Management of Gallstone Cholangitis in the Era of Laparoscopic Cholecystectomy

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Hypothesis: The combined endoscopic and laparoscopic approach is safe and effective in managing gallstone cholangitis in the era of laparoscopic cholecystectomy (LC).

Design: Retrospective case series.

Setting: University teaching hospital.


Interventions: The main treatments were endoscopic retrograde cholangiopancreatography (ERCP) and endoscopic sphincterotomy (ES) followed by interval LC. Open or laparoscopic common bile duct exploration (OCBDE or LCBDE) was used when ERCP or ES failed.

Main Outcome Measures: Success of various interventions, morbidity and mortality, and long-term incidence of recurrent biliary symptoms.

Results: Endoscopic retrograde cholangiopancreatography was successful in 175 patients (95%), with bile duct stones found in 147 (84%). Endoscopic stone clearance by ES was achieved in 132 patients (90%). Morbidity rate after ERCP or ES was 4.0% (n=7), and overall mortality rate from cholangitis was 1.6% (n=3). After bile duct stone clearance, 82 patients underwent LC with a conversion rate of 9.8% (n=8) and a morbidity rate of 3.6% (n=3). Eighteen patients underwent OCBDE with a morbidity rate of 33% (n=6), and 3 underwent LCBDE with 1 conversion and no morbidity. There was no operative mortality. Seventy-eight patients were managed conservatively after endoscopic clearance of bile duct stones. Follow-up data were available in 101 patients with cholecystectomy and 73 patients with gallbladder in situ. During a median follow-up of 24 months, recurrent biliary symptoms occurred in 5.9% (n=6) and 25% (n=18), respectively (P=.001). In both groups, the most common recurrent symptom was cholangitis (n=5 and n=14, respectively). Gallbladder in situ (risk ratio, 4.16; 95% confidence interval, 1.39-12.50; P=.01) and small-size papillotomy (risk ratio, 2.94; 95% confidence interval, 1.07-8.10; P=.04) were significant risk factors for recurrent biliary symptoms.

Conclusions: Endoscopic sphincterotomy for biliary drainage and stone removal, followed by interval LC, is a safe and effective approach for managing gallstone cholangitis. Patients with gallbladder left in situ after ES have an increased risk of recurrent biliary symptoms. Laparoscopic cholecystectomy should be recommended after endoscopic management of cholangitis except in patients with prohibitive surgical risk.

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A CUTE CHOLANGITIS is a serious complication of gallstones, occurring in 6% to 9% of patients admitted to the hospital with gallstone disease. Prior to the introduction and acceptance of endoscopic management, open common bile duct exploration (OCBDE) was the standard treatment, with a mortality rate of 10% to 40%. The advent of endoscopic retrograde cholangiopancreatography (ERCP) and endoscopic sphincterotomy (ES) has remarkably decreased the mortality rate of acute cholangitis to between 0.4% and 7%. A prospective randomized trial previously conducted by our department has shown that endoscopic biliary drainage reduced the mortality rate of severe cholangitis compared with emergency surgical decompression. Endoscopic management followed by elective open surgery became an accepted approach in the 1980s.

In the 1990s, laparoscopic cholecystectomy (LC) has replaced open surgery as the standard treatment for symptomatic gallstone disease, and the use of ERCP and ES for the diagnosis and management of common bile duct (CBD) stones has been further popularized. How-
PATIENTS AND METHODS

During a 4-year period between January 1995 and December 1998, 184 consecutive patients with acute cholangitis due to gallstone disease were admitted through the Accident and Emergency Department and managed in the Department of Surgery, Queen Mary Hospital, Hong Kong, China. Patients with intrahepatic ductal stones or previous cholecystectomy were excluded from this study. There were 98 men (53%) and 86 women (47%). The mean age was 70.5 years (SD, 13.1 years; age range, 25-96 years), and 98 patients (53%) were aged 70 years or older. Comorbid illnesses, including hypertension, cardiac disease, chronic respiratory disease, diabetes mellitus, chronic renal insufficiency, and cirrhosis were present in 112 patients (61%). The diagnosis of acute cholangitis was based on a combination of upper abdominal pain, jaundice, chills, and fever (temperature >37.5°C). Sixty patients (33%) had severe cholangitis defined by the presence of septic shock, mental confusion, or persistent high fever despite antibiotic treatment.

MANAGEMENT PROTOCOL

All patients were admitted under the care of a single hepatobiliary surgical team and managed according to a standard protocol. Patients began fasting and were given intravenous fluid after admission. After routine blood tests including blood culture, a broad-spectrum intravenous antibiotic, ticaricillin clavulanate (3.2 g every 8 hours), was administered immediately after a clinical diagnosis of acute cholangitis was made. Urgent ultrasonography was performed in the Department of Diagnostic Radiology to confirm the diagnosis. For patients with severe cholangitis, emergency ERCP was performed after initial stabilization within the same day of admission. For clinically mild cholangitis, ERCP was performed the next day after admission in most cases, and in any case not later than 72 hours after admission.

Endoscopic retrograde cholangiopancreatography was performed by the hepatobiliary surgeons in the surgical endoscopy unit, which provided 24-hour emergency ERCP service. All surgeons in the hepatobiliary team have been fully trained in ERCP procedures. The procedure was carried out under local pharyngeal anesthesia and intravenous sedation, with close monitoring of patients’ hemodynamic conditions. A diagnostic cholangiogram with selective CBD cannulation was performed first to detect any CBD stone. For patients with unstable hemodynamic status or expected difficulty of stone removal, initial drainage was obtained by insertion of endoprosthesis using a polyethylene double pigtail catheter to control the sepsis, followed by ES and stone removal in an elective session. Otherwise, ES and stone removal were performed in the same session. The size of papillotomy was gauged by the balloon size that could pass through. A small papillotomy was defined as one that admitted balloons smaller than 2 mL, and a large papillotomy was defined as one that admitted a 2-mL or larger balloon. Stone removal was carried out using a basket, balloon catheter, or mechanical lithotripsy.

For patients in whom endoscopic clearance of CBD stones was successful, an interval LC was performed in 6 to 12 weeks. For elderly patients with comorbid illnesses, LC was offered unless the operative risk was considered prohibitive. High-risk patients, such as those with severe cardiopulmonary disease, and patients who refused surgery were managed conservatively with regular follow-up to monitor for any recurrent biliary symptoms.

For patients in whom ERCP or endoscopic stone clearance failed, the management was governed by the severity of cholangitis. Patients with severe cholangitis were managed by emergency OCBDE or percutaneous transhepatic biliary drainage if the patients were considered too unstable for an emergency operation. Patients with mild cholangitis that subsided with antibiotic treatment were managed by early elective OCBDE. Laparoscopic common bile duct exploration was performed in selected patients with failed ES in whom laparoscopic stone extraction was not deemed too technically demanding. Patients with multiple large CBD stones that failed to be extracted by endoscopic means were not considered for LCBDE.

PATIENT FOLLOW-UP

All patients were offered regular follow-up in the outpatient clinic, regardless of whether definitive surgical treatment had been given. Patients were initially seen at intervals of 2 to 3 months in the first year, and then every 4 to 6 months. Patients with recurrent biliary symptoms were readmitted for investigation for possible recurrent CBD stones or cholangitis.

Patients’ clinical data and treatment outcomes were obtained from hospital records. Details of endoscopic findings were retrieved from a computerized record database, with review of ERCP films to clarify any uncertain findings if necessary. Follow-up data were obtained from outpatient records and readmission charts. For patients who did not attend regular follow-up, a telephone interview directly with the patient (or with the relative if the patient had died) for any recurrent biliary symptoms was conducted by the principal investigator.

STATISTICAL ANALYSIS

Continuous data were expressed as mean ± SD. Comparison between groups was performed using the χ² test with Yates correction (or Fisher exact test where appropriate) for nominal variables, and the unpaired t test for numerical variables. Risk factors for recurrent biliary symptoms were analyzed using logistic regression analysis. P < .05 was taken to be statistically significant.
gallstone cholangitis in the laparoscopic era, with a particular reference to the efficacy of the combined endoscopic and laparoscopic approach, and the long-term outcomes of ES alone for gallstone cholangitis.

### RESULTS

The overall management of the 184 patients is summarized in the flow chart in the Figure.

**ENDOSCOPIC MANAGEMENT OF ACUTE CHOLANGITIS**

The overall success rate of a diagnostic ERCP was 95% (175/184). Cannulation of CBD failed in 9 patients because of previous Billroth II gastrectomy (n = 6), technical difficulty (n = 2), or anatomical distortion by peritumoral diverticulum (n = 1). Among the 175 patients with successful ERCP, no CBD stone was found in 28 patients (16%), presumably due to spontaneous stone passage. Common bile duct stones were present in 147 patients (84%), and biliary decompression was achieved in all patients by either ES with stone removal in the same session (n = 103) or temporary stenting (n = 44). Subsequently, ES was performed in 33 of the patients with initial stenting. Overall, 136 (93%) of 147 patients with CBD stones underwent ES. Eventually, endoscopic stone clearance was achieved in 132 patients (90%) after a mean of 1.6 sessions of ERCP (range, 1-4 sessions). Nine patients (5.1%) had post-ERCP pancreatitis, which resolved with conservative management. Two patients (1.5%) developed postphincterotomy bleeding, both managed successfully by endoscopic hemostasis. There was no other morbidity or any mortality related to ERCP or ES. Among the 9 patients in whom ERCP failed, 3 underwent emergency OCBDE, 3 underwent early elective OCBDE after control of cholangitis with antibiotics, and 3 patients with septic shock underwent emergency percutaneous transhepatic biliary drainage (n = 3).

Overall, 3 (1.6%) of 184 patients died. The mortality rate among patients with severe cholangitis was 5.0% (3/60). All 3 deaths occurred in patients with advanced septic shock and disseminated intravascular coagulation. One 68-year-old woman died of persistent shock 36 hours after admission despite emergency stenting for CBD stones. Another 69-year-old woman, also with endoscopic stenting, died of massive intracerebral hemorrhage 24 hours after admission. An 86-year-old man underwent emergency percutaneous transhepatic biliary drainage because of failed ERCP, but died of refractory shock 4 hours after the procedure.

### SURGICAL MANAGEMENT OF GALLSTONE DISEASE

After successful endoscopic stone extraction, 82 patients underwent interval LC. Only 2 patients (2.4%) had recurrent biliary symptoms (1 recurrent cholangitis and 1 biliary colic) while waiting for LC. Conversion to open surgery was required in 8 patients (9.8%), due to dense adhesion in the Calot triangle (n = 7) or around the gallbladder (n = 1). The conversion rate was higher compared with that of 4.4% (30/688) among patients who underwent elective LC during the same period for uncomplicated gallstone disease; ie, presentation with biliary colic (P = .04). Three patients (3.6%) developed postoperative complications, including subumbilical wound infection in 2 patients without conversion and chest infection in 1 patient requiring conversion to open surgery.

Early elective LCBDE was attempted in 3 patients in whom ES failed, and was successful in 2 by laparoscopic choledochotomy without T-tube drainage. Both patients had a stent in situ, and the endoprosthesis was removed after recovery from the operation. One patient required conversion due to dense adhesion in the Calot triangle. No morbidity occurred in these 3 patients. Including these 3 patients, the overall conversion rate of laparoscopic surgery in this series was 10.6% (9/85), and the morbidity rate was 3.5% (3/85).

A total of 18 patients underwent OCBDE, including the 3 patients with emergency OCBDE. Six of these patients had previous Billroth II gastrectomy. Subphrenic abscess occurred in 1 patient after emergency OCBDE and required reoperation for drainage. One patient had pneumonia and 4 had wound infections after elective OCBDE. The overall morbidity rate of OCBDE was 33% (6/18), which was significantly higher than the 3.5% among the 85 patients who underwent laparoscopic surgery with or without conversion (P = .02).

Altogether, 103 patients underwent definitive surgical treatment without any operative mortality. The mean ± SD age of these patients was 66.2 ± 11.7 years (age range, 25-84 years), and the frequency of comorbid illnesses was 57% (59/103). Seventy-eight patients were managed conservatively after initial endoscopic management of cholangitis. Twenty-eight patients, all with severe comorbid illnesses, were considered high risk for surgery. The age
Table 1. Follow-up Status of Patients With and Without Cholecystectomy

<table>
<thead>
<tr>
<th>No. (%) of Patients</th>
<th>With Cholecystectomy (n = 101)</th>
<th>Without Cholecystectomy (n = 73)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alive with no recurrent biliary symptoms</td>
<td>93 (93)</td>
<td>49 (67)</td>
</tr>
<tr>
<td>Recurrent cholangitis</td>
<td>5 (5)</td>
<td>14 (19)*</td>
</tr>
<tr>
<td>Jaundice due to recurrent common bile duct stones</td>
<td>1 (1)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Biliary colic</td>
<td>0 (0)</td>
<td>3 (4)</td>
</tr>
<tr>
<td>Deaths from unrelated conditions</td>
<td>2 (2)</td>
<td>6 (8)</td>
</tr>
</tbody>
</table>

* One death from recurrent cholangitis.

of this group of patients (mean ± SD, 78.7 ± 8.6 years; range, 61-96 years) was significantly higher than that of the operated group (P<.001). The other 50 patients were considered fit for surgery but refused surgical intervention, mostly because of advanced age. The age of this group (mean ± SD, 68.0 ± 12.3 years; range, 55-90 years) was not significantly different from that of the group undergoing surgery (P=.41), and comorbid illnesses were present in 44% (22/50) of these patients.

**LONG-TERM OUTCOME**

Of the 181 patients who survived the initial cholangitis, complete follow-up data were available from outpatient notes or readmission records in 112 (62%). For the remaining 69 patients, telephone interviews were successfully conducted in 62. Follow-up data were available in 174 patients (96%), including 101 patients with cholecystectomy and 73 patients with gallbladder in situ. By the time of analysis, 8 patients had died of unrelated medical conditions. When the end of follow-up was taken as the patient’s death, last follow-up, or interview date, the median follow-up was 24.0 months (range, 7.0-56.0 months). The follow-up duration in patients with and without cholecystectomy was similar (median, 24.0 and 23.5 months, respectively).

The follow-up status among the 101 patients with cholecystectomy and 73 patients without cholecystectomy by the time of analysis is given in **Table 1**. The overall incidence of recurrent biliary symptoms was significantly higher among patients with gallbladder in situ compared with those with cholecystectomy (25% vs 5.9%, P=.001). The incidence of recurrent biliary symptoms among patients not operated on because of high surgical risk was 27% (7/26), and among patients who refused operation was 23% (11/47). By far the most common recurrent symptom was cholangitis (79%). Recurrent cholangitis was associated with recurrent CBD stones in all cases, and only one patient had evidence of stenosed papillotomy. All 19 patients with recurrent cholangitis were managed initially with ERCP. One patient in the group without cholecystectomy had severe cholangitis with septic shock and died despite endoscopic drainage. Open common bile duct exploration was required in 2 patients because of failure of endoscopic stone clearance. The other 16 patients with cholangitis and 2 patients with CBD stones and jaundice had successful endoscopic stone clearance. Two patients subsequently agreed to LC and underwent the operation uneventfully. Three patients with biliary colic were managed conservatively.

**Table 2** presents a comparison of 10 clinical and endoscopic variables between patients with and without recurrent biliary symptoms. By multivariate analysis, gallbladder in situ (risk ratio, 4.16; 95% confidence interval, 1.39-12.50; P=.001) and small papillotomy (risk ratio, 2.94; 95% confidence interval, 1.07-8.10; P=.04) were the only significant risk factors of recurrent biliary symptoms.

This study documented for the first time the efficacy of the combined endoscopic and laparoscopic approach in a series of patients with acute gallstone cholangitis. The results of endoscopic management in this study corroborate data from other reports in which endoscopic decompression was employed for the management of acute...
cholangitis. An aggressive policy of early endoscopic biliary drainage has resulted in a low mortality rate of 1.7% in this series, which comprised predominantly elderly patients. Expeditious decompression of the biliary tree is particularly important to prevent mortality in elderly patients compromised by comorbid illnesses, who could decompensate quickly in the face of sepsis. A recent study has shown that delay in ERCP in patients with severe cholangitis resulted in increased mortality and morbidity.

Endoscopic biliary drainage can be accomplished by ES, followed by clearance of stones in the same session, or by placement of a biliary endoprosthesis. In septic patients with unstable hemodynamic status or multiple large stones, temporary drainage without sphincterotomy followed by elective ES for stone removal is a safer approach. Previously, we have used nasobiliary drainage for acute cholangitis, but in recent years we have used an endoprosthesis instead. In accordance with others’ experience, we have found it equally effective in biliary drainage and more convenient to use.

Apart from biliary drainage for control of sepsis, ERCP and ES allow endoscopic CBD stone removal before LC, thus avoiding the need for exploration of CBD. In the laparoscopic era, preoperative ERCP has been widely used for the management of patients with suspected choledocholithiasis, but this approach has been criticized for a high negative rate, resulting in unnecessary ERCP in many patients. In agreement with others’ findings, our data show a high incidence of CBD stones in patients with cholangitis and a high success rate of ES in CBD clearance. Gallstone cholangitis is particularly suited to a combined approach with ERCP for initial management followed by LC.

No mortality and minimal morbidity was observed with interval LC after endoscopic clearance of CBD stones in our patients. Although relatively high compared with LC for uncomplicated gallstone disease, the conversion rate of 9.8% is acceptable. The main reason for conversion was dense adhesion around the Calot triangle as a result of previous cholangitis. Our experience with interval LC for acute cholecystitis also showed that adhesion was the main cause of conversion, and early conversion was recommended to prevent complications. Early conversion is also important when severe adhesion is encountered during LC for gallstone cholangitis, as persistent dissection in the presence of severe scarring may risk bile duct injury. We have previously demonstrated in a randomized trial that early LC within 72 hours after admission resulted in a lower conversion rate compared with interval LC for patients with acute cholecystitis. Early LC for gallstone cholangitis would have the added merit of avoiding any recurrence of biliary symptoms between ES and interval LC. However, such an approach is usually not possible in cases of cholangitis, as it usually takes a few days before the sepsis is fully controlled even after biliary drainage, and more than one ERCP session is often required for complete CBD stone clearance. Experience with LC for acute cholecystitis has demonstrated a high conversion rate if delayed for more than 72 hours, owing to the onset of adhesion combined with residual inflammation. Studies are required to clarify the optimal timing for LC in patients with gallstone cholangitis, but early interval LC appears to be a reasonable approach.

Although there is little controversy that severe cholangitis is best managed by endoscopic drainage followed by surgery, whether this is the best approach for patients with mild cholangitis is less clear. An alternative option for these patients is early LCBDE after control of cholangitis with antibiotics. In experienced centers, LCBDE by either choledochotomy or transpapillary duct exploration is successful in 85% to 95% of patients. Urgent LCBDE for cholangitis has also been reported. Whether ES followed by LC or LCBDE is preferable for mild gallstone cholangitis is a subject for future studies, but the preferred approach would also depend on the local expertise available. Our main approach for choledocholithiasis is preoperative ERCP followed by LC, but we also attempt LCBDE in selected patients with failed endoscopic stone clearance. For those with difficult CBD stones that failed to be extracted by endoscopic means, we offered OCBDE because LCBDE was expected to be difficult. Open common bile duct exploration was associated with a high rate of infective complications, presumably related to the presence of infected bile. However, it still has a role in the laparoscopic era, at least in patients with previous Billroth II gastrectomy, and in those in whom ES or LCBDE fails to clear CBD stones.

Several studies have evaluated the long-term outcome after ES for CBD stones without cholecystectomy. This study provides unique data on the long-term risk of recurrent biliary symptoms after ES specifically in patients with cholangitis. In particular, we have evaluated the long-term efficacy of ES alone for high-risk or elderly patients. Our study shows that patients managed with ES alone were at a significantly higher risk of recurrent biliary symptoms compared with those with cholecystectomy. A 25% incidence of recurrent biliary symptoms after a short median follow-up of 24.5 months was strikingly high compared with an incidence of 5% to 20% after an average follow-up of 24 to 61 months in previously reported series of patients with gallbladder in situ after ES. A finding that deserves emphasis is that cholangitis is by far the most common recurrent biliary symptom in this study, whereas in previous studies gallbladder symptoms like biliary colic or acute cholecystitis were the main recurrent symptoms after ES.

Although repeated ERCP was effective in the management of recurrent cholangitis in most of the cases, 1 patient died as a result of recurrent cholangitis and 2 required OCBDE. The risk of recurrent cholangitis was particularly high in patients with a small papillotomy. While every attempt should be made to perform an adequate papillotomy, the size of the papillotomy is often limited by anatomical factors such as the presence of a periampullary diverticulum or technical factors. Our findings suggest that for patients with gallstone cholangitis, ES alone is insufficient to prevent further attacks of cholangitis due to passage of stones from the gallbladder, probably because cholangitis is usually caused by stones of substantial size. In contrast, studies have shown that ES alone is effective in preventing recurrent pancreatitis among patients with acute pancreatitis.
atitis, because stones causing pancreatitis are usually small.3,32 Cholecystectomy should be advocated in patients with gallstone cholangitis unless the operative risk is extremely high. A previous randomized trial has shown that in elderly or high-risk patients, open cholecystectomy with bile duct exploration is preferable to ES with the gallbladder left in situ as a definitive treatment of CBD stones.33 With the availability of laparoscopic surgery, the risk of cholecystectomy is even lower for elderly or high-risk patients. Studies have shown that LC can be accomplished in elderly patients with low mortality and morbidity rates comparable to younger patients even for complicated gallstone disease,33,34 and it has also been shown that LC is associated with a lower complication rate than open cholecystectomy in elderly patients.35 While further studies are required to establish the safety limit for LC in high-risk elderly patients, LC following ES is recommended for the majority of elderly patients with gallstone cholangitis. For patients with an extremely high surgical risk or those who refuse operation after ES, long-term follow-up should be offered, especially if papillotomy size is inadequate. These patients should also be advised about the high risk of recurrent cholangitis and the importance of early readmission for any biliary symptoms.

In conclusion, this study has demonstrated that ES followed by LC is a safe and effective approach for the management of gallstone cholangitis in the laparoscopic era. Endoscopic sphincterotomy alone with gallbladder left in situ was associated with a high risk of recurrent biliary symptoms, especially recurrent cholangitis, and thus LC should be recommended unless the surgical risk is prohibitive.

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