Gastrointest Interv 2017;6:171–175

Gastrointestinal Intervention

journal homepage: www.gi-intervention.org

Original Article

Clinical outcomes of biliary and duodenal self-expandable metal stent placements for palliative treatment in patients with periampullary cancer

Hong Joo Kim*

A B S T R A C T

Background: Endoscopic self-expandable metal stent (SEMS) insertions for palliation of malignant biliary and duodenal obstructions have been revealed to be an effective treatment. We present our clinical experience with the use of SEMS for malignant biliary and duodenal obstructions caused by periampullary cancer.
Methods: We performed a retrospective review of all patients who underwent endoscopic biliary and duodenal SEMS insertion for palliation of malignant biliary and duodenal obstruction caused by periampullary cancer between July 2007 and October 2016. The patients received simultaneous or sequential endoscopic biliary stenting and duodenal stenting with COMVI™ stents (partially covered; Taewoong, Seoul, Korea).
Results: The final diagnoses of our enrolled patients were 15 pancreas head cancer, and 3 distal common bile duct (CBD) cancer. The main stricture site in the duodenum was bulb (n = 4, 22.2%), 2nd portion (n = 9, 50.0%), and 3rd portion (n = 5, 27.8%). The technical success rates of CBD and duodenal stenting were 100% (18/18), and 100% (18/18), respectively. The clinical success rates of CBD and duodenal stenting were 100% (18/18), and 88.9% (16/18), respectively. Median actuarial stent patency for biliary and duodenal SEMS were 6.5 months (range, 1–12 months) and 4.5 months (range, 1–14 months), respectively. Three patients (16.7%) had recurrent biliary obstruction and all of them underwent percutaneous trans-hepatic biliary drainage (PTBD) with biliary SEMS reinsertion. Three other patients (16.7%, totally different from patients with CBD restenosis) had recurrent duodenal obstruction and all of them underwent upper gastrointestinal endoscopy with duodenal SEMS reinsertion.
Conclusion: Endoscopic SEMS insertions for simultaneous palliation of malignant biliary and duodenal obstruction in patients with periampullary cancer may provide a safe, and less invasive alternative to surgical palliation with a successful clinical outcome.

Keywords: Biliary obstruction; Duodenal obstruction; Periampullary cancer; Restenosis; Self expandable metallic stents

Introduction

Periampullary cancer, which includes pancreas head cancer, distal common bile duct (CBD) cancer, and ampulla of Vater and surrounding duodenal cancer, generally has a poor prognosis.[1] In majority of patients the disease is either locally advanced or metastatic at the time of diagnosis which hinder the application of potentially curative pancreaticoduodenectomy. In addition, the high morbidity and considerable mortality associated with pancreaticoduodenectomy may preclude it being offered to certain patients with significant medical comorbidities. Patients with periampullary cancer frequently develop symptomatic biliary and duodenal obstruction.[2–4] Historically, such patients have been treated by surgical bypass procedures such as hepaticojejunostomy or choledochojejunostomy for biliary obstruction and gastrojejunostomy for duodenal or gastric outlet obstruction.[5,6] Palliative management of biliary and duodenal stenosis in patients with unresectable periampullary cancer is effective in enhancing the quality of life of patients and in reducing pruritus, ascending cholangitis, vomiting and cachexia. Endoscopic and percutaneous transhepatic biliary stenting have a well-established efficacy in the palliative management of malignant biliary stenosis.[7] Recently, the use of self-expandable enteral metal stents has been reported, providing safe and effective palliative treatment in gastric and duodenal obstruction.[2,8]

An association between the development of jaundice and the

Department of Internal Medicine, Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine, Seoul, Korea
Received June 30, 2017; Revised July 31, 2017; Accepted August 13, 2017
* Corresponding author. Department of Internal Medicine, Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine, 29 Saemunan-ro, Jongno-gu, Seoul 03181, Korea.
E-mail address: hongjoo3.kim@samsung.com (H.J. Kim).

pISSN 2213-1795 eISSN 2213-1809 https://doi.org/10.18528/gii170013

subsequent development of duodenal obstruction has been reported.[9] Freeman and Cass[10] referred a case report describing the use of interlocking metal stents for simultaneous treatment of malignant biliary and duodenal obstruction. However, there have been not enough studies looking at the clinical outcome of sequential self-expandable metal stent (SEMS) for malignant biliary obstruction and malignant duodenal obstruction in patients with periampullary cancer. The aim of the present study was to evaluate the short- and long-term efficacy and clinical outcome of sequential SEMS placements for malignant biliary and duodenal obstruction in patients with periampullary cancer.

Methods

We performed a retrospective review of all patients who underwent biliary and duodenal SEMS for palliation of malignant biliary and duodenal obstruction caused by periampullary cancer between July 2007 and October 2016 in our hospital. The reasons of not performing surgery were advanced stage (n = 16, 88.9%; tumor status of locally advanced in 8 patients and metastatic disease in 8 patients) and medically unfit for surgery (n = 2, 11.1%; old age with poor performance status in 1 patient and advanced chronic obstructive pulmonary disease in 1 patient), respectively. Final confirmative diagnoses of periampullary cancer in our enrolled patients were established by explorative laparotomy in 1 patient (5.6%), endoscopic biopsies for duodenal mass lesion in 8 patients (44.4%), and endoscopic ultrasound-guided fine needle aspiration (EUS-FNA) for primary lass lesion in 9 patients (50.0%), respectively. The final diagnoses of our enrolled patients were pancreas head cancer in 15 patients (83.3%), and distal CBD cancer in 3 patients (16.7%), respectively (Table 1). Enrolled patients were followed-up until their death or January 2016. During the follow-up, all duodenal and biliary restenosis were retrospectively explored by searching relevant documents in electronic medical record system and relevant imaging files in Pi View PACS program (INFINITT, Seoul, Korea). In our institution, systematic approaches of endoscopic treatment of CBD and/or duodenal stenosis are first intention in patients who had unresectable periampullary cancer or medically unfit for surgical treatment. Surgical bypass is suggested only in patients in whom R0 resection is not possible during attempted curative resection. This study was conducted in accordance with the Principles of Declaration of Helsinki. The protocol of this study was obtained the approval of the Ethics Committee of Kangbuk Samsung Hospital (approval no. KBSMC17002) and informed consents were obtained from all patients.

Our enrolled patients had relevant evidences of biliary and duodenal obstruction by imaging and clinical findings. The patients received simultaneous or sequential endoscopic biliary stenting with COMVI™ biliary stent (partially covered; Taewoong, Seoul, Korea) and endoscopic duodenal stenting with COMVI™ duodenal stent (partially covered; Taewoong). Biliary and duodenal stents were inserted in the stenotic legions with partially overlapping region in all patients (Fig. 1). Technical success was defined as satisfactory deployment and precise positioning of the both CBD and duodenal stents through the stenosis. Clinical successes for CBD and duodenal stenting corresponded to improvements in jaundice with liver blood tests (total bilirubin < 5 mg/dL within 14 days after the procedure) and the ability to tolerate a normal oral diet without vomiting or the requirement of parenteral nutrition for duodenal stenting, respectively.

Endoscopic procedure

At the time of the stents placement, side-viewing duodenoscope (TJF-260V; Olympus Korea, Seoul, Korea) was used for biliary stent insertion, and both direct-viewing two-channel endoscope (GIF-2T240; Olympus Korea) and side-viewing duodenoscope were used for duodenal stent insertion. All the procedures were performed with the patients under monitored anesthesia care using intravenous midazolam® (Bukwang Pharm., Seoul, Korea)

Table 1 Patient Characteristics

Characteristic	Overall patients with biliary and duodenal SEMS insertion (n = 18)
Age (yr)	71.2 ± 10.0
Male gender	9 (50.0)
Final diagnosis	
Pancreas head cancer	15 (83.3)
Distal CBD cancer	3 (16.7)
Diagnostic confirmation	
Surgical pathology	1 (5.6)
EUS-FNA	9 (50.0)
Endoscopic (including ERCP) forcep biopsy	8 (44.4)
Site of duodenal stricture	
Bulb	4 (22.2)
2nd portion	9 (50.0)
3rd portion	5 (27.8)
Reasons of inoperability	
Advanced tumor stage	16 (88.9)
Medically unfit for surgery	2 (11.1)
WHO performance grade	
0	11 (61.1)
1	5 (27.8)
3	2 (11.1)
Tumor status	
Operable	2 (11.1)
Locally advanced	8 (44.4)
Metastatic	8 (44.4)
Chemotherapy	
First line	10 (55.6)
Second line	1 (5.6)
No chemotherapy	7 (38.9)
Endoscope used for duodenal SEMS insertion	
Forward-viewing scope	14 (77.8)
Side-viewing scope	4 (22.2)
Median length of duodenal SEMS (cm)	10 (8–12)
Median time interval between biliary and duodenal SEMS (mo)	0 (–2 to 13)

Values are presented as mean ± standard deviation, number (%), or median (range).
SEMS, self-expandable metal stent; CBD, common bile duct; EUS-FNA, endoscopic ultrasound-guided fine needle aspiration; ERCP, endoscopic retrograde cholangiopancreatography; WHO, World Health Organization.

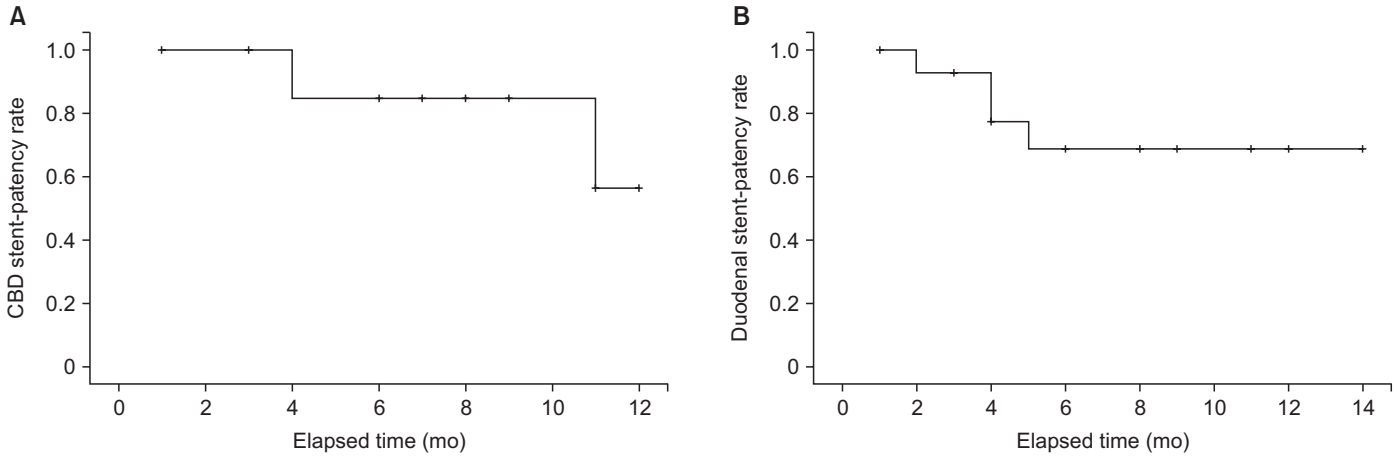

Fig. 1. Actuarial common bile duct (CBD; A) and duodenal (B) metallic stent patency in 18 patients with malignant biliary and duodenal obstruction caused by periampullary cancer.

following institutional guideline for patients and procedures at high risk. Cimetropium bromide (Algiron®; Boehringer Ingelheim Korea, Cheongju, Korea) was used for duodenal relaxation whenever necessary. Initially, side-viewing duodenoscope was inserted into the 2nd portion of duodenum in a standard fashion. Major papilla was identified, and a cholangiogram was obtained after contrast was injected (Omnipaque 300®; GE Healthcare, Seoul, Korea). In patients with a preexisting plastic biliary stent, the stent was removed using a snare grasping, and cholangiogram was obtained to define the biliary stricture. All our enrolled patients underwent biliary SEMS placement using the standard technique. The biliary stent used was COMVI™ biliary stent with a diameter of 10 mm and a length of 50 to 80 mm. Of 18 patients, 10 patients (55.6%) underwent biliary and duodenal SEMS, simultaneously. In these 10 patients, duodenal stenosis was sequentially dilated using the 12 to 20 mm sized through-the-scope controlled radial expansion balloons (CRE®; Boston Scientific/Microvasive, Natick, MA, USA) and side-viewing duodenoscope was passed through the stenotic area to major papilla, and then sequential CBD and duodenal SEMS insertions were done. Duodenal SEMS was firstly done and subsequently biliary SEMS was performed in 2 patients (11.1%) after 1, and 2 months. In remaining 6 patients (33.3%), biliary SEMS was followed by duodenal SEMS by median period of 10 months (range, 2–13 months). Duodenal SEMS was performed after a stiff, 0.035-inch guidewire (Kink resistant guidewire; MTW Korea, Seoul, Korea) was passed through the stricture. With the aid of fluoroscopic guidance, COMVI™ duodenal stent with a diameter of 20 mm, a length of 8–12 cm, and a delivery system of 8.5-Fr was deployed across the stricture, with the assistance maintaining constant tension on the outer sheath.

Results

Eighteen patients (9 men and 9 women) were enrolled in the current study. Mean ± standard deviation (SD) age of our enrolled patients was 71.2 ± 10.0 years. The final diagnoses of our enrolled patients were 15 pancreas head cancer (83.3%), and 3 distal CBD cancer (16.7%). The methods of diagnostic confirmation were EUS-FNA (n = 9, 50.0%), endoscopic biopsy for duodenal lesion (n = 8, 44.4%), and explorative laparotomy (n = 1, 5.6%). One patient underwent laparotomy because tumor appeared operable on preoperative staging. The cancer was operable in 2 cases (11.1%, who were medically unfit for surgery due to poor performance

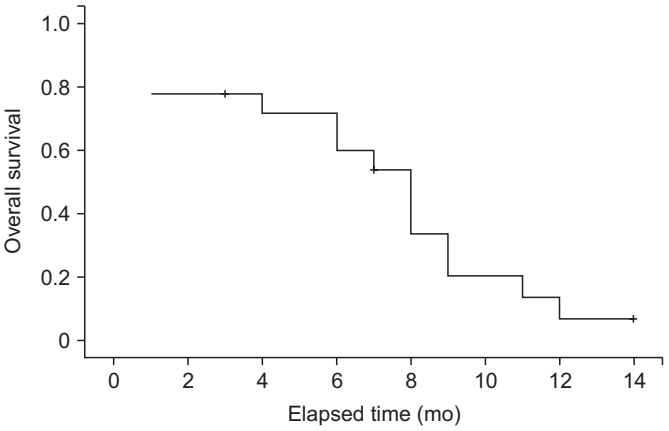

Fig. 2. Overall survival in 18 patients with malignant biliary and duodenal obstruction caused by periampullary cancer.

and comorbid conditions), locally advanced in 8 cases (44.4%) and metastatic in 8 cases (44.4%). The main stricture site in the duodenum was bulb (n = 4, 22.2%), 2nd portion (n = 9, 50.0%) and 3rd portion (n = 5, 27.8%). Eleven patients (61.1%) received at least one line of chemotherapy. Among them, 10 patients (55.6%) received first line chemotherapy including gemcitabine alone, combination of gemcitabine and erlotinib, and combination of gemcitabine and cisplatin. One patient (5.6%) received second line chemotherapy composed of 5-fluorouracil-leucovorin-cisplatin. No one of our enrolled patients received radiotherapy. The median length of inserted duodenal stent was 10 cm (range, 8–12 cm). For insertion of duodenal stent, direct-viewing two-channel endoscope (GIF-2T240) and side-viewing duodenoscope (TJF-260V) were used in 14 (77.8%) and 4 patients (22.2%), respectively. Median time interval between biliary and duodenal SEMS insertion was 0 month (range, –2 to 13 months; Table 1). The technical success rates of CBD and duodenal stenting were 100% (18/18), and 100% (18/18), respectively. The clinical success rates of CBD and duodenal stenting were 100% (18/18), and 88.9% (16/18), respectively. There were no immediate stents-related complications. Two patients in the arm of clinically unsuccessful outcomes after the duodenal SEMS insertion showed persistent intolerance to oral intake and nausea/vomiting. Follow-up

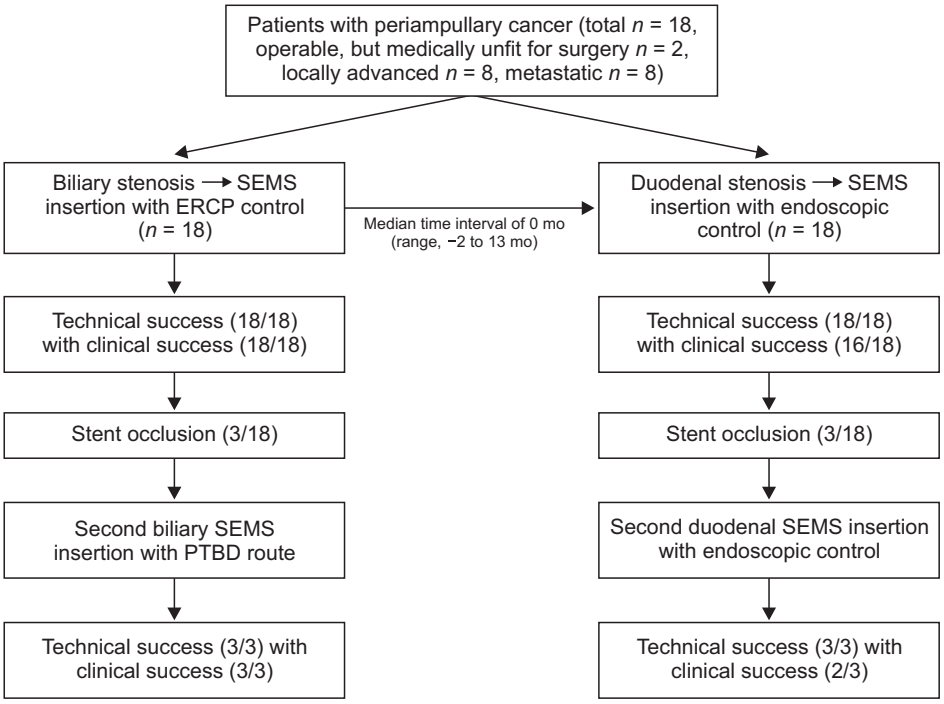

Fig. 3. Management of the biliary and duodenal obstructions in 18 patients with periampullary cancer who were inoperable or medically unfit for surgery. SEMS, self-expandable metal stent; ERCP, endoscopic retrograde cholangiopancreatography; PTBD, percutaneous trans-hepatic biliary drainage.

computed tomography scans for these two patients revealed the multiple small and large bowel obstructions probably due to the peritoneal metastases of cancer lesion. Median actuarial stent patency for biliary and duodenal SEMS were 6.5 months (range, 1–12 months) and 4.5 months (range, 1–14 months), respectively (Fig. 1). Median survival time was 7 months (range, 1–14 months) (Fig. 2). Three patients (16.7%) had recurrent biliary obstruction from tumor ingrowth or overgrowth at 2, 4, and 5 months, respectively, after the biliary stenting, and all of them underwent percutaneous trans-hepatic biliary drainage (PTBD) with biliary SEMS reinsertion. Three other patients (16.7%, totally different from patients with CBD restenosis) had recurrent duodenal obstruction from tumor ingrowth or overgrowth at 2, 4, and 5 months after the duodenal stenting, respectively, and all of them underwent duodenal SEMS reinsertion with upper gastrointestinal endoscopic control. Entire these 3 patients with duodenal SEMS reinsertion showed technical success, and two of these 3 patients could resume oral intake after the duodenal SEMS reinsertion (Fig. 3).

Discussion

The strength of the current study may be the uniformed application of endoscopic techniques by an experienced endoscopist, same biliary and duodenal SEMS (COMVI™ type) used, and one strategy of treatment by single institution which permits the accurate appraisal of the effectiveness and safety of the interventional technique. Additionally, the composition of enrolled patients was relatively uniformed (periampullary cancer with most of them were pancreas head cancer), and these strengths are contrasted to the heterogenous characteristics of previously reported data[2–10] in terms of adopted SEMS types, endoscopic and interventional techniques, and performed endoscopists and interventional radiologists.

In the current study, our attentions were focused on the feasibility and clinical outcomes of biliary and duodenal SEMS insertion in a consistent series of consecutive patients with malignant biliary and duodenal stenosis caused by periampullary cancer who were inoperable due to advanced stage or unfit for surgery due to poor performance status and comorbid conditions. Technical success rates for biliary and duodenal SEMS insertion were all 100% in our enrolled patients. This figure of high technical success rates is in accordance with series in the literature.[2,7,8,11] The stent patency is still a matter of debate. In the current study, the median actuarial stent patency for biliary and duodenal SEMS were 6.5 months (range, 1–12 months) and 4.5 months (range, 1–14 months), respectively (Fig. 1). We speculated that relatively short stent patency for biliary and duodenal SEMS was attributed to poor survival (median survival time were only 7 months; Fig. 2) of our enrolled patients because the restenosis of biliary and duodenal SEMS were only occurred in 3 patients (16.7%) and 3 patients (16.7%) of biliary and duodenal SEMS insertion, respectively. A previous report[12] suggested that all patients with WHO performance scores of 0–2, who are theoretically eligible to receive chemotherapy, should undergo metallic stenting on primary intention because their life expectancy usually exceeds 6 months. In the current study, entire enrolled patients had WHO performance score 0–1, except for two patients with WHO performance score 3. For these two patients, simultaneous biliary and duodenal SEMS insertions were done for the alleviation of symptoms for obstructive cholangitis and gastric outlet obstruction.

The cumulative restenosis rate (16.7%) of duodenal SEMS in the current study was comparable to those of previous reports.[3,4,13] Several studies have shown that duodenal stenting is a safe and effective method to palliate gastric or duodenal obstruction. Technical and clinical success rates reported in the literature are 75% to 100% and 77% to 100%, respectively.[8,13–17] A recent report by Telford et al,[18] showed that 84% of patients resumed oral intake after enteral stent insertion in a large multicenter series. The current study also confirms the excellent feasibility (100%) and clinical efficacy (88.9%) of endoscopic duodenal SEMS placement. Most patients (83.3%) with duodenal obstruction required a single duodenal stenting during follow-up. Stent failure (failure to

achieve clinical success) reported in two patients was probably a result of multiple small or large bowel obstruction caused by peritoneal carcinomatosis that was not diagnosed before endoscopic treatment. Peritoneal cancer metastasis should be carefully excluded by both conventional imaging before the endoscopic duodenal SEMS placement, especially for the bowel below the level of duodenal stenosis. Three patients (16.7%, totally different from patients with CBD restenosis) had recurrent duodenal obstruction from tumor ingrowth or overgrowth underwent duodenal SEMS reinsertion with upper gastrointestinal endoscopic control, and entire 3 patients showed technical success; however, only two of these 3 patients resumed oral intake after the SEMS insertion (Fig. 3).

Patients who were treated with endoscopic biliary SEMS insertion are prone to develop symptomatic duodenal obstruction due to duodenal tumor invasion.[19] Given the difficulties in obtaining access to the CBD through a duodenal stent placed across the major papilla, a SEMS should be inserted before the duodenal SEMS is positioned if there is known biliary obstruction. If a plastic biliary stent has already been used, the plastic stent should be replaced by a SEMS.[4,19] When the CBD and duodenal stenosis were simultaneously occurred (10 patients in the current study) sequential endoscopic CBD SEMS placement followed by endoscopic duodenal SEMS insertion was successfully done. If the CBD stenosis occurred after a duodenal SEMS positioning across the major papilla (2 of our enrolled patients), a percutaneous transhepatic route might be required for biliary drainage. Such procedure was successful in all two patients in the current study.

Our study design had inherent limitations including retrospective nature. Prospective randomized controlled trial will be a decisive clinical study to determine the effectiveness and safety of SEMS in palliating both malignant CBD and duodenal obstruction. However, due to ethical problem, it will be very difficult to design and perform such a kind of clinical studies. Second, the number of enrolled patients is relatively small to draw concrete conclusion, and future study design including multicenter setting will resolve the limitation.

In conclusion, SEMS insertions for simultaneous palliation of malignant biliary and duodenal obstruction in patients with periampullary cancer who were inoperable due to advanced tumor stage or unfit for surgery due to poor performance status and comorbid conditions, may provide a safe, and less invasive alternative to surgical palliation with a successful clinical outcome. Our results suggest that “exclusive endoscopic approach” for the treatment of biliary and duodenal obstructions is feasible, safe and clinically effective in short- and long-term in these patients. Endoscopic approach could afford the patients to provide palliation and permit immediate use of cancer chemotherapeutic agents.

Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

References

1. Sohn TA, Yeo CJ, Cameron JL, Koniaris L, Kaushal S, Abrams RA, et al. Resected adenocarcinoma of the pancreas-616 patients: results, outcomes, and prognostic indicators. *J Gastrointest Surg.* 2000;4:567-79.
2. Profili S, Feo CF, Meloni GB, Strusi G, Cossu ML, Canalis GC. Combined biliary and duodenal stenting for palliation of pancreatic cancer. *Scand J Gastroenterol.* 2003;38:1099-102.
3. Kaw M, Singh S, Gagneja H, Azad P. Role of self-expandable metal stents in the palliation of malignant duodenal obstruction. *Surg Endosc.* 2003;17:646-50.
4. Kaw M, Singh S, Gagneja H. Clinical outcome of simultaneous self-expandable metal stents for palliation of malignant biliary and duodenal obstruction. *Surg Endosc.* 2003;17:457-61.
5. Feduska NJ, Dent TL, Lindenauer SM. Results of palliative operations for carcinoma of the pancreas. *Arch Surg.* 1971;103:330-4.
6. Sarr MG, Cameron JL. Surgical palliation of unresectable carcinoma of the pancreas. *World J Surg.* 1984;8:906-18.
7. Prat F, Chapat O, Ducot B, Ponchon T, Pelletier G, Fritsch J, et al. A randomized trial of endoscopic drainage methods for inoperable malignant strictures of the common bile duct. *Gastrointest Endosc.* 1998;47:1-7.
8. Dumas R, Demarquay JF, Caroli-Bosc FX, Paolini O, Guenenna D, Peten EP, et al. Palliative endoscopic treatment of malignant duodenal stenosis by metal prosthesis. *Gastroenterol Clin Biol.* 2000;24:714-8.
9. Maetani I, Ogawa S, Hoshi H, Sato M, Yoshioka H, Igarashi Y, et al. Self-expanding metal stents for palliative treatment of malignant biliary and duodenal stenoses. *Endoscopy.* 1994;26:701-4.
10. Freeman ML, Cass OW. Interlocking expandable metal stents for simultaneous treatment of malignant biliary and duodenal obstruction. *Gastrointest Endosc.* 1996;44:98-9.
11. Flamm CR, Mark DH, Aronson N. Evidence-based assessment of ERCP approaches to managing pancreaticobiliary malignancies. *Gastrointest Endosc.* 2002;56(6 Suppl):S218-25.
12. Maire F, Hammel P, Ponsot P, Aubert A, O'Toole D, Hentic O, et al. Long-term outcome of biliary and duodenal stents in palliative treatment of patients with unresectable adenocarcinoma of the head of pancreas. *Am J Gastroenterol.* 2006;101:735-42.
13. Nassif T, Prat F, Meduri B, Fritsch J, Choury AD, Dumont JL, et al. Endoscopic palliation of malignant gastric outlet obstruction using self-expandable metallic stents: results of a multicenter study. *Endoscopy.* 2003;35:483-9.
14. Dormann A, Meisner S, Verin N, Wenk Lang A. Self-expanding metal stents for gastroduodenal malignancies: systematic review of their clinical effectiveness. *Endoscopy.* 2004;36:543-50.
15. Adler DG, Baron TH. Endoscopic palliation of malignant gastric outlet obstruction using self-expanding metal stents: experience in 36 patients. *Am J Gastroenterol.* 2002;97:72-8.
16. Maetani I, Tada T, Ukita T, Inoue H, Sakai Y, Nagao J. Comparison of duodenal stent placement with surgical gastrojejunostomy for palliation in patients with duodenal obstructions caused by pancreaticobiliary malignancies. *Endoscopy.* 2004;36:73-8.
17. Shand AG, Grieve DC, Brush J, Palmer KR, Penman ID. Expandable metallic stents for palliation of malignant pyloric and duodenal obstruction. *Br J Surg.* 2002;89:349-50.
18. Telford JJ, Carr-Locke DL, Baron TH, Tringali A, Parsons WG, Gabbrielli A, et al. Palliation of patients with malignant gastric outlet obstruction with the enteral Wallstent: outcomes from a multicenter study. *Gastrointest Endosc.* 2004;60:916-20.
19. Hyodo T, Yoshida Y, Yamanaka T, Imawari M. Duodenal stenosis after endoscopic biliary metallic stent placement for malignant biliary stenosis. *Gastrointest Endosc.* 2000;52:64-6.