Fully Covered Metal Biliary Stents: Current and Future Uses

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 to 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. Endoscopic placement of the first plastic endoprosthesis was described in 1980. Endoscopic stenting was shown to be as effective as surgical drainage relieving obstructive jaundice with fewer complications. In addition, stenting has resulted in shorter hospital stays, is accompanied by less morbidity and mortality, less cost and an improved quality of life.

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 cholangiopancreatography (ERCP) and stent exchange. 10F stents perform better than smaller 8F stents in malignant obstruction.

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.
Fully Covered Metal Biliary Stents

SEMS have been described since the late 1980’s and are of proven benefit in both malignant and benign biliary obstruction. 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). 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. 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.

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 to 10 mm (30 Fr) at full deployment. 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) 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. These occlusions require further insertion of plastic stents within the SEMS or deployment of another SEMS within the initial one and sometimes mechanical cleaning. 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.
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 orthotopic 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. Traditionally these strictures have been treated surgically, but stricture resolution may be achieved endoscopically. 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 1½ 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 strictureting 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. 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. 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. 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. Long-term resolution rates for chronic pancreatitis related strictures were low at 20% to 30%. 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...
Fully Covered Metal Biliary Stents

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

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

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 liver transplantation (continued on page 27)
### Table 2. Use of Fully Covered Self-Expandable Metal Stents in Benign Biliary Strictures

<table>
<thead>
<tr>
<th>Study</th>
<th>Method</th>
<th>Stent Type</th>
<th>Patients</th>
<th>Indication</th>
<th>Clinical Success, %*</th>
<th>Adverse Events, %†</th>
<th>Migrations, %</th>
<th>Recurrence, %</th>
<th>Follow Up, Mo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tarantino et al.¹¹</td>
<td>Prospective, multicenter</td>
<td>Niti-S ComVi</td>
<td>62</td>
<td>Mixed 38 OLT</td>
<td>90.3</td>
<td>1.6</td>
<td>24.2</td>
<td>7.1 (all OLT)</td>
<td>16</td>
</tr>
<tr>
<td>Sauer et al.²¹</td>
<td>Prospective, single center</td>
<td>Wallflex</td>
<td>19</td>
<td>OLT</td>
<td>78.9</td>
<td>15.8</td>
<td>31.6</td>
<td>5.2</td>
<td>12</td>
</tr>
<tr>
<td>Moon et al.²⁶</td>
<td>Prospective, single center</td>
<td>Bonastent M-Intraductal</td>
<td>21</td>
<td>Mixed 3 OLT</td>
<td>95.2</td>
<td>0</td>
<td>19</td>
<td>4.8</td>
<td>13.8</td>
</tr>
<tr>
<td>Poley et al.¹³</td>
<td>Prospective, single center</td>
<td>Hanaro</td>
<td>23</td>
<td>Mixed 6 OLT</td>
<td>60.8 64% CP 80% non-CP</td>
<td>87.0</td>
<td>4.3</td>
<td>Unknown</td>
<td>15</td>
</tr>
<tr>
<td>Haapamaki et al.²³</td>
<td>Retrospective, single center</td>
<td>Allium BIS Wallstent</td>
<td>17</td>
<td>OLT</td>
<td>100</td>
<td>35.3</td>
<td>23.5</td>
<td>11.8</td>
<td>21.7</td>
</tr>
<tr>
<td>Park et al.²⁷</td>
<td>Prospective, multicenter</td>
<td>AF: M.I. Tech FE: Standard Sci-Tech Inc.</td>
<td>43</td>
<td>Mixed 2 OLT</td>
<td>84</td>
<td>27.9 31.8 AF 23.8 FE</td>
<td>16.3 0 AF 33.3 FE</td>
<td>16.3 13.6 AF 19 FE</td>
<td>4</td>
</tr>
<tr>
<td>Hu et al.²⁴</td>
<td>Prospective, single center</td>
<td>Micro-Tech</td>
<td>13</td>
<td>OLT</td>
<td>92.3</td>
<td>7.7</td>
<td>0</td>
<td>8.3</td>
<td>12.1</td>
</tr>
<tr>
<td>Park et al.⁴²</td>
<td>Prospective, single center</td>
<td>Anchor Biliary Stent Nonanchor</td>
<td>33 16 Anchor, 17 Nonanchor</td>
<td>Mixed No OLT</td>
<td>93.8 anchor, 70.5 nonanchor</td>
<td>3.0</td>
<td>6.3 anchor, 41.2 nonanchor</td>
<td>3.0</td>
<td>14 anchor, 15 nonanchor</td>
</tr>
<tr>
<td>Garcia-Pajares et al.²⁰</td>
<td>Retrospective, single center</td>
<td>Not Stated</td>
<td>22</td>
<td>OLT</td>
<td>95.5</td>
<td>40.9</td>
<td>22.7</td>
<td>4.5</td>
<td>12.5</td>
</tr>
<tr>
<td>Traina et al.²²</td>
<td>Prospective, single center</td>
<td>Niti-S ComVi</td>
<td>16</td>
<td>OLT</td>
<td>87.5</td>
<td>6.3</td>
<td>37.5</td>
<td>7.1</td>
<td>6</td>
</tr>
<tr>
<td>Mahajan et al.¹²</td>
<td>Prospective, single center</td>
<td>Gore-Viabil</td>
<td>44</td>
<td>Mixed 9 OLT</td>
<td>82.9</td>
<td>27.3</td>
<td>4.5</td>
<td>Unknown</td>
<td>3.8</td>
</tr>
<tr>
<td>Cahen et al.¹⁰</td>
<td>Prospective, single center</td>
<td>Hanaro</td>
<td>6</td>
<td>CP</td>
<td>66.7</td>
<td>33.3</td>
<td>33.3</td>
<td>25.0</td>
<td>36</td>
</tr>
</tbody>
</table>

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.¹⁰ 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. The strictures may be non-anastomotic (presenting earlier) or anastomotic. Non-anastomotic strictures have less favorable outcomes.

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. In another series of 11 patients with complications after liver transplantation, placement of CSEMS was successful in avoiding hepaticojejunostomies. 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.

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.

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.

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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Table 3. FCSEMS Used in Bleeding After ERCP

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

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

From Valats et al. with permission.
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%).

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.

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. 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.

**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. Technical success was achieved in 98% with uncomplicated acute removal when required. In addition there were low rates of stent migration and occlusion. 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).

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...
seemed to be more cost effective compared to other options. 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. 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. 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. 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.

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. 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.

Non-Stricture Indications for FCSEMS

Biliary Leaks

Bile leaks may occur following cholecystectomy, traumatic injury, OLT, or liver resection. The most common sites of biliary leaks are at the cystic duct stump or the duct of Luschka. 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%. 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). 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 the 17 patients (94%). Minimal complications were noted in 5 of the 17 patients (29%). In a prospective study of 16 patients, FCSEMS were shown to be effective for postoperative biliary strictures and bile leaks not responding to plastic stents, with a success rate of 94% after a median follow-up of 13 months. 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. In a retrospective analysis including 13 patients with complex biliary leaks, the FCSEMS device helped to increase the patency rate to 100%.

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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 44 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. Antireflux stents have now been developed that prevent duodenal biliary reflux and thereby improve biliary drainage, prolong stent patency and also, reduce chances of cholangitis. 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, 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. 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. Mucosal hyperplasia after stent placement is partly responsible for stent occlusion; inflammation and fibrous reaction are thought to be contributing factors for mucosal hyperplasia. 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.

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.

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. Further prospective trials are needed to evaluate the long-term effectiveness, particularly when compared to multiple plastic stents.

References

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