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Novel anti-reflux biliary metal stent with a distal tapered end for distal malignant biliary obstruction: a feasibility study ▶

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ABSTRACT

Background and study aims We developed a self-expandable metallic stent (SEMS) with a distal tapered end to reproduce the physiological bile flow with a pressure gradient due to the difference in the diameter. We aimed to evaluate the safety and efficacy of the newly developed distal tapered covered metal stent (TMS) for distal malignant biliary obstruction (DMBO).

Patients and methods This single-center, prospective, single-arm study was conducted in patients with DMBO. The primary endpoint was time to recurrent biliary obstruction (TRBO), and the secondary endpoints were the survival time and incidence of adverse events (AEs).

Results Thirty-five patients (15 men, 20 women; median age, 81 years [range: 53–92]) were enrolled between December 2017 and December 2019. The primary diseases were pancreatic head cancer in 25 cases, bile duct cancer in eight cases, and ampullary cancer in two cases. TMS was successfully placed in all cases. Acute cholecystitis occurred as an early AE (within 30 days) in two cases (5.7%). The median TRBO was 503 days, median survival time was 239 days. RBO was observed in 10 cases (28.6%), and the causes were distal migration in six cases, proximal migration in two cases, biliary sludge in one case, and tumor overgrowth in one case.

Conclusions Endoscopic placement of the newly developed TMS in patients with DMBO is technically feasible and safe, and the TRBO was remarkably long. The anti-reflux mechanism based on the difference in diameter may be effective, and a randomized controlled trial with a conventional SEMS is required.

Introduction

Endoscopic placement of a self-expandable metal stent (SEMS) is the first-line treatment option for unresectable distal malignant biliary obstruction (DMBO) [1–3]. In particular, a covered SEMS is expected to have a longer patency period by preventing tumor ingrowth through the mesh of the stent [4–7].

A SEMS for DMBO is usually placed across the papilla. This impairs the function of the sphincter of Oddi and leads to SEMS occlusion due to biliary sludge or impaction of food residue [8–10]. To prevent duodenal biliary reflux, an SEMS with an anti-reflux valve at the lower end, an anti-reflux metal stent (ARMS), has been developed [11–21]; however, it is becoming clear that stent occlusion due to biliary sludge and micro-food particles cannot be prevented.

We hypothesized that a SEMS with a narrower distal tip side is less likely to cause bile flow stagnation due to the pressure gradient and can reproduce more physiological bile outflow

compared to a conventional SEMS with a uniform diameter. Therefore, we developed a new covered SEMS with a tapered structure at the distal end. In this study, we prospectively evaluated the efficacy and safety of a distal tapered metal stent (TMS) in patients with DMBO.

Patients and methods

Study design

This clinical study was a single-center, prospective, single-arm study conducted at Teikyo University Mizonokuchi Hospital. The study was approved by the Institutional Review Board for Human Research, and written informed consent was obtained from all participating patients. This study was registered with the University Hospital Medical Information Network Clinical Trials Registry (UMIN000042078) (http://www.umin.ac.jp/ctr/index.htm).

Study population

Consecutive patients with unresectable DMBO were enrolled in this study. The inclusion criteria were as follows: (1) pathologically proven malignant biliary obstruction (MBO); (2) patients not eligible for surgical resection because of the tumor stage or surgical risk; (3) those older than 20 years of age; (4) those able to provide informed consent; (5) those with an expected prognosis of >2 months; and (6) those with a performance status ≤2. The exclusion criteria were as follows: (1) massive ascites; (2) serious complications in other organs; (3) hilar biliary obstruction (within 10 mm from the hilar bifurcation); (4) altered anatomy following Billroth-II or Roux-en-Y reconstruction; (5) inability to undergo endoscopic retrograde cholangiopancreatography (ERCP); (6) more duodenal stenosis on the anal side than on the duodenal papilla (patients who showed improved with the duodenal stent could be enrolled); and (7) cases in which the physician judged inappropriate for some reason.

### Newly designed SEMS with a tapered distal end

The TMS used in this study was manufactured based on the braided-type covered SEMS, Niti-S (Taewoong Medical, Inc., Gimpo, Korea), but with a special design: a tapered distal end (▶Fig. 1). The TMS was 8 mm in diameter with a full silicone cover. Two lengths were available during the study (60 and 80 mm). The length of the tapered part was 15 mm from the distal end, and the tip diameter was 6 mm. A thread was attached to the boundary between the tapered and non-tapered parts for visibility during endoscopic placement. Radiopaque markers were attached to the entire part of the tapered part and proximal end. The delivery system was 9F in diameter.

Procedures

TMS placement was performed using standard ERCP procedures with a duodenoscope (TJF-260V; Olympus, Tokyo, Japan) and the patient under conscious sedation. Standard techniques were used to cannulate the biliary tract, and contrast was injected to identify the location and length of the stricture. Endoscopic sphincterotomy (ES) was performed before stent inser-
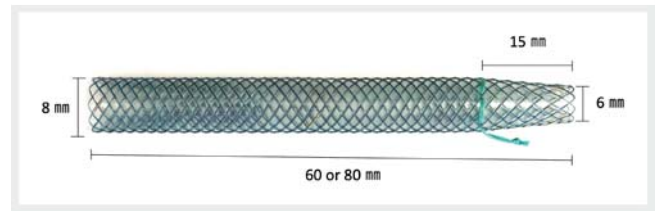
▶ **Fig. 1** The newly developed self-expandable metal stent with a distal tapered end. A thread is attached to the boundary between the tapered and non-tapered parts. a
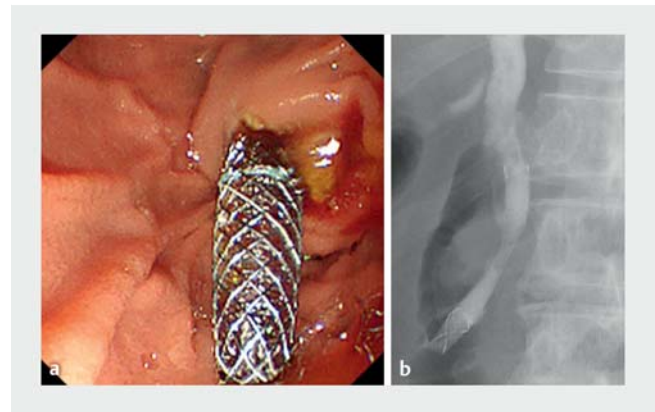
▶ **Fig. 2** **a** Endoscopic view of the distal tapered metal stent. **b** Fluoroscopic view of the distal tapered metal stent.

tion in all patients. The TMS was deployed while confirming with a fluoroscopic image that the position of the radiopaque marker and the air in the duodenum overlapped; finally, based on an endoscopic image, it was confirmed that the thread was in the duodenum (▶Fig. 2a, ▶Fig. 2b, ▶Video 1).
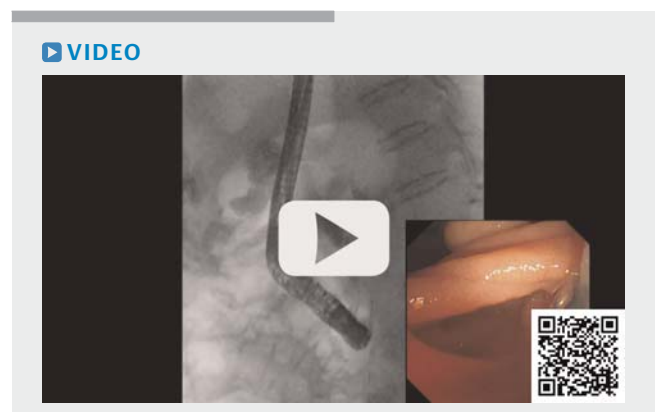
▶ **VIDEO**

▶ **Video 1** A tapered metal stent is deployed while confirming the positions of the radiopaque marker and thread on fluoroscopic and endoscopic images, respectively.

Outcome measurements

The primary endpoint was the time to recurrent biliary obstruction (TRBO). The secondary endpoints were the survival time and incidence of adverse events (AEs). If any of the subjective symptoms of fever, abdominal pain, or jaundice was observed during the follow-up period, clinical evaluation by medical examination, blood test, and radiological imaging were performed, and recurrent biliary obstruction (RBO) was evaluated based on the Tokyo Criteria 2014 [22]. RBO was defined as the coexistence of abnormal liver enzyme levels in blood tests and bile duct dilatation on imaging tests. TRBO was defined as the period from the date of stent placement to the date of RBO diagnosis. The evaluation of intraoperative AEs was based on the 2010 American Society of Gastrointestinal Endoscopy lexicon [23]. Postoperative AEs were evaluated according to the Tokyo Criteria 2014 [22]. AEs were classified as early AE within 30 days after the procedure and late AE occurring after 30 days.

Statistical analysis

The number of patients was set at 34 based on the threshold and expected median TRBO of 12 and 24 months, respectively, with a one-sided alpha error of 0.05 and power of 0.80. Continuous variables are presented as medians and ranges. Categorical variables are described as frequencies and percentages. Cumulative TRBO and overall survival were estimated using the Kaplan-Meier method. All statistical analyses were performed using JMP software version 14.2.0 (SAS Institute, Cary, North Carolina, United States).

Results

Patient characteristics

From December 2017 to December 2019, 35 patients (15 men and 20 women, median age, 81 years [range: 53–92]) were enrolled (▶Table 1). The primary diseases were pancreatic head cancer in 25 cases, bile duct cancer in eight cases, and ampullary cancer in two cases.

TMS placement

TMS placement was successful in all cases (▶Table 2). In 22 cases, previous drainage was placed before TMS placement, of which 21 cases were endoscopic biliary drainage (EBD) and one case was endoscopic nasobiliary drainage (ENBD). In these cases, the TMS was placed after removal at the time of EBD/ENBD removal. ES was performed in 21 cases (60%), excluding 14 cases in which ES had already been performed. The lengths of the TMS used was 6 cm in 17 cases and 8 cm in 18 cases.

TRBO and survival

After TMS placement, patients were followed up until the date of death or December 2020. Chemotherapy was administered in 20 patients, and best supportive care was provided in 15 cases. Thirty-three patients (94.3%) died, with a median survival of 239 days. The remaining two cases were confirmed to be alive as of December 2020, at the end of the observation period, and all reasons for censoring were due to deaths from can-

▶ **Table 1** Patient characteristics.

No. patients	35
Age, median (range), years	81 (53–92)
Sex, male/female	15/20
Cause of DMBO	
▪ Pancreatic cancer	25 (71.4%)
▪ Distal cholangiocarcinoma	8 (22.9%)
▪ Ampullary cancer	2 (5.7%)
▪ Distant metastasis	15 (42.9%)
Performance status	
▪ 0–1	26 (74.3%)
▪ 2–3	9 (25.7%)
Treatment after stent placement	
▪ Chemotherapy	20 (57.1%)
▪ Best supportive care	15 (42.9%)

DMBO, distal malignant biliary obstruction.

▶ **Table 2** Technical outcomes.

Sphincterotomy	
▪ Previous	14 (40%)
▪ Simultaneous	21 (60%)
▪ Technical success	35 (100%)
▪ Functional success	35 (100%)
Previous drainage	
▪ None	13 (37.1%)
▪ ENBD	1 (2.9%)
▪ EBD	21 (60%)
Length of the TMS	
▪ 60 mm	17 (48.6%)
▪ 80 mm	18 (51.4%)

ENBD, endoscopic nasobiliary drainage; EBD, endoscopic biliary drainage; TMS, tapered metal stent.

cer. The median observation period was 230 days (range: 25–1004), and RBO occurred in 10 patients (28.6%). The median TRBO was 503 days (▶Fig. 3). The causes of RBO were distal migration in six cases, proximal migration in two cases, sludge impaction in one case, and tumor overgrowth in one case (▶Table 3). The causes of DMBO in the six distal migrations were pancreatic cancer in four cases, cholangiocarcinoma in two cases, and proximal migration in two cases, all of which were pancreatic cancer. In two cases of proximal migration, the TMS was removed by grasping it with biopsy forceps during ERCP. In two cases (1 case of sludge impaction and 1 case of non-occlusion
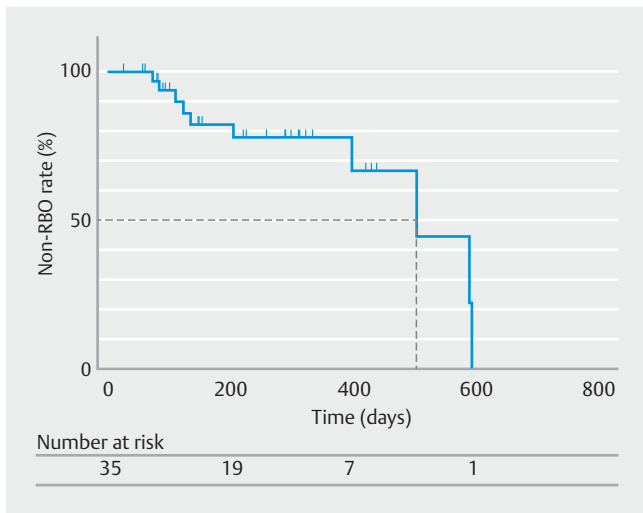
▶ **Fig. 3** Kaplan-Meier curve of the time to recurrent biliary obstruction (RBO). Small vertical bars on the solid line indicate censored cases.

▶ **Table 3** Clinical outcomes.

Recurrent biliary obstruction	
▪ Migration (distal)	6 (17.1%)
▪ Migration (proximal)	2 (5.7%)
▪ Overgrowth	1 (2.9%)
▪ Sludge	1 (2.9%)
Early AE (within 30 days)	
▪ Acute cholecystitis	2 (5.7%)
Late AE (≥31 days)	
▪ Non-occlusion cholangitis	1 (2.9%)
▪ Pseudoaneurysm bleeding	1 (2.9%)

AE, adverse event.

cholangitis), the TMS was removed by grasping the stent body with a snare. The SEMS with flared structures on both ends were used for re-intervention. In one case of overgrowth in which TMS could not be removed, a 7F plastic stent was implanted in a stent-in-stent manner. No patient had obvious duodenal stenosis prior to TMS placement. In three cases, duodenal stenosis on the oral side of papilla developed during follow-up, and a duodenal SEMS was placed.

Adverse events

Acute cholecystitis was observed in two cases as an early AE. In these two cases, preoperative computed tomography and fluoroscopic imaging showed no tumor invasion at the cystic duct orifice. In each case, percutaneous transhepatic gallbladder aspiration was performed, and no recurrence of cholecystitis was observed thereafter. Late AEs were found in two cases. In one case, pseudoaneurysm bleeding from the gastroduode-

nal artery was observed, and transcatheter arterial embolization was performed. In the other case, the hepatobiliary enzyme level was temporarily elevated 289 days after TMS placement, and when ERCP was performed for diagnosis, the stent was not occluded, and the stent was replaced. This patient was diagnosed as having non-occlusion cholangitis. There were no cases of duodenal ulcer, bleeding, or perforation caused by injury of the duodenum.

Discussion

Occlusion caused by sludge or food impaction is a major cause of RBO in cases of covered SEMSs, and it is believed to result from duodenal biliary reflux [8,9]. Recently, various designs of ARMSs have been developed so far; however, according to the results of ARMSs developed in the past, occlusion due to sludge or food impaction still occurs with a frequency of 3.8% to 80.0% [12–16, 18,20,21,24]. Intestinal bacteria produce enzyme, which acts on bile to form biliary sludge or stones leading to stent occlusion. The ARMS is thought to reduce both duodenal biliary reflux and bile forward flow, and it is thought that a small amount of bacterial contamination on the ARMS gradually forms a biofilm, eventually leading to ARMS occlusion. We hypothesized that narrowing the distal end of the SEMS might maintain physiological bile outflow based on pressure gradients due to the difference in diameter. The TMS, which was developed based on this idea, is a new type of SEMS developed that focuses on hydrodynamic bile dynamics; this is the first study to evaluate the efficacy and safety of a TMS for DMBO.

The TMS and ARMS are intended to prevent duodenal biliary reflux, but their structures are completely different. The ARMS has almost closed distal openings, the accumulation of bile in the bile duct increases the pressure in the bile duct, and bile is released into the duodenum through the gap in the valves. However, months of exposure to intestinal juices and food residue can damage anti-reflux valves made of silicone or polytetrafluoroethylene. In fact, past studies of the ARMS have also reported cases of RBO resulting from valve collapse [16,20, 21]. Because the distal opening of the TMS is 6mm, which is wider than the opening of the ARMS, it seems that food residue and duodenal juice flowed back into the bile duct, but the tapered structure can be expected to provide physiological washout. In reality, there was only one case (2.9%) of RBO due to sludge impaction, and the median TRBO was ≥500 days, which was remarkably longer than that in the existing reports on the ARMS. Therefore, it seems that the anti-reflux function of the TMS worked well.

The most common RBO observed in this study was distal migration. In this study, the time to migration was 83 to 593 days (median 96), and the SEMS was placed again in all cases. The developed TMS has a straight structure on the proximal side, so it seems to be a structure that can easily migrate. Among the ARMSs reported in the past, an SEMS with a flared structure on the proximal end has been developed to reduce the risk of migration; however, even this ARMS has been reported to have a distal migration [15,16]. Although the laser-cut SEMS is generally considered to have a low frequency of migration, a recent

study also reported that distal migration occurred with the laser-cut ARMS [20, 21]. Regardless of whether it is an ARMS or TMS, a SEMS with an anti-reflux mechanism is expected to have a higher internal pressure of the bile duct than the conventional SEMS; therefore, the issue of distal migration is more significant when using an ARMS/TMS than when using other SEMSs. Adding features to make it less migratory will be a challenge for future improvements. In this study, ES was performed before SEMS placement in all patients, but ES might have been one of the risk factors for migration. Several studies on pancreatic cancer have shown that ES prior to SEMS placement does not contribute to reducing the risk of pancreatitis [25, 26]. However, Kawakubo et al. reported that non-pancreatic cancer and high axial force SEMS are significant risk factors for postoperative pancreatitis after SEMS placement [27]. In the future, at least for pancreatic cancer cases, not performing ES may be a useful solution to reduce migration.

We were also concerned about the risk of proximal migration and how to manage it. Previous studies have reported that chemotherapy is a risk factor for stent migration [24, 28]. Because the TMS was thought to be structurally easy to migrate proximally when the tapered part was placed across the papilla, we confirmed that the entire tapered part was sufficiently protruding into the duodenum. In this study, two cases of proximal migration were observed. The times to migration were 589 and 122 days, respectively. Chemotherapy was administered in both cases, and bile duct stenosis may have improved with some therapeutic effects. In both cases, the lower end of the TMS moved upstream of the bile duct stenosis, but it could be easily removed by grasping the distal end with biopsy forceps. We thought that the tapered distal end was easier to grasp than the distal end of the other SEMS, which has anti-migration features such as a flared structure. On the other hand, it can be difficult to place a stent-in-stent beyond the distal tapered end. Hence, for patients who are planning to undergo chemotherapy, it may be necessary to take measures such as lengthening the duodenal part of the TMS across the papilla so it is longer than that of the conventional SEMS.

The optimal parameters for preventing duodenal biliary reflux are unknown. In this study, a stent with a body diameter of 8 mm and a tip diameter of 6 mm was used. SEMS with a body diameter of 10 mm is more common, but due to technical limitations of the manufacturer, SEMS with a body/tip diameter of 8 mm/6 mm was adopted. To our knowledge, no basic research on SEMS with a tapered distal end has been reported to date. Interestingly, even in the field of fluid mechanics, no previous study has verified the mechanism by which a tapered tip diameter prevents fluid backflow. More research and verification of the optimum parameters are needed.

A limitation of the present study is that it was a single-arm, single-center, small-sample study. In the future, it will be necessary to confirm our results using a multicenter randomized controlled trial. On the other hand, the observation period was sufficiently long, and of 35 cases, 33 cases of death were confirmed, and the remaining two cases were still being followed up. Therefore, we believe that the possibility of overestimation is low. Additionally, the stent placement procedure, especially

the positioning of the distal end, is unique compared to that of the conventional SEMS, so it requires some familiarity. The boundary of the tapered structure is invisible unless the TMS is fully expanded, but full stent expansion takes several days, as with other SEMSs. By using the thread as a marker, the boundary part can be seen; however, the position of the thread can only be confirmed after the TMS has been completely released. Even when the tapered part is 15 mm, a total length of approximately 20 mm protrudes into the duodenum. When determining the length of the TMS to be placed, a longer stent should be placed in consideration of the taper part. We were also concerned that the protruding stent would catch duodenal contents, but in reality, such a problem did not occur. Nevertheless, if the duodenum is narrowed due to pancreatic cancer, TMS placement may not be suitable, and alternative options should be considered.

Conclusions

In conclusion, our prospective observational study demonstrated that the endoscopic placement of the newly developed TMS in patients with DMBO is technically feasible and safe, and the TRBO was remarkably long. In addition, the anti-reflux mechanism based on the difference in diameter may be effective. Further validation will be needed in larger multicenter studies.

Competing interests

The authors declare that they have no conflict of interest.

Clinical trial

UMIN Japan (http://www.umin.ac.jp/english/)
UMIN000042078
TRIAL REGISTRATION: Prospective study UMIN000042078 at UMIN Japan

References

[1] Davids PHP, Groen AK, Rauws EAJ et al. Randomised trial of self-expanding metal stents versus polyethylene stents for distal malignant biliary obstruction. Lancet 1992; 340: 1488–1492

[2] Knyrim K, Wagner HJ, Pausch J et al. A prospective, randomized, controlled trial of metal stents for malignant obstruction of the common bile duct. Endoscopy 1993; 25: 207–212

[3] Prat F, Chapat O, Ducot B et al. A randomized trial of endoscopic drainage methods for inoperable malignant strictures of the common bile duct. Gastrointest Endosc 1998; 47: 1–7

[4] Isayama H, Komatsu Y, Tsujino T et al. Polyurethane-covered metal stent for management of distal malignant biliary obstruction. Gastrointest Endosc 2002; 55: 366–370

[5] Isayama H, Komatsu Y, Tsujino T et al. A prospective randomised study of "covered" versus "uncovered" diamond stents for the management of distal malignant biliary obstruction. Gut 2004; 53: 729–734

[6] Kahaleh M, Talreja JP, Loren DE et al. Evaluation of a fully covered self-expanding metal stent with flared ends in malignant biliary obstruction: a multicenter study. J Clin Gastroenterol 2013; 47: e96–e100

[7] Kitano M, Yamashita Y, Tanaka K et al. Covered self-expandable metal stents with an anti-migration system improve patency duration without increased complications compared with uncovered stents for distal biliary obstruction caused by pancreatic carcinoma: a randomized multicenter trial. Am J Gastroenterol 2013; 108: 1713–1722

[8] Okamoto T, Fujioka S, Yanagisawa S et al. Placement of a metallic stent across the main duodenal papilla may predispose to cholangitis. Gastrointest Endosc 2006; 63: 792–796

[9] Misra SP, Dwivedi M. Reflux of duodenal contents and cholangitis in patients undergoing self-expanding metal stent placement. Gastrointest Endosc 2009; 70: 317–321

[10] Loew BJ, Howell DA, Sanders MK et al. Comparative performance of uncoated, self-expanding metal biliary stents of different designs in 2 diameters: final results of an international multicenter, randomized, controlled trial. Gastrointest Endosc 2009; 70: 445–453

[11] Hu B, Wang T-T, Shi Z-M et al. A novel antireflux metal stent for the palliation of biliary malignancies: a pilot feasibility study (with video). Gastrointest Endosc 2011; 73: 143–148

[12] Lee KJ, Chung MJ, Park JY et al. Clinical advantages of a metal stent with an S-shaped anti-reflux valve in malignant biliary obstruction: Anti-reflux valve biliary metal stent. Digestive Endoscopy 2013; 25: 308–312

[13] Kim DU, Kwon C, Kang DH et al. New antireflux self-expandable metal stent for malignant lower biliary obstruction: In vitro and in vivo preliminary study. Digestive Endoscopy 2013; 25: 60–66

[14] Hamada T, Isayama H, Nakai Y et al. Novel antireflux covered metal stent for recurrent occlusion of biliary metal stents: A pilot study: ARMS for recurrent occlusion. Digestive Endoscopy 2014; 26: 264–269

[15] Hu B, Wang T, Wu J et al. Antireflux stents to reduce the risk of cholangitis in patients with malignant biliary strictures: a randomized trial. Endoscopy 2014; 46: 120–126

[16] Lee YN, Moon JH, Choi HJ et al. Effectiveness of a newly designed antireflux valve metal stent to reduce duodenobiliary reflux in patients with unresectable distal malignant biliary obstruction: a randomized, controlled pilot study (with videos). Gastrointest Endosc 2016; 83: 404–412

[17] Hamada T, Isayama H, Nakai Y et al. Antireflux metal stent as a first-line metal stent for distal malignant biliary obstruction: a pilot study. Gut Liver 2017; 11: 142–148

[18] Morita S, Arai Y, Sugawara S et al. Antireflux metal stent for initial treatment of malignant distal biliary obstruction. Gastroenterol Res Pract 2018: Jan 31; 2018: 3805173. doi:10.1155/2018/3805173

[19] Renno A. Antireflux valve metal stent versus conventional self-expandable metal stent in distal malignant biliary obstruction: a systematic review and meta-analysis. Ann Gastroenterol 2019; 32: 605–613

[20] Kin T, Ishii K, Okabe Y et al. Feasibility of biliary stenting to distal malignant biliary obstruction using a novel designed metal stent with duckbill-shaped anti-reflux valve. Digestive Endoscopy 2020; 33: 648–655

[21] Yamada Y, Sasaki T, Takeda T et al. A novel laser-cut fully covered metal stent with anti-reflux valve in patients with malignant distal biliary obstruction refractory to conventional covered metal stent. J Hepatobiliary Pancreat Sci 2021; 28: 563–571

[22] Isayama H, Hamada T, Yasuda I et al. TOKYO criteria 2014 for transpapillary biliary stenting: Reporting system of biliary stenting. Digestive Endoscopy 2015; 27: 259–264

[23] Cotton PB, Eisen GM, Aabakken L et al. A lexicon for endoscopic adverse events: report of an ASGE workshop. Gastrointest Endosc 2010; 71: 446–454

[24] Hamada T, Isayama H, Nakai Y et al. Antireflux covered metal stent for nonresectable distal malignant biliary obstruction: Multicenter randomized controlled trial. Digestive Endoscopy 2019; 31: 566–574

[25] Hayashi T, Kawakami H, Osanai M et al. No benefit of endoscopic sphincterotomy before biliary placement of self-expandable metal stents for unresectable pancreatic cancer. Clin Gastroenterol Hepatol 2015; 13: 1151–1158

[26] Artifon ELA, Sakai P, Ishioka S et al. Endoscopic sphincterotomy before deployment of covered metal stent is associated with greater complication rate: a prospective randomized control trial. J Clin Gastroenterol 2008; 42: 815–819

[27] Kawakubo K, Isayama H, Nakai Y et al. Risk factors for pancreatitis following transpapillary self-expandable metal stent placement. Surg Endosc 2012; 26: 771–776

[28] Nakai Y, Isayama H, Kogure H et al. Risk factors for covered metallic stent migration in patients with distal malignant biliary obstruction due to pancreatic cancer: Migration in covered metallic stent. J Gastroenterol Hepatol 2014; 29: 1744–1749