



## A RANDOMISED LONGITUDINAL TRIAL COMPARED THE EFFECTS OF EARLY CHOLECYSTECTOMY VERSUS DELAYED CHOLECYSTECTOMY IN PATIENTS WITH MILD TO SEVERE ACUTE BILIARY PANCREATITIS

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### ABSTRACT

In developing countries, gallstone disease is the most common cause of acute pancreatitis, accounting for up to 75% of cases. Biliary calculi were the aetiology in nearly half of the patients (25.1 percent) admitted for acute pancreatitis in Malaysia, according to a retrospective study conducted over several years (10.7 percent). Patients who have had biliary pancreatitis may have repeated episodes of biliary pancreatitis, CBD obstruction, cholangitis, or biliary colics. To avoid repeated biliary events, cholecystectomy and biliary tree stone removal remain the mainstay of care. We are aimed to achieve the effectiveness of Cholecystectomy in Early Vs Delayed treatment in patients with Severe to Mild Acute Biliary Pancreatitis compared through a Randomized Longitudinal Trail. Due to a clear assumption of CBD stones based on laboratory biochemical parameters and imaging results, 15 patients (50 percent) in the early group and 15 patients (50 percent) in the delayed group underwent an ERCP prior to cholecystectomy. ES and stone extraction were performed on 30 of the 24 patients. ERCP revealed no signs of a CBD stone in the remaining patient. In terms of patients undergoing pre cholecystectomy ERCP, there is no substantial difference between the two classes. As compared to delayed laparoscopic cholecystectomy, the results of this study of patients with mild to moderate ABP show that laparoscopic cholecystectomy with IOC performed within the same index admission reduces recurrent biliary events and reduces overall duration of hospital stay. Furthermore, there is no difference in the need for open surgery conversion, surgery length, or complication rate between early and delayed cholecystectomy. As a result, we suggest early laparoscopic cholecystectomy in patients with mild to moderate ABP, and we hope that as more evidence and research become available, early laparoscopic cholecystectomy will become the standard of care in the treatment of mild to moderate ABP in the near future.

**Key words:** Early And Delayed Cholecystectomy, Acute Biliary Pancreatitis, Surgery, Comparison.

### INTRODUCTION

In developing countries, gallstone disease is the most common cause of acute pancreatitis, accounting for up to 75% of cases. Biliary calculi were the aetiology in nearly half of the patients (25.1 percent) admitted for acute pancreatitis in India, according to a retrospective study conducted over several years (10.7 percent). Patients who have had biliary pancreatitis may have repeated episodes of biliary pancreatitis, CBD obstruction, cholangitis, or

biliary colics. To avoid repeated biliary events, cholecystectomy and biliary tree stone removal remain the mainstay of care [1- 3]. Acute biliary pancreatitis (ABP) is usually mild and self-limiting; however, 10% to 20% of patients experience extreme pancreatitis, which is associated with a high rate of morbidity and mortality [4].

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In patients with clinically serious pancreatitis and local complications such as pancreatic necrosis and organ failure, cholecystectomy is postponed until the local complications have resolved, which usually takes four weeks. For mild to moderate ABP, international guidelines recommend early cholecystectomy [5, 6]. The guidelines, however, differ in their definitions of "early." All patients with gallstone pancreatitis should have a cholecystectomy as soon as they have healed from the attacks, according to the International Association of Pancreatology (IAP), while the British Society of Gastroenterology recommends cholecystectomy during the same hospital admission or up to one week after discharge [7].

The differences in suggested cholecystectomy timing between these recommendations are due to varying viewpoints and procedures, but more importantly, the lack of evidence from prospective randomised controlled trials addressing the timing and safety of early operative intervention [8]. Three-quarters of patients hospitalised with mild biliary pancreatitis had cholecystectomy four weeks after discharge, according to a national survey in the Netherlands. Because of the confusion about the effectiveness and safety of an early cholecystectomy, the majority of specialists perform an interval cholecystectomy. This may be due to a lack of data from prospective randomised controlled trials. The use of ERCP and ES without cholecystectomy as a definitive treatment for ABP is still debatable [9, 10]. Even when typical bile duct exploration was performed, ERCP, with its higher incidence of post procedure pancreatitis, resulted in a longer hospital stay when compared to laparoscopic cholecystectomy and intraoperative cholangiogram (IOC). 18 ES can, however, be used as an approved definitive procedure in elderly patients with multiple comorbid conditions who are unable to undergo surgery to avoid pancreatitis recurrence [11].

### **Aims & Objectives:**

We are aimed to achieve the effectiveness of Cholecystectomy in Early Vs Delayed treatment in patients with Severe to Mild Acute Biliary Pancreatitis compared through a Randomized Longitudinal Trail.

### **Methodology:**

This is a prospective randomised controlled trial with an open label. Patients with mild to moderate ABP who met the inclusion criteria and gave informed consent to participate in the study were randomly assigned to one of two groups: early or delayed cholecystectomy. Due to the design of this study, concealing the allocation for investigators or study participants is impossible due to the fact that study participants must be scheduled for an early or postponed cholecystectomy. After informed consent was obtained, an independent party randomly

assigned participants by drawing a sealed, unlabeled, unordered envelope from a container. When patients in the early group no longer needed opioid analgesics, could tolerate a regular oral diet, and had a serum C-reactive protein concentration of less than 100 mg/L, cholecystectomy with IOC was performed within the index admission. Interval cholecystectomy with IOC was performed on an elective basis in the delayed community, approximately 4 weeks after the pancreatitis episode, after hospital discharge from the index admission. Cholecystectomy was done laparoscopically unless it was contraindicated, in which case an open cholecystectomy was done. A single specialist hepatobiliary surgeon performed all of the procedures. Both of the patients were given the proper antibiotic prophylaxis before surgery.

### **Inclusion Criteria:**

A participant was diagnosed with acute pancreatitis if at least two of the following three features were present:

- (1) Pancreatitis symptoms, such as upper abdominal pain an elevated serum amylase level of at least thrice the upper limit of normal;
- (2) characteristic findings of acute pancreatitis on abdominal imaging; and
- (3) pain, nausea, vomiting, and epigastric tenderness.

The existence of the following symptoms was used to diagnose biliary pancreatitis: (1) radiological imaging confirms the presence of gallstones and/or sludge; and (2) clinical consistency with hospital admission not requiring intensive care unit (ICU) or high dependency unit (HDU) care; and (3) absence of concomitant acute cholangitis.

### **Exclusion Criteria:**

Patients were not allowed to participate if they had any of the following conditions: (1) extreme pancreatitis (presence of three or more Ranson's or Imrie criteria on admission); (2) admission to ICU or HDU; (3) alleged concomitant acute cholangitis; (4) severe pre existing medical comorbidity contraindicating cholecystectomy (as determined by the primary physician). At the conclusion of the report, a computer-assisted analysis was performed.

Midway through the report, an interim review showed a substantial difference in the incidence of chronic biliary events and those requiring hospital readmissions in the delayed cholecystectomy group versus the early cholecystectomy group. The thesis was decided to be terminated after discussion with the supervising and ethics committees. A total of 72 patients had completed the study by the time it was terminated.

### **Results & Discussion:**

In this sample, there were 28 male patients (41.06%) and 43 female patients (58.94%). The

participants ranged in age from 20 to 56 years old, with an average age of 40. Malays made up the bulk of the study population (35.56%), followed by foreigners (29.44%), and Indians (18.06%). This ethnic distribution mirrored the ethnic makeup of the general Malaysian patient population receiving care in the public health system. There were 30 patients in the early group and 30 in the delayed group. In terms of age, gender, and ethnicity, there is no discernible difference between the two classes. The early group had a median time span of 6 days from ABP diagnosis to cholecystectomy, while the delayed group had a median time of 44 days.

Due to a clear assumption of CBD stones based on laboratory biochemical parameters and imaging results, 15 patients (50 percent) in the early group and 15 patients (50 percent) in the delayed group underwent an ERCP prior to cholecystectomy. ES and stone extraction were performed on 30 of the 24 patients. ERCP revealed no signs of a CBD stone in the remaining patient. In terms of patients undergoing pre cholecystectomy ERCP, there is no substantial difference between the two classes. Two patients in the delayed community had ERCP after

cholecystectomy to remove a small CBD stone that was discovered on IOC during cholecystectomy by chance.

Pancreatitis after cholecystectomy has been reported, and there have been cases of pancreatitis recurring after cholecystectomy. These symptoms may be the result of CBD sludge or stones that have remained in the system. A patient with post cholecystectomy pancreatitis was included in this report. Though there was no proof of CBD stone in the IOC, fine 'sandy' stones or sludge that was not picked up may be an explanation.

In this analysis, a larger sample size would have been better for statistical significance. The surgical procedure in this study was performed by a hepatobiliary surgeon, and although having a single surgeon perform all procedures decreases bias in operative data and outcomes, the results do not reflect cholecystectomy procedures in everyday practise, which are typically performed by general surgeons. However, since the aim of the research is to compare the outcomes of the two classes, this should not influence the analysis

**Table 1: Clinical Data Of Study Population**

	<b>Early group (n =38)</b>	<b>Delayed group (n=34)</b>	<b>p*</b>
<b>Patients</b>			
Age (y), median	42.5	42.5	0.657
and IQR	(29.75-52)	(30.75-54.25)	
<b>Sex</b>			0.385
Male	18 (47.37%)	13 (38.24%)	
Female	20 (52.63%)	21 (61.76%)	
<b>Race</b>			0.258
Malay	24 (63.16%)	16 (47.06%)	
Chi.se	6 (15.79%)	7 (20.59%)	
Indian	1 (2.63%)	4 (11.76%)	
Foreigner	7 (18.42%)	7 (20.59%)	
<b>Procedures</b>			
ERCP	19 (50%)	17 (50%)	> 0.99
Preop	19	15	0.644
Postop	0	2	0.220

Time to cholecystectomy (d), median, and IQR	6 (5-9)	44 (36-56)	a
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## CONCLUSION

As compared to delayed laparoscopic cholecystectomy, the results of this study of patients with mild to moderate ABP show that laparoscopic cholecystectomy with IOC performed within the same index admission reduces recurrent biliary events and reduces overall duration of hospital stay. Furthermore, there is no difference in the need for open surgery

conversion, surgery length, or complication rate between early and delayed cholecystectomy. As a result, we suggest early laparoscopic cholecystectomy in patients with mild to moderate ABP, and we hope that as more evidence and research become available, early laparoscopic cholecystectomy will become the standard of care in the treatment of mild to moderate ABP in the near future.

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