

Retrospective Study

# Efficacy and safety of limited endoscopic sphincterotomy before self-expandable metal stent insertion for malignant biliary obstruction

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## Abstract

### AIM

To evaluate the safety and efficacy of limited endoscopic sphincterotomy (ES) before placement of self-expandable metal stent (SEMS).

### METHODS

This was a retrospective analysis of 244 consecutive patients with unresectable malignant biliary obstruction, who underwent placement of SEMSs following limited ES from December 2008 to February 2015. The diagnosis of malignant biliary obstruction and assessment of patient eligibility for the study was established by a combination of clinical findings, laboratory investigations, imaging and pathological results. All patients were monitored in the hospital for at least 24 h following endoscopic retrograde cholangiopancreatography (ERCP). The incidence of immediate or early post-ERCP complications such as post-ERCP pancreatitis (PEP) and bleeding related to limited ES were considered as primary outcomes. Also, characteristics and complications according to the cancer type were classified.

### RESULTS

Among the 244 patients included, the underlying diagnosis was cholangiocarcinoma in 118 patients,

pancreatic cancer in 79, and non-pancreatic or non-biliary malignancies in the remaining 47 patients. Early post-ERCP complications occurred in 9 patients (3.7%), with PEP in 7 patients (2.9%; mild, 6; moderate, 1) and mild bleeding in 2 patients (0.8%). There was no significant association between the incidence of post-ERCP complications and the type of malignancy (cholangiocarcinoma *vs* pancreatic cancer *vs* others,  $P = 0.696$ ) or the type of SEMS used (uncovered *vs* covered,  $P = 1.000$ ). Patients who had more than one SEMS placed at the first instance were at a significantly higher risk of post-ERCP complications (one SEMS *vs* two SEMS,  $P = 0.031$ ). No other factors were predictive of post-ERCP complications.

## CONCLUSION

Limited ES is feasible and safe, and effectively facilitates the placement of SEMS, without any significant risk of PEP or severe bleeding.

**Key words:** Endoscopic sphincterotomy; Endoscopic retrograde cholangio pancreatography; Complications; Pancreatitis; Bleeding; Cholestasis; Self-expandable metal stent

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**Core tip:** The role of routine endoscopic sphincterotomy (ES) is still controversial in biliary stenting and there is a lack of systematic study for the extent of ES and its correlation with the incidence of complications. We retrospectively evaluated the safety and efficacy of limited ES before self-expandable metal stent insertion. We have proved in this study that limited ES doesn't increase the risk of post-procedure complications such as post-endoscopic retrograde cholangio pancreatography pancreatitis and bleeding. Also, it is advantageous in facilitating the more complex stenting procedures. Therefore, limited ES can be a safe, feasible, and effective therapeutic strategy in the placement of self-expandable metal stent.

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## INTRODUCTION

Malignant biliary obstruction is mainly caused by cholangiocarcinoma, pancreatic cancer, gallbladder cancer, and metastatic disease. The prognosis is very poor because the lesions are unresectable at diagnosis in the majority of these patients, with less than 20% of the patients being suitable for surgical resection<sup>[1]</sup>.

Endoscopic retrograde cholangiopancreatography (ERCP) along with biliary stenting is a minimally invasive procedure for palliation of biliary obstruction that provides relief from jaundice and improves the quality of life of patients with unresectable malignant biliary obstruction<sup>[2]</sup>.

Self-expandable metal stents (SEMS), compared to plastic stents, have superior patency and are cost-effective options in selected preoperative patients or in patients whose life expectancy exceeds six months<sup>[3-5]</sup>. They are, however, reported to be associated with a higher incidence of pancreatitis<sup>[6,7]</sup>. Previous studies indicate that performing endoscopic sphincterotomy (ES) before stent insertion may lower the incidence of post-ERCP pancreatitis (PEP)<sup>[8-10]</sup>. ES may also facilitate cannulation of the bile duct during difficult ERCPs, reduce resistance to the passage of stents, improve immediate stent deployment, and increase the luminal diameter of the distal common bile duct (CBD)<sup>[9-12]</sup>. Many endoscopists routinely perform ES before SEMS placement. However, the role of routine ES before stenting is still controversial and no clear guidelines exist to govern its use. Additionally, ES is also an independent risk factor for complications such as pancreatitis, bleeding, and perforation, with a reported complication rate of approximately 10% and an overall direct or indirect procedure-related mortality of 0.42%, even when performed by experienced endoscopists<sup>[2,13-17]</sup>. However, an accurate assessment of the incidence of complications based on the extent of ES is difficult to make owing to the lack of such data in previous studies. Herein, we studied the incidence of early post-ERCP complications, such as PEP and bleeding following limited ES accompanying SEMS placement for biliary drainage in patients with malignant biliary obstruction.

## MATERIALS AND METHODS

### Patients

This was a retrospective analysis of all patients who underwent endoscopic biliary SEMS placement for the first time for malignant biliary obstruction at the Pusan National University Yangsan Hospital during the six-year period from December 2008 to February 2015. Patients that underwent transpapillary SEMS placement after limited ES for a diagnosis of distal or hilar malignant biliary strictures were included in this study. Diagnosis of the disease and assessment of patient eligibility for the procedure was based on a combination of clinical findings, laboratory investigations and radiological studies including computed tomography (CT) scan, magnetic resonance imaging (MRI) and/or endoscopic ultrasound (EUS). In case of without cholangitis, painless jaundice and/or pruritus, sometimes anorexia, weight loss and malaise were main clinical symptoms. The main laboratory parameters recorded were complete blood count (CBC), total bilirubin, liver

function tests including alanine aminotransferase, alkaline phosphatase,  $\gamma$ -glutamyltransferase and tumor markers such as CEA and CA 19-9. CT scan was performed for all patients as an initial test, while MRI was performed in all patients with suspicious malignant biliary strictures. MRI was not performed in uncooperative patients or if contraindicated owing to the presence of intracorporeal metallic device or foreign body. EUS was not routinely performed, and was limited to investigating indeterminate biliary strictures, nonvisible masses, or when tissue acquisition was required for definite diagnosis. Pathology results were reviewed in cases where biopsy was performed during ERCP or EUS. Exclusion criteria were previous ES or stent placement, coagulopathy (international normalized ratio > 1.5), low platelet count (< 50000/mL), current use of anticoagulant or antiplatelet drugs, severe cholangitis with or without septic shock, Billroth II anatomy or Roux-en-Y gastrojejunostomy, and severe heart or pulmonary disease. The study protocol was approved by the ethics committee of the Institutional Review Board of Pusan National University Yangsan Hospital (IRB No. 05-2015-081).

### Study protocol

Patient characteristics including age, sex, history of previous procedures and baseline biochemical and hematological values were collected prior to performing ERCP. SEMS placement was performed in all patients by one of two experienced endoscopists (endoscopist A had performed > 10000 ERCPs over 20 years; endoscopist B had performed > 2000 ERCPs over 10 years). All patients received intravenous (IV) broad-spectrum antibiotics. Nafamostat mesilate (20 mg) was administered for all patients for preventing post-ERCP pancreatitis. Nonsteroidal anti-inflammatory drugs were not used routinely. All procedures were performed under conscious sedation by using IV midazolam and pethidine, with the patient in the supine or left lateral decubitus position. Cimetropium bromide 10 mg IV was administered to reduce duodenal peristalsis. All ERCPs were performed by using a standard side-viewing duodenoscope (JF-260 V or TJF-240; Olympus Optical Co., Ltd., Tokyo, Japan). Selective cannulation of the bile duct was achieved by using a pull-type double-lumen sphincterotome (Ultratome XL, Boston Scientific, Natick, Mass) or by a conventional ERCP catheter (Fluoro Tip, Boston Scientific), with or without a hydrophilic guidewire (0.025- or 0.035-inch Jagwire, Boston Scientific). A wire-guided cannulation technique was attempted first, followed by the conventional contrast-assisted cannulation technique if biliary cannulation was not achieved within 10 min. After successful guidewire placement, limited sphincterotomy was performed with blended current. Limited ES was defined as ES limited to one-third the extent of major ES. A metal stent was then inserted over the guidewire under fluoroscopic control. Stent length (4 cm to

12 cm) and the need for unilateral or bilateral stent placement were determined based on the location and length of the biliary stricture. Stent placement ensured that the stent spanned the stricture with either end of the stent extending a minimum of 1 cm beyond the stricture. In the case of distal biliary strictures, the distal end of SEMS was placed across the papilla with 1 cm of the distal end of the stent exposed in the duodenum. In the case of hilar biliary strictures, SEMS was placed above the sphincter of Oddi. All patients were monitored in the hospital for at least 24 h after ERCP to identify early post-ERCP complications. CBC, serum amylase, and lipase levels were routinely evaluated at 4 h and 24 h after the procedure. Endoscopy was performed to evaluate ES-related-bleeding on the day following stent placement. All adverse events were recorded. During the follow up period, ERCP was repeated on suspecting stent complications such as occlusion or migration.

### Definitions

According to updated Tokyo guidelines (TG13) for diagnosis and severity grading of acute cholangitis, cholangitis was defined as fever and/or shaking chills, increased inflammatory response (abnormal white blood cell counts, increased serum C-reactive protein levels) and jaundice (total bilirubin  $\geq$  2 mg/dL) or abnormal liver function tests ( $> 1.5 \times$  upper limit of normal value)<sup>[18]</sup>. Severe cholangitis is defined as the presence of accompanying organ dysfunction caused by biliary sepsis, and requiring intensive care such as respiratory and circulatory support<sup>[18]</sup>. Limited ES was defined as sphincterotomy less than one-third the extent of major ES<sup>[19]</sup>. Definitions of individual post-procedure complications were according to the descriptions given by Cotton *et al.*<sup>[20]</sup>. PEP was defined as new-onset or worsening abdominal pain lasting more than 24 h after the procedure, in conjunction with pancreatic enzyme (amylase and/or lipase) elevation that was at least three times the upper limit of the normal, with or without radiographic evidence of acute pancreatitis. The severity of PEP was graded by using the number of hospitalization days: mild, when hospitalization was prolonged by 2 to 3 d, moderate, by 4 to 10 d, and severe, by more than 10 d<sup>[20]</sup>. Bleeding was defined as the presence of melena or hematemesis, irrespective of the need for blood transfusion or repeat endoscopy. Mild bleeding was defined as hemoglobin drop within 2 g/dL, with no necessity for blood transfusion. The presence of bleeding was identified based on patient's history (melena or hematemesis) and a drop in hemoglobin level following the procedure. Perforation was considered as perforation of retroperitoneum or bowel walls documented by any of the radiographic techniques<sup>[21]</sup>. Complications were graded according to the grading system described by Cotton *et al.*<sup>[20]</sup>. Early complications or adverse events were defined as any ERCP-related complications occurring within 30 d

**Table 1 Patient characteristics and endoscopic retrograde cholangio pancreatography related data *n* (%) (*n* = 244)**

Characteristics	Value
Age (yr), mean $\pm$ SD (range)	70.8 $\pm$ 10.2 (44-95)
Sex	
Male	130 (53.3)
Female	114 (46.7)
Aspirin	3 (1.2)
Total bilirubin (mg/dL), pre-procedure, mean $\pm$ SD (range)	7.09 $\pm$ 6.45 (0.2-28.9)
Normal	53 (21.7)
Elevated	191 (78.3)
Hyperamylasemia, pre-procedure	14 (5.7)
Cholangitis, pre-procedure	68 (27.9)
Diagnosis	
Cholangiocarcinoma	118 (48.4)
Hilar	75 (63.6)
Distal	43 (36.4)
Pancreatic cancer	79 (32.4)
Head	68 (86.1)
Body/Tail	11 (13.9)
Gallbladder cancer	21 (8.6)
Ampullary cancer	18 (7.4)
Hepatocellular carcinoma	3 (1.2)
Others	5 (2.0)
Pancreatic duct invasion	
Yes	85 (34.8)
No	159 (65.2)
Lymph node metastasis	
Yes	170 (69.7)
No	73 (29.9)
Pancreatic duct injection	
0	187 (76.6)
1-2	24 (9.8)
$\geq 3$	33 (13.5)
ERPD	4 (1.6)
Stent success rate	244 (100)
Number of initially inserted SEMS	
1	230 (94.3)
2	14 (5.7)
Stent type	
Uncovered	190 (77.9)
Covered	54 (22.1)
Post-ERCP complication	
Present	9 (3.7)
Absent	234 (95.9)
Post-ERCP complication type	
Pancreatitis	7 (2.9)
Mild / moderate	6 (2.5)/1 (0.4)
Bleeding, mild	2 (0.8)
Perforation	0 (0)
Post-ERCP hyperamylasemia	30 (12.3)
Stent complication	
None	199 (81.6)
Stent occlusion	44 (18.0)
Stent migration	1 (0.4)
Patency	
No further procedure	199 (81.6)
ERBD restent	1 (0.4)
SEMS restent	32 (13.1)
PTBD	12 (4.9)

SEMS: Self-expandable metal stent; ERPD: Endoscopic retrograde pancreatic drainage; ERBD: Endoscopic retrograde biliary drainage; PTBD: Percutaneous transhepatic biliary drainage.

of the procedure. Patency interval was defined as the period between the first SEMS deployment and the occurrence of stent complications such as occlusion or migration.

### Statistical analysis

The primary outcomes measured were immediate or early complications within 30 d of the procedure. For inter-group differences, Student's *t*-test was performed for continuous variables, and  $\chi^2$  test or Fisher's exact test were performed for categorical variables. Results were considered statistically significant at a *P* value < 0.05. Data were analyzed by using SPSS software version 18.0 (SPSS, Chicago, IL, United States).

## RESULTS

A total of 244 patients that underwent limited ES and biliary stenting for malignant biliary obstruction between December 2008 and February 2015 were included in the study. The etiology of malignant biliary obstruction included cholangiocarcinoma (*n* = 118, 48.4%), pancreatic cancer (*n* = 79, 32.4%), and others including gallbladder cancer (*n* = 21, 8.6%), ampullary cancer (*n* = 18, 7.4%), and hepatocellular carcinoma and metastatic cancer (*n* = 8, 3.2%). Mean age was 70.8  $\pm$  10.2 (range, 44-95) years and 130 (53.3%) were males and 114 (46.7%) were females. Stents were successfully deployed in all patients.

Early post-ERCP complications occurred in 9 patients (3.7%), including PEP in 7 patients (2.9%; mild, 6; moderate, 1), and mild bleeding in 2 patients (0.8%). All patient with post-ERCP complications responded to conservative management. Stent occlusion and migration developed in 44 patients (18.0%) and 1 patient (0.4%), respectively. Patients with late complications underwent repeat ERCP or percutaneous transhepatic biliary drainage. Patient characteristics and ERCP related data are summarized in Table 1.

On categorizing patients into three groups on the basis of cancer location, PEP developed in 4 patients (3.4%, 4/118) with cholangiocarcinoma, 1 patient (1.3%, 1/79) with pancreatic cancer, and 2 patients (4.3%, 2/47) with non-pancreatic, non-biliary cancers (*P* = 0.681). There were no significant differences among these three groups as to the incidence of immediate or early complications (*P* = 0.696) (Table 2). In the cholangiocarcinoma group, the incidence of PEP was 4.0% and 2.3% with hilar and distal cholangiocarcinoma, respectively (*P* = 0.537). One patient with hilar cholangiocarcinoma had mild bleeding (Table 3). In the pancreatic cancer group, one patient had PEP and another had mild bleeding. Both complications developed in patients with pancreatic head cancer and none were reported in cases of pancreatic body and/or tail cancer (Table 4).

**Table 2** Characteristics and complications according to the cancer type *n* (%)

	Cholangiocarcinoma <i>n</i> = 118	Pancreatic cancer <i>n</i> = 79	non-pancreaticobiliary cancer <i>n</i> = 47	<i>P</i> value
Age (yr), mean ± SD	73.5 ± 9.4	67.8 ± 10.4	69.3 ± 10.3	0.002
Hyperamylasemia, pre-procedure	6 (5.1)	3 (3.8)	5 (10.6)	0.273
Cholangitis, pre-procedure	28 (23.7)	19 (24.1)	21 (44.7)	0.021
Pancreatic duct invasion				< 0.001
Yes	12 (10.2)	64 (81.0)	9 (19.1)	
No	106 (89.8)	15 (19.0)	38 (80.9)	
Lymph node metastasis				0.345
Yes	77 (65.3)	58 (73.4)	35 (74.5)	
No	41 (34.7)	21 (26.6)	12 (25.5)	
Pancreatic duct injection				0.606
0	92 (78.0)	59 (74.7)	36 (76.6)	
1-2	8 (6.8)	9 (11.4)	7 (14.9)	
≥ 3	18 (15.3)	11 (13.9)	4 (8.5)	
Number of initially inserted SEMS				0.004
1	106 (89.8)	79 (100.0)	45 (95.7)	
2	12 (10.2)	0 (0.0)	2 (4.3)	
Post-ERCP complication				0.696
Present	5 (4.2)	2 (2.5)	2 (4.3)	
Absent	113 (95.8)	77 (97.5)	45 (95.7)	
Post-ERCP complication type				0.914
Pancreatitis	4 (3.4)	1 (1.3)	2 (4.3)	0.681
Mild/moderate	3 (2.5)/1 (0.8)	1 (1.3)/0 (0)	2 (4.3)/0 (0)	
Bleeding, mild	1 (0.8)	1 (1.3)	0 (0)	
Perforation	0 (0)	0 (0)	0 (0)	
Post-ERCP hyperamylasemia	13 (11.0)	9 (11.4)	8 (17.0)	
Stent complication				0.539
None	90 (76.3)	70 (88.6)	39 (83.0)	
Stent occlusion	27 (22.9)	9 (11.4)	8 (17.0)	
Stent migration	1 (0.8)	0 (0)	0 (0)	
Patency				0.161
No further procedure	90 (76.3)	70 (88.6)	39 (83)	
ERBD restent	1 (0.8)	0 (0)	0 (0)	
SEMS restent	20 (16.9)	9 (11.4)	3 (6.4)	
PTBD	7 (5.9)	0 (0)	5 (10.6)	

SEMS: Self-expandable metal stent; ERBD: Endoscopic retrograde biliary drainage; PTBD: Percutaneous transhepatic biliary drainage.

**Table 3** Rates of complications on biliary stenting with limited endoscopic sphincterotomy according to location of cholangiocarcinoma *n* (%)

	Hilar <i>n</i> = 75	Distal <i>n</i> = 43	<i>P</i> value
Post-ERCP complication type			0.717
Pancreatitis	3 (4.0)	1 (2.3)	
Mild/moderate	2 (2.7)/1 (1.3)	1 (2.3)/0 (0)	
Bleeding, mild	1 (1.3)	0 (0.0)	
Perforation	0 (0.0)	0 (0.0)	
Post-ERCP hyperamylasemia	7 (9.3)	5 (11.6)	
Stent complication			0.756
None	57 (76.0)	33 (76.7)	1.000
Stent occlusion	17 (22.7)	10 (23.3)	
Stent migration	1 (1.3)	0 (0.0)	

ERCP: Endoscopic retrograde cholangio pancreatography.

On categorizing patients based on the type of SEMS deployed, 190 patients (78%) had uncovered SEMS while 54 patients (22%) had covered SEMS. Rates of PEP with uncovered and covered SEMS were 2.6% (5/190; mild, 4; moderate, 1) and 3.7% (2/54, both mild), respectively ( $P = 0.652$ ). Mild bleeding

occurred in 2 patients (1.1%) in the uncovered SEMS group alone. No significant differences were found between these two groups as to the incidence of post-ERCP complications ( $P = 1.000$ ) (Table 5).

On comparing patients with no complications ( $n = 235$ ) and those with complications ( $n = 9$ ), the only



**Table 4** Rates of complications on biliary stenting with limited endoscopic sphincterotomy according to location of pancreatic cancer *n* (%)

	Head <i>n</i> = 68	Body / Tail <i>n</i> = 11	<i>P</i> value
Post-ERCP complication type			1.000
Pancreatitis	1 (1.5)	0 (0.0)	
Mild/moderate	1 (1.5)	0 (0.0)	
Bleeding, mild	1 (1.5)	0 (0.0)	
Perforation	1 (1.5)	0 (0.0)	
Post-ERCP hyperamylasemia	8 (11.8)	2 (18.2)	0.624
Stent complication			1.000
None	60 (88.2)	10 (90.9)	
Stent occlusion	8 (11.8)	1 (9.1)	
Stent migration	0 (0.0)	0 (0.0)	

ERCP: Endoscopic retrograde cholangio pancreatography.

**Table 5** Rates of complications on biliary stenting with limited endoscopic sphincterotomy according to stent type *n* (%)

	Uncovered <i>n</i> = 190	Covered <i>n</i> = 54	<i>P</i> value
Normal	181 (95.3)	49 (90.7)	
Abnormal	9 (4.7)	5 (9.3)	
Post-ERCP complication			1.000
Present	7 (3.7)	2 (3.7)	
Absent	183 (96.3)	52 (96.3)	
Post-ERCP complication type			0.838
Pancreatitis	5 (2.6)	2 (3.7)	
Mild / moderate	4 (2.1) / 1 (0.5)	2 (3.7) / 0 (0)	
Bleeding, mild	2 (1.1)	0 (0)	
Perforation	0 (0)	0 (0)	
Post-ERCP hyperamylasemia	25 (13.2)	5 (9.3)	0.638
Stent complication			0.758
None	156 (82.1)	43 (79.6)	
Stent occlusion	33 (17.4)	11 (20.4)	
Stent migration	1 (0.5)	0 (0)	
Patency			0.012
No further procedure	156 (82.1)	43 (79.6)	
ERBD restent	1 (0.5)	0 (0)	
SEMS restent	28 (14.7)	4 (7.4)	
PTBD	5 (2.6)	7 (13)	

SEMS: Self-expandable metal stent; ERBD: Endoscopic retrograde biliary drainage; PTBD: Percutaneous transhepatic biliary drainage; ERCP: Endoscopic retrograde cholangio pancreatography.

factor that was significantly different between the two groups was the number of SEMS initially deployed [one SEMS vs two SEMS (bilateral), *P* = 0.031] (Table 6). Of the 231 patients with one SEMS, 5 patients developed PEP and 2 patients developed mild bleeding, while of the 13 patients with two SEMS, 2 patients developed PEP.

## DISCUSSION

ES is an established technique and is commonly used to facilitate biliary stone removal. In contrast, the role of routine ES prior to stent insertion is still controversial. Many endoscopists prefer to perform ES before stenting to reduce the risk of PEP, achieve better biliary drainage, and facilitate stent placement. However, sphincterotomy carries risks such as bleeding, perfora-

tion and pancreatitis<sup>[9]</sup>. Some studies have reported that the risks of ES might exceed any benefits owing to a high incidence of ES-related complications<sup>[15]</sup>. Cotton *et al*<sup>[20]</sup> reported bleeding and pancreatitis as major early complications with ES. Freeman *et al*<sup>[15]</sup> evaluated early complications following ES and reported their incidence as 9.8% (pancreatitis, 5.4%; bleeding, 2.0%).

Previous studies, however, lack details regarding the extent of ES and its correlation with the incidence of complications. In this study, we performed limited ES before SEMS placement and described the safety of limited ES by evaluating early post-ERCP complications in patients with malignant biliary obstruction. The overall rate of early post-ERCP complications after SEMS placement with limited ES was 3.7%, including a 2.9% incidence of PEP, and 0.8% of mild bleeding. These

**Table 6** Characteristics according to complications on biliary stenting with limited endoscopic sphincterotomy *n* (%)

	No complication <i>n</i> = 235	Complication <i>n</i> = 9	<i>P</i> value
Age (yr), mean ± SD (range)	70.61 ± 10.33	75.27 ± 5.55	0.993
Gender			1.000
Male	126 (53.6)	5 (55.5)	
Female	109 (46.6)	4 (44.5)	
Total bilirubin (mg/dL), pre-procedure, mean ± SD	7.00 ± 6.46	8.38 ± 6.54	0.362
Normal	52 (22.2)	1 (11.1)	0.453
Elevated	183 (77.8)	8 (88.9)	
Hyperamylasemia, pre-procedure	13 (5.5)	1 (11.1)	0.485
Cholangitis, pre-procedure	64 (27.2)	4 (44.4)	0.472
Diagnosis			0.748
Cholangiocarcinoma	112 (47.6)	6 (66.7)	
Hilar	71 (30.2)	4 (44.4)	
Distal	41 (17.4)	2 (22.2)	
Pancreatic cancer	77 (32.8)	2 (22.2)	
Head	66 (28.1)	2 (22.2)	
Body/tail	11 (4.7)	0 (0.0)	
Gallbladder cancer	20 (8.5)	1 (11.1)	
Ampullary cancer	18 (7.7)	0 (0.0)	
Hepatocellular carcinoma	3 (1.3)	0 (0.0)	
Others	5 (2.1)	0 (0.0)	
Pancreatic duct invasion			0.324
Yes	80 (34.0)	5 (55.6)	
No	155 (66.0)	4 (44.4)	
Lymph node metastasis			0.176
Yes	166 (70.6)	5 (55.6)	
No	69 (29.4)	4 (44.4)	
Pancreatic duct injection			0.662
0	181 (77.0)	6 (66.7)	
1-2	23 (9.8)	1 (11.1)	
≥ 3	31 (13.2)	2 (22.2)	
Number of inserted SEMS			0.031
1	224 (95.3)	7 (77.8)	
2	11 (4.7)	2 (22.2)	
Stent type			1.000
Uncovered	183 (77.9)	7 (77.8)	
Covered	52 (22.1)	2 (22.2)	
Stent complication			1.000
Stent occlusion	42 (17.9)	2 (22.2)	
Stent migration	1 (0.4)	0 (0.0)	
Patency			0.512
No further procedure	192 (81.7)	7 (77.8)	
ERBD restent	1 (0.4)	0 (0.0)	
SEMS restent	31 (13.2)	1 (11.1)	
PTBD	11 (4.7)	1 (11.1)	

SEMS: Self-expandable metal stent; ERBD: Endoscopic retrograde biliary drainage; PTBD: Percutaneous transhepatic biliary drainage; ERCP: Endoscopic retrograde cholangio pancreatography.

rates of complications are relatively low compared to the complication rates of approximately 10% and an overall mortality of 0.42% in published data<sup>[2,13-17]</sup>.

Bleeding is a serious complication of ES and its incidence is reported to be between 1 and 10%<sup>[12,22-25]</sup>. In our study, only 2 patients (0.8%) developed mild bleeding, which could be managed by conservative treatment. No instances of moderate or severe bleeding were reported. Wang *et al.*<sup>[26]</sup>, in their analysis of delayed hemorrhage following ES in 1741 patients did not find delayed bleeding in any patient who underwent small ES (*n* = 194). These results might be related to the limited extent of the ES and the compressive effect of the SEMS<sup>[27]</sup>. On the basis of these

studies, limited ES does not seem to be associated with clinically significant bleeding.

A recent meta-analysis by Cui *et al.*<sup>[28]</sup>, analyzing biliary stenting for malignant biliary obstruction reported that the incidence of PEP was significantly lower with ES than without ES (3.5% vs 8.9%, *P* = 0.04, OR = 0.34, 95%CI: 0.12-0.93) and recommended ES before stent placement as a useful option to reduce the incidence of PEP. Similar low rates (2.2%) were reported by Giorgio *et al.*<sup>[29]</sup> in their randomized control trial involving 10 Fr plastic stent after ES for inoperable malignant common bile duct (CBD) obstruction. In our study, despite the absence of a control group, the low rate of PEP (2.9%) is comparable to the results of the

two above-mentioned studies. Our PEP rates are also low compared to the rates of 9.4% and 6.3%, with metal stent placement following ES for distal biliary strictures, reported by Hayashi *et al.*<sup>[17]</sup> and by Kahaleh *et al.*<sup>[30]</sup>, respectively. In our study, the incidence of PEP was 4.0% in hilar cholangiocarcinoma and 2.3% in distal cholangiocarcinoma. Although the outcomes with ES for malignant biliary strictures, especially cholangiocarcinoma, are controversial, several previous studies have demonstrated a lower incidence of PEP in the ES group compared to the non-ES group<sup>[8,9,31]</sup>. Jeong *et al.*<sup>[8]</sup> investigated the risk of pancreatitis in patients with malignant obstructive jaundice following percutaneous or transpapillary stent placement. They also studied the effect of preliminary ES in the transpapillary stent group. Their results demonstrated a higher rate of pancreatitis in the transpapillary stent group ( $P = 0.502$ ) and the authors concluded that SEMS placement through the intact sphincter of Oddi may increase the risk pancreatitis.

The management of hilar obstruction is more difficult than distal bile duct strictures because of the underlying anatomical and technical complexity. Bilateral stent placements for Bismuth type II to IV hilar cholangiocarcinoma are also very complicated and result in increased endoscopic manipulations<sup>[32]</sup>. The higher incidence of post-ERCP complications in patients who had two SEMS (bilateral stents) placed could be related to these reasons. In these situations, limited ES before stenting could be an effective strategy for facilitating more complex stenting procedures<sup>[33]</sup>. Limited ES may allow for easier stent placement and reduce resistance to biliary instrumentation. Additionally, proximal bile duct strictures may contribute to a fulcrum effect resulting in medial displacement of the distal stent and, consequently, stent related compression of the pancreatic duct<sup>[9]</sup>. Limited ES might prevent the risk of pancreatitis by reducing stent-related pancreatic duct obstruction. In case of distal CBD strictures, ES may allow the stent to achieve a better final diameter, and thus, better drainage.

Our data demonstrated a lower rate of PEP in patients with cholangiocarcinoma compared to previous studies. Limited ES, therefore, could be an effective and useful technique to prevent PEP following stenting for cholangiocarcinoma, especially hilar tumors. The incidence of PEP was lesser in pancreatic cancers than in cholangiocarcinoma in this study (1.3% vs 3.4%,  $P = 0.681$ ). Some studies demonstrated that pancreatic cancers with obstruction of the main pancreatic duct had a lower degree of PEP, possibly due to diminished pancreatic exocrine function and suggested that ES may be unnecessary in such cases<sup>[12,17,28,32]</sup>. Although further confirmation is required, we noted that performing limited ES prior to SEMS placement in patients with unresectable pancreatic cancers did not result in a higher incidence of adverse events compared to published data<sup>[17]</sup>. Additionally, it is pos-

sible that ES may be advantageous in selected cases, depending on pancreatic duct status, stent diameter, stent type (especially fully covered SEMS) or ampulla size, in rendering the procedure easier as biliary strictures secondary to pancreatic cancer tend to be narrow and rigid. ES may also facilitate stent exchange during the follow-up period<sup>[32]</sup> as demonstrated in our study, where the success rate of SEM restenting, when indicated, was 97%.

Stent migration is a late complications of biliary stenting with ES. Stent migration seems to be associated with stent type as well as ES. Covered SEMS are not fully embedded in bile duct, and therefore, are associated with the potential risk of stent migration. A previous study reported increased frequency of stent migration when ES was performed before placement of covered SEMS<sup>[16]</sup>. In contrast, other studies did not support this finding<sup>[29,34]</sup>. In our study, stent migration occurred in only 1 patient (0.4%) and limited ES did not seem to be a significant factor associated with migration, regardless of the stent type.

This retrospective study has a few limitations. First, the possibility of inaccurate data collection cannot be overlooked. For example, procedure-related abdominal pain is difficult to distinguish from the breakthrough pain of malignancy and may have contributed to a bias in measuring the rate of PEP. Second, this study had a single-center design without a control group (non-ES group), which might influence the interpretation of the effect of limited ES. Further prospective multicenter studies with the inclusion of control groups are needed to overcome these limitations.

In conclusion, limited ES is a feasible, safe and effective procedure to facilitate placement of SEMS in patients with malignant biliary obstruction. Limited ES is not significantly associated with complications like severe bleeding or PEP and its use may represent a better strategy to achieve successful stent placement, especially in cases like hilar strictures that require complex procedural techniques.

## COMMENTS

### Background

Endoscopic biliary stent placement has become the primary management therapy for palliation in patients with malignant biliary obstruction. Endoscopic sphincterotomy (ES) is performed to reduce the risk of post-ERCP pancreatitis (PEP) and facilitate stent placement. Although many endoscopists routinely perform ES before self-expandable metal stent (SEMS) placement, the role of ES is still controversial in biliary stenting. Effects and complications on the degree of ES also need to be investigated. There have been few studies on the complications or effects of limited ES.

### Research frontiers

At present, there have been some reports to evaluate the safety and efficacy of ES before placement of SEMS and the existing data is contradictory. Currently, there are no guidelines regarding ES for biliary stenting. There is a lack of detail, regarding the extent of ES, and its correlation with complications.

### Innovations and breakthroughs

Limited ES is not significantly associated with complications like severe



bleeding or PEP. It may be useful to achieve successful stent placement. Limited ES is a feasible, safe and effective procedure to facilitate placement of SEMS in patients with malignant biliary obstruction.

## Applications

This retrospective study showed that limited ES could be useful to facilitate placement of SEMS, especially in cases, like hilar strictures, requiring complex procedural techniques without major complications. Further large randomized controlled trials are required.

## Terminology

ES is a method to provide access to the biliary system for therapy, which means cutting of the sphincter or muscle that lies at the juncture of the intestine with both the bile and pancreatic ducts. Limited ES is defined as sphincterotomy less than one-third the extent of major ES.

## Peer-review

This is an interesting manuscript that has not been published extensively. The authors showed in this study that the clinical outcomes in patients who did undergo limited ES before placement of SEMS for malignant biliary obstruction. The results provide new evidence that limited ES could be a feasible strategy for SEMS placement without significant complications.

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