

Original Article

A RANDOMIZED COMPARATIVE STUDY OF EARLY AND DELAYED LAPAROSCOPIC CHOLECYSTECTOMY IN ACUTE CHOLECYSTITIS: A TERTIARY CENTER EXPERIENCE AND REVIEW OF LITERATURE

RAHUL YADAV^{1*}, HARSHITA RAO², GAURAB GOEL³

¹Department of Surgical Oncology, Aaiims Jodhpur, Rajasthan, India, ²Department of Anaesthesia, Senior Resident, Sms Medical College, Jaipur, Rajasthan, India. ³Department of General Surgery, Sms Medical College, Jaipur, Rajasthan, India
*Corresponding author: Rahul Yadav; *Email: rahul073@gmail.com

Received: 11 Jun 2023, Revised and Accepted: 27 Jul 2023

ABSTRACT

Objective: It is established that the standard treatment for acute cholecystitis is laparoscopic cholecystectomy. However, the question of the timing of surgery remains controversial. To compare early laparoscopic cholecystectomies (within 72 h of symptom onset) and delayed laparoscopic cholecystectomies (beyond 72 h) for acute cholecystitis in terms of intra-operative difficulties and post-operative complications.

Methods: The patients operated on for acute cholecystitis, between December 2018 and December 2021, were included in a prospective study. They were divided into two groups based on whether surgery was performed before (group 1) or after (group 2) 72 h after the onset of symptoms. We conducted a comparison between the two groups.

Results: The two groups were comparable in terms of demographics, clinical presentation, and radiological findings. The duration of surgery was significantly longer for group 2 (53.6 min versus 30.7 min, $p < 0.001$). There was more conversion in group 2 than in group 1, without a significant difference (6% versus 0%, $p = 0.17$). There were no postoperative deaths during the study period. Specific post-operative complications were comparable between the two groups. The post-operative hospital stay was significantly longer in group 2 (9.3 d versus 5.4 d)

Conclusion: In the case of acute cholecystitis, early surgery can reduce the cost of care, the duration of surgery and the hospital stay while the conversion rate and postoperative morbidity are comparable to the delayed treatment.

Keywords: Cholelithiasis, Acute cholecystitis, Laparoscopic cholecystectomy

© 2023 The Authors. Published by Innovare Academic Sciences Pvt Ltd. This is an open access article under the CC BY license (<https://creativecommons.org/licenses/by/4.0/>)
DOI: <https://dx.doi.org/10.22159/ijcpr.2023v15i5.3059>. Journal homepage: <https://innovareacademics.in/journals/index.php/ijcpr>

INTRODUCTION

Cholelithiasis has increasingly become a major cause of abdominal pain and discomfort in the developing world. Its occurrence has been found to be high (7.4%) in the adult population of North India [1]. Acute cholecystitis is one of the most significant acute gallbladder diseases associated with gallstones and presents with a spectrum of symptoms ranging from only mild pain and nausea to a severe, life-threatening illness with complications.

The principal complication is recurrent biliary colic and cholestasis. The latter may lead to ascending cholangitis, and whilst this can be managed with antibiotics, other complications cannot be cured conservatively, such as gangrenous changes, gall bladder perforation and biliary leakage, and acute necrotic gallstone pancreatitis [2-5]. Liver abscesses and underlying incidental carcinoma have also been reported in some cases [2, 6]. The risk of developing second and subsequent episodes of acute cholecystitis is higher than the risk of suffering an initial episode [7, 8].

For the management of acute cholecystitis with cholelithiasis the appropriate timing for laparoscopic cholecystectomy remains controversial [9].

Two approaches are available for the treatment of acute cholecystitis:

- The first approach is early (within 7 d of onset of symptoms) laparoscopic cholecystectomy as a definitive treatment after establishing the diagnosis and surgical fitness of the patient in the same hospital admission [10-13].
- The second approach is conservative treatment, which is successful in about 90% of the cases, and then delayed cholecystectomy is performed in the second hospital admission after an interval of 6-12 w [14].

Early open cholecystectomy had been established as the preferred treatment of acute cholecystitis to reduce morbidity, mortality, and total hospital stay [15]; however, with the advent of Laparoscopic Cholecystectomy, the benefits of early surgery have been the subject of some contention.

On the other hand, Delayed cholecystectomy potentially increases the chance of further gallstone-related complications [12] during the waiting interval and thus additional hospital admission. Thus, the choice of approach still depends largely upon hospital infrastructure, surgical expertise, and the patient's condition.

MATERIALS AND METHODS

Study area

This study was conducted on patients admitted Department of General Surgery, SMS Hospital, Jaipur, Rajasthan.

Study type

Hospital-based Randomized comparative study.

Study period: From December 2018 to December 2021.

Sample size

60 patients operated between December 2018 to December 2021 as per the inclusion and exclusion criteria. During the study period, all patients were operated by the same surgical unit and were given uniform conservative/medical treatment.

Sampling technique

Single random technique through chit box method.

Inclusion criteria

- Age group (>18 y) and either sex.

• Patients come to the Emergency/Out Patient Department with acute symptoms and are diagnosed as a case of acute cholecystitis based on clinical and laboratory investigations.

• Confirmed cases of cholelithiasis either by Ultrasonography (USG)/Computed Tomography (CT)/Magnetic Resonance Cholangiopancreatography (MRCP).

• One who has given written informed consent.

Exclusion criteria

• History of bleeding disorders.

• USG or CT evidence of cirrhosis, intrahepatic gall bladder, liver mass or abscess or periampullary neoplasm.

• Clinical or USG evidence of suppurative or necrotizing cholecystitis, gall bladder empyema, or perforation.

• Multiple prior laparotomies.

• Morbid obesity.

• Pregnancy

• Severe systemic organ dysfunction (chronic liver, renal or heart diseases).

Workup of patients

Eligible patients were explained about the two options of treatment (early and delayed laparoscopic cholecystectomy) and informed consent was obtained. Patients were then randomized into two groups, "early" and "delayed" groups by chit-box method.

Division of groups

Group 1-Early LC Early laparoscopic cholecystectomy will be defined as an operation performed within 72 h of admission to the hospital.

GROUP 2-DELAYED LC In the delayed group, conservative management with intravenous fluids and antibiotics was done. Patients who responded to conservative management underwent an elective laparoscopic cholecystectomy 6–8 w after the acute episode.

RESULTS

Preoperative clinical features

Group 1 exhibited a higher prevalence of thickened gallbladder (33.3% vs. 86.7%) and distended gallbladder (53.3% vs. 86.7%) compared to Group 2. The incidence of Murphy's sign was consistent in both groups (83.3% for both). However, pericholecystic fluid was significantly more prevalent in Group 2 (6.6%) than in Group 1 (33.3%).

Operative parameters and postoperative outcomes

Operative time was significantly shorter in Group 1 (30.7±4.3 min) compared to Group 2 (53.6±9.6 min) (p<0.001). Blood loss showed no significant difference between the groups (88.3±45.3 ml in Group 1, 94.16±51.5 ml in Group 2; p = 0.6435). The occurrence of severe adhesions during surgery was higher in Group 2 (37%) compared to Group 1 (13%) (p = 0.03). Conversion to open cholecystectomy was observed in two operations (6%) in Group 2, while no conversions occurred in Group 1 (p = 0.176). Total hospital stay was significantly shorter in Group 1 (5.4±1.5 d) compared to Group 2 (9.3±1.4 d) (p<0.001).

Postoperative complications

The use of a drain showed no significant difference between Group 1 (13%) and Group 2 (20%) (p = 0.468). Wound infections were observed in 6% of patients in Group 2, while none occurred in Group 1 (p = 0.176). Chest infection was reported in 3% of patients in Group 2, with no cases in Group 1 (p = 0.3432). Notably, major bile duct injury was not observed in either group.

Table 1: Preoperative clinical features

	Group 1	Group 2
Thickened gallbladder	10 (33.3%)	26 (86.7%)
Distended gallbladder	16 (53.3%)	26 (86.7%)
Murphy's sign	25 (83.3%)	25 (83.3%)
Pericholecystic fluid	2 (6.6%)	10 (33.3%)

Table 2: Operative parameters and postoperative outcomes

	Group 1	Group 2	p-value
Mean operative time (Range)	30.7 ± 4.3 (23-40) min	53.6 ± 9.6 (34-68) min	<0.001
Average blood loss	88.3 ± 45.3 ml	94.16 ± 51.5 ml	0.6435
Severe adhesions	4/30 (13%) Patients	11/30 (37%) Patients	0.03
Conversion to open cholecystectomy	None (0%)	2/30 (6%) Operations	0.176
Total hospital stay	5.4 ± 1.5 d	9.3 ± 1.4 d	<0.001

Post-operative complications

Table 3: Postoperative complications

	Group 1	Group 2	p-value
Use of drain	4/30 (13%) patients	6/30 (20%) patients	0.468
Wound infections	NONE	2/30 (6%) patients	0.176
Chest infection	NONE	1/30 (3%) patients	0.3432
Major bile duct injury	NONE	NONE	0

DISCUSSION

Laparoscopic cholecystectomy (LC) was started in 1987 and in a few years became the "gold standard" for the treatment of symptomatic cholelithiasis. However, the application of LC in the setting of acute cholecystitis is still controversial.

In the early years of laparoscopic surgery, acute cholecystitis was considered a relative contraindication to LC [12, 16]. However, reports in the last decade [9-15, 17-24] have suggested that LC is a

feasible and safe procedure for acute cholecystitis also, although the complications and conversion rates are variable. However, more studies are required for conclusive results.

We, therefore, undertook a prospective randomized study comparing early versus delayed LC for acute cholecystitis and also to evaluate the feasibility and safety in our set-up. There was no significant difference in age, biochemical parameters, and radiological findings between 2 groups of patients.

The mean operation time in our study was 30.7 min in the early group and 53.6 min in the delayed group. The difference was statistically significant ($p < 0.001$). It is in contrast to the reports from other trials, which showed no significant difference in operative time between the two groups.

Optimal timing of surgery

More surgeons agree that in acute cholecystitis, timing of cholecystectomy is an important factor in determining outcome. In the past, the optimal timing for laparoscopic cholecystectomy for patients with acute cholecystitis had generally been considered to be 6 to 8 w after the acute phase to allow the resolution of the acute inflammation of the gallbladder [28]. However, several clinical trials proved that early laparoscopic cholecystectomy is safe and shorten hospital stay, with morbidity and mortality similar to those of elective delayed cholecystectomy [25, 29, 30].

In a retrospective analysis of 100 patients, Ohta *et al.* [30] compared 4 timing groups of laparoscopic cholecystectomy (≤ 72 h, 4–14 d, 3–6 w, and > 6 w after the onset of symptoms) and found that the best timing for laparoscopic cholecystectomy for acute cholecystitis is within 72 h, which provides the shortest total hospital stay versus operations performed later.

In addition to the clinical studies, the meta-analyses of randomized clinical trials in the literature also demonstrated that early laparoscopic cholecystectomy (24–72 h of onset) provides a benefit over delayed laparoscopic cholecystectomy (6–12 w later) in terms of total hospital stay, with conflicting results on conversion rates and postoperative complications [31, 32].

Siddiqui *et al.* [9] 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.

More than 90% of our patients in the early group had surgery within 24 h of admission, after initial stabilization and this early intervention has been translated into early resolution of main pathology and systemic inflammation, which led to shorter hospital stay and less exposure to higher antibiotics.

Intraoperative findings

The technical difference of LC is related to operative findings during early surgery. As shown in our study, 33 per cent of patients in the delayed group presented with severe adhesions, due to which Calot's triangle anatomy was not visible, in contrast to 13 per cent of patients who were operated early. Although not statistically significant, these adhesions were prime reasons behind increased operative times and more blood loss.

There was no significant difference in blood loss between the two groups; the mean blood loss in the early group was 88.37 ml and 94.16 ml in the delayed group. Although there are not many studies which compared the difference in blood loss, this one study has documented more blood loss in the early group [9], due to highly vascular adhesions around inflammatory gallbladder and oozing from the inflammatory gallbladder bed.

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 the organization of the adhesions, leading to scarring and contraction, occurs during the cool-down period.

Conversion rate

Most of the studies have failed to demonstrate any significant difference in conversion rates between both types of interventions and this provides a strong jolt to the prior belief of increased inflammation in acute cases.

In this study also, a very small number of cases needed to be converted from laparoscopic to open technique. In the early LC group, not even a single patient needed a conversion, while in delayed LC, two cases were converted due to severe adhesions, non-visualization of planes and inability to progress. This supports the feasibility of LC in early periods.

Postoperative complications

In a best-evidence topic that analyzed 92 papers (meta-analyses, randomized control trials, prospective controlled studies, and retrospective cohort studies), it was concluded that [32] 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, we found that intraoperative and postoperative complications were not common with either early or delayed laparoscopic cholecystectomy.

None of the patients had postoperative wound infection or chest infection, requiring prolonged hospital stay, in cases of early intervention. The patients in the other group also showed similar results except two patients developing wound infections and one developing hospital-acquired chest infection, which may be attributed to their old age and diabetic status.

Subhepatic drains were placed in 4 and 6 patients in the early LC group and delayed LC group, respectively. No major bile duct injury was reported in any patient, in any of the groups.

Total hospital stay

Falor *et al.* [28] performed early laparoscopic cholecystectomy (within 48 h of admission) in 117 of 303 patients with mild gallstone pancreatitis; for the rest of the patients, the operation was delayed until the normalization of laboratory values. They suggested that early laparoscopic cholecystectomy is safe, resulting in shortened hospital stays and decreased use of endoscopic retrograde cholangiopancreatography (ERCP) without increased morbidity and mortality.

Chang *et al.* [25] 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 h) 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 [31].

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 [33].

Similar to the above clinical studies, we found that hospitalization duration was significantly shorter, 5.4 d in the early LC group and 9.3 d in the delayed LC group (p -value < 0.001) and treatment-related costs were lower with early laparoscopic cholecystectomy compared with delayed laparoscopic cholecystectomy for acute cholecystitis.

Table 4: Comparison of operative parameters and postoperative outcomes in early and delayed laparoscopic cholecystectomy

	Early laparoscopic cholecystectomy			Delayed laparoscopic cholecystectomy				
	Operation duration (mean)	Conversion rate	Early complications	Duration of hospitalization (mean)	Operation duration	Conversion rate	Early complications	Duration of hospitalization
Rajcock <i>et al.</i> 2016	75.9 min	3.2 %	12.9 %	7.4 d	90.0 min	16.1%	32.3 %	11.5 d
Kolla <i>et al.</i> 2004	104 min	25%	15%	4.1 d	93 min	25%	20%	10.1 d
Ozkardes <i>et al.</i> 2014	67 min	13.3%	26.7%	5.2 d	71.3 min	0%	0%	7.8 d
ACDC trial	71 min	9.9%	14.4%	5.4 d	80 min	11.9%	40.4%	10.03 d
Verma <i>et al.</i>	65.78 min	10%			56.83 min	6.6%		

CONCLUSION

In conclusion, both early and delayed laparoscopic cholecystectomy have been shown to be feasible and safe treatment options for acute cholecystitis. However, early cholecystectomy offers several advantages. It provides definitive treatment during the initial hospital admission, avoiding the complications and challenges of failed conservative management and recurrent symptoms that may necessitate emergency surgery later on. This early intervention can lead to better patient outcomes and reduced morbidity.

Another significant benefit of early laparoscopic cholecystectomy is the shorter total hospital stay compared to delayed cholecystectomy. This is particularly advantageous from an economic perspective, as it reduces the burden on the healthcare system, especially in our country. Shorter hospital stays also contribute to patient satisfaction and faster recovery.

Moreover, early laparoscopic cholecystectomy was associated with shorter operation times and lower conversion rates. The reduced severity of adhesions in patients operated on early in the course of the disease likely contributed to these improved surgical outcomes. Minimizing the complexity of the surgical procedure can lead to better surgical efficiency and decreased risk of complications.

FUNDING

Nil

AUTHORS CONTRIBUTIONS

All the authors have contributed equally.

CONFLICT OF INTERESTS

Declared none

REFERENCES

- Pitchumoni CS. Gallstone disease and its complications. Med Update. 2010;20(5):383-9. Available from: www.apiindia.org/pdf/medicine_update_2010/ge_and_hepatology_05b.pdf.
- Lubasch A, Lode H. Antibiotic therapy in cholecystitis, cholangitis and pancreatitis. Internist. 2000;41(2 Pt 1):168-74. doi: 10.1007/s001080050021, PMID 10743597.
- Tokunaga Y, Nakayama N, Ishikawa Y, Nishitai R, Irie A, Kaganoji J. Surgical risks of acute cholecystitis in elderly. Hepato Gastroenterology. 1997;44(15):671-6. PMID 9222669.
- Ziessman HA. Acute cholecystitis, biliary obstruction, and biliary leakage. Semin Nucl Med. 2003;33(4):279-96. doi: 10.1016/S0001-2998(03)00032-1, PMID 14625840.
- Browning JD, Horton JD. Gallstone disease and its complications. Semin Gastrointest Dis. 2003;14(4):165-77. PMID 14719767.
- Schirmer BD, Winters KL, RF E. Cholelithiasis and cholecystitis. J Long Term Eff Med Implants. 2005;15:329-38. doi: 10.1615/JLongTermEffMedImplants.v15.i3.90.
- Bakalagos EA, Melvin WS, Kirkpatrick R. Liver abscess secondary to intrahepatic perforation of the gallbladder, presenting as a liver mass. Am J Gastroenterol. 1996;91(8):1644-6. PMID 8759679.
- Hoem D, Viste A, Horn A, Gislason H, Søndena K. Cholecystectomy improves long-term success after endoscopic treatment of CBD stones. Hepato Gastroenterology. 2006;53(71):655-9. PMID 17086862.
- 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. 2008;195(1):40-7. doi: 10.1016/j.amjsurg.2007.03.004, PMID 18070735.
- Sinha R, Sharma N. Acute cholecystitis and laparoscopic cholecystectomy. JSLS J Soc Laparoendosc Surg. 2002;6(1):65-8. PMID 12002300.
- Lo CM, Liu CL, Lai EC, Fan ST, Wong J. Early versus delayed laparoscopic cholecystectomy for treatment of acute cholecystitis. Ann Surg. 1996;223(1):37-42. doi: 10.1097/0000658-199601000-00006, PMID 8554416.
- Lo CM, Liu CL, Fan ST, Lai EC, Wong J. Prospective randomized study of early versus delayed laparoscopic cholecystectomy for acute cholecystitis. Ann Surg. 1998;227(4):461-7. doi: 10.1097/0000658-199804000-00001, PMID 9563529.
- Johansson M, Thune A, Blomqvist A, Nelvin L, Lundell L. Management of acute cholecystitis in the laparoscopic era: results of a prospective, randomized clinical trial. J Gastrointest Surg. 2003;7(5):642-5. doi: 10.1016/s1091-255x(03)00065-9, PMID 12850677.
- Kolla SB, Aggarwal S, Kumar A, Kumar R, Chumber S, Parshad R. Early versus delayed laparoscopic cholecystectomy for acute cholecystitis: a prospective randomized trial. Surg Endosc. 2004;18(9):1323-7. doi: 10.1007/s00464-003-9230-6, PMID 15803229.
- Van Der Linden W, Edlund G. Early versus delayed cholecystectomy: the effect of a change in management. Br J Surg. 1981;68(11):753-7. doi: 10.1002/bjs.1800681102, PMID 7296243.
- Lai PBS, Kwong KH, Leung KL, Kwok SP, Chan AC, Chung SC. Randomized trial of early versus delayed laparoscopic cholecystectomy for acute cholecystitis. Br J Surg. 1998;85(6):764-7. doi: 10.1046/j.1365-2168.1998.00708.x, PMID 9667702.
- Madan AK, Aliabadi Wahle S, Tesi D, Flint LM, Steinberg SM. How early is early laparoscopic treatment of acute cholecystitis? Am J Surg. 2002;183(3):232-6. doi: 10.1016/s0002-9610(02)00789-4, PMID 11943117.
- Peng WK, Sheikh Z, Nixon SJ, Paterson Brown S. Role of laparoscopic cholecystectomy in the early management of acute gallbladder disease. Br J Surg. 2005;92(5):586-91. doi: 10.1002/bjs.4831, PMID 15779079.
- Bhattacharya D, Ammori BJ. Contemporary minimally invasive approaches to the management of acute cholecystitis: a review and appraisal. Surg Laparosc Endosc Percutan Tech. 2005;15(1):1-8. doi: 10.1097/01.sle.0000153730.24862.0a, PMID 15714147.
- Shikata S, Noguchi Y, Fukui T. Early versus delayed cholecystectomy for acute cholecystitis: a meta-analysis of randomized controlled trials. Surg Today. 2005;35(7):553-60. doi: 10.1007/s00595-005-2998-3, PMID 15976952.
- Lau H, Lo CY, Patil NG, Yuen WK. Early versus delayed-interval laparoscopic cholecystectomy for acute cholecystitis: a metaanalysis. Surg Endosc. 2006;20(1):82-7. doi: 10.1007/s00464-005-0100-2, PMID 16247580.
- Papi C, Catarci M, D'Ambrosio L, Gili L, Koch M, Grassi GB. Timing of cholecystectomy for acute calculous cholecystitis: a meta-analysis. Am J Gastroenterol. 2004;99(1):147-55. doi: 10.1046/j.1572-0241.2003.04002.x, PMID 14687156.
- Casillas RA, Yegiyants S, Collins JC. Early laparoscopic cholecystectomy is the preferred management of acute cholecystitis. Arch Surg. 2008;143(6):533-7. doi: 10.1001/archsurg.143.6.533, PMID 18559744.
- Gonzalez Rodriguez FJ, Paredes Cotore JP, Ponton C, Rojo Y, Flores E, Luis Calo ES. Early or delayed laparoscopic cholecystectomy in acute cholecystitis? Conclusions of a controlled trial. Hepato Gastroenterology. 2009;56(89):11-6. PMID 19453020.
- Chang TC, Lin MT, Wu MH, Wang MY, Lee PH. Evaluation of early versus delayed laparoscopic cholecystectomy in the treatment of acute cholecystitis. Hepato-Gastroenterology. 2009;56(89):26-8. PMID 19453022.
- Kum CK, Eypasch E, Lefering R, Paul A, Neugebauer E, Troidl H. Laparoscopic cholecystectomy for acute cholecystitis: is it really safe? World J Surg. 1996;20(1):43-8. doi: 10.1007/s002689900008, PMID 8588411.
- Al-Haijar N, Duca S, Molnar G, Vasilescu A, Nicolescu N. Incidents and postoperative complications of laparoscopic cholecystectomies for acute cholecystitis. Rom J Gastroenterol. 2002;11(2):115-9. PMID 12145667.
- Falor AE, de Virgilio C, Stabile BE, Kaji AH, Caton A, Kokubun BA. Early laparoscopic cholecystectomy for mild gallstone pancreatitis: time for a paradigm shift. Arch Surg. 2012;147(11):1031-5. doi: 10.1001/archsurg.2012.1473, PMID 22801992.
- Macafee DA, Humes DJ, Bouliotis G, Beckingham IJ, Whyne DK, Lobo DN. Prospective randomized trial using cost-utility analysis of early versus delayed laparoscopic cholecystectomy

- for acute gallbladder disease. *Br J Surg.* 2009;96(9):1031-40. doi: 10.1002/bjs.6685, PMID 19672930.
30. Ohta M, Iwashita Y, Yada K, Ogawa T, Kai S, Ishio T. Operative timing of laparoscopic cholecystectomy for acute cholecystitis in a Japanese institute. *JLS.* 2012;16(1):65-70. doi: 10.4293/108680812X13291597716023, PMID 22906333.
31. 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):141-50. doi: 10.1002/bjs.6870, PMID 20035546.
32. 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.* 2012;10(5):250-8. doi: 10.1016/j.ijssu.2012.04.012, PMID 22525382.
33. 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):480-6. doi: 10.3109/00365521.2012.763177, PMID 23356689.
34. Wilson E, Gurusamy K, Gluud C, Davidson BR. Cost-utility and value-of-information analysis of early versus delayed laparoscopic cholecystectomy for acute cholecystitis. *Br J Surg.* 2010;97(2):210-9. doi: 10.1002/bjs.6872, PMID 20035545.
35. Johner A, Raymakers A, Wiseman SM. Cost-utility of early versus delayed laparoscopic cholecystectomy for acute cholecystitis. *Surg Endosc.* 2013;27(1):256-62. doi: 10.1007/s00464-012-2430-1, PMID 22773234.