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Current treatment of benign biliary strictures

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Abstract

Endoscopy is a widely used approach for the treatment of benign biliary strictures. Most common benign biliary strictures amandable to endoscopic treatment are post-cholecystectomy, dominant biliary strictures due to primary sclerosing cholangitis, biliary anastomotic strictures occurring after liver transplantation, and common bile duct strictures due to chronic pancreatitis. Surgery is a valid option in cases of complete transection or ligation of the common bile duct, in selected patients with benign strictures related to chronic pancreatitis, and in noncompliant patients. In any case, even in these patients, endoscopy should always be attempted, because it is safe and repeatable. Endoscopic treatment consists of passing the stricture and placement of at least one large bore plastic stent, followed by further sessions of stenting with multiple plastic stents. Temporary placement of multiple plastic stents is the recommended approach in patients with benign biliary strictures. Self-expandable metal stents have a larger diameter compared to plastic stents, and can be covered and uncovered. Placement of uncovered metal stents in patients with benign biliary strictures is strongly discouraged. However, covered self-expandable metal stents can be safely placed in selected patients.

Keywords Endoscopy, benign biliary strictures, surgery

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Introduction

The endoscopic treatment of benign biliary strictures (BBS) has become widely used in the last decade. Postoperative biliary injuries (mainly post-cholecystectomy), dominant biliary strictures in the setting of primary sclerosing cholangitis (PSC), biliary strictures occurring after liver transplantation, and common bile duct (CBD) strictures due to chronic pancreatitis can all be treated endoscopically. Other, less frequent, causes of BBS, which can be diagnosed and/or treated endoscopically, are listed in Table 1.

The incidence of iatrogenic injuries of the bile ducts has increased 2-3-fold (0.3-0.7%) after the advent of laparoscopic cholecystectomy [1-3]. This is mostly due to misidentification of anatomic structures during laparoscopic surgery, acute inflammation or fibrous adhesions in the gallbladder fossa, excessive use of electrocautery, inaccurate placement of clips, sutures and ligations [4].

Benign biliary strictures can also occur in 3-6% of patients after liver transplantation; when these strictures are anastomotic (choledocho-choledochostomy), they are amenable to endoscopic therapy [5].

In patients with advanced chronic pancreatitis, a symptomatic biliary stricture can be found in approximately 10-30% of the cases [4].

In the past, surgery was the treatment of choice for postoperative biliary strictures, and ERCP was limited to the diagnosis and definition of the level and extent of the stricture [6]. For BBS related to chronic pancreatitis, surgery is still considered the gold standard treatment [7].

BBS can also be approached percutaneously. However,

Table 1 Less frequent causes of benign biliary strictures

Ischemia of the bile ducts (including polyarteritis nodosa)
Post-sphincterotomy
Radiation therapy
Portal biliopathy
Post-treatment of biliary lymphoma
Papillary mucinous biliary tumor
Autoimmune pancreatitis
IgG4 involvement of the bile ducts
Abdominal trauma
Endoscopic injection sclerotherapy of duodenal ulcer bleeding
Post-radiofrequency ablation
Tuberculosis

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this approach is generally limited by the complication rates, discomfort due to longstanding indwelling catheters and high stricture recurrence rates [5,6]. Still, the percutaneous approach can be useful in case of failure of ERCP for "rendezvous" techniques and in patients with surgically modified anatomy and non-accessible papilla.

ERCP for the treatment of BBS is preferred over surgery and the percutaneous approach due to its low invasiveness, because it is more patient friendly, safer and repeatable.

Diagnosis

Biliary strictures may present with pain, jaundice, cholangitis, pruritus, or only with alteration of liver function tests. If left untreated, they can lead to secondary biliary cirrhosis [8].

Dilatation of the intrahepatic biliary tree or of the CBD can be found on ultrasound, but is not always present. MRCP can accurately delineate the biliary anatomy, site and length of the stenosis, being therefore very useful before ERCP for planning therapy [9].

Several diagnostic tools for assessment of biliary strictures and for intraluminal tissue characterization have been developed in the last years. These include intraductal ultrasound, peroral video-cholangioscopy and SpyGlass, Confocal Laser Endomicroscopy and Optical Coherence Tomography [10]. The majority of these techniques are still under evaluation in clinical trials.

Technique of endotherapy

After endoscopic sphincterotomy, the crucial step is to overcome the stricture with a guidewire. The stricture can be negotiated only if there is a continuity of the CBD. With some exceptions, in cases of complete transection or ligation of the CBD a surgical reconstruction is indicated. In postoperative stricture the negotiation of the stricture can be much more difficult than in tumors because the stenotic tract, even if short, can be asymmetric, angulated and rich in fibrous tissue. It is very important to choose the adequate guide wire according to the morphology of the stricture. Hydrophilic guidewires (0.035, 0.021 or 0.018-inch in diameter) with a straight or curved (J-shaped) tip are to be preferred.

Manipulation of guidewires requires patience, skill and optimal fluoroscopic imaging. Another hint is to make sure that the direction of the catheter and the wire are in the same axis as the stricture. This can sometimes be achieved by straightening the CBD by pulling an inflated stone extraction balloon just below the stricture. Straight or steerable catheters and papillotomes can also be useful in some cases to orientate the guidewire. To avoid false passages, manipulation of the guidewire must be very gentle, and should be done with a torque-device.

The aim of the first treatment session is the placement of at least one large bore (10 Fr) plastic stent.

In some cases dilatation of the stricture is therefore required. Balloon dilatation alone is immediately effective, but is considered inadequate "*per se*" because of a high restenosis rate (up to 47%) [11-13]. Pneumatic dilatations should be performed only in cases of effective need and only during the very first endoscopic procedure. It is very likely that the forceful disruption of the scar may add further traumatic damage to the tissue and consequential development of a new fibrotic reaction. This is why pneumatic dilatation should be avoided during further procedures, especially in plastic multistenting procedures.

Stent placement keeps the stricture open for a prolonged period, allowing scar remodeling and consolidation. In case the stricture has not been dilated enough to place a stent, insertion of a 5 or 6 Fr nasobiliary drain for 24 to 48 h is important to guarantee immediate biliary drainage. The nasobiliary drain acts as a mechanical dilator and at the next ERCP, stent placement is usually possible.

Treatment of BBS can be done with plastic stents and self-expandable metal stents (SEMS). Biodegradable biliary stents until now have been experimented only in animal models [14].

Benign strictures and types of stents

The choice of the type of stent is dependent mainly on the etiology of biliary stricture. For example, in patients with sclerosing cholangitis, balloon dilatation alone or short-term (2-3 weeks) placement of a single stent for a dominant CBD stricture can be sufficient. This is not the case for strictures related to chronic pancreatitis or iatrogenic strictures of the CBD, where the endoscopic treatment must be more aggressive and usually requires multiple stenting. Actually, placement of a single stent has produced unsatisfactory long-term outcomes in these settings [15].

Today, the standard endoscopic strategy for post-operative CBD strictures consists of the temporary simultaneous placement of multiple large bore plastic stents, over a period of one year [16,17]. Stent exchanges are usually done every three months, with progressive increment of the number of stents, until complete resolution of the stricture. Stricture recurrences can usually be successfully re-treated by ERCP [16,17]. The mechanism of action of multiple plastic stents is probably their "massaging" effect on the stricture, allowing it to adapt slowly to the increasing number of stents.

The European Society of Gastrointestinal Endoscopy (ESGE) recently published clinical guidelines for endoscopic biliary drainage [18].

According to ESGE guidelines, simultaneous placement of multiple plastic stents for benign strictures of the CBD is technically feasible in >90% of patients; endoscopy provides the highest long-term biliary patency rate in 90% of postoperative biliary strictures and in 65% of strictures related to chronic pancreatitis [18].

The main limitation of the multistenting strategy is the need for multiple ERCP sessions over the one-year period,

Table 2 Main causes of benign biliary strictures and the respective role of endoscopic treatment

	Balloon dilatation	Single stent	Multiple stents	Fully covered SEMS
Sclerosing cholangitis	+++	+	-	-
Post-cholecystectomy	-	-	+++	++
Post-OLT	-	-	+++	++
Chronic pancreatitis	-	+	++	+++

OLT, orthotopic liver transplantation; SEMS, self-expandable metal stents

which increases costs and may decrease patient compliance, which is of paramount importance for this type of treatment.

SEMS have a larger diameter compared to plastic stents and therefore, higher patency rate. The idea to use them for BBS has been proposed several years ago.

In a way to avoid ingrowth (tissue hyperplasia) and to make them easily removable, SEMS for this purpose must be partially, or even better, fully covered. On the other hand, the covering of metal stents can increase the risks of stent migration. Partially covered SEMS for BBS were used by Kahaleh *et al* [19]. SEMS were removed in 65 patients and stricture resolution was obtained in 90% at a median follow-up of 12 months after removal. In 14% of patients the metal stents migrated and in 9% there was mucosal hyperplasia at the level of the uncovered part of the stents.

Fully covered SEMS were placed by Mahajan *et al* [20] in 44 patients with BBS of various etiology. Stricture resolved in 83% of patients. Pancreatitis was the most important complication in this study, and occurred in 14% at stent placement and in 9% at stent removal. There were also one proximal and one distal stent migration.

In order to reduce the risk of migration of covered stents, the idea to make stents with anchoring flaps and flared ends have been studied by Park *et al* [21]. This stents were placed in patients with BBS of different causes. Nevertheless, stent migration was found in 33% of patients with stents with flared ends.

Recently, we published a case series of 17 patients with BBS related to chronic pancreatitis [22]. We placed unflared-end SEMS in 7 patients, but due to the high migration rate (100%) we changed the strategy and continued to place only flared-end SEMS (10 patients). However, even flared-end SEMS migrated in 40% of patients. In our case series, resolution of the BBS was found in 47% of the patients after a median follow-up time of 24 months.

Preliminary data of a multicenter study on the use of fully-covered SEMS in benign strictures have been recently reported by Devière *et al* in abstract form at the Digestive Disease Week 2012 [23]. The authors enrolled 187 patients with BBS related to chronic pancreatitis (CP), orthotopic liver transplantation (OLT) and biliary surgery, with mean follow-up after removal of 209 days. Overall stricture resolution was found in 82% (CP 86%, n=44; OLT 68%, n=15; post-cholecystectomy 100%, n=6) of the patients. The study is still ongoing, but results are however encouraging.

The respective role of the different strategies of endotherapy for BBS is shown in Table 2.

Conclusions

According to ESGE guidelines, in compliant patients with benign CBD strictures, temporary placement of multiple plastic stents is recommended. Placement of uncovered SEMS in these patients is strongly discouraged. Covered SEMS can be safely placed in selected patients.

Surgery is a valid option in cases of complete transection or ligation of the CBD, in selected patients with CP-related CBD stricture, and in noncompliant patients. In any case, endoscopy should be always attempted, because it is safe and repeatable.

Finally, endoscopists should bear in mind that those patients who do not present for ERCP at scheduled dates must be encouraged and contacted, in a way to avoid the risk of potentially fatal septic complications related to "forgotten" stents.

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