Impact of endoscopic intervention in 100 patients with suspected postcholecystectomy bile leak


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Background: Bile leak is a recognized complication of cholecystectomy. Endoscopic intervention is widely accepted as a treatment for this complication, but the optimal form is not well defined.

Methods: An ERCP database was reviewed retrospectively to identify all cases of bile leak related to cholecystectomy. Patient records and endoscopy reports were reviewed, and structured telephone interviews were conducted to collect data.

Results: A total of 100 patients (61 women, 39 men; mean age, 53 [17] years) with suspected postcholecystectomy bile leak were referred for ERCP. Cholecystectomy was commenced laparoscopically in 83 patients (with an open conversion rate of 30%). The most common symptoms were pain (n = 62) and fever (n = 37). Cholangiography was obtained in 96 patients. A leak was identified in 80/96 patients, the most common site being the cystic-duct stump (48), followed by ducts of Luschka (15), the T-tube site (7), and other sites (10). Treatment included stent insertion alone (40), sphincterotomy alone (18), combination stent/sphincterotomy (31), none (6), and other (1). Three patients with major bile-duct injuries were excluded from the analysis. Endoscopic therapy was unsuccessful in 7 patients (6 in the sphincterotomy alone group; p = 0.001). Four patients underwent surgery subsequent to ERCP to control the leak. All 4 were in the sphincterotomy alone group (p = 0.001). Post-ERCP pancreatitis developed in 4 patients (3 mild, 1 moderate).

Conclusions: The optimal endoscopic intervention for postcholecystectomy bile leak should include temporary insertion of a biliary stent. (Gastrointest Endosc 2005;61:269-75.)

Iatrogenic injury to the biliary tree is a well-documented complication of cholecystectomy, the most commonly reported injury being bile leak. The advent of laparoscopic cholecystectomy, together with its sudden and widespread implementation in the early 1990s, led to a dramatic increase in the frequency of bile-duct injury.1-5 A significant postoperative bile leak occurs in approximately 0.8% to 1.1% of patients.6,7 In several published series, surgery often was used as first-line management for such cases,2,7-10 despite the widespread availability of ERCP and a large body of data supporting its use in this setting.11-21

The goal at ERCP, in addition to a diagnosis of the biliary lesion, is to negate the transpapillary pressure gradient, thereby permitting preferential transpapillary bile flow instead of extravasation via the leak. Endoscopic management of bile leaks is safe and efficacious, but the optimal endoscopic intervention is not established. Long-term follow-up data regarding efficacy and complication rates also are lacking. The aim of this study was to assess the different endoscopic measures used to treat post-cholecystectomy bile leak, together with the short- and long-term outcomes of these interventions.

PATIENTS AND METHODS

The endoscopy database of a tertiary referral, university-affiliated hospital was reviewed retrospectively to identify all patients referred for ERCP because of suspected bile leak related to cholecystectomy (open or laparoscopic). Patient records and endoscopy reports were reviewed, and structured telephone interviews were conducted to collect data. Data were collected regarding clinical features of bile leaks, referral time, healing and discharge times, and
follow-up. Retrograde cholangiograms and other imaging data were reviewed to correctly categorize lesions and to determine the site of the leak. Diagnostic and therapeutic interventions, including all forms of surgical therapy were recorded.

All procedures were performed or supervised by two experienced pancretobiliary endoscopists; each had performed more than 5000 ERCPs, with annual volumes of more than 500 ERCPs. The therapeutic protocol for a demonstrated bile leak included sphincterotomy alone (early years), biliary stent insertion alone (straight polyethylene stents), or sphincterotomy plus stent (later years). The endoscopist, based on personal experience and published information, determined the choice of treatment at the time of the procedure. A stent (7F or 10F) was inserted to eliminate the transpapillary biliary-duodenal pressure gradient. The stent was not routinely inserted proximal to the site of the bile leak. In general, it is routine in our unit to perform biliary sphincterotomy by completely dividing the sphincter and by extending the incision to the maximum safe limit. We believe this minimizes the risk of subsequent sphincter stenosis.

A biloma was defined as a collection of bile, usually in the region of the gallbladder fossa (>2 cm diameter). However, this definition also was used in patients with more diffuse bilious fluid collections (bile ascites and bile surrounding the liver). Clinical healing of the leak was defined as the resolution of symptoms or, in patients with a drain in situ, by cessation of drainage or removal of the drain without adverse outcome.

Patient management was primarily determined by the surgeon who performed the cholecystectomy. Failure of endoscopic treatment(s) was defined as the need for further intervention to control the leak, including surgery, repeat ERCP, and/or percutaneous drainage of the biliary tree. Outcomes were assessed according to the type of endoscopic treatment performed. Patients with major duct injuries (defined as not amenable to endoscopic treatment, including complete bile-duct ligation and large-duct transaction) were not considered in the evaluation of the success or the failure of endoscopic treatment.

ERCP complications were classified and graded according to consensus criteria. Statistical methods

Mean and standard deviation, or median and interquartile range (IQR) in the case of skewed distributions, were used to summarize data for continuous variables; percentages were used for categorical variables. Kruskal-Wallis nonparametric analysis of variance was used to test for associations between the continuous outcome variables and type of treatment. Spearman rank correlation was used to quantify the amount of association between two continuous outcome variables. The Fisher exact test was used to test for association between categorical variables. A significance level of 5% was used throughout. The statistical analyses were performed with a statistical software package (SPSS for Windows, version 11; SPSS Inc, Chicago, Ill).

RESULTS

Over 5000 ERCP procedures were performed between 1992 and 2002. There were 125 patients referred for ERCP because of suspected bile leak. The suspicion of a bile leak arose in the setting of cholecystectomy in 100 patients (61 women, 39 men; mean age 53.2 [17.4] years). Open cholecystectomy was performed in 17 patients. Laparoscopic cholecystectomy was undertaken in 83 patients, but, in 25 (30%), the operation was converted to an open procedure. Mean follow-up for the entire patient group was 21.5 months (range 1-135 months).

Presentation

The majority of patients (62) presented with postoperative pain. Twenty-eight were asymptomatic and presented with bile drainage from a surgically placed drain, and 33 had bile drainage associated with symptoms. Of the patients with bile drainage, 8 had leakage related to a surgically placed T-tube (Fig. 1); 4 were symptomatic. The most common clinical symptoms are outlined in Table 1.

Median time from surgery to ERCP was 7.0 days (range 1-51 days). This was composed of the time from surgery to diagnosis of bile leak (median 2 days [range 0-45]), the time from diagnosis to patient referral for ERCP (median 1 day [range 0-21]), and the interval from referral to the ERCP procedure (two scheduled sessions per week).

ERCP success and treatment

A cholangiogram was obtained in 96 patients. In 4 patients, cholangiography could not be obtained, this was
because of an intradiverticular location of the papilla in one and prior gastrectomy with Billroth II anastomosis in another; in two patients, there was no obvious explanation. There were no further attempts to obtain cholangiography in 3 of these patients; in each, the leak resolved without further intervention. Percutaneous transhepatic cholangiography with insertion of a bile-duct drain was required in the patient with the Billroth II anastomosis because of pain and fever, and thereafter there was rapid resolution of the leak.

ERCP demonstrated a leak in 80 (83%) of patients. Of the 16 in whom a leak was not identified, 3 had a major bile-duct injury, two had complete duct obstruction because of a surgical clip, and one had a complete transection of the right hepatic duct.

The most common site of the leak was the cystic-duct stump (Fig. 2), followed by ducts of Luschka (Fig. 3) (Table 1). Endoscopic interventions are listed in Table 1. Stent insertion was the most common intervention (performed in 72 patients). A 10F stent was placed in 57 patients, and a 7F stent was placed in 15 patients, the latter primarily those in whom a sphincterotomy was not performed. In 6 patients, no leak was identified and no intervention was performed.

Biloma

A biloma was found in 31 patients, 17 before ERCP, and 14 after ERCP. One of the 17 in whom the biloma was diagnosed before ERCP required further drainage after ERCP. Treatments for biloma are summarized in Table 2.

**Short-term outcomes**

On an intention-to-treat basis, endoscopic intervention at ERCP had a success rate for resolution of the leak of 92% (92/100). If the 3 cases of major bile-duct injury are excluded, the success rate was 95% (92/97). Of the 80 patients with a demonstrated leak, 76 were successfully treated (95%). The median time for resolution of the leak was 3 days (range 1-39 days).

**Need for intervention/surgery after ERCP**

The need for surgery, percutaneous intervention, and/or repeat ERCP in relation to the type of endoscopic intervention is outlined in Figure 4. The number of patients in whom further intervention was required was significantly higher in the sphincterotomy alone group.

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**TABLE 1. Presentation, findings, and endoscopic treatment for patients with suspected bile leak**

<table>
<thead>
<tr>
<th>Presentation</th>
<th>No. patients (%)</th>
</tr>
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<tbody>
<tr>
<td>Asymptomatic drainage</td>
<td>28</td>
</tr>
<tr>
<td>Symptomatic</td>
<td>72</td>
</tr>
<tr>
<td>Pain</td>
<td>62</td>
</tr>
<tr>
<td>Fever</td>
<td>37</td>
</tr>
<tr>
<td>Jaundice</td>
<td>7</td>
</tr>
<tr>
<td>Distention</td>
<td>3</td>
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</table>

<table>
<thead>
<tr>
<th>Findings</th>
<th>No. patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Successful cholangiogram</td>
<td>96</td>
</tr>
<tr>
<td>Leak seen</td>
<td>80 (83%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Leak site</th>
<th>No. patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cystic</td>
<td>48 (60%)</td>
</tr>
<tr>
<td>Duct of Luschka</td>
<td>15 (19%)</td>
</tr>
<tr>
<td>T-tube related</td>
<td>7 (9%)</td>
</tr>
<tr>
<td>IHD</td>
<td>4 (5%)</td>
</tr>
<tr>
<td>CBD/CHD</td>
<td>5 (6%)</td>
</tr>
<tr>
<td>Unsure</td>
<td>1 (1%)</td>
</tr>
<tr>
<td>Choledocholithiasis</td>
<td>11 (14%)</td>
</tr>
</tbody>
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<table>
<thead>
<tr>
<th>Treatment</th>
<th>No. patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stent only</td>
<td>40</td>
</tr>
<tr>
<td>Sphincterotomy and stent</td>
<td>31</td>
</tr>
<tr>
<td>Sphincterotomy only</td>
<td>18</td>
</tr>
<tr>
<td>Nil</td>
<td>6</td>
</tr>
<tr>
<td>Papilla dilation and stent</td>
<td>1</td>
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</table>

**IHD,** intra hepatic duct; **CBD,** common bile duct; **CHD,** common hepatic duct.
compared with the stent alone group, or with the stent and sphincterotomy group \( (p < 0.01) \). When the 3 patients with major bile-duct injury are excluded, the need for surgery to control the leak subsequent to ERCP is comparable for all endoscopic treatment groups except sphincterotomy alone, which was associated with significantly more surgical procedures \( (p = 0.001, \text{ Fisher exact test}) \). One asymptomatic patient in the stent alone group had an ongoing leak detected at follow-up ERCP 4 weeks after stent insertion. The stent was exchanged, and, at ERCP 6 weeks later, the leak was closed. Three patients (1 treated by stent alone, 2 sphincterotomy alone) required repeat ERCP to control an ongoing leak. Stent insertion in the two patients treated initially by sphincterotomy alone

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**Table 2. Management of biloma (all patients)**

<table>
<thead>
<tr>
<th></th>
<th>Surgery</th>
<th>Percutaneous</th>
<th>Conservative</th>
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<tbody>
<tr>
<td>Pre-ERCP biloma</td>
<td>6</td>
<td>7*</td>
<td>4</td>
</tr>
<tr>
<td>(n = 17)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Post-ERCP biloma</td>
<td>4</td>
<td>11</td>
<td>Nil</td>
</tr>
<tr>
<td>(n = 14)</td>
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*One patient had percutaneous biloma drainage and laparoscopic drainage before ERCP.*

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**Figure 2.** A, Retrograde cholangiogram demonstrating stone in basket after biliary sphincterotomy, together with escape of contrast medium and insufflated air via cystic-duct stump into subhepatic space. B, Radiograph obtained after insertion of 10F plastic stent, showing air more prominently in subhepatic space.

**Figure 3.** Retrograde cholangiogram showing leakage of contrast from peripheral branches of right hepatic ductal system (duct of Luschka-type leak).
resulted in closure of the leak. The patient treated initially by stent alone (10F) had a new stent inserted after a sphincterotomy and bile-duct stone extraction; the leak resolved without sequelae.

Hospital stay
Median (IQR) hospital stay overall was 12 days (range 9-22 days). There was no significant difference between type of intervention at ERCP and total time in the hospital ($p = 0.9$) or time in the hospital after ERCP ($p = 0.3$). There was no significant association between delay in referral for ERCP and time in the hospital after ERCP ($r = 0.14, p = 0.2$). However, delay in referral was associated with a significant increase in total time in the hospital ($r = 0.39, p < 0.001$).

Bile-duct stricture
A bile-duct stricture developed in 4 patients during follow-up. One required no intervention, because the stricture was not associated with obstruction. In two other patients, the stricture resolved in response to a short period of stent insertion. The remaining patient had a high-grade stricture related to the original surgery (T-tube site) and required 11 ERCP procedures with serial stent insertion. One ERCP was complicated by severe pancreatitis associated with pancreatic pseudocyst formation. This patient recovered without sequelae. It is likely that the strictures in these 4 patients were the result of the original surgery.

Long-term outcomes
Four patients failed to return for a scheduled ERCP for stent removal and presented with a retained stent at a later date: two, 1 year later; one, 2 years later; and one, 4 years after stent insertion. One complained of pain alone; the other 3 patients presented with cholangitis. After stent removal and clearance of debris from the biliary tree, cholangiography was normal in all 4 patients. All 4 remain asymptomatic during follow-up.

Changes similar to those of primary sclerosing cholangitis developed in the right hepatic ductal system in one patient 6 weeks after stent insertion. These were thought to be caused by ischemic duct injury during the surgery. This patient was asymptomatic at 18 months’ follow-up. Bile-duct sludge-related cholangitis developed in one patient 15 months after stent insertion. Acute pancreatitis occurred in one patient 2 months after stent insertion. Cholangiography after the episode of pancreatitis was normal. One patient died at 15 months’ follow-up from an incidental gallbladder cancer discovered in the cholecystectomy specimen. One patient presented with cholangiocarcinoma 2 years after endoscopic treatment for the bile-duct leak and subsequently died as a result of the malignancy.

Complications of ERCP
ERCP resulted in pancreatitis in 4 patients (mild 3, moderate 1). All 4 patients recovered without long-term sequelae. Of these patients, 3 were treated with stent insertion alone and one had no treatment at ERCP. The occurrence of ERCP-related pancreatitis did not affect the ultimate outcome in any of these patients.

DISCUSSION
Bile leak as a result of cholecystectomy is uncommon. The frequency in large series is less than 2%.1-7 There are several possible treatment strategies for such leaks. A large body of data supports the early use of ERCP to exclude significant bile-duct injury and to effect closure of the leak by various endoscopic means.11-21 However, there is no consensus as to the optimal endoscopic intervention. Flow rates are better in vitro through straight compared with pigtail stents, and fistula closure is more rapid in dogs with stent alone compared with sphincterotomy alone.23,24 Strategies for stent insertion include “crossing” the leak site with the stent vs. elimination of the transpapillary pressure gradient without crossing the leak. The latter two approaches have not been thoroughly evaluated, but, in general, the diameter of the biliary tree proximal to the leak site (e.g., cystic duct) exceeds the diameter of the stent, and it seems unlikely that crossing the leak provides any additional therapeutic benefit, such as occlusion of the defect.
Potential treatment strategies, other than the conventional forms of intervention at ERCP, are aimed at decreasing basal sphincter of Oddi pressure. For example, a case has been described in which topically applied nitroglycerine (which relaxes the sphincter of Oddi) was used to heal a postcholecystectomy bile leak.25 Also, botulinum toxin has been shown in an animal model to heal bile leaks with an efficacy equal to stent insertion.26 At present, these strategies are experimental, and data from clinical trials are needed before that can be considered for clinical practice.

The present series of patients with postcholecystectomy bile-duct leaks treated endoscopically is the largest published to date. Significantly more patients in the group treated by sphincterotomy alone required further intervention to control the leak, surgery in particular, compared with the groups in which other forms of endoscopic intervention were used. This observation is consistent with the results of studies in animals, which suggests that stent insertion is superior to sphincterotomy alone.23 In the present series, the diameter of the stent did not influence outcome. Thus, insertion of a 7F stent should be adequate, especially when the goal is to avoid sphincterotomy in young patients. The analysis of our series indicates that stent insertion, as a universal practice, may be superior to sphincterotomy alone in patients with postcholecystectomy bile leak. Consequently, we changed our therapeutic protocol to routine stent insertion alone. Among patients treated by sphincterotomy alone, 4 went on to have open surgery to control the leak. Potentially, early repeat ERCP with stent insertion might have precluded surgery in these patients.

The proportion of laparoscopic cholecystectomies converted to open operations in the present series is 30%. Because the reported conversion rate for experienced surgeons is less than 10%, this suggests that a relatively high proportion of the operations in the present series were complex and consequently were associated with a higher risk of bile leak. A similar observation was made in at least two series.7,8 For patients with persistent symptoms after a cholecystectomy that was converted intraoperatively from laparoscopic to open, the index of suspicion for bile leak should be high.

Biliary stricture also is an infrequent, albeit serious, complication of cholecystectomy. This complication occurred in only 4 patients (4%) in the present series. Many factors can contribute to stricture formation, including local ischemia, electrosurgical injury at surgery, and peri-biliary inflammation as a result of leaking bile. The strictures in 3 of our patients were of mild severity, although one patient with a severe high-grade stricture had to be managed by endoscopic insertion of serial stents. The biliary injury that led to this stricture most likely occurred during the initial surgery with subsequent T-tube insertion.

Many of the clinical findings among the patients in the present series are relatively common after cholecystectomy. Thus, clinical features alone are unreliable for the diagnosis of bile leak. However, the constellation of symptoms in the appropriate setting should heighten clinical suspicion for a bile leak and prompt noninvasive imaging. When the volume of bile drainage is large, the diagnosis is readily apparent and prompt ERCP is indicated. When bile leak is suspected, we advocate early ERCP to determine the nature of the injury and to facilitate treatment, either endoscopically for bile leak or surgically for major ductal injury. Early ERCP may decrease the total hospital stay, because the increased time in the hospital in the present series was directly related to waiting time for ERCP.

Based on the present series, the optimal endoscopic treatment for a simple bile-duct leak is insertion of a straight plastic stent at least 7F in diameter. The stent should be removed after 4 weeks, and, in the majority of cases, follow-up cholangiography will not be required, particularly for uncomplicated cystic-duct stump or peripheral duct of Luschka leaks. However, cholangiography should be obtained if there is known or probable stricture formation, for example, if the leak had arisen directly from the bile duct or the right hepatic duct. The decision for a follow-up ERCP, as opposed to stent removal alone, has both ethical implications and economic considerations.

In summary, this study found that stent insertion alone for postcholecystectomy bile leak is superior to sphincterotomy alone, because fewer patients required additional intervention (particularly surgery) to control the leak. However, the retrospective design of the study has inherent limitations, and a prospective randomized study comparing treatment options and timing of intervention is needed.

REFERENCES


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Abstract presentation at Australian Gastroenterology Week, October 4-8, 1999 (J Gastroenterol Hepatol 1999;14 Suppl:A137).

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