$, respectively). Duration of operation was also significantly shorter in Group 2 than Group 3 ($P < 0.001$).

Table 1: Macroscopic adhesion score

Grade 0	No adhesion
Grade 1	Single adherence between two organs or between an organ and the abdominal wall
Grade 2	Two adherences between organs or one organ and the abdominal wall
Grade 3	More than two adherences between organs or a massive generalized adherence of the intestine with no adherence to the abdominal wall
Grade 4	Generalized adherences between organs and the abdominal wall or massive adherence among all organs

Mild (grade 0-1), Moderate (grade 2-3), Severe (grade 4)

Table 2: Histopathological Sakuramoto classification: Degree of inflammation and histopathological findings

None	Free of acute findings
Mild	Only mild neutrophil infiltration
Moderate	Moderate neutrophil infiltration, mucosal edema, erosion
Severe	Severe neutrophil infiltration, mucosal hyperemia, bleeding, ulcer, abscess

Table 3: Distribution of adhesion score across groups

Adhesion Score	Group 1 (*n*=22)	Group 2 (*n*=24)	Group 3 (*n*=11)	Total (*n*=57)
Mild (grade 0-1)	8 (36.3%)	4 (16.6%)	2 (18.1%)	14 (24.5%)
Moderate (grade 2-3)	8 (36.3%)	9 (37.5%)	0	17 (29.8%)
Severe (grade 4)	6 (27.2%)	11 (45.8%)	9 (81.8%)	26 (25.6%)

Table 4: Distribution of bile culture proliferations by study groups

Positive bile culture	Group 1 (*n*=22)	Group 2 (*n*=24)	Group 3 (*n*=11)	Total (*n*=57)
Proliferation*	4 (18.1%)	11 (45.8%)	8 (72.7%)	23 (40.3%)

*Enterobacter spp, 69.5%; Enterococcus spp, 21.7%; and E. coli, 8.6%

Table 5: Distribution of histopathological classification by study groups

Histopathological classification	Group 1 (*n*=22)	Group 2 (*n*=24)	Group 3 (*n*=11)
Mild	13 (59%)	9 (37.5%)	0
Moderate	8 (36.3%)	12 (50%)	4 (36.3%)
Severe	1 (4.5%)	3 (12.5%)	7 (63.6%)

Comparison of the groups in terms of adhesion score was summarized in Table 3. Group 1 had significantly fewer adhesions compared to Group 2 and Group 3 ($P < 0.05$ and $P < 0.001$, respectively), and no significant difference was found between Group 2 and Group 3 ($P > 0.05$). In six of 57 patients (1 in Group 1, 3 in Group 2, and 2 in Group 3), gallbladder was perforated during the operation. However, there were no significant difference between three groups with respect to the perforation rates ($P > 0.05$). Only one patient in Group 2 experienced bile duct injury which was primarily sutured in open surgery. No statistical difference was found between the three groups with respect to bile duct injury ($P > 0.05$). A total of six patients (three males, three females) were converted to open surgery. The rate of conversion to open surgery was 11% in our study group. There was a significant difference between Group 1 and Group 3 with respect to conversion to open surgery ($P < 0.001$). Other inter-group comparisons with respect to conversion to open surgery were not statistically significant ($P > 0.05$). Indications of conversion to open surgery were advanced adhesions in Group 3 ($n = 3$) and advanced adhesions and bile duct injury in Group 2 ($n = 2$ and $n = 1$, respectively).

Statistical analysis revealed that there were no significant correlation between gender, gall bladder wall thickness on ultrasonography, CRP level, leukocyte count, and conversion to open surgery ($P > 0.05$, for each). The effect of age on the conversion rates was examined by dividing the patients into four different age groups and this analysis demonstrated more often convertion rate in the age group of 63–74 years ($P < 0.05$).

Average duration of hospital stay was 1.9 day (1–4 days) in Group 1, 4.5 days (2–20 days) in Group 2, and 7.2 (3–24 days) in Group 3. Duration of hospital stay was significantly shorter in Group 1 compared to Group 2 and Group 3 ($P < 0.001$) and also was significantly shorter in Group 2 than Group 3 ($P < 0.05$).

Postoperative complications were found in two patients (minor bile fistula) in Group 1, in one patient (intra-abdominal abscess) in Group 2 and in one patient (minor bile fistula) in Group 3. No statistical difference was found between three groups with regard to morbidity ($P > 0.05$). All minor bile fistula were treated with sphincterotomy, following endoscopic retrograde cholangio-pancreaticography. There was no mortality observed in either group.

Bile culture results showed that 23 patients had proliferation [*Enterobacter spp.*, 69.5%; *Enterococcus spp*., 21.7%; and *E. coli*, 8.6%; Table 4]. Group 1 had significantly lower rate of culture positivity than Group 3 ($P < 0.001$), whereas no significant differences were evident in other inter-group analyses ($P > 0.05$, for each).

Histopathological examination revealed AC with gallstones in all patients. Sakuramoto classification confirmed the severity of inflammation in each groups [Table 5].

Discussion

In epidemiological studies, the incidence of bile stone disease has been reported to be 10% to 20% in United States of America and Western Europe.[1,2] Approximately, 50–70% of patients with bile stone disease are asymptomatic; however, the possibility of being complicated when the disease is left untreated increases at a rate of 1–2% each year.[2] AC was considered to be contraindication for LC at a time when it just began to be applied. The rationale of this view included fear of inability to do sufficient exploration due to inflammation during the course of acute attack, increased possibility of injury to extra-hepatic bile ducts and vascular structures, and high rate of conversion to open surgery. Until the second half of nineties many surgeons suggested to give an interval of 8-12 weeks

after medical therapy before operating on patients with LC in management of AC. However, this INT-C method has begun to be questioned after 1995, as the experience with LC has increased.[3] Previous studies had reported that 25% of patients in whom an interval was given after medical therapy were readmitted to hospital with acute complications of gallbladder stones during the interval.[7] Gallbladder dissection may become more difficult in patients operated upon with INT-C as a result of diffuse fibrotic adhesions on the basis of AC. Some studies have reported higher complication and conversion rates in cases operated upon with interval LC.[4,5] However, no differences have been found between early LC and interval LC with terms of conversion rates, duration of hospital stay, and morbidity and mortality rates.[6] According to these results, it has been recognized that carrying out a LC within 72 hours of symptom onset, a period which is also called "golden period", is a safe and effective method in treatment of AC.[11,12]

Currently, the chief innovation in surgical therapy of AC is timing of LC. According to many authors, time from the symptom onset is a factor that influences rates of conversion to open surgery, duration of operation and hospital stay. It has also been reported that time from symptom onset to operation is parallel to histological changes and inflammation grade in the gallbladder wall.[8] In a prospective clinical study, Pessaux *et al*. compared LC operations performed within 72 hours of symptom onset or later.[13] They found a conversion rate of 27% in first 72 hours, whereas it increased to 59.5% in cases operated later than 72 hours. In an a nother study which included 137 patients, a 7% conversion rate in patients operated within 72 hours and 9% in those operated later than 72 hours.[14] Furthermore, they found no difference between both groups in terms of morbidity and mortality rates as well as duration of operation and hospital stay. Discrepancies in these studies may be explained by the fact that conversion and complication rates have decreased as number of and experience in LC operations have increased in cases with AC. Considering the above-mentioned results as well as the difficulties of interval LC, surgeons have now begun to debate performance of LC also in patients with a symptom duration of more than 7 days.

In some retrospective studies on this topic, patients undergoing LC for AC were grouped into three as early (three days), intermediate three to seven and late (after the seventh day), according to the time from symptom onset to operation table.[15,16] No difference was found between groups with respect to conversion rates, duration of operation and hospital stay, and morbidity rate. However, in our study group, these intervals were assessed prospectively. There existed no difference between in all three groups with respect to demographics, time from admission to operation, and rates of gallbladder perforation, bile duct injury, and fistulae whereas significant differences were detected between the groups in terms of duration of operation, adhesion score, conversion rate, duration of hospital stay, and proliferation in bile culture. We found that duration of operation was significantly shorter in Group 1 compared to Groups 2 and 3 and also it was significantly shorter in Group 2 than Group 3. A reduction in duration of operation is expected as more experience is gained.

Various studies investigated the causes of conversion to open surgery in AC during LC and late surgery, male gender, advanced age, gallbladder wall thicker than 5 mm, gangrenous cholecystitis were revealed as factors effective in conversion to open surgery.[17,18] Advanced age, history of biliary disease, and recurrent inflammations lead to scar and fibrotic adhesions in gallbladder. In our study, advanced age was related with conversion; however, gender, wall thickness of gallbladder, CRP, and leucocyte levels were not predictive of conversion to open surgery. Although we detected a difference between Group 1 and 3 in terms of conversion to open surgery, we failed to find any difference between Group 2 and Group 3 in terms of the conversion to open surgery. As for the adhesion scoring, Group 1 had less adhesion compared to Group 2 and Group 3, whereas no difference was evident between Group 2 and Group 3. Incidence of AC increases in geriatric population; complication rates have been reported to increase in patients with a higher ASA score and especially patients with AC.[18] We found a significantly higher conversion rate in the age group of 63–74 years in our study group. Three patients in Group 3 had gangrenous cholecystitis, each of them was above 60 years of age, and all were converted to open surgery.

The most common complication of LC pertaining to bile ducts is bile leaks.[16] It usually occurs as small bile leakage on the cut liver surface or through the stump of cystic canal. We observed postoperative bile leak in three patients (5.3%). Sphincterotomy was performed and bile leaks ceased, without a need for any other intervention. No mortality was observed in our study. Histopathological diagnosis of AC is not always correlated with signs of intraoperative cholecystitis. In our study, it was correlated in all patients. Intraoperative findings are sufficient for the diagnosis of AC even though they are not histopathologically confirmed. LC can be performed by experienced centers with

reasonable conversion and complication rates in patients with AC. One should not hesitate to proceed with open surgery in cases when the anatomy of the Calot's triangle cannot be delineated. This decision should be made before a complication develops. In agreement with previous literature, we observed in our study that results of LC operations performed within the first 3 days from the symptom onset had better results. We also determined that the intermediate group operated upon between 4th and 7th days had better results than the groups operated upon after the 7th day with respect to duration of hospital stay and operation. Although we had a few cases operated upon after the 7th day following the symptom onset, a LC operation may be scheduled in such patients.

Our results suggest that early LC is associated with shorter duration of operation and hospital stay, as well as less adhesion and lower rates of conversion to open surgery. Clinics that have established LC a routine practice in cases with AC have begun to report better results with this approach as surgical experiences and the numbers of cases have increased over time.

In conclusion, LC can be safely performed within 7 days of symptom onset in cases with AC. More prospective studies with large sample size are needed to implement LC after the 7th day widely in clinical practice.

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Conflicts of interest

There are no conflicts of interest.

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