

Sphincter of Oddi Dysfunction: Introduction

Sphincter of Oddi dysfunction refers to structural or functional disorders involving the biliary sphincter that may result in impedance of bile and pancreatic juice flow. Up to 20% of patients with continued pain after cholecystectomy and 10–20% of patients with idiopathic recurrent pancreatitis may suffer from sphincter of Oddi dysfunction. This condition is more prevalent among middle-aged women for unclear reasons

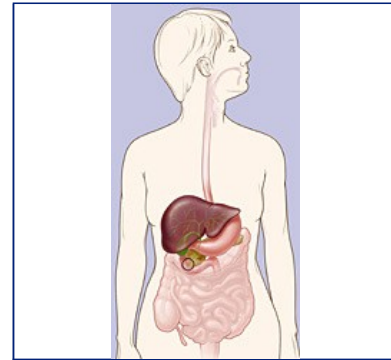


Figure 1. Location of the sphincter of Oddi in the body.

What is Sphincter of Oddi Dysfunction?

The sphincter of Oddi has three major functions: 1) regulation of bile and pancreatic flow into the duodenum, 2) diversion of hepatic bile into the gallbladder, and 3) the prevention of reflux of duodenal contents into the pancreaticobiliary tract. With the ingestion of a meal, the gallbladder contracts and there is a simultaneous decrease in the resistance in the sphincter of Oddi zone.

The sphincter of Oddi consists of circular and longitudinal smooth muscle fibers surrounding a variable length of the distal bile and pancreatic duct. There are three discrete areas of muscle thickness, or mini sphincters: the sphincter papillae, the sphincter pancreaticus, and the sphincter choledochus (Figure 2).

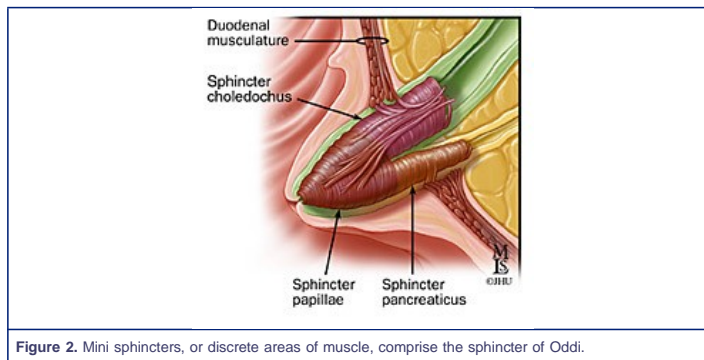


Figure 2. Mini sphincters, or discrete areas of muscle, comprise the sphincter of Oddi.

The major physiologic role of the sphincter is the regulation of the flow of bile and pancreatic juice. Cholecystokinin (CCK) and nitrates decrease the resistance offered by the sphincter. Laboratory studies observing the effects of numerous peptides, hormones, and medications on the sphincter have suggested a multifactor control mechanism for the sphincter of Oddi.

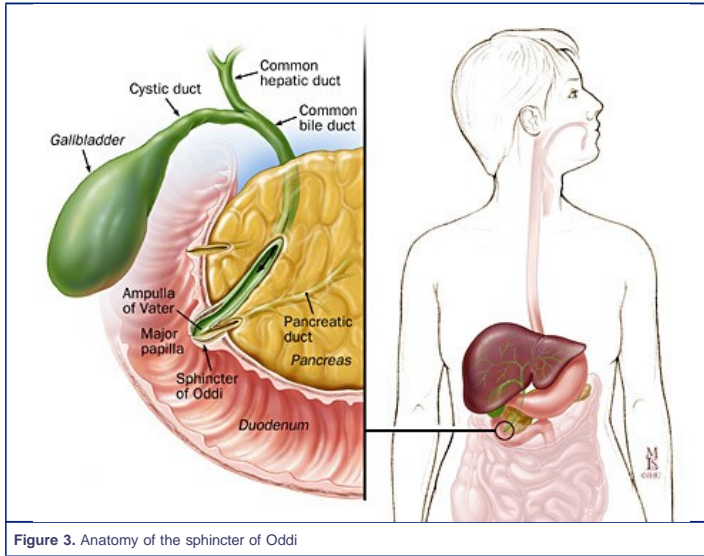
There are two types of sphincter of Oddi dysfunction: 1) papillary stenosis and 2) sphincter of Oddi dyskinesia. Papillary stenosis is a fixed anatomic narrowing of the sphincter, often due to fibrosis. Sphincter of Oddi dyskinesia refers to a variety of manometric abnormalities of the sphincter of Oddi.

Symptoms

The major presenting symptom in patients with sphincter of Oddi dysfunction is abdominal pain. The pain is characteristically sharp, postprandial, and located in the right upper quadrant or epigastrium. The pain may be associated with nausea and/or vomiting, may last for several hours, and may radiate to the back or shoulder blades. Fever, chills, and jaundice are uncommon symptoms. Patients may also present with acute recurrent pancreatitis.

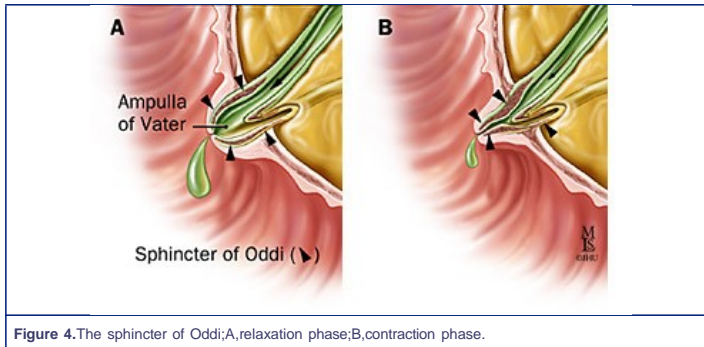
Sphincter of Oddi Dysfunction: Anatomy

The smooth circular muscle surrounding the end of the common bile duct (biliary sphincter) and main pancreatic duct (pancreatic sphincter) fuse at the level of the ampulla of Vater to become the sphincter of Oddi (Figure 3).



This musculature is embryologically, anatomically, and physiologically different from the surrounding smooth musculature of the duodenum. The normal appearance through the endoscope includes the major and minor papilla. The major papilla extends 1 cm into the duodenum with an orifice diameter of 1 mm. The minor papilla is 20–30 mm proximal and medial. Its orifice is tiny and may be difficult to identify. Dysfunction of this muscle may result in unexplained abdominal pain or pancreatitis.

The sphincter of Oddi is a dynamic structure that relaxes and contracts to change the dimensions of the ampulla of Vater (Figure 4).



Sphincter of Oddi dysfunction is a result of anatomic and physiologic abnormalities in the distal choledochus and sphincter. A variable length of the distal choledochus and the pancreatic duct are invested with circular and longitudinal smooth muscle fibers that interdigitate with the extra-ampullary muscle fibers of the duodenal wall to form the sphincter of Oddi. Mini sphincters, or three discrete areas of muscle thickness (sphincter papillae, sphincter pancreaticus, and sphincter choledochus), comprise the sphincter of Oddi.

Upon ingestion of food, the gallbladder contracts, with a simultaneous decrease in the resistance in the sphincter of Oddi zone. The sphincter of Oddi is an independent motor unit that has a high-pressure zone in the distal choledochus approximately 5 mm Hg greater than the pressure in the distal common bile duct. This zone is approximately 5–6 mm long. The basal pressure of the sphincter is 5–15 mm Hg greater than the common bile duct pressure, and 15–30 mm Hg greater than the pressure in the duodenum. Superimposed on this resting pressure are rhythmic phasic wave contractions at an amplitude of 50–150 mm Hg and a frequency of 2–5 contractions/minute.

The major physiologic role of the biliary sphincter is regulation of bile passage, with CCK and nitrates decreasing the resistance offered by the sphincter. Laboratory studies observing the effects of numerous peptides, hormones, and medications on the sphincter have suggested that there is a multifactor control mechanism of the sphincter of Oddi, and this mechanism is adapted to provide occlusive and propulsive influences on the flow of bile. Abnormalities in this control mechanism and/or process result in biliary colic.

Sphincter of Oddi Dysfunction: Causes

Overview

Papillary stenosis and sphincter of Oddi dyskinesia are the major forms of dysfunction (Figure 5).

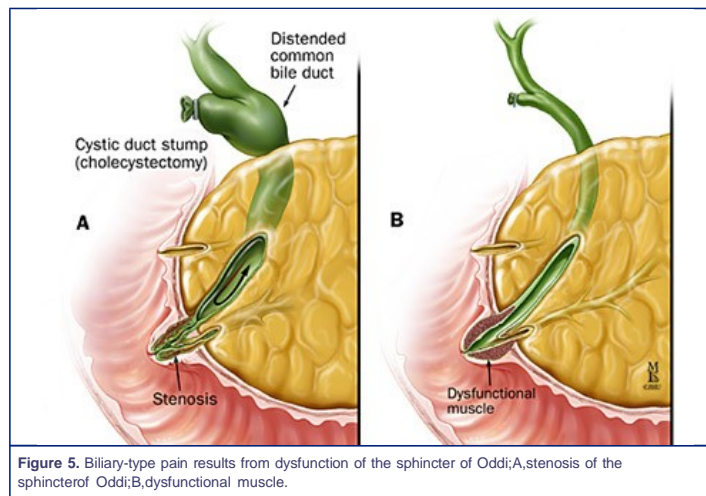


Figure 5. Biliary-type pain results from dysfunction of the sphincter of Oddi; A, stenosis of the sphincter of Oddi; B, dysfunctional muscle.

Papillary stenosis is a structural abnormality with partial or complete narrowing of the sphincter of Oddi due to chronic inflammation and fibrosis (Figure 5A). Overall incidence of papillary stenosis is 2–3%. Associated conditions thought to result in papillary stenosis include choledocholithiasis, pancreatitis, traumatic surgical manipulation, nonspecific inflammatory conditions, and rarely, juxtaampullary duodenal diverticula.

In sphincter of Oddi dyskinesia, functional abnormalities of the sphincter may result in biliary-type pain (Figure 5B). Up to one-third of patients with unexplained biliary pain, often in the setting of postcholecystectomy syndrome with normal extrahepatic biliary and pancreatic systems, have manometric evidence of sphincter of Oddi dysfunction. This type of dysfunction is caused by a paradoxical response to CCK, elevated baseline pressures, or an increase in the amplitude and frequency of the phasic contractions.

Postcholecystectomy Syndrome

Postcholecystectomy syndrome is the most common syndrome associated with sphincter of Oddi dysfunction, and occurs in approximately 20% of patients who have undergone cholecystectomy surgery.

Ampullary or Papillary Tumors

Tumors that involve the ampulla and/or the papillary orifice may also cause stenosis and resultant dysfunction of the sphincter of Oddi.

Sphincter of Oddi Dysfunction: Diagnosis

Overview

The diagnosis of sphincter of Oddi dysfunction is based on a high index of clinical suspicion in patients with persistent or recurrent biliary pain after cholecystectomy. The presence of abnormal biochemical tests of liver function and dilation of common bile duct is helpful in confirming sphincter of Oddi dysfunction. Noninvasive screening tests such as biliary scintigraphic and ultrasound studies are also useful. The gold standard for diagnosis of sphincter of Oddi dysfunction, however, remains sphincter of Oddi manometry.

The Milwaukee Biliary Group Classification of sphincter of Oddi dysfunction (Table 1) suggests categories based on clinical and laboratory findings. The Classification also predicts outcome from endoscopic sphincterotomy or surgical sphincteroplasty.

	Biliary-type pain	Abnormal LFTs (a)	Dilated CBD (b)	Delayed drainage (c)
Type I	+	+	+	+
Type II	+	One or two of above		
Type III	+	None of the above		

(a) ALT and AST levels are more than two times normal values on at least two separate occasions.

(b) Common bile duct diameter greater than 12mm on ultrasonography, or greater than 10 mm on cholangiography.

(c) More than 45 minutes at ERCP while patient in supine position.

Table 1. Milwaukee Biliary Group Classification for Biliary Dyskinesia

For Type II and III patients, endoscopic manometry is important to diagnose sphincter of Oddi dysfunction. Type I patients are believed to have papillary stenosis and may be treated without further investigations.

Laboratory Tests

Biochemical tests of liver function may be normal or may demonstrate moderate elevations of serum aminotransferases (at least two-fold). Tests of liver synthetic function are invariably normal in the absence of other disease.

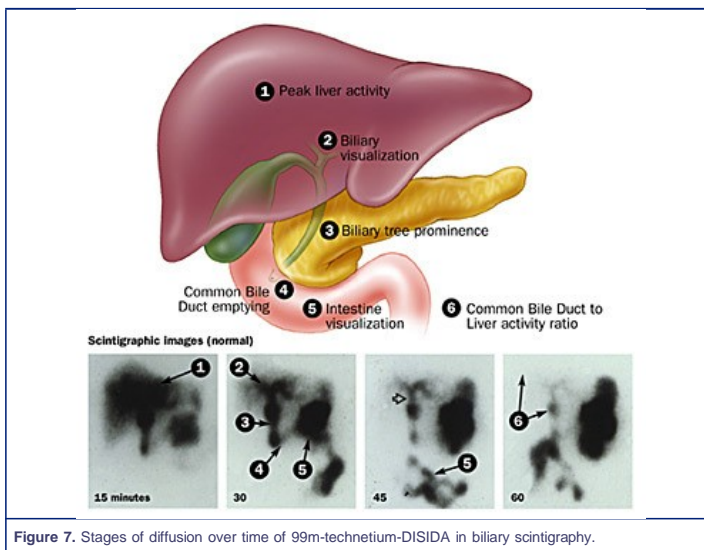
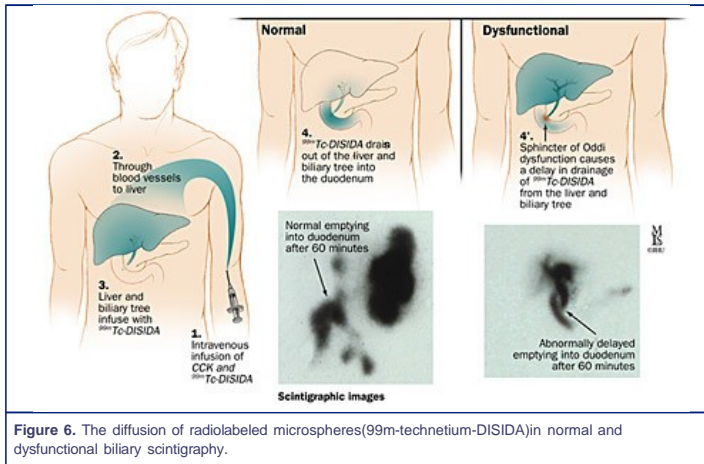
Noninvasive Diagnostic Studies

Biliary Scintigraphy

Dynamic hepatobiliary scintigraphy after stimulation with cholecystokinin has been utilized as a noninvasive tool in the early evaluation of sphincter of Oddi dysfunction. Researchers at Johns Hopkins developed a quantitative scoring system (Hopkins Scintigraphic Scoring System) utilizing multiple scintigraphic parameters (Table 2). A total score of 5 or greater is abnormal. This scoring system demonstrates correlations with 100% sensitivity and specificity with the manometric diagnosis of sphincter of Oddi dysfunction (Figures 7 and 8).

	Criteria	Score
1. Peak Time	a. Less than 10 minutes	0
	b. 10 or more minutes	1
2. Time of Biliary Visualization	a. Less than 15 minutes	0
	b. 15 or more minutes	1
3. Prominence of Biliary Tree	a. Not prominent	0
	b. Prominent major intrahepatic ducts	1
	c. Prominent small intrahepatic ducts	2
4. Bowel Visualization	a. Less than 15 minutes	0
	b. 15-30 minutes	1
	c. More than 30 minutes	2
5. CBD Emptying	a. More than 50%	0
	b. Less than 50%	1
	c. No change	2
	d. Shows increasing activity	3
6. CBD-to-Liver Ratio	a. $CBD_{60} < Liver_{60}$	0
	b. CBD_{60} higher than $Liver_{60}$ but lower than $Liver_{15}$	1
	c. CBD_{60} higher than $Liver_{60}$ and equal to $Liver_{15}$	2
	d. CBD_{60} higher than both $Liver_{60}$ and $Liver_{15}$	3

Table 2. Johns Hopkins Criteria for Scoring Scintigrams



Ultrasound

Fatty meal-stimulated ultrasound is used as a screening test for sphincter of Oddi dysfunction. In this test, dilation of the bile duct after a fatty meal suggests an obstruction to bile flow and sphincter of Oddi dysfunction. Unfortunately, the sensitivity and specificity of this test is low, so it is not widely used. More recently, secretin-stimulated endoscopic ultrasound has shown some promise, but results are still too preliminary to recommend widespread use.

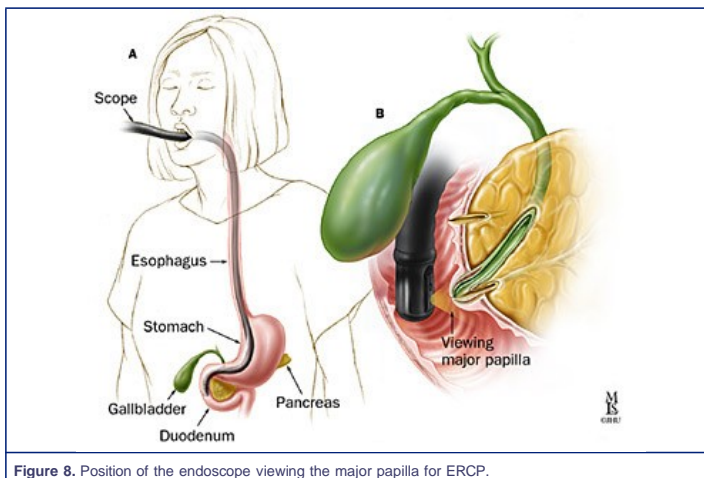
Secretin enhanced Magnetic resonance Cholangiopancreatography (MRCP)

Secretin is a hormone that results in increased secretion of pancreatic juice and hepatic bile and hence results in better visualization of the pancreaticobiliary ductal anatomy during MRCP. This method is attractive since it obviates the complications of ERCP and manometry. Preliminary studies have shown that it may be useful in patients with type II SOD dysfunction but more studies are needed before recommending widespread use of this modality.

Endoscopic Diagnosis

Endoscopic Retrograde Cholangiopancreatography (ERCP)

Endoscopic retrograde cholangiopancreatography (ERCP) is an endoscopic technique for visualization of the bile and pancreatic ducts. During this procedure, the physician places a side-viewing endoscope in the duodenum facing the major papilla (Figure 8).



The side-viewing endoscope (duodenoscope) is specially designed to facilitate placement of endoscopic accessories into the bile and pancreatic ducts. The endoscopic accessories may be passed through the biopsy channel (Figure 9) into the bile and pancreatic ducts.

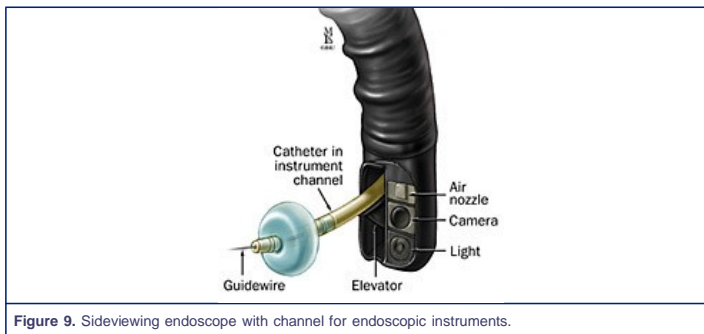


Figure 9. Sideviewing endoscope with channel for endoscopic instruments.

A catheter is used to inject dye into both pancreatic and biliary ducts to obtain x-ray images using fluoroscopy. During this procedure, the physician is able to see two sets of images: the endoscopic image of the duodenum and major papilla, and the fluoroscopic image of the biliary and pancreatic ducts (Figure 10).

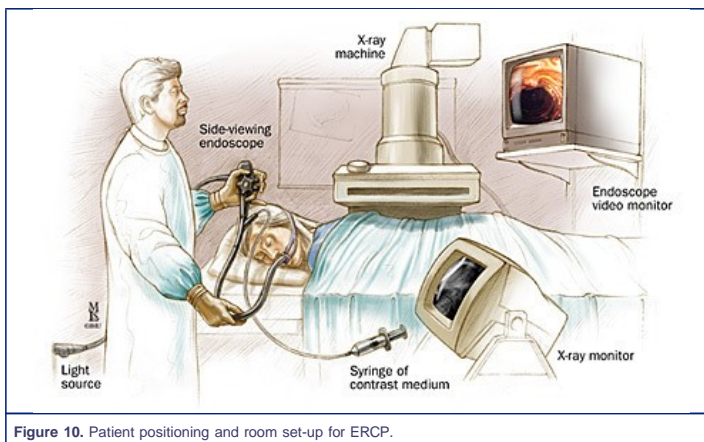


Figure 10. Patient positioning and room set-up for ERCP.

The scope is held in the left hand with the thumb operating up and down angulation. The index finger operates the suction and air/water operations. The right hand is responsible for advancing, withdrawing, and torquing the insertion tube. The right hand also operates left and right angulation of the scope and passes accessories through the instrument.

A variety of instruments can be utilized through the endoscope (Figure 10). Cameras may be attached for photo documentation and dual-examiner viewing. Video cameras may also be attached for full-color motion picture viewing during endoscopic procedures or for later review.

The gold standard for diagnosis is direct endoscopic manometry of the sphincter of Oddi. Retrograde cannulation of the sphincter with a water-perfused catheter records the amplitude and phasic contractions of the sphincter of Oddi. Manometric abnormalities include a basal sphincter of Oddi pressure greater than or equal to 40 mm Hg, increased amplitude of phasic contractions (greater than 240 mm Hg), increased frequency (greater than 10 contractions/min); or paradoxical response of the sphincter to CCK. Elevated basal pressure is the most reliable finding that predicts resolution of symptoms with sphincterotomy.

ERCP and Sphincter of Oddi Manometry

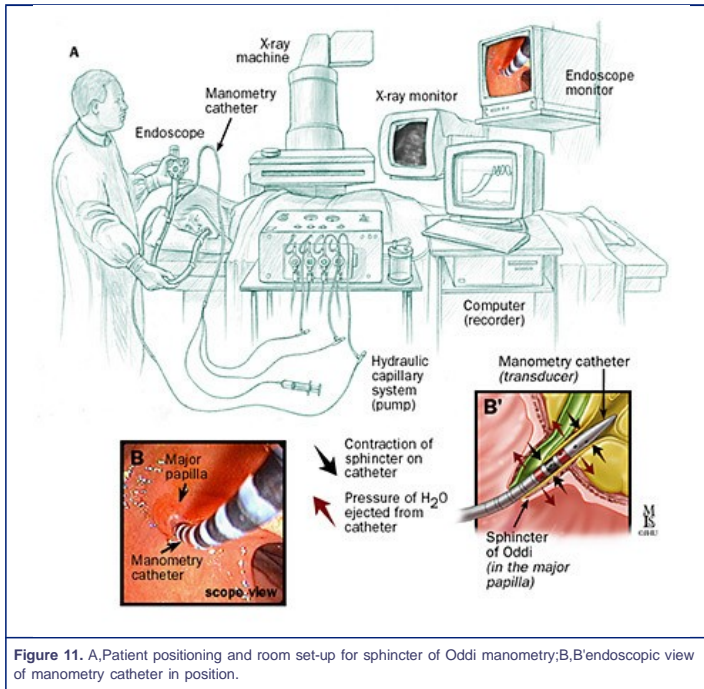


Figure 11. A, Patient positioning and room set-up for sphincter of Oddi manometry; B, B' endoscopic view of manometry catheter in position.

Manometry of the sphincter of Oddi requires a sophisticated system by which the motility pattern of the sphincter is recorded (Figure 11). Measurements are obtained using a special system of manometry catheters, a hydraulic capillary infusion system, and a computer software program. The fluid infusion system is of low compliance, allowing direct measurements of the sphincter of Oddi. The standard manometry catheters are triple lumen and made of polyethylene or Teflon. Each catheter lumen has an internal diameter of 0.5 mm, with three side holes at 2 mm intervals starting at 10 mm from the tip. The catheters, which are 200 cm long, have an outer diameter of 1.7 mm. The pneumatic capillary system perfuses de-ionized, bubble-free water at a pressure of 750 mm Hg and at a rate of 0.125 ml/min. Basal sphincter pressure, amplitude, frequency of contractions, and sequences of sphincter contractions may be obtained (Figure 12). Sphincter of Oddi dysfunction is diagnosed when the basal sphincter pressure is greater than 40 mm Hg.

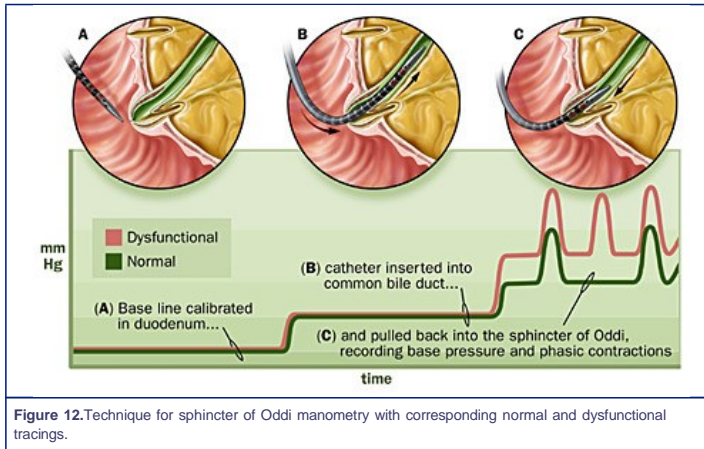


Figure 12. Technique for sphincter of Oddi manometry with corresponding normal and dysfunctional tracings.

Sphincter of Oddi Dysfunction: Therapy

Overview

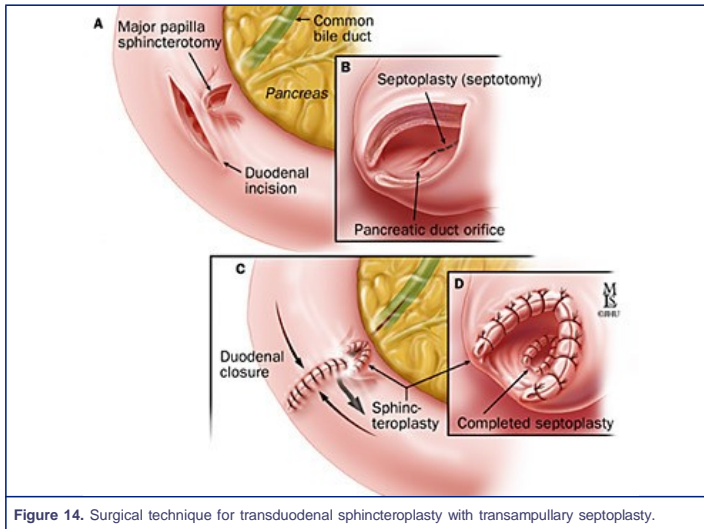
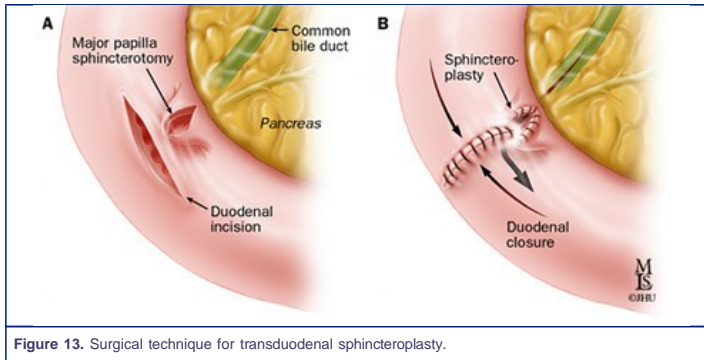
The goal of treatment is to reduce sphincter of Oddi pressure, thereby improving drainage of biliary and pancreatic secretions into the duodenum. This may be accomplished through medical, endoscopic, or surgical therapy.

Medical Therapy

Medical therapy for sphincter of Oddi dysfunction is an attractive approach mainly because it is noninvasive (as compared with endoscopic or surgical therapy), thereby avoiding the occasionally severe complications of sphincterotomy. Because the sphincter of Oddi is composed of smooth muscle, it is reasonable to assume that drugs that relax smooth muscle may be effective in patients with sphincter of Oddi dyskinesia and not in patients with papillary stenosis. Agents such as calcium channel blockers and long-acting nitrates have been shown to reduce sphincter of Oddi basal pressure and improve symptoms. However, there are several drawbacks to medical therapy. First, side effects may be seen in up to one-third of patients. Second, a response rate of only about 75% is expected in patients with the spastic-type of sphincter of Oddi dysfunction. Third, medical therapy utilizing muscle-relaxing agents is not expected to be effective in the patient with papillary stenosis.

Surgical Therapy

Surgical treatment consists of transduodenal sphincteroplasty with or without transampullary septectomy (Figures 13 and 14). This procedure has shown long-term benefit in follow-up at 1–2 years in uncontrolled trials.



There are no randomized trials comparing surgical sphincteroplasty with endoscopic sphincterotomy.

Endoscopic Therapy

Endoscopic Sphincterotomy

Endoscopic sphincterotomy is the current standard of therapy for sphincter of Oddi dysfunction (Figure 15, A-D). Controlled studies document the short-term and long-term efficacy of endoscopic sphincterotomy with relatively low morbidity and mortality rates. The presence of an elevated basal sphincter pressure appears to predict good benefit from sphincter ablating procedures. In appropriate situations, benefits of endoscopic sphincterotomy are greater than 90%, with good results in long-term follow-up. Because of the high complication rate of pancreatitis after endoscopic sphincterotomy for sphincter of Oddi dysfunction, prophylactic short-term pancreatic stenting is recommended, and often yields good results.

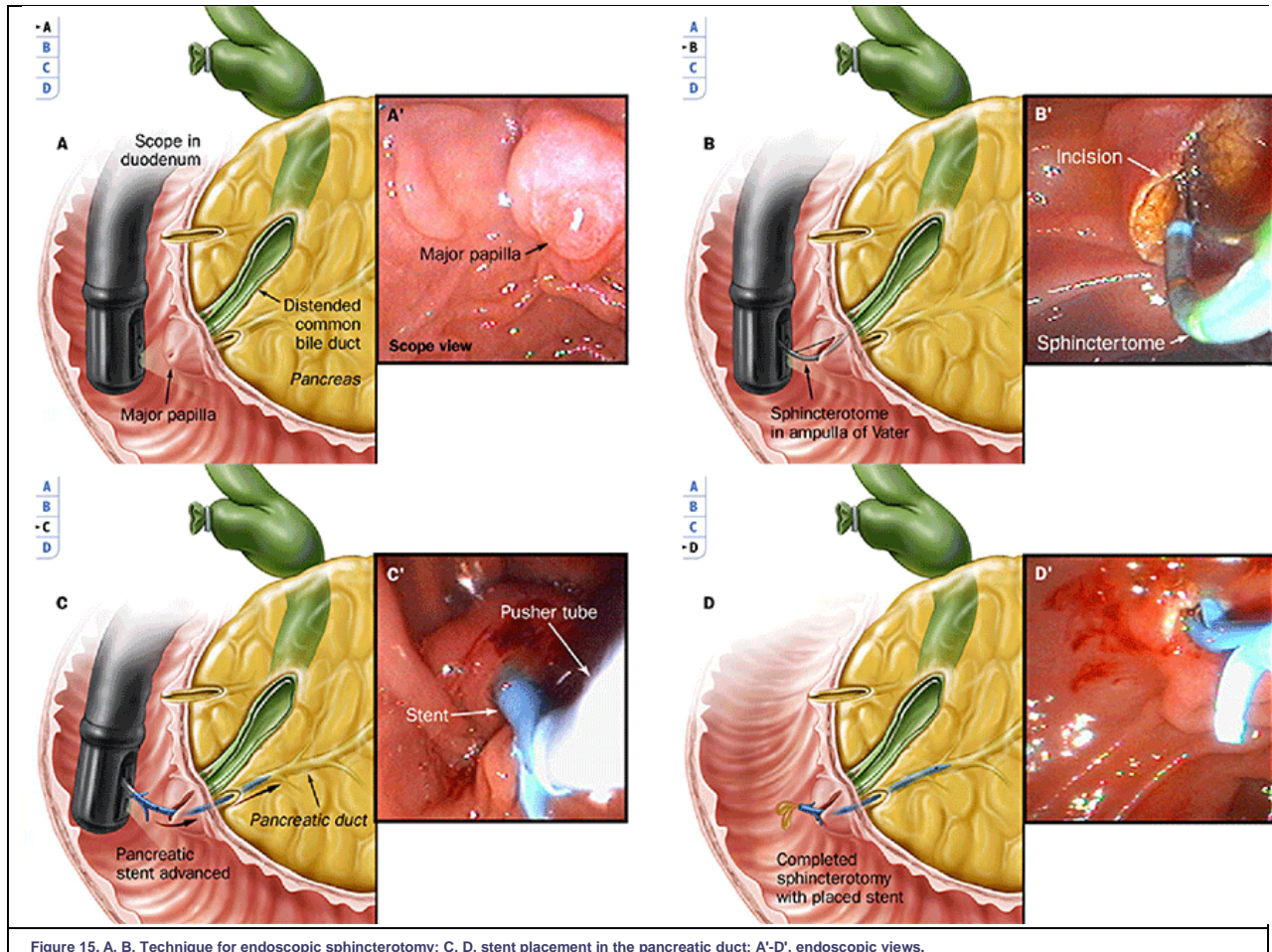


Figure 15. A, B, Technique for endoscopic sphincterotomy; C, D, stent placement in the pancreatic duct; A'-D', endoscopic views.

Other Endoscopic Therapy

Endoscopic balloon dilation and stenting, in an attempt to preserve sphincter function, have not been found to be effective in reducing sphincter of Oddi pressure or symptoms. This technique is also associated with unacceptably high complication rates.

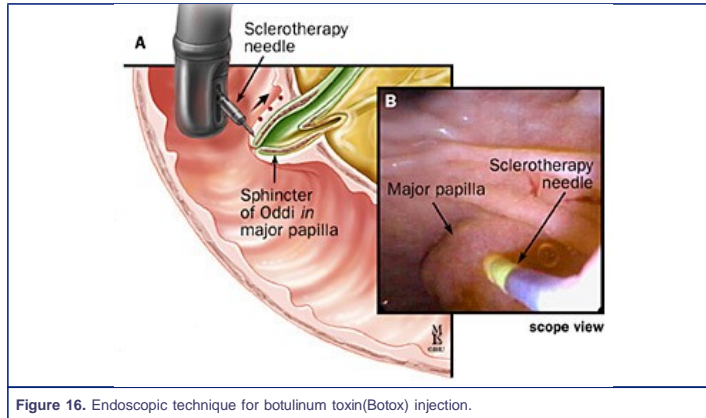


Figure 16. Endoscopic technique for botulinum toxin(Botox) injection.

Recent success has been reported using botulinum toxin (Botox) injections to reduce sphincter of Oddi pressure and to improve bile flow dynamics (Figure 16). This technique, pioneered at the Johns Hopkins Hospital, has shown promise both as a diagnostic and therapeutic modality. The mechanism of action of Botox occurs at the nerve endings within the sphincteric muscle. Botox inhibits the release of acetylcholine (a neurotransmitter), preventing the contraction of the muscle (Figure 17).

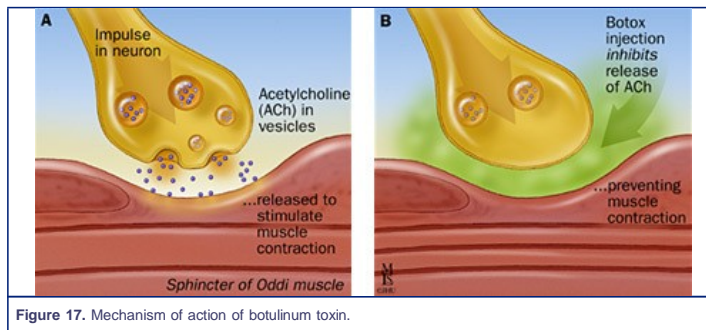


Figure 17. Mechanism of action of botulinum toxin.