Is peripapillary choledochoduodenal fistula an indication for endoscopic sphincterotomy?

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Background: Most patients with a peripapillary choledochoduodenal fistula undergo fistulotomy by endoscopic sphincterotomy for the treatment of bile duct stones. However, whether sphincterotomy should be performed in patients with the fistula but without stones is controversial.

Methods: Among 165 patients in whom a benign peripapillary choledochoduodenal fistula was diagnosed at ERCP, the clinical outcome was retrospectively analyzed and compared between those who underwent fistulotomy by endoscopic sphincterotomy (group 1) and those whose fistula was left untreated (group 2). All patients with hepatolithiasis, residual stones, biliary diversion, or transduodenal papillotomy were excluded (32, leaving 133). Fistulas were divided into types I and II according to the location of the fistula (Ikeda classification).

Results: Follow-up data collected during a median period of 124 months were available for 127 of 133 patients (95%), 76 in group 1 and 53 in group 2. Late complications were bile duct stone recurrence (17 patients), acute cholangitis (7 patients), and biliary carcinoma (2 patients). The incidence of stone recurrence was not significantly different between the 2 groups ($p = 0.1$). In group 2, 4 patients (8%) with an untreated type II fistula had 1 to 3 episodes of presumed reflux cholangitis, which resolved quickly with conservative treatment.

Conclusions: Endoscopic sphincterotomy is not always necessary for peripapillary choledochoduodenal fistulas if bile duct stones are absent because reflux cholangitis is a relatively rare complication that can be easily managed. (Gastrointest Endosc 2001;53:313-7.)

Peripapillary choledochoduodenal fistula, mostly caused by spontaneous penetration of common bile duct stones into the duodenum,1,2 was formerly considered extremely rare3-5 but has been recognized more frequently since the introduction of ERCP.1,2 Currently, most patients with a peripapillary choledochoduodenal fistula undergo endoscopic sphincterotomy (ES) for the treatment of bile duct stones rather than operative procedures such as transduodenal papillotomy or papilloplasty.6-8 However, the most appropriate treatment for patients with a fistula but without stones is unknown. Although the etiology and clinical features of the choledochoduodenal fistula have been well documented,1,2,9 little information is available on the clinical outcome. Persistent fistula may lead to cholangitis and/or pancreatitis by the same mechanism as that of biliary sump syndrome.10,11 If this is the case, fistulotomy may be justified, even in patients with a fistula who had no bile stones at the time of diagnosis. If not, the fistula may be left untreated, thereby obviating the need for ES. The aim of this study was to analyze the outcome of patients with persistent fistula but without stones to clarify whether the fistula alone constitutes an indication for ES.

**PATIENTS AND METHODS**

Medical records were retrospectively reviewed for 165 patients in whom a diagnosis was made with ERCP of benign peripapillary choledochoduodenal fistula between 1970 and 1998. The first 80 patients were described in our previous report on the etiology and diagnosis of the fistula.1,2 In all 165 patients, bile duct stones or a history suggestive of stones was present. There were 74 men and 91 women, and the mean age was 61.9 years (range 24 to 92 years). Eighty-seven patients (53%) had undergone various types of biliary surgery before the diagnosis of the fistula, whereas the other 78 (47%) had no history of biliary disease.

The fistulas were divided into 2 types according to the classification of Ikeda and Okada1 previously reported from our institution: type I on the orad prominence of the papilla and type II at or just proximal to the upper margin of the orad prominence (Fig. 1).

Patients with hepatolithiasis were excluded from this outcome analysis because residual intrahepatic stones were considered a significant risk for subsequent biliary septic complications even without a fistula.12 Moreover,
intrahepatic stones migrating into the bile might be indistinguishable from recurrent bile duct stones.

Patients were divided into 2 groups according to the treatment performed; group 1 underwent fistulotomy by ES, and group 2 received no treatment for the fistula. All patients who underwent Billroth II diversion gastrectomy, transduodenal papilloplasty, or biliary diversion by means of choledochoduodenostomy or Roux-en-Y hepaticojejunostomy were excluded. Patients with residual stones after the treatment were also excluded.

Stones obtained during the treatment were classified as cholesterol, bilirubinate, or black pigment stones by chemical analysis. This analysis was conducted by the preliminary separation of stone constituents into subgroups with solvent partition and column chromatography followed by gas-liquid chromatography.

Follow-up data were obtained from outpatient records or by mail questionnaire, telephone call, interview, or ERCP when indicated. All the patients were asked about the presence and timing of certain symptoms: abdominal pain, fever, jaundice, and dark urine. The presence of residual stones was confirmed by ERCP at the completion of treatment. Recurrent stones were defined as stones that developed after extraction and completion of treatment. Data on patients who died during the follow-up period were included in the analysis to determine whether death was related to treatment and/or biliary disease. The incidence and frequency of late complications such as stone recurrence, cholangitis, sump syndrome, and development of biliary cancer were compared between groups 1 and 2. These same data were compared for patients with type I and type II fistulas in group 2.

Comparisons between groups were performed by using chi-square test or Fisher exact test. The level of \( p < 0.05 \) was considered significant.

RESULTS

At the time of diagnosis of the fistula in 165 patients, 96 (58%) had a type I fistula and 64 (39%) type II. Two fistula orifices were found in the remaining 5 patients (3%): a combination of types I and II in 2 patients and two type I fistulas in 3 patients. Air or barium was observed in the biliary tree in 40 patients (24%). Seven of them had a type I fistula, and 32 had type II. One had a combination of the 2 types. Of 112 patients (68%) with bile duct stones, 23 also had gallbladder stones and 13 had intrahepatic stones. The stones were composed of calcium bilirubinate in 109 patients and of cholesterol in the other 3. Fourteen patients (8%) had stones only in the gallbladder, and 7 patients had them only in the intrahepatic ducts. Thirty-two patients (19%) had no stones in the biliary tract. Twenty patients in all (12%) had hepatolithiasis.

Of 145 patients, excluding the 20 with hepatolithiasis, 10 patients who underwent biliary diversion and/or transduodenal papilloplasty and 2 patients with residual stones were also excluded from the outcome analysis. Of the remaining 133 patients, 6 could not be tracked for long-term follow-up. Thus, follow-up data were available in 127 patients (95%) (Fig. 2).

Table 1 shows the treatments performed in the 127 patients for whom follow-up data were complete, 76 patients of group 1 and 51 of group 2. In group 1, 13 patients subsequently underwent cholecystectomy. In group 2, 38 patients were not treated, and 24 underwent cholecystectomy and/or bile duct exploration without treatment of the fistula. These untreated fistulas in group 2 consisted of 27 type I, 23 type II, and 1 multiple.

Of these 127 patients, 42 (33%) died during the
follow-up period. After ERCP, 1 patient died of acute cholangitis and 1 died of biliary carcinoma. The cause of death was unrelated to biliary disease in 28 patients and unknown in the remaining 12 patients.

During a median period of 124 months (range 11 days to 28 years), 26 patients (20%) developed late complications including recurrence of bile duct stones (17 patients, 13%), acute cholangitis (7 patients, 6%), and biliary carcinoma (2 patients, 2%) (Table 2). The incidence of stone recurrence tended to be higher in group 1 (17%) than in group 2 (8%), but the difference was not statistically significant ($p = 0.13$). All recurrent bile duct stones were bilirubinate and easily treated again by endoscopy. Seven patients had stone recurrence 2 to 4 times. Acute cholangitis associated with recurrent stones occurred in 3 patients.

In group 2, only 4 patients (8%) had 1 to 3 episodes of cholangitis without evidence of biliary stones or tumors or a history of drug use or injury during the follow-up period. Under the presumptive diagnosis of reflux cholangitis, they received medical treatment, which rapidly improved their condition. All of them had an untreated type II fistula (Table 3). In group 2, a 74-year-old man died of bile duct carcinoma 2 years after the initial diagnosis of the fistula, and a 65-year-old woman developed early stage gallbladder carcinoma 7 years after fistula diagnosis.

**DISCUSSION**

The present study of the clinical outcomes of peripapillary choledochoduodenal fistula demonstrated that (1) the incidence of stone recurrence was not significantly different between patients who underwent ES and those whose fistula remained untreated, (2) reflux cholangitis sometimes occurred in patients with untreated type II fistulas even without recurrent stones, but it could be resolved quickly with conservative treatment, and (3) biliary carcinoma was found in 2 patients with a persistent fistula.

There are only 2 previous reports available on treatment strategy for the fistula. Sheu et al. suggested aggressive therapy to correct the fistula based on an analysis of 1-year follow-up data on 24 patients with this type of fistula. In contrast, a review of 19 cases led other researchers to the conclusion that an uncomplicated peripapillary choledochoduodenal fistula probably does not require treatment. Both analyses included only small numbers of patients and follow-up was short. Our study consists of a relatively large number of patients with follow-up for a median of 124 months. It is our belief that the 34% mortality rate at the time of follow-up does not affect the reliability of the follow-up data because most patients were elderly at the time of diagnosis of the fistula, and their deaths were not related to the fistula.

ES has been considered the standard for treatment of fistula if bile duct stones are present because both removal of the stones and fistulotomy are achieved nonoperatively. Although some investigators have described the effectiveness of enlarging the fistula in a cephalad direction through the fistula orifice with the standard ES technique, an incision of excessive length results in an increased risk of hemorrhage and perforation. In addition, an incision positioned well proximal may predispose a patient to biliary sump syndrome. Ramsey et al. reported the use of a needle knife to open the sump portion between the fistula and the papilla in a caudal direction. This maneuver may be helpful when access to the common bile duct through the ampullary orifice is impossible in patients with a fistula.

In our present series of patients with fistulas, all recurrent bile duct stones were bilirubinate stones, the formation of which has been considered to be associated with the activity of β-glucuronidase released from gram-negative bacteria. ES has

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**Table 1. Treatments performed in 127 patients with peripapillary choledochoduodenal fistula with complete follow-up**

<table>
<thead>
<tr>
<th>Group 1</th>
<th>No. of patients</th>
<th>Group 2</th>
<th>No. of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>ES</td>
<td>63</td>
<td>No treatment</td>
<td>31</td>
</tr>
<tr>
<td>ES + cholecystectomy</td>
<td>13</td>
<td>Cholecystectomy + BDE</td>
<td>9</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cholecystectomy</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td></td>
<td>BDE</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Extraction of stones through fistula</td>
<td>2</td>
</tr>
<tr>
<td>Total</td>
<td>76</td>
<td>Total</td>
<td>51</td>
</tr>
</tbody>
</table>

**Table 2. Late complications of peripapillary choledochoduodenal fistula after treatments**

<table>
<thead>
<tr>
<th></th>
<th>Group 1</th>
<th>Group 2</th>
<th>$p$ Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recurrence of stones</td>
<td>13 (17%)</td>
<td>4 (8%)</td>
<td>0.13</td>
</tr>
<tr>
<td>Cholangitis with recurrent stones</td>
<td>3 (4%)</td>
<td>0</td>
<td>0.15</td>
</tr>
<tr>
<td>Cholangitis without stones</td>
<td>0</td>
<td>4 (8%)</td>
<td>0.01</td>
</tr>
<tr>
<td>Biliary carcinoma</td>
<td>0</td>
<td>2 (4%)</td>
<td>0.08</td>
</tr>
</tbody>
</table>

*BDE,* Bile duct exploration.
been considered one of the causes that may promote stone recurrence because ablation of the sphincter mechanism leads to ascending biliary infection. Because the incidence of stone recurrence in our present study was not significantly different between patients who underwent ES and those whose fistula was left untreated, it is also possible that the existence of a fistula may contribute to the formation of bile duct stones due to infection through the fistula.

Reflux cholangitis sometimes occurs in patients with untreated type II fistula even in the absence of recurrent stones. Ikeda et al.1 and Sheu et al.6 reported that the fistula orifice and the bile duct stones were larger in patients with type II fistula than in those with type I fistula. In many patients with type II fistula, air or barium is seen in the biliary tree at the time of diagnosis of the fistula.1,2,7 In our present series, air or barium was observed in the bile duct in 40 patients (24%), 33 of whom had type II fistula.

Biliary sump syndrome is a rare problem after side-to-side choledochoduodenostomy or choledochojunostomy.10,11 Accumulation of stones, gravels, sludge, or food residue in the sump results in cholangitis, pancreatitis, or unexplained upper abdominal pain and fever. The large diameter of a type II fistula seems to offer a route of ascending biliary infection and to be a cause of the sump syndrome. Indeed, all 4 patients who presented with cholangitis during the follow-up period of the present study had an untreated type II fistula. ES has proved to be effective in eliminating this problem, thereby obviating the need for relaparotomy.10,11 However, because the incidence and frequency of recurrence of cholangitis are low and the symptoms can be managed without difficulty, as shown in this study, prophylactic ES for preventing sump syndrome may be unnecessary for patients with fistula who do not have bile duct stones.

Intentional creation of a type I fistula on the papillary orad prominence is often attempted with the use of a needle knife to achieve cholangiography when conventional endoscopic cannulation cannot be achieved.19,20 However, the long-term effect of this procedure has not been determined. In this series no patients with an untreated type I fistula developed sump syndrome. This finding may be supportive evidence for the use of this procedure.

Hakamada et al.21 reported that 8 (7.4%) of 108 patients developed bile duct cancer after transduodenal papilloplasty. The bile was infected in 7 of the 8 patients, and histopathology showed cholangiocarcinoma and various degrees of atypical hyperplasia secondary to chronic cholangitis. They postulated that chronic cholangitis due to reflux of duodenal contents with activated pancreatic juice and bacterial flora into the bile duct could be an important causative factor in late development of bile duct cancer after sphincteroplasty. No data have been presented to indicate that ES might increase the incidence of biliary carcinoma. Although the high incidence of intrahepatic cholangiocarcinoma in patients with hepatolithiasis,22,23 bile duct carcinoma in patients with congenital choledochal cyst,24 and gallbladder carcinoma in patients with the pancreaticobiliary maljunction are well known,25 the relation between carcinogenesis and fistula remains unclear. The 2 biliary carcinomas in patients with a persistent fistula in this study may be coincidental.

In conclusion, reflux cholangitis sometimes occurs in patients with an untreated fistula even in the absence of recurrent stones. However, the incidence and recurrence frequency of cholangitis are low, and the symptoms can be managed without difficulty. When bile duct stones are absent, ES is not always necessary, and the fistula may be left untreated.

### REFERENCES


### Table 3. Late complications among patients with untreated peripapillary choledochoduodenal fistula (group 2)

<table>
<thead>
<tr>
<th>Complication</th>
<th>Type I</th>
<th>Type II</th>
<th>Multiple</th>
<th>Total</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recurrence of stones</td>
<td>3</td>
<td>1</td>
<td>0</td>
<td>4</td>
<td>0.38</td>
</tr>
<tr>
<td>Cholangitis without stones</td>
<td>0</td>
<td>4</td>
<td>0</td>
<td>4</td>
<td>0.02</td>
</tr>
<tr>
<td>Biliary carcinoma</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>2</td>
<td>0.9</td>
</tr>
</tbody>
</table>

*p value compared between types I and II.*