Mild To Moderate Acute Gallstone Pancreatitis: A Comparative Study of Early Versus Delayed Cholecystectomy

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ABSTRACT

Objective — *To compare the duration of surgery, conversion rate, perioperative complications, hospital stay and the rate of gallstone related recurrent complications for patients undergoing early versus delayed cholecystectomy after an episode of mild to moderate acute gallstone pancreatitis (AGP).*

Study design — *Experimental study.*

Place & Duration of study — *Department of General Surgery Unit 4, Jinnah Postgraduate Medical Centre Karachi and Ziauddin University Hospital Clifton Campus Karachi, from January 2017 to December 2017.*

Methodology — *This study included 80 patients who were randomized alternatively into an early cholecystectomy (EC) and a delayed cholecystectomy group (DC).The median time interval from diagnosis of AGP to cholecystectomy was seven days in the EC group and 28 days in the DC group. Patients in both the groups were compared for conversion rate to open surgery, perioperative complications, duration of surgery, length of postoperative hospital stay and the rate of recurrent biliary events.*

Results — *The conversion rate to open surgery, perioperative complication rate and the duration of surgery were higher in the EC group. However DC was associated with a higher rate of recurrent biliary events which ultimately lead to greater morbidity and hospital cost. The length of hospital stay remained similar between two groups.*

Conclusion — *Laparoscopic early cholecystectomy is the procedure of choice for patients admitted in the hospital with mild to moderate acute gallstone pancreatitis*

Key words — *Early cholecystectomy, Acute pancreatitis, Acute gallstone pancreatitis.*

INTRODUCTION:

In developed countries, up to 75% of all cases of acute pancreatitis are caused by gallstone related diseases.[1] The pathogenesis of acute gallstone pancreatitis is best explained by persistent biliopancreatic obstruction which leads to progressive inflammation of the pancreas.[2] After AGP, there may be recurrent episodes of acute pancreatitis, common bile duct obstruction, acute cholangitis or self-limiting biliary colic episodes.[3,4] The mainstay of treatment for the prevention of recurrent biliary events is cholecystectomy and biliary tree clearance.[1,5] Episodes of AGP are usually mild and self-limiting, however 10-20% of patients develop severe pancreatitis which is associated with a high morbidity and mortality rate.[5]

In patients presenting with severe pancreatitis and its complications such as pancreatic necrosis and organ failure, cholecystectomy is delayed until the resolution of local complications.[6] Patients with severe

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pancreatitis should be considered, candidates for endoscopic retrograde cholangiopancreaticography (ERCP) and endoscopic sphincterotomy(ES).[7] Laparoscopic cholecystectomy remains the treatment of choice for mild to moderate acute pancreatitis.[1,5]

The International Association of Pancreatology (IAP) recommend that all patients who experience an episode of AGP should undergo cholecystectomy as soon as they have recovered from the acute attack and the American College of Gastroenterology recommended it within the index admission.[1,7] The British Society of Gastroenterology and The American Gastroenterological Association recommend that cholecystectomy should be performed in the index admission or up to 2 weeks after discharge from the hospital and in no case beyond 2-4 weeks after discharge.[3,4]

The rationale for performing early cholecystectomy is to prevent the rate of recurrent AGP as that can be severe and associated with high morbidity and mortality. However, delayed cholecystectomy may be deemed preferable by most surgeons, due to the high complication and mortality rate associated with early cholecystectomy.[1,6,8]

There also remains a high risk of conversion to open cholecystectomy(OS) in patients undergoing EC because acute inflammation in the perihepatic area may result in anatomic distortion. This may also have an adverse effect on the duration of the surgery and complications encounteredduring the surgery may also increase the postoperative length of hospital stay.[9] This is a comparative study of the length of surgery, conversion rate, perioperative complications, length of in hospital stay and the rate of gallstone related recurrent complications for patients undergoing early or delayed cholecystectomy after an episode of mild to moderate acute AGP.

METHODOLOGY:

This randomized controlled trial was carried out in the Department of General Surgery, Unit 4 at Jinnah Postgraduate Medical Centre and Ziauddin Medical Centre Clifton Karachi, from January 2017 to December 2017. The study was approved by the ethical review committee of the hospital. Patients above 18 years of age who presented to the surgical department with the diagnosis of mild to moderate AGP and gave written and informed consent for participation, were included in this study. Patients with, severe pancreatitis having a Ranson's score of >6, patients with pancreatic necrosis, peripancreatic inflammation or pleural effusion on imaging and patients with persistent raised LFTs were excluded from the study.

Patients were alternatively randomized to either an Early cholecystectomy (EC) or a Late Cholecystectomy(LC) group. A patient was labelled as having AGP if they fulfilled the following criteria: a history of acute upper abdominal pain, nausea, vomiting and tenderness in the epigastrium, an increase in the levels of serum amylase more than three times the upper limit of normal, an increase in the levels of serum lipase and detection of gallstones on ultrasonography. The classification of mild to moderate pancreatitis was based on the following criteria: A Ranson's score (RS) of <3 was labelled as mild and 3-6 was considered moderate pancreatitis, no evidence of pancreatic necrosis on abdominal imaging and no evidence of organ failure.

In patients who were randomized to the EC group, cholecystectomy was planned within the index admission whereas DC was performed 4 weeks after discharge from the hospital. Laparoscopic cholecystectomy was performed in both the groups. Preoperatively, a second-generation cephalosporin was administered intravenously at the time of induction of anesthesia to all the patients. Open and laparoscopic techniques were similar for all the patients. A standard right subcostal incision was used during OC, and a standard 4 port cholecystectomy was done laparoscopically. Following discharge, all postoperative patients were followed in the outpatient department of the hospital for a period of six months.

Preoperative, intraoperative and postoperative progress data was collected on a pre-designed form. The data was analyzed for the length of surgery, conversion rate, perioperative complications, the in hospital stay length and the rate of gallstone related recurrent complications. Statistical analysis was done using SPSS. Dichotomous variable data was expressed as percentage and was compared by a Fischer's Exact test. P-value of less than 0.05 was considered as significant.

RESULTS:

A total of 96 patients were admitted in the Department of Surgery with the diagnosis of AGP. Among these, only 80 of the patients met the inclusion criteria. Sixteen of the patients had severe pancreatitis and they were excluded from our study. The age range was 18 to 75 year with a mean of 45.05 year. Forty patients were randomized into the EC group and forty in to the DC group. There was no significant difference between the two groups in terms of age, gender and ethnicity.

The median time interval from the diagnosis of AGP to LC was seven days in the EC group and twenty-

eight days in the DC group. In terms of RS, 26 (65%) patients had RS <3 and 14 (35%) patients RS >3 in EC group and 16 (40%) patients had RS <3 and 24 (60%) patients RS>3 in DC group. Among the 80 patients who underwent laparoscopic cholecystectomy, 6 (7.5%) were converted to open surgery, 4 (10%) in the EC group and 2(5%) in the DC group. Out of those 4 patients in the EC group, 3 (7.5%) had RS >3 and 1 (2.5%) had RS <3. In DC group both patients had RS >3.

There was no significant difference between the EC and the DC group in the length of surgery (mean of 55 minutes in the EC group and 40 minutes in the DC group). Obscure anatomy with adhesions between the omentum, gall bladder, peritoneum and surrounding structures in the Calot's triangle and peripancreatic fluid collection was found in 1 (2.5%) patient in EC group and 1 (2.5%) patient in DC group. Acute inflammation with gallbladder empyema was encountered in 1 (2.5%) patient in EC group and none in DC group. Common bile duct injury occurred in 1 (2.5%) patient in EC group and none in DC group. Uncontrolled excessive bleeding was encountered in 1 (2.5%) patient only from the DC group. Bowel injury occurred in 1 (2.5%) patient in EC group. Perioperative complications occurred in 10 (12.5%) of the 80 patients, 7 (17.5%) in the EC group and 3 (7.5%) patients in DC group. Out of these 10 patients, 6 (7.5%) were converted into open surgery for other reasons. Of the other 4 (5%) patients, 3 (7.5%) in EC group and 1 (2.5%) in DC group, all were found to have friable and edematous tissue around the Calot's triangle. However the dissection was easily carried out through the laparoscopic technique and there was no need to convert into open surgery (table-I).

Postoperative complications were observed in 5 (12.5%) patients in total, 3 (7.5%) in EC group and 2 (5%) in DC group, all who had been converted into open surgery. Among these five patients, two developed superficial surgical site infections, which resolved on daily dressings, 2 patients developed seroma and one patient developed an intrabdominal abscess which resolved with antibiotics. The mean length of postoperative hospital stay was 48+ hours in both groups except for the patients with bowel and CBD injury who were discharged on 5th and 7th postoperative day respectively. Their hospital course however remained uneventful. Among the 40 patients who underwent EC within the same hospital admission, there was no episode of any recurrent gallstone related event in the short interval between recovery from the acute attack of pancreatitis and cholecystectomy. Patients in both the groups were followed for a period of 6 months following laparoscopic cholecystectomy and except for the patients who underwent DC and who presented in the interval period with recurrent biliary events, none of the patients had any symptoms of AGP postoperatively. Among the patients who were planned for DC, about one third of them presented in the interval period with recurrent biliary events, with most of them presenting with symptoms that warranted hospital admission (Table-II). No deaths occurred in this series.

Table I: Perioperative Outcome in Early and Delayed Cholecystectomy

	Early Cholecystectomy (n=40)	Delayed Cholecystectomy (n=40)	P[a]
Conversion to open surgery	4 (10%)	2 (5%)	0.6752[b]
Perioperative complications	7 (17.5%)	3 (7.5%)	0.3109[b]
Duration of surgery (mins), median, IQR[C]	55 (40-60)	40 (30-60)	>0.99[b]
Postoperative complications	3 (7.5%)	2 (5%)	>0.99[b]
Postoperative hospital stays (days), median, IQR[C]	2 + 1.5	2 + 1.4	>0.99[b]
Postoperative complications	3 (7.5%)	2 (5%)	>0.99[b]
Postoperative hospital stay (days), median, IQR[C]	2 +.5	2+1.4	>0.99[b]
Recurrent biliary events	0	12 (30%)	0.0001[b]
Mortality	0	0	

[a] p<0.05=significant [b] Fischer exact test [C]Inter Quartile Range

Table II: Recurrent Biliary Events in Delayed Cholecystectomy		
	Delayed Cholecystectomy (n=40)	**Hospital Re admission (n=12)**
Number of recurrent biliary events	12 (30%)	7 (58.33%)
Biliary colic	5 (12.5%)	0
Acute cholecystitis	4 (10%)	4 (33.33%)
Recurrent biliary pancreatitis	3 (7.5%)	3 (25%)

DISCUSSION:

The standard treatment for removal of the gallbladder is laparoscopic cholecystectomy (LC) and its safety and efficacy for the treatment of acute cholecystitis is well accepted.[10-13] The instigating factor for acute gallstone pancreatitis (AGP) is the transient or persistent obstruction of the ampulla of Vater by biliary calculi.[14] AGP is often self-limiting, but can be associated with significant morbidity and mortality, especially in patients with severe pancreatitis.[15] Therefor the management of AGP includes removal of the gallbladder and evaluation and clearance of CBD, if needed. After an episode of severe AGP, cholecystectomy is delayed until the resolution of local and systemic complications.[6] The timing of cholecystectomy, in mild to moderate AGP, has remained a subject of debate.

Early cholecystectomy (EC) provides complete treatment during a single admission. Proponents of DC believe that LC during the same hospital admission is associated with difficult dissection due to the distortion of anatomy caused by acute pancreatitis, which leads to more perioperative complications and has a higher chance of conversion to open surgery. However, studies have demonstrated that DC is associated with an increase in the rate of recurrent gallstone related complication and had no significant advantage regarding perioperative and postoperative complications or the length of postoperative hospital stay.

In this study, the frequency of biliary complications and the rate of conversion to open surgery, was higher in the EC than in the DC group, however this difference was not statistically significant. Patients in the DC group had a higher incidence of readmission with subsequent biliary events which was associated with increased morbidity, prolonged in hospital stay and the difference was statistically significant. There is also a possibility of patients being lost to follow up once discharged from the hospital after resolution of symptoms from the acute attack. The recurrence rate of acute gallstone pancreatitis, if un treated, is reported as 32-61%.[16] Therefore, early laparoscopic cholecystectomy is the safe and recommended treatment of choice. The operative time was almost the same for both the groups and so was the length of the postoperative in hospital stay.

In mild to moderate AGP, the risk of recurrent gallstone related events is reduced with EC, with no increase in operative difficulty or perioperative morbidity.[17] It was observed in this study that the conversion rate in patients who underwent EC, the frequency was much higher in those with moderate pancreatitis with a higher RS score as compared to those with mild pancreatitis. This was considered as the primary reason for the higher conversion rate in both the groups. We propose that for patients admitted with moderate pancreatitis with RS>3, both EC and DC should be performed by a qualified surgeon, to prevent further morbidities. It is recognized that obscure biliary tract anatomy due to pancreatitis makes dissection difficult in acute gallstone pancreatitis, and this could be the primary reason for the higher rate of conversion in this study, but the difference was not statistically significant. Other underlying causes included acute empyema with inflammation, excessive uncontrolled bleeding, CBD and bowel injury. The rate of these complications was less in mild than those with moderate pancreatitis. Patients with moderate pancreatitis who underwent EC had a much lower rate of recurrent gallstone related complications than those with DC though the complication and conversion rate was higher but when compared with the morbidity rate and hospital expense associated with recurrent biliary events, EC was deemed preferable over DC. Patients in both the groups had a similar length of postoperative stay except for those with CBD and bowel injury. Only patients who were converted to open surgery presented with complications in the postoperative period, however they were not associated with any significant morbidity.

Recurrent biliary events are associated with morbidity and mortality and a greater hospital cost and early laparoscopic cholecystectomy is safe and cost effective in mild to moderate acute pancreatitis.[18]

Same was observed in this study.

In a tertiary care hospital, when the morbidity associated with DC was compared with that associated with perioperative complication rate, it was observed that EC had better results. Though the perioperative complication rate was higher in patients with moderate pancreatitis, but easily managed and the hospital course in most of the patients remained uneventful. None of the postoperative complications were severe enough to warrant hospital admission. This is in comparison with rate of hospital readmission associated with recurrent biliary events in the interval period following resolution of an acute attack of AGP. Pancreatitis is associated with both local and systemic complications and morbidity and mortality. No mortality was observed in this study.

CONCLUSIONS:

Laparoscopic early cholecystectomy is the procedure of choice in patients with AGP. The procedure can be easily and safely performed in both mild and moderate pancreatitis after the acute attack has resolved. The rate of conversion to open surgery was higher in the EC as compared with the DC group, however DC was associated with a higher rate of recurrent biliary events and hospital readmission rate which ultimately leads to greater morbidity and hospital cost.

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