Benign Biliary Strictures Related to Chronic Pancreatitis: Balloons, Stents, or Surgery

Sami Arslanlar, MD
Rajeev Jain, MD

Corresponding author
Rajeev Jain, MD
Department of Medicine, Presbyterian Hospital of Dallas,
8230 Walnut Hill Lane, Suite 610, Dallas, TX 75231, USA.
E-mail: rjain@tddctx.com

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Opinion statement

Benign biliary strictures are seen in a subset of patients with chronic pancreatitis. Most patients are asymptomatic and require no intervention. In some patients, benign strictures can become symptomatic. In these patients, the aim of biliary drainage is to prevent long-term complications such as recurrent cholangitis and secondary biliary cirrhosis. The possibility of a malignant stricture should always be excluded. Successful endoscopic drainage of biliary obstruction has no influence on pain pattern in patients with chronic pancreatitis. At the first diagnosis of a symptomatic biliary stricture due to chronic pancreatitis, a polyethylene stent can be inserted endoscopically. If the stricture is still present despite stent exchange with serial insertion of multiple stents every 3 months for 1 year, surgery is indicated as definitive treatment. The role of self-expandable metal stents in the management of benign biliary strictures due to chronic pancreatitis is unclear, but they may be useful for nonoperative candidates and a select group of patients in whom surgery is planned. The aim of surgical therapy is to definitively treat the benign biliary stricture, especially in younger patients, who presumably have a longer lifespan.

Introduction

Chronic pancreatitis is an inflammatory disease characterized by progressive anatomic and functional damage to the pancreas. With repeated attacks of pancreatitis, the glandular parenchyma is replaced by fibrous scar tissue that can exert extrinsic pressure on the intrapancreatic portion of the common bile duct (CBD). The end result of this process is mechanical obstruction of the CBD. The incidence of CBD obstruction among patients hospitalized for chronic pancreatitis ranges from 3% to 23%, with a mean of 6% [1]. The highest incidence of biliary obstruction occurs in patients who have had an inflammatory mass in the head of the pancreas [1]. Most CBD strictures in chronic pancreatitis are clinically insignificant and do not require intervention [2••].

The anatomic relationship between the distal CBD and the head of the pancreas is the main factor responsible for biliary obstruction in patients with chronic pancreatitis. The CBD is completely ensheathed by the pancreas as it courses to the duodenum in 80% to 85% of people [1]. The other 15% to 20% will have their CBD located adjacent and immediately posterior to the pancreas. The pancreatic portion of the CBD is defined as the segment extending from the junction of the CBD with the superior margin of the duodenum at the level of the head of the pancreas to its point of entry into the duodenum. This portion of the CBD is frequently enveloped by a fibrous sheath joined to the pancreatic septae by fibrous cords. Extrahepatic biliary obstruction occurring concomitantly with chronic pancreatitis can be due to choledocholithiasis, periampullary cancer, pancreatic pseudocyst, or fibrosis. In chronic pancreatitis, fibrosis can cause concentric narrowing of the distal CBD. On endoscopic retrograde cholangiopancreatography (ERCP), the stricture associated with chronic pancreatitis can be seen as a long, smoothly tapered ste-

Table 1. Indications for biliary drainage in patients with chronic pancreatitis

Cholangitis
Biopsy evidence of biliary cirrhosis
CBD stones
Progression of the CBD stricture
Persistent high elevations of alkaline phosphatase and/or bilirubin for more than a month

CBD—common bile duct.
(*Adapted from* Frey et al. [3].)

Table 2. Summary of studies on benign biliary strictures in chronic pancreatitis treated with endoscopic biliary polyethylene stent insertion

Reference	Year	*n*	Long-term success, %	Follow-up, *months*	Stent dysfunction, %	
					Clogging	Migration
Deviere et al. [18]	1990	25	12	14	32	40
Barthet et al. [19]	1994	19	10	18	0	1
Smits et al. [20]	1996	58	28	49	36	4
Kiehne et al. [21]	2000	14	16	NM	36	NM
Vitale et al. [22]	2000	25	80	32	12	8
Farnbacher et al. [23]	2000	31	45	28	29	23
Eickhoff et al. [24]	2001	39	31	58	33	10
Catalano et al. [8•]	2004	46	41	48	0	13
Pozsar et al. [25]	2004	29	60	13	24	0
Cahen et al. [6•]	2005	58	38	45	48	2
Bartoli et al. [26]	2005	9	44	16	11	11

NM—not mentioned.

nosis throughout the intrapancreatic portion of the CBD. The proximal dilated duct often appears as a "bent knee" deformity superior to the pancreas. An "hourglass"- or "funnel"-shaped narrowing localized to the upper border of the pancreas is commonly found. The length of the stricture varies from 1 to 5 cm and depends on the length of the intrapancreatic portion of the CBD [1].

In patients with biliary obstruction from chronic pancreatitis, the most common presenting symptom is epigastric abdominal pain, which is often associated with weight loss, jaundice, nausea, vomiting, fever, chills, or pruritus. In patients who develop jaundice, the total bilirubin tends to rise and fall with each exacerbation of pancreatitis, and rarely does the total bilirubin remain above 10 mg/dL in chronic pancreatitis [3]. The incidence of both cholangitis and biopsy-proven biliary cirrhosis is 10% [1].

Benign biliary strictures secondary to chronic pancreatitis can be divided into two types: 1) reversible due to pancreatic edema or compression from a pseudocyst and 2) nonreversible due to pancreatic fibrosis. The hepatic damage caused by CBD stenosis due to chronic pancreatitis occurs in 6% to 29% of patients and can progress rapidly to fibrosis within as short a period of time as 11 weeks. Relief of the obstruction can have rapid effects on biochemical tests, as well as reverse histologic changes of secondary biliary fibrosis [1,4]. The indications for biliary drainage are listed in Table 1. The aim of biliary drainage is to prevent long-term complications such as recurrent cholangitis and secondary biliary cirrhosis. The possibility of a malignant stricture should always be evaluated by brush cytology, especially in an asymmetrical stenosis [2••]. Successful endoscopic drainage of biliary obstruction has no influence on pain pattern in patients with chronic pancreatitis, as CBD obstruction in the absence of cholangitis does not cause pain in patients with chronic pancreatitis [5•].

In patients with chronic pancreatitis who have a symptomatic CBD stricture, biliary drainage may be achieved by ERCP with stenting, percutaneous transhepatic biliary drainage (PTBD), or surgery. There are few data for the use of balloon dilation as sole therapy in patients with CBD strictures due to chronic pancreatitis. In patients with symptomatic biliary stricture due to chronic pancreatitis, endoscopic drainage with a polyethylene stent is indicated. A summary of studies on benign biliary strictures in chronic pancreatitis treated with endoscopic biliary polyethylene stent insertion is presented in Table 2. The success rate, defined as stricture resolution, is variable. Concomitant acute pain relapse at the time of biliary stenosis diagnosis is predictive of successful outcome in stricture resolution after stent removal due to pancreatic

Table 3. Summary of studies on benign biliary strictures in chronic pancreatitis treated with endoscopic biliary SEMS insertion

Reference	Year	Number of patients	Follow-up (mean), *months*	Patency, %
Deviere et al. [9]	1994	20	33	95
Kahl et al. [10]	2002	3	37	100
van Berkel et al. [11]	2004	13	50	75
Cantu et al. [12]	2005	14	22	37
Yamaguchi et al. [13]	2006	8	84	?

SEMS—self-expandable metal stent.

edema resolution [6•]; the presence of pancreatic calcifications is associated with a higher failure rate [7,8•]. One retrospective study demonstrated that multiple simultaneous stents were superior to single stent changes [8•]. If the stricture is still present despite stent exchange with serial insertion of multiple stents every 3 months for 1 year, surgery is indicated as definitive treatment. Self-expandable metal stents (SEMS) may be an option in patients who refuse or who are unfit for surgery. Also, SEMS may be useful as a "temporary bridge" to surgery in selected patients. In five published series, SEMS were deployed in patients with chronic pancreatitis and biliary stricture that did not respond to serial plastic stenting or in patients unfit for or unwilling to have surgery [9–13] (see Table 3). The success rate was quite variable (37%–100%), with lowest patency rate seen in the only study in which a covered SEMS was deployed [12]. PTBD should be reserved for patients in whom ERCP fails or those patients who for anatomical reasons are not candidates for ERCP.

Multiple surgical approaches are available for the treatment of CBD strictures due to chronic pancreatitis. The choice of surgical approach should be determined by patient characteristics and the associated complications of pancreatitis, such as pseudocysts. Hepaticojejunostomy is more appropriate than choledochoduodenostomy for younger patients with benign strictures due to chronic pancreatitis. Cholecystoenterostomy is a simpler operation than the choledochoenterostomy, but the failure rate is unacceptably high at 23% [1]. Overall, surgery has greater long-term success than endoscopic therapy, but surgery is associated with longer recovery and higher morbidity. Ultimately, the choice of therapy for benign biliary strictures in patients with chronic pancreatitis will depend on patient characteristics and local expertise.

Treatment

Diet and lifestyle

- Alcohol consumption should be avoided.

Pharmacologic treatment

- The main purposes of medical therapy for benign biliary strictures are to control pruritus related to cholestasis and to improve liver enzymes.
- Patients should avoid drugs that may worsen cholestasis (ie, cyclosporine, sirolimus, troglitazone, glibenclamide, COX-2, infliximab, fosinopril).
- Pruritus can be treated with cholestyramine, opioid antagonists, or sertraline [14,15].

Endoscopic therapy

- Polyethylene stents are indicated in patients with biliary strictures secondary to chronic pancreatitis as short-term drainage before surgery. Biliary strictures disappear in 8% to 15% of patients who undergo plastic stenting for 3 to 6 months. SEMS are a long-term option in high-risk surgical cases. SEMS could be considered a "bridge to surgery" in patients who refuse operation in first instance.

Getting over the stricture

- Standard 0.035-inch guidewires (ie, Teflon [DuPont, Wilmington, DE] coated) are adequate for most of the strictures due to chronic pancreatitis.
- If fibrosis makes strictures tight, it often is necessary to use smaller-caliber guidewires (0.021- and 0.018-inch).
- In tight or angled strictures, once the stricture is passed, it may be necessary to exchange the hydrophilic guidewire for a stiff or "super-stiff" guidewire in order to proceed with dilation and/or stent insertion.

Balloon dilation

Standard procedure	After a sphincterotomy is performed, a 4- to 12-mm pneumatic balloon is advanced over a guidewire across the stricture under fluoroscopic guidance. The balloon is inflated with a mixture of saline and radio-opaque contrast medium. The balloon is maintained fully inflated for 30 to 60 seconds, until complete disappearance of the waist on the balloon.
Contraindications	Lack of informed consent, coagulopathy (ie, International Normalized Ratio [INR] > 1.5), cardiopulmonary instability, duodenal obstruction.
Complications	ERCP-related complications such as acute pancreatitis, bleeding from sphincterotomy, perforation, and cholangitis.
Special points	There are few data for the use of balloon dilation as sole therapy in patients with CBD strictures due to chronic pancreatitis. Main use is for subsequent biliary stent placement. Small-caliber angioplasty balloons can be used for dilation with subsequent stent placement of biliary strictures that are refractory to standard endoscopic approaches because of the tightness of the stricture or other anatomic factors [16].
Cost effectiveness	Unknown.

Endoscopic stenting

Standard procedure	In patients with biliary strictures due to chronic pancreatitis, a single, large-bore polyethylene or plastic stent (10 F or 11.5 F) usually is inserted across the stricture. Patients with chronic pancreatitis are more likely to benefit from scheduled stent exchange every 3 months.
Contraindications	Lack of informed consent, coagulopathy (ie, INR > 1.5), cardiopulmonary instability, duodenal obstruction.
Complications	ERCP-related complications such as acute pancreatitis, bleeding from sphincterotomy, perforation, and cholangitis. Stent dysfunction such as clogging or migration occurs at significant rates (Table 3).
Special points	Concomitant acute pain relapse is predictive of successful outcome in stricture resolution after stent removal due to pancreatic edema resolution [6•]. The presence of pancreatic calcifications is an independent risk factor for the failure in biliary stricture resolution after plastic stent removal [7,8•].
Cost effectiveness	Stenting is probably cost effective for chronic pancreatitis patients considering that almost one fourth of them have resolution of the stricture after single-stent removal at more than 3 years of follow-up.

Endoscopic stenting with multiple stents

Standard procedure	In patients with biliary strictures due to chronic pancreatitis, multiple, large-bore plastic stents (10 F or 11.5 F) are inserted across the stricture. With each scheduled stent exchange, the stricture is reevaluated and stents are placed with the goal of increasing the number of or total diameter of stents placed in order to relieve the CBD stricture.
Contraindications	Lack of informed consent, coagulopathy (ie, INR > 1.5), cardiopulmonary instability, duodenal obstruction.

Complications	ERCP-related complications such as acute pancreatitis, bleeding from sphincterotomy, perforation, and cholangitis.
Special points	The placement of multiple biliary stents to achieve persistent stricture dilation after stent removal seems to have better results than standard single stenting [8•].
Cost effectiveness	Unknown.

SEMS

Standard procedure	After access to the bile duct is obtained, the SEMS is deployed across the stricture over a guidewire under fluoroscopic guidance. Covered and uncovered metal stents are available.
Contraindications	Lack of informed consent, coagulopathy (ie, INR > 1.5), cardiopulmonary instability, duodenal obstruction.
Complications	ERCP-related complications such as acute pancreatitis, bleeding from sphincterotomy, perforation, and cholangitis.
Special points	Covered and uncovered stents have similar patency.
Cost effectiveness	Unknown.

Surgery

- The aim of surgical therapy is to definitively treat the benign biliary stricture, especially in younger patients, who presumably have a longer lifespan.

Choledochoduodenostomy

Standard procedure	A side-to-side anastomosis between the bile duct and duodenum is created.
Contraindications	Unacceptable anesthesia risk.
Complications	Anastomotic stricture, cholangitis, "sump syndrome."
Special points	Considered the operation of choice, as the failure rate is approximately 2%.
Cost effectiveness	Unknown.

Roux-en-Y choledochojejunostomy

Standard procedure	An end-to-side anastomosis between the bile duct and jejunum is created.
Contraindications	Unacceptable anesthesia risk.
Complications	Anastomotic stricture, cholangitis.
Special points	Low failure rate of 2%, but an additional suture line is required. This operation may be preferred in younger patients to avoid the risk of "sump syndrome," or in those patients requiring concomitant pseudocyst drainage.
Cost effectiveness	Unknown.

Cholecystoenterostomy

Standard procedure	An anastomosis between the cystic duct and duodenum or jejunum is created.
Contraindications	Unacceptable anesthesia risk.
Complications	Anastomotic stricture, cholangitis, jaundice.
Special points	Although this is a simpler operation than the choledochoenterostomy, the failure rate is unacceptably high at 23% [1].
Cost effectiveness	Unknown.

Interventional radiology

Percutaneous transhepatic biliary drainage (PTBD)

Standard procedure	Under local and parenteral anesthesia, a needle is inserted through the right flank into a dilated intrahepatic biliary duct. The biliary system is

	opacified with contrast, and a catheter is advanced into the CBD and secured to external drainage.
Contraindications	Lack of informed consent.
Complications	Intra-abdominal hemorrhage, bleeding from the puncture site, catheter occlusion/dislodgement, bile leak, pneumothorax, hemothorax.
Special points	PTBD should be reserved for patients in whom ERCP fails or those patients who for anatomical reasons are not candidates for ERCP.
Cost effectiveness	Unknown.

Emerging therapies

- Self-expanding bioabsorbable biliary stents have been tested in animals and may be another possibility for the future endoscopic treatment of benign biliary strictures [17].
- Endoscopic ultrasound may help to identify those patients who would not benefit from stent placement, so that surgery can be pursued in a timely fashion.
- Investigational agents that have the potential to alter the course of pancreatitis may affect the development of chronic pancreatitis and subsequent biliary obstruction.

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have been highlighted as:
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