Rad M. Agrawal, M.D., Series Editor

Sphincter of Oddi Dysfunction

Abhijit Kulkarni

Sphincter of Oddi dysfunction (SOD) is a complex disorder with an often frustrating clinical course and therapeutic outcome for both the patient and the physician. The diagnosis and therapy require a high-level of understanding of the anatomy and pathophysiology of the area. Although, sphincter of Oddi manometry (SOM) is the gold standard in the diagnosis and management of the disorder, it is limited by several factors, including post-procedural complications (e.g., pancreatitis), requirement for highly-specialized equipment, and the need for an expert endoscopist, as the procedure is technically challenging and requires significant skill and experience in both performance and interpretation. Endscopic sphincterotomy is the current standard therapy for treating patients with SOD, though medical therapy should generally be tried first, especially in patients with type III disease or type II disease with mild symptoms. This review discusses the classification, diagnosis, and treatment of SOD.

INTRODUCTION

Sphincter of Oddi dysfunction (SOD) is a benign acalculous obstruction to the flow of biliopancreatic secretions through the sphincter of Oddi (1,2). In the general population, its prevalence is 1.5% (3). It is one of the known causes of post-cholecystectomy syndrome, and is observed in 14%–23% of these patients (4,5). The post-cholecystectomy syndrome can loosely be defined as a persistent or recurrent upper abdominal pain (usually right) following cholecystectomy and may be caused by gastroesophageal reflux, gastroparesis, or visceral hyperalgesia. Alternatively, retained common bile duct stones, which may be seen in 4%–7% of patients following cholecystectomy, or complications of the cholecystectomy including bile duct injuries and resultant bile leaks may be responsible for persistent post-cholecystectomy abdominal pain (6). However, if these causes are excluded and cholecystectomy was performed for only clinical biliary symptoms, SOD is the more likely cause for recurrent or persistent symptomatology.

(continued on page 31)

Abhijit Kulkarni, M.D., Director, G.I. Lab., Allegheny General Hospital, Drexel University College of Medicine, Pittsburgh, PA.

(continued from page 28)

SOD, commonly referred to as either papillary stenosis or ampullary spasm, can be a difficult disorder to diagnose and treat with an often frustrating course for both the patient and the clinician.

CLASSIFICATION

SOD became a disorder that gained widespread acceptance following the landmark 1989 publication by Geenen and colleagues (7), which introduced the Hogan-Geenen Milwaukee Classification system for SOD. Using this system, patients with biliary pain are classified into 3 categories based on symptoms, laboratory tests, and radiological imaging. Type I patients have 1) biliary pain with elevated liver enzymes (AST, ALT, or ALP) >2 times the upper limit of normal on at least 2 separate occasions with normalization within 24–48 hours, 2) dilation of extrahepatic bile duct to ≥12 mm in diameter, and 3) delayed bile duct drainage following cholangiography >45 minutes. Type II patients have biliary pain and 1 or 2 of the criteria of type I patients. Type III patients have only biliary type pain (7).

Over time, these original criteria have been modified as more data regarding SOD have become known. For example, the last criterion, delayed bile duct drainage following cholangiography is not frequently used in clinical practice as biliary drainage is difficult and sometimes impractical to measure (8,9). Other modifications include liver function test (LFT) elevations of *either* serum transaminase (AST or ALT) or serum ALP to more than 1.5 times the upper limit of normal (10). By convention, normalization of serum transaminases is not mandatory, which certainly allows patients with other causes of persistently abnormal LFTs (e.g., obese patients with steatosis) to be included in the definition. Biliary dilation, originally defined as ≥12 mm, is now considered to include ducts more than 10 mm in size (10).

However, even the revised classification system most likely eliminates a sizable portion of patients. For example, the upper limit of normal for bile duct size is 7 mm, and a few millimeters increase following cholecystectomy is considered normal. However, a large retrospective study found that there was no difference between bile duct size of pre- and post-cholecystectomy patients (11).

Table 1.
Modified Milwaukee Classification System (13)

SOD Type	*Definition*
Type I	Pain + abnormal hepatic or pancreatic enzymes on 2 occasions + dilated common bile duct/pancreatic duct
Type II	Pain + either abnormal enzymes or dilated common bile duct/pancreatic duct
Type III	Pain alone

The Milwaukee classification has traditionally focused on biliary sphincter dysfunction. With the recognition that isolated sphincter pancreatitis dysfunction may occur in up to 18.9% of patients with SOD (12), the Milwaukee classification has been modified and categorizes presumptive SOD into 3 biliary and 3 pancreatic types (Types I-III; Table 1) (13).

DIAGNOSIS

The diagnosis of suspected SOD is initially clinical, requiring exclusion of other causes of pancreaticobiliary pain by means of noninvasive testing (2). It is, however, sometimes difficult to distinguish the clinical manifestations of SOD from those caused by organic pancreaticobiliary disorders (e.g., stones, tumors) or other functional bowel disorders (e.g., irritable bowel syndrome).

The initial evaluation of all patients suspected to have SOD includes a detailed history and physical examination with special attention to the nature, quality, severity, and character of the pain. The "typical" pancreaticobiliary pain syndrome is described as epigastric or right upper quadrant in location and is usually episodic with intervening normal spells (2,14). The pain often radiates directly to the back ("knife-like") and is often precipitated by meals, usually occurring within half hour post-prandially. It generally lasts approximately 45 minutes and is relieved spontaneously or with the aid of medications (14,15). This is, however, a "classic" description, and in our experience, it is rare to find the patient who falls into this category. In our practice, patients commonly present with near continuous pain that is not always postprandial in

nature. However, pain that crosses the midline and is relieved by defecation or is exclusively left sided is almost never pancreaticobiliary in nature.

The next series of evaluations includes biochemical investigations including LFTs, amylase, and lipase (2). These should be drawn both in an asymptomatic state as well as during an attack of pain. As mentioned earlier, classic "objective" findings include an elevation of biliary (AST, ALT or alkaline phosphatase) or pancreatic enzymes of >2 times the upper limit of normal on at least 2 separate occasions with normalization within 48 hours, although most authorities have relaxed the definition using an elevation of either serum transaminases or the serum ALP to >1.5 times the upper limit of normal (7,10).

Routine imaging studies including transabdominal ultrasonography and CT scanning are usually normal but should be performed to evaluate for a dilated pancreaticobiliary system as well as to exclude other etiologies of abdominal pain (2). An upper endoscopy to evaluate for peptic ulcer disease, gastroesophageal reflux, and other upper gastrointestinal anatomic abnormalities should also be done.

In the absence of mass lesions, stones, or response to a therapeutic trial of acid suppression, the likelihood of SOD is increased. This then necessitates further diagnostic testing, including noninvasive and invasive modalities.

DIAGNOSTIC METHODS

Noninvasive Methods

While the gold standard for diagnosis of SOD is sphincter of Oddi manometry (SOM), it is invasive, of limited availability, and difficult to perform (2,9,16). Thus, several noninvasive tests have been developed to identify patients with SOD. As opposed to conventional imaging studies such as ultrasonography and CT scanning which look for anatomic abnormalities, noninvasive methods used to diagnose SOD are aimed at identifying functional issues with the disorder.

Morphine-prostigmin provocative test (Nardi test). The Nardi test is performed by an intramuscular or subcutaneous injection of morphine 10 mg and neostigmine 1 mg (15). This test relies on the property of morphine sulfate to cause sphincter of Oddi contraction and neostigmine to stimulate pancreaticobiliary secretions through cholinergic pathways. Endpoints include a reproduction of the patient's typical pain as well as a 4-fold elevation of the serum ALT, AST, alkaline phosphotase, amylase, or lipase at 30 minutes following the injection (15). However, this test is limited due to its low specificity and sensitivity and has therefore fallen out of clinical favor despite its ease of use and low cost (17).

Fatty meal-stimulated assessment of pancreaticobiliary system. This noninvasive method uses a standardized fatty meal (usually 250 mL of whole milk) to stimulate gallbladder contraction, increase hepaticoduodenal bile flow, and cause sphincter of Oddi relaxation (15). In cases of SOD where there may be a paradoxical contraction of the sphincter of Oddi in response to stimulation, an increase of the pancreaticobiliary ductal diameter may be seen when compared to baseline. This assessment is usually performed using transabdominal ultrasonography or by magnetic resonance cholangiopanctreatography (MRCP) (15). In patients with a gallbladder in situ, the gallbladder dyskinesia is evaluated by assessing the ejection fraction of the gallbladder in response to stimulation. Although this test is easy to perform and inexpensive, it's clinical utility is limited by the lack of standardization of the fatty meal and the variable response to fatty meals. This test has largely been supplanted by intravenous stimulation of the pancreaticobiliary system using secretin or cholecystokinin (15).

Secretin-stimulated assessment of the pancreatic system. Naturally occurring secretin is a hormone that increases the volume and bicarbonate concentration of pancreatic juice. Synthetically-derived porcine secretin used for commercial purposes has a similar effect on the exocrine pancreas (18). This property can be used to better assess anatomic abnormalities of the pancreatic duct when administered intravenously. SecreFlo™ contains 16 μg of porcine secretin in a vial of lyophilized powder which is reconstituted with 8 mL of normal saline (19). A dose of 0.4 μg/kg is

(continued on page 34)

(continued from page 32)

administered intravenously, and the effects are monitored for 10 minutes (19). Assessment of the pancreatic duct can then be made using a variety of techniques, including MRCP, endoscopic ultrasound (EUS), or even transabdominal ultrasonography. A size increase as compared to baseline of the pancreatic duct measured at 1 min, 2 min, 5 min and 10 min following injection as compared to baseline may imply a functional obstruction of the sphincter.

Invasive Methods

Cholangiography. A diagnostic cholangiopancreatogram is essential to rule out organic disease such as tumors, stones, or strictures (20). An extrahepatic bile duct >10 mm or a pancreatic duct >5 mm is considered abnormal. Drainage of contrast is then timed, usually in the supine position. A bile duct that retains dye 45 minutes after injection is considered abnormal. Although definitive pancreatic drainage times in the supine position have not been clearly defined, retention of dye in the pancreatic duct for ≥9 min is generally indicative of SOD (20).

Sphincter of Oddi Manometry. SOM is a procedure that has been central to the understanding of the physiology of the sphincter of Oddi as well as to the pathophysiology of sphincter dysfunction, and it is considered to be the "gold standard" in the diagnosis and management of this disorder (21). SOM is recommended in the evaluation of pancreaticobiliary pain with or without enzyme abnormalities or in evaluation of idiopathic recurrent pancreatitis in which a structural abnormality can not be identified. Typically, these patients are considered for the diagnosis of SOD. They are classified clinically using the Hogan-Geenen Milwaukee classification system as described earlier. Patients with type I SOD usually have a fibrotic cause for sphincter dysfunction (papillary stenosis), and SOM is not necessary (22,23). The majority of type I SOD patients respond to endoscopic sphincterotomy. Furthermore, up to 65% of patients with type I SOD may in fact have normal readings during SOM, and therefore performance of the manometry may simply confuse the issue (22,23). SOM is highly recommended in patients with type II SOD, and is mandatory in patients with type III SOD, with sphincterotomy response rates predicted by the presence of abnormal sphincter of Oddi readings (22,23). Approximately 50%–60% of type II SOD patients will have an abnormal manometry, with response rates of up to 75% to sphincterotomy in those with abnormal pressure findings (22,23). Type III SOD patients are far more complex, with only 25% of these patients having an abnormal reading, though 50% of type III SOD patients respond to sphincterotomy (22,23).

SOM is usually performed endoscopically at tertiary referral centers, almost always at the time of endoscopic retrograde cholangiopancreatography (ERCP) (21). The performance of SOM is however limited by several factors. First, patients with SOD are at highest risk for post-ERCP complications, specifically ERCP-induced severe pancreatitis and even death (16,21). Given the risks, these procedures should be reserved for patients with severe or disabling symptoms and may not be performed unless an endoscopic sphincterotomy could be done due to abnormal findings (21). Secondly, SOM requires equipment that is highly specialized, not widely available, and is often prone to equipment failure. The equipment may be temperamental and a skillful technique is needed for proper patient sedation and positioning of devices. The procedure in and of itself is technically challenging and requires significant skill and experience in both performance and interpretation (16,24). Static measurements taken over a few minutes may not accurately represent dynamic changes in sphincter pressures over a 24-hour period. Finally, there is often a lack of reproducibility and uniformity in findings which may lead to significant inter-observer variability (25,26). However, despite these limitations, most tertiary care centers, especially those that specialize in pancreaticobiliary disorders, have access to manometry techniques and equipment.

Sedation during SOM—Sedation for ERCP and SOM has long utilized diazepam as a sole agent due to absence of significant effects on normal sphincter motility (27,28). Although midazolam similarly has no effect on normal sphincter pressures (27,29), it may lower the pressure of a hypertensive sphincter and is therefore avoided during sedation for SOM (30). With regard to opioids, both meperidine and morphine have

(continued on page 36)

(continued from page 34)

been shown to alter only phasic pressure and not the basal pressure, and thus, may be used as an adjunct to diazepam sedation during SOM (31). Propofol has also been shown to not alter the sphincter of Oddi pressure in patients with normal basal sphincter pressures, but the data are limited (32).

SOM Equipment—The most commonly used system for manometry utilizes a water-perfused catheter hooked up to a low compliance pump. A triple lumen size 5-French catheter with a long nose is generally used with passage of the wire into the duct over a guide wire (33). This catheter usually has 2 or 3 spirally placed transducers at the tip which serve as recording ports. Most catheters will permit the passage of a 0.018-inch guidewire throughout the length of the catheter. The catheter is typically calibrated using a standard air-tight chamber (33).

Alternatively, a solid-state catheter system can be used for pressure recording. The theoretical advantage over a water-perfused system is a lower incidence of post-manometry pancreatitis, although no data exist comparing the 2 with regard to post-procedural complications. Disadvantages of the solid-state catheter are that it is expensive, fragile, and prone to damage during insertion across the elevator of a duodenoscope.

It is generally recommended to position the monitor on which the sphincter pressures are recorded adjacent to the endoscopic monitor so that the endoscopist may simultaneously view both procedures. Alternatively, a second physician may perform and interpret the manometry.

Technique—SOM is almost always performed during the time of ERCP using standard techniques. At our institution, it is sometimes recommended that the patient is in a prone position to allow gravitational flow of bile through the papilla as the bile duct courses naturally from an anterior position at the hilum to a more posterior positioned papilla. However, the prone position is not mandatory, and many centers will perform this procedure in the left lateral or supine position.

Medications that may adversely affect the sphincter (e.g., glucagon, nitrates, anticholinergics) should generally be avoided. The 5-French, triple lumen catheters with spirally placed transducers as described above are placed over a 0.018-inch guidewire positioned within the duct. During initial cannulation of the duct using a standard cannula, overfilling with dye should be avoided to prevent fluctuations in sphincteric pressure. The manometry catheter is then passed monorail style over the guidewire taking care to calibrate it with the resting duodenal pressure. The sphincteric pressure is measured with the duodenum as a reference.

Care should be taken to avoid catheter impaction against a sidewall which will alter pressure readings (16). Standard manometry catheters are generally marked over distal 2 cm every 2 mm. The catheter is then placed deep intraductally and withdrawn across the sphincter at 1-mm to 2-mm intervals (stations) allowing 15 to 30 seconds at each station.

Ideally, manometry is recorded from both sphincters using at least 2 passes each (16). Sacrificing the wire guided port and aspiration of intraductal juices from that port has been shown to significantly reduce the risk of pancreatitis following pancreatic manometry (34) and is, thus, strongly recommended.

The initial assessment of the manometry tracing involves measurement of the basal pressure (16). Again, this is measured in reference to the duodenal pressure and is defined as the sustained high pressure zone at the sphincter area. Normal pressures for SOM are listed in Table 2. An average pressure of the passes is generally used and is considered abnormal if ≥35 mmHg (16). Next, the phasic waves are measured evaluating their amplitude, duration, and frequency (16). Response to an intravenous injection of cholecystokinin is also sometimes assessed with the normal response of relaxation being replaced with a paradoxical excitation in patients with SOD (16). Furthermore, intraductal biliary pressure may correlate well with intrasphincteric basal pressure and may be used as a surrogate marker.

Table 2.
Normal Values for Sphincter of Oddi Manometry

Basal sphincter pressure	<35 mmHg
Intraductal pressure	<13 mmHg
Phasic waves	
Amplitude	<220 mmHg
Duration	<8 seconds
Frequency	<10/min

Complications of SOM—The most common complication described after SOM remains pancreatitis (20). Rates of pancreatitis of up to 31% have been described (33). It is widely believed that perfusion of the pancreatic duct using standard catheters is the cause for this complication (21), although SOM is not by itself an independent risk factor for the development of post-ERCP pancreatitis (21). The underlying disease, namely SOD, is more likely responsible for the high rates of pancreatitis following manometry. Measures to reduce the incidence of pancreatitis following ERCP include: 1) routine use of pancreatic stents following all SOM cases (21); 2) use of an aspirating catheter during pancreatic SOM (34); 3) reducing the flow rates during pancreatic SOM to 0.05 mL/min to 0.1 mL/min; and 4) using a solid-state microtransducer system or avoiding pancreatic SOM altogether (35).

Pancreatic or Biliary Stents—The use of a pancreatic or biliary stents to maintain sphincter patency and create a temporary state of "sphincter ablation" has fallen out of favor as a diagnostic tool for SOD. Used mainly at centers without access to SOM or in cases of equivocal SOM findings, pancreatic stenting can lead to fibrotic strictures of the pancreatic duct. Some of these strictures are severe and may need endoscopic or even surgical therapy (36). Biliary stent placement has also been studied, but the high rate of pancreatitis (38% in one series) has limited its use (32). Therefore, the routine use of pancreaticobiliary stent placement as a therapeutic trial for SOD is strongly discouraged.

THERAPY

The management of SOD is often difficult and frustrating except in patients with true papillary stenosis (type I SOD). Complication rates, especially after endoscopic therapy, tend to be high and the presence of associated visceral hypersensitivity tends to complicate the issue further (33). Success, even if obtained, can sometimes be short-lived and patients are often misdiagnosed for years before an accurate diagnosis is provided. Data regarding long-term results are often hampered by the fact that many of these patients seek care from multiple specialists due to the incomplete response obtained from conventional therapies.

The goal of therapy is to improve the impaired flow of bilio-pancreatic secretions into the duodenum, which can be accomplished using medical, endoscopic, or surgical means (20,23,37).

Medical Therapy

A variety of agents designed to produce smooth muscle relaxation and subsequent sphincter of Oddi relaxation have been used. Nitrates and calcium channel blockers have been the most extensively studied pharmacotherapies. A placebo-controlled, cross-over study found that nifedipine reduced pain scores, emergency room visits, and use of oral analgesia in 75% of patients with manometrically documented SOD (38). With regard to nitrates, these agents have been shown to cause relaxation of the sphincter of Oddi in animal models and in humans (39). The efficacy of nitrates in SOD patients was described in a case report of a patient treated with nitrates whose pain resolved and was associated with a decrease in both basal and phasic sphincter of Oddi activity (40). However, there are no controlled trials of nitrate therapy in patients with SOD. Other agents used at our institution include low-dose tricyclic antidepressants, selective serotonin reuptake inhibitors (SSRIs), gabapentin, and even non allopathic agents such as peppermint oil. The latter agents are all designed to reduce visceral hypersensitivity, which is usually coexistent in patients with type III SOD.

Several drawbacks of medical therapy exist. First, systemic side effects of these agents limit their long-term use (20). Second, improvement is often temporary, short lived, or incomplete. Lastly, patients with the mechanical form of SOD (sphincter of Oddi stenosis) usually fail to respond to any medical therapy (20). Regardless, given the relative safety of this approach compared to more aggressive endoscopic or surgical techniques, medical therapy should be offered first to all type III SOD patients and those type II patients without disabling symptoms.

Alternative Approaches

An intriguing area of therapy revolves around the use of alternative approaches. In 1 pilot study, acupuncture

along the right lateral tibia resulted in a significant decrease in basal pressure, amplitude duration, and frequency of basal contractions of the sphincter of Oddi (41). There has also been interest in the use of therapeutic touch, hypnosis, and stress relaxation in treating patients with type III SOD, although the clinical relevance of these modalities remains to be determined.

Endoscopic Therapy

The principles of endoscopic therapy revolve around ablation of the dysfunctional sphincter, which may be achieved by a variety of techniques that are described below.

Biliary Stenting. Biliary stenting can be used as a short-term alternative to sphincterotomy as well as a therapeutic trial to determine response to a sphincterotomy. However, the risk of complications has limited its widespread use, and it is not a recommended procedure.

Botulinum Toxin Injection. Botulinum toxin, a potent inhibitor of acetylcholine release, has wide clinical utility in the management of spastic sphincteric diseases throughout the gastrointestinal tract. Best studied in the management of esophageal achalasia, it has also been described in the management of SOD.

In 1 study of 22 patients with type III SOD, 100 units of botulinum toxin was injected into the major papilla as a single injection (42). A 5% rate of pancreatitis was observed with about half the patients deriving symptom relief at 6 weeks (42). These data show that this approach can be used a therapeutic alternative to endoscopic sphincterotomy in selected patients with a short duration of response.

Endoscopic Sphincterotomy. Endscopic sphincterotomy is the current standard therapy for treating patients with SOD. Using conventional techniques, the biliary and/or pancreatic segment of the sphincter of Oddi can be severed by electrocautery during ERCP. Due to significant complications, this procedure should ideally be done by endoscopists with sufficient training and expertise in a high-volume center.

An endoscopic sphincterotomy should cause ablation of the hypertensive or dysfunctional sphincter with a theoretical improvement in pancreaticobiliary flow. The main aims of treatment are the relief of pancreaticobiliary pain and the avoidance of recurrent pancreatitis.

The landmark, prospective study by Geenen et al. (7) was conducted in postcholecystectomy type II SOD patients who were randomized to undergo endoscopic or sham sphincterotomy. All patients underwent SOM. The study found that a finding of an abnormal SOM highly predicted a positive response to endoscopic sphincterotomy but not to a sham sphincterotomy (7). During a 4-year follow up, 95% of patients with an abnormal SOM responded to endoscopic sphincterotomy (7).

The performance of a pancreatic sphincterotomy in addition to a biliary sphincterotomy (ie, dual sphincterotomy) may improve long-term outcomes. Long-term data for this approach are however limited. At our institution, dual sphincterotomy is performed in all type III SOD patients in whom pancreatic manometry is abnormal or in those who present with recurrent symptoms following a recent prior biliary sphincterotomy. Manometry is performed on both sphincters at the time of the original ERCP and clinical decisions are made based on the results.

Complications following endoscopic sphincterotomy in patients with SOD mainly include pancreatitis, which may be seen in up to 20% of patients (23). Most cases tend to be mild, although some are severe and may even be life threatening. In one study, the presence of a hypertensive pancreatic sphincter strongly correlated with post-biliary sphincterotomy pancreatitis which can be reduced by the placement of a pancreatic duct stent (43). In our practice, it is customary to place a long (usually 9 cm), 4F pigtail stent in the pancreatic duct following all SOM. This can then be removed in 1 week if it has not spontaneously passed. Duodenal perforation can also occur due to the small size of the ducts involved.

When the etiology of idiopathic recurrent pancreatitis has been studied, SOD was found to be the primary cause in up to 47% of patients (44), although a positive response to sphincterotomy may also be seen in patients with microcrystalline gallbladder disease, another common cause of idiopathic recurrent pancre-

(continued on page 40)

(continued from page 38)

atitis. In these patients however, ablation of both the biliary and pancreatic sphincters is necessary for long term success. In a study of 69 patients with idiopathic pancreatitis and documented SOD, 81% of patients undergoing dual sphincterotomy improved as compared to 28% of patients undergoing biliary sphincterotomy alone (45).

Surgical Therapy. A transduodenal approach is utilized to perform a biliary sphincteroplasty along with a transampullary pancreatic septoplasty (33). This is usually accomplished by laparotomy. The theoretical advantage over an endoscopic approach is the decreased incidence of duodenal perforation and the complete ablation by means of septoplasty of the pancreatic meatus. Additionally, a surgical approach may have a decreased likelihood of restenosis. Patients with pancreaticobiliary pain may respond better than those with recurrent pancreatitis (33).

However, surgical sphincteroplasty is now rarely done due to the significant morbidity, cost, and cosmetic appearance. There are limited long term data for this form of therapy, and it largely reserved for those patients with restenosis following endoscopic sphincterotomy in whom symptom relief has been unequivocally linked to sphincter ablation (33). Surgical therapy can also be considered in those patients with endoscopically inaccessible papillae (e.g., Roux-en-Y gastrojejunostomy).

SUMMARY

SOD is a complex disorder with an often frustrating clinical course and therapeutic outcome for both the patient and the physician. The diagnosis and therapy require a high-level of understanding of the anatomy and pathophysiology of the area. Enthusiasm for therapy of this condition should be limited and avoided due to complications from sphincterotomy. Manometry can assist in the diagnosis of this disorder but requires access to specialized equipment along with expert endoscopic skills. Medical therapy should generally be tried first, especially in patients with type III disease and type II disease with mild symptoms. Failure of medical therapy warrants an endoscopic approach for both diagnosis and therapy. Unsatisfactory or unexpected response to therapy in patients with well established SOD may be a result of restenosis, pancreatic sphincter dysfunction, or duodenal hyperalgesia.

In conclusion, due to the technical difficulty, patients with SOD should be evaluated and treated in centers that are specialized in advanced ERCP techniques. ■

References

1. Fogel EL, Eversman D, Jamidar. Sphincter of Oddi dysfunction: pancreaticobilary sphincterotomy with pancreatic stent placement has a lower rate of pancreatitis that biliary sphincterotomy alone. *Endoscopy*, 2002;34:280-285.
2. Bistritz L, Bain VG. Sphincter of Oddi dysfunction: managing the patient with chronic biliary pain. *World J Gastroenterol*, 2006;12:3793-3802.
3. Drossman DA, Li Z, Andruzzi E, et al. US householder survey of functional gastrointestinal disorders. Prevalence, sociodemography, and health impact. *Dig Dis Sci*, 1993;38:1569-1580.
4. Bar-Meir S, Halpern Z, Bardan E, et al. Frequency of papillary dysfunction among cholecystectomized patients. *Hepatology*, 1984;4:328-330.
5. Meshkinpour H, Mollot M. Sphincter of Oddi dysfunction and unexplained abdominal pain: clinical and manometric study. *Dig Dis Sci*, 1992;37:257-261.
6. Hermann RE. The spectrum of biliary stone disease. *Am J Surg*, 1989;158:171-173.
7. Geenen JE, Hogan WJ, Dodds WJ, et al. The efficacy of endoscopic sphincterotomy after cholecystectomy in patients with sphichter-of-Oddi dysfunction. *New Engl J Med*, 1989;320: 82-87.
8. Elta GH, Barnett JL, Ellis JH, et al. Delayed biliary drainage is common in asymptomatic post-cholecystectomy volunteers. *Gastrointest Endosc*, 1992;38:435-439.
9. McLoughlin MT, Mitchell RMS. Sphincter of Oddi dysfunction and pancreatitis. *World J Gastroenterol*, 2007;13:6333-6343.
10. Baillie J. Sphincter of Oddi dysfunction: overdue for an overhaul. *Am J Gastroenterol*, 2005;100:1217-1220.
11. Majeed Aw, Ross B, Johnson AG. The preoperatively normal bile duct does not dilate after cholecystectomy: results of a five year study. *Gut*, 1999;45:741-743.
12. Eversman D, Fogel EL, Rusche M, et al. Frequency of abnormal pancreatic and biliary sphincter manometry compared with clinical suspicion of sphincter of Oddi dysfunction. *Gastrointest Endosc*, 1999;50:637-641.
13. Peterson BT. Sphincter of Oddi dysfunction, part 2: evidence-based review of the presentations, with "objective" pancreatic findings (types I and II) and of presumptive type III. *Gastrointest Endosc*, 2004;59:670-686.
14. Toouli J, Craig A. Clinical aspects of sphincter of Oddi function and dysfunction. *Curr Gastroenterol Rep*, 1999;1:116-122.
15. Sgouros SN, Pereira SP. Systematic review: sphincter of Oddi dysfunction-noninvasive diagnostic methods and long-term outcome after endoscopic sphincterotomy. *Aliment Pharmacol Ther*, 2006;24:237-246.
16. Hogan WJ, Sherman S, Pasricha P, et al. Sphincter of Oddi manometry. *Gastrointest Endosc*, 1997;342-348.
17. Steinberg WM, Salvato RF, Toskes PP. The morphine-prostigmin provactive: is it useful for making clinical decisions? *Gastroenterology*, 1980;78:728-731.
18. Jowell PS, Robuck-Mangum G, Mergener K, et al. A double-blind, randomized dose response study testing the pharmacologi-

cal efficacy of synthetic porcine secretin. *Aliment Pharmacol Ther*, 2000;14:1679-1684.
19. SecreFlo™ Prescribing Information. ChiRhoClin, Inc. Silver Spring, MD, 2002.
20. Piccinni G, Angrisano A, Testini M, et el. Diagnosing and treating sphincter of Oddi dysfunction. *J Clin Gastroenterol*, 2004; 38:350-359.
21. Cohen S, Bacon BR, Berlin JA, et al. National Institutes of Health state-of-the-science conference statement: ERCP for diagnosis and therapy, January 14-16, 2002. *Gastrointest Endosc*, 2002; 56:803-809.
22. Sherman S, Troiano FP, Hawes RH, et al. Frequency of abnormal sphinchter of Oddi manometry compared with the clinical suspicion of sphincter of Oddi dysfunction. *Am J Gastroenterol*, 1991;86:586-590.
23. Sherman S. What is the role of ERCP in the setting of abdominal pain of pancreatic or biliary origin (suspected sphincter of Oddi dysfunction)? *Gastrointest Endosc*, 2002;56:S258-S266.
24. Gilbert DA, DiMarino A, Jensen DM, et al. Status evaluation: sphincter of Oddi manometry. American Society for Gastrointestinal Endoscopy. Technology Assessment Committee. *Gastrointest Endosc*, 1992;38:757-759.
25. Smithline A, Hawes R, Lehman G. Sphincter of Oddi manometry: interobserver variability. *Gastrointest Endosc*, 1993;39:486-491.
26. Thune A, Scicchitano J, Roberts-Thomson I, et al. Reproducibility of endoscopic sphincter of Oddi manometry. *Dig Dis Sci*, 1991;36:1401-1405.
27. Allescher HD. How to sedate endoscopic sphincter of Oddi manometry? *Endoscopy*, 1993;25:399-400.
28. Garciia JP, Garrigues, V, Sala T, et al. Diazepam does not modify the motility of the sphincter of Oddi. *Endoscopy*, 1988;20:87.
29. Cuer JC, Dapoigny M, Bommelaer G. The effect of midazolam on motility of the sphincter of Oddi in human subjects. *Endoscopy*, 1993;25:384-386.
30. Rolny P, Arleback A. Effect of midazolam on sphincter of Oddi motility. *Endoscopy*, 1993;25:381-383.
31. Sherman S, Gottlieb K, Uzer MF, et al. Effects of meperidine on the pancreatic and biliary sphincter. *Gastrointest Endosc*, 1996;44:239-242.
32. Goff JS. Effect of propofol on human sphincter of Oddi. *Dig Dis Sci*, 1995;40:2364-2367.
33. Sherman S, Lehman G. Sphincter of Oddi dysfunction: diagnosis and treatment. *JOP*, 2001;2:382-400.
34. Sherman S, Troiano FP, Hawes RH, Lehman GA. Sphincter of Oddi manometry: decreased risk of clinical pancreatitis with use of a modified aspirating catheter. *Gastrointest Endosc*, 1990;36:462-466.
35. Botoman VA, Koszarek RA, Novell LA, et al. Long-term outcome after endoscopic sphincterotomy in patients with biliary colic and suspected sphincter of Oddi dysfunction. *Gastrointest Endosc*, 1994;40:165-170.
36. Kozarek RA. Pancreatic stents can induce ductal changes consistent with pancreatitis. *Gastrointest Endosc,* 1990;36:93-95.
37. Corazziari E, ShafferA, Hogan WJ, et al. Functional disorders of the bilary tract and pancreas. *Gut*. 1999;45:48-54.
38. Khuroo MS, Zargar SA, Yattoo GN. Efficacy of nifedipine therapy in patients with sphincter of Oddi dysfunction: a prospective, double-blind, randomized, placebo-controlled, cross over trial. *Br J Clin Pharmacol*. 1992;33:477-485.
39. Brandstatter, G, Schinzel, S, Wurzer, H. Influence of spasmolytic analgesics on motility of sphincter of Oddi. *Dig Dis Sci*. 1996;41:1814-1818.
40. Bar-Meir, S, Halpern, Z, Bardan, E. Nitrate therapy in a patient with papillary dysfunction. *Am J Gastroenterol*. 1983;78:94-95.
41. Lee SK, Kim MH, Kim HG, et al. Electroacupuncture may relax the sphincter of Oddi in humans. *Gastrointest Endosc*. 2001;53:211-216.
42. Wehrmann T, Seifert H, Seipp M, et al. Endoscopic injection of botulinum toxin for biliary sphincter of Oddi dysfunction. *Endoscopy*, 1998;30:702-707.
43. Tarnasky P, Cunningham J, Cotton P, et al. Pancreatic sphincter hypertension increases risk of post-ERCP pancreatitis. *Endoscopy*, 1997;29:252-257.
44. Coyle WJ, Pineau BC, Tarnasky PR, et al. Evaluation of unexplained acute and acute recurrent pancreatitis using endoscopic retrograde cholangiopancreatography, sphincter of Oddi manometry and endoscopic ultrasound. *Endoscopy*, 2002;34:617-623.
45. Guelrud M, Plaz J, Mendoza S, et al. Endoscopic treatment in type II pancreatic sphincter dysfunction. *Gastrointest Endosc*, 1995;41:A398.

Fellows' Corner
is open to
Trainees and Residents ONLY.

Section Editor: C. S. Pichumoni, M.D.

Send in a brief case report. No more than one double-spaced page. One or two illustrations, up to four questions and answers and a three-quarter to one-page discussion of the case. Case to include no more than two authors. A $100.00 honorarium will be paid per publication.

Case should be sent to:

C. S. Pitchumoni, M.D.
Chief, Gastroenterology, Hepatology
and Clinical Nutrition
St. Peter's University Hopsital
254 Easton Avenue, Box 591
New Brunswick, NJ 08903
E-mail: pitchumoni@hotmail.com