

## Original

# A Two-institution study of risk factors for pancreatitis after endoscopic retrograde cholangiopancreatography for transpapillary biliary stent placement in patients with malignant biliary obstruction

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**【Objective】**To evaluate the risk factors for pancreatitis following endoscopic retrograde cholangiopancreatography (ERCP) for biliary stent placement in patients with malignant biliary obstruction (MBO).

**【Methods】**This retrospective study included consecutive MBO patients who underwent ERCP-guided transpapillary biliary stent placement over a period of 5.5 years at two tertiary referral academic medical centers. Of 100 eligible patients identified, 67 received a Wallflex™ self-expandable metallic stent (Boston Scientific Cooperation, Japan; SEMS group) and 33 received a Flexima™ plastic stent (Boston Scientific; PS group). The etiology of MBO was similar between the two groups, with pancreatic cancer accounting for 53% cases. The main outcome measurements were identifiable risk factors for post-ERCP pancreatitis (PEP).

**【Results】**The overall PEP rate was 3.0%, with no significant difference between the SEMS and PS groups. Totally, 7.1% and 2.3% patients who did and did not undergo endoscopic sphincterotomy (EST) before biliary stenting, respectively, developed PEP. The median duration of stent patency in the 8-mm SEMS, 10-mm SEMS, and PS groups was 136, 140, and 79 days, respectively, for patients with pancreatic cancer and in the 8-mm SEMS, 10-mm SEMS, and PS groups was 126, 166, and 137 days, respectively, for patients without pancreatic cancer. Multivariate analysis identified 6 factors that were not associated with PEP. PEP rates according to the presence or absence of EST before stent placement, stent type, stent size, and indications were not significantly different.

**【Conclusion】**The characteristics of the biliary stent and the performance of EST before stent placement are not significant risk factors for PEP in patients with MBO who underwent transpapillary biliary stent placement.

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## Introduction

Malignant biliary obstruction (MBO) is frequently

encountered in the practice of gastroenterology<sup>1-3)</sup>. Endoscopic retrograde cholangiopancreatography (ERCP) is the preferred method of providing biliary

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drainage because of its cost-effectiveness, and it is also the first-line therapy for the treatment of MBO<sup>4,5</sup>. Biliary stent placement using ERCP resolves jaundice and pain and improves the quality of life in patients with MBO<sup>6</sup>. Post-ERCP pancreatitis (PEP) is the most common complication of ERCP-guided biliary stent placement for MBO. Although it is generally mild, severe complications and death have been reported to occur in patients with PEP<sup>1-3</sup>. This study aimed to evaluate the risk factors for PEP in patients with MBO who underwent ERCP-guided biliary stent placement.

## Methods

The medical records of 100 patients with MBO who underwent ERCP-guided transpapillary biliary stent placement from April 2005 to August 2011 at the Saitama Medical Center of Saitama Medical University and Ageo Central General Hospital were retrospectively reviewed. This study was approved by the Saitama Medical Center, Saitama Medical University Institutional Review Board (No. 785). Of the 100, 67 patients received a Self-Expandable Metallic Stent (SEMS group; 39 covered stents and 28 uncovered stents) and 33 received a Plastic Stent (7Fr-10Fr) (PS group). The clinical characteristics of the patients included in the study are summarized in Table 1. The Single-step group included 33 men (49.3%) and 34 women (50.7%) with a mean age of 74.6 years, whereas the PS group included 18 men (54.5%) and 15 women (45.5%) with a mean age of 66.9 years. Pancreatic

cancer was the cause of MBO in 36 patients (53.7%) in the SEMS group and 16 patients (48.5%) in the PS group, whereas cholangiocarcinoma and gallbladder cancer were the cause in 31 patients (46.3%) in the SEMS group and 17 patients (51.5%) in the PS group. Patient demographics and data regarding stricture location and stent sizes are shown in Fig. 1. PEP was defined using standard criteria: new or worsening acute postprocedural abdominal pain in conjunction with an elevation in serum amylase or lipase levels greater than 3 times the upper limit of normal, with or without radiographic evidence of acute pancreatitis<sup>6</sup>.

## Statistical analysis

We reviewed the medical records and radiological images of each patient undergoing the stent placement procedure. The following variables were assessed by multivariate analysis (Chi-square test or Fisher's exact test) to identify the potential risk factors for PEP: gender, age, etiology of MBO (pancreatic cancer vs. non-pancreatic cancer), MPD tumor involvement, procedure for the ampulla, and type of SEMS used (covered or uncovered). Odds ratios (ORs) with 95% confidence intervals (CIs) were computed for all variables. Statistical tests were two-sided, and a *P* value of <0.05 was considered statistically significant.

## Results

The rates of PEP in the two groups in this study are summarized in Tables 2 and 3. The overall rate of PEP

Table 1.

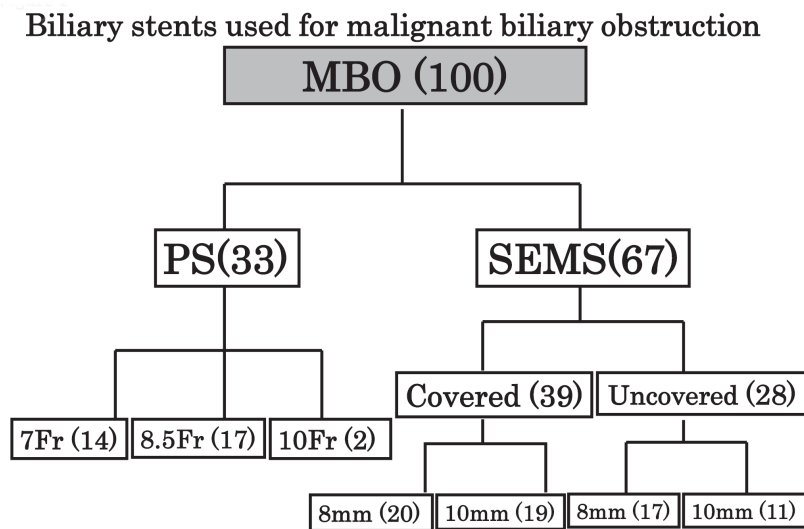
### Patient characteristics

Variable	SEMS (n= 67)	PS (n=33)	<i>P</i>
Mean age (years)	74.6	66.9	NS
Gender (n)			
Male	33	18	NS
Female	34	15	
Etiology of MBO:			
pancratic cancer (%)	53.7	48.5	NS
MPD tumor involvement			
present (%)	50.8	36.4	NS
Sphincterotomy (%)	13.4	15.2	NS

SEMS; Self -Expandable Metallic Stent PS; Plastic Stent

was 3.0%. We classified all cases of PEP as mild using consensus criteria. Hospitalization was required for all patients, with a mean post-ERCP length of stay of 11 days. No significant difference in PEP rate was observed between the PS group and SEMS group (3.0% vs. 2.99%,  $P = 0.54$ ). The performance of EST prior to stenting was not associated with a lower rate of PEP; 7.1% (1/14) patients who underwent EST developed PEP while 2.3% (2/86) patients who did not undergo the procedure developed PEP ( $P = 0.89$ ). The duration of stent patency in patients with and without

pancreatic cancer are shown in Fig. 2 and 3. The median duration of stent patency in the 8-mm SEMS group, the 10-mm SEMS group, and the PS group was 136, 140, and 79 days, respectively for the patients with pancreatic cancer ( $P = 0.88$ ) and 126, 166, and 137 days, respectively, in the PS group ( $P = 0.82$ ). A multivariate analysis of risk factors for PEP are shown in Table 4. PEP rates according to the presence or absence of EST before stent placement, stent type, stent size, and indications were not significantly different.



**Fig. 1.** Patient demographics and data regarding stricture location and stent sizes are shown.

**Table 2.**

**Rates of PEP in SEMS and PS groups**

	n	PEP	%	P
SEMS	67	2	2.99	<b>0.54</b>
PS	33	1	3.0	

PEP: Post ERCP Pancreatitis

**Table 3.**

**Rates of PEP in sphincterotomy and no sphincterotomy groups**

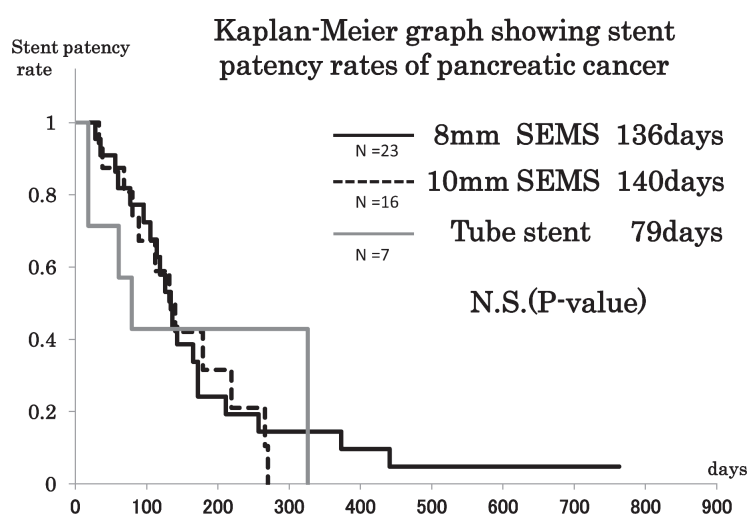
	n	PEP	%	P
Sphincterotomy	14	1	7.1	<b>0.89</b>
No sphincterotomy	86	2	2.3	

## Discussion

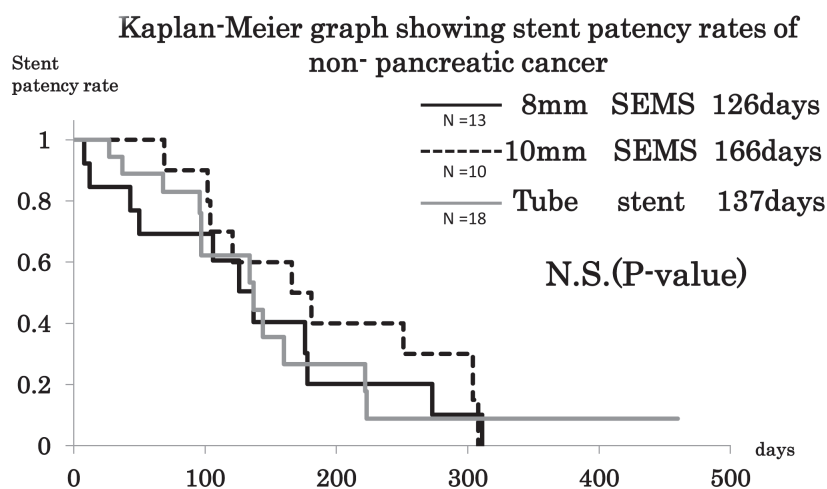
The performance of EST before biliary stenting is an established technique used in selected patients to facilitate biliary stone extraction, enhance the placement of large-diameter (10-11.5 Fr) plastic stents, and treat bile leakage, among other indications<sup>7-9</sup>. There is currently no standardization of the indications for EST before transpapillary SEMs placement. This is an important clinical question that should be addressed for several reasons.

First, the reported incidence of pancreatitis in patients with tumors of the main pancreatic duct (MPD) is low<sup>10, 11</sup>. In addition, because of their greater diameter compared with that of PSs, SEMs have superior patency and are increasingly preferred for the treatment of unresectable MBO in patients whose life expectancy is at least 6 months<sup>12-13</sup>. Nevertheless, among patients with unresectable MBO and a reasonable life expectancy, SEMs remains the preferred device because of its superior patency rate.

The overall rate of PEP was 3.0% in the total



**Fig. 2.** Duration of stent patency in patients with pancreatic cancer are shown. No significant difference was observed among the 8 mm SEMS, 10 mm SEMS and PS groups.



**Fig. 3.** Duration of stent patency in patients without pancreatic cancer are shown. No significant difference was observed among the 8 mm SEMS, 10 mm SEMS and PS groups.

Table 4.

**Multivariate analysis of risk factors for pancreatitis**

Variables	OR	95% CI	P
Pancreatic cancer (yes versus no)	1.01	0.21-1.61	0.98
MPD tumor involvement (yes versus no)	1.03	0.17-1.83	0.97
Sphincterotomy (yes versus no)	1.11	0.21-1.79	0.90
Type of stent (PS or MS)	0.82	0.15-1.51	0.81
Covered stent (yes or no)	1.15	0.20-1.91	0.87
Size of SEMS (8mm or 10mm)	1.23	0.28-1.70	0.78

MPD; Main Pancreatic Duct

\* OR odds ratio,

CI confidence interval

population of patients who underwent transpapillary biliary stenting for MBO between April 2005 and August 2011 in this study.

No significant difference in PEP rate was observed between the SEMS group and the PS group (3.0% vs. 2.99%,  $P = 0.54$ ). In addition, the performance of EST prior to biliary stenting was not associated with a lower rate of PEP (with EST, 7.1% (1/14 patients); without EST, 2.3% (2/86 patients);  $P = 0.89$ ).

The results of multivariate analysis of risk factors for PEP are shown in Table 4. There was no significant difference in PEP rates calculated according to the presence or absence of EST prior to stent placement, stent type, stent size, and indications. Although SEMSs have superior patency compared with PSs, the risk factors for PEP following transpapillary stent placement should be taken into consideration. Prior studies have reported that self-expanding metal stent placement without biliary sphincterotomy was not associated with pancreatitis<sup>14-16</sup>. The physician must use sound clinical judgement while making the decision to perform EST prior to transpapillary SEMS placement.

SEMS have superior patency to plastic stents due to their greater diameter, which may increase the incidence of pancreatitis. However, in the present study, we did not identify a relationship between stent size and the incidence of pancreatitis. Covered SEMS are associated with a higher risk of pancreatitis because of obstruction of the pancreatic duct orifice by the cover. However, our study showed that none of the SEMS-specific risk factors, including the use of covered SEMS, contributed to pancreatitis.

Our study has some limitations. First, the study population was too small for meaningful analysis of the risk factors for PEP. Second, this was not a prospective study; therefore, selection biases were present with regard to the type of SEMS used and the procedure employed for cannulation of the ampulla. The type of procedure was selected at the discretion of the endoscopists, so its impact on the incidence of pancreatitis could not be clearly established.

**Conclusions**

The characteristics of the biliary stent and the performance of EST before stent placement are not significant risk factors for PEP in patients with MBO who undergo transpapillary biliary stent placement.

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悪性胆道狭窄に対する内視鏡的胆管ステント留置におけるERCP後膵炎危険因子の検討－ 2 施設共同研究－  
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【目的】悪性胆道狭窄に対する内視鏡的胆管ステント留置におけるERCP後膵炎の危険因子を明らかにする。

【対象と方法】対象は2005年4月から2011年8月の間に埼玉医科大学総合医療センター及び上尾中央総合病院にて悪性胆道狭窄に対しERCP下に内視鏡的胆管ステント留置した100例。Self expandable metallic stent (SEMS)を留置した67例をSEMS groupとしPlastic stent (PS)を留置した33例をPS groupとした。ERCP後膵炎に寄与する危険因子を検討した。

【結果】全症例のERCP後膵炎の発症率は3.0%でありSEMS groupは7.1%, PS groupは2.3%であり両群に差を認めなかった。膵癌患者のステントの開存期間中央値はSEMS group (8 mm)は136日, SEMS group (10 mm)は140日, PS groupは79日であった。膵癌以外の患者のステントの開存期間中央値はSEMS group (8 mm)は126日, SEMS group (10 mm)は166日, PS groupは137日であった。ERCP後膵炎に寄与する因子として膵癌か否か, 主膵管の閉塞の有無, ステント留置前のESTの有無, PSかMS, MSにおけるcoverかuncover, SEMSの径が8 mmか10 mmの6因子にて多変量解析したところいずれも寄与しなかった。

【結論】悪性胆道狭窄に対する内視鏡的胆管ステント留置においてステントの種類や径, ステント留置前のESTの有無はERCP後膵炎に寄与しない。

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