

Endoscopic Management of Benign Biliary Strictures

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Abstract Benign biliary strictures are a common indication for endoscopic retrograde cholangiopancreatography (ERCP). Endoscopic management has evolved over the last 2 decades as the current standard of care. The most common etiologies of strictures encountered are following surgery and those related to chronic pancreatitis. High-quality cross-sectional imaging provides a road map for endoscopic management. Currently, sequential placement of multiple plastic biliary stents represents the preferred approach. There is an increasing role for the treatment of these strictures using covered metal stents, but due to conflicting reports of efficacies as well as cost and complications, this approach should only be entertained following careful consideration. Optimal management of strictures is best achieved using a team approach with the surgeon and interventional radiologist playing an important role.

Keywords Chronic pancreatitis · Cholecystectomy · Transplant · Hilar · SEMS · Stents · Dilatation · Confocal · ERCP · Cholangioscopy

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Introduction

Endoscopic retrograde cholangiopancreatography (ERCP) is commonly performed for the diagnosis and treatment of biliary strictures. A thorough understanding of etiologies, diagnostic techniques, and therapeutic options available is important for the interventional endoscopist.

Benign biliary strictures (BBS) have diverse etiologies which result in local inflammation or ischemia with secondary fibrosis and scarring (Table 1). Postoperative and inflammatory strictures are the most common causes of BBS. Surgical injury to the bile duct during cholecystectomy accounts for the majority of postoperative BBS, whereas chronic pancreatitis is the most common etiology for inflammatory biliary strictures. The diagnosis of biliary strictures is based on signs and symptoms of biliary obstruction and evidence of upstream biliary dilatation on imaging. Clinical presentation varies, depending on the severity of the biliary obstruction, from subclinical mild elevation of liver function tests to a complete cholestatic syndrome (jaundice, pruritus, dark urine, and white feces) with or without cholangitis. Delayed presentation up to several years after the initial insult can be seen with ischemic bile duct injury. A detailed history and identification of risk factors for causative diseases may facilitate diagnosis.

Routine imaging techniques such as computed tomography or ultrasonography can guide in stricture localization by identifying a transition point to dilatation. Subsequent confirmation of the biliary stricture and evaluation of stricture characteristics requires cholangiography. Magnetic retrograde cholangiopancreatography (MRCP) provides noninvasive accurate evaluation in most cases and can play an important role in planning of endoscopic therapy. ERCP is the gold standard diagnostic modality for evaluation of biliary strictures and has also emerged as the therapeutic intervention of choice for managing biliary strictures. This review focuses on the endoscopic management of BBS and

Table 1 Causes of benign biliary strictures

Causes	
Postoperative	<ul style="list-style-type: none"> • Cholecystectomy • Liver transplantation • Hepatic resection • Biliary-enteric anastomosis • Biliary anastomosis/reconstruction
Inflammatory	<ul style="list-style-type: none"> • Chronic pancreatitis • Primary sclerosing cholangitis • IgG4-related sclerosing cholangitis • Choledocholiathiasis • Vasculitides: SLE and ANCA-associated vasculitis
Other	<ul style="list-style-type: none"> • Traumatic • Infectious: recurrent pyogenic cholangitis, <i>Ascaris lumbricoides</i>, <i>Clonorchis sinensis</i>, <i>Opisthorchis viverrini</i>, tuberculosis, histoplasmosis, HIV • Ischemic: hypotension, hepatic artery thrombosis, portal biliopathy, TACE • Radiation • Mirizzi syndrome • ERCP related: biliary sphincterotomy and metal stenting

elaborates on optimal treatment strategies for the more common causes.

General Principles of Endoscopic Management

The primary goals of endoscopic management of BBS are diagnosis of the underlying etiology with exclusion of malignancy and provision of biliary decompression. Biliary decompression is critical to prevent secondary complications of cholestasis such as cholangitis and secondary biliary cirrhosis. The majority of BBS require multiple endoscopic interventions for sustained response or complete resolution, with high rates of relapse in particular subgroups such as chronic calcific pancreatitis [1, 2]. Surgical options should be considered in patients with refractory strictures.

Selective cannulation of the CBD during ERCP is the prerequisite for all diagnostic and therapeutic biliary procedures. Once biliary cannulation is achieved, important considerations include the choice of guidewire, the need and method of tissue sampling, the need and size of dilatation, the selection of stent (type, length, diameter), and whether unilateral vs. bilateral stenting will be attempted for hilar strictures. A biliary sphincterotomy is usually performed to enable the placement of multiple plastic stents and ensure biliary access on subsequent ERCPs.

Guidewire Passage

Guidewires are critical in maintaining biliary access, directing the catheter and stent into the correct segment, and can aid in minimizing contrast contamination of the biliary tree. Standard 0.035-in. guidewires are most commonly used to traverse BBS. Traversing tight strictures, however, may require specialized guidewires, such as those with an angulated tip, hydrophilic coating, or small diameter 0.021 and 0.018 in. There are numerous guidewires available with different characteristics; however, there exists a paucity of comparative data to guide the best choice of wire in traversing difficult strictures. The authors find that a hydrophilically coated guidewire is extremely useful in traversing difficult strictures. A stone extraction balloon may be inflated below the stricture while gently applying traction distally to help straighten the duct and allow for optimal guidewire passage and positioning. Additional options for traversing difficult biliary strictures include using a steerable catheter with a 3.9- to 4.9-Fr tapered tip or using angioplasty balloons mounted on 3-Fr catheters [3, 4]. In patients with complete biliary obstruction in whom guidewire passage is difficult, a rendezvous technique (via endoscopic ultrasound [EUS] or percutaneous transhepatic cholangiography [PTC]) or surgical approach should be considered.

A cholangiogram is obtained to confirm the stricture, further defining its characteristics, as well as estimate the diameter of the biliary ducts to aid in diagnosis of the underlying etiology and guide endoscopic management. Strictures involving the distal CBD can be related to disorders in the pancreatic head such as chronic pancreatitis (benign biliary stricture) and pancreatic cancer (malignant stricture). Hilar strictures are concerning for cholangiocarcinoma or an iatrogenic injury. Long strictures, particularly ≥ 14 mm in length or with irregular or asymmetric appearance, are more suspicious of a malignant process [5, 6]. Diffuse stricturing and sclerosis is concerning for a systemic inflammatory or infective cause.

Stricture Classification

Anatomic classification guides optimal management strategy. The most commonly used Bismuth classification is based on stricture location in relation to the confluence, whereas the Strasberg classification describes the anatomy and characteristics of the stricture (size and bile leakage) (Tables 2 and 3) [7, 8]. The endoscopic management of hilar and intrahepatic strictures is complex and technically more challenging, and may require PTC for management. In hilar lesions involving both left and right ducts, the endoscopic drainage of both lobes is not always possible. Reviewing high-quality cross-sectional imaging prior to endoscopic intervention is critical to ascertain which segments will benefit most from drainage.

Table 2 Bismuth classification for benign biliary strictures

Bismuth class	Location
I	>2 cm distal to hepatic confluence
II	<2 cm distal to hepatic confluence
III	At the level of the hepatic confluence
IV	Involves the right or left hepatic duct
V	Extends into the left or right hepatic branch ducts

The right lobe typically drains most of the liver, and decompressing the right hepatic duct usually provides the most clinical benefit. Assessing for lobar atrophy (<30 % of volume) on imaging may also guide management decisions.

Exclusion of Malignancy

Malignancy should always be considered and excluded in the management of biliary strictures. Tissue sampling is performed at the initial and subsequent ERCPs, most routinely via stricture brushing for cytology or endobiliary forceps biopsy with or without direct cholangioscopic visualization. Biliary epithelial brushings are usually obtained after biopsy or dilatation, but this approach has not consistently been proven to increase diagnostic yield [9, 10]. Bile duct brush cytology has relatively lower sensitivity than that of forceps biopsy (30–57 vs. 43–81 %, respectively); however, both have similar specificity ranging from 90 to 100 % [11–13].

Depending on the availability and expertise, several other endoscopic modalities can be used in cases where a definite diagnosis is not obtained on cholangiography and tissue sampling during ERCP.

Table 3 Strasberg classification for benign biliary strictures

Strasberg Class	Description
A	Injury to small ducts in continuity with biliary system, with cystic duct leak
B	Injury to sectoral duct with consequent obstruction
C	Injury to sectoral duct with consequent bile leak from a duct not in continuity with biliary system
D	Injury lateral to extrahepatic ducts
E1	Stricture located >2 cm from bile duct confluence
E2	Stricture located <2 cm from bile duct confluence
E3	Stricture located at bile duct confluence
E4	Stricture involving right and left bile ducts
E5	Complete occlusion of all bile ducts

Endoscopic Ultrasonography (EUS)

EUS is usually the next step and enables detailed visualization of the bile ducts, ampulla, head of the pancreas, and other surrounding structures such as lymph nodes with the advantages of permitting FNA and staging for malignant lesions. EUS findings of a pancreatic head mass, an irregular bile duct wall, or duct wall thickness of ≥ 3 mm have been associated with malignancy [14]. The pooled sensitivity and specificity of EUS without FNA in differentiating malignant from benign biliary obstruction were 78 and 84 % in a meta-analysis of nine studies (555 patients), whereas EUS-FNA has been shown to have a sensitivity and specificity ranging from 43–89 and 100 %, respectively [14, 15, 16, 17, 18]. The diagnostic yield of EUS-FNA is much higher for distal biliary strictures and in cases where a mass is visualized on EUS [18–21].

Cholangioscopy

Cholangioscopy enables the direct visualization of the bile duct strictures. Over last few years, single-operator direct peroral cholangioscopy using ultraslim pediatric or transnasal endoscopes or, more recently, wire-guided direct cholangioscopy (SpyGlass Direct Visualization System; Boston Scientific, Natick, MA) has become popular with increasing application in the evaluation of indeterminate biliary strictures. Aside from targeted biopsies, several cholangioscopic findings have been associated with malignancy including friability, irregular surface, and the presence of capillary sign or tumor vessel sign (irregularly dilated and tortuous vessels) in a bile duct stricture [16, 21–23].

The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy of single-operator cholangioscopy-directed biopsy ranges from 49 to 82, 82 to 100, 100, 72 to 100, and 75 to 82 %, respectively [16, 24, 25]. In one study, addition of peroral cholangioscopy to ERCP/tissue sampling was shown to significantly increase the sensitivity (from 78.1 to 93.4 %), NPV (from 68.6 to 100 %), and accuracy (from 78.1 to 93.4 %) in the diagnosis of malignant bile duct strictures without significantly impacting its specificity and PPV [26].

Confocal Laser Endomicroscopy (CLE)

Probe-based CLE (pCLE) uses a probe introduced through the working channel of the duodenoscope or cholangioscope which permits real-time histologic assessment by obtaining high-resolution images of the biliary epithelium [16, 21, 27, 28]. The Miami classification has been developed to identify criteria predictive of malignancy including thick dark bands (>40 μ m), thick white bands (>20 μ m), dark clumps, visualized epithelium, and fluorescein leakage [28, 29]. pCLE has

been reported to have high sensitivity (98 %) for detecting malignant strictures, and the combination of ERCP and pCLE has been shown to have a significantly higher accuracy compared with that of ERCP with tissue acquisition (90 vs. 73 %; $p=0.001$) [30•]. The Paris Classification including four descriptive features: vascular congestion, dark granular patterns with scales, increased inter-glandular space, and thickened reticular structure, has been recently suggested for diagnosing benign inflammatory strictures and to further improve the accuracy of pCLE [31]. Although studies have shown the increased utility of pCLE in the diagnostic work-up of indeterminate biliary strictures, its use is currently limited by the lack of availability and expertise, low specificity (60–70 %), and a poor to fair interobserver agreement even among experienced operators [31–33].

Stricture Dilation

The dilation of benign bile duct strictures by either balloon or bougie is typically performed before stenting and is particularly required before the placement of multiple large-bore plastic stents. The size of dilating balloon is determined by the size of the bile duct distal to the stricture. The dilating balloon is advanced over a guidewire across the stricture under fluoroscopic guidance and is maintained fully inflated for 30 to 60 s. Dilatation soon after biliary anastomosis (<30 days after surgery) carries a higher risk of dehiscence and resultant bile leak, so a less aggressive approach is recommended in this setting [34, 35]. In most cases, except in select cases such as dominant strictures in primary sclerosing cholangitis (PSC), the dilation of benign biliary strictures should be followed with stenting, as dilation alone is associated with the high recurrence rates of up to 50 % depending on the underlying etiology.

Stent Choice

Plastic Stents

Are still considered the stent of choice for most benign strictures, although self-expandable metal stent (SEMS) are increasingly being used for the treatment of benign strictures with some literature supporting their utility. Many different plastic stents are available with different stent characteristics varying in their construction material, coating (to reduce biofilm formation), length, angulation, and antimigration properties (to prevent the reflux of dietary fibers which contribute to occlusion), but studies have failed to establish consistent superiority of one type over another. One or two plastic biliary stents are initially placed side by side depending on the

stricture diameter and diameter of distal bile duct. Stent exchange and periodic dilation with the placement of the increasing number of stents (up to six) is performed every 3–4 months over the next 12–18 months. The placement of multiple side-by-side, large-bore plastic stents has been shown to improve long-term outcomes of BBS compared with one or two stents alone [36, 37•, 38]. In addition, multiple plastic biliary stent insertion in distal strictures might decrease the number of ERCP procedures as it has been shown to have a lower rate of obstruction at 6 months, because bile can flow along the grooves that lie between stents [39].

Metal Biliary Stents

SEM have the advantage of a larger expansion diameter with a narrow deployment system that does not require aggressive dilation before stent placement. Large diameter also minimizes the risk of stent occlusion resulting in the longer duration of stent patency and reduced need for frequent stent exchanges. Moreover, SEMs are appealing as they may require fewer ERCP procedures than that of plastic stents [40•].

Three main types of SEMS are available: uncovered, partially covered, and fully covered stents. Uncovered SEMS have a median patency of approximately 20 months, and reinterventions are frequently required to manage stent occlusion from reactive tissue hyperplasia. These stents are not recommended for benign disease because of problems with stent embedment making them nonremovable [41–43].

Fully covered SEMS (FCSEMS) have a full external covering to prevent stent occlusion from reactive tissue hyperplasia and tumor ingrowth, enabling the prolonged duration of patency and easy removal. Treatment with FCSEMS results in stricture resolution ranging from 60 to 100 % at the time of stent removal. There has been some concern about the development of strictures proximal to the stent especially with long indwell times. A significant additional drawback is the high rates of stent migration ranging from 5 to 40 % depending on the type of FCSEMS used. In addition, FCSEMS migration risk may be related to the patient population. In a recent large prospective multinational study including 187 patients with benign biliary strictures, the lowest stent migration rate was observed in chronic pancreatitis (CP) patients, which remained below 5 % at 6 months of indwell, increasing to 18.6 % by 12 months [44•]. This was significantly lower compared to the orthotopic liver transplantation (OLT) (74.7 % by 6 months) and cholecystectomy (CCY) groups (22.2 % at 6 months and 66.7 % by 12 months) [44•]. Stent migration can be partial distal, complete distal, or proximal and is associated with biliary reobstruction and failure of stricture resolution.

Partially covered SEMS (PCSEMS) have uncovered proximal and distal ends in an effort to decrease the rate of stent

migration but have been associated with difficulty in stent removal because of the increased risk of tissue embedment in the end portions [45].

It is important to appreciate that in the USA, currently all metal stents are FDA approved solely for the treatment of malignant strictures, and using them for benign diseases is a strictly off-label indication.

Management of Benign Biliary Strictures Associated With Specific Disorders

Chronic Pancreatitis

Distal CBD strictures are found in 10–30 % of patients with chronic pancreatitis [21, 46–52]. Patients with symptoms and/or signs of cholestasis should undergo surgical or endoscopic decompression to prevent cholangitis, choledocholithiasis, and secondary biliary cirrhosis [3, 21, 46, 51–53]. Surgical interventions offer a definitive solution but are associated with significant morbidity and mortality [54]. Therefore, endoscopic therapy has become the preferred option, especially in poor surgical candidates [3, 21, 51, 52, 54–56]. However, BBS secondary to chronic pancreatitis, particularly in chronic calcific pancreatitis, are more resistant to endoscopic therapy because of the resiliency of pancreatic fibrosis, resulting in the high rate of relapse and are unlikely to represent a long-term solution to this difficult problem [1, 2, 21, 51, 52, 54, 57–64].

The type of endotherapy does to some extent depend on the underlying pathophysiology, though more than one mechanism may contribute to the development of biliary stricture in CP patients. The vast majority of these strictures result from severe progressive fibrosis of the pancreatic head parenchyma due to recurrent acute or chronic inflammation, which compresses and narrows the distal CBD leading to permanent periductal fibrosis. Endotherapy involves endoscopic stenting with or without balloon dilation. CBD strictures resulting from periductal edema and secondary obstruction secondary to inflammation during an acute attack usually resolve spontaneously within a few days or weeks after the clinical onset. Biliary strictures caused by the extrinsic compression of the CBD from a pseudocyst, a pancreatic retention cyst, or a walled off pancreatic necrosis is usually temporary and best managed by the endoscopic drainage of the fluid collection. Lastly, CBD strictures can also be caused by pancreatic cancer and should always be carefully excluded, especially when the patient is seen for the first time or in case of a long-lasting disease [21, 50, 52, 54, 62–64].

For persistent BBS, temporary placement of simultaneous multiple, side-by-side plastic stents has become the current endoscopic standard of care as this has been shown to achieve

significantly improved long-term outcomes compared with placement of a single plastic stent [3, 21, 38, 46, 51, 53, 63, 65]. The exchange of plastic stents with an increasing number of stents is usually scheduled at 3-month intervals for a total stenting duration of 12 months without additional benefit with a more prolonged treatment [2, 38, 46, 51, 63, 65, 66]. However, recently, it has been suggested that with multiple, side-by-side plastic stents, the interval between stent exchanges may be extended to up to 6 months [39].

“Definitive” insertion of an uncovered SEMS without intended stent removal for benign biliary strictures has been largely abandoned due to the development of biliary epithelial hyperplasia that leads to late biliary obstruction [51, 63]. The increasing number of studies support the use of the temporary placement of “removable” covered SEMS with a migration of interest from partially covered to fully covered SEMS designs [44, 67, 68]. Spontaneous SEMS migration has been the main drawback with FCSEMS, with stent migration associated with a 78–82 % reduction in the odds of stricture resolution [44, 69]. New stent designs aiming to prevent migration including the adjunction of anchoring fins, the positioning of the stent covering on the internal side of the SEMS, and a flared ends design have been designed to address the problem of migration.

If FCSEMS are used to treat benign biliary strictures, a stenting duration over 3 months should be considered as this has been independently associated with stricture resolution in a multicenter trial that included 44 patients with CP-related benign biliary strictures [69]. Another recent large, prospective, multinational study evaluated the rate of stricture resolution and removal success of FCSEMS in 127 chronic pancreatitis patients after extended indwell. Of these patients, 82.7 % had prior plastic stenting. The overall stricture resolution rate was 79.7 % with a removal success of 80.5 % after median indwell periods of 11.3 months (IQR, 10.9–12.0 months) [44]. FCSEMS currently are the most promising alternative to multiple, side-by-side plastic biliary stents and are technically less complex and less demanding. Despite several advantages such as the reduced number of endoscopy procedures and a lower incidence of stent obstruction, FCSEMS need further improvements in their design as well as randomized trials before they can possibly be recommended as a first-line option for the endoscopic treatment of CP-related biliary strictures.

Postoperative Strictures

Postoperative benign biliary strictures occur most frequently after liver transplantation with a reported incidence of about 20 to 30 % [3, 21, 70–72]. Patients who undergo cholecystectomy, particularly via laparoscopic approach, are at the second highest risk of developing postoperative biliary strictures with the incidence of approximately 0.5 % [73–76].

Transplant Biliary Strictures

Bile strictures are one of the most common biliary complications following OLT and may present at a variable period of time after OLT, ranging from days to more than 2 years [70–72, 77]. Posttransplant biliary strictures are classified as anastomotic or nonanastomotic based on etiology and early (<30 days after OLT) or late based on the timing of stricture formation. Early strictures are generally related to perioperative events (excessive cautery, dissection, or tension of the duct anastomosis), surgical technique (hepaticojejunostomy), or donor-recipient CBD diameter mismatch and are mostly anastomotic. Late strictures are mainly caused by ischemic injury and fibrosis [71, 72, 78]. Endoscopic therapy is now widely accepted as the first-line management approach for posttransplant biliary strictures, with PTC and surgical bypass reserved for unsuccessful cases. In patients with Roux-en-Y anastomosis, ERCP may be more complex and technically challenging (with the use of balloon-assisted enteroscope, colonoscope, transgastric ERCP (via laparotomy or PEG), and PTC with dilatation) and catheter placement may be required if unsuccessful.

Anastomotic stricture is typically a single, short stricture in the mid-CBD which is caused by focal stenosis at the junction of the recipient's CBD with the donor's common hepatic duct. Anastomotic strictures account for up to 80 % of biliary strictures following OLT [79]. Early anastomotic strictures, developing within the first 1 to 2 months after OLT, are usually caused by local edema and inflammation and have an excellent response to endotherapy with stricture resolution over an average of 3 months and are less likely to recur [79, 80]. Late-onset anastomotic strictures, caused by fibrosis, often require a more protracted course of therapy. Balloon dilation to a maximal diameter of the duct up to 10 mm followed by plastic stenting reduces stricture recurrence by 62 to 31 % compared with that of balloon dilation alone [35, 81]. Furthermore, balloon dilatation with 3 monthly stent changes with the placement of the increasing numbers of side-by-side plastic stents seems to be the most effective approach, increasing the success rate to 80 to 90 % [35, 80, 81, 82, 83–88]. Small studies using fully covered metal stents have shown favorable results, however, further needing evaluation.

Nonanastomotic strictures (NAS), comprising 10 to 25 % of all post-OLT strictures, are typically more numerous, diffuse, proximal to the anastomosis, and often involve the hilum and intrahepatic biliary ducts [34, 89–94]. Majority of NAS are caused by biliary ischemia due to hepatic artery thrombosis or stenosis; therefore, evaluation with CTA, MRA, or Doppler ultrasonography should be considered and may require endovascular stenting, thrombolysis, or surgery for treatment [3, 94–97]. In addition, prolonged pretransplant ischemia time and ABO blood type incompatibility have also been

associated with the development of NAS [93, 94, 96, 98–100]. Long-term response to endoscopic therapy is low, ranging from 50 to 75 %, with up to 25 to 50 % of patients with NAS eventually requiring retransplantation or expiring [34, 53, 71, 72, 86, 93, 97, 101, 102]. In addition, NAS usually require more endoscopic interventions and a longer duration of therapy compared with that of anastomotic strictures [34, 53, 71, 72, 86, 93, 97, 101, 102]. However, the extraction of biliary sludge and casts and the dilatation of accessible strictures, followed by placement of plastic stents every 3 months, should be considered as first-line therapy or as a bridge to retransplantation if endoscopic therapy fails [3, 97].

Post-cholecystectomy

The incidence of bile duct injuries including postoperative biliary strictures have increased since the widespread application of laparoscopic approach to cholecystectomy [74–76]. Several factors contributing to post-CCY biliary stricture formation have been described including confusion of the cystic duct with the CBD (most common), biliary ischemia, unintentional application or extension of thermal injury, and excessive traction on the gallbladder neck [103]. The presentation can be delayed for several weeks to months after the surgery, particularly when related to ischemic injury. Endoscopic therapy is an effective first-line approach with success rates comparable to surgical repair. Most studies have reported a significantly higher rate of success with the insertion of multiple plastic stents exchanged intermittently every 3 months over a period of 6 to 18 months [3, 36, 37, 104–107]. A success rate ranging from 74 to 90 % at the end of the 12 months of treatment has been reported, with a relapse rate of 20 to 30 % within 2 years of stent removal.

Over the last few years, several studies have demonstrated successful use of covered SEMS in achieving the permanent dilation of postoperative biliary strictures including post-CCY strictures [44]. Although plastic stenting is currently the first-line approach, FCSEMS should be considered in patients with refractory post-CCY strictures or strictures associated with refractory bile leak [75].

Primary Sclerosing Cholangitis

Primary sclerosing cholangitis (PSC) is a chronic progressive inflammatory disorder characterized by the development of multiple, diffuse, fibrotic strictures, and the saccular dilations of the intrahepatic and extrahepatic bile ducts [3, 21, 53, 108, 109, 110–113]. The destruction of the intrahepatic and extrahepatic bile ducts through inflammation and fibrosis leads to cholestatic liver disease. However, endoscopic management is predominantly focused on the treatment of dominant strictures which can cause biliary obstruction in approximately 40–50 % of PSC patients [114–118]. A dominant

stricture is defined as a stenosis ≤ 1.5 mm in the common bile duct or ≤ 1 mm in the hepatic duct [119]. Malignancy always needs to be considered and excluded in the management of dominant strictures because patients with PSC have a 20 to 30 % risk of developing cholangiocarcinoma, particularly in the presence of a dominant stricture [3, 21, 109•, 120–122]. Imaging (CT and MRI/MRCP), serum tumor markers (CA19-9), brushing cytology, biopsy, and fluorescent in situ hybridization (FISH) in cytology samples have varying sensitivity and specificity and may be combined to yield higher accuracy. The expansion of dominant strictures by endoscopic balloon dilation to 6- to 8-mm diameter, usually over multiple sessions, is the standard endoscopic approach. Balloon dilation alone or dilation followed by endoprosthesis stent placement can achieve long-term clinical and biochemical (alkaline phosphatase $<1.5 \times$ ULN) response in around 80 % of cases and has also been shown to improve outcomes than predicted by the Mayo model of PSC [3, 21, 109•, 117, 121, 123–126]. Although there are no randomized controlled studies comparing these methods, endoscopic stenting following dilation compared with balloon dilation alone was associated with a higher rate of complications including stent occlusion and cholangitis in a large retrospective study [126]. Typically, short-term stenting for a duration as short as 10 days up to 6–8 weeks should be reserved for strictures in which dilation alone is unsuccessful [3, 21, 109•, 120]. The administration of prophylactic antibiotics during and after dilation and/or stenting for a minimum of 5 days has been recommended to reduce the risk of cholangitis [109•, 119].

IgG4 Cholangiopathy

IgG4 cholangiopathy, autoimmune cholangiopathy, or IgG4-related sclerosing cholangitis (IgG4-SC) is a systemic inflammatory condition characterized by an IgG4-positive lymphoplasmacytic infiltration resulting in sclerosing cholangitis. Most patients with IgG4-SC have associated autoimmune pancreatitis, whereas approximately 20 % of patients with autoimmune pancreatitis have IgG4-SC. Biliary obstruction from stricture formation can occur at any point in the biliary tree from primary bile duct inflammation or secondary to chronic inflammation or mass in the head of the pancreas from autoimmune pancreatitis. Biliary strictures in IgG4-SC may resemble benign strictures caused by PSC. IgG4-SC strictures are usually longer and more segmental and commonly involve the distal CBD but may be difficult to differentiate based on cholangiography alone. The presence of continuous as opposed to skip disease in the bile ducts, gallbladder involvement, and single-wall common bile duct thickness greater than 2.5 mm on MRI has been shown to favor a diagnosis of IgG4-SC over PSC [127]. Immunosuppression with corticosteroids remains the primary therapy with endoscopic management playing a supportive role.

Endoscopic stent placement can be performed to temporarily relieve jaundice while awaiting response to medical therapy.

Conclusion

Benign biliary strictures are an important and difficult challenge for endoscopists and biliary surgeons. There have been significant advances in the endoscopic diagnosis and management of these strictures over the past two decades. Understanding of the etiology as well as the exclusion of underlying malignancy is vital for the selection of the optimal therapeutic approach.

Currently, the placement of multiple plastic stents, possibly with endoscopic dilatation, is the current standard of care. Covered metal stents can be considered and, while attractive in many ways, possess significant limitations and in no way represent a panacea. It is also worth remembering that the use of metal stents in benign biliary strictures constitutes off-label use in the USA.

The value of good cross-sectional imaging prior to embarking on endoscopic therapy cannot be understated, and both the interventional radiologist and surgeon have important roles to play in difficult to access and refractory biliary strictures.

Compliance with Ethics Guidelines

Conflict of Interest Tarun Rustagi and Priya A. Jamidar declare no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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