Clinical manifestations and diagnosis of sphincter of Oddi dysfunction

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INTRODUCTION

The sphincter of Oddi is a muscular structure that encompasses the confluence of the distal common bile duct and the pancreatic duct as they penetrate the wall of the duodenum (figure 1). The term sphincter of Oddi dysfunction (SOD) has been used to describe a clinical syndrome of biliary or pancreatic obstruction related to mechanical or functional abnormalities of the sphincter of Oddi.

The literature regarding SOD is often difficult to interpret because of differences in nomenclature [1]. The terms papillary stenosis, sclerosing papillitis, biliary spasm, biliary dyskinesia, and postcholecystectomy syndrome have been used synonymously with SOD. Despite this source of confusion, two separate pathologic entities are widely recognized based upon their distinct pathogenic mechanisms [2,3].

- Sphincter of Oddi stenosis
- Sphincter of Oddi dyskinesia

The term sphincter of Oddi dysfunction encompasses both sphincter of Oddi stenosis and sphincter of Oddi dyskinesia.

SOD has been associated with two clinical syndromes: biliary pain and idiopathic recurrent acute pancreatitis. Idiopathic recurrent acute pancreatitis is defined as two or more attacks of well documented acute pancreatitis of unclear cause despite an exhaustive work-up (laboratory and noninvasive imaging) with complete resolution of clinical and laboratory findings between attacks. (See "Clinical manifestations and diagnosis of acute pancreatitis" and "Etiology of acute pancreatitis".)

Evidence that SOD can cause acute pancreatitis was suggested in an animal model in which transient sphincter contraction induced by application of topical carbachol abolished trans-sphincteric flow and increased pancreatic exocrine secretion and pancreatic duct pressure to levels comparable with those seen in pancreatic duct ligation [4]. The addition of cholecystokinin/secretin stimulation of pancreatic secretion plus carbachol application caused pancreatic tissue damage and an increase in serum amylase levels.

This topic will review the clinical manifestations and diagnosis of sphincter of Oddi dysfunction. The treatment of sphincter of Oddi dysfunction, other causes of postcholecystectomy syndrome, and functional gallbladder disorder are discussed separately. (See "Treatment of sphincter of Oddi dysfunction" and "Laparoscopic cholecystectomy", section on 'Postcholecystectomy syndrome' and "Functional gallbladder disorder in adults".)

ANATOMY

The sphincter of Oddi is composed of small circular and longitudinal muscular segments that are approximately 6 to 10 mm in total length and are contained mostly within the wall of the duodenum (figure 1) [5]. The muscle fibers surround the intraduodenal segment of the common bile duct and the ampulla of Vater (picture 1). A circular aggregate of muscle fibers known as the sphincter choledochus (or sphincter of Boyden) maintains resistance to bile flow and thereby permits filling of the gallbladder during fasting and prevents retrograde reflux of duodenal contents into the biliary tree. A separate structure, the sphincter pancreaticus, encircles the distal pancreatic duct. The muscle fibers of the sphincter pancreaticus are interlocked with those of the sphincter choledochus in a figure eight pattern. Although the pancreatic and biliary sphincter portions of the sphincter of Oddi can be distinguished anatomically, their manometric features are similar, and a direct anatomic and manometric correlation has not been established.

The muscle fibers of the sphincter of Oddi function independently from those of the duodenal musculature. The motility of the sphincter of Oddi is complex and not completely understood, but it is known to vary in the fasting and fed states.

- During fasting, sphincter of Oddi motility is integrated with the migrating motor complex (MMC), permitting coordinated release of bile into the duodenum. The MMC is the pattern of gastrointestinal motor activity present during fasting [6]. It is divided into three phases: phase I is a quiescent period and lasts 45 to 60 minutes; phase II is comprised of random intermittent contractions and lasts approximately 30 minutes; phase III is a period of bursts of rapid, evenly-paced, uninterrupted peristaltic contractions and lasts for 5 to 15 minutes. Myoelectrical

potentials within the sphincter of Oddi increase during phase I of the MMC, reach a maximum during phase III, and then decrease rapidly.

- During the fed state, myoelectrical potentials within the sphincter of Oddi vary depending upon the type and quantity of nutrients ingested and may be influenced by endogenous hormones such as cholecystokinin [7,8].

PATHOPHYSIOLOGY

Sphincter of Oddi stenosis is an anatomic abnormality associated with narrowing of the sphincter of Oddi. It can result from any process leading to inflammation or scarring, such as pancreatitis, passage of a gallstone through the papilla, intraoperative trauma, infection, and adenomyosis. Sphincter of Oddi stenosis is associated with abnormal sphincter of Oddi motility and elevated basal pressure.

Sphincter of Oddi dyskinesia refers to a functional disturbance of the sphincter of Oddi, leading to intermittent biliary obstruction. The cause of sphincter of Oddi dyskinesia is not well understood. Spasm and relaxation of the sphincter of Oddi can be induced pharmacologically with agents known to affect smooth muscle function (such as nitroglycerin), suggesting that the spasm may be influenced by local hormonal or neurologic disturbance.

EPIDEMIOLOGY

The prevalence of sphincter of Oddi dysfunction (SOD) among patients with biliary pain or idiopathic recurrent pancreatitis is difficult to estimate because of several potential sources of bias among studies evaluating SOD:

- The amount of investigation for other causes of symptoms differed
- The diagnostic "gold-standard" for SOD varied
- The use of different manometry systems, which may lead to variable results [9]
- Lack of adequate control groups in many studies because the diagnosis of SOD usually involves invasive testing
- The studies were performed in tertiary medical centers and are thus potentially vulnerable to referral bias

However, available data suggest that both biliary and pancreatic SOD occur more often in women than in men [10,11]:

- In a survey of 5430 participants from randomly sampled US households, women were significantly more likely to have functional biliary pain than men (2.3 versus 0.6 percent, odds ratio 3.3) [10].

- In a second study of 49 patients with sphincter of Oddi stenosis and recurrent pancreatitis, 43 of the patients (88 percent) were female [11]. The median age of the patients was 43 years.

Epidemiology of biliary SOD — Biliary SOD is most commonly recognized in patients who have undergone cholecystectomy (hence the name postcholecystectomy syndrome). The reasons for this are not well understood, but may be related to unmasking of pre-existing SOD due to removal of the gallbladder, which may have served as a reservoir to accommodate increased pressure in the biliary system occurring during sphincter spasm [12]. Another possible explanation is that there is alteration of sphincter of Oddi motility because of the severing of nerve fibers that pass between the gallbladder and the sphincter of Oddi via the cystic duct [13]. However, SOD also occurs in patients whose gallbladders are intact, suggesting that other pathophysiologic mechanisms are involved [14].

Despite the association of SOD with cholecystectomy, SOD is an uncommon occurrence following cholecystectomy [15]. In one series of 454 patients who had undergone cholecystectomy, the prevalence of SOD was estimated to be less than 1 percent [16]. However, among patients complaining of symptoms following cholecystectomy, the prevalence was 14 percent.

Epidemiology of pancreatic SOD — SOD is one of the most common diagnoses found in patients with idiopathic recurrent acute pancreatitis. In an illustrative report, SOD was noted in 41 of 126 patients (33 percent) who underwent endoscopic retrograde pancreatography with sphincter of Oddi manometry and bile crystal analysis for microlithiasis [17]. Similar findings were noted in a series of 90 patients with unexplained acute pancreatitis, in which 28 patients (31 percent) had elevated pancreatic basal sphincter pressures (table 1) [18].

CLINICAL MANIFESTATIONS

Clinical manifestations of biliary SOD — Sphincter of Oddi dysfunction (SOD) is suspected in patients who have biliary-type pain without other apparent causes. Typically the pain is located in the right upper quadrant or epigastrium and lasts from 30 minutes to several hours [19]. Characteristics that are **not** suggestive of biliary SOD include lancinating pain that lasts for seconds, constant pain that lasts all day, pain that is exacerbated by eating, pain that is relieved by defecation, or pain that is associated with diarrhea. In addition, the pain is not relieved by anticholinergic antispasmodics, antacids, H2-blockers, or proton pump inhibitors.

Laboratory abnormalities may include elevations in the alanine aminotransferase, aspartate aminotransferase, and alkaline phosphatase that normalize between attacks. Patients with biliary SOD have normal amylase and lipase levels.

On imaging such as ultrasound, the common bile duct may appear dilated (>8 mm in diameter).

Clinical manifestations of pancreatic SOD — Patients with pancreatic SOD present with recurrent episodes of pancreatitis. The episodes typically occur months apart and are associated with elevations in the amylase and lipase. Liver transaminases and bilirubin may also be elevated, and there may be dilation of the pancreatic duct. (See "Clinical manifestations and diagnosis of acute pancreatitis".)

CLINICAL CRITERIA

Rome IV criteria — Clinical criteria for diagnosis of functional gallbladder and sphincter of Oddi disorders have been proposed, based mainly upon expert consensus [20,21]. The Rome IV criteria specify three subsets of functional gallbladder and sphincter of Oddi disorders:

- Functional gallbladder disorder
- Functional biliary sphincter disorder
- Functional pancreatic sphincter disorder

The guidelines stress that patients with upper abdominal pain who do not meet the Rome IV symptom-based criteria should not be submitted to sphincter of Oddi manometry. Those who fulfill the criteria should undergo further evaluation with liver and pancreatic enzymes, ultrasound, and, for selected patients, sphincter of Oddi manometry. (See 'Diagnostic approach' below.)

The following are the Rome IV criteria for biliary pain. In order to fulfill the Rome IV criteria, **all** of the following conditions must be met:

- Pain located in the epigastrium and/or right upper quadrant
- Episodes lasting 30 minutes or longer
- Recurrent symptoms occurring at different intervals (not daily)
- The pain builds up to a steady level
- The pain is severe enough to interrupt the patient's daily activities or lead to an emergency department visit
- The pain is not significantly (<20 percent) related to bowel movements
- The pain is not significantly (<20 percent) relieved by postural change or acid suppression

Supportive criteria include:

- Pain associated with nausea and vomiting
- Pain radiating to the back and/or right infrascapular region
- Pain awakening the patient from sleep

Functional gallbladder disorder — The following are the Rome IV criteria for functional gallbladder disorder (see "Functional gallbladder disorder in adults"):

- Criteria for biliary pain are fulfilled
- Absence of gallstones or other structural pathology

Supportive criteria include:

- Low ejection fraction on gallbladder scintigraphy
- Normal liver enzymes, conjugated bilirubin, and amylase/lipase

Functional biliary sphincter of Oddi disorder — The following are the Rome IV criteria for functional biliary sphincter of Oddi disorder:

- Criteria for biliary pain are fulfilled
- Absence of bile duct stones or other structural abnormalities
- Elevated liver enzymes or dilated bile duct, but not both

Supportive criteria include

- Normal amylase/lipase
- Abnormal sphincter of Oddi manometry
- Abnormal hepatobiliary scintigraphy

Functional pancreatic sphincter of Oddi disorder — The following are the Rome IV criteria for functional pancreatic sphincter of Oddi disorder:

- Documented recurrent episodes of pancreatitis (typical pain with amylase or lipase >3 times normal and/or imaging evidence of acute pancreatitis)
- Other etiologies of pancreatitis excluded
- Negative endoscopic ultrasound
- Abnormal sphincter manometry

DIFFERENTIAL DIAGNOSIS

Biliary and pancreatic sphincter of Oddi dysfunction (SOD) both present with pain in the right upper quadrant or epigastrium, a symptom that is common to multiple disorders, most of which are more

common than SOD [22]. The differential diagnosis of right upper quadrant or epigastric pain includes gastroesophageal reflux disease, irritable bowel syndrome, functional dyspepsia, cholelithiasis, cholecystitis, and pancreatitis due to other causes. (See "Etiology of acute pancreatitis".)

The evaluation for alternate diagnoses may include studies such as transabdominal ultrasound, abdominal computed tomography, magnetic resonance cholangiopancreatography, upper endoscopy, endoscopic ultrasound, and endoscopic retrograde cholangiopancreatography (ERCP). Which tests to pursue will depend upon their availability and the patient's clinical presentation. In addition, therapeutic trials of medications such as antispasmodics or proton pump inhibitors should be considered in patients with symptoms suggestive of possible irritable bowel syndrome or gastroesophageal reflux/functional dyspepsia, respectively, prior to invasive testing for SOD [22]. (See "Evaluation of the adult with abdominal pain", section on 'Epigastric pain'.)

DIAGNOSTIC APPROACH

The approach to a patient with suspected sphincter of Oddi dysfunction (SOD) depends upon the patient's clinical presentation as well as the results of laboratory testing and abdominal imaging. In general, only patients fulfilling the Rome IV criteria should undergo invasive evaluation for SOD. This decreases the chance of patients being inappropriately subjected to invasive testing for SOD that is associated significant complications (primarily pancreatitis). (See 'Rome IV criteria' above and 'Sphincter of Oddi manometry' below.)

To determine if patients fulfill the Rome IV criteria, liver tests (transaminases, alkaline phosphatase, bilirubin) and pancreatic enzymes (amylase, lipase) should be checked, and structural abnormalities need to be excluded. Transabdominal ultrasound is typically the initial imaging study obtained for suspected biliary SOD. It can look for structural abnormalities such as gallstones while also providing an estimate of the common bile duct diameter. However, transabdominal ultrasound may not adequately visualize the pancreas because of overlying bowel gas, so alternate imaging techniques, such as magnetic resonance cholangiopancreatography (MRCP), may be required for evaluation of the pancreatic duct. Additional testing that may help to rule out structural abnormalities includes abdominal computed tomography, endoscopic ultrasound, and endoscopic retrograde cholangiopancreatography (ERCP).

In appropriately selected patients, the diagnosis of SOD is established by sphincter of Oddi manometry (SOM), which is performed during ERCP. Several less invasive methods have also been evaluated for establishing the diagnosis, but none has been shown to approach the diagnostic accuracy of SOM [23,24]. (See 'Sphincter of Oddi manometry' below.)

Diagnosis of biliary SOD — Biliary SOD may be suspected based upon the presence of biliary-type pain, abnormal liver tests (aminotransferases, bilirubin or alkaline phosphatase >2 times normal values) that normalize between attacks, and dilation of the common bile duct. The diagnosis may be supported by provocation tests or hepatobiliary scintigraphy, but definitive diagnosis requires SOM. (See 'Specific diagnostic tests' below.)

The Rome IV consensus conference statement suggests that in patients who have had a cholecystectomy, a reasonable approach is to start with liver and pancreatic biochemical tests, followed by an upper endoscopy and abdominal imaging (ultrasound, computed tomography scan, MRCP, or endoscopic ultrasound).

Subsequent evaluation in the patient with biliary-type pain depends on the presence of abnormal liver tests, and a dilated common bile duct [22].

- **Both abnormal liver tests and a dilated common bile duct** – Patients with elevated liver tests and a dilated common bile duct likely have an underlying obstruction and do not require additional testing. These patients should be referred directly for ERCP with endoscopic sphincterotomy.

- **Either abnormal liver tests or a dilated common bile duct** – Sphincter of Oddi dysfunction should be suspected in patients with biliary type pain and either abnormal liver tests or a dilated common bile duct. Patients with suspected SOD should undergo SOM to confirm the diagnosis and to select patients who are likely to respond to treatment. However, some authorities recommend empiric sphincterotomy in such patients, a strategy that was supported by a cost-effectiveness analysis [25]. Our approach is to proceed with SOM in such patients, which is consistent with the Rome IV consensus statement [20]. (See 'Sphincter of Oddi manometry' below and "Treatment of sphincter of Oddi dysfunction", section on 'Biliary pain'.)

  If a provider with significant experience in SOM is not available, hepatobiliary scintigraphy (in patients whose gallbladder is intact) or a fatty meal ultrasound study (in patients with or without a gallbladder) is a reasonable alternative, provided that local standards for these tests have been established. However, these tests are inferior to SOM, and when possible, patients should be referred to centers experienced in performing SOM. (See 'Biliary provocation tests' below and 'Correlation of noninvasive tests with sphincter of Oddi manometry for biliary SOD' below.)

- **Normal liver tests and bile duct** – Symptoms in patients with biliary type pain and normal liver tests and bile duct may be due to functional biliary type pain or other functional bowel diseases, such as dyspepsia or irritable bowel syndrome. To further complicate matters, these conditions may coexist and may result from generalized smooth muscle dysfunction, duodenal hyperalgesia [26], or somatosensory hypersensitivity following cholecystectomy [27].

Our approach begins with an evaluation focused on detecting clinical features associated with irritable bowel syndrome or functional dyspepsia (algorithm 1). Patients whose clinical features are more consistent with one of these diagnoses are treated accordingly. (See "Clinical manifestations and diagnosis of irritable bowel syndrome in adults" and "Approach to the adult with dyspepsia".)

For other patients, we proceed based upon whether or not the gallbladder is intact. In patients who have **not** undergone cholecystectomy, we obtain a gallbladder ejection fraction to determine whether the gallbladder may be the source of symptoms. For those who have an ejection fraction <40 percent or reproduction of symptoms during intravenous cholecystokinin administration, we suggest laparoscopic cholecystectomy.

Patients with biliary pain alone should not routinely undergo SOM. SOM and sphincterotomy should be performed in these patients only as part of a research protocol as there is poor correlation between the results of SOM and response to sphincterotomy in these patients [19]. Such patients are commonly encountered and represent a difficult diagnostic and management challenge [28]. In such patients, pharmacologic trials should be tried (eg, proton pump inhibitors, spasmolytic drugs, calcium channel blockers [nifedipine], and psychotropic agents).

Diagnosis of pancreatic SOD — Patients fulfilling the Rome IV criteria for suspected pancreatic sphincter of Oddi disorders will typically require manometric evaluation of the sphincter of Oddi. In particular, recordings from the pancreatic portion of the sphincter should be obtained. (See 'Functional pancreatic sphincter of Oddi disorder' above and 'Sphincter of Oddi manometry' below.)

SPECIFIC DIAGNOSTIC TESTS

Noninvasive tests

Transabdominal ultrasound — Otherwise unexplained dilation of the common bile duct on ultrasound is associated with sphincter of Oddi dysfunction (SOD) and may predict a favorable response to sphincterotomy in patients with other clinical evidence of biliary obstruction (eg, pain, abnormal liver function tests) [29]. However, common bile duct dilation (>6 mm) may be observed in up to one-third of patients after cholecystectomy [30-32]. Furthermore, the size of the common bile duct increases with age [33]. As a result, dilation of the common bile duct alone is insufficient evidence for establishing the diagnosis of SOD. It should be considered in the context of symptoms, liver and pancreatic biochemical tests, and a history of multiple gallbladder stones or past removal of common bile duct stones. In most instances, mild dilation is an incidental finding warranting only observation.

Biliary provocation tests — To increase the specificity of common bile duct diameter measurement for determining SOD, several provocation tests have been developed that use either a fatty meal (fatty meal ultrasonography) or cholecystokinin (CCK) to increase bile flow [34,35]. In patients who have normal sphincter of Oddi function, the bile duct diameter remains constant or decreases following stimulation; an increase of more than 2 mm is considered to be abnormal [34].

Correlation of these provocation tests with sphincter of Oddi manometry is poor, and abnormal findings may be seen in non-biliary diseases. As an example, an abnormal response of the sphincter of Oddi to CCK stimulation or the Nardi test (a provocative test using morphine and prostigmin) has been observed in patients with irritable bowel syndrome [36,37]. Thus, provocation tests are not performed routinely in clinical practice.

Magnetic resonance cholangiopancreatography — Secretin stimulated magnetic resonance cholangiopancreatography (MRCP) has also been used for the diagnosis of biliary SOD.

One prospective study included 47 patients with suspected type II or III SOD who underwent secretin MRCP [38]. Results were compared with conventional manometry where the diagnosis was based upon a mean basal pressure of >40 mmHg (table 1). Results were also correlated with long-term outcomes with or without endoscopic sphincterotomy.

Of the 47 patients, 27 (57 percent) were considered to have SOD based upon manometry and underwent biliary and/or pancreatic sphincterotomy. Secretin MRCP was abnormal in 10 of 16 (63 percent) of type II and 0 of 11 type III cases. The overall diagnostic accuracy was estimated to be 73 and 46 percent for types II and III, respectively.

During a mean follow-up of 32 months, 9 of 13 patients with normal manometry (and thus no sphincterotomy) and 14 of 16 patients with type II SOD treated with sphincterotomy experienced a significant reduction in symptoms. By contrast, only 2 of 11 patients with type III SOD treated with sphincterotomy had a reduction in symptoms. All patients with SOD by manometry and an abnormal secretin MRCP (n = 12) had long-term symptom improvement following sphincterotomy. The authors concluded that secretin MRCP was useful in predicting abnormal manometry and a response to endotherapy in patients with suspected type II SOD, but it was insensitive for predicting abnormal manometry in patients with suspected type III SOD.

Hepatobiliary scintigraphy — Hepatobiliary scintigraphy using technetium-99m labeled dyes can provide a standardized, semiquantitative assessment of delayed biliary drainage in patients whose gallbladder is absent [12,39-41]. (See "Acute calculous cholecystitis: Clinical features and diagnosis", section on 'Cholescintigraphy (hepatic iminodiacetic acid [HIDA] scan)'.)

Studies on the utility of hepatobiliary scintigraphy have had variable results:

- In one study, 26 consecutive patients underwent hepatobiliary imaging, ERCP, and sphincter of Oddi manometry (SOM) [39]. A scintigraphic score (referred to as the Hopkins score) was constructed from quantitative and visual criteria that successfully discriminated all patients with SOD.

- Substantially different conclusions were reached in another report in which scintigraphy results were compared with sphincter of Oddi manometry in 27 patients with suspected SOD following cholecystectomy [42]. Scintigraphy with CCK infusion was performed within one month of manometry. Scoring of the scans and measurement of the transit time from the hepatic hilum to the duodenum (HDTT) was performed by independent, blinded observers.

  Eight patients had abnormal SOM (basal sphincter of Oddi pressure >40 mmHg). Scintigraphy scoring had a sensitivity of 25 to 38 percent, a specificity of 86 to 89 percent, a positive predictive value of 40 to 60 percent, and a negative predictive value of 75 to 79 percent. The coefficient of variation between observers was 0.72 (ie, moderately good correlation). The sensitivity, specificity, positive, and negative predictive values of the HDTT were 13, 95, 50, and 74 percent, respectively. The authors concluded that scintigraphy correlated poorly with manometry in postcholecystectomy patients with suspected SOD.

A problem with hepatobiliary scintigraphy is that clearance rates in patients with SOD overlap with those in a normal population [12]. In addition, scintigraphy may be falsely positive in patients who have extrahepatic biliary obstruction from a variety of causes, or it may be falsely negative in patients who have sphincter of Oddi dyskinesia in whom the obstruction to bile flow may be intermittent. Furthermore, hepatobiliary scintigraphy cannot detect obstruction to flow arising from the pancreatic portion of the SO. Thus, scintigraphy should have only a supportive role in the evaluation of suspected SOD.

Correlation of noninvasive tests with sphincter of Oddi manometry for biliary SOD — As noted above, several studies have compared the accuracy of the noninvasive tests for SOD with manometry. One of the largest studies comparing the most commonly used methods involved 304 patients with suspected SOD who underwent manometry, fatty meal ultrasonography, and hepatobiliary scintigraphy [43]. The following observations were made:

- 73 patients (24 percent) were diagnosed with SOD by manometry.

- Compared with SOM as the gold-standard, the sensitivity and specificity of fatty meal ultrasonography were 21 and 97 percent, respectively.

- The sensitivity and specificity of hepatobiliary scintigraphy were 49 and 78 percent, respectively.

- Hepatobiliary scintigraphy and fatty meal ultrasonography (either one or both) were abnormal in 91, 50, and 44 percent of patients with type I, II, and III SOD dysfunction, respectively.

- A durable clinical response was observed in 40 of 73 patients (55 percent) who underwent sphincterotomy. Of those with SOD, 11 of 13 (85 percent) with both abnormal hepatobiliary scintigraphy and fatty meal ultrasonography had a good long-term response.

These data suggest that the correlation of fatty meal ultrasonography and hepatobiliary scintigraphy with sphincter of Oddi manometry is poor, though the combined use of hepatobiliary scintigraphy and fatty meal ultrasonography increases sensitivity compared with either alone. In addition, the accuracy of these tests appears to decrease in relation to the probability of SOD as determined by the Milwaukee Biliary Group classification. The authors suggest that despite the poor test characteristics, fatty meal ultrasonography and hepatobiliary scintigraphy may provide assistance in predicting the long-term response to sphincterotomy in patients with manometrically proven SOD.

Pancreatic provocation tests — Provocation tests for evaluating pancreatic SOD are based upon a similar principle as provocation tests for biliary SOD. An increase in pancreatic duct diameter following secretin stimulation of >1.5 mm (assessed by ultrasound, computed tomography, or magnetic resonance cholangiopancreatography [MRCP]) lasting for >30 minutes is considered to be pathologic [44].

In one report evaluating this technique, a positive test was associated with good operative outcomes in 90 percent of patients with suspected SOD [45]. However, these results have not been duplicated in other centers. In another study, the accuracy of the secretin ultrasound test was compared with manometry as the gold standard in 47 patients with acute pancreatitis. Ultrasound findings in 35 healthy patients were used as controls [46]. The sensitivity and specificity of the secretin ultrasound were 88 and 82 percent, respectively.

The addition of endoscopic ultrasound to the secretin stimulation test has been attempted to improve accuracy. In one report, 20 patients underwent dynamic imaging of the pancreas using real-time endoscopic ultrasonography with secretin stimulation [47]. Of the seven patients who had SOD based upon manometric results, only four (57 percent) had an abnormal endoscopic ultrasound measurement. Only 1 of 13 patients with normal SOM had an abnormal endoscopic ultrasound study. The results suggested excellent negative and positive predictive values but poor overall sensitivity for this test (table 2). (See "Glossary of common biostatistical and epidemiological terms".)

The secretin stimulation test has also been performed with MRCP with similar results. In two studies, the sensitivities of secretin stimulated MRCP for diagnosing pancreatic SOD ranged from 57 to 67 percent, with specificities of 100 percent [48,49].

Invasive tests

Sphincter of Oddi manometry — Sphincter of Oddi manometry (SOM) remains the gold standard for diagnosing of SOD. Basal pressure and phasic wave contractions are routinely recorded from the common bile duct and pancreatic duct segments of the sphincter of Oddi. The mechanical and electrical activity is similar between the two segments (figure 2A-B) [50]. Measurement of basal pressures from either the biliary or pancreatic duct alone may miss up to one-quarter of patients with abnormal sphincter pressures [51]. Because of this, we recommend that patients undergoing SOM have measurements taken from both the biliary and pancreatic ducts.

Patients with SOD have been divided into two groups based upon manometric findings:

- Patients with structural alterations of the sphincter of Oddi (stenosis)
- Patients with functional abnormalities (dyskinesia)

Patients with stenosis are identified by an abnormally elevated basal sphincter of Oddi pressure (>40 mmHg), which is the most widely clinically accepted diagnostic finding for SOD (figure 3A-B). This finding is reproducible, and the elevated sphincter of Oddi pressure does not relax following administration of smooth muscle relaxants. Other abnormalities have also been described (table 1) [27].

Patients with sphincter of Oddi dyskinesia may also have elevated basal sphincter of Oddi pressure. However, in contrast to sphincter of Oddi stenosis, the elevated pressure decreases dramatically following amyl nitrite inhalation or glucagon bolus injection, which relaxes smooth muscle. Other manometric characteristics of this group are: rapid sphincter of Oddi contraction frequency (>7/min) or tachyoddia, an excess in retrograde phasic contractions (>50 percent), and a substantial basal sphincter of Oddi pressure increase (paradoxical response) following administration of cholecystokinin-octapeptide (CCK-8) (waveform 1). Manometric findings in patients with sphincter of Oddi dyskinesia are less well reproduced upon repeat measurement compared with patients with sphincter of Oddi stenosis.

Limitations — Although SOM remains the gold standard for diagnosis of SOD, it is invasive, technically demanding, and has several limitations:

- The cut-off point for what is considered elevated basal pressure for biliary and pancreatic sphincters was based upon a single study of 50 South American subjects [52].
- The procedure has been associated with an increased risk of pancreatitis.
- The technique, equipment, and method of sedation used can affect the results.
- The interpretation of results can vary among observers depending in part upon experience [53].

Most series have suggested that SOM is associated with an increased risk of pancreatitis compared with ERCP for other indications, which carries with it a risk of approximately 5 percent. (See "Post-endoscopic retrograde cholangiopancreatography (ERCP) pancreatitis".) In an illustrative series of 100 consecutive patients who underwent sphincter of Oddi manometry, the overall incidence of pancreatitis (defined as upper abdominal pain associated with an elevation in serum amylase or lipase 24 hours after manometry) was 17 percent [54]. Pancreatitis developed in 6 of 38 patients with type II SOD (16 percent) and in 11 of 62 patients with type III SOD (18 percent). Among the 54 patients with normal SOM, the rate of pancreatitis was 13 percent, and among the 46 patients with abnormal SOM, the rate was 22 percent. The incidence was significantly increased in patients who had manometry plus ERCP during one session compared with those who had manometry alone (26 versus 9 percent). On multivariable analysis, only the performance of ERCP was associated with pancreatitis.

Placement of a pancreatic stent following biliary sphincterotomy may reduce the incidence of pancreatitis in patients with pancreatic sphincter hypertension [55]. In one report in which stenting was used, the level of the serum amylase obtained three hours after SOM predicted the development of pancreatitis [56]. (See "Treatment of sphincter of Oddi dysfunction" and "Prophylactic pancreatic stents to prevent ERCP-induced pancreatitis: When do you use them?".)

On the other hand, some reports suggest that the risk is related to the SOD itself and that patients undergoing SOM and ERCP are not at higher risk for pancreatitis than patients undergoing ERCP alone. A retrospective study of 268 patients who underwent elective ERCP categorized patients into two major groups: those with suspected SOD (cases), and those with a bile duct stone (controls) [57]. The case group was further subclassified into two groups: those who underwent sphincter of Oddi manometry followed by immediate ERCP, and those who had an ERCP without manometry. Similar to other reports, the rate of pancreatitis was much higher in the group with suspected SOD (27 versus 3.2 percent). However, there was no significant difference in the rate of pancreatitis in those with SOD who underwent manometry and ERCP compared with those who had ERCP without manometry (OR 0.72, 95% CI 0.08 to 9.2). On multivariable analysis, biliary sphincterotomy and pancreatography were independent predictors of pancreatitis. Thus, the authors concluded that the higher risk of pancreatitis was not due to the manometry, but rather to the underlying presence of SOD.

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Biliary infection and obstruction".)

SUMMARY AND RECOMMENDATIONS

Prior to subjecting patients to invasive testing for sphincter of Oddi dysfunction, it is important to ensure that they have been adequately evaluated for alternative explanations for their pain. In addition, the evaluation of patients with suspected sphincter of Oddi dysfunction (SOD) should consider the availability of local expertise, since the accuracy of the various diagnostic tests is operator dependent. (See 'Differential diagnosis' above and 'Diagnostic approach' above and 'Specific diagnostic tests' above.)

Evaluation of suspected biliary SOD — Biliary SOD may be suspected based upon the presence of biliary-type pain, abnormal liver tests, and dilation of the common bile duct. The diagnosis may be supported by provocation tests or hepatobiliary scintigraphy, but definitive diagnosis requires sphincter of Oddi manometry (SOM). Patients who fulfill the Rome IV clinical criteria for functional biliary sphincter of Oddi disorders should undergo SOM to confirm the diagnosis and to select patients likely to respond to treatment. (See 'Rome IV criteria' above and 'Specific diagnostic tests' above.)

Evaluation of suspected pancreatic SOD — Patients with pancreatic SOD present with recurrent episodes of pancreatitis and have a negative evaluation for alternate causes. Patients fulfilling the Rome IV criteria for suspected pancreatic sphincter of Oddi disorders will typically require manometric evaluation of the sphincter of Oddi. In particular, recordings from the pancreatic portion of the sphincter should be obtained. (See 'Functional pancreatic sphincter of Oddi disorder' above and 'Diagnosis of pancreatic SOD' above.)

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Topic 5654 Version 26.0

GRAPHICS

Sphincter of Oddi in relation to the ampulla of Vater

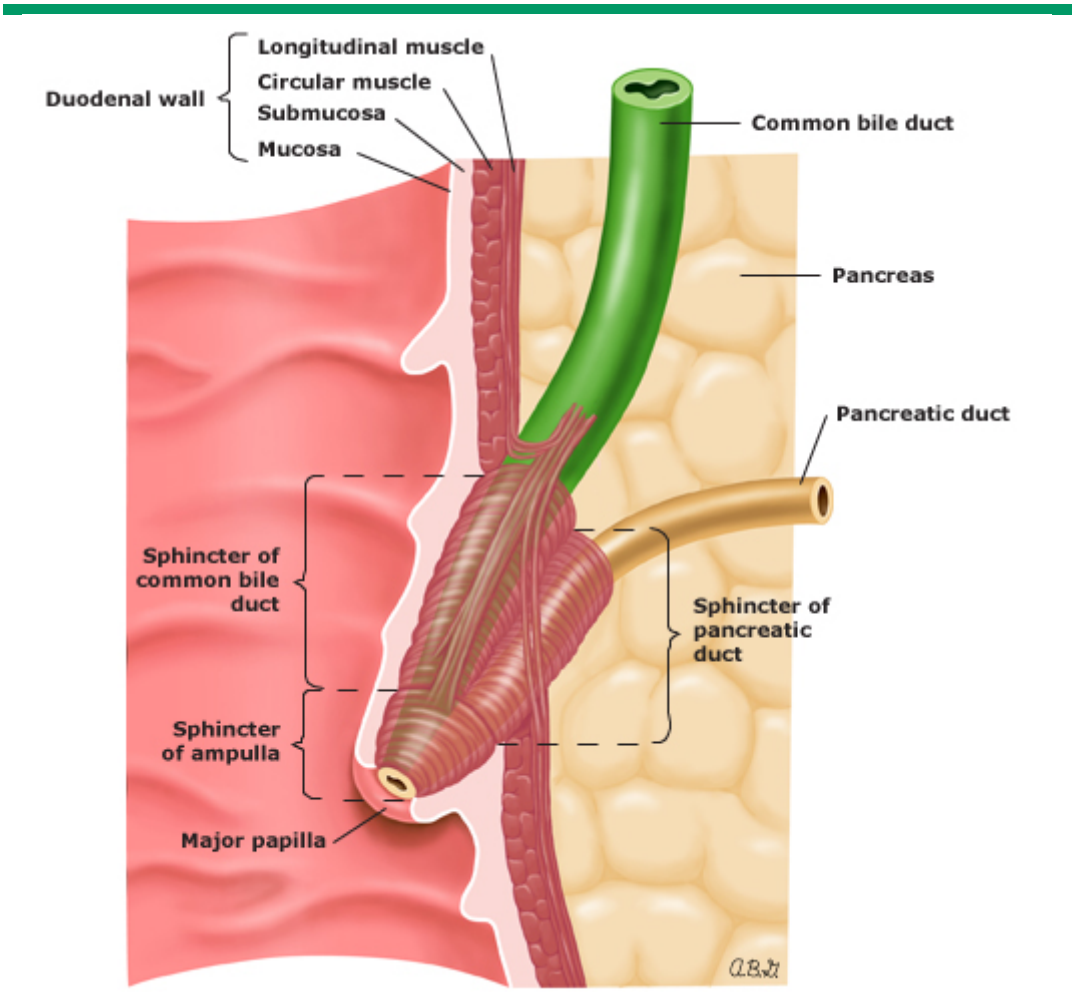
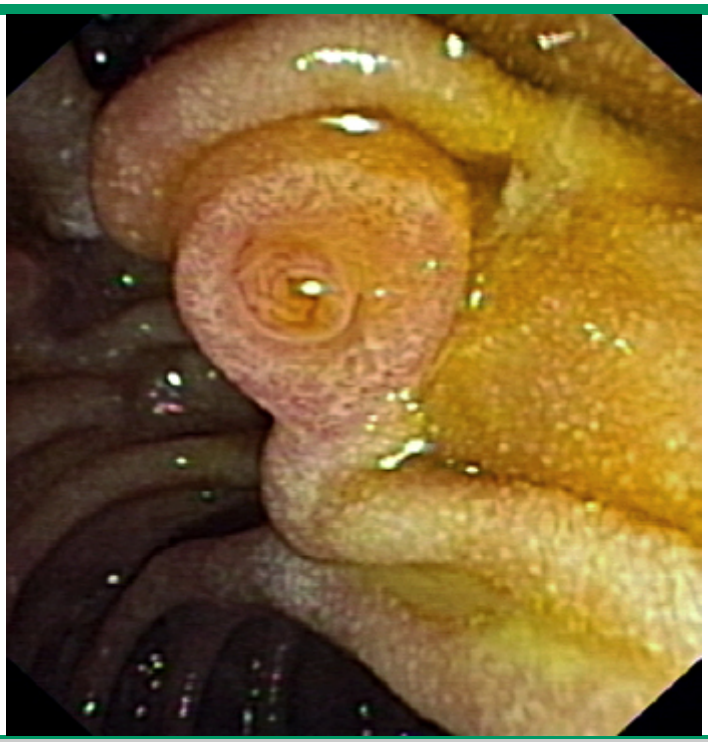


Diagram of the anatomy of the sphincter of Oddi and ampulla of Vater. The muscle fibers of the sphincter of Oddi surround the intraduodenal segment of the common bile duct and the ampulla of Vater. A circular aggregate of muscle fibers, known as the sphincter choledochus (or sphincter of Boyden), keeps resistance to bile flow high, and thereby permits filling of the gallbladder during fasting and prevents retrograde reflux of duodenal contents into the biliary tree. A separate structure, called the sphincter pancreaticus, encircles the distal pancreatic duct. The muscle fibers of the sphincter pancreaticus are interlocked with those of the sphincter choledochus in a figure eight pattern.

Graphic 78786 Version 3.0

Endoscopic view of the papilla of Vater



The papilla of Vater, also known as the ampulla, is a small nipple-like structure located in the duodenum (first part of the intestine). Bile is coming out through the orifice.

Courtesy of Silvano Loperfido, MD.

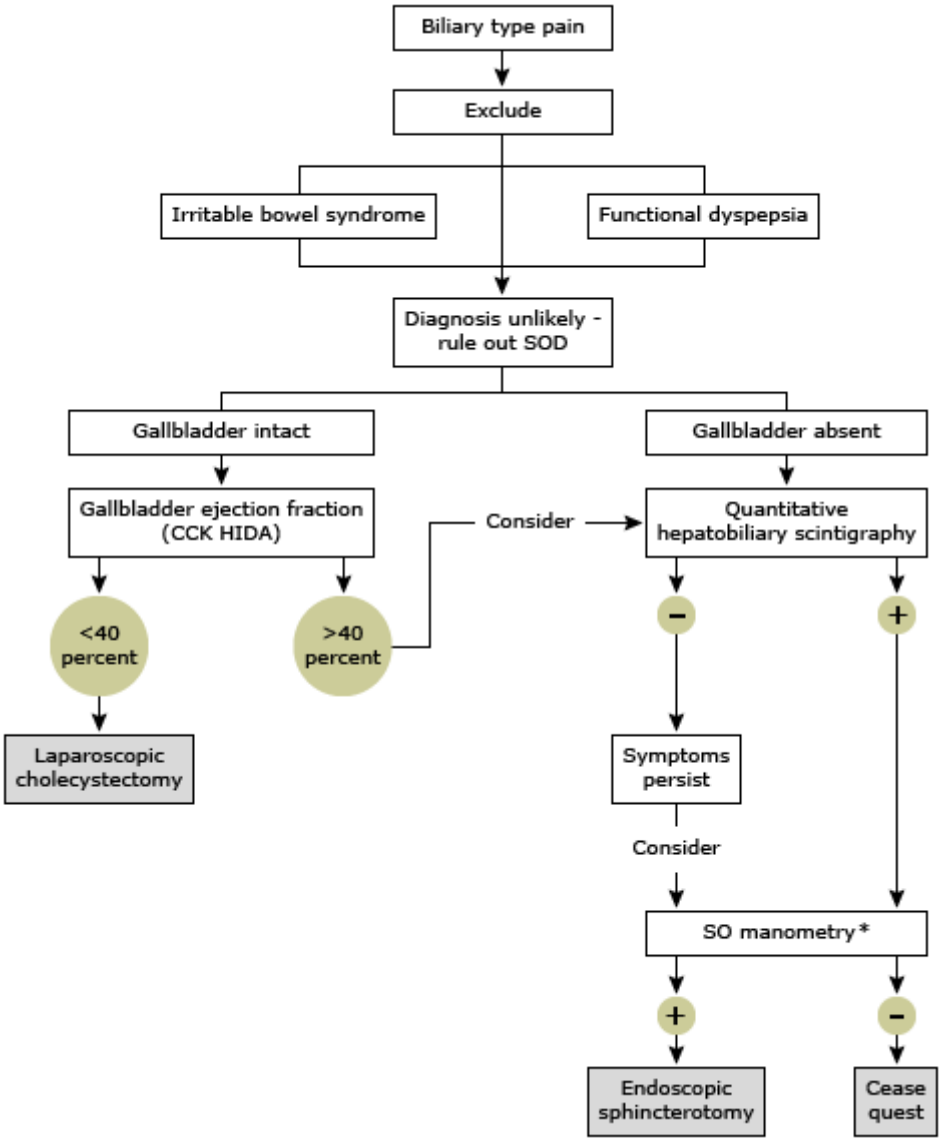
Graphic 63728 Version 2.0

Abnormal pressure profile of sphincter of Oddi measured at common bile duct and pancreatic duct

Basal pressure (mmHg)	>40
Phasic contractions (mmHg)	>350
Frequency (per minute)	>7
Retrograde sequence (percent)	>50

Graphic 65380 Version 1.0

Approach to suspected sphincter of Oddi dysfunction



SO: sphincter of Oddi.
* SO manometry and sphincterotomy should be performed in these patients only as part of a research protocol.

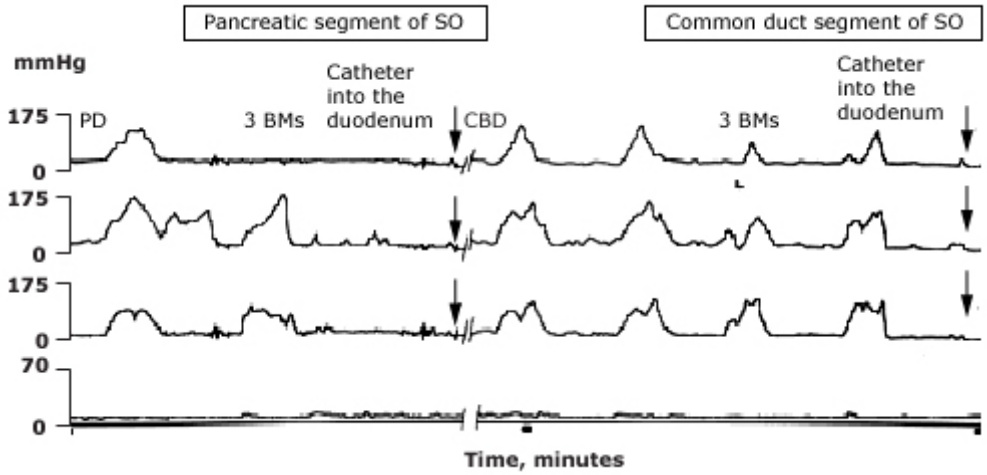
Graphic 60587 Version 3.0

Definitions of sensitivity, specificity, and positive and negative predictive values

	Disease present	Disease absent
Test positive	**A**	**B**
Test negative	**C**	**D**
Sensitivity = A ÷ (A + C)		
Specificity = D ÷ (B + D)		
Positive predictive value = A ÷ (A + B)		
Negative predictive value = D ÷ (C + D)		

Graphic 77832 Version 3.0

Comparison of pressures in the pancreatic and common duct segments of the sphincter of Oddi

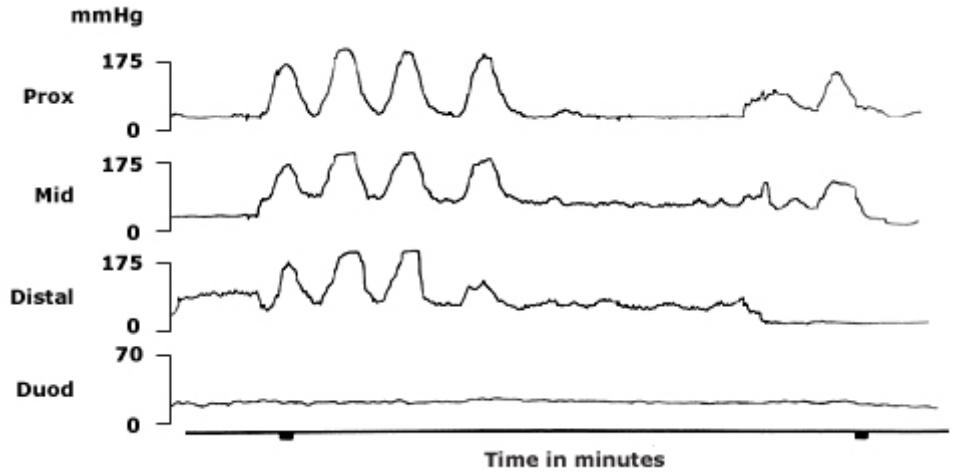


Sphincter of Oddi manometry. Comparison of the sphincter of Oddi (SO) pressures obtained from both the pancreatic segment (PD) and common duct (CBD) segment of the SO during catheter pull-through of the sphincter in the same patient. The pressures are equivalent. (BM refers to "black marks" noted on the catheter.)

Courtesy of Walter J Hogan, MD.

Graphic 57960 Version 1.0

Sphincter of Oddi manometry

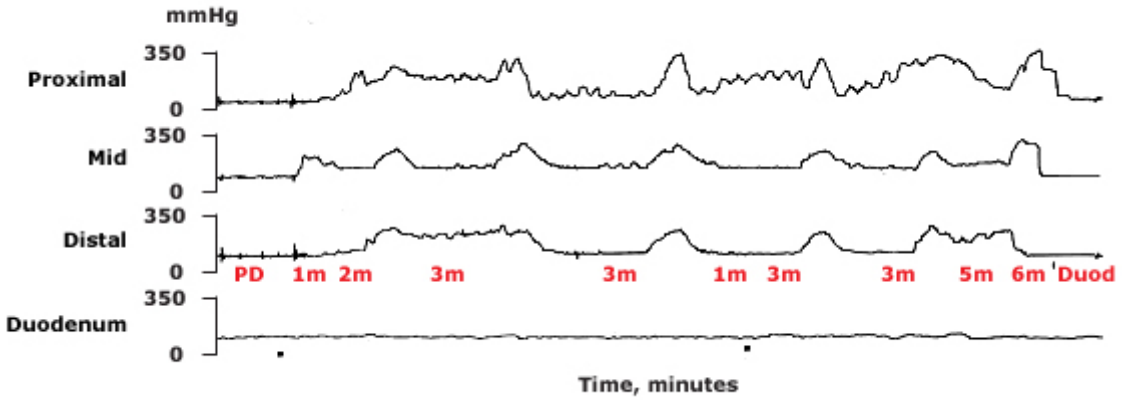


Sphincter of Oddi (SO) pressure profile obtained by catheter pull-through from the common bile duct (CBD) into the duodenum. The three recording tips (proximal to distal) encompass a 4 mm length. The basal SO pressure and superimposed SO phasic waves are demonstrated in all tips.

Courtesy of Walter J Hogan, MD.

Graphic 54223 Version 1.0

Sphincter of Oddi manometry

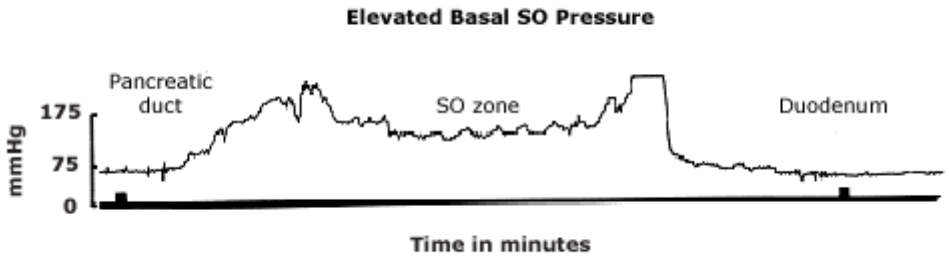


Example of elevated basal sphincter of Oddi (SO) pressure in the pancreatic segment (PD) of the SO.

Courtesy of Walter J Hogan, MD.

Graphic 80705 Version 1.0

Sphincter of Oddi manometry

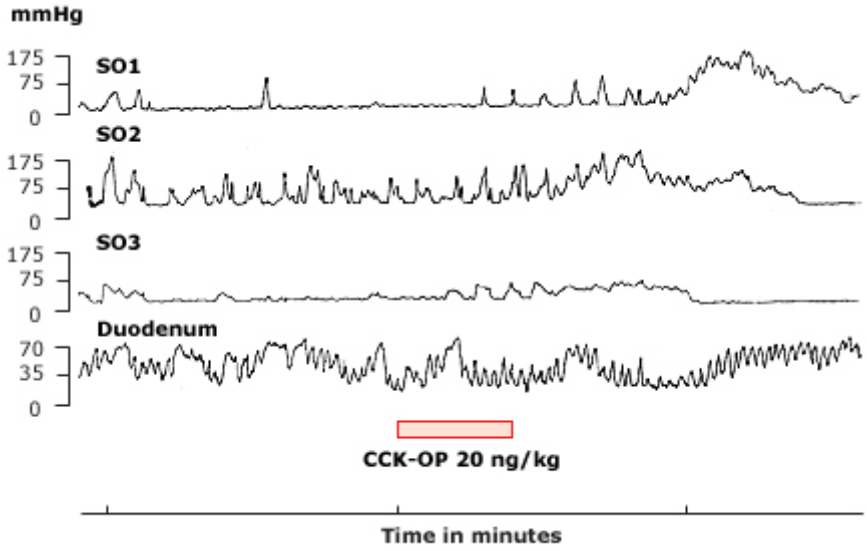


Example of elevated basal sphincter of Oddi (SO) pressure and a pressure gradient between the pancreatic duct and duodenum obtained during manometric catheter pull-through of the pancreatic segment of the SO.

Courtesy of Walter J Hogan, MD.

Graphic 57715 Version 1.0

Sphincter of oddi manometry



Example of a paradoxical basal sphincter of Oddi (SO) pressure elevation following the intravenous administration of cholecystokinin-octapeptide (20 ng/kg). Normally, CCK reduces SO basal pressure. This finding suggests possible denervation of the sphincteric zone.

Courtesy of Walter J Hogan, MD.

Graphic 61411 Version 2.0

Contributor Disclosures

Marc F Catalano, MD, FACG, FACP, FASGE, AGAF Nothing to disclose **Nirav C Thosani, MD, MHA** Nothing to disclose **Douglas A Howell, MD, FASGE, FACG** Grant/Research/Clinical Trial Support: Cook Endoscopy (Research support). Consultant/Advisory Boards: Cook Endoscopy-Consultant [Advanced Endoscopy]; Olympus America [Endoscopy (General and Advanced). Patent Holder: Cook Endoscopy [advanced interventional endoscopy (ERCP devices/stents)]. **Shilpa Grover, MD, MPH, AGAF** Nothing to disclose

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