

Retrospective Study

## Multicenter study of endoscopic preoperative biliary drainage for malignant distal biliary obstruction

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## Abstract

**AIM:** To determine the optimal method of endoscopic preoperative biliary drainage for malignant distal biliary obstruction.

**METHODS:** Multicenter retrospective study was conducted in patients who underwent plastic stent (PS) or nasobiliary catheter (NBC) placement for resectable malignant distal biliary obstruction followed by surgery between January 2010 and March 2012. Procedure-related adverse events, stent/catheter dysfunction (occlusion or migration of PS/NBC, development

of cholangitis, or other conditions that required repeat endoscopic biliary intervention), and jaundice resolution (bilirubin level < 3.0 mg/dL) were evaluated. Cumulative incidence of jaundice resolution and dysfunction of PS/NBC were estimated using competing risk analysis. Patient characteristics and preoperative biliary drainage were also evaluated for association with the time to jaundice resolution and PS/NBC dysfunction using competing risk regression analysis.

**RESULTS:** In total, 419 patients were included in the study (PS, 253 and NBC, 166). Primary cancers included pancreatic cancer in 194 patients (46%), bile duct cancer in 172 (41%), gallbladder cancer in three (1%), and ampullary cancer in 50 (12%). The median serum total bilirubin was 7.8 mg/dL and 324 patients (77%) had  $\geq 3.0$  mg/dL. During the median time to surgery of 29 d [interquartile range (IQR), 30-39 d]. PS/NBC dysfunction rate was 35% for PS and 18% for NBC [Subdistribution hazard ratio (SHR) = 4.76; 95%CI: 2.44-10.0,  $P < 0.001$ ]; the pig-tailed tip was a risk factor for PS dysfunction. Jaundice resolution was achieved in 85% of patients and did not depend on the drainage method (PS or NBC).

**CONCLUSION:** PS has insufficient patency for preoperative biliary drainage. Given the drawbacks of external drainage *via* NBC, an alternative method of internal drainage should be explored.

**Key words:** Endoscopic preoperative biliary drainage; Malignant distal biliary obstruction; Periapillary cancer; Plastic stent; Nasobiliary drainage

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**Core tip:** To determine the optimal method of endoscopic preoperative biliary drainage for malignant distal biliary obstruction, we conducted a multicenter retrospective study in 419 patients who underwent plastic stent (PS) or nasobiliary catheter (NBC) placement for resectable malignant distal biliary obstruction followed by surgery. The dysfunction rate for PS was significantly higher than that for NBC. Since the current limitations of nasobiliary catheter may not be overcome by a plastic stent, further studies may need to focus on the use of other stents that could remain patent for a longer period of time.

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## INTRODUCTION

Surgical resection is the only treatment option for cure in patients with periampullary cancers, including pancreatic and biliary tract cancers. In such patients, obstructive jaundice is often complicated. The efficacy of preoperative biliary drainage on improving peri- and postoperative outcomes for jaundice due to periampullary cancers is controversial<sup>[1-6]</sup>; however, biliary drainage is widely incorporated into clinical practice in many centers as a procedure following diagnostic cholangiography combined with pathological confirmation of malignancy or for the prevention of jaundice progression when the waiting time to a major surgery is prolonged, especially in tertiary centers<sup>[7,8]</sup>. Endoscopic biliary drainage (EBD) is preferred over percutaneous transhepatic biliary drainage (PTBD) for preoperative management of malignant distal biliary obstruction, because PTBD is more invasive, imposed considerable patient discomfort<sup>[9,10]</sup>, and more importantly, is frequently susceptible to catheter tract recurrence after surgery<sup>[11]</sup>. Although EBD is usually performed *via* plastic stent (PS) or nasobiliary catheter (NBC), NBC is unacceptable, especially in western countries, because of patient intolerance. However, NBC is considered advantageous in preventing reflux cholangitis and for early resolution of jaundice and is often employed in Japan.

In this multicenter retrospective study entitled endoscopic preoperative biliary drainage (E-POD) study, we evaluated the outcomes of preoperative EBD using both PS and NBC and analyzed the risk factors for PS/NBC dysfunction.

## MATERIALS AND METHODS

### Patients

In this study, data from 33 referral centers in Japan were consecutively collected. Patients who were diagnosed with distal biliary obstruction due to periampullary cancer and who underwent EBD *via* PS or NBC followed by surgical resection with curative intent between January 2010 and March 2012 were included. Patients who underwent initial drainage by PTBD or underwent surgery more than 100 d after initial EBD were excluded. This study was approved by the ethics committee at each hospital and was registered with UMIN-CTR (clinical trial registration number: UMIN000008492).

### Data collection

Data on baseline patient characteristics, procedures of EBD, procedure-related adverse events, outcomes of PS/NBC, types of surgery, and survival were collected retrospectively. All data were made anonymous and were collected from a collaborative web-based database.

### Definitions

Distal biliary obstruction was defined as biliary stricture located  $\geq 2$  cm downstream from the hilar bifurcation. Performance status was determined using the World Health Organization classification. Tumor invasion to the duodenum<sup>[12]</sup> was diagnosed on the basis of pathological findings of resected specimens. Dysfunction of PS/NBC was defined as occlusion or migration of PS/NBC, development of cholangitis, or suspected insufficient drainage that required repeat endoscopic biliary intervention. Occlusion or cholangitis included jaundice or re-elevation of liver enzyme with or without fever-up, and fever-up without other causes even if no elevation of liver enzyme. Insufficient drainage included persistent liver dysfunction or limited improvement of the elevated liver enzyme even though it is sometimes difficult to distinguish from other causes of liver dysfunction. Designed PS replacement was defined as NBC replacement with PS in patients without NBC dysfunction. Diagnostic re-endoscopic retrograde cholangiopancreatography (re-ERCP) was defined as further endoscopic examination (*e.g.*, confirmation of pathological diagnosis and re-evaluation of biliary system) that was required without PS/NBC dysfunction. The jaundice was defined as 3.0 mg/dL by using the application with modifications of Child-Pugh classification for cirrhotic patients, which was clinically used as one of the indications for surgery. Jaundice resolution was defined as reduction of serum total bilirubin from a pre-drainage level of  $\geq 3.0$  mg/dL to  $< 3.0$  mg/dL. The time to jaundice resolution and dysfunction of PS/NBC was defined as the interval between the initial EBD and each outcome. Procedure-related adverse events were diagnosed and graded according to the American Society of Gastrointestinal Endoscopy lexicon's severity grading system<sup>[13]</sup>.

### Statistical analysis

Results are expressed as numbers and percentages of patients or as medians and interquartile ranges (IQRs). Continuous variables were compared using Student's *t*-test or Wilcoxon's rank-sum test, as appropriate. Categorical variables were compared using the  $\chi^2$  or Fisher exact test, as appropriate. Cumulative incidence of jaundice resolution and dysfunction of PS/NBC were estimated using competing risk analysis<sup>[14]</sup> and were compared using the Gray's test<sup>[15]</sup>. During the analysis of the cumulative incidence of jaundice resolution, surgery prior to jaundice resolution was considered as a competing risk event. On the other hand, during the analysis of the cumulative incidence of PS/NBC dysfunction, surgery without PS/NBC dysfunction, PS/NBC removal at the time of diagnostic re-ERCP, or designed PS replacement was considered as a competing risk event. Patient characteristics and preoperative biliary drainage were evaluated for association with the time to jaundice resolution and PS/NBC dysfunction using competing

**Table 1** Characteristics of 419 patients who underwent endoscopic preoperative biliary drainage *via* plastic stent and nasobiliary catheter *n* (%)

	All patients ( <i>n</i> = 419)	PS ( <i>n</i> = 253)	NBC ( <i>n</i> = 166)	<i>P</i> value
Sex, male	269 (64)	163 (64)	106 (64)	0.905
Age (yr)	69 (63-75)	69 (62-75)	70 (63-76)	0.274
Performance status, 0/1/2	331/81/7 (79/19/2)	201/50/2 (79/20/1)	130/31/5 (78/19/3)	0.781
Primary cancer, pancreas/biliary tract/ampullary	194/175/50 (46/42/12)	133/91/29 (53/36/11)	61/84/21 (37/51/13)	0.003
Primary tumor size (mm)	20 (15-30)	20 (14-28)	22 (18-30)	0.008
Length of biliary stricture (mm)	16 (11-22)	15 (11-22)	17 (12-23)	0.154
Diameter of proximal bile duct (mm)	15 (12-18)	15 (12-18)	14 (11-17)	0.050
Involvement of intrapancreatic bile duct	354 (84)	221 (87)	133 (80)	0.048
Tumor invasion into duodenum	213 (51) <sup>1</sup>	132 (53)	81 (51)	0.823
Cholangitis on admission	64 (15)	34 (13)	30 (18)	0.200
Total bilirubin (mg/dL)	7.8 (3.3-13.2)	7.5 (3.3-12.6)	8.6 (3.4-13.5)	0.536

<sup>1</sup>Data were not obtained in nine patients. Data are expressed as numbers (%) or median (interquartile range). PS: Plastic stent; NBC: Nasobiliary catheter.

risk regression analysis<sup>[16]</sup>. Factors with a *P*-value of < 0.20 in the univariate analysis were further analyzed in multivariate models. Subdistribution hazard ratios (SHRs) and 95% CIs were calculated for each factor. A *P*-value of < 0.05 was considered statistically significant. All analyses were performed using R software version 2.12.0 (R Development Core Team) and its *cmprsk* package.

## RESULTS

### Patients

In total, 425 consecutive patients who underwent preoperative EBD for resectable periampullary cancers were identified. Six patients with placement of metal stent in this setting were excluded from the analyses. The characteristics of 419 patients are summarized in Table 1 (Those in patients with pancreatic and biliary tract cancer were shown separately in Supplementary Table 1A and B). Primary cancers included pancreatic cancer in 194 patients (46%), bile duct cancer in 172 (41%), gallbladder cancer in three (1%), and ampullary cancer in 50 (12%). Eighty-four patients (20%) had diabetes, three (1%) had liver cirrhosis, and three (1%) had dementia. Sixty-four patients (15%) had acute cholangitis at the initial drainage. The median serum total bilirubin was 7.8 mg/dL and 324 patients (77%) had  $\geq 3.0$  mg/dL. Two patients underwent neoadjuvant chemotherapy. The following surgeries were performed: pancreatoduodenectomy in 166 patients (39.6%), pylorus-preserving pancreatoduodenectomy in 142 (33.9%), subtotal stomach-preserving pancreatoduodenectomy in 90 (21.5%), choledochectomy in 10 (2.4%), total pancreatectomy in four (1.0%), and other surgeries in seven (1.7%). Cancer invasion of the duodenum was confirmed in the resected specimens obtained from 213 patients (51%).

### Procedures and procedure-related adverse events after initial EBD

PS and NBC were placed in 253 (60%) and 166 (40%) patients, respectively. NBC was placed in 30 of 64 patients (47%) with acute cholangitis and in 136 of

355 patients (38%) without acute cholangitis. The procedure for initial EBD is shown in Table 2 (Those in patients with pancreatic and biliary tract cancer was shown separately in Supplementary Table 2A and B). The diameters of PSs were 5 Fr in 18 patients (7%), 7 Fr in 150 (59%), and 8.5 Fr or 10 Fr in 85 (34%), whereas those of NBCs were 5 Fr or 6 Fr in 80 patients (48%), 7 Fr in 80 (48%), and 7.5 Fr in 6 (4%). An NBC with a diameter larger than  $\geq 8.5$  Fr was not commercially available; thus, the mean diameter of NBCs were significantly smaller than that of PSs (*P* < 0.001). Approximately two-thirds of PSs were straight tipped, whereas almost the same proportion of NBCs was pig-tail tipped. Endoscopic sphincterotomy (39%) or endoscopic papillary balloon dilation (3%) was performed before placement of PS/NBC. During the initial EBD procedure, biliary biopsy or brushing cytology examination was performed in 362 patients (86.4%), and 250 of them (69.1%) were found to be positive for cancer. There were no significant differences in the initial EBD procedures between pancreatic cancer and biliary tract cancer.

PEP was noted in 40 patients (9.5%). The PEP rate was higher in patients with bile duct cancer than in those with pancreatic or ampullary cancer (12.0% vs 7.8%, *P* = 0.15), but it was not related to PS/NBC (10.3% vs 8.4%, *P* = 0.53), the PS/NBC diameter (9.7% in < 7.5 Fr vs 9.4% in > 7.5 Fr, *P* = 0.91), and necessity for sphincterotomy (7.3% vs 11.3%, *P* = 0.17).

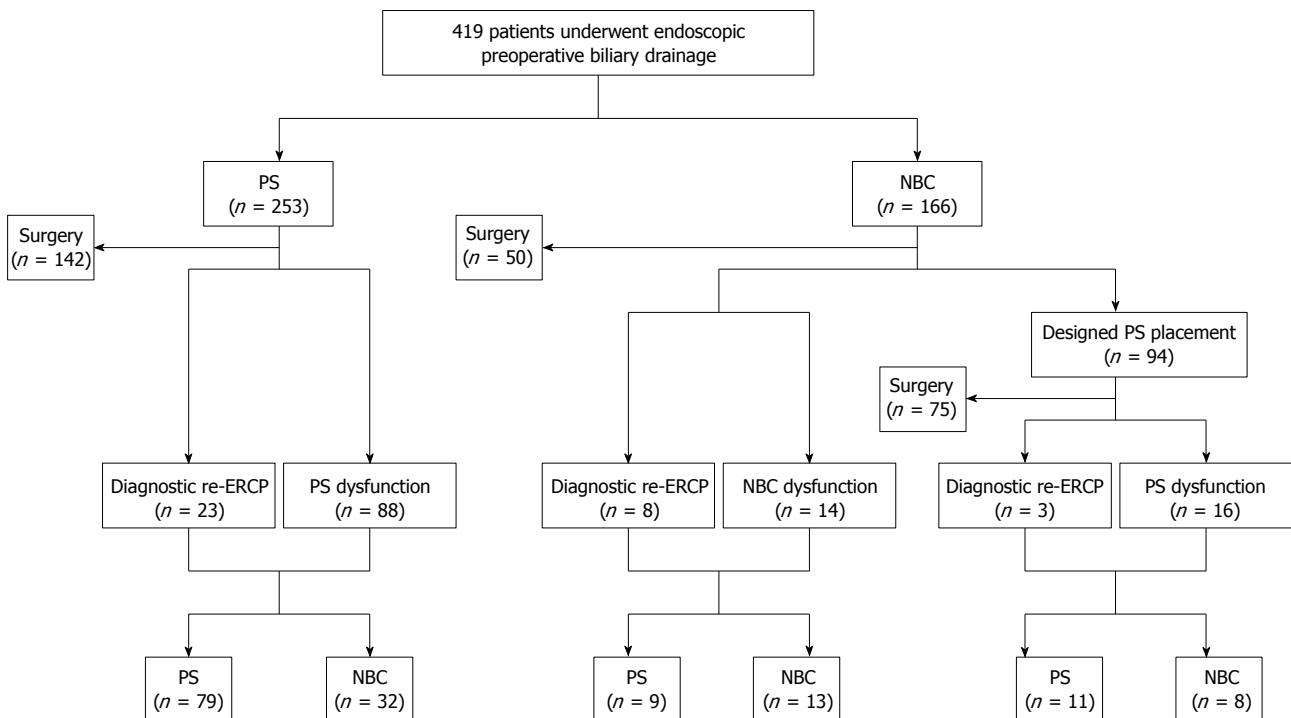
### Outcomes of preoperative biliary drainage via PS and NBC

The median time to surgery was 29 d (IQR, 30-39 d). Figure 1 demonstrates the clinical course of the patients after the initial drainage. In the PS group, 111 of 253 patients (44%) underwent additional ERCP (23 for diagnostic re-ERCP and 88 for PS dysfunction) and NBC was replaced in 32 of them. In the NBC group, 94 of 166 patients (57%) underwent designed PS replacement after a median of 8.4 d (IQR, 6-10 d). There were 41 patients (25%) who underwent

**Table 2** Procedures, adverse events, and causes of dysfunction in patients who underwent preoperative plastic stent and nasobiliary catheter placement *n* (%)

	All patients ( <i>n</i> = 419)	PS ( <i>n</i> = 253)	NBC ( <i>n</i> = 166)	<i>P</i> value
Procedures of the initial ERCP				
EST or EPBD	178 (43)	101 (40)	77 (46)	0.202
Biopsy or brushing of the bile duct	362 (86)	214 (85)	148 (89)	0.234
Positive for cancer	250 (60)	150 (59)	100 (60)	
Biliary stents/catheters placed				
Diameter 5-6/7-7.5/8.5-10 Fr	98/236/85 (23/56/20)	18/150/85 (7/59/34)	80/86/0 (48/52/0)	< 0.001
Pig-tailed tip/straight tip	152/224 <sup>1</sup>	74/177 (29/71)	78/47 (62/38)	< 0.001
Placement of pancreatic stent	41 (10)	25 (10)	16 (10)	0.935
Adverse events (other than cholangitis)				
Pancreatitis	40 (10)	26 (10)	14 (8)	0.612
Mild/moderate/severe	30/10/0			
Cholecystitis	4 (1)	2 (1)	2 (1)	0.650
Others	4 (1)	2 (1)	2 (1)	0.650
Stent/catheter dysfunction	118 (36)	88 (35)	30 (18)	< 0.001
Causes of PS/NBC dysfunction				
Occlusion or cholangitis	85	69 (27)	16 (10)	0.013
Insufficient drainage	19	14 (6)	5 (3)	0.330
Migration	10	5 (2)	5 (3)	0.526
Inadvertent removal	4	NA	4 (2)	NA
Number of ERCPs	2 (1-2)	1 (1-1)	2 (1-2)	< 0.0001

<sup>1</sup>Data was not obtained in 43 patients. A part of data on tips of PS/NBC was missing. "Occlusion or cholangitis" included jaundice or re-elevation of liver enzyme with or without fever-up, and fever-up without other causes even if no elevation of liver enzyme; "Insufficient drainage" included persistent liver dysfunction or limited improvement of the elevated liver enzyme, which is sometimes difficult to distinguish from other causes of liver dysfunction. PS: Plastic stent; NBC: Nasobiliary catheter; ERCP: Endoscopic retrograde cholangiopancreatography; EST: Endoscopic sphincterotomy; EPBD: Endoscopic papillary balloon dilation; NA: Not applicable.



**Figure 1** Flowchart of the clinical course of 419 patients who underwent preoperative biliary drainage via plastic stent and nasobiliary catheter followed by surgery. PS: Plastic stent; NBC: Nasobiliary catheter.

additional ERCP (11 for diagnostic re-ERCP, 14 for initial NBC dysfunction, and 16 for designed PS dysfunction).

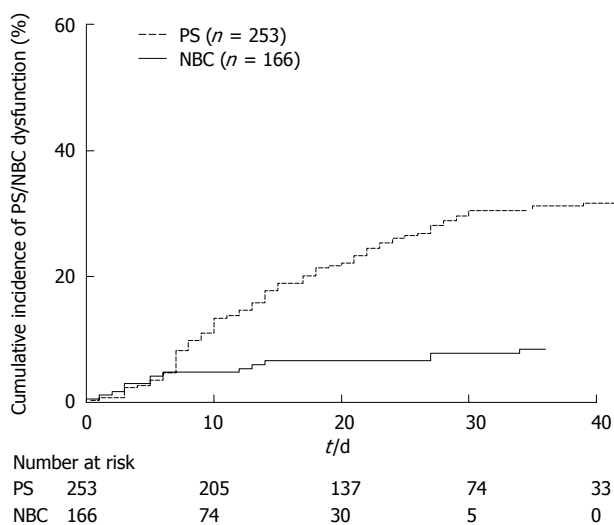
**Risk factors for PS/NBC dysfunction**

Multivariate analysis showed that PS placement had a significantly higher risk for dysfunction than NBC

**Table 3** Univariate and multivariate competing risks regression analyses to identify risk factors for dysfunction of plastic stent or nasobiliary catheter in 419 patients who underwent endoscopic preoperative biliary drainage

	Univariate analysis		Multivariate analysis	
	SHR (95%CI)	P value	SHR (95%CI)	P value
Sex, male	0.96 (0.64-1.44)	0.839		
Age > 70 yr	1.06 (0.72-1.56)	0.773		
Performance status ≥ 1	0.67 (0.39-1.14)	0.139	0.70 (0.39-1.24)	0.221
Primary cancer				
Biliary tract	Reference		Reference	
Pancreas	1.61 (1.06-2.44)	0.025	1.30 (0.84-2.03)	0.240
Ampullary	0.89 (0.43-1.84)	0.758	0.81 (0.40-1.65)	0.568
Primary tumor size > 20 mm	0.90 (0.61-1.33)	0.603		
Length of biliary stricture > 20 mm	1.04 (0.71-1.53)	0.854		
Diameter of proximal bile duct > 15 mm	0.94 (0.64-1.38)	0.755		
Tumor invasion into duodenum	1.10 (0.75-1.63)	0.621		
Cholangitis on admission	0.77 (0.44-1.37)	0.378		
Total bilirubin ≥ 8 mg/dL	1.16 (0.79-1.71)	0.447		
Placement of PS	4.76 (2.63-8.33)	< 0.001	4.76 (2.44-10.0)	< 0.001
Diameter of biliary stent/catheter				
5-6 Fr	Reference		Reference	
7-7.5 Fr	1.92 (1.07-3.43)	0.029	0.95 (0.50-1.83)	0.885
8.5-10 Fr	2.44 (1.28-4.66)	0.007	0.93 (0.44-1.99)	0.850
Pig-tailed tip	1.05 (0.71-1.57)	0.796		

PS: Plastic stent; NBC: Nasobiliary catheter; SHR: Subdistribution hazard ratio.



**Figure 2** Cumulative incidences of plastic stent/nasobiliary catheter dysfunction. PS: Plastic stent; NBC: Nasobiliary catheter.

placement (SHR = 4.76, 95%CI: 2.44-10.0,  $P < 0.001$ ) (Table 3). Figure 2 illustrates the cumulative incidences of PS/NBC dysfunction. The cumulative incidences of PS vs NBC was 13% vs 5% at 10 d, 22% vs 7% at 20 d, and 30% vs 8% at 30 d.

Table 4 shows the results of the analyses for identifying risk factors for PS dysfunction. Only the pig-tailed tip stent was an independent risk factor for PS dysfunction (SHR = 1.72, 95%CI: 1.13-2.64,  $P = 0.012$ ); a larger diameter of PS did not decrease the risk for PS dysfunction.

**Jaundice resolution after preoperative biliary drainage**

Jaundice was resolved at the time of surgery in 275 of

324 patients (84.9%). The other 49 patients (15.1%) underwent surgery without resolution of jaundice after a median of 21 d (IQR, 14-31 d) from the initial EBD. The prognostic factors for jaundice resolution are shown in Table 5. Placement of PS or NBC did not result in earlier resolution of jaundice, and only a high total bilirubin level (SHR = 0.43, 95%CI: 0.32-0.58,  $P < 0.001$ ) was identified as the significant risk factor for jaundice resolution.

**DISCUSSION**

In this multicenter retrospective study of 419 patients who underwent preoperative EBD for malignant distal biliary obstruction, PS placement was a risk factor for PS/NBC dysfunction, whereas NBC placement was not, and the cumulative incidence of PS dysfunction increased almost linearly with time after the initial drainage.

Preoperative biliary drainage in patients with distal biliary obstruction has been a major matter of debate for decades. Although randomized controlled trials and meta-analyses failed to demonstrate the effectiveness of routine preoperative biliary drainage, this procedure is still performed widely, particularly in symptomatic patients with an expected long waiting time who have complication such as cholangitis or intense pruritus or because of some other reasons. In the 33 hospitals that participated in the present study, most patients with jaundice underwent preoperative biliary drainage because a major surgery that lasts for 5-10 h cannot always be scheduled immediately after a diagnosis of cancer<sup>[17]</sup> and such drainage also allows time for further staging of primary cancer, physical work-up of comorbidities, and potentially, for

**Table 4** Univariate and multivariate competing risk regression analyses to identify risk factors for plastic stent dysfunction in 253 patients who underwent endoscopic preoperative plastic stent placement

	Univariate analysis		Multivariate analysis	
	SHR (95%CI)	P value	SHR (95%CI)	P value
Sex, male	1.00 (0.65-1.55)	0.993		
Age > 70 yr	1.15 (0.76-1.74)	0.509		
Performance status $\geq$ 1	0.84 (0.49-1.45)	0.534		
Primary cancer				
Biliary tract	Reference			
Pancreas	1.27 (0.81-1.99)	0.303		
Ampullary	0.83 (0.39-1.79)	0.637		
Primary tumor size > 20 mm	1.10 (0.72-1.69)	0.657		
Length of biliary stricture > 20 mm	1.01 (0.66-1.54)	0.957		
Diameter of proximal bile duct > 15 mm	0.85 (0.56-1.28)	0.432		
Tumor invasion into duodenum	1.10 (0.72-1.67)	0.659		
Cholangitis on admission	0.79 (0.41-1.52)	0.479		
Total bilirubin $\geq$ 8 mg/dL	1.32 (0.87-2.00)	0.192	1.43 (0.94-2.18)	0.096
Diameter of biliary stent/catheter				
5-6 Fr	Reference			
7-7.5 Fr	0.76 (0.37-1.56)	0.446		
8.5-10 Fr	0.67 (0.31-1.46)	0.314		
Pig-tailed tip	1.73 (1.14-2.63)	0.010	1.72 (1.13-2.64)	0.012

PS: Plastic stent; SHR: Subdistribution hazard ratio.

**Table 5** Univariate and multivariate competing risks regression analyses to identify prognostic factors for jaundice resolution after endoscopic preoperative biliary drainage in 325 patients

	Univariate analysis		Multivariate analysis	
	SHR (95%CI)	P value	SHR (95%CI)	P value
Sex, male	0.90 (0.71-1.14)	0.387		
Age $\geq$ 69 yr	1.01 (0.80-1.27)	0.932		
Performance status $\geq$ 1	1.00 (0.73-1.39)	0.979		
Primary cancer				
Biliary tract	Reference			
Pancreas	1.07 (0.84-1.36)	0.602		
Ampullary	1.19 (0.80-1.77)	0.389		
Primary tumor size > 20 mm	0.81 (0.63-1.04)	0.094	0.91 (0.69-1.20)	0.524
Length of biliary stricture > 20 mm	0.80 (0.63-1.01)	0.059	0.82 (0.63-1.06)	0.134
Diameter of proximal bile duct > 15 mm	0.78 (0.62-0.98)	0.033	0.81 (0.63-1.05)	0.107
Tumor invasion to duodenum	0.96 (0.76-1.21)	0.721		
Cholangitis on admission	1.11 (0.80-1.54)	0.528		
Total bilirubin $\geq$ 8 mg/dL	0.41 (0.31-0.55)	< 0.001	0.43 (0.32-0.58)	< 0.001
EST or EPBD	1.02 (0.81-1.28)	0.897		
Diameter of biliary stent/catheter				
5-6 Fr	Reference			
7-7.5 Fr	0.96 (0.73-1.25)	0.738		
8.5-10 Fr	0.97 (0.70-1.34)	0.859		
Pig-tailed tip	1.05 (0.83-1.34)	0.681		
Placement of NBC	0.83 (0.66-1.06)	0.129	0.92 (0.71-1.19)	0.520

In these competing risks regression analyses, jaundice resolution was set as the outcome and thus, a higher SHR indicated a higher probability of early resolution of jaundice. SHR: Subdistribution hazard ratio; CI: Confidence interval; EST: Endoscopic sphincterotomy; EPBD: Endoscopic papillary balloon dilation; NBC: Nasobiliary catheter.

neoadjuvant chemotherapy, which is increasingly utilized for pancreatic cancer.

EBD is preferred over PTBD for preoperative drainage because it is less invasive and insusceptible to tumor seeding. During EBD, PSs are preferred over NBCs with regard to comfort, but the rate of PS dysfunction before surgery is reported to be as high as 34%-70%<sup>[18-20]</sup>. Although Sugiyama *et al.*<sup>[20]</sup> demonstrated that the time to dysfunction of PS and NBC did not differ

significantly in a retrospective study of 76 patients, the rate of PS dysfunction was significantly higher than that of NBC dysfunction in the present study. In the PS group, a pig-tailed PS was the only risk factor for stent dysfunction and PS with a larger diameter failed to prolong the time to stent dysfunction. Interestingly, although the cumulative incidences of PS/NBC dysfunction were quite similar within a week of the initial biliary drainage, the cumulative incidence of PS

dysfunction linearly increased thereafter, whereas that of NBC dysfunction almost plateaued. At 30 d after the initial EBD, which was almost the median time to surgery in the present cohort, the cumulative incidence of dysfunction reached as high as 30% in the PS group, whereas that in the NBC group remained at 8%. In this study, the PS dysfunction rate and median time to dysfunction of 14 d were similar to those reported in a prospective study by van der Gaag *et al.*<sup>[4]</sup> (30% and 13 d, respectively).

NBC has other advantages such as repetitions of bile cytology to confirm malignancy<sup>[21]</sup> and contrast medium injection for cholangiography to evaluate longitudinal tumor spreading, especially in patients with bile duct cancer. However, there are several obvious disadvantages. For example, external bile drainage by NBC may impair enterohepatic circulation of bile, potentially leading to deterioration of intestinal immunity and coagulopathy, and prolonged placement of NBC may impose discomfort in the pharynx. NBC followed by the replacement of PS is another option for preoperative drainage, although it requires additional ERCP.

Longer patency of self-expandable metal stent (SEMS) compared with PS has been well-established in unresectable distal biliary obstruction<sup>[22,23]</sup> and recently, SEMS in the preoperative setting has been reported to be effective because of its longer patency and lower dysfunction rate (< 20%)<sup>[24-27]</sup>. Therefore, despite some potential disadvantages of SEMS, including cholecystitis<sup>[28]</sup>, pancreatitis<sup>[29]</sup>, and cost, SEMS is a promising device for preoperative biliary drainage and deserves further investigation. Considering that the ultimate endpoint of endoscopic preoperative biliary drainage for malignant distal biliary obstruction is overall survival rather than outcomes, the most appropriate method should be determined by a randomized controlled trial that compares PS, NBC, and SEMS, with the survival time set as the primary endpoint.

We acknowledge some limitations of this study. First, it was based on a non-randomized retrospective design and did not evaluate surgical outcomes. A randomized controlled trial is required to draw a definite conclusion of the optimal endoscopic preoperative biliary drainage procedure for malignant distal biliary obstruction, surgical outcomes (R0 resection rate, rate of surgical adverse events, and ultimately, overall survival), length of hospitalization, and cost-effectiveness. Second, we included only patients who underwent EBD and subsequent surgery; some patients in whom surgery could not be performed because of unsuccessful biliary drainage may have been excluded. Third, various types of PSs and NBCs were used in the present study.

In conclusion, PS was associated with a higher rate of cholangitis or occlusion compared with NBC. Because internal bile drainage is not susceptible to inherent disadvantages of external bile drainage,

internal bile drainage *via* SEMS should be evaluated in a preoperative setting.

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## COMMENTS

### Background

Although the efficacy of preoperative biliary drainage on improving peri- and postoperative outcomes for jaundice due to periampullary cancers is controversial, biliary drainage is widely incorporated into clinical practice in many centers as a procedure following diagnostic cholangiography combined with pathological confirmation of malignancy or for the prevention of jaundice progression when the waiting time to a major surgery is prolonged, especially in tertiary centers. Endoscopic biliary drainage is usually performed *via* plastic stent (PS) or nasobiliary catheter (NBC). NBC is unacceptable, especially in western countries, because of patient intolerance. However, NBC is considered advantageous in preventing reflux cholangitis and for early resolution of jaundice and is often employed in Japan.

### Research frontiers

The results of this study contribute to clarifying the outcomes of preoperative EBD using both PS and NBC and the risk factors for PS/NBC dysfunction in the largest cohort.

### Innovations and breakthroughs

At 30 d after the initial EBD, which was almost the median time to surgery in the present cohort, the cumulative incidence of dysfunction reached as high as 30% in the PS group, whereas that in the NBC group remained at 8%. The PS



dysfunction rate and median time to dysfunction of 14 d were similar to those reported in a prospective randomized study by van der Gaag *et al* (30% and 13 d, respectively).

### Applications

As the NBC has an obvious disadvantages of imposing discomfort in the pharynx, NBC followed by the replacement of PS is one of the options for preoperative drainage, although it requires additional ERCP. Preoperative placement of self-expandable metal stent should be investigated instead of plastic stent.

### Terminology

Endoscopic naso-biliary drainage: Naso-biliary drainage has some advantages such as repetitions of bile cytology to confirm malignancy and contrast medium injection for cholangiography to evaluate longitudinal tumor spreading, especially in patients with bile duct cancer. However, it has several obvious disadvantages; external bile drainage by NBC may impair enterohepatic circulation of bile, potentially leading to deterioration of intestinal immunity and coagulopathy, and prolonged placement of NBC may impose discomfort in the pharynx.

### Peer-review

Authors studied superiority between PS and NBC for preoperative drainage in a retrospective setting. This attempt is clinically valuable and the study is well-organized. Their results and conclusions are simple and reasonable.

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