Early Laparoscopic Cholecystectomy for Mild Gallstone Pancreatitis

Time for a Paradigm Shift

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Hypothesis: Patients with mild gallstone pancreatitis may undergo an early laparoscopic cholecystectomy (LC) within 48 hours of hospital admission without awaiting the normalization of pancreatic and liver enzyme levels. This may decrease the hospital stay without increasing morbidity or mortality and may minimize the unnecessary use of endoscopic retrograde cholangiopancreatography.

Design: A retrospective review.

Setting: Two university-affiliated urban medical centers.

Patients: A total of 303 patients with mild gallstone pancreatitis, of whom 117 underwent an early LC and 186 underwent a delayed LC.

Main Outcome Measures: Hospital length of stay, morbidity and mortality rates, and the use of endoscopic retrograde cholangiopancreatography.

Results: Similar hospital admission variables were observed in the early and delayed LC groups, although the delayed group was older (P = .006). The median hospital length of stay was significantly less for the early group than for the delayed group (3 vs 6 days; P < .001). There were no patients who died, and the complication rates were similar for both groups. However, the patients who underwent an early LC were less likely than patients who underwent a delayed LC to undergo endoscopic retrograde cholangiopancreatography (P = .02).

Conclusions: An early LC may be safely performed for patients with mild gallstone pancreatitis, without concern for increased morbidity and mortality, resulting in shortened hospital stays and a decrease in the use of endoscopic retrograde cholangiopancreatography. The practice of delaying an LC until normalization of laboratory values appears to be unnecessary.


ACUTE BILIARY PANCREATITIS is a common clinical scenario encountered by the general surgeon. The etiology can be explained by the "common channel" theory, in which the ampulla of Vater is transiently obstructed by a gallstone, leading to pancreatic inflammation and autodigestion. Historically, the symptomatic management of gallstone pancreatitis involved the delay of a cholecystectomy until the normalization of laboratory values and the resolution of abdominal pain. Ranson's earlier articles in the era of the open cholecystectomy investigated the timing of biliary surgery in mild (<3 Ranson signs) and severe (≥3 Ranson signs) pancreatitis. He concluded that "definitive correction of cholelithiasis should usually be carried out as soon as evidence of acute pancreatitis has resolved" to avoid exacerbating the severity or recurrence of disease. Recent evidence, with the introduction of laparoscopic surgery, has suggested that patients with mild gallstone pancreatitis, which comprises 80% to 90% of all patients with gallstone pancreatitis, may be better served with earlier intervention.

Two previous studies from our institution demonstrated that, in patients with mild gallstone pancreatitis, an LC could be...
safely performed within 48 hours of admission regardless of resolution of abdominal pain or normalization of serum enzyme levels. This approach resulted in a significant decrease in length of hospitalization without increasing complications.5,6 There remains continued concern, however, that prediction of mild pancreatitis is uncertain and that some patients may incur an exacerbation of their disease as a result of early operative intervention.

To further address these concerns and to minimize the possible bias of a single-institution study, we set out to expand our database by collecting patient data from 2 university-affiliated urban medical centers during a 5-year period, with the goal of reaffirming the results of our previous, more limited investigations. Hospital lengths of stay, perioperative complications, and readmission rates were examined to determine the efficacy and safety of an early LC in patients with mild gallstone pancreatitis.

METHODS

Our study included patients from 2 UCLA School of Medicine-affiliated institutions that are both public teaching hospitals: Harbor–UCLA Medical Center in Torrance, California, and Olive View–UCLA Medical Center in Sylmar, California. Institutional review board approval for our study was obtained from the Los Angeles Biomedical Research Institute at Harbor–UCLA Medical Center.

A retrospective review was performed that included all patients who underwent an LC for the indication of gallstone pancreatitis during the period from 2006 to 2011. Patients were diagnosed with gallstone pancreatitis if they had (1) midepigastric or right upper quadrant abdominal pain, nausea, vomiting, or abdominal tenderness; (2) no history of ethanol use; (3) elevated serum amylase and/or lipase levels to at least 3 times the upper limit of normal; and (4) the presence of gallstones on an ultrasonographic or computed tomographic scan. Mild pancreatitis was defined as (1) the presence of fewer than 3 Ranson criteria on admission; (2) the patient being admitted to a nonmonitored ward bed; (3) the absence of acute cholangitis defined as the patient having a temperature greater than 38.6°C, hyperbilirubinemia, and right upper quadrant pain and tenderness or purulence seen during endoscopic retrograde cholangiopancreatography (ERCP); (4) the absence of significant signs of hypovolemia, which is defined, at hospital admission, as a serum urea nitrogen level of greater than 15 mg/dL (to convert to millimoles per liter, multiply by 0.357) and a heart rate of 110 beats/min or less; and (5) low suspicion for retained common bile duct (CBD) stones, which is defined as no CBD stones seen on an ultrasonographic scan, in conjunction with a total bilirubin level of less than 4 mg/dL (to convert to micromoles per liter, multiply by 17.104).

Patients were excluded (1) if they demonstrated severe pancreatitis, which is defined as having 3 or more Ranson criteria at hospital admission; (2) if they were suspected of having concomitant acute cholangitis; (3) if they showed evidence of cholecystolithiasis, as demonstrated by a total bilirubin level of 4 mg/dL or greater or by the presence of CBD stones on ultrasonographic scan; (4) if they were admitted to a monitored unit; or (5) if they showed evidence of marked dehydration, which is defined, at hospital admission, as a heart rate of greater than 110 beats/min or a serum urea nitrogen level of greater than 15 mg/dL. Patients were also excluded if they showed evidence of acute cholecystitis on an abdominal ultrasonographic scan, including a sonographic Murphy sign, pericholecystic fluid, and/or gallbladder wall thickening. Patients who had a final pathologic diagnosis of acute cholecystitis were similarly excluded.

The demographic data collected included age, race, and presence of medical comorbidities (including coronary artery disease, diabetes mellitus, and renal failure). Vital signs at presentation, laboratory values, and findings from abdominal ultrasonography were also noted. The outcome data collected included the timing of the operative intervention, defined in terms of days after admission; the length of hospitalization; the incidence of conversion to open cholecystectomy; and the presence of CBD stones during preoperative and postoperative ERCP.

Given the retrospective nature of our study, it was not possible to ascertain the indications for preoperative and/or postoperative ERCP in every patient. However, as a general rule, the vast majority of preoperative ERCPs were performed for persistent elevation of the total bilirubin level and/or a dilated (>1 cm) CBD. Postoperative ERCP was performed because of either elevated pancreatic and liver enzyme levels determined by use of postoperative liver function tests or the existence of a filling defect determined by use of intraoperative cholangiography, which is routinely performed at Harbor–UCLA Medical Center but not at Olive View–UCLA Medical Center, for all patients with a diagnosis of gallstone pancreatitis at admission.

For purposes of analysis, patients were divided into 2 groups according to the timing of the LC. Patients who underwent an early LC (performed within 48 hours of admission) were compared with patients who underwent a delayed LC (after 48 hours). The primary end point was length of hospitalization. Secondary end points were the use of ERCP, the incidence of conversion to open cholecystectomy, the presence of major complications requiring a secondary intervention, and the need for readmission within 30 days.

Patient data were entered into an Excel database (Microsoft Corp) and translated into a native SAS format using DBMS/Copy (Dataflux Corp). Descriptive statistics were calculated for all variables. When comparing the early vs the delayed group, normally distributed continuous variables are reported as means with 95% CIs, whereas non-normally distributed continuous numerical variables were compared using the nonparametric Wilcoxon rank sum test and are reported as medians with interquartile ranges. For the primary outcome of interest (i.e., length of hospital stay), both the mean and median lengths of stay are described. To identify whether there were differences between the early vs delayed cohorts with respect to the incidence of the use of ERCP, conversion to open cholecystectomy, complications, and readmission, the χ2 test or the Fisher exact test were used, as appropriate. P < .05 was considered statistically significant.

RESULTS

PATIENT CHARACTERISTICS

During the study period, 396 patients with gallstone pancreatitis underwent an LC. In total, 93 patients (23.5%) were excluded, including 72 patients (18.2%) with a total bilirubin level of 4 mg/dL or greater, 53 patients (13.4%) with an elevated serum urea nitrogen level, 12 patients with severe pancreatitis (3.0%), 7 patients (1.8%) with a heart rate of more than 110 beats/min, and 6 patients (1.5%) with a diagnosis of concomitant cholangitis, leaving 303 patients for analysis. Several patients had more than 1 exclusion criteria. Of the 303 patients included, 122 were treated at Harbor–UCLA Medical Center, and 181 were treated at Olive View–UCLA Medical Center.
None progressed to severe pancreatitis or required transfer from a nonmonitored to a monitored bed. The mean age was 37 years, and 78.2% were female patients. All patients underwent an LC during the index hospital admission. An intraoperative cholangiogram was performed for 116 patients (38.3%).

**EARLY VS DELAYED LC GROUPS**

Of the 303 patients, 117 (38.6%) underwent an early LC, and 186 (61.4%) underwent a delayed LC. A comparison of the demographics is shown in Table 1. There were no significant differences between the early and delayed LC groups with respect to sex, laboratory results at admission, or Ranson score at admission. The early LC group was slightly older than the delayed LC group (35 vs 40 years; \( P = .006 \)) (Table 1). The most common reason for delay in LC was awaiting normalization of bilirubin or pancreatic enzyme levels, and this was secondary to surgeon preference.

**PRIMARY END POINT**

For the early LC group, the median length of hospital stay was 3 days (interquartile range, 3-4 days), and the mean length of hospital stay was 3.4 days (95% CI, 3.1-3.8); for the delayed LC group, the median length of hospital stay was 6 days (interquartile range, 4-7 days), and the mean length of hospital stay was 6.3 days (95% CI, 5.9-6.6) (\( P < .001 \)).

**SECONDARY END POINTS**

There were no differences in mortality rates (0%) or complication rates (4.2% in early LC group vs 4.8% in delayed LC group; \( P = .99 \)), in readmission within 30 days (3.4% in early LC group vs 1% in delayed LC group; \( P = .20 \)), or in conversion from LC to open cholecystectomy (2.5% in early LC group vs 7.5% in delayed LC group; \( P = .80 \)) (Table 2). Complications in the early LC group included urinary tract infection, CBD leak, recurrent pancreatitis, choleodocholithiasis, and postoperative pain. In the delayed LC group, complications included intraoperative hypotension, cystic duct leak, presence of pancreatic pseudocyst, CBD leak, wound infection, and recurrent pancreatitis.

Use of ERCP was significantly higher in the delayed LC group than in the early LC group (27.4% vs 16.2%); \( P = .02 \). Preoperative ERCP use was higher in the delayed LC group than in the early LC group (6% vs 17%; \( P = .004 \)), whereas there was no difference between groups in the use of postoperative ERCP (10.3% vs 10.2%; \( P = .99 \)) (Table 2).

**COMMENT**

To our knowledge, the present retrospective study of 303 patients at 2 university-affiliated institutions is the largest to date to analyze the timing of early LC in mild gallstone pancreatitis. The primary finding was that patients who underwent an early LC had a significantly decreased median length of hospitalization compared with patients who underwent a delayed LC. The decrease in length of hospital stay was achieved without an increase in adverse outcomes. Complication rates and early readmission rates were similar, as were the rates of conversion to open cholecystectomy and the use of postoperative ERCP.

The timing of a cholecystectomy in gallstone pancreatitis remains controversial. In the era of open cholecystectomy, Kelly and Wagner demonstrated that an early cholecystectomy (48 hours after admission) worsened outcomes in patients with severe pancreatitis. In patients with mild pancreatitis, there was no difference between an early and delayed open cholecystectomy. The authors concluded that, because early removal of the gallbladder does not impact the progression of the disease and because patients with severe pancreatitis have significantly higher morbidity and mortality with early intervention, an operation should only be performed after the "pancreatitis had subsided." As a result, surgeons have historically delayed cholecystectomy in all patients with gallstone pancreatitis.

More recently, in the era of LC, several studies have shown that delaying surgery in patients with mild pan-

### Table 1. Patient Characteristics in Early vs Delayed Laparoscopic Cholecystectomy

<table>
<thead>
<tr>
<th>Variable</th>
<th>Early LC (n=117)</th>
<th>Delayed LC (n=186)</th>
<th>( P ) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>35 (28-45)</td>
<td>40 (31-56)</td>
<td>.006</td>
</tr>
<tr>
<td>Glucose, mg/dL</td>
<td>109 (98-129)</td>
<td>117 (98-146)</td>
<td>.07</td>
</tr>
<tr>
<td>Ranson score at admission</td>
<td>1 (0-1)</td>
<td>1 (0-1)</td>
<td>.20</td>
</tr>
<tr>
<td>WBC count, /µL</td>
<td>10.5 (8.0-13.9)</td>
<td>10.9 (8.0-13.2)</td>
<td>.90</td>
</tr>
<tr>
<td>Amylase, U/L</td>
<td>819 (287-1669)</td>
<td>985 (227-1999)</td>
<td>.50</td>
</tr>
<tr>
<td>Lipase, U/L</td>
<td>929 (355-2989)</td>
<td>1129 (422-2940)</td>
<td>.60</td>
</tr>
<tr>
<td>Total bilirubin, mg/dL</td>
<td>1.6 (1.0-2.1)</td>
<td>1.7 (1.0-2.4)</td>
<td>.30</td>
</tr>
</tbody>
</table>

**Abbreviations:** IQR, interquartile range; LC, laparoscopic cholecystectomy; WBC, white blood cell.

SI conversion factors: To convert glucose to millimoles per liter, multiply by 0.0555; to convert WBC count to \( /000/L \), multiply by 0.001; to convert amylase and lipase to microkatal per liter, multiply by 0.0167; and to convert total bilirubin to micromoles per liter, multiply by 17.104.

### Table 2. Clinical Outcomes in Early vs Delayed Laparoscopic Cholecystectomy

<table>
<thead>
<tr>
<th>Variable</th>
<th>Early LC (n=117)</th>
<th>Delayed LC (n=186)</th>
<th>( P ) Value</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary Endpoint</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median length of hospital stay, d</td>
<td>3 (3-4)</td>
<td>6 (4-7)</td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td><strong>Secondary End Points</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Length of hospital stay, d</td>
<td>3 (3-4)</td>
<td>6 (4-7)</td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td>Postoperative ERCP</td>
<td>12 (10.3)</td>
<td>19 (10.2)</td>
<td>.99</td>
<td>1.0 (0.9-1.1)</td>
</tr>
<tr>
<td>Total</td>
<td>19 (16.2)</td>
<td>51 (27.4)</td>
<td>.02</td>
<td>0.5 (0.3-0.9)</td>
</tr>
<tr>
<td>Complications</td>
<td>5 (4.2)</td>
<td>9 (4.8)</td>
<td>.99</td>
<td></td>
</tr>
<tr>
<td>Readmission</td>
<td>4 (3.4)</td>
<td>2 (1)</td>
<td>.20</td>
<td></td>
</tr>
</tbody>
</table>

**Abbreviations:** ERCP, endoscopic retrograde cholangiopancreatography; IQR, interquartile range; LC, laparoscopic cholecystectomy; OR, odds ratio.

*\( a \) Determined by use of the Fisher exact test.*
creatitis may be unnecessary. Taylor and Wong\(^a\) compared 2 groups of patients with mild gallstone pancreatitis who underwent an LC performed by 1 of 2 surgeons. Surgeon 1 delayed surgery until the resolution of abdominal pain and the normalization of enzyme levels, whereas surgeon 2 proceeded to LC as soon as the serum amylase level began to decrease and the abdominal pain began to lessen. The finding of this study\(^a\) of 46 patients was that an earlier LC, performed once the serum amylase level began to decrease and once the abdominal pain began to lessen (but not yet normalized), resulted in a significant decrease in the length of hospital stay, from 4.7 to 3.5 days, without an increase in complication rates (10% vs 11%; \(P = .12\)). Our observational retrospective and prospective trial\(^b\) from Harbor–UCLA Medical Center reported similar findings. The study\(^b\) compared 177 patients (retrospectively reviewed) who underwent a delayed LC with a prospective group of 43 patients who deliberately underwent an early LC. The length of hospitalization in the early LC group was reduced from 7 to 4 days (\(P < .001\)) without an increase in complications (4.5% vs 4.8%; \(P = .70\)).\(^c\) Our subsequent prospective randomized trial\(^c\) compared 25 patients who underwent an early LC with 25 patients who underwent a cholecystectomy following resolution of symptoms and normalization of laboratory values. Again, the mean length of hospital stay was reduced to 3.5 days, from a mean of 5.8 days, with no difference observed in perioperative complication rates.\(^d\)

Despite the growing evidence supporting the safety and efficacy of an early LC in the management of mild gallstone pancreatitis, concerns remain with regard to the safety of this approach. One issue is whether mild gallstone pancreatitis can be accurately predicted at admission because calculating the total Ranson score requires 48 hours. Studies\(^e\,f\) have suggested that from 5% to 10% of patients with presumed mild pancreatitis progress to severe pancreatitis during their hospitalization. A policy of early LC might result in increased morbidity and mortality in a patient who was misdiagnosed as having mild pancreatitis who then progresses to more severe disease. It is important to note that, in the present study, which spanned 5 years and included 303 patients at 2 institutions, no patient with mild pancreatitis progressed to severe pancreatitis. We believe that the safety of an early LC lies in the identification and exclusion of patients who may be at risk of progressing to a more severe pancreatitis, such as those with tachycardia, elevated serum urea nitrogen level, or evidence of cholangitis at hospital admission. Our previous study\(^g\) has verified the utility of these criteria in predicting mild pancreatitis. It is worth noting that, in the present study, more than 75% of the patients admitted were eligible for an early LC following application of these exclusion criteria.

Another concern is that an early LC may lead to a higher incidence of postoperative ERCP. In gallstone pancreatitis, most CBD stones pass within 48 to 72 hours of admission.\(^3\) Performing an LC, along with an intraoperative cholangiography, too early might result in a higher rate of detection of CBD stones that would otherwise have passed harmlessly into the duodenum. In one of the previously cited studies,\(^a\) there was no difference in the percentage of ERCPs performed between the early and delayed LC groups (6% in early LC group vs 4% in delayed LC group; \(P = .38\)). The present study also demonstrates no difference between early or delayed LC in the necessity for postoperative ERCP. Interestingly, the overall rate of ERCP was significantly less in the early LC group compared with the delayed LC group, owing to increased use of preoperative ERCP in the delayed group. Given the similar complication rates in the 2 groups, this latter finding suggests that many of the ERCPs performed in the delayed LC group may have been unnecessary.

The results of our study, in conjunction with our previous investigations, provide further validation that an early LC (within 48 hours of admission) for mild gallstone pancreatitis can safely be performed without the need for normalization of laboratory values or complete resolution of clinical symptoms. Provided patients are carefully selected, this strategy will not increase the rates of complications; the rates of readmission, the need for conversion to an open cholecystectomy, or the need for ERCP. As such, our opinion is that the policy of delaying an LC for normalization of laboratory values is unnecessary and that an early operation is safe and should be the preferred approach.

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REFERENCES

The article by Falor and colleagues, “Early Laparoscopic Cholecystectomy for Mild Gallstone Pancreatitis: Time for a Paradigm Shift,” represents a potentially important retrospective study. By providing real data, Falor and colleagues once again show that some of our cherished biases and beliefs may be incorrect. Their study examined the impact of early vs delayed laparoscopic cholecystectomy in uncomplicated acute gallstone pancreatitis and demonstrated outcomes that were statistically indistinguishable. Specifically, they found no increase in the number of complications, in the incidence of conversion to open cholecystectomy, or in the need for postoperative endoscopic retrograde cholangiopancreatography. The article did demonstrate a significant 3-day decrease in hospital length of stay in the early laparoscopic cholecystectomy group. They concluded that a laparoscopic cholecystectomy can be safely performed early in gallstone pancreatitis, without waiting for normalization of laboratory values.

The study does have limitations that arise from the retrospective nature of the study. Gallstone pancreatitis was diagnosed if there were gallstones, epigastric pain, and pancreatic enzyme levels that were more than 3 times the normal level. Our practice has been to use the trend in pancreatic enzyme levels to guide the timing of an operation. That is, if levels are decreasing, the patient is considered for an earlier laparoscopic cholecystectomy. In the face of increasing pancreatic enzyme levels, our practice is to delay the operation until the levels stabilize or begin to decrease. In this study, it is conceivable that the timing of a single level could adversely impact decision making. In addition, when each patient presented to the emergency department with acute gallstone pancreatitis, each could have been managed differently, depending on which service the patient was admitted to, yet this was not specified or defined in the study.

For example, if the majority of patients in the delayed group were admitted to the medical or gastrointestinal service with a delayed surgical consult, this might impact the time-line of a laparoscopic cholecystectomy. The duration of time between surgical evaluation and laparoscopic cholecystectomy was not specified, but this may be the crucial determining factor for early operation. It would have been most interesting if the data had been made available to show whether differences in the length of hospital stay were attributable to the preoperative delay in surgical involvement. Our experience is that there is relatively little difference in postoperative lengths of hospital stay for most patients undergoing a laparoscopic cholecystectomy, but we often have significant differences in time prior to operation. Finally, in the present study, almost two-thirds of the patients underwent a delayed laparoscopic cholecystectomy, despite prior work by the authors documenting the safety of early laparoscopic cholecystectomy. This apparent disparity suggests either that, despite good evidence, it can be difficult to change surgical practice or that preoperative delays thwart good surgical care. Based on this study, surgeons should feel more comfortable proceeding with an early laparoscopic cholecystectomy to shorten hospital length of stay without sacrificing outcomes.

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