PO Box 2345, Beijing 100023, China
Fax: +86-10-85381893
E-mail: wjg@wjgnet.com www.wjgnet.com

World J Gastroentero, 2000; 6(5):643-646
World Journal of Gastroenterology
 ISSN 1007-9327

Metallic biliary stents for malignant obstructive jaundice: a review

Richard A. Kozarek

Subject headings pancreatic neoplasms; bile duct neoplasms; cholangiopancreatography, endoscopic retrograde; cholestasis; stents

Kozarek RA. Metallic biliary stents for malignant obstructive jaundice: a review. ***World J Gastroentero***, 2000;6(5):643-646

Affecting 8-10 patients per 100 000 population, pancreatic cancer is the primary cause of malignant obstructive jaundice and is the presenting feature in over three quarters of these patients[1]. Unfortunately, using modern imaging techniques, such as endoscopic ultrasound or pancreatic protocol computed tomography with vascular reconstruction, 80% - 90% prove unresectable for cure[2,3]. Historically, this jaundice was treated surgically with biliary bypass. Over the past 10 years, however, multiple studies have shown comparable palliation (3-6 month survival) with percutaneous or endoscopic placement of a polyethylene prostheses[4-6]. Moreover, our group, as well as others, have shown that despite comparable survivals, resource utilization (costs) to time of death for the endoscopic group are approximately one-half of those expended in surgically treated patients[7].

Despite this palliative advance in an often aged and infirm group of patients, however, stent occlusion has proven problematic. A consequence of bacterial biofilm development, attempts to prolong patency with chronic antibiotic therapy, ursodeoxycholic acid, change in the type of polymer used or coating the inner lining with a variety of agents to preclude bacterial colonization have all proven unsuccessful[8]. It was with this background that the first expandable metallic stent was introduced. This review will summarize the current state of our knowledge, new developments in self-expandable metal stent (SEMS) technology, and areas in which additional studies are needed.

WHAT DO WE KNOW ABOUT EXPANDABLE STENT TECHNOLOGY IN THE BILIARY TREE?

For one, we know that the vast majority of literature has utilized the open mesh stainless-steel Wallstents[9-16] (Microvasive Inc. Natick, MA). However, a number of additional SEMS (Table 1) have recently been introduced and variably studied. The latter included closed-weave prostheses fashioned from nitinol (Diamond stent, Microvasive Inc., Natick, MA; and Za stent, Wilson-Cook Inc., Winston-Salem, MA) or stainless steel (Spiral Z, Wilson-Cook Inc.)[17-23]. They also included the Biliary Endocoil (Intratherapeutics, Eden, Prairie, MN), a tightly coiled nitinol spiral which ostensibly precludes tumor ingrowth[24]. Not only these stents have different physical properties by virtue of wire material, guage, and configuration, but also their delivery systems and their degree of foreshortening at time of delivery differ. For instance, neither Spiral Z nor Za stents foreshorten. Diamond and Wallstents shorten by a third and Endocoils by a half.

We also know that, to date, there has been no study which has randomized metallic stent placement against surgical bypass in the palliation of malignant obstructive jaundice. There are, however, numerous randomized and controlled studies randomizing Wallstents against plastic prostheses, all showing superior patency of the former[4,10-13]. In a largest study, 182 patients with inoperable distal bile duct obstruction were randomized to plastic stent versus SEMS. At 30 days, one-quarter of the plastic prostheses were occluded compared with 5% of the Wallstents[11]. Although survival was unchanged, there was a two-fold prolongation in patency rate compared to plastic stents. Comparable, albeit longer stent survival (Wallstent 273 days, plastic 126 days) was reported by Davids *et al* in a well-designed European trial[10]. Additional, non-randomized studies have looked at the use of single or dual Wallstents in Klatskin-type tumor[15-17]. Dual stenting was not only associated with a decreased risk of cholangitis, but a decreased need for reintervention, and, in one study, approximately a two-fold survival[16].

Table 1 Commercially available self-expandable biliary stents for malignant obstructive jaundice

Stent	Wallstent	Endocoil	Diamond	Spiral Z	Za
Design	Mesh	Spiral coil	Mesh	Mesh	Mesh
Material	Stainless steel	Nitinol	Nitinol	Stainless steel	Nitinol
Length (cm)	4.2/6.8/8	6/7.5	4/6/8	5.7/7.5	4/6/8
Diameter (mm)	8/10	6/8	10	10	10
Stent foreshortening	Yes	Yes	Yes	No	No
Introducer diameter (Fr)	7.5/8	8/10	9	8.5	8.5

Richard A. Kozarek, MD, Section of Gastroenterology, Virginia Mason Medical Center, Seattle, WA, USA
Correspondence to: Richard A. Kozarek, MD, Chief of Gastroenterology, Virginia Mason Medical Center, 1100 9th Avenue, Seattle, WA 98111, USA
Fax. 206-223-6379
Email.GASRAK@VMMC.ORG
Received 2000-07-26 **Accepted** 2000-08-02

CAN THE ABOVE RESULTS BE GENERALIZED TO OTHER METALLIC PROSTHESES?

Probably not. Up to now there has been no study randomizing patients to Wallstents versus other SEMS. Dumonceau *et al*, however, reported 23 patients with malignant obstructive jaundice treated with Diamond stents and retrospectively compared them with an age and illness matched group treated with Wallstents[18]. Technical insertion, incidence of recurrent jaundice, and life table analyses of bile duct patency were comparable with both types of prostheses. In contrast, Raijman *et al* placed Diamond stents in 21 patients noting delivery system kinking in 2 and stent distortion or displacement in 3[22]. Moreover, mean patency was only 2.1 months compared to the 9.7 months of Wallstent patency in their historical controls. Seecoomar *et al* have also noted similar results[23]. In one of the few comparative studies reported to date, Yoo *et al* placed Diamond stents in 75 patients, plastic prostheses in 58 and Spiral Z stents in 20. The success rate of insertion was comparable whereas the patency at 4 months was 63%, 24%, and 77%, respectively[25]. They concluded that the patency rate of both SEMS was comparable and improved over plastic prostheses.

In addition to the above, there have been a few studies looking at biliary Endocoils but no comparative studies. In the latest series abstracted, 25 patients, including 6 with benign stenoses had Endocoil insertion and were followed for a mean of 13 months[26]. Stents were successfully deployed in 23/25 (92%) and jaundice improved in 22/24 (92%). However, 50% of stents were dysfunctional at a mean of 7 months. Data are even sparser for the Spiral Zstent[21] although a multi-center US trial is currently underway.

WHAT ELSE DO WE KNOW?

We recognize that in contrast to bacterial biofilm occlusion of plastic prostheses[8], SEMS dysfunction is usually a consequence of tumor ingrowth or overgrowth or elicitation of mucosal hyperplasia at the site of individual metal stents[27] Whether all wire materials and gauges elicit comparable hyp erplasia is unknown but common sense suggests that larger weave stents may allow more tumor ingrowth than tighter weaves. Wallstents may also become dysfunction al by local duct perforation at the proximal or distal ends, particularly if acutely angulated. Likewise, their exposed distal wires may cause prosthesis dysfunction by ulceration and impaction into the contralateral duodenal wall. Finally, Endocoils fail by virtue of migration or stent infolding. The latter may allow elicitation of granulation tissue or tumor ingrowth[28].

Despite our knowledge about the mechanism of dysfunction, the ideal therapy of recurrent jaundice in a patient with an imbedded SEMS remains controversial. Extraction of cholesterol and bile salt debris above a partially occluded stent is temporizing only and attempts to cauterize lumenal tissue are usually unsuccessful. Most endoscopists will usually place one or two plastic stents through a SEMS although an additional SEMS may sometimes prove useful. This is currently my sole use of the biliary Endocoil[9].

IN ADDITION TO WHAT WE DO KNOW, WHAT DO WE THINK WE KNOW?

We think that despite a 30 to 40-fold increase in cost of plastic stents as opposed to Wallstents, the latter are still cost-effective in patients with malignant obstructive jaundice[10]. These data are derived from the incremental expense associated with repeat ERCP in patients who outlive their plastic stents. In an attempt to better define which patients with malignant jaundice would benefit from a SEMS, Prat *et al* reviewed a variety of clinical, biochemical, and imaging criteria. Patients with small tumors (< 3cm) and normal albumen as well as those with good performance status were most likely to survive >6 months and were felt to benefit from a Wallstent[13]. Those who survived < 3 months were more likely to have larger tumors, metastases, low proteins, and poor performance status and should be considered for plastic prostheses. Unfortunately, this leaves a large number of patients in whom treatment remains uncertain. I would personally add that SEMS should be con sidered in patients who repeatedly occlude plastic prostheses or those who reside in geographically distant locations or those who do not have access to ERCP in their community.

We also think that covering a SEMS does not necessarily increase the patency rate [29]. Not only is the migration rate increased if the stent is fully covered, but bacterial biofilms and mucosal hyperplasia are problematic in stents that are only partially covered. Recent studies, most using historical controls, have questioned this[30-36]. For instance, Shim *et al* placed polyure thane- covered Z stents in 29 patients, following them for a mean of 15 months[30]. Successfully inserting 32/34 (94%) prostheses, there were early complications related to sludge in 19% and tumor/tissue ingrowth or overgrowth in another 21%. Median patient survival was 15.8 months and the authors concluded that covered Z stents improved long-term palliation of malignant biliary strictures. Recent abstracts have also recently been publis hed placing covered Wallstents and Diamond stents with variable results[31-36].

WHAT DO WE NEED TO KNOW FOR THE FUTURE?

We desperately need comparative studies between different SEMS and need true prospective studies

randomizing covered versus uncovered SEMS. We need better algorithms using clinical data to predict survival and define who is likely to benefit from a SEMS as opposed to selecting patients who would be equally well palliated with a much cheaper plastic prosthesis. We need better knowledge about the elicitation of mucosal hyperplasia and mechanisms to prevent this. Ultimately, we will need new materials, perhaps expandable mesh plastic polymers, cotton weaves impregnated with not only hardening agents but also antibiotics or chemotherapeutic agents, or metals that use a magnetic field or thermocouple to limit local tumor growth or treat ingrowth. If the precursor 10 years are any indication of the future 10, there will be new technologies that will be introduced and marketed before their advantages or disadvantages are fully known.

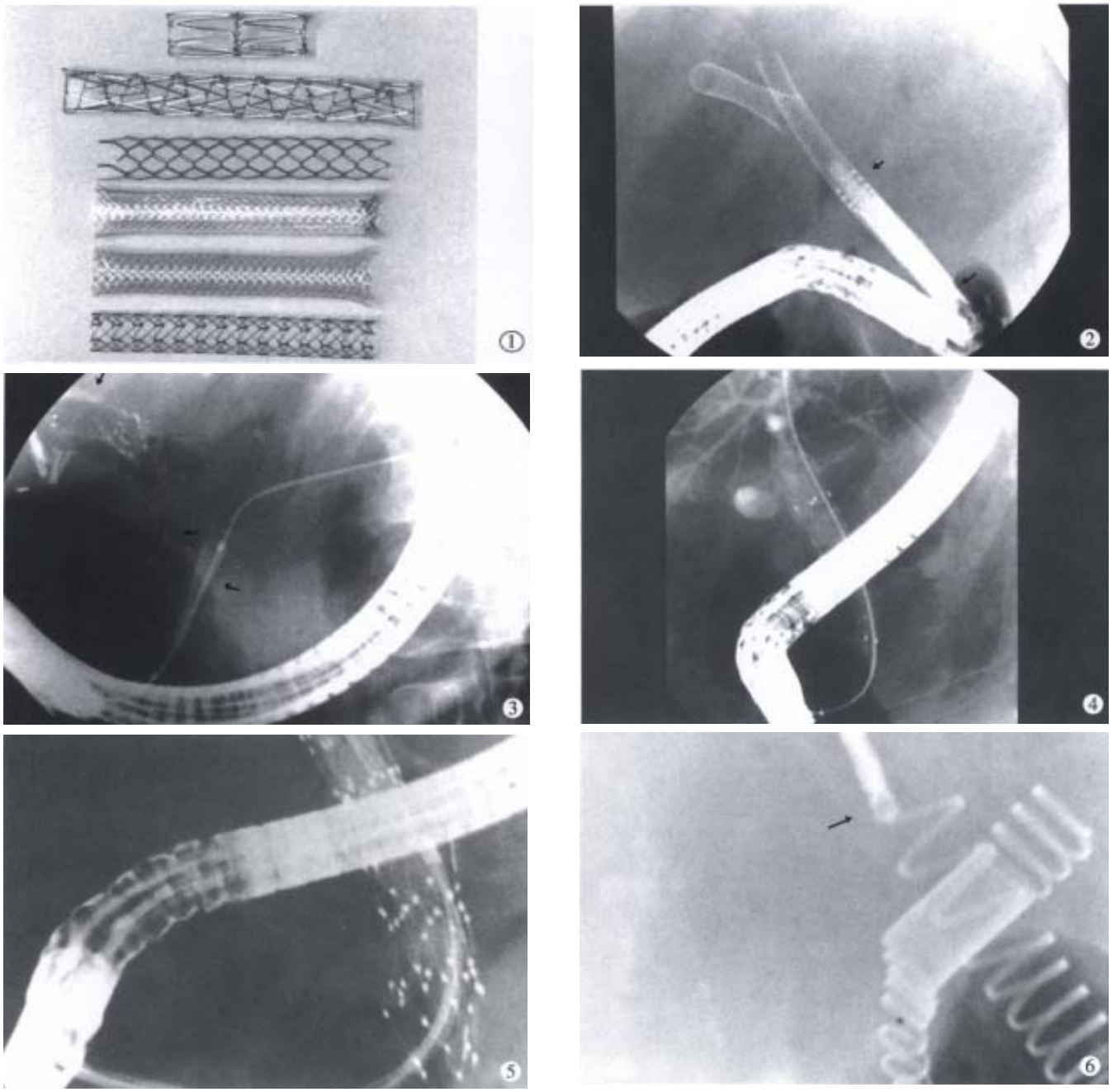

Figure 1 Currently available expandable metallic prostheses top to bottom: conventional Z, Spiral Z, Diamond, covered and uncovered Wallstent, and Za stent.

Figure 2 Dual Wallstents in patient with multiple bi liary strictures from metastatic colorectal carcinoma. Arrows depict Biliary Endocoil placed for mucosal hyperplasia and recurrent jaundice.

Figure 3 Diamond stent (large arrows) placed into th e biliary tree, and Wallstent (small arrow) placed into the pancreatic duct in patient with islet cell cancer and recurrent pancreaticobiliary sepsis.

Figure 4 Za stent placement in patient with distal malignant biliary stricture.

Figure 5 Spiral Z stent inserted in patient with obstructive jaundice from cholangiocarcinoma.

Figure 6 Expandable biliary endoprostheses imbed in tissue and cannot be retrieved. The exception is the biliary endocoil which can theoretically be retrieved by grabbing the distal end with a foreign body retriever.

REFERENCES

1 Enns RA. Expandable biliary stents: more questions than answers. *Am J Gastroenterol*, 2000;95:575-577
2 Kozarek RA. Endoscopy in the management of malignant obstructive jaundice. *Gastrointest Endosc Clin N Am*, 1996;6:153-176
3 Gudjonsson B. Cancer of the pancreas. 50 years of surgery. *Cancer*, 1987;60:2284-2303
4 Naggar E, Krag E, Matzen P. Endoscopically inserted biliary endoprosthesis in malignant obstructive jaundice. A survey of the literature. *Liver*,1990;10:321-324
5 Smith AC, Dowsett JF, Russell RC, Hatfield AR,Cotton PB. Randomized trial of endoscopic stenting versus surgical bypass in malignant low bile duct obstru ction. *Lancet*, 1994;344:1655-1660
6 Shepherd HA, Royle G, Ross AP, Diba A, Arthur M, Colin Jones D. Endoscopic biliary endoprosthesis in the palliation of malignant obstruction of the distal common bile duct:a randomized trial. *Br J Surg*, 1988;75:1166-1168
7 Brandabur JJ, Kozarek RA, Ball TJ, Hofer BO, Ryan JA Jr., Traverso LW, Freeny PC,Lewis GP. Nonoperative versus operative treatment of obstructive jaundice in pancreatic cancer: cost and survival analysis. *Am J Gastroenterol*, 1988;83:1132-1139
8 Sung JY, Leung JW, Shaffer EA, Lam K, Costerton JW. Bacterial biofilm, brownpigment stone and blockage of biliary stents. *J Gastroenterol Hepatol*, 1993;8:28-34
9 Kozarek RA. Expandable endoprostheses for gastrointestinal stenoses. *Gastrointest Endosc Clin N Am*, 1994;4:279-295
10 Davids PH, Groen AK, Rauws EA, Tytgat GN, Huibregtse K. Randomized trial of self expanding metal stents versus polyethylene stents for distal malignant biliary obstruction. *Lancet*, 1993;240: 1488-1492
11 Carr Locke, Ball TJ, Connors PJ, Cotton PB, Geenen JE, Hawes RH, Jowe ll PS, Kozarek RA, Lehman GA, Meier PB, Ostroff JW, Shapiro HA, Silvis SE, Vennes JA. Multicenter, randomized trial of Wallstent biliary endoprosthesis versus plastic stents (abstract). *Gastrointest Endosc*, 1993;39:310
12 Knyrim K, Wagner HJ, Pausch J, Vakil N. A prospective, randomized, controlled trial of metal stents for malignant obstruction of the common bile duct. *Endoscopy*, 1993;25:207-212
13 Prat F, Chapat O, Ducot B, Ponchon T, Pelletier G, Fritsch J, Choury A D, Buffet C. A randomized trial of endoscopic drainage methods for inoperable malignant strictures of the common bile duct. *Gastrointest Endosc*, 1998;47:1-7
14 Lammer J, Hausegger KA, Flückiger F, Winkelbauer FW, Wilding R, Klein GE, Thurnher SA, Havelec L. Common bile duct obstruction due to malignancy : treatment with plastic versus metal stents. *Radiology*, 1996;201:167-172
15 Dumas R, Demuth N, Buckley M, Peten EP, Manos T, Demarquay JF, Hastier P, Caroli Bosc FX, Rampal P, Delmont JP. Endoscopic bilateral metal stent placement for malignant hilar stenoses: identification of optimal technique. *Gastrointest Endosc*, 2000;51: 334-338
16 Mehta S, Ozden Z, Dhanireddy S, Pleskow DP, Chuttani R. Endoscopic single *vs* double (bilateral) Wallstents for palliation of malignant Bismuth type III/IV hilar strictures comparison of clinical outcome and hospital costs. *Gastrointest Endosc*, 1999;49:AB234
17 Kozarek RA, Ball TJ, Patterson DJ. Metallic self expanding stent applications in the upper gastrointestinal tract. caveats and concerns. *Gastrointest Endosc*, 1992;38:1-6
18 Dumonceau JM, Cremer M, Auroux J, Delhaye M, Deviere J. A comparison of Ultraflex Diamond stents and Wallstents for palliation of distal malignant biliary strictures. *Am J Gastroenterol*, 2000;95:670 -676
19 Smits M, Huibregtse K, Tytgat G. Results of the new nitinol self-expa ndable stents for distal biliary strictures. *Endoscopy*, 1995;27: 505-508
20 Gostout CJ, DeLuca L, Sorbi D, Conio M, Geller A. Endoscopic palliative treatment of inoperable pancreatic cancer using metal stents. *Gastrointest Endosc*, 1999;49:AB231
21 Howell DA, Nezhad SF, Dy RM. Endoscopically placed Gianturco endoprost hesis in the treatment of malignant and benign biliary obstruction. *Gastrointest Endosc Clin N Am*, 1999;9:479-490
22 Raijman I, Amin V, Siddique I, Curley S, Patt Y, Lynch P, Lahoti S, Pisters P, Lee J, Evans D, Catalano MF. The use of the Diamond stent (DS) in the treatment of malignant bile duct stricture (MBDS). *Gastrointest Endosc*, 1999;49:AB235
23 Seecoomar LF, Cohen SA, Kasmin FE, Siegel JH. Preliminary experience with the Ultraflex Diamond stent for the management of malignant biliary obstruction. *Gastrointest Endosc*, 1999;49: AB236
24 Goldin E, Beyar M, Safra T, Globerman O, Verstanding A, Wengrower D, Fich A. A new self expandable and removable metal stent for biliary obstruction a preliminary report. *Endoscopy*, 1993;25:597-599
25 Yoo B, Kim J, Roe I, Kim HG, Lee J, Park S, Lee D. Prospective study for the usefulness of self expanding nitinol biliary stents in patients with malignant obstruction of extrahepatic bile duct. *Gastrointest Endosc*, 1999;49:AB237
26 Cozart JC, Haber GB, Kortan PP, Kandel GP, Marcon NE.A nitinol self-expandable metallic stent for biliary obstruction: long term outcome in 25 pts. *Gastrointest Endosc*, 1999;49:AB230
27 Silvis SE, Sievert CE Jr., Vennes JA, Abeyta BK, Brennecke LH. Comparison of covered versus uncovered wire mesh stents in the canine biliary tract. *Gastrointest Endosc*, 1994;40:17-21
28 Kozarek RA. Endoscopic maneuvers for diagnosis and palliative treatment of pancreatic cancer. In: traverso LW (ed) Pancreatic Cancer. New York: Lippircott Raven, 1997:13-26
29 Born P, Neuhaus H, Roisch T, Ott R, Allescher H, Frimberger E, Classen M. Initial experience with a new, partially covered Wallstent for malignant biliary obstruction. *Endoscopy*, 1996;28:699-702
30 Shim CS, Cho YD, Kim YS, Moon JH, Lee MS. Long term follow up results of membrane covered self expanding metal stent in patients with malignant biliary obstruction. *Gastrointest Endosc*, 1999;49:AB131
31 Isayama H, Komatsu Y, Tsujino T, Toda N, Tada M, Yoshida H, Shiratori Y, Hamada T, Yamada H, Tagawa K, Kawabe T, Omata M. A prospective randomized study of "covered" vs "uncovered" metallic stent for distal malignant biliary obstruction. *Gastrointest Endosc*, 2000;51:AB191
32 Ponnudurai R, Haber GB, Kortan PP, Repici A, May G, Guerra J, Gordon R. A new covered biliary Wallstent: effectiveness in the palliation of malignant obstructive jaundice. Results from a multicenter trial. *Gastrointest Endosc*, 2000;51:AB191
33 Suh JH, Song SY, Park SW, Chung JB, Kang JK. A prospective randomized trial of a new covered biliary metal stent versus uncovered Wallstent for malign ant biliary obstruction. *Gastrointest Endosc*, 2000;51:AB192
34 Takasaki M, Takamatsu M, Yamamoto R, Emori Y, Saito T, Morita S, Yorimitsu Y. "Bare" versus "polyurethane covered" self-expandable metallic stent for malignant biliary obstruction. *Gastrointest Endosc*, 2000;51:AB192
35 Kim HD, Kim JH, Yoo BM, Lee KJ, Kim YS, Hahm KB, Cho SW, Lee DK, Park JJ, Park SH, Roe IH. Preliminary results of new covered biliary nitinol stent in patients with malignant obstruction of extrahepatic bile duct (EHD). *Gastrointest Endosc*, 2000;51:AB193
36 Shim CS, Cheon YK, Moor JH, Cho YD, Lee MS. Preliminary results of the new membrane covered self expandable nitinol biliary metal stent. *Gastrointest Endosc*, 2000;51:AB194

Edited by Ma JY