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Asia–Pacific Consensus Guidelines for Endoscopic Management of Benign Biliary Strictures

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Asia–Pacific Consensus Guidelines for Endoscopic Management of Benign Biliary Strictures

Short title: International consensus for BBS

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Abstract

Benign biliary strictures (BBSs) are commonly caused by surgical injury, chronic pancreatitis, and inflammatory cholangiopathies. Although advanced imaging tests and tissue acquisition methods have been developed for evaluation of indeterminate biliary strictures, differentiation of BBSs from biliary malignancies remains a challenge to clinicians. The majority of BBSs have good response to nonsurgical treatment and surgical intervention mainly serves as a rescue when nonsurgical approaches fail. Endoscopic management is a safe, effective, and less-invasive treatment for BBSs compared with other approaches. Endoscopic biliary stricture dilation followed by placement of multiple plastic stents has been the first-line choice with good long-term ductal patency. Recently, covered self-expanding metal stents (CSEMSs) has been increasingly used in the management of BBSs with similar effectiveness but easier deployment, fewer endoscopic sessions compared with plastic stents. Moreover, other technologies are emerging in the diagnosis and management of BBSs. To assist clinicians in managing BBSs, the Asia-Pacific ERCP Club (APEC) has developed this statement through a systematic review of the literature.

Key words: Consensus statements; benign biliary strictures; cholangiopancreatography, endoscopic retrograde; stent

Introduction

The primary goal of treatment for benign biliary strictures (BBSs) is to resolve bile duct obstruction, to achieve a long-term ductal patency and to maintain liver
function. Endoscopic approach has become the first-line option for most cases of
BBSs. Biliary drainage can be maintained through combination of endoscopic
striction dilation and biliary stenting. The effectiveness, clinical success, and
outcomes of endoscopic intervention for BBSs largely depend on specific etiologies,
endoscopic techniques used, and the selection of appropriate accessories and stents,
which varies in the literature. New endoscopic techniques have also been developed
to improve the success of endotherapy. Therefore, we established this consensus
recommendation to better assist clinical decision making and standardize
endoscopic techniques in endoscopic management of BBSs.

**Methods**

A comprehensive literature searching of the PubMed/Medline and EMBASE
databases was conducted for the English language publications on BBSs. Search
items included “benign strictures,” “biliary,” and pertinent to specific statements.
After screening the corresponding abstracts of the retrieved articles, the full text of
the articles relevant to this review were downloaded. Electronic searches were then
supplemented by manual searches of reference of these articles.

Before the consensus meeting, a list of statements was generated by the Chinese
co-authors and were divided into the following topics: diagnosis, pre-procedure
preparation, biliary access, stricture dilation, stenting, alternate therapy, and specific
indications for endoscopic treatment of BBSs including post-liver transplantation,
surgical injury, chronic pancreatitis (CP), primary sclerosing cholangitis (PSC), IgG-4
related sclerosing cholangitis (IgG-4 SC), bilio-enteric anastomotic stricture. B. Hu, B.
Sun, and X. Zheng wrote the commentaries on all the statements. The draft of statement was distributed electronically in advance to all consensus members. The first vote was conducted electronically by e-mail with a response rate of 85% (17/20). All feedbacks were collected and the draft statement was revised before the face-to-face meeting.

A face-to-face meeting of all consensus members was held in October 21, 2016, in Shenyang, Liaoning Province of China. Nineteen of 20 (95%) consensus members participated in the meeting (S. Lakhtakia didn’t participate but voted through email again). All statements, commentaries and relevant evidence were reviewed, discussed, and revised accordingly. The evidence level and recommendation grade were rated using the grading system developed by the Scottish Intercollegiate Guidelines Network Grading Review Group (Table 1). The voting system used was a 4-point scale (Table 2). The second vote was conducted in this meeting. Consensus was considered to be achieved when the majority (≥80%) of voting members indicated “agree completely” or “agree with some reservation.” The final revised version was approved by all members of the Asia-pacific ERCP Club committee before publication. All approved statements were enlisted in Table 3.

**Consensus statements**

**GENERAL PRINCIPLES**

**Etiology**

1. BBSs arise from diverse etiologies, most commonly postoperative injury and chronic inflammation.
BBSs have heterogeneous etiologies and are commonly caused by surgical bile duct injury, chronic pancreatitis and chronic cholangiopathy (eg, primary or secondary sclerosing cholangitis) (table 4). Cholecystectomy and liver transplantation (LT) are the most common etiologies of surgical related biliary strictures. The reported incidence of post-LT biliary strictures is approximately 10% to 40% with anastomotic biliary strictures (ABS) the most common adverse event.\textsuperscript{2,3} Cholecystectomy is another important etiology of BBSs, which is mostly caused by direct bile duct injury during surgery. The incidence of post-cholecystectomy biliary stricture is approximately 0.5% which has not been influenced by the increasing experience with laparoscopy.\textsuperscript{4} Among the non-surgical etiologies, chronic pancreatitis associated biliary strictures normally occur in the distal common bile duct and tends to be refractory due to fibrosis and calcification of periductal tissue. A multi-center survey covering a 10-year period of 2008 Chinese patients with chronic pancreatitis showed that biliary strictures developed in 13.4% of study patients.\textsuperscript{5} Due to the diversity of etiologies, the effectiveness of treatment for BBSs is not uniform. The clinical presentation of BBSs is related directly to the degree and onset of biliary obstruction, and ranges from asymptomatic to severe or even life-threatening
condition. The outcome also varies and depends on the etiology, pathogenesis, and response to treatment.

**Diagnosis**

2. The diagnosis of BBS should be made carefully by the combination of history review, cross-section imaging studies and endoscopic procedures. Histological diagnosis by cytology or biopsy, as well as long-term clinical follow-up are recommended to confirm the diagnosis.

   Level of evidence: 1+

   Recommendation grade: A

   Level of agreement: A, 85%; B, 15%; C, 0%; D, 0%

Diagnosis of biliary strictures remains a clinical challenge due to either the risk of missing resectable malignancy or the expenditure and morbidity related to unnecessary operation in patients with benign etiologies. A multidisciplinary approach is required to confirm the diagnosis, which includes history review, basic laboratory work-ups, cross-section abdominal imaging, and other advanced intraductal imaging tests. Taking a thorough clinical history into consideration may be beneficial in clarifying the etiology of a biliary stricture. Typical etiologies of benign strictures are listed in Table 4. Cross-section imaging tests and EUS are preferred initial investigation for biliary strictures, whereas ERCP-directed tissue acquisition and EUS-guided fine-needle aspiration or biopsy are the only way to provide cytohistological diagnosis. ERCP-guided brushing cytology and/or transpapillary forceps biopsy (TPFB) is widely applied with high specificity, but low
sensitivity in diagnosing biliary strictures. A recent meta-analysis showed that the pooled sensitivity and specificity for the diagnosis of malignant biliary strictures were 45% and 99% for brushing cytology, and 48.1% and 99.2% for TPFB.\(^8\) Therefore, other technologies have been applied to improve the diagnosis when brush cytology and TPFB are indeterminate, which include, but not limited to, Fluorescent in-situ hybridization (FISH), EUS-FNA, intraductal ultrasound (IDUS), per-oral cholangioscopy and confocal laser endomicroscopy.\(^9,10\) In addition, clinical follow-up of at least 6 months with a benign clinical course is required to support a benign stricture. This is supported by a prospective single center, long-term (182.8 person-years) follow-up study involving 104 patients with indeterminate biliary strictures, in which the detection of biliary cancer was more common during the first 6 months of follow-up.\(^11\) Long-term follow-up is also mandatory in those with risk of developing malignancy, such as PSC.\(^12\)

3. Non-invasive imagings such as MRCP and/or MD-CT are necessary before ERCP procedure, as it can provide useful roadmap and clarify the preprocedure plan.

Level of evidence: 1++

Recommendation grade: A

Level of agreement: A, 75%; B, 25%; C, 0%; D, 0%

Abdominal imaging tests are widely used in patients with biliary obstruction, such as magnetic resonance imaging (MRI), computed tomography (CT), and trans-abdominal US. MRCP has been increasingly used as a noninvasive alternative
to ERCP, which provides high-quality imaging information of biliary tree just as radiocontrast cholangiography and allows pre-ERCP evaluation of biliary strictures with regard to the location, stricture margin, and length. On MRCP, a BBS is characterized by regular, symmetric and short-segment narrowing, whereas malignant strictures usually present with irregular, asymmetric, and long-segment narrowing, particularly ≥14 mm in length. A randomized clinical trial showed that MRCP has a comparable accuracy with ERCP in differentiating extrahepatic cholangiocarcinoma (CCA) from benign strictures, and a strategy of pre-ERCP MRCP decreased the need for subsequent ERCPs in patients with suspected biliary obstruction. Meta-analysis demonstrated that MRCP has a high sensitivity and specificity for evaluation of post-LT biliary strictures. When noninvasive imaging tests fail to identify the cause of biliary strictures, EUS, when available, can be performed before ERCP in a single session and is useful to provide more diagnostic information. As a result, we believe MRCP, as well as other non-invasive or less invasive diagnostic modalities should be selected for the initial evaluation of patients with biliary strictures before ERCP procedure.

Role of endotherapy

4. ERCP is the first-line interventional option for the management of most BBS patients with accessible papilla.

Level of evidence: 2++
Recommendation grade: B

Level of agreement: A, 95%; B, 5%; C, 0%; D, 0%

The goal of treatment for BBSs is to obtain a long-term bile duct patency through surgical or non-surgical approaches (eg, endoscopic and/or percutaneous intervention). Long-term follow-up study revealed that endoscopic therapy for BBSs is safe, effective, less-invasive, and repeatable. Therefore, it has become the first therapeutic choice for relieving bile duct obstruction in most cases of BBSs. Standard endoscopic techniques include stricture dilation with balloon or bougie catheter followed by insertion of multiple plastic stents. Plastic stents are required to be exchanged periodically for up to 12 months to maintain ductal patency. Placement of fully covered self-expanding metal stent (FCSEMS) is becoming an accepted method for BBSs given its safety, high success rate, easier insertion technique, and requiring fewer endoscopic sessions. In a large prospective multinational study of 177 patients with BBSs received FCDEMS by Deviere, et al, endoscopic removal of FCSEMS was achieved in all 131 patients who were shceduled for stent removal, 94.7% (124/131) of whom had no removal related serious adverse events, and stricture resolution were achieved in 135 patients (76.3%). In addition, FCSEMSs have been established as an alternative therapy to plastic stents for BBSs or stands as a rescue therapy when multiple plastic stents failed. In a prospective study, placement of FCSEMS for 6 months achieved stricture resolution in 70.6% (12/17) of patients who had CBD strictures secondary to chronic pancreatitis and were not respond to single 10F plastic stent placement. Eight patients completed a 2-year follow-up without
stricture recurrence. Percutaneous biliary interventions are reserved for patients with surgically altered anatomy or inaccessible papilla (e.g., history of Roux-en-Y gastric bypass and biliary-enteric anastomosis), who are not candidates for endoscopic intervention. Finally, surgical technique plays a role in the setting of bile duct dissection or unsuccessful endoscopic and percutaneous intervention.

**Preparation**

5. Prophylactic antibiotics should be administered in selected patients, such as those with complex hilar strictures, post liver transplantation and PSC.

   Level of evidence: 1++

   Recommendation grade: A

   Level of agreement: A, 85%; B, 10%; C, 5%; D, 0%

Cholangitis and sepsis are known adverse events of ERCP. ERCP in patients with biliary strictures has been associated with a higher rate of bacteremia than in those without bile duct obstruction. Traditionally, use of prophylactic antibiotics before the procedure has been administered to reduce the incidence of ERCP-related infective adverse events. However, an early meta-analysis of 5 randomized, controlled trials revealed that prophylactic antibiotics before ERCP procedures could not significantly reduce the incidence of cholangitis and bacteremia. This has been further supported by another recent meta-analysis of 7 clinical trials with 1389 patients, which concluded that prophylactic antibiotics were not effective to prevent
ERCP-induced cholangitis in unselected patients. Therefore, antibiotics cannot be routinely recommended to prevent ERCP-induced cholangitis in unselected patients. However, increased risk of post-procedure infection has been associated with incomplete biliary drainage, which is commonly seen in post-liver transplantation biliary strictures and PSC due to complex or multiple biliary strictures. A longer duration of procedures with multiple intraductal manipulations such as brush cytology, forceps biopsies, balloon dilation and intraductal cholangioscopy/US examination could also contribute to a higher incidence of post-ERCP cholangitis in PSC patients than non-PSC patients. Therefore, antibiotic prophylaxis is recommended in the setting of biliary obstruction and anticipated incomplete biliary drainage. However, adequate drainage of the biliary obstruction is fundamental to reduce post-ERCP cholangitis. Antibiotics that cover biliary flora, such as enteric gram-negative organisms, enterococci, and pseudomonas, are recommended.

**Biliary access**

6. Negotiating the biliary stricture with guidewire requires reasonable skill from endoscopist and assistant, and use of appropriate catheter and guidewire.

**Level of evidence:** 4

**Recommendation grade:** D

**Level of agreement:** A, 75%; B, 15%; C, 10%; D, 0%
Success deep biliary cannulation with guidewire is critical in maintaining biliary access and is prerequisite for therapeutic ERCP. In cases of difficult bile duct cannulation, various techniques have been developed and are effective to facilitate selective biliary cannulation, such as early precut fistulotomy, double-guidewire cannulation method, wire-guided cannulation over a pancreatic stent, and precut after placement of a pancreatic stent. However, attempts at guidewire passage beyond the BBS is still challenging depending on the severity and anatomic location of obstruction. Although there exists a paucity of comparative studies to guide the best choice of guidewire, standard 0.035-inch hydrophilic guidewires are most commonly used to traverse a stricture. In severe and complex strictures, specialized guidewires with smaller diameter and better maneuverability (eg, 0.025, 0.021, and 0.018-inch) with or without an angulated tip may be required. Additionally, when conventional methods fail to achieve guidewire passage of BBSs, other techniques, such as inflated balloon extraction, Spyglass cholangioscopy-assisted guidewire placement, may be required. Nevertheless, forceful maneuvers should be avoided to prevent the creation of a false tract or biliary perforation.

**Dilation**

7. Serial incremental (balloon or bougie catheter) dilation is usually necessary for the management of severe BBSs, but particular caution should be taken during early postoperative period.
Serial incremental endoscopic dilation followed by multiple plastic stent placement is often required for benign, severe fibrotic biliary strictures. Either balloon dilators or bougie-like tapered catheter can be used but balloon dilation is often needed in tight strictures. The dilating balloon is advanced over a guidewire across the stricture under fluoroscopic guidance, and is suggested to be maintained fully inflated for 30 to 60s, or until the stricture waist disappears under fluoroscopy. However, forceful dilation of an early post-operative stricture (<4 weeks after surgery) should be avoided to reduce the risk of dehiscence of bile duct and resultant bile leak. Moreover, early postoperative bile duct strictures often accompanied with bile leaks, in which circumstances aggressive dilation of the stricture should also be avoided.

8. Balloon dilation alone, without subsequent stenting, is associated with a high rate of BBS recurrence.

Level of evidence: 1++
Recommendation grade: A
Level of agreement: A, 80%; B, 20%; C, 0%; D, 0%
Balloon dilation followed by biliary stent placement is a widely applied strategy in management of most types of BBSs with excellent long-term outcomes. Balloon dilation alone of post-liver transplant anastomotic strictures (PLTASs) showed a high recurrence rate whereas single or multiple stents insertion after initial balloon dilation could maintain ductal patency. A recent systematic review of 19 studies concluded that longer stenting duration for PLTASs predicted less recurrence (OR=0.95, P=0.002). The pooled stricture resolution rate was 86% in 18 studies using plastic stents and the pooled recurrence rate was 9%. In those with biliary strictures secondary to chronic pancreatitis, biliary dilation followed by multiple 10F plastic stents placement with regular stent exchange for 12 months resulted in stricture resolution in up to 90% of patients. Another recent systematic review of 25 studies showed that treatment with covered self-expanding metal stents achieved a better treatment success rate (77%) at 12-month follow-up than multiple plastic stents (33%) in 946 patients with biliary strictures associated with CP. The only exception is PSC related strictures, in which dilation alone appeared effective and no additional benefit was observed in those undergoing stricture dilation and stenting. Repeated endoscopic balloon dilations of dominant strictures in PSC patients has been associated with a good long-term outcome.

Stenting

9. To place multiple plastic stents side-by-side for up to 1 year, using the strategy of either several sessions with an increasing number of stents or one session
with maximal stents, has become current standard of care for the majority of
BBSs.

Level of evidence: 1++

Recommendation grade: A

Level of agreement: A, 65%; B, 30%; C, 5%; D, 0%

To maintain a long-term patency of bile duct is the major goal in the management of
BBSs. Placement of multiple, large-bore plastic stents side-by-side across the
stricture after stricture dilation has been established as a standard treatment for
BBSs, whose long-term outcomes may be equivalent or superior to surgical
management but with less morbidity. This strategy is suitable for patients with
non-hilar extrahepatic BBSs, who have available endoscopic access to the duodenum
and accept multiple endoscopic procedures. A systematic review of 47 trials with
1116 patients found that multiple plastic stent placement had a higher overall
clinical success rate (94.3%) and less adverse events (20.3%) compared with
placement of a single plastic stent in the management of BBSs. Stents are
exchanged tri-monthly with increasing number and/or diameter of stents for up to
12 months. An alternative strategy is by insertion of maximal stents over a single
session, which may lessen the need for frequent stent exchange. Symptomatic
stent occlusion rates appeared similar between patients with indwelling multiple
plastic stents undergoing exchange within 6 months and those exchanged more than
6 months after placement. \(^46\)

10. Placement of uncovered SEMS in patients with BBS or indeterminate biliary stricture is strongly discouraged.

Level of evidence: 4

Recommendation grade: D

Level of agreement: A, 80%; B, 15%; C, 0%; D, 5%

Placement of covered SEMSs is technically easy, which could prevent tissue ingrowth or stent embedment and is easy to be removed from the bile duct after successful treatment in most patients with BBSs. \(^47\) In contrast to fully covered SEMSs, ingrowth of reactive tissue occurs through the mesh of uncovered or partially covered SEMSs after being deployed for a certain period, which may eventually cause stent embedment, making it unable to be removed endoscopically. Although a stent-in-stent technique has been recently reported to help retrieve uncovered SEMSs in case series, \(^48\) uncovered SEMS placement is not recommended for treating BBSs and indeterminate biliary strictures.

11. Placement of fully covered SEMSs has similar successful outcome to that of multiple plastic stents therapy, but requires fewer endoscopic sessions and
shorter stenting duration in BBSs such as post-liver transplantation anastomotic biliary stricture.

Level of evidence: 1++

Recommendation grade: A

Level of agreement: A, 90%; B, 10%; C, 0%; D, 0%

Covered SEMS placement is a promising alternative therapy to multiple plastic stents (MPSs) for selected benign CBD strictures. Despite the higher expenditure of SEMSs, placement of a CSEMS that opens to a diameter of 10 mm is technically easier than insertion of MPSs side by side to obtain a comparable diameter of bile duct dilation. A randomized trial comparing FCSEMS with MPS in post-liver transplantation anastomotic biliary strictures showed a higher successful stricture resolution rate (81%-92% vs 76%-90%), shorter median stent dwelling time (3.8 vs 10.1 months), fewer median ERCP sessions (2.0 vs 4.5), and lower adverse event rate (10% vs 50%) in the FCSEMS group compared with the MPS group. The cost of stent therapy was lower in the FCSEMS arm than in the MPS group. When post-protocol consumption was added, the FCSEMS arm was still more cost-effective than the MPS arm. Similar result has been proven in a recently published multicenter RCT study. Therefore, FCSEMS placement is proved as the more patient-friendly and cost-effective strategy, and achieves similar stricture resolution rate to conventional MPS, with fewer procedures and procedure-related adverse events.
Considering that hilar strictures have a relatively poor response to endoscopic stenting, and CSEMS crossing hilar bifurcation may prevent bile drainage of non-stenting hepatic lobe, CSEMS therapy can only be recommended as management of choice for non-hilar BBSs.\textsuperscript{57,58-64} Cholecystitis is another concern when placement of FCSEMS in patients with BBSs and gallbladder in situ.\textsuperscript{67,69} The optimal duration of stenting with CSEMSs has not been determined. Recently published study results suggested that post-LT anastomotic biliary strictures can be successfully managed with FCSEMS with stent dwell time of around 6 months (Table 5), but it takes longer time to remove FCSEMS in chronic pancreatitis or cholecystectomy associated biliary strictures.\textsuperscript{47} The treatment success of benign distal biliary strictures with FCSEMS placement can be compromised by high stent dislocation rates.\textsuperscript{74} On the other hand, long time of stent indwelling is associated with cholangitis resulting from stent occlusion or migration, and may cause difficult stent removal due to mucosal hyperplasia on the extremities of the SEMS.\textsuperscript{65, 66} Removal success of FCSEMS appeared less frequent in post-cholecystectomy biliary strictures than in chronic pancreatitis.\textsuperscript{47}

12. To improve the effectiveness of FCSEMS therapy, efforts should be attempted to prevent stent migration.

Level of evidence: 2++
Recommendation grade: B

Level of agreement: A, 65%; B, 35%; C, 0%; D, 0%

Compared with uncovered or partially covered SEMSs, FCSEMSs can efficiently prevent the ingrowth of reactive tissue and stent embedment. However, stent migration is frequently encountered, which could compromise the effectiveness of treatment and may cause serious adverse events.\(^\text{20,60,64}\) Meanwhile, enough stent indwelling period and absence of stent migration have been related to stricture resolution in patients with BBSs treated by FCSEMS.\(^\text{71}\) In order to prevent stent migration, several anti-migration features have been designed. Insertion of a double-pigtail stent within FCSEMS for anchoring appeared as a simple, safe, and effective strategy with significantly lower stent migration rate and longer stent dwelling time compared with FCSEMS alone.\(^\text{72}\) A newly designed FCSEMS with novel anchoring flap at the proximal portion of the stent was associated with a much lower stent migration rate than stents with a flared end (0% vs 33%, \(P = 0.004\)).\(^\text{73}\) An anatomy-shaped design of FCSMS also appeared effective to reduce the stent migration rate.\(^\text{74}\)

**Percutaneous intervention**

13. Percutaneous approach may be useful in case of failed ERCP for “rendezvous” techniques and in patients with surgically alerted anatomy and inaccessible papilla
Level of evidence: 2++

Recommendation grade: B

Level of agreement: A, 75%; B, 20%; C, 5%; D, 0%

ERCP is a feasible first choice in the management of BBSs. However, endoscopic access to the major papilla can be failed in patients with gastric outlet obstruction, duodenal indwelling stents, or surgically altered anatomy such as Roux-en-Y hepaticojejunostomy. In these circumstances, percutaneous transhepatic biliary drainage (PTBD) usually is considered as an alternative treatment for biliary decompression and to avoid invasive surgical management.\(^{75}\) PTBD followed by balloon dilation is a minimally invasive, safe, and effective option offering the patient a quicker recovery and far less morbidity than surgery.\(^{76}\) Prospective data showed that percutaneous catheter placement in extrahepatic, single-site biliary stricture for 6 to 8 months, with progressive catheter insertion upsizing to 18F to 20F was effective and achieved stricture resolution in 64% of patients with post-liver transplantation biliary strictures and in 86.4% of patients with BBSs caused by other etiologies.\(^{77}\) Percutaneous transhepatic placement of retrievable covered metal stents also appeared feasible for the treatment of BBSs with satisfied short or mid-term outcomes.\(^{75}\)

**Surgical intervention**
14. Surgery is a valid option in cases of complete transection or ligation of bile duct, in selected patients with unsuccessful to ERCP therapy.

Level of evidence: 2++

Recommendation grade: B

Level of agreement: A, 85%; B, 15%; C, 0%; D, 0%

Complete transection or ligation of biliary tract is a serious adverse event of hepatobiliary surgery due to inadequate visualization of anatomical features in the surgical field and/or insufficiency of surgeon experience. Endoscopic therapy or percutaneous treatment is generally ineffective to re-establish physical biliary drainage when bile duct is completely obstructed or ligated, and surgical repair will be required. Surgical intervention is also indicated in patients with refractory BBSs or in those who are not compliant to endoscopic management. This can be particularly encountered in patients with chronic pancreatitis or post-LT non-anastomotic strictures. A prospective follow-up study found that patients with chronic pancreatitis, who have calcifications in the head of pancreas, having a 17-fold increased risk of failure to standard endoscopic management. These patients may ultimately need surgical treatment which was reported having better long-term outcomes, and similar treatment success rate compared with endoscopic intervention for biliary strictures caused by chronic pancreatitis. Similarly, endoscopic drainage has a lower success rates in patients with post-liver transplantation non-anastomotic strictures than in those with anastomotic strictures,
and some may eventually require re-transplantation.  

**Innovative techniques**

15. Novel techniques, such as magnetic compression anastomosis, intraductal bipolar radiofrequency ablation & biodegradable biliary stenting, may have potential role in selected cases when conventional endoscopic and percutaneous approaches are not successful.

Level of evidence: 3

Recommendation grade: D

Level of agreement: A, 45%; B, 35%; C, 10%; D, 10%

Conventional endoscopic or percutaneous interventions may fail to achieve successful biliary drainage in severe BBSs. Other novel techniques, such as magnetic compression anastomosis (MCA), have been developed as rescue methods which appeared effective and safe in case reports or series.  

In a recent case series by Jang, et al., MCA achieved biliary recanalization in 89.7% (35/39) of patients with complete postoperative or traumatic biliary obstruction. Adverse events only occurred in 1 patient with mild cholangitis, and restenosis occurred in 2 patients during a mean follow-up of 41.8 months.  

A smaller magnet (2.4mm in diameter) has also been developed recently to facilitate the deployment and appeared
excellent results in treating complete post-liver transplantation BBSs.\textsuperscript{82} Hu et al applied intraductal bipolar radiofrequency ablation with or without biliary stenting in 9 patients with refractory BBSs. Immediate stricture improvement was achieved in all patients without significant adverse events, and only 1 patient developed restenosis during a median follow-up of 12.6 months.\textsuperscript{86} Mauri et al reported using biodegradable biliary stent to treat refractory postsurgical biliary strictures. Strictures were resolved in all 10 patients without restenosis during a median follow-up of 16.5 months.\textsuperscript{87} These novel techniques are promising in the future management of BBSs, especially when conventional non-surgical methods failed. However, more large-scale and randomized studies are warranted to further confirm their efficacy and safety, as well as long-term outcome.

**BBS WITH SPECIFIC DISORDERS**

Post-LT

16. ERCP therapy is the first-line management approach for the patients with anastomotic biliary stricture (ABS) and localized non-anastomotic biliary stricture (NABS). Earlier intervention provides better response.

Level of evidence: 1+

Recommendation grade: A

Level of agreement: A, 85%; B, 15%; C, 0%; D, 0%
Biliary stricture is one of the common adverse events after liver transplantation with an incidence rate reported of 4% to 43%.

Post-LT biliary strictures are classified as ABS or NABS. ABS occurs at the biliary anastomotic site, which is usually single and more commonly associated with living donor LT than deceased donor LT. Endoscopic treatment is effective and has been established as a first-line therapy for ABSs. Retrospective studies showed that endoscopic stricture dilation followed by multiple plastic stent placement achieved a high stricture resolution rate ranging from 66.7% to 100% in the management of ABS. In recent years, covered SEMS has been increasingly used in ABSs. A small scale, prospective, randomized, multi-center study showed a sustained stricture resolution in 52% of ABS patients by temporary placement of partially CSEMSs. Another small, prospective, randomized trial revealed that fully CSEMSs achieved a comparable stricture resolution rate but reduced number of ERCPs compared with MPS insertion. However, ABSs presenting beyond 6 months after LT needed more episodes of ERCP therapy than those presenting within 6 months after LT.

NABSs are located at least 5 mm proximal to the anastomosis and are characterized by multiple intra- or extra-hepatic bile duct strictures with recurrent biliary sludge or cast formation. Late-onset NABSs (presented 1 year after LT) are more likely seen at the peripheral branched biliary tree compared with early onset NABSs (within 1 year). Compared with ABS, NABSs are often associated with ischemic events, which are more resistant to endotherapy. Endoscopic management of NABSs, especially in late-onset NABSs, is more challenging, which features repeated stricture dilation,
longer period of stenting, a lower success rate ranging from 40% to 81.8%, and a higher stricture recurrence rate.\textsuperscript{94, 95}

**Surgical injury**

17. Endoscopic therapy with biliary stenting is an effective approach for post-operative bile duct stricture with successful long-term outcome comparable with surgical repair.

Level of evidence: 2+

Recommendation grade: C

Level of agreement: A, 70%; B, 25%; C, 5%; D, 0%

Cholecystectomy has been associated with a 0.5% incidence of bile duct injury.\textsuperscript{4} Surgery is considered the treatment of choice for post-cholecystectomy bile duct strictures (PCBDSs), particularly in patients with total biliary obstruction.\textsuperscript{96} Endoscopic dilation of postoperative biliary strictures followed by placement of multiple large-bore plastic stents with trimonthly exchange for a 1-year period has become an alternative treatment strategy (table 6).\textsuperscript{42, 96-98} Retrospective studies showed a similar treatment success rate between surgery and endotherapy for PCBDS.\textsuperscript{96, 99} In an early study, Davids et al retrospectively compared endoscopic stenting (66 patients) with surgical therapy (35 patients) in the management of BBSs.
Excellent and good result was achieved in 83% in both surgically (mean follow-up of 50 months) and endoscopically treated patients (mean follow-up of 42 months after stent removal). Compared with the surgery group, endoscopically treated patients featured a less early adverse event (8% vs 26%, $p<0.03$), but higher late adverse events (27% vs 0%). Stricture recurrence occurred in 17% of patients in both surgical and endoscopic groups. In another retrospective study by Tocchi et al, a total of 42 patients with PCBDS underwent endoscopic stenting (20) or surgical biliary-digestive reconstruction (22). Excellent and good outcomes were achieved in 77.3% (17/22) in the surgery group and in 80% (16/20) in endoscopically treated patients during a follow-up longer than 60 months. Morbidity occurred more frequently in patients treated with endoscopic stenting (9 vs 2; $p=0.34$).

**Chronic pancreatitis**

18. Fully covered SEMS therapy is associated with optimal resolution rate in BBSs caused by chronic pancreatitis.

Level of evidence: 1++

Recommendation grade: A

Level of agreement: A, 80%; B, 15%; C, 5%; D, 0%

Chronic pancreatitis is frequently associated with CBD strictures that require
endoscopic or surgical intervention. Endoscopic therapy is less invasive than surgery, and therefore is the preferred initial management for CP-related CBD strictures when malignancy can be excluded. However, CP-related CBD strictures are more difficult to treat endoscopically compared with other types of BBSs, particularly in patients with calcific CP. Biliary stenting with multiple plastic stents has been recommended to relieve biliary obstruction, but covered SEMSs are being increasingly used in the management of CP-related distal bile duct strictures due to their larger diameter and the lesser number of therapeutic ERCP sessions. Systematic review and meta-analysis of the literature showed that CSEMSs achieved a higher success rate (77%) than multiple plastic stents (30%) at 12-month follow-up in resolving CP-related biliary strictures. The median number of ERCP interventions with CSEMSs was significantly lower than multiple plastic stents (1.5 vs 3.9, P=0.002). In a recent prospective, multicenter, randomized study, Haapamaki et al, compared the effectiveness of single CSEMS with multiple plastic stents in 60 patients with CP-related CBD strictures. Patients were randomized to receive either a single 10 mm CSEMS or three 10F plastic stents initially. Another three 10F plastic stents were added to patients in plastic stent group at 3 months and all stents were removed at 6 months. The 2-year stricture free success rates were 92% in the CSEMS group and 90% in the plastic stent group (P=0.405). There was no significant difference with regard to stent migration rates between plastic stent group and CSEMS group. These results support CSEMSs as an effective therapy in CP setting with high long-term stricture resolution. Nevertheless, patients with chronic pancreatitis and significant calcification in the head of pancreas have an increased risk of not responding to endoscopic therapy, which may ultimately require surgical
management.

**PSC**

19. Differentiating benign strictures from CCA in PSC patients is crucial but challenging.

Level of evidence: 2++

Recommendation grade: B

Level of agreement: A, 70%; B, 25%; C, 5%; D, 0%

PSC is associated with an increased risk of CCA. However, early diagnosis of dysplastic change and localized CCA is difficult. Meta-analysis showed that endoscopic transpapillary brush cytology has a high specificity of 97% but a modest sensitivity of 43% for detecting CCA in patients with PSC. As a result, advanced cytological and newer endoscopic techniques such as cholangioscopy with biopsy, brush cytology with fluorescence in situ hybridization (FISH) and probe-based confocal laser endomicroscopy (pCLE) have been used and are likely to improve the sensitivity for the diagnosis of malignant biliary change. FISH is currently recommended with transpapillary tissue sampling to differentiate benign dominant strictures from malignancies, especially in patients with suspicious or atypical cytological diagnosis. The pooled sensitivity and specificity of FISH for diagnosis of CCA in patients with PSC were reported 68%, and 70%, respectively in meta-analysis. Cholangioscopy allows direct visualization of bile duct epithelial change, guides targeted biopsy of bile duct strictures, may increase diagnostic rate in suspicious
lesions when combined with narrow-band imaging, and therefore is considered superior to ERC for detecting malignant bile duct strictures.\textsuperscript{106} Arnelo et al prospectively assessed the clinical utility of single-operator per-oral cholangioscopy (SOPOC) guided sampling of biliary strictures in 47 patients with PSC. Sample quality was adequate in 98% of cytology brushings and 95% of the mini-forceps biopsies. The sensitivity, specificity, accuracy and negative predictive value were 33%, 100%, 96%, and 95%, respectively.\textsuperscript{107} Another recent prospective study showed that SOPOC acquired adequate samples for cytological and histological diagnosis in 82% and 91% of patients, respectively.\textsuperscript{108} In addition, pCLE can be used with cholangioscopy to visualize biliary epithelium. Limited data suggest that pCLE may have a high sensitivity and negative predictive value to exclude neoplasia in patients with PSC.\textsuperscript{109}

\textbf{20.} ERCP intervention is recommended for symptomatic PSC patient with dominant stricture by balloon or bougie catheter dilation without or with short-term stent placement.

Level of evidence: 2++

Recommendation grade: B

Level of agreement: A, 75%; B, 25%; C, 0%; D, 0%

PSC is characterized by progressive fibrotic inflammation and multifocal strictures of biliary tree leading to jaundice, cholangitis, deteriorating liver function and
decreased long-term survival rate.\textsuperscript{110} Although the optimal treatment of dominant bile duct strictures remains unclear due to the lack of randomized controlled trials, cumulative evidence supports the effectiveness of endoscopic intervention in symptomatic PSC patients with dominant strictures to relieve the obstruction and preserve liver function.\textsuperscript{111, 112} Limited data suggest that repeat endoscopic therapy could achieve longer survival time than predicted survival time in patients with PSC and dominant strictures.\textsuperscript{113} Gotthart et al prospectively evaluated the outcome of long-term endoscopic treatment in PSC patients. A total of 500 balloon dilations were performed in 96 patients with dominant biliary strictures and 5 patients underwent biliary stenting. Long-term follow-up results showed successful preservation of a functioning CBD in all patients with a 5-year and 10-year survival free of liver transplantation rate of 81% and 52%, respectively.\textsuperscript{39} Other long-term follow-up studies also indicated that repeated endoscopic therapy with balloon dilation and/or stenting appeared safe with acceptable low adverse event rates ranging from 1% to 4.3%.\textsuperscript{39, 110, 114}

IgG4-SC

21. For patients with IgG4-related bile duct stricture, ERCP with biliary stenting maybe unnecessary, unless deep obstructive jaundice or acute cholangitis occurs.
IgG4-associated cholangiopathy is an inflammatory disease that can be associated with autoimmune pancreatitis as well as other multiple systematic diseases.\textsuperscript{115} Patients with IgG4-SC can present with obstructive jaundice and intra- or extra-hepatic biliary strictures that are difficult to discriminate from other benign or malignant biliary strictures such as PSC and CCA. Moreover, IgG4-SC overlapping with PSC has also been reported.\textsuperscript{116} Response to steroid trial is supportive for the diagnosis of IgG4-SC in suspected patients. A small cohort study of 29 patients with IgG4-SC suggested that treatment responsiveness could be evaluated in more than 50% of patients by biochemistry and on MRCP or ERC as early as 1 to 2 weeks, but response was lower in the hilar or intrahepatic lesion.\textsuperscript{117} Corticosteroids are currently the mainstay of treatment in patients with confirmed or highly suspicious IgG4-SC with good response in most patients.\textsuperscript{118} Immunomodulators and biological therapy have been also reported effective.\textsuperscript{119} A prospective study of 23 patients with IgG4-SC by Sandanayake, et al reported 100% response a rate over 6 weeks of prednisolone treatment.\textsuperscript{120} In another prospective study of 24 patients with IgG4-SC conducted by Bjornsson et al, most patients (18, 75%) were treated with corticosteroids and 8 (33%) were treated with biliary stenting for a median time of 4 months. Ninety percent (9/10) of patients with elevated bilirubin improved after treatment and biliary stents could be removed in all after treatment.\textsuperscript{121} Biliary drainage is only performed in
selected cases with significant obstructive jaundice or acute cholangitis as a bridge therapy before patients having response to corticosteroids.\textsuperscript{122}

\textbf{Bilio-enteric anastomotic stricture}

22. In experienced hands, ERCP using balloon-assisted enteroscopy has acceptable success and adverse event rate in treating BBS with surgically altered anatomy.

Level of evidence: 1++

Recommendation grade: A

Level of agreement: A, 75%; B, 25%; C, 0%; D, 0%

Endoscopic treatment of BBS challenges endoscopists substantially in surgically altered anatomy such as Roux-en-Y gastric bypass, hepaticojejunostomy, and Whipple procedure, mostly due to the length of afferent limb, complicated angulation in anastomosis, and adhesion.\textsuperscript{123} In the last decade, single- and double-balloon enteroscopy (SBE, and DBE) have been applied to conquer the long distance and gain access to the bile duct.\textsuperscript{124,125} The short type DBE is even more preferred because of its shorter working length of 152cm which is compatible with most ERCP catheters. Literature has shown a high overall success rate of balloon enteroscopy assisted ERCP in surgically altered anatomy with acceptable adverse event rate. A recent meta-analysis of 15 trials with 461 patients showed that the
pooled success rates were 80.9% for SBE in reaching the biliary anastomosis or the papilla, 69.4% for obtaining a cholangiogram, and 61.7% for providing successful biliary interventions. A total of 32 (6.5%) adverse events occurred in 489 procedures including pancreatitis (n=11), bleeding (n=1) and perforation (n=4) but nearly half of enrolled studies reported no adverse events.\textsuperscript{125} Another systematic review analyzed 23 reports with 697 patients who underwent a total of 945 enteroscopy-assisted ERCP procedures including anastomotic stricture balloon dilation. The overall ERCP success rate was 74% and adverse events occurred in 32 procedures (3.4%).\textsuperscript{126} In a retrospective study of 32 patients with biliary-enteric strictures, Lee et al reported balloon dilation alone to be successful in 66% of patients with only 1 (5%) recurrence over a mean follow-up duration of 13.1 years.\textsuperscript{76}

References


23. Harris A, Chan AC, Torres-Viera C et al. Meta-analysis of antibiotic prophylaxis in endoscopic


42. 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. Gastrointest Endosc 2010;72:551-7.


51. Haapamäki C, Kylänpää L, Udd M et al. Randomized multicenter study of multiple plastic


113. Johnson GK, Saeian K, Geenen JE. Primary sclerosing cholangitis treated by endoscopic


123. Shimatani M, Takaoka M, Tokuhara M et al. Review of diagnostic and therapeutic endoscopic retrograde cholangiopancreatography using several endoscopic methods in patients with


Table 1. Definitions for evidence levels and recommendation grades used

<table>
<thead>
<tr>
<th>Levels of evidence</th>
<th>Grades of recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1++ High-quality meta-analysis, systematic reviews of RCTs, or RCTs with a very low risk of bias</td>
<td>A  At least 1 meta-analysis, systematic review, or RCT rated as 1++ and directly applicable to the target population or a systematic review of RCTs or a body of evidence consisting principally of studies rated as 1+ directly applicable to the target population and demonstrating overall consistency of results</td>
</tr>
<tr>
<td>1+ Well conducted meta-analysis, systematic reviews of RCTs, or RCTs with a low risk of bias</td>
<td>B  A body of evidence including studies rated as 2++ directly applicable to the target population and demonstrating overall consistency of results or extrapolated evidence from studies rated as 1++ or 1+</td>
</tr>
<tr>
<td>1- Meta-analysis, systematic reviews or RCTs with a high risk of bias</td>
<td></td>
</tr>
<tr>
<td>2++ High-quality systematic reviews of case-control or cohort studies; high-quality case-control or cohort studies with a very low risk of confounding, bias, or chance and a high probability that the relationship is causal</td>
<td></td>
</tr>
<tr>
<td>2+ Well-conducted case-control or cohort studies with a low risk of confounding, bias, or chance and a moderate probability that the relationship is causal</td>
<td></td>
</tr>
<tr>
<td>2- Case-control or cohort studies with a high risk of confounding, bias, or chance and a significant risk that the relationship is not causal</td>
<td></td>
</tr>
<tr>
<td>3 Non-analytic studies (eg, case reports or case series)</td>
<td></td>
</tr>
<tr>
<td>4 Expert opinion</td>
<td></td>
</tr>
</tbody>
</table>
C A body of evidence including studies rated as 1- or 2+ directly applicable to the target population and demonstrating overall consistency of results or Extrapolated evidence from studies rated as 2++

D Evidence level 2-, 3 or 4 or extrapolated evidence from studies rated as 2+

Table 2. Voting on recommendation

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Completely agree</td>
</tr>
<tr>
<td>B</td>
<td>Agree with some reservation</td>
</tr>
<tr>
<td>C</td>
<td>Disagree with some reservation</td>
</tr>
<tr>
<td>D</td>
<td>Completely disagree</td>
</tr>
</tbody>
</table>
Table 3. Summary of statements

<table>
<thead>
<tr>
<th>Topics</th>
<th>Statements</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>GENERAL PRINCIPLES</strong></td>
<td></td>
</tr>
<tr>
<td>Etiology</td>
<td>1. BBSs arise from diverse etiologies, most commonly post-operative injury and chronic inflammation (evidence level: 2++, recommendation level: B).</td>
</tr>
<tr>
<td>Diagnosis</td>
<td>2. The diagnosis of BBS should be made carefully by the combination of history review, cross-section imaging studies and endoscopic procedures. Histological diagnosis by cytology or biopsy, as well as long-term clinical follow-up are recommended to confirm the diagnosis (evidence level: 1+, recommendation level: A).</td>
</tr>
<tr>
<td></td>
<td>3. Non-invasive imagings such as MRCP and/or MD-CT are necessary before ERCP procedure, as it can provide useful roadmap and clarify the pre-procedure plan (evidence level: 1++, recommendation level: A).</td>
</tr>
<tr>
<td>Role of endotherapy</td>
<td>4. ERCP is the first-line interventional option for the management of most BBS patients with accessible papilla (evidence level: 2++, recommendation level: B)</td>
</tr>
<tr>
<td>Preparation</td>
<td>5. Prophylactic antibiotics should be administered in selected patients, such as those with complex hilar strictures, post liver transplantation and PSC (evidence level: 1++, recommendation level: A)</td>
</tr>
<tr>
<td>Biliary access</td>
<td>6. Negotiating the biliary stricture with guidewire requires reasonable skill from endoscopist &amp; assistant, and use of appropriate catheter and guidewire (evidence level: 4, recommendation level: D)</td>
</tr>
<tr>
<td>Dilation</td>
<td>7. Aggressive (balloon or bougie catheter) dilation is usually necessary for the management of severe BBSs, but particular caution should be taken during early post-operative period (evidence level: 4, recommendation level: D).</td>
</tr>
</tbody>
</table>
8. Balloon dilation alone, without subsequent stenting, is associated with a high rate of BBS recurrence (evidence level: 1++, recommendation level: A).

9. To place multiple plastic stents side-by-side for up to 1 year, using strategy of either several sessions with increasing number of stents or one session with maximal stents, has become current standard of care for the majority of BBSs (evidence level: 1++, recommendation level: A).

10. Placement of uncovered SEMS in patients with BBS or indeterminate biliary stricture is strongly discouraged (evidence level: 4, recommendation level: D).

11. Placement of fully covered SEMS has similar successful outcome to that of multiple plastic stents therapy, but requires less endoscopic sessions and shorter stenting duration in BBSs such as post-liver transplantation anastomotic biliary stricture (evidence level: 1++, recommendation level: A).

12. To improve the effectiveness of FCSEMS therapy, efforts should be attempted to prevent stent migration (evidence level: 2++, recommendation level: B).

13. Percutaneous approach may be useful in case of failed ERCP for "rendezvous" techniques and in patients with surgically alerted anatomy and inaccessible papilla (evidence level: 2++, recommendation level: B).

14. Surgery is a valid option in cases of complete transection or ligation of bile duct, in selected patients with unsuccessful to ERCP therapy (evidence level: 2++, recommendation level: B).

15. Novel techniques, such as magnetic compression anastomosis, intraductal bipolar radiofrequency ablation & biodegradable biliary stenting may have potential role in selected cases when conventional endoscopic and
percutaneous approaches are not successful (evidence level: 3, recommendation level: D).

BBS WITH SPECIFIC DISORDERS

Post-LT

16. ERCP therapy is the first-line management approach for the patients with anastomotic biliary stricture (ABS) and localized non-anastomotic biliary stricture (NABS). Earlier intervention provides better response (evidence level: 1+, recommendation level: A).

Surgical

17. Endoscopic therapy with biliary stenting is an effective approach for post-operative bile duct stricture with successful long-term outcome comparable to surgical repair (evidence level: 2+, recommendation level: C)

Chronic

18. Fully covered SEMS therapy is associated with optimal resolution rate in BBSs caused by chronic pancreatitis (evidence level: 1++, recommendation level: A)

PSC

19. Differentiating benign strictures from CCA in PSC patients is crucial but challenging (evidence level: 2++, recommendation level: B).

20. ERCP intervention is recommended for symptomatic PSC patient with dominant stricture by balloon or bougie catheter dilation without or with short-term stent placement (evidence level: 2++, recommendation level: B).

IgG4-SC

21. For patients with IgG4-related bile duct stricture, ERCP with biliary stenting maybe unnecessary, unless deep obstructive jaundice or acute cholangitis occurs (evidence level: 2+, recommendation level: C).

Bilio-enteric anastomotic stricture

In experienced hands, ERCP using balloon-assisted enteroscopy has high successful rate and acceptable adverse event rate in treating BBS with surgically altered anatomy (evidence level: 1++, recommendation level: A).
Table 4. Etiologies of benign biliary strictures

<table>
<thead>
<tr>
<th>Categories</th>
<th>Etiologies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lategenous</td>
<td>Liver transplantation</td>
</tr>
<tr>
<td></td>
<td>Cholecystectomy (open or laparoscopic)</td>
</tr>
<tr>
<td></td>
<td>Partial hepatectomy</td>
</tr>
<tr>
<td></td>
<td>Bilio-enteric anastomosis</td>
</tr>
<tr>
<td></td>
<td>Sphincterotomy</td>
</tr>
<tr>
<td></td>
<td>TACE</td>
</tr>
<tr>
<td></td>
<td>Radiation therapy</td>
</tr>
<tr>
<td>Inflammatory cholangiopathy</td>
<td>Acute or chronic pancreatitis of any etiology</td>
</tr>
<tr>
<td></td>
<td>Primary or secondary sclerosing cholangitis</td>
</tr>
<tr>
<td></td>
<td>IgG4-related cholangiopathy</td>
</tr>
<tr>
<td></td>
<td>Eosinophilic cholangiopathy</td>
</tr>
<tr>
<td>Ischemia</td>
<td>Hypotension</td>
</tr>
<tr>
<td></td>
<td>Hepatic artery thrombosis</td>
</tr>
<tr>
<td>Others</td>
<td>Papillary stenosis</td>
</tr>
<tr>
<td></td>
<td>Mirizzi syndrome</td>
</tr>
<tr>
<td></td>
<td>Portal biliopathy</td>
</tr>
<tr>
<td></td>
<td>Parasitic infection</td>
</tr>
<tr>
<td></td>
<td>Trauma</td>
</tr>
</tbody>
</table>
Cold injury
Table 5. Results of recently published series on endoscopic treatment of benign extrahepatic biliary strictures with FCSEMs

<table>
<thead>
<tr>
<th>Design</th>
<th>No. pts</th>
<th>Etiology (%)</th>
<th>Stent dwell time (mo)</th>
<th>Stricture Resolution (%)</th>
<th>f/u period (mo)</th>
<th>Adverse event rate (%)</th>
<th>Re (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Park et al. (2016)</td>
<td>19</td>
<td>GS (38.1), CP (35.1), PS (17.9), O (9)</td>
<td>3.1</td>
<td>77.4</td>
<td>32</td>
<td>30.8(M)</td>
<td>25.2</td>
</tr>
<tr>
<td>Saxena et al. (2015)</td>
<td>65</td>
<td>AS (6.5), BS (30), CP (24.3), PLTAS (13), PSC (7.3), PS (6.5), ID (6.5), O (8.1)</td>
<td>6.1</td>
<td>81</td>
<td>18.5</td>
<td>9.7(M), 4.1(C)</td>
<td>4.1</td>
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<tr>
<td>Haapamaki et al. (2015)</td>
<td>67</td>
<td>CP (100)</td>
<td>6</td>
<td>92</td>
<td>40</td>
<td>7 (M), 14 (C), 6.7</td>
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</tr>
<tr>
<td>Hu et al. (2014)</td>
<td>68</td>
<td>PS (28.9), PLTAS (66.7), CP (4.4)</td>
<td>8.6</td>
<td>91</td>
<td>18.9</td>
<td>2.2(Pan), 6.7</td>
<td></td>
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<tr>
<td>Kaffes et al. (2014)</td>
<td>52</td>
<td>PLTAS (100)</td>
<td>3</td>
<td>100</td>
<td>24.5</td>
<td>10(C), 0(M), 30(3/1) pts</td>
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<tr>
<td>Irani et al. (2014)</td>
<td>69</td>
<td>BEA (8.3), BS (9.7), CP (50.3), O (6.2), PLTAS (6.9), PS (7.6), PSC (2.8), PST (8.3)</td>
<td>6.5</td>
<td>66</td>
<td>3</td>
<td>11.7 (C), 3.4 (Pan), 8</td>
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</tr>
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</table>

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<table>
<thead>
<tr>
<th>Study</th>
<th>Type</th>
<th>Patients</th>
<th>PS (%)</th>
<th>GS (%)</th>
<th>CP (%)</th>
<th>PLTAS (%)</th>
<th>Mean</th>
<th>SD</th>
<th>Mean</th>
<th>SD</th>
<th>Mean</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kahaleh et al. (2013)</td>
<td>R</td>
<td>13</td>
<td>3.2</td>
<td>27.6</td>
<td>10.5</td>
<td>2</td>
<td>NA</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wagh et al. (2013)</td>
<td>P</td>
<td>23</td>
<td>6.0</td>
<td>96</td>
<td>18.8</td>
<td>39</td>
<td>16.7</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Tarantino et al. (2012)</td>
<td>P</td>
<td>62</td>
<td>3.2</td>
<td>90.3</td>
<td>15.9</td>
<td>24.2</td>
<td>7.1</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

Table 6. Endoscopic treatment of postoperative biliary strictures with CSEMS or multiple plastic stents

<table>
<thead>
<tr>
<th>Design</th>
<th>No.</th>
<th>Location or type of BBS (%)</th>
<th>Type of stent</th>
<th>Duration of stenting</th>
<th>Mean No. of PS inserted</th>
<th>Overall success rate (%)</th>
<th>Mean F/U period</th>
</tr>
</thead>
<tbody>
<tr>
<td>Saxena et al.(2015)</td>
<td>65</td>
<td>Extrahepatic (not hilum)</td>
<td>FCSEMS</td>
<td>Mean 24.4 +/- 2</td>
<td>86 (6/7 pts)</td>
<td>86.5</td>
<td>18.5 mo</td>
</tr>
<tr>
<td>Kahaleh et al.(2013)</td>
<td>49</td>
<td>Distal CBD</td>
<td>FCSEMS</td>
<td>Mean 95.5 +/- 4</td>
<td>91.6 (11/12 pts)</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Tarantino et al.(2012)</td>
<td>14</td>
<td>Extrahepatic</td>
<td>FCSEMS</td>
<td>Mean 97.6 d</td>
<td>100 (14/14 pts)</td>
<td>100 (14/14 pts)</td>
<td>15.9 mo</td>
</tr>
<tr>
<td>Tuvignon et al.(2011)</td>
<td>96</td>
<td>Type I (6.3), II (68.8), III (20.8), IV (4.2)</td>
<td>MPS</td>
<td>Median 1.9 +/- 0.</td>
<td>89</td>
<td>82.3</td>
<td>6.4 +/- 3 yr</td>
</tr>
<tr>
<td>Costamagna et al.(2010)</td>
<td>40</td>
<td>Type I (36), II (21%), III (17), IV (19), V (7)</td>
<td>MPS</td>
<td>NA</td>
<td>NA</td>
<td>88.6*</td>
<td>13.7 yr</td>
</tr>
<tr>
<td>Kuzela et al.(2005)</td>
<td>43</td>
<td>Type I</td>
<td>MPS</td>
<td>Median 3.4 +/- 0.</td>
<td>100</td>
<td>16.0 +/- 13.5 yr</td>
<td>11.1 mo</td>
</tr>
</tbody>
</table>


* Postsurgical, not included post-liver transplantation
£ Bismuth-lazardthes classification of postsurgical benign biliary strictures

§ Four patients (11.4%) had biliary stricture recurrence and 3 developed CBD stones

# Five died of unrelated causes
Abbreviations used in this paper:

ABS (anastomotic biliary strictures), APEC (Asia-Pacific ERCP Club), BBSs (benign biliary strictures),
CCA (cholangiocarcinoma), CP (chronic pancreatitis), CSEMS (covered self-expanding metal
stents), CT (computed tomography), DBE (double balloon enteroscopy), EUS (Endoscopic
ultrasound), EUS-FNA (EUS-guided fine needle aspiration), FCSEMS (fully covered self-expanding
metal stent), FISH (fluorescent in-situ hybridization), IDUS (intraductal ultrasound), IgG-4 SC
(IgG-4 related sclerosing cholangitis), LT (liver transplantation), MCA (magnetic compression
anastomosis), MPS (multiple plastic stents), MRI (magnetic resonance imaging), PCBDS
(post-cholecystectomy bile duct strictures), pCLE (probe-based confocal laser endomicroscopy),
PLTASs (post-liver transplant anastomotic strictures), PSC (primary sclerosing cholangitis), PTBD
(percutaneous transhepatic biliary drainage), SBE (single balloon enteroscopy), TPFB
(transpapillary forceps biopsy), US (trans-abdominal ultrasound)