The role of endoscopic biliary sphincterotomy for the treatment of type 1 biliary dysfunction (papillary stenosis) with or without biliary stones

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Abstract

BACKGROUND: This study assesses the safety and effectiveness of endoscopic biliary sphincterotomy (ES) in the treatment of papillary stenosis (PS) with and without biliary stones.

METHODS: The records of all patients who had endoscopic retrograde cholangiopancreatography (2,689 patients) from January 1, 1991, to August 1, 2010, were reviewed. There were 117 patients with PS who had ES.

RESULTS: All patients had biliary pain, a dilated common bile duct (CBD) with a maximum diameter of 10 to 25 mm, and elevated liver function tests. There were 46 patients who had prior cholecystectomy of whom 20 patients had CBD stones. The remaining 71 patients had no prior biliary surgery; there were no biliary stones in 14 patients. All patients were symptom free after ES with or without CBD stone retrieval.

CONCLUSIONS: ES is the optimal treatment for PS in patients with or without biliary stones. ES eliminates pain, corrects CBD dilation, and restores LFTs to normal.

Sphincter of Oddi dysfunction (SOD) is a benign, obstructive disorder of the ampullary sphincter. SOD causes pain by impeding the flow of bile and/or pancreatic juice, resulting in ductal hypertension. SOD is a possible cause of 3 clinical conditions: (1) persistent or recurrent biliary-type pain after cholecystectomy; (2) recurrent idiopathic pancreatitis; and (3) biliary-type pain in patients with an intact gallbladder but without choledolithiasis. The pathogenesis of SOD can be divided into 2 subtypes: stenosis, which results from passive obstruction at the sphincter of Oddi caused by fibrosis, inflammation, or both; and dyskinesia, which results from intermittent obstruction caused by sphincter muscle spasm.
The Modified Milwaukee Classification (MMC) categorizes SOD into 3 types. Type 1 SOD causes biliary pain, elevated liver function tests, and dilation of the common bile duct (CBD) beyond 9 mm; this is also known as stenosis or fibrosis of the sphincter of Oddi or ampullary or papillary stenosis (PS). Type 2 SOD causes pain plus either elevated liver function tests or CBD dilation; type 3 SOD causes only pain without elevated liver function tests or CBD dilation.

A significant body of literature has shown that endoscopic sphincterotomy (ES) is an effective and safe modality for PS. However, the literature is less informative about the role of ES in the treatment of PS in patients with coexistent biliary stones. Cholecystectomy alone or with CBD exploration and stone removal may not be effective at resolving biliary pain when PS and ductal hypertension are not corrected. The purpose of this study was to investigate the role of ES in the management of PS in patients with or without biliary stones and with or without prior cholecystectomy.

Materials and Methods

After Wayne State University/Detroit Medical Center Human Investigational Committee approval, the records of patients with PS who subsequently underwent ES by a single endoscopist (CS) from 1991 through 2010 were reviewed. During this interval, 2,689 patients underwent endoscopic retrograde cholangiopancreatography (ERCP) including patients with endoscopic biliary sphincterotomy; 127 patients (4.7%) were diagnosed with PS.

Ten patients were excluded. ES was not performed in 5 patients without CBD stones but with severe comorbidities including liver cirrhosis in 2, severe cardiopulmonary disease in 2, and refractory coagulopathy in 1. ES was successfully performed in 4 patients with concomitant sickle cell disease but not included because of confusion in determining the cause of subsequent pain. ES was not technically possible in 1 patient although PS was diagnosed by successful ERCP. The remaining 117 patients had successful ES. These 117 patients were followed for an average of 72 ± 38.3 months and a median of 48.7 months; this includes 2 patients who have been followed over 20 years.

Preoperative workup always included liver function tests (LFTs), including aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, total bilirubin, and an abdominal ultrasound. An upper endoscopy was performed to rule out disease in the esophagus, stomach, and duodenum. Ninety-eight percent of the study population underwent a computed tomographic scan of the abdomen to examine the distal bile duct and pancreas followed by ERCP to look for retained stones or strictures of the bile duct. All patients included in this study had the classic MMC triad for PS with the triad of biliary pain, dilated CBD, and elevated LFTs.

ES was performed using a Valley Laboratory (Force FX, Boulder, CO) cautery unit with a setting of blend 1, cutting of 55, and coagulation of 30. Sphincter pressure was not measured. The length of the sphincterotomy cut varied depending on the size of the intraduodenal portion of the bile duct. The papilla was cut as large as possible without perforation usually a papillary bulge in the duodenal wall; the papillotomy length was measured by using a bowing sphincterotomy knife and/or pulling out an inflated balloon catheter in the CBD through the papillotomy site in some patients. Endpoints of treatment efficacy were symptomatic resolution of pain and the return of LFTs to normal.

Results

The 117 patients included 84 women and 33 men with a mean age of 48 years. All patients presented with biliary type pain; 29% had nausea with vomiting, and 19% had pancreatitis. All patients had bile duct dilatation that averaged 12.8 ± 0.33 mm and ranged from 10 to 25 mm. All patients had abnormal LFTs; the mean values were aspartate aminotransferase (U/L) of mean 220.2, SD 80.5, alanine aminotransferase (U/L) of mean 203.8, SD 70.5, alkaline phosphatase (U/L) of mean 280, SD 95.3, and total bilirubin (mg/dL) of 3.2, SD 1.2. Endoscopic cannulation of the duct was difficult, which was defined as more than 4 attempts at cannulation, in 67 patients; a guide wire papillotome was used in 35 patients, and precutting before cannulation was required in 2 patients. There were no acute complications such as pancreatitis, perforations, bleeding, or cholangitis after ES. However, 1 patient who had CBD stones after a prior cholecystectomy and 3 patients with no prior cholecystectomy and no CBD stones developed a moderate restenosis of the papilla months or years after ES requiring repeat ES. They subsequently did well.

Endoscopic biliary sphincterotomy after prior cholecystectomy

There were 46 PS patients who had prior cholecystectomy; 20 had CBD stones present at the time of ES (Fig. 1). The retrieval of CBD stones was successful in all 20 patients. The ES with stone removal was performed less than 1 month after cholecystectomy in 9 of these 20 patients. The 26 patients who had prior cholecystectomy with no evidence of CBD stones were further divided into 5 who had CBD exploration performed at the time of prior cholecystectomy and 21 who had no prior CBD exploration. The ES was performed less than 1 month after cholecystectomy in 7 of the 21 patients who had no prior CBD exploration; 4 of these 7 patients had ES within 1 week after cholecystectomy because of persistent right upper quadrant pain, jaundice, and CBD dilatation. One of the 5 patients who had prior CBD exploration had ES performed within 3 weeks of surgery because of a persistent high
output of bile (>700 mL/d) from the T tube; the drainage fell off immediately.

**Endoscopic biliary sphincterotomy without prior cholecystectomy**

The 71 PS patients without prior cholecystectomy (Fig. 1) included 26 patients with both gallstones and CBD stones, 15 patients with CBD stones only, 16 patients with gallstones only, and 14 patients with neither gallbladder nor CBD stones. ES was successful in all 71 patients. CBD stone removal failed in 2 of the 26 patients with CBD and gallstones because of multiple large CBD stones. These 2 patients had open cholecystectomy with CBD exploration. Seven of the 15 patients with CBD stones only had ES and CBD stone removal, whereas 8 patients had ES, CBD stone removal, and cholecystectomy. The 16 PS patients with gallbladder stones only underwent subsequent cholecystectomy; most were completed laparoscopically. Two of the 14 patients with no stones had laparoscopic cholecystectomy later.

Thus, the total therapy in 117 patients included ES alone (38 patients), ES with CBD stone removal (27 patients), ES with CBD stone removal and follow-up cholecystectomy (32 patients), and ES with follow-up cholecystectomy (18 patients). ES with later cholecystectomy and CBD exploration was performed in 2 patients. One of these latter 2 patients required ES with lithotripsy and CBD stone removal for recurrent stones 1 year after the initial ES. All 117 patients who underwent treatment achieved the therapeutic endpoint of pain relief and normalization of LFTs.

**Comments**

SOD is classified as either PS or sphincter of Oddi dyskinesia.11–13 PS is a structural abnormality in which there is narrowing of a portion or the entire sphincter because of chronic inflammation and fibrosis.14,15; etiologies include pancreatitis, injury from gallstone migration through the papilla, trauma from intraoperative manipulation of the CBD, and nonspecific inflammatory conditions. Anderson et al14 reported that wedge specimens of the sphincter of Oddi obtained at surgical sphincteroplasty showed evidence of inflammation, muscular hypertrophy, fibrosis, or adenomyosis within the papillary zone in approximately 60% of patients. The remaining 40% of patients with normal histology were thought to have a motor dyskinesia. The PS patients had the diagnostic triad of biliary pain, dilated CBD, and elevated liver function tests. Sphincter of Oddi dyskinesia is often difficult to distinguish from PS; the classic MMC triad of PS was noted in all patients in this study.

Manometry may be helpful in diagnosing SOD. When elevated levels of LFTs were present, Cicala et al16 noted that 10 of 25 patients with gallbladder stones but without bile duct stones had an elevated basal CBD pressure. Ruffolo et al17 reported that half of 81 patients with biliary-type pain and intact gallbladders without stones had delayed gallbladder emptying, SOD, or both. The constellation of symptoms and signs that persist after cholecystectomy has been termed the “postcholecystectomy syndromes.” The frequency approaches 10% to 20% of postcholecystectomy patients.18 Several conditions may be responsible for this syndrome, including biliary and pancreatic disease, irritable bowel syndrome, peptic ulcer disease, liver diseases, angina, and neuritis. A small percentage of patients with postcholecystectomy syndrome have PS. When the gallbladder has been removed, PS may be observed in up to 14% of patients with continued biliary pain and elevated LFTs.19 When other causes of postcholecystectomy pain have been excluded and sphincter manometry has been performed, the frequency of PS rises to 30% to 60%.20 The present study showed that there were 127 patients with PS of 2,689 patients (4.7%) imaged by ERCP.

The sphincter of Oddi is composed of layers of smooth muscle that are embedded in the muscular duodenal wall. This sphincter has 3 portions, namely, a small segment that covers the common channel (sphincter ampullae), a second small portion that surrounds the beginning of the main pancreatic duct (sphincter pancreateicus), and the largest portion, which covers the distal CBD (sphincter choledochus). Biliary sphincterotomy involves cutting both the sphincter choledochus and the sphincter ampullae. Biliary sphincterotomy is generally recommended for all PS patients and for patients with type 2 and 3 SOD patients when they have abnormal manometric findings.21–23

![Figure 1](image-url) The therapeutic intervention for each subgroup.
Patients who meet the classic MMC triad for PS do well with ES.\(^1\) Manometric studies are not needed before ES in PS patients.\(^1,2,24-26\) The efficacy of ES in PS patients with an abnormal manometric finding is no better than those patients who had normal manometric values. For these reasons, manometry was not performed in the PS patients reported in this study. All of the patients had classic PS based on the MMC criteria of biliary pain, CBD dilation, and abnormal LFTs. ES in this setting of CBD dilation without stones is very beneficial.\(^1,2,25-27\) When ES was performed after cholecystectomy in 26 patients without CBD stones, there was a total resolution of symptoms and normalization of LFTs. Eight of these 26 patients had ES less than 1 month after cholecystectomy (4 within a week) because of persistent pain caused by PS. This practice of postcholecystectomy ES as a routine management strategy for classic PS patients is well established.\(^1,2,25-27\)

The 1 patient who had jaundice (bilirubin = 4.5 mg/dL) had a dilated CBD and an enlarged gallbladder. He also had pancreatitis. A diagnosis of PS was made by preoperative ERCP. At operation, hydrops of the gallbladder without stones was noted. Suspected bile stasis was confirmed by liver biopsy (Fig. 2). His pain persisted after cholecystectomy; therefore, 1 week later, ES was performed for PS. Biopsy confirmed papillary fibrosis. He has remained asymptomatic after ES for 12 years.

Indications of biliary sphincterotomy include choledocholeithiasis and type 1 biliary dysfunction (PS).\(^2,28\) PS is a possible cause of the clinical condition with biliary-type pain in patients with an intact gallbladder but without cholelithiasis.\(^1\) For the 14 PS patients without prior surgery or stones, 12 were successfully managed with ES alone; in most patients, the bile duct was cleared with a balloon catheter after ES to remove possible small stones or debris. However, 3 of these patients were restenosed and required repeat ES. The increased restenosis rate in this subset of patients is consistent with the literature, which reports that patients undergoing ES for PS alone are 5 times more likely to develop restenosis compared with patients who have ES with calculi.\(^30,31\) Overall, ES is a safe and effective treatment option that is recommended for any patient presenting with classic PS even though no stones are present.

As might be expected, all 20 patients with PS and CBD stones after cholecystectomy did well. All had complete retrieval of CBD stones. Likewise, 24 of 26 patients with CBD stones and gallstones who had no prior history of cholecystectomy were successfully managed with ES and CBD stone removal followed by laparoscopic cholecystectomy. The combined treatment of CBD stones by ES and stone removal will treat both the symptomatic stone as well as PS. These results are consistent with those of Anderson et al,\(^14\) who reported that ES was effective in 109 patients, which was performed for CBD stones in 53 patients. They found that the best clinical result was obtained in the group of patients with CBD stones. Juxtaposing our experience with the conclusions of this report suggests that most patients presenting with PS and CBD stones without prior cholecystectomy will require subsequent cholecystectomy to achieve complete relief of symptoms and resolution of laboratory abnormalities. However, ES is probably very important to the successful management of these patients. Patients with PS and gallstones without CBD stones may respond well to ES followed by cholecystectomy. All 16 patients in this subgroup were cured.

Early post-ES complications include pancreatitis, hemorrhage, perforation, and cholangitis.\(^32\) Pancreatitis can be prevented by avoiding repeated cannulations of the pancreatic duct. Incidence of developing pancreatitis by ES is less common when treating type 1 biliary dysfunction (PS) compared with type 3 biliary dysfunction. Bleeding can be prevented by careful endoscopic sphincterotomy using blended current and cutting in short increments in patients without coagulopathy. Perforation can be prevented by not cutting too long and using a stepwise incision. To prevent cholangitis, it is necessary to obtain successful and complete biliary drainage using a large papillotomy. To prevent late complications of restenosis of the papilla, it is necessary to incise the papilla as long as possible initially. This complication is successfully treated by recutting the papilla. With careful attention to patient selection and details of the ES technique, complications of ES can be minimized. Endoscopic experience is reflected in the complication rate.\(^32\) In this report, ES was performed by a single endoscopist who had performed more than 2,800 ERCP examinations (1972 to 1990).

Preoperative ERCP and ES is a reasonable management strategy in PS patients with gallbladder stones even when there is no radiographic/ultrasonographic evidence of CBD stones. Wu et al\(^33\) looked at the role of perioperative ERCP and found that in carefully selected patients the identification of missed CBD stones was 67%. Even when no CBD
stones are identified preoperatively, ES with ductal clearance by a balloon catheter is a safe and important part of the management of PS and may play a critical role in decreasing postcholecystectomy syndrome.  

Conclusions

This study elucidates the relationship between PS, cholelithiasis, and cholecdocholithiasis and assesses the role of ES in the management of patients with both PS and CBD stones. ES is an effective and safe treatment for classic PS patients with no biliary stones. Furthermore, cholecystectomy with or without CBD exploration and stone removal may be insufficient to relieve pain caused by isolated PS. The addition of ES in this group of patients often brings complete relief. Overall, ES is a safe and effective modality for the treatment of PS in patients with CBD stones with or without cholecystectomy. These conclusions need to be verified with a long-term evaluation of a larger number of patients.

References