Early versus Delayed Laparoscopic Cholecystectomy in Acute Calculus Cholecystitis in Southern Odisha - A Prospective Comparative Study

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ABSTRACT

BACKGROUND

Acute cholecystitis is a pathology of inflammatory origin, usually associated with cholelithiasis, with a high incidence in the world. Its treatment involves an important socioeconomic impact. There are two surgical therapeutic options: early laparoscopic cholecystectomy (ELC) done within 72 hours of onset of pain or delayed laparoscopic cholecystectomy (DLC) done after 6 weeks of conservative treatment. The present study intends to compare between the effectiveness of ELC vs DLC in the management of acute cholecystitis in a tertiary care setup.

METHODS

The study sample included 65 patients who were clearly documented and radiologically proven cases of acute calculous cholecystitis, met the inclusion criteria, admitted to the surgery department of MKCG MCH, Berhampur, between August 2018 and July 2020. Out of 65 patients, 33 and 32 patients were selected randomly for ELC and DLC respectively. In ELC group surgery was done within 72 hours of the onset of pain while in DLC group surgery was done after 6 weeks of initial conservative treatment. The study was conducted using a case record proforma, prepared in their local language. The questionnaire included timing of cholecystectomy, duration of antibiotic coverage, mean duration of hospital stay, number of intraoperative and postoperative complications, conversion to open cholecystectomy, and follow-up. The data was compiled and tabulated in MS ® Excel and statistically analysed using IBM ® SPSS 22.0.

RESULTS

The overall morbidity and mortality were less in ELC compared to DLC. The mean duration of surgery was less in ELC (47.36 minutes) compared to DLC (65.75 minutes). The mean duration of antibiotic coverage was lesser in ELC (3.58 days) compared to DLC (5.50 days).The mean hospital stay was less in ELC (4.67 days) to DLC (6.50 days). The overall morbidity and mortality were less in ELC.

CONCLUSIONS

ELC is considered to be a safe modality of treatment in patients with acute cholecystitis and leads to an economical treatment.

KEYWORDS

Acute Calculus Cholecystitis, Early Laparoscopic Cholecystectomy, Delayed Laparoscopic Cholecystectomy

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BACKGROUND

Gallstone disease remains one of the major causes of abdominal morbidity and mortality throughout the world.[1] Nowadays, gallbladder disease is a frequent problem in developed countries representing a major health problem.[2] It's a chronic recurrent hepatobiliary disease, the basis for which is the impaired metabolism of cholesterol, bilirubin, and bile acids, which is characterized by the formation of gallstones in the hepatic bile duct, common bile duct, or gallbladder.[3] Gallstone disease and cardiovascular disease, common diseases worldwide, are strongly associated and have a considerable economic impact.[4] Acute cholecystitis is a pathology of inflammatory origin, usually associated with cholelithiasis, with a high incidence in the world. The treatment of acute cholecystitis involves an important socioeconomic impact.[5] There are two surgical therapeutic options: early laparoscopic cholecystectomy (ELC) in which surgery is done within 72 hours of the onset of pain or delayed laparoscopic cholecystectomy (DLC) done after six weeks of initial conservative treatment.[6] The first studies that assessed early cholecystectomy as a treatment for acute cholecystitis dates back to the 1950s. In 1970, the first controlled study was published by Vander Linden and Sunzel, demonstrating better morbidity and shorter average hospital stay after open early cholecystectomy.[7]

The exponential development of laparoscopic surgery occurred during the 1990s. Some of the earlier publications about ELC did not show favouring results in terms of morbidity and mortality and a higher incidence of complications. Based on these results, ELC was discouraged and even considered a contraindication for treatment of acute cholecystitis, favouring initial conservative treatment followed by DLC.[8,9] Kiviluoto et al. reported similar results in terms of morbidity and mortality in early laparoscopic cholecystectomy and open cholecystectomy.[10] Lo et al. presented the first controlled study that compared ELC and DLC, with lower morbidity and hospital stay in the ELC.[11] However, it is important to note that many recent works of literature and articles favour ELC as a treatment of choice in acute cholecystitis. The present study intends to have a comparison between the effectiveness of ELC vs DLC in the management of acute cholecystitis in a tertiary care setup.

METHODS

The study sample included sixty-five patients who were clearly documented and radiologically proven cases of acute calculous cholecystitis, also met with the inclusion criteria, and were admitted to the Surgery department of MKCG Medical College and Hospital, Berhampur. It is a hospital-based cross-sectional, prospective comparative study conducted between August 2018 to July 2020. The present study was approved by Institutional Ethical Committee of MKCG Medical College and Hospital, Berhampur on human subject research. The IEC Number of study is 713. Out of 65 cases, 33 patients were selected randomly for ELC, and 32 were selected randomly for DLC. ELC means surgery done within 72 hours of the onset of pain while DLC means patients were discharged with conservative treatment initially for 6weeks then they were subjected to surgery.

Inclusion Criteria

All radiologically proven cases of acute calculous cholecystitis.

Exclusion Criteria

1. Patient with acalculous cholecystitis.
2. Patients with carcinoma gallbladder.
3. Patients with cholangitis, choledocholithiasis.
4. Patients who were not willing to be part of the study

Patient Data Collection and Evaluation

A detailed clinical history and physical examination was carried out and recorded in a standard proforma which included demographic factors (age and gender), dietary status (pure vegetarian, mixed: vegetarian, poultry, meat, eggs). All clinical presentations (dyspepsia, acute upper abdominal pain, jaundice, nausea/vomiting) were taken into account and then a standard physical and systemic examination was done. Murphy's sign, tenderness in right hypochondrium, palpable lump in the right hypochondrium, hepatomegaly etc. were looked for in per-abdominal examination. Laboratory investigations were sent at the time of admission — hematological (haemoglobin, TLC, DC, ESR), biochemical (FBS2hour PPBS, serum - urea, creatinine, sodium, potassium, amylase, lipase) [Liver function test (LFT) (serum – SGOT, SGPT, ALP, Bilirubin)], PT - INR, serological (HbsAg, ICTC, HCV) and urine (albumin, sugar, bile salts, bile pigments).

All patients underwent abdominal ultrasonography (echogenic focus, acoustic shadow, gravitational dependence, gallbladder thickening and pericholecystic fluid, multiple/solitary stones, CBD – diameter, thickness, echogenic foci present / not), plain X - ray abdomen erect posture AP View (10 % gallstones are radio opaque) and contrast-enhanced CT with pancreatic protocol (better anatomical delineation, biliary obstruction due to stones, evaluation of hepatic and pancreatic parenchyma or neoplastic masses and presence of enhancing lesion in the gallbladder fossa, aortic and para aortic area – mass lesion present / absent), Magnetic resonance cholangiopancreatography (MRCP) - provides superior anatomic definition of intrahepatic and extrahepatic biliary tree and pancreas, focal mass lesion at the time of admission. The Tokyo guidelines were taken into account as is practical and in accordance with the pathophysiological aspects involved in the inflammation progression from gallbladder wall to regional and systemic complications. Therefore, grade I – represents a mild disease with only wall inflammation. Th grade II - associated with local signs of complications such as palpable mass, pericholecystic fluid; onset of symptoms > 72hours; laboratory data showing leucocytosis > 18,000 / mm^3 and elevated C-reactive protein level. Finally grade III - is associated with organ dysfunction

– cardiovascular (refractory hypotension to hypovolemic resuscitation at 30 ml / kg / hour), decrease of consciousness, respiratory failure (PaO_2 / FiO_2: < 300), oliguria (creatinine: > 2 gm / dL), PT- INR > 1.5 and platelet count < 100,000 / mm^3).

Then patients were selected randomly for ELC (within 72 hours) or DLC (after 6 weeks) and the following parameters: 1. operative timing of surgery, 2. number of days of antibiotic coverage, 3. complications during intra-op and post-op, 4. number of days in hospital stay and 5. Follow up period ,were noted and evaluated. Adequate time was given to each subject. Patient's comfort was maintained during the interview. The data was collected after obtaining informed consent in their local language, in the presence of eye witness. The operative findings, intraoperative and post-operative complications were recorded and carefully analysed. The effectiveness of ELC vs DLC was compared with all the parameters recorded. The gallbladder specimen of all the cases were sent for Histopathological examination. The follow up period was taken to be 1 month from the day of discharge. The patients were subjected to investigations (TLC, serum-creatinine, LFT, serum- amylase, lipase, USG), then all the details were noted including the complications present if any. Then both ELC and DLC group were also compared on the basis of follow-up period.

Statistical Analysis

The data was collected according to the given Case proforma and compiled and tabulated in Microsoft ® Excel. Observation and statistical analysis were done using mean, standard deviation, and proportions. The statistical conclusion was done using an unpaired t-test and chi-square test. All the measurements were done using IBM SPSS version 22.0. P < 0.05 was considered as statistically significant.

RESULTS

	Timing				t-Value	P-Value
	ELC		DLC			
Age (Years)	Mean	SD	Mean	SD	2.297	0.02*
	41.76	7.838	46.63	9.210		

Table 1. Age Distribution

*indicates statistically significant difference

In the study sample of 65 patients of acute calculous cholecystitis, it was found that, in the age group of 20-30 years the incidence was only 3%. The majority of patients belonged to the age group 41 - 50 years and the mean age was 41 years in ELC and 46 years in DLC. The second most common age group was found to be 31 - 40 years. The mean age of DLC group was more than mean age of the ELC group and was found to be statistically significant. (P < 0.05).

	Timing				X^2 - Value	P-Value
Sex	ELC		DLC			
	Count	Frequency (%)	Count	Frequency (%)		
Male	12	36.4	11	34.4	0.0281	0.8
Female	21	63.6	21	65.6		

Table 2. Sex Distribution

In the study population of 65 patients the incidence of female: male ratio was 1.9:1. The total number of male subjects was 36 % in ELC and DLC was 34 %, female subjects 63 % in ELC and DLC 65 %. Sex was not significant for deciding early and delayed laparoscopic cholecystectomy (P = 0.8).

	Timing				t-Value	P-Value
	ELC		DLC			
Operative Time (min)	Mean	SD	Mean	SD	14.074	< 0.0001*
	47.36	6.909	65.75	2.664		

Table 3. Operative Timing

*indicates statistically significant difference at $P < 0.05$

The mean operative time on an average in ELC was 47 minutes and in delayed was 65 minutes. The difference in timing on an average was 18 minutes with P < 0.0001. This is statistically significant. Hence, it appeared that ELC took less time as compared to DLC which was highly beneficial for the patient and the treating surgeon in managing the intra-op and post-op comorbidities.

	Timing				t-Value	p Value
Number of days of antibiotic coverage	ELC		DLC			
	Mean	SD	Mean	SD	13.0768	< 0.05*
	3.58	0.561	5.50	0.622		

Table 4. Number of Days of Antibiotic Coverage

*indicates statistically significant difference at $P < 0.05$

The number of days of antibiotic coverage in ELC was 3.58 days and in DLC was 5.50 days. The P - value calculated using unpaired t-test was statistically significant (P < 0.05). Hence, it appeared that patients who underwent ELC had lesser amount of complications as compared to DLC, as they required less number of days of antibiotic coverage.

	Timing				t-Value	P Value
Number of days in hospital stay	ELC		DLC			
	Mean	SD	Mean	SD	14.947	<0.0001*
	4.67	0.479	6.5	0.508		

Table 5. Number of Days of Hospital Stay

*indicates statistically significant difference at $P < 0.05$

Complications	Timing ELC n (%)	DLC n (%)	X^2 – Value (p Value)
Adhesions			
Yes	5 (15.0)	5 (16.0)	0.003
No	28	27	(0.956)
Bleeding[ᵃ]			
Yes	0 (0.0)	5 (16.0)	0.0244*
No	33	27	
Bile leak[ᵃ]			
Yes	1 (3.0)	0 (0.0)	1
No	32	32	

Table 6A. Complications

ᵃ Fisher's exact test applied

*indicates statistical significance at $P < 0.05$

With lesser number of days of antibiotic coverage, lesser number of complications, the mean duration of hospital stays for patients who underwent ELC was less as compared to DLC. The average number of days of hospital stay in ELC was 4.67 days while in DLC was 6.5 days. P - value calculated using unpaired t-test was statistically significant (P < 0.0001). The hospital stays in the ELC group was 2 days lesser than the DLC group.

The complications like adhesions, bleeding and bile leak was found in both the groups. Five patients of each group

had the intra-op complication of adhesion with omentum of intestinal loops which had to be managed carefully. The adhesions were found to be 15 % and 16 % respectively in the ELC and DLC groups. Similarly, other complications like bleeding and bile leak were of similar frequencies in both groups. The bleeding was due to frozen calot's triangle and it caused difficulty during dissecting cystic artery, cystic duct and gallbladder from its fossa. The P - value calculated using the chi - square test was not significant.

Complications	Timing			
	ELC		DLC	
	Count	Frequency (%)	Count	Frequency (%)
Gall bladder perforation	3	9	1	3
Conversion to open	6	18	9	28

Table 6B. Other Complications

Other complications like gall bladder perforation during the surgery and conversion of laparoscopic cholecystectomy into open cholecystectomy were of similar frequency in both the groups. The P - value calculated using the chi-square test was found to be 0.21 which was not statistically significant. Despite all the above complications, there was no death in either group. Hence, the frequency of complications was not significant.

Follow up Period	Timing			
	ELC		DLC	
	Count	Frequency (%)	Count	Frequency (%)
Bile leak	3	9	2	6
Pancreatitis	2	6	7	21

Table 7. Follow Up

In the follow-up, period bile leak was seen a bit higher in the ELC group while gallstone induced pancreatitis was seen more in the DLC group. The P - value calculated using the chi-square test was 0.157 which was not statistically significant.

DISCUSSION

The common approach for management of acute calculous cholecystitis consists of initial control of inflammation followed by interval cholecystectomy after a period of 6weeks. But with the recent advances in laparoscopic methods recent works of literature favour ELC as a method of preferred treatment in patients of acute calculous cholecystitis.

In the present study, evaluation of the mean duration of operative timing, number of days of antibiotic coverage, and number of days of hospital stay using unpaired t-test are significant ($P < 0.05$) in the ELC group as compared to the DLC group.

Overall Morbidity

Various arguments were made against early laparoscopic cholecystectomy include a high conversion rate to open cholecystectomy and other complications. Also, it was thought that delayed laparoscopic cholecystectomy leads to a technically easier surgery with a lower conversion rate. However, gallstone-induced pancreatitis, recurrent attacks were more in the DLC group. So, with the advancement of laparoscopic techniques recent articles advocate that early laparoscopic cholecystectomy is the treatment of choice for acute calculous cholecystitis. In the present study, the morbidity rate was the same in both the groups as no cases got converted to open cholecystectomy. But, there is always an increased risk in a waiting period in the delayed group, with an increase in the number of complications in the intra-op, post-op, and follow-up period. In a study conducted by Guruswamy KS et al. it was concluded that overall morbidity is lower in the ELC group than the DLC group.[6]

Surgical Morbidity

Surgical intraoperative complications like bile leak and gallbladder perforation are lower in the ELC group compared to the DLC group where there were more bile leak and gallbladder perforation. Other complications, like adhesions, were similar in both groups. The adhesions were seen to the omentum of intestinal loops etc. The calot's triangle was also found to be frozen in some cases which lead to difficult dissection of cystic artery, cystic duct and gallbladder from its fossa which lead to increased chances of intra-operative bleeding. There were comparatively more complications like gallstone induced pancreatitis, bile leak in the post-op and follow-up period in the DLC group as compared to the ELC group. But the differences were not statistically significant (P - value < 0.05). Similar results were shown in the study conducted by Senthil RM et al. which proved that ELC is the preferred treatment in treating acute calculous cholecystitis.

Timing

Most surgeons agree that the timing of cholecystectomy in the early group is important in determining the outcome. Ideally, surgery should be performed within 72 hours of onset of symptoms because after that more inflammatory changes occur and the gallbladder will be more edematous. In this study, the ELC group was operated within a 72 hours golden period.

In the DLC group patients had been treated conservatively in their first admission and operated on after an interval of 6 weeks from the onset of symptoms. The mean timing of surgery was reduced in ELC as compared to DLC that was 47.36 minutes and 65.75 minutes respectively. The plane of dissection was easier in ELC which contributed to the less duration of surgery.

Hence, it appears that ELC takes less time as compared to DLC which is highly beneficial for the patient and the treating surgeon in managing the intra-op and post-op comorbidities.

The P - value calculated was found to be statistically significant ($P < 0.05$) Another study conducted by Guruswamy KS et al. showed the mean duration to be 55 minutes and 70 minutes respectively in the ELC and DLC groups.[6]

Days of Antibiotic Coverage

In the present study, the mean duration of antibiotic coverage was found to be 3.58 days in the ELC group and 5.50 days in the DLC group. The number of days of antibiotic coverage was less as compared to that of the DLC group as the number of infections, complications in the ELC group were comparatively less as compared to the DLC group. Another study conducted by Senthil RM et al. showed the number of days of antibiotic coverage was 3.97 days in the ELC group and 5.30 days in the DLC group.[5] The studies revealed that ELC had significantly reduced the number of days of antibiotic coverage as compared to the DLC group.

Days of Hospital Stay

In the present study mean duration of hospital stay in ELC and DLC was found to be 4.67 days and 6.50 days respectively and an average of 4 days in the previous admission in the DLC group. With lesser amount of days of antibiotic coverage, less number of complications, the mean duration of hospital stay for ELC patients was less as compared to DLC patients.

ELC patients had a significantly lower average hospital stay than DLC patients. All of the articles published to date offer significantly lower results of hospital stay in the ELC group with differences in days of stay ranging from 2 days in the population study of Banz et al.[12] to 4.97 days in the study of Senthil RM et al. to Lai et al. 7.6 days. Hence, ELC has a lower hospital stay in turn direct effect on cost savings and time savings.

CONCLUSIONS

ELC provides better morbidity results, less operative timing, less duration of antibiotic coverage, less duration of hospital stay which shows a clear trend towards a lower mortality rate. This, in turn, has a direct effect on cost savings and manpower. Hence, ELC is the preferred modality of treatment in patients with acute calculous cholecystitis.

Data sharing statement provided by the authors is available with the full text of this article at jebmh.com.
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