

Timing of Cholecystectomy in Mild Acute Biliary Pancreatitis.

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Abstract

Background: Acute biliary pancreatitis (ABP) is one of the most common gastrointestinal events that requires acute admission to the hospital with considerable risks of mortality & morbidity. Laparoscopic cholecystectomy has become the gold standard for the treatment of ABP. Our aim was to determine the safety of cholecystectomy during the first admission by performing a review of the current literature. Waiting for 6 - 8 weeks to perform cholecystectomy may result with an increased incidence of recurrent ABP attacks, which may increase morbidity and the length of the hospital stay. On the contrary, cholecystectomy during the index admission for mild ABP appears to be a preferable and safe approach with better surgical outcomes providing a definitive treatment.

Keywords: *Pancreatitis, cholecystectomy, general surgery*

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Full Text

Gallstone disease and its complications

Gallstone disease is considered as an important health problem worldwide, affects quality of life and causes severe morbidity and even mortality. Globally, the incidence of gall stone disease is approximately 10-15% [1]. The prevalence of this entity is dependent on variable risk factors, which could be identified as modifiable and non-modifiable (Table 1) [1]. The incidence increases over the years, especially due

to non-modifiable risk factors and there is a concordant increase in complication rates such as acute biliary pancreatitis (ABP) [2]. ABP is a common gastrointestinal inflammatory condition and most patients develop a mild course; however, some patients may have severe inflammatory response and mortality is usually associated with multiorgan dysfunction in this group [3].

Non-modifiable	Modifiable
Family history	Obesity / metabolic syndrome / diabetes mellitus / dyslipidemia
Genetic factors	Drugs - ceftriaxone, thiazide diuretics, octreotide, female sex hormones
Ethnicity	Decreased physical activity
Female gender	Rapid weight loss
Age	Total parenteral nutrition
	Dietary factors
	Underlying disease - cirrhosis

Table 1. Risk factors for gallstone disease [1].

Acute biliary pancreatitis

The definition of acute pancreatitis is that it is an inflammatory condition of the pancreas with a wide spectrum of pathophysiological aspects that shows different types of severeness; such as

edema or necrosis that is associated with poor or no fibrosis [4]. Concomitant stones in the biliary ducts are present in 6-12% of people with gallstones, and based on the

differences in site of formation and pathogenesis, common bile duct (CBD) stones can be classified as primary and secondary biliary stones [5,6]. If a stone forms in the CBD, it's called a primary stone, whereas migrated stones from the gallbladder that locate in the CBD are called secondary stones [7]. Migration of gallstones especially smaller than 3 mm through the cystic duct to the CBD is thought to be the pathophysiology behind ABP. In 1901, Opie observed impacted stones at the site of the sphincter of Oddi in two mortal cases. Temporary obstruction of the ampulla of Vater by stones causes bile reflux towards the pancreas via the common channel and regurgitation continues through the pancreatic duct. Normally, inactive digestive zymogens and lysozyme hydrolase stay apart in pancreatic cells. If ductal obstruction occurs, they colonize together in vacuoles in the cells and uncontrolled activation of trypsin leads to autodigestion of the pancreas and local inflammation [8,9]. Biliary stones are considered to be responsible for ABP in 30-70% of cases. In addition to the aforementioned risk factors, male gender is associated with increased possibility of complicated forms leading to morbidity and mortality [10].

Severity assessment in acute biliary pancreatitis

Scoring systems based on clinical, laboratory and radiological findings to predict the prognosis of pancreatitis have been identified and used in medical practice for decades. The most frequently used are the Balthazar and Ranson's scoring systems as well as the Atlanta Classification.

In 1992, the Atlanta Classification was created for a standardized clinical approach and revised in 2012 [11,12]. According to the Revised Atlanta Classification, the clinical presentation must meet the criteria as follows: acute onset of severe, persistent, epigastric pain often radiating to the back. The pain relieves by leaning forward and is aggravated by food in most cases. According to the laboratory findings, the serum lipase level is at least three times increased. Radiologic work-up is unnecessary to be carried out immediately if the first two criteria are present [11]. The Revised Atlanta classification of acute pancreatitis identified three grades of severity, which were the "mild form" (no organ dysfunction, or local/systemic complications), the "moderate form" (organ failure that ameliorates within 48 hours and/or local or systemic complications), and the "severe form" (persistent organ failure lasting for >48 hours, single or multiple) [11]. There also had been changes in radiological severity in the Revised Atlanta Classification [12] (Table 2).

Another approach to foresee the prognosis of ABP is the Ranson’s score which was first described in 1974 by Ranson *et al*, and then modified in 1979 based on the etiology for biliary disease [13,14] (Table 3).

Balthazar *et al* published two studies in 1985 and 1990 about the prognostic value of computerized

tomography (CT) in acute pancreatitis [15,16]. Patients without peripancreatic inflammation were found to be associated with the uncomplicated (mild) form, whereas patients with one or several peripancreatic collections were associated with the severe form, and were more likely to develop serious complications [16] (Table 4).

	Original Atlanta Classification	Revised Atlanta Classification
Acute pancreatitis	Interstitial pancreatitis	Interstitial edematous pancreatitis
	Steril necrosis	Necrotizing pancreatitis (pancreatic and/or peripancreatic necrosis)
	Infected necrosis	Sterile necrosis Infected necrosis
Fluid collections during acute pancreatitis	Pancreatic pseudocyst Pancreatic abscess	<4 weeks after onset of acute pancreatitis - Acute peripancreatic fluid collection Sterile necrosis Infected necrosis - Acute necrotic collection
		Sterile necrosis Infected necrosis <4 weeks after onset of acute pancreatitis - Pancreatic pseudocyst Sterile necrosis Infected necrosis - Walled-off pancreatic necrosis Sterile necrosis Infected necrosis

Table 2. Comparison of the Original and Revised Atlanta Classification systems [12].

Parameter	Gallstone-induced pancreatitis
<i>On admission</i>	
Age	>70
WBC	>18000
Glucose (mg/dL)	>220
LDH (IU/L)	>400
AST (IU/L)	>250
<i>Within 48 h</i>	
Hct decrease (%)	5
BUN increase (mg/dL)	>2
Calcium (mg/dL)	<8
PaO ₂ (mmHg)	52
Base deficit (mEq/L)	>5
Fluid (L)	>4

Table 3. Ranson's criteria [17].

Inflammatory process – Balthazar's morphological index for acute pancreatitis		
Grade	Tomographic finding	Scoring
A	Normal pancreas.	0
B	Focal or diffuse pancreatic enlargement.	1
C	Pancreatic alternations associated with peripancreatic inflammation.	2
D	Single fluid collection.	3
E	Two or more fluid collections and/or presence of gas within the pancreas or within peripancreatic inflammation.	4
Pancreatic necrosis		
Tomographic finding	Scoring	
Absence of necrosis.	0	
< 30% necrosis.	2	

30-50% necrosis.	4
>50% necrosis.	6

Table 4. Balthazar's scoring system [18].

Cholecystectomy for acute biliary pancreatitis

The definitive treatment of mild ABP is cholecystectomy after resolution of the symptoms and clinical improvement. Several approaches are applied based on the optimal timing for cholecystectomy. Early cholecystectomy during the the first admission, after the resolution of clinical and laboratory parameters, is suggested by current guidelines [19,20]. In their prospective study, published in 1981, Stone *et al* compared early and delayed open cholecystectomy after biliary pancreatitis, and given the surgical outcomes, complication rates, and hospital stay, they concluded that early and delayed surgery were equally safe [21].

Although there is no consensus on the timing for delayed cholecystectomy, performing surgery up to 8 weeks after the pancreatitis attack can be defined as interval surgery. Cholecystectomy during the first admission is recommended by the International Association of Pancreatology, while the American Gastroenterological Association suggests delayed cholecystectomy after 2-4 weeks following discharge [22,23]. The British Society of

Gastroenterology recommends cholecystectomy at first admission or up to 2 weeks after admission [24].

Recurrence and readmission

In his study of 80 patients with pancreatitis, published in 1979, Ranson operated on 59 patients and suggested that although early surgical treatment for the associated biliary condition could be carried out safely in many patients with "mild" acute pancreatitis, early definitive surgery was insecure in "severe" pancreatitis and should, if possible, be delayed until pancreatitis subsided and that most patients should be operated before hospital discharge [14]. In a meta-analysis by Baal *et al*, increased rates of readmissions after ABP attacks were reported to be associated with the interval time periods between the first admissions and the delayed surgical interventions of the patients [25]. The risk of developing a recurrent biliary attack was reported as 9-60% following discharge before delayed surgery [26]. Ito *et al* suggested that a two-weeks-interval between the first attack and surgical intervention might be too long

because 31% of recurrences occurred within two weeks after the first admission [27]. According to three prospective randomized controlled studies and 10 retrospective studies evaluating the surgical outcomes, complications, hospital stay, and readmission rates analyzed in a review, when compared between early and delayed cholecystectomy operations, the rates of conversion to open surgery were similar, and early cholecystectomy was associated with decreased incidence of recurrent ABP attacks, morbidity and hospital stay [20].

Complications

A meta-analysis showed no variation in complication rates between early and delayed surgery [28]. In another meta-analysis it was found that delayed laparoscopic cholecystectomy resulted in higher rates of complications and readmission than early laparoscopic cholecystectomy while the rates of conversion to open cholecystectomy between early laparoscopic cholecystectomy and delayed laparoscopic cholecystectomy were comparable [20].

One of the indicators for difficult surgery is operative time. When the studies were analyzed in our review, it was found that the timing of cholecystectomy did not affect the

duration of surgery. Early surgery decreases the risk of recurrent biliary complications. In our opinion, cholecystectomy in patients with mild to moderately severe biliary pancreatitis can be performed safely during the first admission.

Conversion to open surgery

Although most guidelines suggest early cholecystectomy because of the high rates of recurrent ABP attacks that are clearly associated with more complicated disease and other gallstone related events, the answer is still unclear for the question: "Why do most surgeons delay surgery?". It can be thought that delayed surgery can be associated with relatively easier surgery due to regressed inflammation and possibly lower conversion rates [29]. Early cholecystectomy, on the other hand, is believed to be harder to perform due to increased inflammation. The conversion rates to open surgery between early and delayed cholecystectomy were approximately 7.5% and 7%, respectively, according to several studies [30,31]. Even though there is an assumption that early cholecystectomy is harder to perform, no difference was shown in concern of operative time or surgical complications between studies according to the available data [20].

Length of hospital stay

Delayed surgery was associated with a significantly longer length of hospital stay and those patients require readmission and a longer duration of conservative treatment. In their study of 72 patients, Jee *et al* reported that the patients who underwent delayed surgery had longer hospital stay than the patients who underwent early surgery during the first admission since 24% of these cases readmitted due to recurrent gall-stone related events most of which could have been preventable with early cholecystectomy [26]. In summary, delayed surgery results with longer hospital stay, increases hospitalization costs and leads to excessive consumption of medical resources.

Conclusions

The timing of cholecystectomy in ABP should be decided according to the severity of the disease and the clinical course of the individual patient. Definitive treatment of mild ABP can be accomplished effectively and safely via cholecystectomy following clinical improvement and normalized levels of laboratory parameters during the first admission. Delayed cholecystectomy following a 6 to 8 weeks' time period may result with recurrent gallstone pancreatitis, which may increase

morbidity rates and the duration of hospital stay.

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