

Which Is Crucial, Strengthen the Foundation or Building the Dream House?

Hiroyuki Isayama^{1,2}, Yousuke Nakai², and Toshio Fujisawa¹

¹Department of Gastroenterology, Graduate School of Medicine, Juntendo University, and ²Department of Gastroenterology, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan

See “Efficacy of a Multiplex Paclitaxel Emission Stent Using a Pluronic® Mixture Membrane versus a Covered Metal Stent in Malignant Biliary Obstruction: A Prospective Randomized Comparative Study” by Sung Ill Jang, et al. on page 567, Vol. 11, No. 4, 2017

I read the article by Jang *et al.*¹ with great interest. However, I was disappointed, because the efficacy of drug-eluting stents (DESs) was not clarified. The authors have studied DESs for quite some time, and I have followed their research on this topic since the beginning.² The DES is considered a very promising stent that additionally possesses an antitumor function, and highly favorable results are expected. However, in this study, most of the DESs became occluded before they could exert their antitumor function. Therefore, we should reconsider the efficacy of the current biliary stents used for malignant biliary obstruction (MBO) as well as their additional indications.

Endoscopic biliary stenting is a widely accepted palliative procedure for patients with unresectable MBO, and many endoscopists perform this procedure. MBO may cause cholestatic liver dysfunction, jaundice, pruritus, body weight loss, and other nonspecific symptoms. It is necessary to improve the quality of life and maintain the condition of patients. The patency of a biliary stent is an important factor in maintaining a patient's condition. The ideal biliary stent improves cholestasis without complications up until death. Self-expandable metallic stents (SEMSs) have shown better patency than plastic stents, but with SEMSs, occlusion due to tumor/tissue ingrowth through the stent's mesh can occur, preventing removal of the stent. Covered SEMSs were developed to prevent tumor/tissue ingrowth, to prolong patency and allow their removal. We performed the first randomized controlled trial comparing covered and uncovered SEMSs using an original covered SEMS made in-house, because no commercially available covered SEMS were available at the time.³ We successfully showed the superiority of the covered SEMS and, subsequently, that of the partially covered

Wallstent, the first commercially available SEMS developed by Boston Scientific Company in 2005. Currently, we use various types of covered SEMSs for drainage of resectable biliary malignancy, benign biliary stricture, transmural biliary drainage, the pancreatic duct, peri-pancreatic fluid correction, gastric-jejunal anastomosis, and other conditions.

For transpapillary biliary drainage, there was still no ideal covered SEMS. Prevention of recurrent biliary obstruction (RBO) as well as other complications should be considered. RBO has various causes, such as tumor/tissue in-/overgrowth, sludge formation, food impaction, stent migration, kinking of the bile duct at the covered SEMS edge, and other rare causes.⁴ Complications other than RBO related to SEMS placement, including pancreatitis, cholecystitis, perforation, and other rare conditions, are completely preventable. Therefore, further improvement of covered SEMSs is necessary to develop the ideal biliary stent.

The mechanical properties of SEMS such as the radial force (RF) and axial force may influence the results of clinical trials. RF is an expansion force related to maintaining luminal patency in the presence of tumor compression. We previously reported that a weak RF may cause a high rate of stent migration.⁵ After placement, the SEMS is surrounded by tumor tissue, causing both sides of the stent body to compress the bile duct wall and orifices of the cystic and pancreatic ducts, potentially causing various complications such as bile duct kinking, cholecystitis, and pancreatitis. We reported a relationship between the mechanical properties and complications of SEMSs.⁶

The smoothness of the inner surface of a covered SEMS may be related to stent occlusion due to sludge and food impaction. Naked wires are exposed on both the outer and inner surfaces

Correspondence to: Hiroyuki Isayama

Department of Gastroenterology, Graduate School of Medicine, Juntendo University, 3-1-3 Hongo, Bunkyo-ku, Tokyo 113-8655, Japan

Tel: +81-3-3813-3111 (PHS:70285), Fax: +81-3-3813-8862, E-mail: isayama-tky@umin.ac.jp

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of the covered SEMS used in the article written by Jang *et al.*,¹ and we previously reported a high incidence of food impaction and sludge formation with short-term use of such stents.⁷ Jang, *et al.* reported similar results of same type of covered SEMS to previous article.

On the other hand, the DES gives additional advantages to the SEMS, including prolongation of the time to RBO and survival in patients with MBO. SEMSs are effective for preventing tumor ingrowth for distal MBO; however, tumor overgrowth is one of the main causes of occlusion with covered SEMSs. DESs are expected to be more effective for the prevention of tumor in-/overgrowth. This and previous studies that have evaluated DESs were not able to reveal the efficacy of SEMSs in prolonging the time to RBO because of early occlusion due to food impaction. A long interval to RBO resulting from causes other than tumor extension can effectively demonstrate the efficacy of DESs.

The aim of the biliary DES is not only prolongation of the time to RBO but also prolongation of patient survival. If a DES is left in place long-term, the tumor volume may be reduced, possibly achieving good oncological outcomes. From this point of view, we should consider the types of anticancer agents used with DESs. Paclitaxel does not appear to be the best option for pancreatobiliary malignancies. Many drugs have been used in DESs for these cancers, including gemcitabine, nab-paclitaxel, fluorouracil, platinum-bases drugs (oxaliplatin, cisplatin), and irinotecan. Previous trials of DESs using carboplatin showed a reduction in tumor volume.⁸ A reduction in tumor volume may cause stent migration, thus necessitating an antimigration function of the stent for development of an ideal SEMS that prevents RBO. The SEMS provides many functions despite being a relatively simple device.

Regarding other indications for DES, placement of a DES as a bridge to surgery in patients with MBO is appropriate. For hilar MBO, a limited number of cases have shown an indication for a covered SEMS, and tumor reduction efforts using ablation therapy (radio frequency ablation, photodynamic therapy, and external and internal radiotherapies) have been made to prolong stent patency. In the case with hilar MBO, we could not use covered type SEMS and should develop the drug eluting uncovered SEMS. As for an indication for a DES for benign biliary stricture, a DES was a good option for preventing tissue

hyperplasia such as coronary artery occlusion.

In conclusion, the DES is promising in terms of prolongation of the time to RBO due to its anticancer effect. To develop the ideal stent, all causes of RBO should be eliminated after SEMS placement. Consideration of the type of drug, and other indications for DES, are the next issues to address. We are waiting for the next generation of DESs, employing high quality covered SEMS.

CONFLICTS OF INTEREST

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

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