

**FABRIZIO FANELLI**

**Biliary Disease and  
Advanced Therapies  
using ePTFE/FEP  
Covered Stents**



**EDIZIONI MINERVA MEDICA**

ISBN: 978-88-7711-786-1

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# PREFACE

An adequate method of treatment for biliary neoplastic pathology has been unsuccessfully investigated for years and only recently mini-invasive techniques have started playing a role of primary importance in this field, even though there are many problems still unresolved, in particular concerning medium- and long-term results.

The introduction of e-PTFE covered stent-grafts has undoubtedly been taking a step forward in providing physicians with a valid tool for the treatment, although palliative, of malignant biliary pathology.

After the very good results initially gained, the use of these new devices has been extended to biliary benign disease, thus eliminating all the problems linked to the use of plastic stents.

The basic aim of this book is to give an overview of the biliary benign and malignant pathology and of the great potentialities that biliary e-PTFE covered stents have. Their use has been analyzed from any point of view, including their different endoscopic or interventional applications. Consequently, this book has been conceived not only for interventional radiologists, but also for endoscopists and surgeons as well as those physicians who have to deal with such diseases in their daily activity.

With this specific aim, some experts, with different backgrounds and experience, have been asked to collaborate in order to analyze the topic in all its aspects. A section of this book deals with the “how to do” description, and specifically addresses the youngest and the least experienced: this book can actually help them in their daily clinical activity and when performing procedures.

Our warmest thanks goes to Dr. Karel Caca, Dr. Adam Hatzidakis, Dr. Miltiadis Krokidis and Dr. Arthur Schmidt and to all the collaborators who, with their enthusiasm and competence, have actively participated in preparing this book.

We are grateful to W.L. Gore & Associates, which is always taking an active part in the educational field and scientific research, and which has kindly supported this project.

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# INTERVENTIONAL RADIOLOGY TREATMENT OF BENIGN BILIARY STRICTURES

*F. Fanelli, P. Lucatelli, C. Cirelli*

Biliary stricture represents a challenging clinical condition with an unknown incidence. Management of this pathology involves an extensive multidisciplinary team, including gastroenterologists, radiologists, interventional radiologists and surgeons.

Due to the lack of clinical manifestation in nearly 20% of patients or to its indolent course, the diagnosis of biliary stricture is often missed or delayed. Protracted and complicated course with life-threatening complications (e.g. ascending cholangitis, liver abscess, secondary biliary cirrhosis) may occur in up to 30% of patients with benign biliary strictures. Moreover, these patients require an intensive multidisciplinary management, and a longer term of in-patient stay on the ward which results in a significant increase in health care costs.

The accurate diagnosis of benign biliary strictures relies on a combination of both clinical, epidemiologic and imaging findings, and histopathological or cytological sample analysis.

## **BENIGN BILIARY STRICTURES**

### *Etiology of the stricture*

Benign biliary stricture can be the result of a wide spectrum of non-neoplastic causes. The most common cause of all benign biliary strictures is iatrogenic damage, accounting for nearly 80-85% of all case studies.<sup>1,2</sup> Of these, cholecystectomy (either open or laparoscopic) and orthotopic liver transplantation are the most common iatrogenic causes of benign biliary stricture.

Other causes of benign biliary stricture include chronic pancreatitis, primary sclerosing cholangitis (PSC), Mirizzi syndrome, autoimmune cholangitis associated with autoimmune pancreatitis, recurrent pyogenic cholangitis, chemotherapy-induced sclerosing cholangitis, and non-iatrogenic trauma (blunt and penetrating).<sup>3</sup>

### *Iatrogenic biliary strictures*

Since the introduction of open cholecystectomy (first performed in 1882)<sup>4, 5</sup> and laparoscopic cholecystectomy-VLC (first performed in 1985),<sup>6</sup> the incidence of bile duct injury and subsequent stricture formation in experienced hands has been quoted as between 0.1% and 0.2%<sup>7, 8</sup> for open surgery and between 0.2% and 2.8% for VLC.<sup>9-14</sup> The slightly higher complication rate of the laparoscopic approach has been classically related to the change from an easy-access surgical field with a three-dimensional view to a technique using video representation of a “remote control” procedure.

The most prevalent problem lies in correctly identifying the insertion of the right hepatic duct and its tributaries, in the attempt to ligate the cystic duct very close to the common bile duct (CBD) or in the inadvertent ligation of the CBD or common hepatic duct during the procedure. For this reason, most post-VLC strictures are located at the common hepatic duct or proximal CBD. Other risk factors apart from aberrant anatomy are acute cholecystitis, obesity, Mirizzi syndrome and fibrosis in Calot’s triangle.<sup>15-18</sup>

Local inflammation of the cystic duct can lead to fibrosis and scarring. Additional causes of strictures in patients who have undergone cholecystectomy include excessive traction on the gallbladder neck, electrocautery injury, biliary ischemia and extension of thermal injury applied to a correctly recognized common bile duct.<sup>16</sup>

Orthotopic liver transplantation (OLT) is the second most common cause of iatrogenic biliary stricture. Biliary complications are estimated in around 8-30% of patients who undergo OLT, and biliary stricture is the most common among these complications.<sup>19</sup> Biliary stricture can be classified as: early (<30 days) or late (>30 days) according to the time of appearance after OLT; this can also be divided, according to the location, into anastomotic or non-anastomotic.<sup>20</sup> The former usually occurs secondary to fibrosis and is less likely to be caused by ischemia from hepatic arterial stenosis;<sup>21</sup> the latter results from biliary ischemia induced by hepatic artery thrombosis, and stenosis.<sup>20</sup> Non-anastomotic strictures are localized at the hilum and could involve the intrahepatic ducts.<sup>22</sup> Multiple factors contribute to non-anastomotic strictures, including ischemic injury, donor hypotension during cardiac death, long ischemic times, and reperfusion injury.<sup>23-27</sup>

Transplanted patients could also suffer other causes of non-anastomotic biliary strictures, including the recurrence of primary liver diseases, such as PSC, or biliary infection.<sup>28</sup> Moreover during OLT, the donor’s biliary tract can also be injured, thus developing strictures, most often at the junction of the common hepatic and the intrahepatic ducts.<sup>29</sup>

Nearly 20% of bile duct injuries are recognized intraoperatively; clinical presentation with various degrees of biliary obstruction could occur within 1 week after surgery (one fourth of patients) or even within 1 month (nearly half of patients).<sup>2</sup>

### *Biliary stricture secondary to chronic pancreatitis*

The second most common cause, in terms of incidence of benign biliary strictures, is chronic pancreatitis, accounting for up to 10% of cases. Distal CBD strictures due to chronic pancreatitis are seen in 3-46% of patients, and are usually incidentally diagnosed following magnetic resonance cholangio pancreatography (MRCP).<sup>30</sup> Most biliary strictures in chronic pancreatitis are clinically insignificant and do not warrant therapeutic intervention.

The mechanism of action is an obstruction of the intrapancreatic CBD secondary to recurrent pancreaticobiliary inflammation, resulting in fibrosis. Pseudocysts can also cause biliary obstruction.

The classical clinical features are jaundice (transient or recurrent, 30-50% of patients), abdominal pain, abnormal liver function test results, recurrent cholangitis, secondary biliary cirrhosis, and choledocholithiasis.<sup>30, 31</sup>

Interventional approaches, either endoscopic or percutaneous, are reserved for patients with jaundice, cholangitis, or abnormal liver function test results.<sup>32-34</sup>

### *Primary sclerosing cholangitis*

Primary sclerosing cholangitis is a chronic inflammatory disorder of unknown cause characterized by an alternating pattern of stricture and dilatation of the biliary tree. The peak of incidence is in the third and fourth decades in men.<sup>35, 36</sup> Clinical features are non-specific constitutional symptoms such as fatigue, weight loss, and fever, often associated with inflammatory bowel disease (most commonly ulcerative colitis),<sup>37</sup> with cholestatic symptoms (pruritus, intermittent jaundice, and cholangitis) being an expression of advanced disease.<sup>38, 39</sup>

In most cases, PSC results in cirrhosis necessitating liver transplantation. Degeneration to cholangiocarcinoma occurs in 3.3-36.4% of patients.<sup>40</sup>

Medical management of PSC involves ursodeoxycholic acid and immunosuppressants such as steroids. Dominant strictures are treated with balloon dilatation.<sup>41-43</sup> The only curative treatment is liver transplantation, which is associated with excellent 1- and 5-year survival rates of 90% and 85%, respectively.<sup>44</sup>

### *Recurrent pyogenic cholangitis*

Recurrent pyogenic cholangitis, also known as Oriental cholangiohepatitis, is characterized by recurrent bacterial cholangitis, intrahepatic pigment stones, and biliary obstruction.

Epidemiologically, the disease is prevalent in Southeast Asia, but an increasing number of cases are being reported in western nations because of the immigrant population.<sup>45</sup>

Malnutrition and biliary parasitosis, such as ascariasis and clonorchiasis, are the two main factors that cause bacterial colonization of the biliary tree, recurrent inflammation, and stone formation.<sup>46, 47</sup> Due to the nature of the infection, a high rate of complications such as biliary fistulas, pancreatitis, hepatic abscesses, sepsis, and biliary cirrhosis are often seen in these patients, thus increasing the overall morbidity.

Typically, presentation is that of recurrent episodes of cholangitis characterized by fever, jaundice, right upper quadrant pain, and leukocytosis. The natural history of disease is highly variable, and some cases may eventually progress to end-stage liver disease. An estimated 2-6% of patients with recurrent pyogenic cholangitis may develop cholangiocarcinoma.

The goals of management of recurrent pyogenic cholangitis include the complete clearance of calculi from the biliary tract and an aggressive antibiotic therapy.<sup>48</sup>

Surgery is reserved for patients with significant parenchymal atrophy, multiple cholangitic abscesses, and concurrent intrahepatic cholangiocarcinoma.

### *Mirizzi syndrome*

Mirizzi syndrome is characterized by obstruction of the common hepatic duct due to impaction of a gallstone in the gallbladder neck or within a long cystic duct with low insertion. Mirizzi syndrome is rare, occurring in 0.1% of gallstone disease patients, with no sex or race predilection.<sup>49, 50</sup>

Mirizzi syndrome is classified into four types on the basis of the presence or absence of a fistula. Type I results from direct compression of the CBD without fistula formation. Types II, III, and IV result from erosion of the common hepatic duct.<sup>50</sup>

Common presenting symptoms include classical cholangitis symptoms such as fever, right upper abdominal pain, jaundice, and elevated liver function test results.

## *Portal biliopathy*

Portal biliopathy results from a mechanical obstruction of the biliary tract due to the large para- and epicholedochal venous plexus in patients with cavernous transformation of the portal vein, usually seen in cirrhotic patients.<sup>51</sup>

## *Miscellaneous causes*

Rare causes of benign biliary strictures include infections such as tuberculosis and non-infectious inflammatory entities such as sarcoidosis, inflammatory pseudotumor, xanthogranulomatous cholangitis, eosinophilic cholangiopathy, radiation, vasculitis (Wegener granulomatosis), and cystic fibrosis.

## *Classification*

The first classification for benign biliary strictures was proposed by Bismuth based on stricture location.<sup>52</sup>

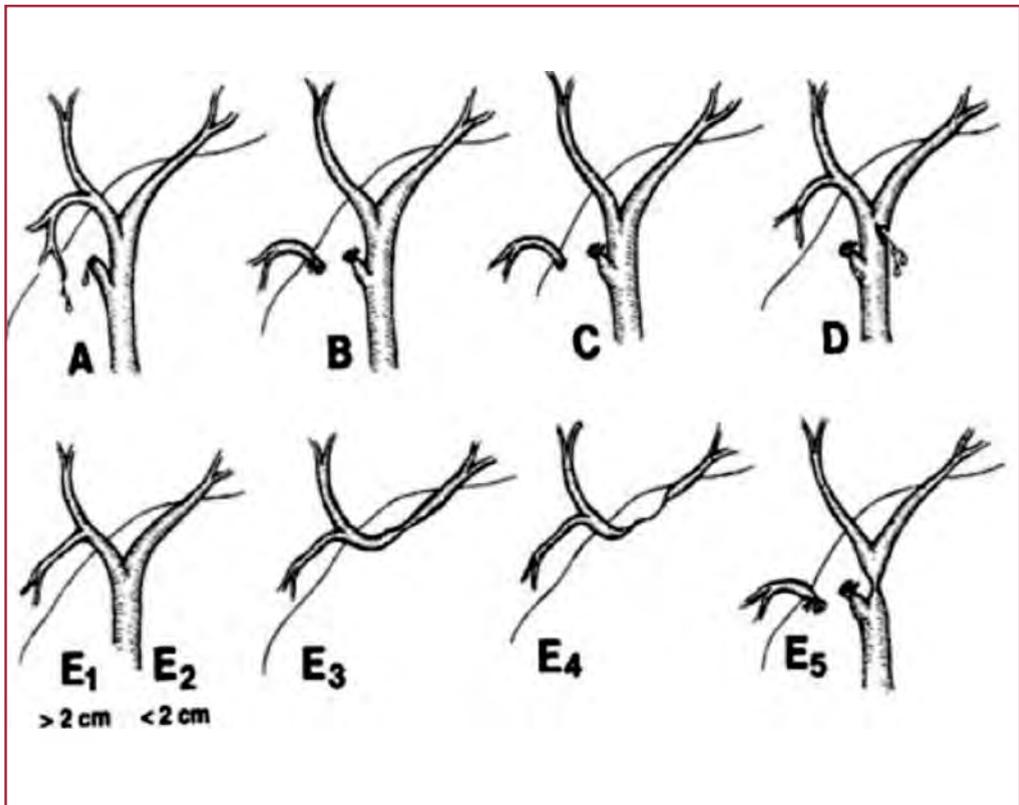
This classification is based on the lowest level where healthy biliary mucosa is available for anastomosis, allowing surgeons to select the best technique for repair. Type I strictures include a CBD stump longer than 2 cm; type II strictures have a CBD stump shorter than 2 cm; type III lesions have only the ceiling of the biliary confluence intact, while the right and left ductal systems communicate; type IV lesions have an interrupted biliary confluence, and separated bile ducts; while type V lesions are strictures of the hepatic duct associated with a stricture on a separate right branch.

Nowadays, the classification introduced by Strasberg is more frequently used (Table 1-I).<sup>53</sup>

This classification divides bile duct injuries into five groups (from A to E) where the E class corresponds to the Bismuth classification. Class A represents a bile leak from the cystic duct or an accessory duct. In both conditions, there is continuity with the common bile duct. Class B is the section of an accessory duct with no continuity with the common bile duct. Class C represents a leak from a bile duct with no continuity with the common bile duct. Class D is a partial section of a bile duct with no complete loss of continuity with the rest of the bile duct system. Class E is a complete section of the bile duct with subtypes according to the length of the stump (E1-E5: E1- Stricture located >2 cm from bile duct confluence; E2 - Stricture located <2 cm from bile duct confluence; E3 - Stricture located at bile

**Table 1-I. Strasberg classification of bile duct injury.**

Type	Criteria
A	Cystic duct leaks or leaks from small duct in the liver bed
B	Occlusion of a part of the biliary tree, almost invariably the aberrant right hepatic ducts
C	Transection without ligation of the aberrant right hepatic ducts
D	Lateral injuries to major bile ducts
E1	Low CBD stricture located >2 cm from bile duct confluence
E2	Proximal CBD stricture located <2 cm from bile duct confluence
E3	Stricture located at bile duct confluence
E4	Stricture involving right and left bile ducts
E5	Involvement of aberrant right sectorial hepatic duct alone or with concomitant stricture of the CBD

**FIGURE 1.1** Strasberg classification of bile duct injury.

duct confluence; E4 - Stricture involving right and left bile ducts; E5 - Complete occlusion of all bile ducts). This class also includes the loss of confluence and injury to accessory duct (Figure 1.1).

## CLINICAL FEATURES

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Clinically, benign biliary stricture can present a wide array of manifestations, ranging from completely asymptomatic individuals or those showing aspecific symptoms (e.g. fatigue, fever, etc.) to more specific ones: jaundice, pain, sepsis, abdominal distension, and abdominal colic due to retained bile duct stones.

The clinical manifestation strongly depends on the underlying cause of biliary stricture and its location. In cases of obstructive causes, symptoms are represented by jaundice, elevated levels of direct bilirubin and alkaline phosphatase and transaminase.

Moreover, sensitive parameters of hepatic synthetic function are levels of plasma albumin and clotting factors of the extrinsic pathway, as assessed by the prothrombin time (PT);  $\gamma$ -glutamyl transferase ( $\gamma$ -GT) is the most sensitive indicator of hepatocellular damage.

Strictures determine biliary stasis and gallstone formation, increasing the chance of bacterial colonization and infection and the consequent onset of recurrent cholangitis, which could be a potentially life-threatening condition.<sup>54</sup>

Currently, no good method exists for predicting the need for treatment in asymptomatic patients. Mild biochemical cholestasis may be monitored for a period of time; however, deterioration in liver function must prompt assessment for intervention. A multidisciplinary approach should be sought, as close collaboration between the surgeon, gastroenterologist and radiologist is required.

## DIAGNOSIS

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Ultrasound is the first-line imaging modality for the detection of biliary dilatation. It is highly sensitive for the detection of biliary obstruction and the level of obstruction (accuracy >90%); however, the accuracy of ultrasound for detection of the underlying cause is limited.<sup>55, 56</sup> Often, post-surgical patients are not compliant to long examination and surgical scars or free fluid around the liver could limit the visibility of the hepatic hilum. Moreover, not all patients are suitable for US examination, with obesity and interposition of bowel being the main limitations.

Multi-detector CT (MDCT) is the preferred second-line imaging because is fast, widespread in all centers, and able to detect the presence of biliary dilatation, the underlying cause of biliary obstruction, and complications such as cholangitis and intrahepatic abscess. Moreover, MDCT is able to differentiate

benign biliary strictures from malignant neoplasms. A malignant stricture is generally characterized by arterial and venous hyperenhancement, a wall thickness of greater than 1.5 mm, and associations with the presence of lymphadenopathy and/or metastases.<sup>57</sup>

Magnetic resonance cholangiopancreatography (MRCP) should be the preferred second line imaging modality due to its high resolution in the assessment of biliary tree damage and strictures. The main limitations are long examination times and the fact that it is not available in all centers. The sensitivity of MRCP for the diagnosis of biliary obstruction is up to 98%; however, its sensitivity to differentiate benign from malignant biliary strictures varies widely (30-98%).<sup>58, 59</sup>

On MRCP, typical malignant common bile duct strictures are shown as asymmetric strictures with a shouldered margin, whereas benign strictures tend to have smooth and symmetric borders with tapered margins.<sup>60</sup> Abrupt narrowing of the distal CBD in contrast to smooth tapering has traditionally been considered a sign of malignancy.

Endoscopic retrograde cholangiopancreatography (ERCP) is a third-line imaging modality; it is the gold standard investigation for the evaluation of biliary obstruction.

Nowadays, due to its invasive nature with associated risks (e.g. sedation, perforation etc.), ERCP is performed only with therapeutic intent because it could involve a wide variety of interventions such as: sphincterotomy, brush cytology, endobiliary fine-needle aspiration (FNA), forceps biopsy, balloon dilatation, and stenting.<sup>61-63</sup>

Endoscopic ultrasound and intraductal sonography are emerging techniques that have been shown to improve the accuracy of ERCP in differentiating benign from malignant strictures.<sup>64, 65</sup>

Positron emission tomography (PET) with 18F-FDG has been shown to be highly sensitive and specific for the differentiation of benign from malignant biliary strictures, with a sensitivity of up to 92.3% and specificity of up to 92.9%; however, this is only available in a few centers.<sup>66</sup>

Associated with all of these general findings, each underlying cause has different specific and characteristic features that have to be investigated.

In OLT patients, ultrasound may show intrahepatic biliary dilatation and may help to define the level of obstruction; Doppler evaluation of the hepatic arteries may reveal the underlying cause (e.g. hepatic arterial stenosis or thrombosis) in patients with non-anastomotic ischemic strictures. Contrast-enhanced MRCP helps to define the level of obstruction and to exclude occult malignancy.

Chronic pancreatitis manifests with various degrees of intra- and extrahepatic biliary dilatation with smooth tapering of the distal CBD. Evidence of chronic pancreatitis (*i.e.*, parenchymal atrophy, calcification, a dilated main pancreatic duct, or pseudocysts) supports the diagnosis of benign strictures related to chronic pancreatitis.

Primary sclerosing cholangitis classical imaging findings are multifocal intra- and extrahepatic biliary strictures with alternating areas of normal segments or minimally dilated segments, giving a “beaded” appearance on MRCP. Isolated involvement of the intrahepatic biliary system is seen in up to 28% of patients, whereas isolated extrahepatic duct involvement is rare.<sup>44</sup> Other typical findings are periportal edema (high T2 signal around the portal tracts), irregular areas of peripheral arterial hyperenhancement, and cirrhosis morphology (e.g. irregular margins, hypertrophy of left lobe etc.).<sup>67</sup> Imaging also plays a crucial role in the detection of PSC complications including choledocholithiasis and cholangiocarcinoma.<sup>40</sup>

Pyogenic cholangitis has typical findings, such as biliary dilatation and intra-ductal stones, that are usually detected on ultrasound, whereas contrast-enhanced CT and MRCP better evaluate the complete extent of disease including the presence of biliary dilatation, lobar atrophy, abscess, fistulas, or bilomas.<sup>68</sup>

Mirizzi syndrome is characterized by a large calculus impacted in the neck of a contracted gallbladder with dilatation of the biliary tree proximal to it and normal caliber CBD distal to it.

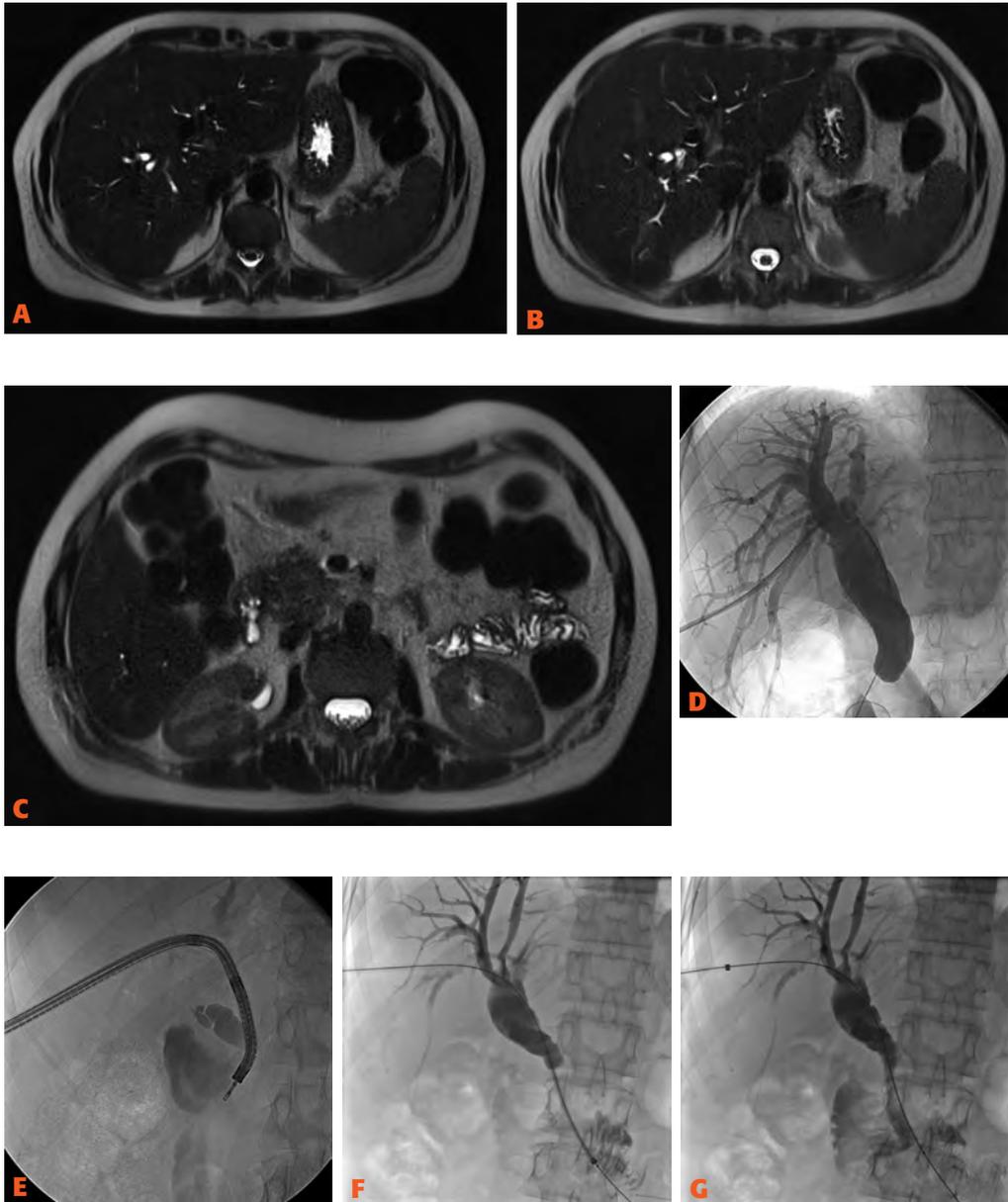
CT and MRCP are substantially used to exclude other causes of obstructive jaundice and exhibit similar findings.<sup>69</sup>

Ultrasound and CT shows cavernous transformation of the portal vein and biliary dilatation.

Single or multifocal smooth strictures of the CBD and central intrahepatic ducts are the most common imaging findings.<sup>51</sup>

The main imaging pitfalls are type I choledochal cysts that may mimic biliary strictures on imaging and may also induce biliary stricture formation due to recurrent infection and stone formation. The presence of moderate to severe fusiform dilatation of CBD without intrahepatic biliary dilatation is the key imaging finding that helps in differentiating a type I choledochal cyst from a distal CBD stricture.

Moreover, CBD cholangiocarcinoma, being a hypervascular thickening of the main biliary duct mucosa, could result in a patient with portal vein cavernoma being misdiagnosed for para- and epicholedochal venous plexus hypertrophy.



**FIGURE 1.2** C,C 54 years-old, female. Pervious cholecystectomy, then colectomy and Kehr's tube positioning. Diagnosis of benign biliary stricture in April 2011. A-C) Axial MRCP demonstrates intrahepatic dilation of the biliary tree, with no significant mass at the level of the pancreatic head. The etiology of benign stricture was suspected to be due to an iatrogenic injury, in July 2008. D) PTC was performed due to ERCP failure as a result of duodenal stenosis. Cholangiogram confirmed a distal CBD short stricture (1.7 cm), whose distance from the hilum was 4.8 cm. E) Percutaneous biopsy, which was negative for neoplasm, was performed under combined cholangioscopy and fluoroscopy guidance. F-G) Percutaneous deployment of 10 mm x 8 cm removable GORE® VIABIL® Biliary Endoprosthesis whose terminal end was placed trans-papillary.

## TREATMENT

The aim of treatment is to overcome the increased resistance to biliary flow offered by the reduction in bile duct lumen. According to Hagen-Poiseuille's law, the resistance to flow in a tube is inversely proportional to the fourth exponent of its radius, meaning that even only a small reduction in the lumen has a significant influence on drainage.

All different modalities of treatment aim to remove the strictured segment or increase its cross-section, thus reducing biliary stasis and the high risk of cholangitis.

Several treatment modalities are available to solve benign strictures: endoscopic, percutaneous interventional, surgical. The advantages of both endoscopic and percutaneous interventional techniques have brought about a shift from open surgery to minimally-invasive therapy.<sup>70</sup> The endoscopic approach is considered the first-line treatment, as this is the least invasive.<sup>1</sup> The percutaneous approach must be considered only when endoscopy fails or is not applicable (e.g. previous surgical biliary anastomosis is not reachable). Surgical management should be left as a bail-out treatment when all others fail.

### *Endoscopy*

See chapter 3.

### *Surgery*

Open surgery options to treat benign bile duct strictures are choledocho-jejunostomy (for distal strictures of the common bile duct), whereas a hepatico-jejunostomy is used as a treatment for high common hepatic duct strictures. In these cases, a loop of small bowel, usually in a Roux-Y configuration, is anastomosed directly to the liver hilum, where implantation of the left and right hepatic duct is performed.

These procedures are considered "major surgery", with important alterations of the enteric anatomy. Complications include bleeding, anastomotic stricture (5-27% of cases) and leakage, vascular injuries, side effects of general anesthesia, laparotomy and extended hospitalization; overall rates are quoted at around 25%.<sup>71,72</sup>

Modification of surgical techniques by positioning a blind-ending access loop to the anastomosis have been proposed to allow percutaneous intervention through this limb in case of recurrent strictures; this should particularly be con-

sidered in patients with high strictures and where surgery has been difficult, especially in patients with previous biliary bypass and where endoscopic access is not possible.

### **Interventional radiology: percutaneous transhepatic cholangiogram (PTC)**

PTC is used as the second option to access to the biliary system when ERCP has failed or is not applicable due to previous bypass surgery. Initial drainage is usually achieved via an internal-external catheter (percutaneous biliary drainage - PBD).

The only absolute contraindication to PTC/PBD is a significant coagulopathy which cannot be corrected. PBD should be avoided in those patients with diffuse polycystic liver disease, or diffuse metastatic disease, or in patients with hepatic cysts due to parasitic infections (e.g. *Echinococcus*).

PTC/PBD is considered an invasive procedure. Major risks are bleeding, sepsis, failure, fistulas, and biliary leaks. Preoperative laboratories such as coagulation, liver function should be carefully checked. Intravenous antibiotic prophylaxis is mandatory for both septic and non-septic patients. In non-septic patients, antibiotics are administered on the day of the procedure and continued for 24 hours after; in contrast, if a patient presents with clinical signs and symptoms of biliary sepsis, cholangitis intravenous antibiotics are started immediately upon admission.

The procedure is performed with the patient in the supine position, usually with intravenous sedation and analgesia with continuous physiologic monitoring (*i.e.*, blood pressure, pulse, and oxygen saturation).

According to the patient's features, the left subxyphoid approach or right mid-axillary approach could be selected to perform a cholangiography using a Chiba needle (21 G.). The biliary tree is identified by withdrawing the needle slowly under fluoroscopic guidance and injecting the contrast media. Once opacification of the biliary anatomy is achieved, multiple images are obtained to accurately define the anatomy. The biliary system can also be punctured under ultrasound guidance.

If a sufficient peripheral duct has not been entered, or the point of duct entry is unfavorable for advancement of a guidewire due for example to an angle that is too acute, a second "one-stick" needle will be used to target a more peripheral duct.

A hydrophilic guidewire (0.035") together with an angulated catheter is generally used to manage the stricture. Once the stenosed segment is passed, an internal/external drainage catheter (8-10 Fr) is positioned to achieve drainage. In case of

very severe stenosis, a bilioplasty, performed with a 6-8 mm balloon catheter, can be used to facilitate the catheter insertion. In case of a biliary stricture at the level of the hilum with separation of the right and left ductal systems, a bilateral PBD may be required.

Normalization of bilirubin is achieved in 70% of cases with a single procedure, and with repeat interventions this approaches 90%.<sup>73, 75</sup>

In case of strictures following liver transplantation, success rates are as low as 27%.<sup>76, 77</sup> Sclerosing cholangitis has the worst reported results (40% long-term success<sup>73</sup>), presumably due to the ongoing inflammatory process and the presence of multifocal disease.

Complication rates range between 25% and 54% including pleural puncture, pneumothorax, bilio-pleural fistula, gallbladder puncture, biliary leak, injury to the bowel or kidney, sepsis, and hemorrhage from puncture of the portal vein or hepatic artery.<sup>78-80</sup>

### *The role of stent*

Minimally-invasive approaches with percutaneous or endoscopic dilation are the most commonly used options to treat benign biliary strictures in order to avoid the need for the traditional surgical approach (bilio-digestive anastomosis). Several reports have shown how stent placement in the CBD is an alternative to surgery in terms of results.<sup>81-83</sup>

Endoscopic management, typically the first-line treatment, consists of dilation and insertion of one or more plastic stents. During follow-up, elective stent exchange (every 3-6 months) is performed to avoid cholangitis caused by stent obstruction.<sup>84</sup> Usually, an increasing number of plastic stents is progressively employed to dilate the stricture in the CBD. The major disadvantages of this method are the need for multiple invasive procedures that require sedation, the morbidity caused by stent dysfunction resulting in recurrent jaundice, and cholangitis.

For more details, see chapter 3 on endoscopy.

### *Plastic stent*

The use of plastic stents is limited by their clogging tendency, which leads to obstruction and the risk of migration. Obstruction is due to microbial colonization and biofilm formation inside the stent lumen, biliary sludge formation, and

duodenal reflux of food contents. The risk of plastic stent occlusion increases progressively after 3 months; therefore, stent exchanges must be scheduled every 3 months.

For more details, see chapter 3.

### *Metal stent*

Percutaneous or endoscopic placement of uncovered self-expandable Nitinol stents (SEMS) has been employed since 1991 in research trials in patients with postsurgical, chronic pancreatitis and postOLT, with reported clinical success rates of 59.6%, 80.4% and 50%, respectively.<sup>85-89</sup> Even though the median duration of stent patency is around 20 months, re-interventions are pretty frequent, mostly due to stent occlusion. Stent occlusion is usually due to mucosal hyperplasia.

Metallic stents have several limitations, and are generally not indicated in case of benign biliary strictures, due to the fact that they cannot be removed. Epithelial hyperplasia causes embedding of the stent into the bile duct mucosa, making removal difficult due to the risk of bleeding, or even impossible.<sup>90</sup>

The overall clinical success rate is higher for endoscopic placement of multiple plastic stents than uncovered SEMS.<sup>91</sup> Moreover, complications occur more frequently with uncovered SEMS than with the endoscopic placement of multiple plastic stents; therefore, uncovered SEMS should not be placed for benign disease.<sup>91</sup>

### *Partially covered metal stent*

Partially covered SEMS (PCSEMS) have been designed to prolong the duration of stent patency by preventing occlusion from reactive tissue hyperplasia and embedding of the metal wires into the tissue, thus permitting removability.

PCSEMS, uncoated at both ends, were used in several studies. Behm *et al.* enrolled 20 patients with benign biliary strictures secondary to chronic pancreatitis who were treated with PCSEMS. Stricture resolution was achieved in 90% of patients 6 months after stent removal and 80% were without stricture recurrence at a median of 22 months after PCSEMS removal. Complications occurred in 20% of patients and included stent migration, worsening pain and worsening pancreatitis.<sup>92</sup>

Chaput *et al.* studied PCSEMS placement in 22 patients with postOLT anas-

tomotic strictures; the treatment success rate was 86% with sustained resolution of strictures in 52% of patients. Stents remained in place for 2 months and were subsequently removed.

Complete stent migration was observed in two patients and partial migration was observed in one patient. All remaining stents were successfully removed, although in six cases this was challenging and required more than one procedure for removal.<sup>93</sup>

Finally, Kahaleh *et al.* reported a study that included 79 patients with benign biliary strictures secondary to multiple etiologies (chronic pancreatitis, biliary stones, OLT, cholecystectomy and inflammation) who underwent placement of PCSEMS.

The stents were left in place for a median of 4 months and patients were followed for a median of 12 months. An intention to treat analysis global success rate of 75% was achieved (higher in patients with strictures not related to chronic pancreatitis). Complications included postERCP pancreatitis (4%) and stent migration (14%).<sup>94</sup>

### Fully-covered metal stent

The fullycovered SEMS (FCSEMS) consists of an expanded polytetrafluoroethylene (ePTFE) and fluorinated ethylene propylene (FEP) tubular lining that is externally supported along its length by a Nitinol stent and incorporates radiopaque rings at both ends.

Temporary placement of FCSEMS has been tried in an attempt to avoid epithelial hyperplasia seen in patients who have received PCSEMS and that may cause difficult removal.<sup>95-97</sup> An acceptable clinical success rate is achieved after the removal of FCSEMS but long-term follow-up studies are needed to confirm these results. There is also some concern regarding FCSEMS because of the high migration rates seen with these stents (range 4.8-33%). However, a 2011 study of FCSEMS by Park *et al.*, including 43 patients with benign biliary strictures of different etiologies, reported that when stents with an anchoring flap as opposed to a flared end were used, no stent migration occurred (0% versus 33%, respectively). All stents were also removed without difficulty in this study.<sup>96</sup> Another study by Hu *et al.*, which included 13 patients with postOLT anastomotic strictures, showed an excellent treatment response rate (92% at a mean follow-up of 12 months) with the placement of a short FCSEMS with a stent retriever that exits the papilla of Vater. The stents were easily removed after a mean duration of 5.4 months.<sup>97</sup>

## Removal procedure

Removal procedure could be performed either endoscopically or percutaneously. For the endoscopic removal procedure, see chapter 3.

Percutaneous removal should be considered only when the endoscopic approach fails or is not feasible (e.g. biliary anastomosis, etc.). The procedure is carried out via a 12 Fr sheath with grasping forceps and/or snare where the stent-graft is withdrawn back into the sheath and then removed.<sup>98, 99</sup>

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