ORIGINAL RESEARCH

An Observational Study To Compare Delayed And Early Cholecystectomy In Acute Cholecystitis At A Tertiary Care Hospital Of Bihar

[1]Rajeev Ranjan, [2]Anand Prakash, [3]Rahul Kumar

[1,2]Assistant Professor, [3]Senior Resident, Department of General Surgery, NMCH, Jamuhar, Bihar, India

Correspondence:
Rajeev Ranjan
Assistant Professor, Department of General Surgery, NMCH, Jamuhar, Bihar, India
Email: drrajeevsingh1982@gmail.com

ABSTRACT

Introduction: Elective laparoscopic cholecystectomy has become the gold standard for treatment of symptomatic gallstones. However, in the early days, acute cholecystitis was a contraindication of laparoscopic cholecystectomy. The aim of this study was to compare the intra-operative and postoperative outcomes of early versus delayed laparoscopic cholecystectomy for acute cholecystitis.

Materials and Methods: A randomized clinical study was conducted by the Department of General Surgery, Narayan Medial College & Hospital, Jamuhar, Bihar from May 2020 to February 2021. A total of 100 patients whose physical, laboratory, and ultrasound findings suggested acute cholecystitis, and who were operated on by laparoscopy, was included in the study. Acute cholecystitis diagnosis was based on a combination of clinical and radiologic criteria. . Each patient gave written informed consent before participation in the study. Approval for this study was obtained from the Institutional Ethics Committee. The statistical analyses were performed using commercially available software (Statistical Package for Social Sciences version 16.0, SPSS Inc, Chicago, Illinois).

Results: The study groups, which underwent early or delayed laparoscopic cholecystectomy, had 50 patients each. Both groups revealed similar findings on physical examination: all patients had tenderness and defense in the abdominal area. On ultrasonography, calculi in the gallbladder were detected in all of the patients, and thickness of the anterior gallbladder wall was increased in majority of the patients of both the groups. There was no significant difference between the early and the delayed laparoscopic cholecystectomy groups in terms of operation time and rates for conversion to open cholecystectomy.

Conclusion: Early laparoscopic cholecystectomy should be preferred by surgeons for treatment of acute cholecystitis with the advantage of shorter hospital stay and early ambulation.

Key Words: Delayed and Early Cholecystectomy In Acute Cholecystitis

INTRODUCTION

Elective laparoscopic cholecystectomy has become the gold standard for treatment of symptomatic gallstones. [1] However, in the early days, acute cholecystitis was a contraindication of laparoscopic cholecystectomy, and patients with acute cholecystitis were managed conservatively and discharged for re-admission in order to have elective surgery performed for the definitive treatment. [2, 3] Then, randomized controlled trials and meta-

analyses had shown the benefits of early surgery (within the acute admission period, which is 24 to 72 hours) compared with delayed cholecystectomy with respect to hospital stay and costs, with no significant difference in morbidity and mortality. [2, 4, 5] Thus, in the late 1980s early surgery for acute cholecystitis had gained popularity. The updated Tokyo Guidelines announced in 2013 by the Japanese Society of Hepato-Biliary-Pancreatic Surgery suggested that early laparoscopic cholecystectomy is the first-line treatment in patients with mild acute cholecystitis, whereas in patients with moderate acute cholecystitis, delayed/elective laparoscopic cholecystectomy after initial medical treatment with antimicrobial agent is the first-line treatment. [6]

With the increased experience in laparoscopy, surgeons started to attempt early laparoscopic cholecystectomy for acute cholecystitis. [2] However, early laparoscopic cholecystectomy is still performed by only a minority of surgeons. [7-9] Furthermore, the exact timing, potential benefits, and cost-effectiveness of laparoscopic cholecystectomy in the treatment of acutely inflamed gallbladder have not been clearly established and continue to be controversial. [1-10]

The aim of this study was to compare the intra-operative and postoperative outcomes of early versus delayed laparoscopic cholecystectomy for acute cholecystitis.

MATERIALS AND METHODS

A randomized clinical study was conducted by the Department of General Surgery, Narayan Medial College &Hospital, Jamuhar, Bihar from May 2020 to February 2021. A total of 100 patients whose physical, laboratory, and ultrasound findings suggested acute cholecystitis, and who were operated on by laparoscopy, was included in the study. Acute cholecystitis diagnosis was based on a combination of clinical and radiologic criteria. All of the following criteria together constituted an acute episode: right subcostal tenderness; positive Murphy sign; leukocytosis; thickened, edematous distended gallbladder; presence of gallstones; and pericholecystic fluid collection on ultrasound examination. Patients with common bile duct stones, acute pancreatitis, previous upper abdominal surgery, or severe concomitant medical problems deeming them unfit for laparoscopic surgery were excluded from the study. Each patient gave written informed consent before participation in the study. Approval for this study was obtained from the Institutional Ethics Committee.

Patients were randomized to the early or delayed operation group. The early operation group was operated on within 24 hours of admission (50 patients), whereas the late operation group was operated on after 6 to 8 weeks following the initial treatment (50 patients). Patients in the delayed group were treated with intravenous fluids, antibiotics, and analgesics. Patients who responded to conservative treatment were discharged after a complete relief of symptoms. They were called for laparoscopic cholecystectomy after 6 or 8 weeks, when the acute episode had subsided.

LAPAROSCOPIC CHOLECYSTECTOMY

Laparoscopic cholecystectomy operations were performed by competent trainees under the supervision of a consultant. The surgical procedure was in line with the literature. [1] The surgery was done with the patient under general anesthesia using endotracheal intubation. Pneumoperitoneum was created by blind puncture with a Veress needle through a subumbilical incision. Four laparoscopic ports were used: 10-mm umbilical for the optical instrument (0 degrees), 10-mm subxiphoidal for working instruments, 5-mm right subcostal along the midclavicular line also for working instruments, and 5 mm on the right flank for retraction instruments. Adhesion release and exposure of Calot triangle were undertaken first. If necessary, the gallbladder was emptied through a laterally inserted Veress needle to allow better grasping. The cystic pedicle was detected to isolate the cystic duct and the artery

separately. Both were then clipped and divided. The gallbladder was dissected off of its bed with a monopolar cautery hook. At completion of the surgery, the gallbladder was placed in a retrieval bag and extracted through the subxiphoidal incision, which was enlarged if necessary. Hemostasis was achieved in the gallbladder bed, and after a through saline lavage, a suction drain was placed if clinically indicated and the incisions closed. When required, a conversion to open surgery was performed through a right subcostal incision.

EVALUATION CRITERIA

Demographics, clinical data, and findings for medical history, physical examination, laboratory tests, and ultrasonography were recorded for all patients. The patients were followed up during postoperative hospitalization. The primary evaluation criteria of the study were operative and postoperative variables, such as operation time, hospitalization duration, intraoperative and postoperative complications, and rate of conversion to open cholecystectomy. For the late operation group, hospitalization duration was considered as total length of stay for both first and second hospitalizations (for initial treatment and operation, respectively) added together.

STATISTICAL ANALYSIS

The study data were summarized with descriptive statistics (mean, SD, frequency, and percentage). The statistical analyses were performed using a commercially available software (Statistical Package for Social Sciences version 16.0, SPSS Inc, Chicago, Illinois). The statistical level of significance was set to $P < 0.05$.

RESULTS

The study groups, which underwent early or delayed laparoscopic cholecystectomy, had 50 patients each. The basic clinical and demographic characteristic has been shown and compared in Table 1.

Table 1: Comparison of various clinical and demographic characteristics between both the groups (N = 50 in each group)

Clinical & demographic character	Early cholecystectomy	Delayed cholecystectomy	P value
Age, years	46.6 (12.3)	49 (11.6)	> 0.05
Female gender	33 (66%)	36 (72%)	> 0.05
Pain duration, hours	29.5 (19.8)	34.5 (21.7)	> 0.05
History duration, days	4.7 (10.2)	5.6 (11.7)	> 0.05
Previous attack	27 (54%)	22 (44%)	> 0.05
H/O abdominal surgery	8 (16%)	7 (14%)	> 0.05
Fever, ^{o}C	37.1 (0.71)	36.5 (0.45)	> 0.05
Comorbidity	11 (22%)	13 (26%)	> 0.05

* Results has been expressed in terms of mean (SD or No (%), as appropriate

Both groups revealed similar findings on physical examination: all patients had tenderness and defense in the abdominal area. On ultrasonography, calculi in the gallbladder were detected in all of the patients, and thickness of the anterior gallbladder wall was increased in majority of the patients of both the groups. Other ultrasonography and physical examination findings has been shown and compared in table 2.

Table 2: Comparison of findings of physical examination, laboratory parameters and Ultrasonography between both the groups (N = 50 in each group)

Physical examination or lab or USG findings	Early cholecystectomy	Delayed cholecystectomy	P value
Physical finding			

Tenderness	50 (100)	50 (100)	> 0.05
Rebound tenderness	10 (20)	13 (26)	> 0.05
Defence in the abdomen	50 (100)	50 (100)	> 0.05
Murphy sign	48 (99)	45 (90)	> 0.05
Laboratory findings			
White Blood Cells (per litre)	12.2 (4.3)	13.4 (3.8)	> 0.05
Alanine transaminase (per litre)	85.7 (130.9)	87.6 (63.8)	> 0.05
Aspartate transaminase (per litre)	116.8 (221.7)	83.7 (56.7)	> 0.05
Gamma Glutamyl transferase (per litre)	121.1 (210.8)	131.3 (221.8)	> 0.05
Alkaline phosphatase (per litre)	82.3 (53.8)	106.8 (35.7)	> 0.05
Amylase (per litre)	84.8 (53.1)	107.5 (33.7)	> 0.05
Total bilirubin (mg/dl)	1.1 (0.8)	3.2 (15.7)	> 0.05
Direct/conjugated bilirubin (mg/dl)	0.4 (0.39)	0.3 (0.21)	< 0.05
USG finding			
Calculi in GB	50 (100)	50 (100)	> 0.05
Increased thickness of the anterior GB wall	39 (78)	36 (72)	> 0.05
Pericholecystic fluid	7 (14)	6 (12)	> 0.05
Intrahepatic bile duct dilation	1 (2)	3 (6)	> 0.05
Extrahepatic bile duct dilation	1 (2)	1 (2)	> 0.05

* Results has been expressed in terms of mean (SD or No (%), as appropriate

There was no significant difference between the early and the delayed laparoscopic cholecystectomy groups in terms of operation time and rates for conversion to open cholecystectomy [Table 3]. On the other hand, total hospital stay was longer in the delayed laparoscopic cholecystectomy group than in the early laparoscopic cholecystectomy group. Intraoperative and postoperative complications were recorded in 5 patients in the early laparoscopic cholecystectomy group, whereas no complications occurred in the delayed laparoscopic cholecystectomy group.

Table 3: Comparison of Intra-operative and Post-operative findings between both the groups (N = 50 in each group)

Intra-operative and Post-operative findings	Early cholecystectomy	Delayed cholecystectomy	P value
Operation time, minutes	68.5 (30.4)	72.6 (25.8)	> 0.05
Hospitalization duration, hours	6.1 (1.8)	7.6 (1.9)	< 0.05
Complications	12 (24)	1 (2)	< 0.05
Conversion to open cholecystectomy	5 (10)	0 (0)	> 0.05

* Results has been expressed in terms of mean (SD or No (%), as appropriate

DISCUSSION

In the past, the optimal timing for laparoscopic cholecystectomy for patients with acute cholecystitis had generally been considered to be 6 to 8 eight weeks after the acute phase to allow for resolution of the acute inflammation of the gallbladder. [8] However, several clinical trials—albeit mostly small and retrospective studies—proved that early laparoscopic cholecystectomy is safe and shortens hospital stay, with morbidity and mortality similar to those of elective delayed cholecystectomy. [2,4,8,9,11] In a retrospective analysis of 100 patients, Ohta et al [11] compared 4 timing groups of laparoscopic cholecystectomy (≤72 hours, 4–14 days, 3–6 weeks, and >6 weeks after onset of symptoms) and found that the best timing for laparoscopic cholecystectomy for acute cholecystitis is within 72 hours, which provides the shortest total hospital stay versus operations performed later. Falor et al [8] performed early laparoscopic cholecystectomy (within 48 hours of admission) in 117 of 303 patients with mild gallstone pancreatitis; for the rest of the patients, operation was delayed

until the normalization of laboratory values. They suggested that early laparoscopic cholecystectomy is safe, resulting in shortened hospital stay and decreased use of endoscopic retrograde cholangiopancreatography without increased morbidity and mortality. Chang et al [4] reported that although early laparoscopic cholecystectomy is associated with a higher rate of wound infections compared with delayed intervention, it shortens the length of hospital stay and reduces the risk of repeat cholecystitis. In a randomized, controlled trial including 75 patients, early laparoscopic cholecystectomy (<24 hours) was found to decrease the morbidity during the waiting period for elective laparoscopic cholecystectomy, the rate of conversion to open cholecystectomy, operating time, and hospital stay. [12] In a recent survey evaluating surgical approaches for acute gallbladder disease between 1989 and 2006 in Sweden, total hospital stay was found to be shorter for patients who had emergency cholecystectomy at first admission compared with patients with elective cholecystectomy. [7]

Similar to the above clinical studies, we found that hospitalization duration was significantly shorter with early laparoscopic cholecystectomy compared with delayed laparoscopic cholecystectomy for acute cholecystitis. Furthermore, operation time and conversion rate were comparable between groups. It should be noted that physical, clinical, and radiologic characteristics of patients in both study groups were similar in our study, except for body temperature and blood direct/conjugated bilirubin level, which were significantly higher in the early laparoscopic cholecystectomy group.

In addition to the clinical studies, the meta-analyses of randomized clinical trials in the literature demonstrated that early laparoscopic cholecystectomy (24–72 hours of onset) provides benefit over delayed laparoscopic cholecystectomy (6–12 weeks later) in terms of total hospital stay, with conflicting results on conversion rates and postoperative complications. [5,13–15] Siddiqui et al [14] analyzed 4 clinical studies containing 375 patients and found shorter hospital stay and longer operation time in early laparoscopic cholecystectomy, but they found no significant difference in conversion rates between early and delayed laparoscopic cholecystectomy. In a best-evidence topic that analyzed 92 papers (meta-analyses, randomized control trials, prospective controlled study, and retrospective cohort studies), it was concluded that early laparoscopic cholecystectomy for acute cholecystitis is advantageous in terms of the length of hospital stay without increases in morbidity or mortality. [15] Although the operating time in early laparoscopic cholecystectomy can be longer, the incidence of serious complications was found to be comparable to the delayed laparoscopic cholecystectomy. In the present study, similar to the findings of studies showing a high rate of wound infections and complications with early laparoscopic cholecystectomy, we found that intraoperative and postoperative complications were more common with early than delayed laparoscopic cholecystectomy. The higher rate of complications in the early laparoscopic cholecystectomy group may also be explained by the significantly higher initial body temperatures and blood direct/conjugated bilirubin levels in this group. However, considering the shorter hospitalization duration, early laparoscopic cholecystectomy still seems advantageous over late intervention.

We believe that inflammation associated with acute cholecystitis creates an edematous plane around the gallbladder, thus facilitating its dissection from the surrounding structures. Maturation of the surrounding inflammation, and thus organization of the adhesions, leading to scarring and contraction, occurs during the cool-down period.

CONCLUSION

Although intraoperative and postoperative complications are associated more with early laparoscopic cholecystectomy compared with delayed intervention, early laparoscopic cholecystectomy should be preferred by surgeons for treatment of acute cholecystitis with the advantage of shorter hospital stay and early ambulation.

REFERENCES

1. Kolla SB, Aggarwal S, Kumar A, Kumar R, Chumber S, Parshad R, et al. Early versus delayed laparoscopic cholecystectomy for acute cholecystitis: a prospective randomized trial. *Surg Endosc.* 2004; 18(9):1323–1327.
2. Macafee DAL, Humes DJ, Bouliotis G, Beckingham IJ, Whynes DK, Lobo D. Prospective randomized trial using cost-utility analysis of early versus delayed laparoscopic cholecystectomy for acute gallbladder disease. *Br J Surg.* 2009; 96(9):1031–1040.
3. Cuschieri A. Approach to the treatment of acute cholecystitis: open surgical, laparoscopic or endoscopic? *Endoscopy.* 1993; 25(6):397–398.
4. Chang TC, Lin MT, Wu MH, Wang MY, Lee PH. Evaluation of early versus delayed laparoscopic cholecystectomy in the treatment of acute cholecystitis. *Hepatogastroenterology.* 2009; 56(89):26–28.
5. Gurusamy K, Samraj K, Gluud C, Wilson E, Davidson BR. Meta-analysis of randomized controlled trials on the safety and effectiveness of early versus delayed laparoscopic cholecystectomy for acute cholecystitis. *Br J Surg.* 2010; 97(2):141–150.
6. Miura F, Takada T, Strasberg SM, Solomkin JS, Pitt HA, Gouma DJ, et al. TG13 flowchart for the management of acute cholangitis and cholecystitis. *J Hepatobiliary Pancreat Sci.* 2013; 20(1):47–54.
7. Sandzen B, Haapamaki MM, Nilsson E, Stenlund HC, Oman M. Surgery for acute gallbladder disease in Sweden 1989–2006 - a register study. *Scand J Gastroenterol.* 2013; 48(4):480–486.
8. Falor AE, de Virgilio C, Stabile BE, Kaji AH, Caton A, Kokubun BA, et al. Early laparoscopic cholecystectomy for mild gallstone pancreatitis: time for a paradigm shift. *Arch Surg.* 2012; 147(11):1031–1035.
9. Panagiotopoulou IG, Carter N, Lewis MC, Rao S. Early laparoscopic cholecystectomy in a district general hospital: is it safe and feasible? *Int J Evid Based Health.* 2012; 10(2):112–116.
10. Sankarankutty A, da Luz LT, De Campos T, Rizoli S, Fraga GP, Nascimento B., Jr Uncomplicated acute cholecystitis: early or delayed laparoscopic cholecystectomy? *Rev Col Bras Cir.* 2012; 39(5):436–440.
11. Ohta M, Iwashita Y, Yada K, Ogawa T, Kai S, Ishio T, et al. Operative timing of laparoscopic cholecystectomy for acute cholecystitis in a Japanese institute. JSLS. 2012;16(1):65–70.
12. Gurusamy KS, Samraj K, Fusai G, Davidson BR. Early versus delayed laparoscopic cholecystectomy for biliary colic. Cochrane Database Syst Rev. 2008 4):CD007196.
13. Lau H, Lo CY, Patil NG, Yuen WK. Early versus delayed-interval laparoscopic cholecystectomy for acute cholecystitis: a metaanalysis. Surg Endosc. 2020;20(1):82–87.
14. Siddiqui T, MacDonald A, Chong PS, Jenkins JT. Early versus delayed laparoscopic cholecystectomy for acute cholecystitis: a meta-analysis of randomized clinical trials. Am J Surg. 2021;195(1):40–47.
15. Skouras C, Jarral O, Deshpande R, Zografos G, Habib N, Zacharakis E. Is early laparoscopic cholecystectomy for acute cholecystitis preferable to delayed surgery?: best evidence topic (BET) Int J Surg. 2022;10(5):250–258.