

A Comparative Study of Clinical Outcome in Early and Interval Cholecystectomy in Acute Calculous Cholecystitis

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Abstract:

Background: The optimal timing of laparoscopic cholecystectomy in the treatment of acute cholecystitis remains controversial. Two approaches are available for the treatment of acute cholecystitis – Early cholecystectomy - performed within 72 hours of the onset of disease. Delayed or interval cholecystectomy - performed 6 to 8 weeks after initial medical treatment with anti-microbial agents.

The study aims: To compare both early and delayed or interval cholecystectomy in acute calculous cholecystitis.

Methodology: Patients with Acute Cholecystitis admitted to the General Surgery department at GMC Kadapa were divided to two groups. Early laparoscopic cholecystectomy is performed in patients of group A and Delayed or interval cholecystectomy is planned in patients of group B who presented after 72 hours.

Conclusion: There is no significant difference observed in overall clinical outcomes in patients managed by early and delayed cholecystectomy in acute calculous cholecystitis. Total overall hospital stay and overall medicine requirements are higher in the delayed cholecystectomy group when compared to the early cholecystectomy group.

Keywords: Acute Calculus Cholecystitis, Open Cholecystectomy, Laparoscopic Cholecystectomy.

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Introduction

One of the frequently occurring diseases in the developed countries of the world is acute cholecystitis. There is always a lack of agreement regarding the timing of the operation in the treatment of acute cholecystitis, since the advent of laparoscopic cholecystectomy. The optimal timing of laparoscopic cholecystectomy in the treatment of acute cholecystitis remains controversial.

Hence, the timing of surgery has been the topic of interest in my study. Mühe (under direct scope vision) first performed laparoscopic cholecystectomy in 1985. Subsequently, the same procedure using a video-laparoscope, used today, was carried out by Mouret in 1987 and was spread worldwide from Europe and the United States by Dubois and Perissat.[1] Two approaches are available for the treatment of acute cholecystitis – Early cholecystectomy - performed within 72 hours of the onset of disease.

Delayed or interval cholecystectomy - performed 6 to 8 weeks after initial medical treatment with anti-microbial agents. The exact timing of surgery, potential benefits, and cost-effectiveness of

laparoscopic cholecystectomy in the treatment of acutely inflamed gallbladder have not been established and continue to be controversial.[2] In the presence of acute inflammation, LC becomes more challenging and difficult because of edema, exudate, adhesions with adjoining structures, and distension of gallbladder, friability of tissues, unclear and distorted ductal and vascular anatomy [3], hyper vascularity, congestion, and dissemination of infection.

These risk factors predispose for the suboptimal outcome and high conversion rate to open cholecystectomy in early cholecystectomy. In delayed cholecystectomy, there is a risk of recurrence of symptoms requiring and emergency surgery, overall prolonged hospital stay, and higher hospital costs.

Hence, this study aims to compare both early and delayed or interval cholecystectomy in acute calculous cholecystitis.

Aims and Objectives

- To compare overall morbidity and mortality

between 30 patients managed with early or delayed laparoscopic cholecystectomy for acute calculous cholecystitis.

- To compare the conversion rate to open cholecystectomy between early and interval laparoscopic cholecystectomy.

Methodology

This is a prospective comparative study of 30 cases diagnosed to have acute calculous cholecystitis in two year period in the Department of General Surgery GGH, Kadapa who underwent laparoscopic cholecystectomy (early or delayed) for Acute Calculous Cholecystitis form the subjects of the study. The plan of study has been submitted to the hospital ethics committee, and their approval is taken.

All the patients were informed about the procedure and consent taken before participating in the study. All patients who are diagnosed to have Acute Calculous Cholecystitis form the subjects of the study. Patients with common bile duct stones (choledocholithiasis), acute pancreatitis, previous upper abdominal surgery, or severe concomitant medical problems and significant systemic disease deeming them unfit for laparoscopic surgery were excluded from the study.

Patients were divided into 2 study groups, and they were categorized as Group A & Group B based on their presentation to OPD with the duration of onset of disease (within or more than 72 hours). Early laparoscopic cholecystectomy is performed in patients of group A within 72 hours of the onset of symptoms. Delayed or interval cholecystectomy is

planned in patients of group B who presented after 72 hours of the onset of symptoms, after 6-8 weeks after the initial treatment with intravenous fluids, antibiotics, and analgesics.

Patients who had recurrent episodes of cholecystitis who are managed conservatively and planned for interval cholecystectomy were excluded from this study. Key outcomes were morbidity, mortality, operating times, the incidence of bile duct injury, length of hospital stay.

Demographics, clinical data were recorded for all patients. The patients are followed up until postoperative hospitalization. The evaluation criteria of the study were both operative and postoperative variables, such as operation time, intra-operative and post-operative complications, hospitalization duration (total and post-operative), and conversion rate to open cholecystectomy. For the delayed operation group, hospitalization duration was considered as the total length of stay for adding both the first and second hospitalizations. The secondary evaluation criteria were treatment-related costs, including costs of surgery, conservative treatment, hospitalization. The total expenses of hospitalization include first hospitalization, second hospitalization (for the late surgery group), and outpatient visits in between and after the admissions. Proforma used for the records of the patients, which are mentioned in annexures.

Statistics: Data collected was entered in Microsoft excel and analysed using SPSS -22.0. Mean and percentages was used for descriptive analysis.

Results

Table 1: Age Distribution

Age group (years)	No of patients (n = 30)	Percentage (%)
21-30	3	10
31-40	7	22
41-50	9	30
51-60	5	18
61-70	5	16
>71	1	4

Table 2: Gender Distribution

Sex	No. of patients (n = 30)	Percentage (%)
Male	11	36
Female	19	64
Total	30	100

Table 3: Open Conversion Rate

	Total operated Cases (n = 30)	No. Of cases converted to open	(%)
Group A	15	1	6.66
Group B	15	0	0

Table 4: Length of Hospital Stay

	Group A	Group B	P Value
Hospital Stay (Days)	5.68±0.85	7.2±0.71	<0.05
Post Op Stay (Days)	3.08±0.95	2.8±0.58	0.22

Table 5: Operating Time

Operating Time	Group A	Group B
50 – 60 Min	0	2
61 – 70 Min	1	4
71 – 80 Min	2	5
81 – 90 Min	5	2
91 – 100 Min	5	1
> 100 Min	2	1
Total	15	15

Table 6: Intra Operative Findings, Intra Op & Post Op Complications

	Group A	Group B
Intra Op Findings	GB Adhesion	2 (13%)
	GB Congestion	1 (6.66%)
	GB Perforation	0
Intra Op Complications	Bile/Stone Spillage	1 (6.66%)
	Hemorrhage	1 (6.66%)
	CBD Injury	0
	Conversion To Open Surgery	0
Post Op Complication	Bile Leakage	0
	Wound Infection	0
	Hemorrhage	0

Table 7: Studies Comparing Age Groups of Presentation

Study	Common age group of presentation
Nis (Nationwide Inpatient Sample) 2005-2009 [3]	40-59 years
Multicentre Rct	55-56 years
Addison Et Al [4]	50-59 years
This Study	41-50 years

Table 8: Studies Showing Gender of Acute Cholecystitis

References	Year	No of patients	Conversion rate	Percentage (%)
Asai [5]	2014	225	7/105	6.7
Kamalapurkar [6]	2014	84	1/60	1.7
Wright [7]	2015	445	7/92	7
Ambe [8]	2015	138	5/79	6.3
Amirthalingam [9]	2016	149	2/84	2.4
This study	2019	15	1/15	6.66

Table 9: Studies Showing Open Conversion Rates

Study	Gender predominance	Percentage (%)
Nis (Nationwide Inpatient Sample) 2005-2009 [3]	Female	64.7
Multicentre RCT	Female	62.8
Addison et al. [4]	Female	69
This Study	Female	64

Table 10: Studies Comparing Operative Times between Early and Delayed Groups

Study	Operative Time (Min)	
	Early Group	Delayed Group
Lo et al.[11]	135	105
Johansson et al.[12]	98	100
Lai et al.[13]	123	107
Kolla et al.[14]	104	93
This study	87	70

Discussion

In Acute calculous cholecystitis, the mean age of presentation in this study was found to be 48.4±14.2 years of total patients, with the common age group of presentation being 41-50 years of age.

This study is in agreement with the above meta-analysis with an open conversion rate of 6.66% in the early group. In this study, average operative duration was found to be 87.04 minutes in the early cholecystectomy group and delayed

cholecystectomy group; it is 70.56 minutes with a p-value of <0.05 , which is suggestive of significant shorter operative duration in interval cholecystectomy. Mean operative time is 80 to 100 minutes in the early laparoscopic cholecystectomy group, while it is 60 to 80 minutes in the interval laparoscopic cholecystectomy group in this study.

Siddiqui et al. analyzed four clinical studies consisting of 375 patients and found shorter hospital stay in early laparoscopic cholecystectomy and longer operation time in early laparoscopic cholecystectomy, but they found no difference observed significantly between early and delayed laparoscopic cholecystectomy groups in terms of conversion rates. [10] This study has prolonged operative time in the early group when compared to the delayed group, which is in agreement with the studies mentioned above.

Overall operating times were faster in both the groups when compared to all studies mentioned above as experienced surgeons performed surgery, increased exposure to laparoscopy as the study done recently, and the compared studies done during periods when laparoscopy was evolving. Catena and colleagues (2009) have proposed the use of a harmonic scalpel for improved hemostasis and bile stasis in laparoscopic cholecystectomy, and preliminary data suggested it may decrease the conversion rate to open procedure in patients undergoing laparoscopic cholecystectomy for acute cholecystitis. A prospective, randomized controlled trial subsequently confirmed these findings (Catena et al., 2009). [15]

In this study, three patients had recurrent symptoms, out of which two patients underwent surgical intervention before the planned time of cholecystectomy, and hence, they were excluded from our study. A study taken from the Cochrane database revealed that 18.3% of the patients were included in the delayed group, in 5 RCTs had to undergo emergency surgery in the interval period for non-resolution or recurrence of symptoms of cholecystitis before their planned operation with 45% conversion rate to open cholecystectomy. [16]

A meta-analysis study taken from the American journal of gastroenterology reviewed that more than 20% of patients planned to delayed surgery failed to respond to conservative management or suffer recurrent cholecystitis during the interval period. [17] Approximately 20% of patients initially admitted for non-operative management failed to respond to medical treatment before the period of planned interval cholecystectomy and required surgical intervention. Initial conservative therapy remains a viable option for patients who present in a delayed fashion and should be decided on an individual basis. [18]

The risk of performing late cholecystectomy (weeks after the diagnosis of cholecystitis) is that a subset of patients has a recurrence of symptoms during the period of medical management between diagnosis and surgical treatment, which leads to recurrent hospital admissions and urgent surgery. [19]

A meta-analysis of these trials demonstrated that more than 20% of patients did not respond to conservative management while waiting for the definitive treatment, and almost half of these patients required emergency surgical treatment as a result. In this same analysis, no increased morbidity in patients undergoing early treatment with laparoscopic ($p = 0.6$) or open ($p = 0.2$) cholecystectomy compared with delayed treatment, but a clear difference in the length of hospital stay, with patients undergoing delayed intervention requiring a more prolonged hospitalization. [19]

In this study, the average total hospital stay in interval cholecystectomy was found to be 7.2 days, and in early cholecystectomy, it was 5.68 days. A meta-analysis study taken from the American journal of gastroenterology stated that total hospital stay (mean \pm SD) in the immediate surgery group (9.6 ± 2.5 days versus 17.8 ± 5.8 days; with $p < 0.0001$) was significantly shorter. [17] S.A. Khuwaith conducted a study that found that the average duration of hospital stay is 18.5 days for delayed cholecystectomy. [20]

A study showed that the total hospital stays in ELC is four days shorter than with delayed surgery. It was because of the patients in the delayed group requiring two treatment episodes, one for the conservative treatment of acute cholecystitis initially, and another for definitive surgical treatment later. Besides, many patients in the delayed group required emergency readmission due to recurrent symptoms. The number of working days lost was also less with ELC in the only trial that reported this outcome. It is found that both intraoperative and postoperative complications like bile and gall stone spillage due to gall bladder perforation, bleeding, wound infection, and biliary fistula were more commonly seen with early than interval laparoscopic cholecystectomy. The higher rate of complications was noted in the early laparoscopic cholecystectomy group may also be explained by the significantly elevated initial body temperatures, and total blood leukocytes count in this group.

However, considering the shorter hospitalization duration and lesser treatment costs, early laparoscopic cholecystectomy still seems advantageous over delayed intervention. In a prospective randomized study, they have found more pre-operative and postoperative complication

rate in early cholecystectomy group than delayed cholecystectomy group similar to our study. [21]

Out of the 15 cases of early cholecystectomy, one patient had developed low output (<200cc) biliary fistula, which was seen as a bile leak in the drain, which was left in-situ. Both patients were managed conservatively with Inj. Hyoscine bromide and fatty meals. The drain output gradually reduced, and after removal of the drain when the production was negligible, patients were discharged. The further follow up of these patients was uneventful, and follow up ultrasonography abdomen didn't show any collection or abnormality in the gallbladder bed. No patients from the interval cholecystectomy group had developed a biliary fistula.

Given the inflammatory process taking place in the porta hepatis, early conversion to open cholecystectomy should be considered when proper delineation of anatomy is not clear or when progress can't be made out laparoscopically. With substantial inflammation, a partial cholecystectomy, transecting the gallbladder at the infundibulum with cauterization of the remaining mucosa, is acceptable to avoid injury to the common bile duct.

Some patients present with acute cholecystitis but have a prohibitively high operative risk. For these patients, a percutaneously placed cholecystostomy tube should be considered. Frequently performed with ultrasound guidance under local anesthesia with some sedation, cholecystostomy can act as a temporizing measure by draining the infected bile.

Percutaneous drainage of bile results in an improvement in symptoms and physiology, allowing a delayed cholecystectomy 3 to 6 months after medical optimization. In patients with cholecystostomy tubes, when fluoroscopy shows a patent cystic duct, the cholecystostomy tube can be removed and the decision for cholecystectomy determined by the patient's ability to tolerate surgical intervention.[18] In this study, the overall requirement of antibiotics and analgesics was significantly higher in the interval cholecystectomy group as compared to the early cholecystectomy group.

Patients after interval cholecystectomy returned to work early during the postoperative period as compared to immediate cholecystectomy, but higher overall morbidity in patients planned for interval cholecystectomy is seen due to recurrence of symptoms during conservative period. Due to the minimal sample size and lack of systematic decision models, cost analysis could not be done adequately in this study. Patients are not being charged for operative interventions/hospital stay, and most of the medications are available free of cost in our hospital, so the cost-effectivity of

immediate and interval cholecystectomy cannot be compared correctly in this study. In this study, we found higher total morbidity related expenses in the interval cholecystectomy group.

In a study on the cost-utility of early versus delayed laparoscopic cholecystectomy for acute cholecystitis, Wilson et al. showed that early laparoscopic cholecystectomy is less costly and results in a better quality of life. [22] A meta-analysis of randomized and other studies performed by Lau and colleagues (2006) concluded that early surgery was more cost-effective because of reduced overall length of hospital stay and avoidance of readmissions for recurrent cholecystitis or biliary colic. In this study, no mortality is noted in either of the group.

Limitations of this study:

The major drawback of this study is that the results cannot be extrapolated to the general population due to the small sample size and lack of systematic decision models in this study. The sample size should be increased furthermore to apply the results obtained to the general population. Another major drawback of the study is that exclusion of other conditions associated with acute calculous cholecystitis like choledocholithiasis, gall stone pancreatitis, severe concomitant medical problems making them unfit for surgery, grade II & III cholecystitis, and patients who are in sepsis, which lead to exclusion of complicated cases from this study which are associated with higher morbidity and mortality rates.

Hence this study obtained favorable results, like less open conversion rates, and no mortality was recorded as only uncomplicated cases are considered as a part of this study. So, the results of this study don't apply to all the cases of acute calculous cholecystitis and hence can't be used to the general population also.

This topic needs furthermore research in-depth as there has been a changing trend now and then regarding the timing of laparoscopic cholecystectomy following Acute Calculous Cholecystitis, as there is more experience, exposure, and evolvments in the field of laparoscopy.

Conclusion

There is no significant difference observed in overall clinical outcomes in patients managed by early and delayed cholecystectomy in acute calculous cholecystitis. Total overall hospital stay and overall medicine requirements are higher in the delayed cholecystectomy group when compared to the early cholecystectomy group. Overall morbidity is more in patients undergoing interval cholecystectomy group. The difficulty of procedure intraoperatively, postoperative morbidity, and

complications are higher in the early cholecystectomy group. Patients should be planned for early or interval cholecystectomy according to their severity of symptoms and the patient's willingness to undergo early surgery or initial conservative management. It still requires many numbers of cases to conclude this study.

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