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Fully Covered Metal Biliary Stents: Current and Future Uses

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Biliary stenting has evolved dramatically since endoscopic placement of the first stent in 1980. Endoscopic stenting has largely supplanted surgical bypass for palliation of malignant biliary obstruction. Plastic stents were traditionally used due their low cost and removability, with albeit limited duration of patency. The development of self-expanding metal stents (SEMS) represents a major advance in the treatment of obstructive biliary disease, providing an increased luminal diameter and patency. Metallic biliary stenting, however, has significant limitations including mucosal hyperplasia occurring within the stent leading to in-stent restenosis, and lack of removability. The recent introduction of fully covered self-expanding metal stents (FCSEMS) has helped overcome some of these limitations. Randomized clinical trials using FCSEMS have shown a reduction in stent ingrowth and an increased ability to remove stents as compared with uncovered metal stents. In this article, we summarize recent developments in the design and applications of FCSEMS, and compare findings of recent clinical studies.

INTRODUCTION

Endoscopic stent placement provides effective drainage in both malignant and benign biliary obstruction as well as in biliary fistulae.[1-3] Endoscopic placement of the first plastic endoprosthesis was described in 1980.[4,5] Endoscopic stenting was shown to be as effective as surgical drainage relieving obstructive jaundice with fewer complications.[6-8] In addition, stenting has resulted in shorter hospital stays, is accompanied by less morbidity and mortality, less cost and an improved quality of life.[9-12]

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Plastic Stents

Plastic stents are attractive because of their efficacy and low cost. These stents are made of Teflon, polyethylene or polyurethane and are easily exchanged. Plastic stents get occluded due to formation of a bacterial biofilm, leading to recurrent jaundice as well as cholangitis requiring repeat Endoscopic retrograde cholangio pancreatography (ERCP) and stent exchange.[13-15] 10F stents perform better than smaller 8F stents in malignant obstruction.[16]

Self-Expanding Metal Stents

Self-expanding metal stents (SEMS) have a larger luminal diameter than plastic stents and were designed to overcome limitations of occlusion and stent patency.

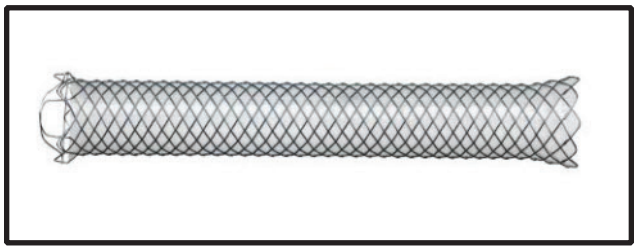

Figure 1. Wallflex fully covered metal stent *(Courtesy: Boston Scientific)*

SEMS have been described since the late 1980's and are of proven benefit in both malignant and benign biliary obstruction.[17-19] SEMS are composed of metal alloys such as stainless steel with nickel shape-retaining titanium (Nitinol), Cobalt, Chromium and Nickel super alloy (Co-Cr-Ni alloy or Elgiloy), and Platinum-cored Nitinol (Platinol).[20] These alloys enable adequate radial expansible force without compromising on flexibility. SEMSs range from 4 to 12 cm in length with diameters of 6 mm to 10 mm when fully expanded. SEMS are radiopaque, and some have markers at the ends made of a different metal such as gold and titanium.

SEMS are more expensive than plastic stents, but present a lower risk of recurring biliary obstruction than do single plastic stents. As they require fewer repeated interventions, placing a SEMS is often more cost effective in patients with malignant obstruction of the common bile duct as compared to placing a plastic stent. Earlier data suggested that this holds true only if the life expectancy is longer than 6 months.[13,21-24] However recent studies demonstrate that metallic stents are more effective than plastic stents, for most patients with obstruction from pancreatic cancer including those expected to survive less than 6 months.[25-27]

SEMS are deployed into the bile duct while constrained ("packed") by a sheath 8.5F or smaller, allowing insertion through the duodenoscope channel. Once correctly placed, the sheath is retracted, and the wire mesh stent expands to a diameter of up to10 mm (30 Fr) at full deployment.[13,14,21] The Viabil stent (Gore Medical, Flagstaff, AZ, USA), is constrained by a thin filament tightly wound around the stent. Once the filament is retracted, the stent expands. Some SEMS shorten after deployment, while others do not. Diamond stents (Boston Scientific, Natick, MA, USA), Wallstents (Boston Scientific), EndoChoice Bonastent (Atlanta, GA, USA), Taewoong Medical Niti–S (S type) and Taewoong Medical Niti–S (D type) (Seoul, Korea) and Merit Medical (South Jordan, Utah, USA)

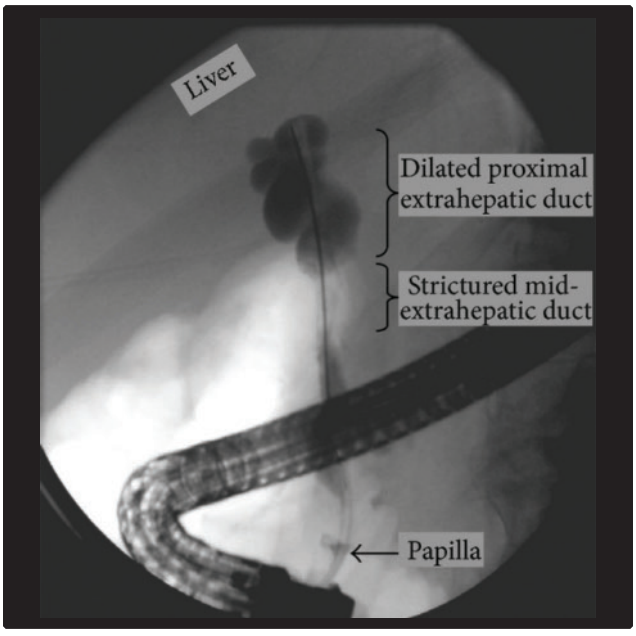

Figure 2a. Fluroscopic images of malignant biliary stricture and WallFlex Biliary Stent placement.[53] *(Courtesy: From Petersen et al. Gastroenterology Research and Practice)(CC)*

and Alimaxx-Borten (Merit Medical Endotek, USA) shorten their length by approximately a third after deployment. This shortening necessitates optimal guide wire placement and assessment of the stricture before deployment. Some stents do not shorten allowing more accurate positioning. (e.g., the Zilver stent (Wilson Cook) and the Olympus X-Suit Nur stent (Olympus America)

SEMS are often complicated by luminal occlusion. In contrast to plastic stents, SEMS occlude due to: (1) tissue ingrowth through the stent mesh; (2) tumor overgrowth around the proximal or distal end of the stent; (3) mucosal hyperplasia into the stent as a result of a chronic inflammatory reaction to the stent mesh; and, less commonly, (4) biliary sludge.[28-30, 31] These occlusions require further insertion of plastic stents within the SEMS or deployment of another SEMS within the initial one and sometimes mechanical cleaning.[32] Removing and exchanging such stents may be challenging and is often impossible.

Stent designs continue to evolve to overcome these limitations. Recently, fully covered self-expanding metal stents (FCSEMS) have been introduced with the goal of prolonging stent patency. We discuss current and future developments in FCSEMS in both malignant and benign strictures.

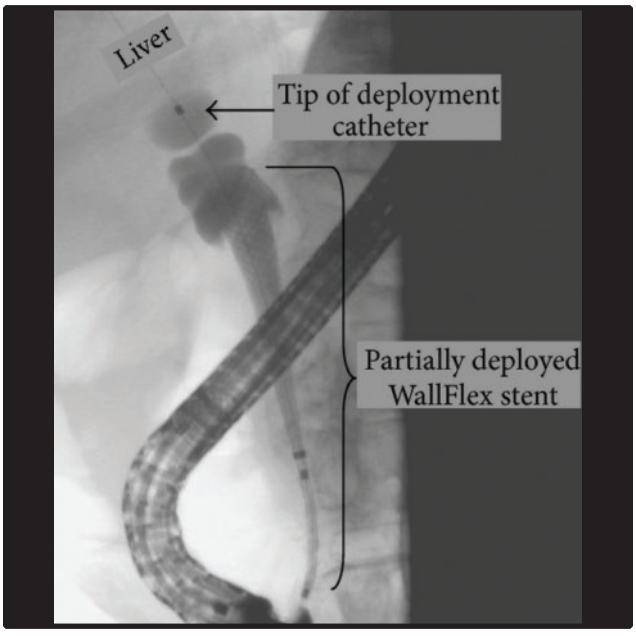

Figure 2b. Fluroscopic images of malignant biliary stricture and WallFlex Biliary Stent placement.[53] *(Courtesy: From Petersen et al. Gastroenterology Research and Practice)(CC)*

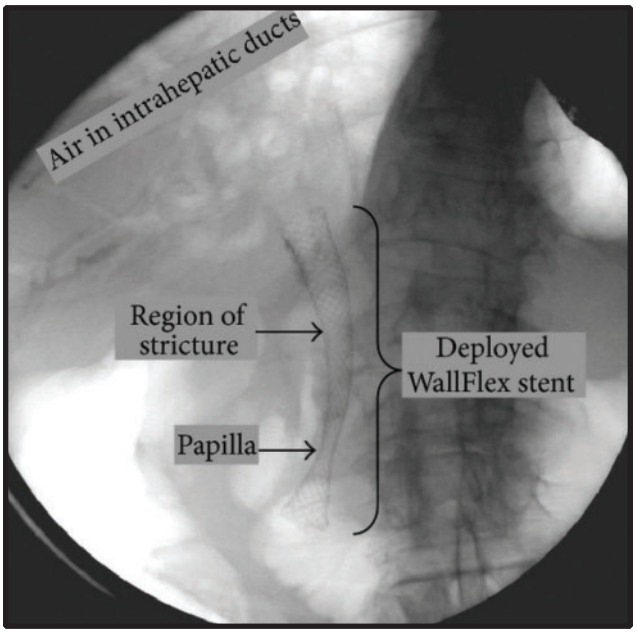

Figure 2c. Fluroscopic images of malignant biliary stricture and WallFlex Biliary Stent placement.[53] *(Courtesy: From Petersen et al. Gastroenterology Research and Practice)(CC)*

Benign Biliary Strictures

The most common etiologies of benign biliary strictures (BBS) are post-cholecystectomy, following bile duct exploration, chronic pancreatitis and anastomotic strictures that develop following orthoptioc liver transplantation (OLT).

Post-Operative BBS

The risk of bile duct injury is significantly greater with laparoscopic (0.5 to 2%) than with open (0.25%) cholecystectomy. The incidence of laparoscopic cholecystectomy-related bile duct injury has not decreased with time, suggesting a higher complication rate inherent to the procedure.[33] Traditionally these strictures have been treated surgically, but stricture resolution may be achieved endoscopially. Typically dilation, followed by the placement of one or more stents across the stricture with exchanges at 3- to 4-month intervals, for approximately 1 to 1 ½ years is conducted. It is postulated that once sufficient dilation is achieved, fibrotic tissue remodeling will prevent elastic recoil and recurrent stenosis. In a study of 74 patients with benign biliary strictures, who underwent therapy with endoscopic stenting (10F plastic stent), 80% of the patients had resolution with recurrent stricturing rates of only 20%, at a median follow up of 9.1 years. Most cases of recurrent stenosis occurred within 2 years of stent removal.[33] Studies have reported that placement of multiple stents (three or more plastic stents) with a dwell time of around 1 year can achieve even greater rates of stricture resolution with excellent long-term results. Technical feasibility may limit placement of multiple stents during the initial procedure especially when the stricture lumen is small.[34-36] The practice as far as endoscopic therapy in BBS, consists of placement of multiple plastic stents with frequent stent exchanges every 3 months, progressively increasing the number of stents placed at subsequent exchanges.[34,35] The clinical success rate in a meta-analysis of 1116 patients treated with multiple stents was 94%, a success rate much higher as compared to those patients treated with single plastic stents and SEMS.[36] Long-term resolution rates for chronic pancreatitis related strictures were low at 20% to 30%.[37] SEMS have longer patency compared to plastic stents. For the aforementioned reasons, (tissue hyperplasia, ingrowth into the mesh), uncovered SEMS are no longer used for benign strictures. To avoid tissue ingrowth and allow endoscopic removal, covered SEMS are often used instead.

FCSEMS are not approved by FDA for use in BBS but are frequently used in an off-label fashion for this indication. FCSEMS have small diameter delivery systems (8.5 Fr), which allow placement without dilation. (See Fig 1) After deployment, the stent expands

Table 1. Summary of Commonly Used Fully Covered Self-Expandable Metal Stents

Stent; Manufacturer	Material	Central Diameter, mm	Length, cm
Niti-S ComVi; Taewoong Medical	Nitinol	6, 8, 10	4, 5, 6, 7, 8, 9, 10, 12
Niti-S Kaffes; Taewoong Medical	Nitinol	6, 8, 10	4, 5, 6, 7, 8
Wallstent; Boston Scientific	Nitinol	8, 10	4, 6, 8, 10
Wallflex; Boston Scientific	Platinol	8, 10	4, 6, 8
Bonastent M-Intraductal; Standard Sci-Tech Inc.	Nitinol	10	6, 7, 8, 9
Hanaro; M.I. Tech	Nitinol	10	4, 6, 8, 10, 12
Micro-Tech; Micro-Tech	Nitinol	10	4, 6, 8
Gore-Viabil; CONMED	Nitinol	8, 10	4, 6, 8, 10
Allium BIS; Allium Medical	Nitinol	8, 10	6, 8, 10, 12

From Kaffes et al.[103] with permission.

to a larger diameter (8-10 mm) and can remain in place for an extended period of time before removal. In a multi-centric analysis FCSEMS have been shown to be removable after 6–355 days with few complications.[38] (See Table 1)

Chronic Pancreatitis

In a prospective study of 44 patients with BBS were stented using a 10-mm diameter FCSEMS, (Viabil; Conmed, Utica, NY, USA) for a median time of 3.3 months. These stents were left in place until adequate biliary drainage was achieved. Stricture resolution was confirmed in 83% patients after a median (post stent removal) follow-up time of 3.8 months. The stents were removed in 41 patients (93%); complications were noted in 6 (14%) patients after stent placement and in 4 patients (9%) after stent removal. The majority of the patients in this study had strictures secondary to chronic pancreatitis (CP) (19/44). Successful stricture resolution was seen in only 58% of CP patients whereas all other etiologies of stricture had higher resolution rates (92%) (Intent-to-treat) (ITT). There was also one proximal and one distal stent migration seen. The complications during stent placement were comparable to those of standard therapeutic ERCP. The results of this study were encouraging for use of FCSEMS at least in the short term. The study also affirmed the lower success rates found with chronic pancreatitis related BBS.[39] Poley et al., in a study of 23 patients, demonstrated similar results: again, the treatment success rate with FCSEMS for BBS in chronic pancreatitis was higher than with plastic stents.[40] In yet another study with similar patients (n=23), placing WallFlex FCSEMS in chronic pancreatitis related common bile duct strictures reported short-term resolution rates of 100% after 6 months of stent removal and 67% at 12 months post stent removal. These success rates are much better than those reported with plastic stents.[41]

Benign Hilar Strictures

Treating benign hilar strictures with fully covered stents has traditionally been contraindicated because of concern that the stents may obstruct the intrahepatic bile ducts, particularly the contralateral hepatic duct. Poley et al. used FCSEMS in combination with a contralateral plastic stent in treating benign hilar strictures in 2 patients without ensuing cholangitis caused by bile duct occlusion.[42]

Anastomotic BBS in OLT

One of the most common complications following

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Table 2. Use of Fully Covered Self-Expandable Metal Stents in Benign Biliary Strictures

Study	Method	Stent Type	Patients	Indication	Clinical Success, %*	Adverse Events, %†	Migrations, %	Recurrence, %	Follow Up, Mo
Tarantino et al.[11]	Prospective, multicenter	Niti-S ComVi	62	Mixed 38 OLT	90.3	1.6	24.2	7.1 (all OLT)	16
Sauer et al.[21]	Prospective, single center	Wallflex	19	OLT	78.9	15.8	31.6	5.2	12
Moon et al.[26]	Prospective, single center	Bonastent M-Intraductal	21	Mixed 3 OLT	95.2	0	19	4.8	13.8
Poley et al.[13]	Prospective, single center	Hanaro	23	Mixed 6 OLT	60.8 46% CP 80% non-CP	87.0	4.3	Unknown	15
Haapamakl et al.[23]	Retrorospective, single center	Allium BIS Wallstent	17	OLT	100	35.3	23.5	11.8	21.7
Park et al.[27]	Prospective, multicenter	AF: M.I. Tech FE: Standard Sci-Tech Inc.	43	Mixed 2 OLT	84	27.9 31.8 AF 23.8 FE	16.3 0 AF 33.3 FE	16.3 13.6 AF 19 FE	4
Hu et al.[24]	Prospective, single center	Micro-Tech	13	OLT	92.3	7.7	0	8.3	12.1
Park et al.[42]	Prospective, single center	Anchor Biliary Stent Nonanchor	33 16 Anchor, 17 Nonanchor	Mixed No OLT	93.8 anchor, 70.5 nonanchor	3.0	6.3 anchor, 41.2 nonanchor	3.0	14 anchor, 15 nonanchor
Garcia-Pajares et al.[20]	Retrorospective, single center	Not Stated	22	OLT	95.5	40.9	22.7	4.5	12.5
Tralna et al.[22]	Prospective, single center	Niti-S ComVi	16	OLT	87.5	6.3	37.5	7.1	6
Mahajan et al.[12]	Prospective, single center	Gore-Viabil	44	Mixed 9 OLT	82.9	27.3	4.5	Unknown	3.8
Cahen et al.[10]	Prospective, single center	Hanaro	6	CP	66.7	33.3	33.3	25.0	36

OLT, Orthotopic liver transplantation; *CP,* chronic pancreatitis; *AF,* anchoring fin; *FE* flared end.
*Clinical success at removal of stent.
†Adverse events other than stent migration.

From Kaffes et al.[103] with permission.

Table 3. FCSEMS Used in Bleeding After ERCP

Age/Sex	Previous Biliary Sphincterotomy	Bleeding Secondary to Sphincterotomy	Bleeding Onset	Stent L/D (cm)	Hemostasis Achieved and Other Benefit	Stent Extraction
71/M	No	Yes	Immediate	8x1	Yes; stenosis treated	No
68/M	No	Yes	Immediate	4x1	Yes; stenosis treated	Yes (2 mo) During Surgery
57/M	No	No; trauma to anostomotic biliary stricture	Immediate	8x1	Yes; stenosis treated	Yes (1 mo)
57/M	No	No CBD trauma	Immediate	6x1	Yes; stenosis treated	No (6 mo) Spontaneous Migration
85/F	No	unknown	Delayed (Day 10 post-ERCP)	4x1	Yes; No	No
66/M	No	Yes	Immediate	6x1	Yes; biliary leak treated	Yes (11 mo)

CBD, Common Bile Duct; *L/D,* Length/Diameter.

From Valats et al.[80] with permission.

liver transplantation is biliary stricture. The incidence of these strictures range from 5% to 15% following deceased-donor transplantations and from 28% to 32% following living-donor transplantations.[43] The strictures may be non-anastomotic (presenting earlier) or anastomotic. Non-anastomotic strictures have less favorable outcomes.[44]

An Italian study followed 54 consecutive patients with biliary complications after orthotopic liver transplantation who were treated with FCSEMS placement and concluded that complication rates were considerable. Stent migration occurred in 33% of the patients, and the authors did not recommend FCSEMS as a first modality of treatment. In a subgroup of 39 patients who failed conventional endoscopic therapy, 72% resolution was seen after stent removal.[45] In another series of 11 patients with complications after liver transplantation, placement of CSEMS was successful in avoiding hepaticojejunostomies.[46] Although all the available data show stent migration as the main complication in OLT, resolution rates were impressive. Newer stents fitted with anti-migration anchoring flaps may mitigate this problem.[47]

A major limitation of FCSEMS is frequent stent migration (5-33%) In order to reduce the risk of migration, anti-migration features such as anchoring flaps and flared ends were introduced. These modified stents have been studied by Park et al., Moon et al. and several others.[48]

In a recent prospective study of 17 patients with FCSEMS (Niti-S; Taewoong Medical) for BBS secondary to chronic pancreatitis, the initial patients had stents with unflared ends and had migrations rates of 100%. The remainder of the patients received stents with flared ends resulting in decreased distal migration rates of 40%. The stricture resolution rate for patients using flared ends (10 patients) at the time of stent removal was 90% and 80 % after 12 months of follow up.[49]

Park et al. compared stents with different anti-migration designs (the anchoring flap (AF) vs. flared end (FE) at the proximal end of the stent in 43 patients) in benign biliary strictures. Patients were assigned to the AF (n = 22) or the FE group (n = 21). After a median period of 6 months no patients in AF group

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and 7 of 21 in FE group (33%) had stent migration, concluding that AF design is superior to FE. The stents were successfully removed in all the patients (100%).[47] (See Table 2)

In another small prospective study with the 8mm fully covered SEMS WallFlex Biliary RX Stents (Boston Scientific Corporation, Natick, MA, USA) for BBS (n=20), the stent was successfully removed without complication following a mean dwell time of over four months.[50]

In a systematic review of plastic stents in BBS, the overall clinical success rate was highest with placement of multiple plastic stents (94.3%), followed by uncovered SEMS (79.5%) and lowest with single plastic stents (59.6%). Comparative data between multiple plastic stents and FCSEMS are still lacking.[51] In addition, further long-term studies are needed to follow up on the durability of the FCSEMS in BBS. Considering the complication rates with stent migration and pancreatitis, FCSEMS should be used in selected groups of patients and the balance between their benefits and risks should be carefully considered before using in BBS as a routine practice.

Malignant Biliary Strictures

Pancreatic cancer is the most common cause of malignant biliary obstruction. In the past, plastic stents were commonly used for palliation. Currently SEMS are preferred due to their increased patency rates.[52]

Extra-Hepatic Non-Hilar Malignant Strictures

Fully covered biliary SEMS (WallFlex Biliary RX Boston Scientific, Natick, MA, USA) were studied in 58 patients with malignant non-hilar extra-hepatic bile duct obstruction. (See Fig 2) Technical success was achieved in 98% with uncomplicated acute removal when required. In addition there were low rates of stent migration and occlusion.[53] In a randomized, controlled trial of 112 patients with unresectable non-hilar biliary malignancies, covered and uncovered metal stents and FCSEMS were found to have longer patency (304 days) compared to uncovered stents (161 days).[54]

Kahaleh et al. studied 101 patients with obstructive jaundice secondary to pancreatic cancer with life expectancy of longer than 6 months, placing FCSEMS or plastic stents regardless of resectability. In 85 patients who did not undergo resection, the median patency of FCSEMS was 5.5 months. Moreover, placing FCSEMS

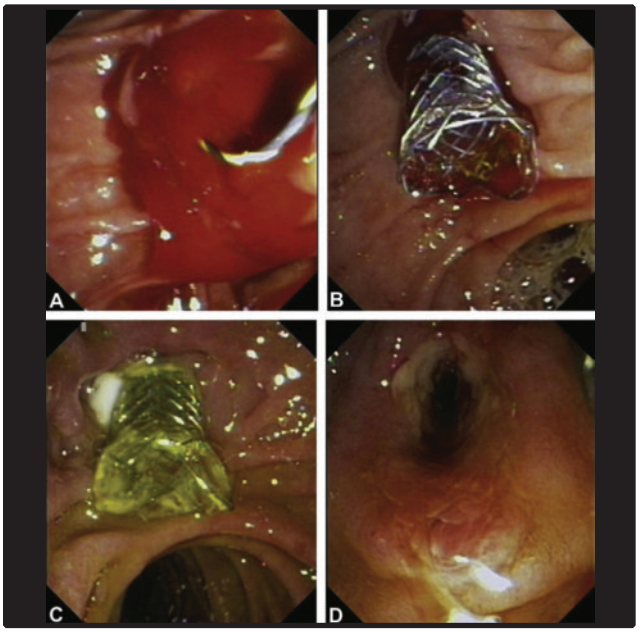

Figure 3. Covered self-expandable biliary stents for the treatment of bleeding after ERCP [80] *(From Valats et. al [80] with permission)*

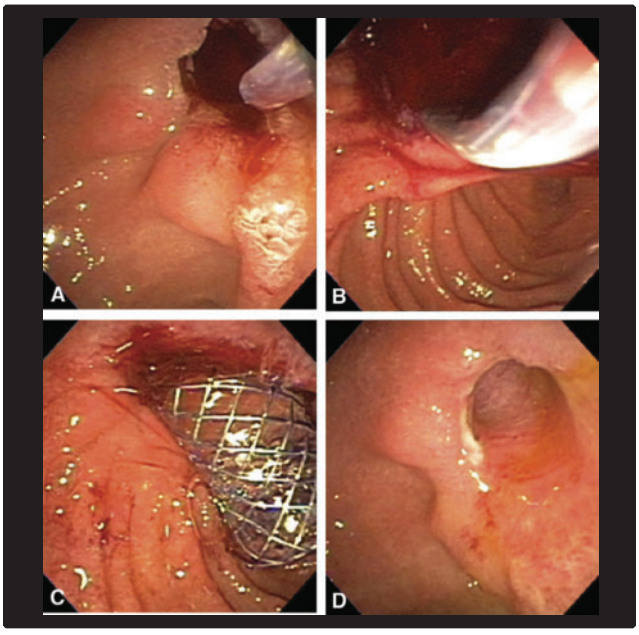

Figure 4. A. Endoscopic image during ERCP reveals active bleeding after biliary sphincterotomy for papillary stenosis. **B.** Fully covered SEMS constrained in delivery sheath is placed across the ampullary orifice. **C.** Deployment of SEMSs results in mechanical tamponade and hemostasis. **D.** Widely patent biliary orifice without stigmata of hemorrhage is seen after SEMS removal at 2 weeks.[76] *(From Shah el al.[76] with permission)*

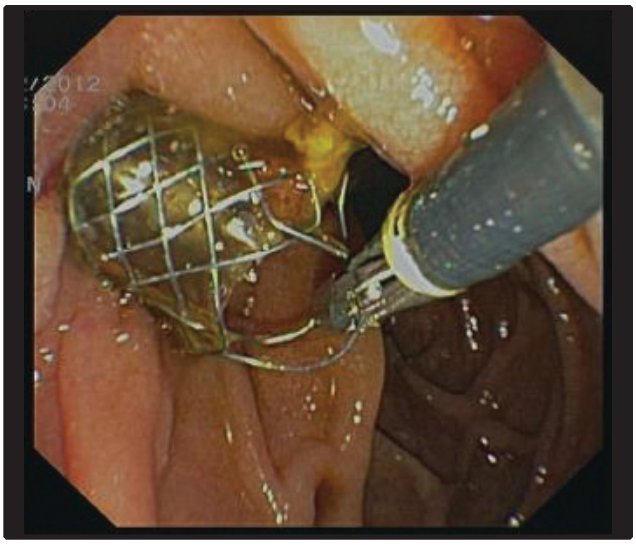

Figure 5. Stent removal with forceps.[104] *(Courtesy : From Abdel Sami A et al. Gastroenterology Research) (CC)*

seemed to be more cost effective compared to other options.[55] This study is similar to another prospective study in 2011, involving 88 pancreatic cancer patients, which concluded that CSEMS can be safely used to relieve malignant biliary obstruction even when the resectability is uncertain.[56] A recent prospective study of 120 patients with distal biliary obstruction with unresectable pancreatic cancer, showed patient survival time without stent dysfunction was significantly longer when covered metal stents with anti-migration system were used.[57] These studies suggest that FCSEMS may be a viable and cost effective option for malignant biliary strictures because of increased patency, lesser tumor in-growth and easy removability.[58] A meta-analysis by Saleem et al. from Mayo Clinic, however, reported similar rates of stent dysfunction with both covered and un-covered biliary stents.[59]

A recent large retrospective study from MD Anderson showed no significant difference in the patency rate or overall survival between FCSEMS and uncovered SEMS in patients with malignant distal bile duct obstruction. In this study involving 749 patients, the FCSEMS group had significantly higher rates of migration and pancreatitis, than did the uncovered SEMS group, making the use of FCSEMS questionable in this situation.[60] A recent meta-analysis by Almadi et al. from Canada, reported no difference in patency and complication rate between FCSEMS and uncovered SEMS in 1061 patients and concluded that FCSEMS has unclear benefit over the uncovered stents.[61]

Malignant Hilar Strictures

Stent placement in malignant hilar stricture is challenging. Covered stent is not usually used in patients with hilar malignancy due to unintentional obstruction of contralateral ducts or side branch ducts. There is still a lack of clear consensus on unilateral versus bilateral drainage for hilar malignant obstruction, although bilateral approach is used in most centers.[62, 63] Biliary stenting with newly designed Y-shaped devices is possible and seems promising, but these devices are not in widespread use.[64, 65]

Non-Stricture Indications for FCSEMS

Biliary Leaks

Bile leaks may occur following cholecystectomy, traumatic injury, OLT, or liver resection.[66 67,68] The most common sites of biliary leaks are at the cystic duct stump or the duct of Luschka.[68] The standard of care in management of bile leaks is transpapillary biliary plastic stent placement, with or without sphincterotomy, with success rates of 70% to 100%.[69,70] Bile leaks may be complex and may be refractory to these usual endoscopic interventions (as with bile leaks following orthotopic liver transplantation or large leaks following complicated cholecystectomy). They can be classified into low grade (leak identified only after intrahepatic opacification) and high grade (leak observed before intrahepatic opacification).[70] FCSEMS placement helps to reduce intra-ductal pressure and to divert bile flow from the leaking site. FCSEMS are not approved for this indication but have been used successfully in an off-label fashion.

In a recent study, Viabil FCSEMS (Conmed, Utica, NY, USA) were placed in 17 patients with bile leaks occurred following cholecystectomy and were located at the cystic duct. After a median stent time of 92 ± 81 days (range 48-251 d), the biliary strictures and bile leaks resolved in 16 of 17 patients (94%). Minimal complications were noted in 5 of the 17 patients (29%).[71]

In a prospective study of 16 patients, FCSEMS were shown to be effective for postoperative biliary strictures and biliary leaks not responding to plastic stents, with a success rate of 94% after a median follow-up of 13 months.[72] Canena et al. demonstrated that in 17 post cholecystectomy patients with refractory bile leaks, temporary placement of FCSEMS (for less than a month) was an effective rescue therapy. [73] In a retrospective analysis including 13 patients with complex biliary

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leaks, temporarily placing FCSEMS with anchoring fins successfully resolved the leaks in all the patients. However, this treatment was associated with bile duct ulcerations and de novo choledocholithiasis. [74]

Post-Sphincterotomy Bleeding

Post-sphincterotomy bleeding is a well recognized complication of biliary sphincterotomy.[75] Temporary placement of FCSEMS may be an effective therapy for difficult-to-control post-endoscopic sphincterotomy bleeding. This was demonstrated in a study of 25 patients that included 4 patients with post-sphincterotomy bleeding. (See Fig 3) The median indwelling time for FCSEMS was 6 days (range 3-15 days).[73] The covered stent was able to tamponade the duct and site and prevent further bleeding. Several small studies have supported the use of FCSEMS for post-sphincterotomy bleeding, but stent migration seems to limit the effectiveness of this intervention.[76-79] (See Table 3) On the other hand, this technique is easy and may be effective for both bleeding originating from the papilla and for bleeding proximally from the common bile duct.[80] (See Fig 4)

Perforations

Perforation may represent a serious complication of ERCP and can be classified into three types:[81]

- Type I: Free duodenal wall perforation
- Type II: Retroperitoneal duodenal perforation or periampullary perforation
- Type III: Perforation of the pancreatic or bile duct from guidewire insertion

Type I perforations can be large and may require surgical treatment if endoscopic closure cannot be achieved. Periampullary perforations (Type II) that are diagnosed early often respond to endoscopic drainage and medical treatment.[81-82] Guidewire (Type III) perforations generally resolve with medical therapy. FCSEMS have been used as an endoscopic therapeutic option to seal the perforation site and permit free bile flow into the duodenum.[83-85]

FCSEMS – Removal

FCSEMS are as easy and safe to remove as are plastic stents. (See Fig 5). In a multicenter study of 37 patients, removal of stents was successful in all the patients.[38] In a prospective trial of 187 patients, Costamagna et al. demonstrated easy removal after a dwelling time of 1 year, [86] and other smaller studies also confirm easy removability. [87]

Complications with FCSEMS

Stent migration is a frequent complication. Recently stents were developed with anti-migration designs (anchoring flaps) to decrease migration.[47] Pancreatitis, Cholecystitis, Stent occlusion and cholangitis are other reported complications. [58]

Cholecystitis has been reported following placement of FCSEMS in patients with gallbladder in-situ, and some have hypothesized the stent can block the opening of the cystic duct.[88] A number of experts believe that this complication could be avoided by using a stent of the correct length and placing the upper end of the stent distal to cystic duct insertion. In a study of 73 patients, gallbladder stent placement with a 7F transpapillary pigtail stent was shown to be effective in preventing cholecystitis if the cystic duct ostium was occluded. [3] It is still unsettled as to whether cholecystitis is from the stent occluding the cystic duct orifice[54] or the tumor growth into the cystic duct orifice.[89-91] In a recent prospective randomized study involving 120 patients with distal biliary obstruction from unresectable pancreatic carcinoma, acute cholecystitis occurred in one patient in the covered FCSEMS group and in two patients in the uncovered SEMS group.[57] Moreover, the prevalence of intact gallbladders among treated patients was not systematically documented; hence the rate of acute cholecystitis among those with intact gallbladders is unknown.[53] Overall, the literature at this time is inconclusive as to whether or not FCSEMS really do increase the risk of cholecystitis and an intact gallbladder cannot be considered a contraindication to FCSEMS use.

NEWER DEVELOPMENTS

Anti-Reflex Stents

Placing a stent across the ampulla of Vater compromises the normal "gatekeeper" valve function of the sphincter of Oddi, which normally allows outflow of bile into the duodenum and prevents ascending duodenal biliary reflux. The presence of pneumobilia after biliary stent placement suggests occurrence of duodenal biliary reflux. Studies using confocal laser-scanning microscopy were done 3 months after placing stents to demonstrate the mechanisms of clogging. Investigators

found large amounts of dietary fibers that were acting like a filter intraluminally.[92] Antireflux stents have now been developed that prevent duodenal biliary reflux and thereby improve biliary drainage, prolong stent patency and also, possibly, reduce chances of cholangitis.[93,94]

Drug-Eluting FCSEMS

FCSEMS are commonly used in unresectable malignant biliary obstruction. The metal stents, even if covered, are susceptible to occlusion by tumor overgrowth and ingrowth. Paclitaxel-eluting covered metal stents (PECMS) were recently introduced to overcome this,[95] but there are conflicting data on their efficacy in preventing occlusion. A prospective study of 52 patients with unresectable distal malignant biliary obstruction found no significant differences in the duration of stent patency or survival time in patients who were given paclitaxel stents and those who got FCSEMS.[96] In porcine models, newer Paclitaxel-eluting stents using membrane containing Pluronic have been shown to be safe, with reported enhanced local drug delivery in the bile ducts.[97] Mucosal hyperplasia after stent placement is partly responsible for stent occlusion; inflammation and fibrous reaction are thought to be contributing factors for mucosal hyperplasia.[98,99] Preliminary animal studies have shown indirectly that Gemcitabine-coated stents are effective in decreasing mucosal hyperplasia by minimizing inflammatory histologic changes in unresectable pancreatic cancer.[100]

Similarly, a pre-clinical study with a Sorafenib-coated metal stent used in human cholangiocellular carcinoma (HuCC)-T1 cells in vitro and a mouse tumor xenograft model in vivo shown to be effective in inhibiting angiogenesis as well as proliferation and invasion of cancer cells, suggesting these drug coated stents as promising candidates in future for local treatment of cholangiocarcinoma.[101]

CONCLUSION

The use of FCSEMS in benign biliary diseases is expanding. Recent data support their consideration in malignant and benign biliary strictures as well as refractory bile leaks, recalcitrant post-sphincterotomy bleeding, and periampullary perforations. Despite higher costs, FCSEMS may be more effective than uncovered stents and plastic stents and reduce the need for additional procedures.[102] Further prospective trials are needed to evaluate the long-term effectiveness, particularly when compared to multiple plastic stents. ■

References

1. Costamagna G, Shah SK, Tringali A. Current management of postoperative complications and benign biliary strictures. Gastrointestinal endoscopy clinics of North America 2003;13:635-48, ix.
2. Levy MJ, Baron TH, Gostout CJ, Petersen BT, Farnell MB. Palliation of malignant extrahepatic biliary obstruction with plastic versus expandable metal stents: An evidence-based approach. Clinical gastroenterology and hepatology : the official clinical practice journal of the American Gastroenterological Association 2004;2:273-85.
3. Gosain S, Bonatti H, Smith L, et al. Gallbladder stent placement for prevention of cholecystitis in patients receiving covered metal stent for malignant obstructive jaundice: a feasibility study. Digestive diseases and sciences 2010;55:2406-11.
4. Soehendra N, Reynders-Frederix V. Palliative bile duct drainage - a new endoscopic method of introducing a transpapillary drain. Endoscopy 1980;12:8-11.
5. Laurence BH, Cotton PB. Decompression of malignant biliary obstruction by duodenoscopic intubation of bile duct. British medical journal 1980;280:522-3.
6. Speer AG, Cotton PB, Russell RC, et al. Randomised trial of endoscopic versus percutaneous stent insertion in malignant obstructive jaundice. Lancet 1987;2:57-62.
7. Andersen JR, Sorensen SM, Kruse A, Rokkjaer M, Matzen P. Randomised trial of endoscopic endoprosthesis versus operative bypass in malignant obstructive jaundice. Gut 1989;30:1132-5.
8. Mitty R, Cave DR. Randomized trial of endoscopic stenting versus surgical bypass in malignant low bile duct obstruction. Gastrointestinal endoscopy 1995;42:281-2.
9. Brandabur JJ, Kozarek RA, Ball TJ, et al. Nonoperative versus operative treatment of obstructive jaundice in pancreatic cancer: cost and survival analysis. The American journal of gastroenterology 1988;83:1132-9.
10. Raikar GV, Melin MM, Ress A, et al. Cost-effective analysis of surgical palliation versus endoscopic stenting in the management of unresectable pancreatic cancer. Annals of surgical oncology 1996;3:470-5.
11. Abraham NS, Barkun JS, Barkun AN. Palliation of malignant biliary obstruction: a prospective trial examining impact on quality of life. Gastrointestinal endoscopy 2002;56:835-41.
12. Luman W, Cull A, Palmer KR. Quality of life in patients stented for malignant biliary obstructions. European journal of gastroenterology & hepatology 1997;9:481-4.
13. Kaassis M, Boyer J, Dumas R, et al. Plastic or metal stents for malignant stricture of the common bile duct? Results of a randomized prospective study. Gastrointestinal endoscopy 2003;57:178-82.
14. Schmassmann A, von Gunten E, Knuchel J, Scheurer U, Fehr HF, Halter F. Wallstents versus plastic stents in malignant biliary obstruction: effects of stent patency of the first and second stent on patient compliance and survival. The American journal of gastroenterology 1996;91:654-9.
15. Ghosh S, Palmer KR. Prevention of biliary stent occlusion using cyclical antibiotics and ursodeoxycholic acid. Gut 1994;35:1757-9.
16. Speer AG, Cotton PB, MacRae KD. Endoscopic management of malignant biliary obstruction: stents of 10 French gauge are preferable to stents of 8 French gauge. Gastrointestinal endoscopy 1988;34:412-7.
17. Huibregtse K, Cheng J, Coene PP, Fockens P, Tytgat GN. Endoscopic placement of expandable metal stents for biliary strictures--a preliminary report on experience with 33 patients. Endoscopy 1989;21:280-2.
18. Neuhaus H, Hagenmuller F, Classen M. Self-expanding biliary stents: preliminary clinical experience. Endoscopy 1989;21:225-8.
19. Irving JD, Adam A, Dick R, Dondelinger RF, Lunderquist A, Roche A. Gianturco expandable metallic biliary stents: results of a European clinical trial. Radiology 1989;172:321-6.
20. Chun HJ, Kim ES, Hyun JJ, Kwon YD, Keum B, Kim CD. Gastrointestinal and biliary stents. Journal of gastroenterology and hepatology 2010;25:234-43.
21. Davids PH, Groen AK, Rauws EA, Tytgat GN, Huibregtse K. Randomised trial of self-expanding metal stents versus polyethylene stents for distal malignant biliary obstruction. Lancet 1992;340:1488-92.
22. 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;25:207-12.

23. Prat F, Chapat O, Ducot B, et al. A randomized trial of endoscopic drainage methods for inoperable malignant strictures of the common bile duct. Gastrointestinal endoscopy 1998;47:1-7.
24. Wagner HJ, Knyrim K, Vakil N, Klose KJ. Plastic endoprostheses versus metal stents in the palliative treatment of malignant hilar biliary obstruction. A prospective and randomized trial. Endoscopy 1993;25:213-8.
25. Aadam AA, Evans DB, Khan A, Oh Y, Dua K. Efficacy and safety of self-expandable metal stents for biliary decompression in patients receiving neoadjuvant therapy for pancreatic cancer: a prospective study. Gastrointestinal endoscopy 2012;76:67-75.
26. Adams MA, Anderson MA, Myles JD, Khalatbari S, Scheiman JM. Self-expanding metal stents (SEMS) provide superior outcomes compared to plastic stents for pancreatic cancer patients undergoing neoadjuvant therapy. Journal of gastrointestinal oncology 2012;3:309-13.
27. Boulay BR. Biliary stents for pancreas cancer with obstruction: the problem with plastic. Journal of gastrointestinal oncology 2012;3:306-8.
28. Lee MJ, Dawson SL, Mueller PR, Krebs TL, Saini S, Hahn PF. Palliation of malignant bile duct obstruction with metallic biliary endoprostheses: technique, results, and complications. Journal of vascular and interventional radiology : JVIR 1992;3:665-71.
29. Hausegger KA, Kleinert R, Lammer J, Klein GE, Fluckiger F. Malignant biliary obstruction: histologic findings after treatment with self-expandable stents. Radiology 1992;185:461-4.
30. Silvis SE, Sievert CE, Jr., Vennes JA, Abeyta BK, Brennecke LH. Comparison of covered versus uncovered wire mesh stents in the canine biliary tract. Gastrointestinal endoscopy 1994;40:17-21.
31. Levy MJ, Baron TH, Gostout CJ, Petersen BT, Farnell MB. Palliation of malignant extrahepatic biliary obstruction with plastic versus expandable metal stents: an evidence-based approach. Clinical Gastroenterology and Hepatology 2004;2:273-85.
32. Tham TC, Carr-Locke DL, Vandervoort J, et al. Management of occluded biliary Wallstents. Gut 1998;42:703-7.
33. Bergman JJ, Burgemeister L, Bruno MJ, et al. Long-term follow-up after biliary stent placement for postoperative bile duct stenosis. Gastrointestinal endoscopy 2001;54:154-61.
34. Lawrence C, Romagnuolo J, Payne KM, Hawes RH, Cotton PB. Low symptomatic premature stent occlusion of multiple plastic stents for benign biliary strictures: comparing standard and prolonged stent change intervals. Gastrointestinal endoscopy 2010;72:558-63.
35. Costamagna G, Tringali A, Mutignani M, et al. Endotherapy of postoperative biliary strictures with multiple stents: results after more than 10 years of follow-up. Gastrointestinal endoscopy 2010;72:551-7.
36. van Boeckel PG, Vleggaar FP, Siersema PD. Plastic or metal stents for benign extrahepatic biliary strictures: a systematic review. BMC gastroenterology 2009;9:96.
37. Farnbacher MJ, Rabenstein T, Ell C, Hahn EG, Schneider HT. Is endoscopic drainage of common bile duct stenoses in chronic pancreatitis up-to-date? The American journal of gastroenterology 2000;95:1466-71.
38. Kasher JA, Corasanti JG, Tarnasky PR, McHenry L, Fogel E, Cunningham J. A multicenter analysis of safety and outcome of removal of a fully covered self-expandable metal stent during ERCP. Gastrointestinal endoscopy 2011;73:1292-7.
39. Mahajan A, Ho H, Sauer B, et al. Temporary placement of fully covered self-expandable metal stents in benign biliary strictures: midterm evaluation (with video). Gastrointestinal endoscopy 2009;70:303-9.
40. Poley JW, Cahen DL, Metselaar HJ, et al. A prospective group sequential study evaluating a new type of fully covered self-expandable metal stent for the treatment of benign biliary strictures (with video). Gastrointestinal endoscopy 2012;75:783-9.
41. Wagh MS, Chavalitdhamrong D, Moezardalan K, et al. Effectiveness and safety of endoscopic treatment of benign biliary strictures using a new fully covered self expandable metal stent. Diagnostic and therapeutic endoscopy 2013;2013:183513.
42. Poley JW, van Tilburg AJ, Kuipers EJ, Bruno MJ. Breaking the barrier: using extractable fully covered metal stents to treat benign biliary hilar strictures. Gastrointestinal endoscopy 2011;74:916-20.
43. Ryu CH, Lee SK. Biliary strictures after liver transplantation. Gut and liver 2011;5:133-42.
44. Verdonk RC, Buis CI, Porte RJ, Haagsma EB. Biliary complications after liver transplantation: a review. Scandinavian journal of gastroenterology Supplement 2006:89-101.
45. Tarantino I, Traina M, Mocciaro F, et al. Fully covered metallic stents in biliary stenosis after orthotopic liver transplantation. Endoscopy 2012;44:246-50.
46. Marin-Gomez LM, Sobrino-Rodriguez S, Alamo-Martinez JM, et al. Use of fully covered self-expandable stent in biliary complications after liver transplantation: a case series. Transplantation proceedings 2010;42:2975-7.
47. Park do H, Lee SS, Lee TH, et al. Anchoring flap versus flared end, fully covered self-expandable metal stents to prevent migration in patients with benign biliary strictures: a multicenter, prospective, comparative pilot study (with videos). Gastrointestinal endoscopy 2011;73:64-70.
48. Moon SH, Kim MH, Park do H, et al. Modified fully covered self-expandable metal stents with antimigration features for benign pancreatic-duct strictures in advanced chronic pancreatitis, with a focus on the safety profile and reducing migration. Gastrointestinal endoscopy 2010;72:86-91.
49. Perri V, Boskoski I, Tringali A, et al. Fully covered self-expandable metal stents in biliary strictures caused by chronic pancreatitis not responding to plastic stenting: a prospective study with 2 years of follow-up. Gastrointestinal endoscopy 2012;75:1271-7.
50. Garcia-Cano J, Taberna-Arana L, Jimeno-Ayllon C, et al. Use of fully covered self-expanding metal stents for the management of benign biliary conditions. Revista espanola de enfermedades digestivas : organo oficial de la Sociedad Espanola de Patologia Digestiva 2010;102:526-32.
51. Gupta R, Reddy DN. Stent selection for both biliary and pancreatic strictures caused by chronic pancreatitis: multiple plastic stents or metallic stents? Journal of hepato-biliary-pancreatic sciences 2011;18:636-9.
52. Jaganmohan S, Lee JH. Self-expandable metal stents in malignant biliary obstruction. Expert review of gastroenterology & hepatology 2012;6:105-14.
53. Petersen BT, Kahaleh M, Kozarek RA, et al. A multicenter, prospective study of a new fully covered expandable metal biliary stent for the palliative treatment of malignant bile duct obstruction. Gastroenterology research and practice 2013;2013:642428.
54. 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;53:729-34.
55. Kahaleh M, Brock A, Conaway MR, et al. Covered self-expandable metal stents in pancreatic malignancy regardless of resectability: a new concept validated by a decision analysis. Endoscopy 2007;39:319-24.
56. Siddiqui AA, Mehendiratta V, Loren D, Hong SK, Kowalski T. Fully covered self-expandable metal stents are effective and safe to treat distal malignant biliary strictures, irrespective of surgical resectability status. Journal of clinical gastroenterology 2011;45:824-7.
57. 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. The American journal of gastroenterology 2013.
58. 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. Journal of clinical gastroenterology 2013.
59. Saleem A, Leggett CL, Murad MH, Baron TH. Meta-analysis of randomized trials comparing the patency of covered and uncovered self-expandable metal stents for palliation of distal malignant bile duct obstruction. Gastrointestinal endoscopy 2011;74:321-7.e1-3.
60. Lee JH, Krishna SG, Singh A, et al. Comparison of the utility of covered metal stents versus uncovered metal stents in the management of malignant biliary strictures in 749 patients. Gastrointestinal endoscopy 2013;78:312-24.
61. Almadi MA, Barkun AN, Martel M. No benefit of covered vs uncovered self-expandable metal stents in patients with malignant distal biliary obstruction: a meta-analysis. Clinical gastroenterology and hepatology : the official clinical practice journal of the American Gastroenterological Association 2013;11:27-37.e1.
62. Kogure H, Isayama H, Kawakubo K, et al. Endoscopic bilateral metallic stenting for malignant hilar obstruction using newly designed stents. Journal of hepato-biliary-pancreatic sciences 2011;18:653-7.

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63. Chahal P, Baron TH. Expandable metal stents for endoscopic bilateral stent-within-stent placement for malignant hilar biliary obstruction. Gastrointestinal endoscopy 2010;71:195-9.
64. Hwang JC, Kim JH, Lim SG, Kim SS, Yoo BM, Cho SW. Y-shaped endoscopic bilateral metal stent placement for malignant hilar biliary obstruction: prospective long-term study. Scandinavian journal of gastroenterology 2011;46:326-32.
65. Kogure H, Isayama H, Nakai Y, et al. Newly designed large cell Niti-S stent for malignant hilar biliary obstruction: a pilot study. Surgical endoscopy 2011;25:463-7.
66. Bridges A, Wilcox CM, Varadarajulu S. Endoscopic management of traumatic bile leaks. Gastrointestinal endoscopy 2007;65:1081-5.
67. Dumonceau JM, Deviere J, Delhaye M, Baize M, Cremer M. Plastic and metal stents for postoperative benign bile duct strictures: the best and the worst. Gastrointestinal endoscopy 1998;47:8-17.
68. Katsinelos P, Kountouras J, Paroutoglou G, et al. A comparative study of 10-Fr vs. 7-Fr straight plastic stents in the treatment of postcholecystectomy bile leak. Surgical endoscopy 2008;22:101-6.
69. Kaffes AJ, Hourigan L, De Luca N, Byth K, Williams SJ, Bourke MJ. Impact of endoscopic intervention in 100 patients with suspected postcholecystectomy bile leak. Gastrointestinal endoscopy 2005;61:269-75.
70. Sandha GS, Bourke MJ, Haber GB, Kortan PP. Endoscopic therapy for bile leak based on a new classification: results in 207 patients. Gastrointestinal endoscopy 2004;60:567-74.
71. Lalezari D, Singh I, Reicher S, Eysselein VE. Evaluation of fully covered self-expanding metal stents in benign biliary strictures and bile leaks. World journal of gastrointestinal endoscopy 2013;5:332-9.
72. Luigiano C, Bassi M, Ferrara F, et al. Placement of a new fully covered self-expanding metal stent for postoperative biliary strictures and leaks not responding to plastic stenting. Surgical laparoscopy, endoscopy & percutaneous techniques 2013;23:159-62.
73. Canena J, Liberato M, Horta D, Romao C, Coutinho A. Short-term stenting using fully covered self-expandable metal stents for treatment of refractory biliary leaks, postsphincterotomy bleeding, and perforations. Surgical endoscopy 2013;27:313-24.
74. Wang AY, Ellen K, Berg CL, Schmitt TM, Kahaleh M. Fully covered self-expandable metallic stents in the management of complex biliary leaks: preliminary data - a case series. Endoscopy 2009;41:781-6.
75. Ferreira LE, Baron TH. Post-sphincterotomy bleeding: who, what, when, and how. The American journal of gastroenterology 2007;102:2850-8.
76. Shah JN, Marson F, Binmoeller KF. Temporary self-expandable metal stent placement for treatment of post-sphincterotomy bleeding. Gastrointestinal endoscopy 2010;72:1274-8.
77. Akbar A, Reddy DN, Baron TH. Placement of fully covered self-expandable metal stents to control entry-related bleeding during transmural drainage of pancreatic fluid collections (with video). Gastrointestinal endoscopy 2012;76:1060-3.
78. Aslinia F, Hawkins L, Darwin P, Goldberg E. Temporary placement of a fully covered metal stent to tamponade bleeding from endoscopic papillary balloon dilation. Gastrointestinal endoscopy 2012;76:911-3.
79. Itoi T, Yasuda I, Doi S, Mukai T, Kurihara T, Sofuni A. Endoscopic hemostasis using covered metallic stent placement for uncontrolled post-endoscopic sphincterotomy bleeding. Endoscopy 2011;43:369-72.
80. Valats JC, Funakoshi N, Bauret P, et al. Covered self-expandable biliary stents for the treatment of bleeding after ERCP. Gastrointestinal endoscopy 2013;78:183-7.
81. Howard TJ, Tan T, Lehman GA, et al. Classification and management of perforations complicating endoscopic sphincterotomy. Surgery 1999;126:658-63; discussion 64-5.
82. Stapfer M, Selby RR, Stain SC, et al. Management of duodenal perforation after endoscopic retrograde cholangiopancreatography and sphincterotomy. Annals of surgery 2000;232:191-8.
83. Vezakis A, Fragulidis G, Nastos C, Yiallourou A, Polydorou A, Voros D. Closure of a persistent sphincterotomy-related duodenal perforation by placement of a covered self-expandable metallic biliary stent. World journal of gastroenterology : WJG 2011;17:4539-41.
84. Jeon HJ, Han JH, Park S, Youn S, Chae H, Yoon S. Endoscopic sphincterotomy-related perforation in the common bile duct successfully treated by placement of a covered metal stent. Endoscopy 2011;43 Suppl 2 UCTN:E295-6.
85. Park WY, Cho KB, Kim ES, Park KS. A case of ampullary perforation treated with a temporally covered metal stent. Clinical endoscopy 2012;45:177-80.
86. Guido Costamagna DNR, Andreas Puspok, Thierry Ponchon, Marco J. Bruno, Michael J. Bourke, Horst Neuhaus, Andre Roy, FerráN. GonzáLez-Huix, Alan N. Barkun, Paul P. Kortan, Claudio Navarrete, Jacques M. Deviere. Stent Removability and Mid-Term Stricture Resolution After Multi-Month Metal Stenting of Benign Biliary Strictures: Interim Report From an International Prospective Trial in 187 Patients. Gastrointestinal endoscopy 2013;77:Supplement, Page AB321.
87. Cahen DL, Rauws EA, Gouma DJ, Fockens P, Bruno MJ. Removable fully covered self-expandable metal stents in the treatment of common bile duct strictures due to chronic pancreatitis: a case series. Endoscopy 2008;40:697-700.
88. Fumex F, Coumaros D, Napoleon B, et al. Similar performance but higher cholecystitis rate with covered biliary stents: results from a prospective multicenter evaluation. Endoscopy 2006;38:787-92.
89. Shimizu S, Naitoh I, Nakazawa T, et al. Predictive factors for pancreatitis and cholecystitis in endoscopic covered metal stenting for distal malignant biliary obstruction. Journal of gastroenterology and hepatology 2013;28:68-72.
90. Isayama H, Kawabe T, Nakai Y, et al. Cholecystitis after metallic stent placement in patients with malignant distal biliary obstruction. Clinical gastroenterology and hepatology : the official clinical practice journal of the American Gastroenterological Association 2006;4:1148-53.
91. Suk KT, Kim HS, Kim JW, et al. Risk factors for cholecystitis after metal stent placement in malignant biliary obstruction. Gastrointestinal endoscopy 2006;64:522-9.
92. van Berkel AM, van Marle J, Groen AK, Bruno MJ. Mechanisms of biliary stent clogging: confocal laser scanning and scanning electron microscopy. Endoscopy 2005;37:729-34.
93. Hu B, Wang TT, Shi ZM, et al. A novel antireflux metal stent for the palliation of biliary malignancies: a pilot feasibility study (with video). Gastrointestinal endoscopy 2011;73:143-8.
94. Dua KS, Reddy ND, Rao VG, Banerjee R, Medda B, Lang I. Impact of reducing duodenobiliary re
vitro evaluation and a prospective randomized clinical trial that used a biliary stent with an antireflux valve. Gastrointestinal endoscopy 2007;65:819-28.
95. Suk KT, Kim JW, Kim HS, et al. Human application of a metallic stent covered with a paclitaxel-incorporated membrane for malignant biliary obstruction: multicenter pilot study. Gastrointestinal endoscopy 2007;66:798-803.
96. Song TJ, Lee SS, Yun SC, et al. Paclitaxel-eluting covered metal stents versus covered metal stents for distal malignant biliary obstruction: a prospective comparative pilot study. Gastrointestinal endoscopy 2011;73:727-33.
97. Jang SI, Kim JH, Kim M, et al. Porcine feasibility and safety study of a new paclitaxel-eluting biliary stent with a Pluronic-containing membrane. Endoscopy 2012;44:825-31.
98. Lee SS, Shin JH, Han JM, et al. Histologic influence of paclitaxel-eluting covered metallic stents in a canine biliary model. Gastrointestinal endoscopy 2009;69:1140-7.
99. Bethge N, Sommer A, Gross U, von Kleist D, Vakil N. Human tissue responses to metal stents implanted in vivo for the palliation of malignant stenoses. Gastrointestinal endoscopy 1996;43:596-602.
100. Chung MJ, Kim H, Kim KS, Park S, Chung JB, Park SW. Safety evaluation of self-expanding metallic biliary stents eluting gemcitabine in a porcine model. Journal of gastroenterology and hepatology 2012;27:261-7.
101. Kim do H, Jeong YI, Chung CW, et al. Preclinical evaluation of sorafenib-eluting stent for suppression of human cholangiocarcinoma cells. International journal of nanomedicine 2013;8:1697-711.
102. Behm B BA, Clarke BW, Adams RB, Northup PG, Yeaton P, Kahaleh M. Cost analysis of temporarily placed covered self expandable metallic stents versus plastic stents in biliary strictures related to chronic pancreatitis (abstract). Gastrointestinal endoscopy 2007;65:AB211.
103. Kaffes AJ, Liu K. Fully covered self-expandable metal stents for treatment of benign biliary strictures. Gastrointestinal endoscopy 2013;78:13-21.
104. Ahmed Abdel Samiea MS, Lorenz Theilmann. Fully Covered Self-Expandable Metal Stents for Treatment of Malignant Biliary Strictures due to Pancreatic Carcinoma. Gastroenterology Research 2012;5:195-9.