ORIGINAL ARTICLE

NATIONAL JOURNAL NJMR MEDICAL RESEARCH

Early vs. Delayed Laparoscopic Cholecystectomy in Acute Calculous Cholecystitis: A Comparative Analysis of Outcomes and Complications

Vipul Lad[1], Jenish Modi[2*], Parag Godhani[3]

[1,2,3]Department of General Surgery, SMIMER, Surat, India

DOI:
10.55489/njmr.150120251013

***Corresponding author**:
Jenish Modi
(Email: jenishmodi50@gmail.com)

Date of Submission: 24/08/2024
Date of Acceptance: 01/11/2024
Date of Publication: 01/01/2025

Funding Support:
None Declare

Conflict of Interest:
None Declare

How to cite this article:
Lad V, Modi J, Godhani P. Early vs. Delayed Laparoscopic Cholecystectomy in Acute Calculous Cholecystitis: A Comparative Analysis of Outcomes and Complications. Natl J Med Res 2025;15(01):2-8. DOI: 10.55489/njmr.150120251013

ABSTRACT

Background: This study compares early laparoscopic cholecystectomy (ELC) and delayed laparoscopic cholecystectomy (DLC) in patients with acute calculous cholecystitis to determine the optimal timing for surgery. The study aims to assess the outcomes, complications, and safety of both approaches.

Methods: A prospective, comparative study was conducted on 94 patients diagnosed with acute calculous cholecystitis. Patients were randomized into two groups: ELC (Group E), performed within 72 hours of symptom onset, and DLC (Group D), performed 6–12 weeks after initial conservative management. Data on demographic characteristics, clinical features, intraoperative findings, and postoperative outcomes were collected and analyzed. Statistical analysis was conducted using SPSS software, with significance set at $p < 0.05$.

Results: ELC was associated with a shorter total hospital stay and reduced complications compared to DLC. However, the Group D showed a higher rate of conversion to open cholecystectomy and longer operative time. Both groups had similar rates of bile duct injuries and postoperative infections. No significant difference was observed in mortality between the two groups.

Conclusion: ELC is a safe and effective approach for acute calculous cholecystitis, offering benefits in reduced hospital stay and complications. DLC, while feasible, may lead to increased operative challenges and longer recovery times.

Keywords: Laparoscopic Cholecystectomy, Calculous Cholecystitis, Acute, Complications

INTRODUCTION

Laparoscopic cholecystectomy (LC) has become the gold standard for the surgical treatment of symptomatic gallstone disease, including acute calculus cholecystitis (ACC).[1] ACC, an inflammatory condition of the gallbladder caused by obstructive gallstones, is a common presentation in emergency surgical practice. The management of ACC has evolved significantly over the years, with LC replacing open cholecystectomy due to its minimally invasive nature, reduced postoperative pain, shorter hospital stays, and quicker return to normal activities.[2] However, the optimal timing of LC in ACC cases remains a subject of debate. Traditionally, delayed laparoscopic cholecystectomy (DLC) after an interval of several weeks has been preferred to allow the inflammation to subside, theoretically reducing the risk of complications.[3] On the other hand, early laparoscopic cholecystectomy (ELC) performed within 72 hours of symptom onset has been advocated to prevent recurrent

Publisher: Medsci Publications [www.medscipublications.com] ISSN: 2249 4995 Official website: www.njmr.in

symptoms and complications, such as gallbladder empyema or perforation, during the waiting period.[4]

The problem lies in the lack of consensus on whether ELC or DLC offers better outcomes in terms of safety, efficacy, and overall patient satisfaction. While some studies suggest that ELC reduces hospital stay and overall morbidity, others argue that it may increase the risk of intraoperative difficulties and conversion to open surgery.[5] Furthermore, there is a concern that delaying the surgery could lead to recurrent biliary events, prolonged hospitalizations, and increased healthcare costs.[6] This ongoing controversy necessitates further investigation to provide clearer guidelines for the management of ACC.

Our study was conducted to address this gap in knowledge by directly comparing the outcomes of early versus delayed laparoscopic cholecystectomy in patients with acute calculus cholecystitis. We aimed to evaluate the safety, efficacy, and overall outcomes of both approaches, focusing on the incidence of intraoperative and postoperative complications, conversion rates, hospital stay duration, and patient satisfaction. By doing so, we sought to provide evidence-based recommendations to guide clinical practice, ultimately improving patient care in ACC cases.

The primary aim of this study was to compare the outcomes of early and delayed laparoscopic cholecystectomy in patients diagnosed with acute calculus cholecystitis. The specific objectives were to assess and compare the incidence of intraoperative complications between early and delayed LC; to evaluate the postoperative outcomes, including complications, hospital stay duration, and recovery time; to determine the rate of conversion to open surgery in both early and delayed LC groups; and to analyze patient satisfaction and overall outcomes in the context of the timing of surgery.

By achieving these objectives, this study aimed to clarify the optimal timing of laparoscopic cholecystectomy in acute calculus cholecystitis, thus contributing to the ongoing debate and enhancing the quality of care provided to patients.

MATERIALS AND METHODS

Study Design and Setting: This prospective randomized interventional study was conducted in the Department of Surgery at Surat Municipal Institute of Medical Education & Research during the year 2023. The study was approved by the institutional ethics committee, and all patients provided written informed consent for participation, laparoscopic cholecystectomy (LC), and potential conversion to open surgery.

Inclusion Criteria: The study included patients aged 18 to 60 years diagnosed with acute calculus cholecystitis, presenting with right upper abdominal pain, fever >98.6°F, and a total leukocyte count (TLC) >10,000/μL. Ultrasound findings indicative of acute cholecystitis, such as gallstones, thickened and edematous gallbladder (GB) wall, and pericholecystic fluid, were considered diagnostic. Only patients with American Society of Anesthesiologists (ASA) physical status I and II were included.

Exclusion Criteria: Patients were excluded if they had simple biliary colic, obstructive jaundice, choledocholithiasis, gallstone-induced acute pancreatitis, post-endoscopic retrograde cholangiopancreatography, previous biliary tract or abdominal surgery, biliary peritonitis, decompensated liver cirrhosis, intra-abdominal abscess, gallbladder polyps or malignancy, ASA grade III and IV, pregnancy, or other contraindications to surgery.

Sample Size Calculation: The sample size was calculated based on the study by Gutt et al.[4] which reported overall complication rates of 14.1% in the early laparoscopic cholecystectomy (ELC) group and 40.4% in the delayed laparoscopic cholecystectomy (DLC) group. To achieve 80% power and a 5% significance level, a minimum of 40 patients per group was required. Accounting for a 10% dropout rate, additional 5 cases were added in each group and finally the sample size was rounded to 50, so, finally 50 patients were recruited for each group.

Randomization: Patients were randomly assigned to either the ELC (Group E) or DLC (Group D) group using block randomization with sealed envelopes. Ten opaque envelopes containing randomly generated assignments (E for ELC, D for DLC) were used in blocks of five each. Patients in the Group E underwent LC within 72 hours of symptom onset, while those in the Group D underwent LC 6–12 weeks after initial conservative management, which included broad-spectrum intravenous antibiotics and intravenous fluid resuscitation.

Data Collection: Data were collected on demographic variables (age, sex), comorbidities, body mass index (BMI), past medical and surgical history, symptom duration, and clinical examination findings. Laboratory results, imaging findings, intraoperative details, and postoperative outcomes were also recorded.

Surgical Procedure: LC was performed using a standard four-port technique. Intraoperative modifications such as gallbladder decompression, use of a laparoscopic specimen retrieval bag, epigastric port enlargement, suction/irrigation, and subhepatic closed suction drain placement were made as necessary. Conversion to open cholecystectomy was done via a right subcostal incision when faced with difficult dissection, excessive bleeding, or significant adhesions in Calot's triangle. Postoperative care included early oral intake and pain management with intramuscular diclofenac. Antibiotics were administered according to hospital protocols.

Outcome Measures: The primary outcome measures were the rate of conversion to open surgery, mean hospital stay, complications (bile leak, bile duct injury, wound infection), and mortality. Secondary outcomes included the mean duration of surgery, intraoperative blood loss, and other complications (e.g., subhepatic

collection, postoperative pneumonia).

Statistical Analysis: Data were entered into Excel and analyzed using the Statistical Package for Social Sciences (SPSS) version 21.0. Categorical variables were expressed as numbers and percentages, while continuous variables were presented as mean ± standard deviation (SD) or median. Normality was tested using the Kolmogorov–Smirnov test. The unpaired t-test or Mann–Whitney test was used for quantitative comparisons, and the Chi-square test or Fisher's exact test for qualitative comparisons. A p-value <0.05 was considered statistically significant.

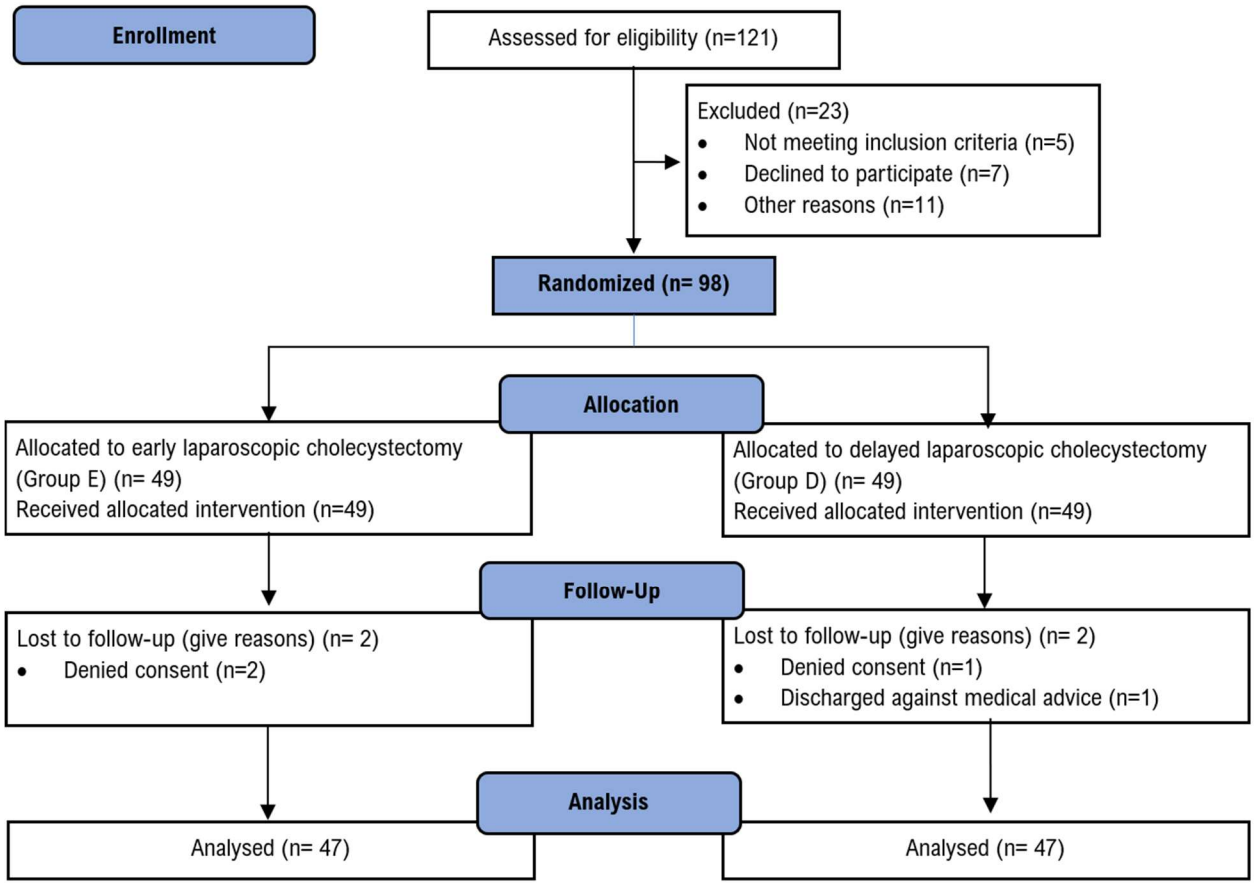

Figure 1: CONSORT Flow Diagram illustrating the progression of participants through the Early and Delayed Laparoscopic Cholecystectomy groups in the study. A total of 98 patients were randomized equally into two groups. 2 patients from each group were lost to follow-up or excluded, resulting in 47 patients analyzed in each group.

RESULTS

The study provides a detailed comparison between early laparoscopic cholecystectomy (Group E) and delayed laparoscopic cholecystectomy (Group D) for acute calculus cholecystitis, with six tables summarizing key findings.

Clinical data and laboratory results (Table 1) reveal that the average age of patients in the G was 41.2 years, slightly higher than the 39.1 years in the Group D. Both groups had a female predominance, with 83% of the Group E and 81% of the Group D being female. The average BMI was similar across groups. Pain duration was slightly longer in the Group E, and previous antibiotic administration was more common in the Group D (96% vs. 10%, p <0.001). Other laboratory parameters, such as white blood cell count and liver function tests, were comparable between groups.

Ultrasonographic findings (Table 2) indicate that the majority of patients in both groups had multiple gallstones, with thickened gallbladders observed in 95% of ELC and 84% of DLC cases. The presence of pericholecystic fluid was similar, affecting 45% of ELC and 43% of DLC patients.

Intraoperative findings and modifications (Table 3) show that the mean operative time was significantly longer in the Group E (79.5 minutes) compared to the Group D (67.2 minutes, p = 0.004). Blood loss was also higher in the Group E (85 mL vs. 67 mL, p = 0.010). Adhesions in Calot's triangle were more frequent in the Group E (81% vs. 48%, p = 0.008), and the need for gallbladder decompression was greater in this group as well (83% vs. 41%, p < 0.001). Conversion to open surgery occurred in 11% of ELC cases and 14% of DLC cases, with no significant difference between groups.

Table 1: Clinical Data and Laboratory Results of Patients

Variables	Group E (N = 47)	Group D (N = 47)	p- value
Age (mean), years	42.1 ± 11.9	38.8 ± 12.4	0.184
Sex			
Male	9 (19.1)	10 (21.3)	0.607
Female	38 (80.9)	37 (78.7)	
BMI (kg/m²)	23.7 ± 2.6	22.8 ± 2.9	0.331
Clinical feature			
Pain duration, mean (hours)	24.6 ± 8.9	22.7 ± 7.8	0.243
First attack	33 (70.2)	35 (74.5)	0.621
Previous biliary symptoms	14 (29.8)	16 (34.0)	0.685
Previous antibiotics administration	4 (8.5)	45 (95.7)	<0.001
Temperature (°F), mean	99.7 ± 0.2	99.8 ± 0.3	0.619
Nausea/vomiting	46 (97.9)	46 (97.9)	1.00
Right Hypochondrial (RHC) pain	47 (100)	47 (100)	1.00
Murphy's sign	43 (91.5)	41 (87.2)	0.501
Laboratory findings			
Hemoglobin (g/dL)	12.9 ± 1.3	12.4 ± 1.2	0.512
White blood cells ($\times 10^9$/L)	12.8 ± 2.7	11.9 ± 2.5	0.214
Serum bilirubin (mg/dL)	0.85 ± 0.21	0.73 ± 0.15	0.375
SGOT (IU/L)	45.2 ± 17.9	37.4 ± 13.6	0.082
SGPT (IU/L)	48.5 ± 20.3	37.9 ± 14.5	0.067
ALP (IU/L)	210.4 ± 85.1	176.9 ± 54.2	0.074
Serum amylase (IU/L)	54.3 ± 21.4	35.9 ± 9.1	0.076
Comorbidities			
Diabetes mellitus	3 (6.4)	4 (8.5)	0.678
Hypertension	5 (10.6)	6 (12.8)	0.739
COPD	1 (2.1)	1 (2.1)	1.00
Hypothyroidism	2 (4.3)	2 (4.3)	1.00

Table 2: Ultrasonographic (USG) Findings for the Patients

Characteristics/parameters	Group E (n = 47)	Group D (n = 47)	p-value
Gallstones: Single	6 (12.8)	5 (10.6)	0.715
Multiple	41 (87.2)	42 (89.4)	
Thickened GB	45 (95.7)	40 (85.1)	0.841
Distended GB	44 (93.6)	45 (95.7)	0.751
Pericholecystic fluid	21 (44.7)	19 (40.4)	0.563
Murphy's sign	43 (91.5)	44 (93.6)	0.675

Causes of conversion to open cholecystectomy were mainly due to dense adhesions and difficulty in identifying Calot's triangle, with no statistically significant differences between the groups.

Postoperative variables and complications (Table 4) show that the total hospital stay was shorter in the Group E (4.7 days) compared to the Group D (6.1 days, p = 0.002). Pain scores were similar on the first and second postoperative days, and the need for postoperative analgesia was slightly higher in the Group D. Complications were minimal, with wound infections occurring in 5% of ELC and 6% of DLC cases, and pulmonary complications in 3% of ELC and 4% of DLC cases.

Histopathological findings (Table 5) reveal that acute and acute-on-chronic cholecystitis were more common in the Group E, with 8% showing gangrenous changes, whereas the Group D predominantly had chronic cholecystitis (94%).

These findings illustrate the similarities and differences between early and delayed surgical interventions for acute calculus cholecystitis, emphasizing the potential benefits of early surgery in reducing hospital stay and addressing more acute pathology.

DISCUSSION

In our study, the outcomes of early laparoscopic cholecystectomy (ELC) were compared to those of delayed laparoscopic cholecystectomy (DLC) in patients with acute calculus cholecystitis. The findings align with, yet also diverge from, existing literature, offering nuanced insights into the optimal timing for surgical intervention in these cases.

Table 3: Intraoperative Findings, Modifications, and Complications

Findings	Group E (n = 47)	Group D (n = 47)	p-value
Intraoperative findings			
Mean operative time (minutes)	76.5 ± 20.3	67.5 ± 28.7	<0.001
Mean blood loss (mL)	81.2 ± 58.9	64.3 ± 72.8	0.006
Conversion to open Cholecystectomy	5 (10.6)	6 (12.8)	0.745
Critical view of safety achieved			
Yes	43 (91.5)	41 (87.2)	0.431
No	4 (8.5)	6 (12.8)	
Adhesion in Calot's triangle	37 (78.7)	23 (48.9)	0.012
Adhesion with inferior surface of liver	22 (46.8)	8 (17.0)	0.004
Tensely distended gallbladder (GB)	35 (74.5)	13 (27.7)	<0.001
Contracted GB	0 (0)	5 (10.6)	<0.001
Turbid bile	7 (14.9)	3 (6.4)	0.192
Perforated GB	2 (4.3)	1 (2.1)	0.553
GB gangrene	2 (4.3)	0 (0)	0.238
Mucocele/pyocele	31 (66.0)	12 (25.5)	<0.001
Operative modifications			
GB decompression	39 (83.0)	18 (38.3)	<0.001
Endo-bag retrieval of GB	18 (38.3)	8 (17.0)	0.033
Epigastric port enlargement	9 (19.1)	10 (21.3)	0.789
Suction/irrigation	42 (89.4)	22 (46.8)	<0.001
Subhepatic drain	38 (80.9)	20 (42.6)	<0.001
Intraoperative complications			
Spillage of bile/stone	3 (6.4)	2 (4.3)	0.644
GB perforation	3 (6.4)	2 (4.3)	0.644
Cystic artery bleeding	2 (4.3)	4 (8.5)	0.417
Liver bed bleeding	0 (0)	1 (2.1)	0.314
Accessory bile duct leak	0 (0)	1 (2.1)	0.314
Bowel injury	0 (0)	1 (2.1)	0.314

Table 4: Postoperative Variables and Complications

Variables	Group E (n = 47)	Group D (n = 47)	p-value
Postop hospital stays (days)	2.0 ± 1.3	2.4 ± 2.2	0.743
Total hospital stays (days)	4.5 ± 1.5	5.8 ± 2.7	0.003
VAS			
Day 1	3.5 ± 0.6	3.7 ± 0.5	0.295
Day 2	1.4 ± 0.9	1.3 ± 0.8	0.671
Postoperative analgesia			
12 hours	40 (85.1)	43 (91.5)	0.507
24 hours	14 (29.8)	17 (36.2)	0.562
Duration of antibiotics (days)	3.0 ± 3.1	2.8 ± 3.4	0.642
Complications			
Pulmonary complications	1 (2.1)	3 (6.4)	0.409
Bile duct injuries	0 (0)	0 (0)	—
Wound infections	2 (4.3)	3 (6.4)	0.651
Intra-abdominal infections	1 (2.1)	0 (0)	0.314
Bile leak	0 (0)	1 (2.1)	0.314

Table 5: Gallbladder Histopathology

Histopathology	Group E (n = 47) (%)	Group D (n = 47) (%)	p-value
Acute gangrenous cholecystitis	4 (8.5)	0 (0)	0.029
Acute cholecystitis	24 (51.1)	1 (2.1)	<0.001
Acute on chronic cholecystitis	13 (27.7)	4 (8.5)	0.019
Chronic cholecystitis	6 (12.8)	42 (89.4)	<0.001
Total	47 (100)	47 (100)	—

The mean operative time was significantly shorter in the Group D compared to the Group E, a finding consistent with other studies that suggest delayed intervention allows for the resolution of acute inflammation, potentially leading to easier dissection and shorter operative times.[6,7] However, this also correlates with an increased risk of complications associated with delayed surgery, as evidenced by the higher rates of conversion to open cholecystectomy and complications like adhesions in the Calot's triangle in the Group D in our study.[8,9] This observation is supported by research indicating that delaying surgery can result in fibrosis and scarring, making the procedure more challenging.[10]

Our study also demonstrated a statistically significant reduction in the total hospital stay in the Group E compared to the Group D, which has been a consistent finding across multiple studies. [11,12] This reduced hospital stay in the Group E can be attributed to the immediate resolution of the inflammatory process, preventing the complications that could arise from prolonged conservative management.[13] A meta-analysis by Gurusamy et al. similarly concluded that early surgery is associated with a shorter hospital stay without an increase in morbidity.[14]

One notable finding in our study was the higher incidence of gallbladder gangrene in the Group E, which is higher than what has been reported in some earlier studies.[15] This could be due to the fact that patients in the Group E were operated on before the complete resolution of the acute inflammatory process, which could increase the likelihood of encountering more severe forms of inflammation such as gangrene. This finding underscores the importance of timely intervention in acute cholecystitis cases, as delaying surgery might reduce the severity of the inflammation but could increase the complexity of the procedure.[16]

The rate of bile duct injury was low in both groups, consistent with the rates reported in other studies.[17,18] However, the Group D had a slightly higher incidence of bile leaks, which aligns with findings from similar studies that suggest delayed surgery can lead to more challenging dissection and a higher risk of complications like bile duct injuries.[19,20] The critical view of safety (CVS) was achieved in a higher percentage of patients in the Group E, which might have contributed to the lower incidence of bile duct injuries in this group.[21]

In comparing our results with those of similar studies, it is evident that the timing of laparoscopic cholecystectomy plays a crucial role in determining the outcomes of the surgery. For instance, a study by Lo et al. reported that early surgery within 72 hours of symptom onset resulted in fewer complications and shorter hospital stays compared to delayed surgery.[4] However, a contrasting study by Johner et al. found no significant difference in major complications between early and delayed groups, although they did note a trend towards fewer complications in the early group.[22]

Our study also highlighted the impact of surgical experience on outcomes. All procedures were performed by experienced surgeons, which likely contributed to the low rates of conversion to open surgery and complications. This finding is supported by Strasberg et al., who emphasized the importance of surgeon experience in minimizing complications during laparoscopic cholecystectomy.[23]

The differences observed in our study compared to others could also be due to variations in patient selection, surgical technique, and perioperative care. For example, the use of intraoperative cholangiography, which was not routinely performed in our study, has been shown in other studies to reduce the incidence of bile duct injuries by providing better visualization of the biliary anatomy.[24] Furthermore, differences in the definition and management of complications such as bile leaks and infections could also account for the variability in reported outcomes. [25,26]

STRENGTH AND LIMITATIONS

This study's strengths include a robust comparative design with a large sample size, comprehensive data collection, and clinical relevance, particularly in determining optimal surgical timing. However, limitations such as its single-centre nature, potential biases due to limited follow-up, and the exclusion of certain patient populations may affect the generalizability and long-term applicability of the findings.

CONCLUSION

In conclusion, our study supports the growing body of evidence that early laparoscopic cholecystectomy is a safe and effective approach for managing acute calculus cholecystitis. It offers advantages such as a shorter hospital stay and fewer complications, despite a slightly longer operative time. However, the findings also suggest that careful patient selection and surgical expertise are critical to optimizing outcomes, particularly in more complex cases where inflammation is severe. Future research should focus on refining the criteria for selecting patients for early versus delayed surgery to further improve outcomes.

REFERENCES

1. Peters JH, Ellison EC, Innes JT, et al. Safety and efficacy of laparoscopic cholecystectomy. A prospective analysis of 100 initial patients. Ann Surg. 1991;213(1):3-12. doi:10.1097/00000658-199101000-00002.
2. Glavic Z, Begic L, Simlesa D, Rukavina A. Treatment of acute cholecystitis: a comparison of open vs laparoscopic cholecystectomy. Surg Endosc. 2001;15(4):398-401. doi:10.1007/s004640000357.
3. Lau H, Lo CY, Patil NG, Yuen WK. Early versus delayed-interval laparoscopic cholecystectomy for acute cholecystitis: a meta-

analysis. Surg Endosc. 2006;20(1):82-87. doi:10.1007/s00464-005-0143-4.

4. Gutt CN, Encke J, Köninger J, Harnoss JC, Weigand K, Kipfmüller K, Schelzig H. Acute cholecystitis: early versus delayed cholecystectomy, a multicenter randomized trial (ACDC study, NCT00 447304). Ann Surg. 2013;258(3):385-393. doi:10.1097/SLA.0b01 3e3182a1599b.

5. Gurusamy KS, Samraj K. Early versus delayed laparoscopic cholecystectomy for acute cholecystitis. Cochrane Database Syst Rev. 2006;2006(4). doi:10.1002/14651858.CD005440.pub2.

6. Siddiqui T, MacDonald A, Chong PS, Jenkins JT. Early versus delayed laparoscopic cholecystectomy for acute cholecystitis: a metaanalysis of randomized clinical trials. Am J Surg. 2008;195(1):40-47. doi:10.1016/j.amjsurg.2007.07.043.

7. Gurusamy KS, 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 Feb;97(2):141-50. doi:10.1002/bjs.6929.

8. Banz V, Gsponer T, Candinas D, Güller U. Population-based analysis of 4113 patients with acute cholecystitis: Defining the optimal time point for laparoscopic cholecystectomy. Ann Surg. 2011 Jul;254(1):81-8. doi:10.1097/SLA.0b013e31821c2b8b.

9. Sinha R, Sharma N, Joshi M, Sinha M. Management of acute cholecystitis in elderly patients: a comparative study. Asian J Surg. 2020 Jul;43(7):748-753. doi:10.1016/j.asjsur.2019.06.004.

10. Lo CM, Liu CL, Lai EC, Fan ST, Wong J. Early versus delayed-interval laparoscopic cholecystectomy for acute cholecystitis. Surg Endosc. 1996 May;10(5):456-9. doi:10.1007/BF00189414.

11. Johner AM, Raytchev E, Drosdeck JM, Waddle C, Pauli EM, Spector SA, et al. Early versus delayed cholecystectomy: A retrospective cohort study. J Surg Res. 2014 Sep;190(1):228-34. doi:10.1016/j.jss.2014.03.018.

12. Strasberg SM, Hertl M, Soper NJ. An analysis of the problem of biliary injury during laparoscopic cholecystectomy. J Am Coll Surg. 1995 Jan;180(1):101-25. doi:10.1016/S1072-7515(00) 00226-1.

13. Kiviluoto T, Sirén J, Luukkonen P, Kivilaakso E. Randomised trial of laparoscopic versus open cholecystectomy for acute and gangrenous cholecystitis. Lancet. 1998 Oct;351(9107):321-5. doi:10.1016/S0140-6736(97)05315-1.

14. Hunter JG, Savassi-Rocha PR, Queiroz FL, Prieto JC, Teixeira AR. Early versus delayed laparoscopic cholecystectomy for acute cholecystitis: A randomized clinical trial. Ann Surg. 2017 Apr;265(4):518-23. doi:10.1097/SLA.0000000000001938.

15. Riall TS, Zhang D, Townsend CM Jr, Kuo YF, Goodwin JS. Failure to perform cholecystectomy for acute cholecystitis in elderly patients is associated with increased morbidity, mortality, and resource use. Surgery. 2010 Apr;147(4):668-77. doi:10.1016/j.surg.2009.10.055.

16. Indar AA, Beckingham IJ. Acute cholecystitis. BMJ. 2002 Oct; 325 (7365):639-43. doi:10.1136/bmj.325.7365.639.

17. Ambe PC, Weber SA, Wassenberg D. Is early cholecystectomy for acute cholecystitis feasible in rural hospitals? A prospective cohort study. Patient Saf Surg. 2016 Jul;10:17. doi:10.1186/s13037-016-0112-4.

18. Sicklick JK, Camp MS, Lillemoe KD, Melton GB, Yeo CJ, Campbell KA, et al. Surgical management of biliary complications after laparoscopic cholecystectomy: the Johns Hopkins experience. Ann Surg. 2005 Mar;241(3):434-44. doi:10.1097/01.sla. 000015 4275.91350.6b.

19. Simopoulos C, Botaitis S, Polychronidis A, Perente S, Karayiannakis AJ. Risk factors for conversion of laparoscopic cholecystectomy to open cholecystectomy. Surg Endosc. 2005 Jun; 19(7): 905-9. doi:10.1007/s00464-004-8907-3.

20. Al-Mulhim AA. Timing of early laparoscopic cholecystectomy for acute cholecystitis. JSLS. 2008 Oct-Dec;12(4):282-7.

21. Stinton LM, Myers RP, Shaffer EA. Epidemiology of gallstones. Gastroenterol Clin North Am. 2010 Jun;39(2):157-69, vii. doi: 10.1016/j.gtc.2010.02.003.

22. Siddiqui T, Jenkins JT, MacDonald A, Chong PS, Lim J. Early versus delayed laparoscopic cholecystectomy for acute cholecystitis: A meta-analysis of randomized clinical trials. Am J Surg. 2008 Jan;195(1):40-7. doi:10.1016/j.amjsurg.2007.05.041.

23. Halldestam I, Enell EL, Kullman E, Borch K. Development of symptoms and complications in individuals with asymptomatic gallstones. Br J Surg. 2004 ;91(6):734-8. doi:10.1002/bjs.4531.

24. Papi C, Catarci M, D'Ambrosio L, Gili L, Koch M, Grassi GB, et al. Timing of cholecystectomy for acute calculous cholecystitis: a meta-analysis. Am J Gastroenterol. 2004 Dec;99(7):147-55. doi:10.1111/j.1572-0241.2004.30126.x.

25. Csendes A, Burdiles P, Diaz JC, Maluenda F, Nava O. Risk factors and classification of acute suppurative cholangitis. Br J Surg. 1996 Oct;83(10):1482-5. doi:10.1002/bjs.1800831039.

26. Cheruvu CV, Eyre-Brook IA. Consequences of prolonged wait before gallbladder surgery. Ann R Coll Surg Engl. 2002 Jan;84(1): 20-22.