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Sphincter of Oddi Dysfunction

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Abstract Sphincter of Oddi dysfunction (SOD) is a poorly-understood disorder, typically presenting as post-cholecystectomy, "biliary-type," right-sided abdominal and/or chest wall pain. Most patients referred to specialist clinics for work-up of presumed SOD do not, in fact, have anything wrong with their bile ducts or biliary sphincter mechanisms. A careful history and focused physical examination will often identify the true source of the pain syndrome, ranging from chest wall costochondritis and nerve injury at surgical trochar sites, to gastroparesis and visceral hypersensitivity ("irritable bowel"). The Rome III classification of functional gallbladder and biliary disorders defines SOD as episodic (not daily) pain lasting more than 30 min, which is disruptive of normal activities and not associated with bowel upset. It is not relieved by gastric acid suppression or antispasmodics. Other causes of abdominal pain must be excluded. Standard work-up includes endoscopic retrograde cholangiopancreatography (ERCP) with biliary manometry, which risks post-ERCP pancreatitis, especially in young women with normal bile ducts and liver serology. Noninvasive tests for SOD, such as timed ("gated") cholecystokinin (CCK)-stimulated hepatobiliary iminodiacetic acid (HIDA) scans and secretin-stimulated magnetic resonance cholangiopancreatography, are imperfect and still evolving. Although many doubt the very existence of SOD, a multidisciplinary approach to the management of pre- and postcholecystectomy abdominal pain syndromes is long overdue.

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Introduction

Sphincter of Oddi dysfunction (SOD) is a difficult subject to discuss without emotion. It is unloved, even by its proponents, misunderstood, and frequently vilified. It is largely ignored outside the United States. SOD burst on the endoscopic retrograde cholangiopancreatography (ERCP) scene in 1989 with a paper in the *New England Journal of Medicine* by Joseph Geenen, Walter Hogan, and colleagues [1] from Racine, Wisconsin. Geenen and Hogan are two of the pioneers in ERCP and sphincter of Oddi (SO) physiology [1]. In an effort to make sense of postcholecystectomy abdominal pain, they studied 47 patients randomly assigned to sphincterotomy or no sphincterotomy prior to SO manometry (SOM). Forty patients were followed prospectively for 4 years. By comparing their symptoms, radiologic findings, and serologic findings with SOM results, these investigators produced what became known as the Milwaukee Criteria: this classification is based on whether SOD patients have "typical biliary pain," elevation of serum transaminases or alkaline phosphatase to 1.5 times the upper limit of normal on two occasions, with normalization between attacks, and bile duct dilatation [2]. The common bile duct dilatation "required" for SOD was

recently revised downward, from ≥ 12 mm to ≥ 8 mm. Patients with all three features are said to have type I SOD; those with pain and one or other—but not both—of the dilated bile duct and serologic abnormalities are type II; and those with pain alone—by far the most commonly seen in biliary clinics—are type III. The most recent iteration of the Rome criteria for functional gastrointestinal disorders, Rome III [3, 4], identifies the following characteristics of *biliary pain*:

- Episodes last longer than 30 min;
- Pain builds up to a steady level;
- Pain is severe enough to disrupt daily activities or lead to an emergency department visit;
- Pain is not relieved by defecation, charge in position, or acid suppression;
- No other structural abnormalities that would explain the pain.

SOD pain is rarely precipitated by eating, and it rarely awakens patients from sleep. Most patients walking in the door of the gastroenterology clinic with an implanted morphine pump, wearing a transdermal fentanyl patch, and having a transcutaneous electrical nerve stimulating device for good measure *do not* have SOD. All too often, patients sent to specialist clinics for evaluation of suspected SOD have not had an adequate history and focused physical examination. Pain that is clearly positional in nature is most likely to be of musculoskeletal origin. Similarly, the complaint of pain on coughing, straining, or lifting may be caused by a chest wall fibromyalgia, costochondritis, or a trigger point where a surgical trochar injured a sensory nerve passing through the abdominal wall. On physical examination, such trigger points should be sought out. If focal pain is acutely exacerbated by the supine patient attempting to roll forward from lying flat (an abdominal "crunch"), this is a positive Carnett's sign. Local injection of long-acting steroid and local anesthetic will frequently take care of such pain; this procedure is typically done in a pain clinic. Gastroparesis is a common cause of episodic epigastric and/or right hypochondrial pain, especially after meals. Certain patients, such as those with insulin-dependent diabetes mellitus (IDDM), are clearly at risk for gastroparesis. Although IDDM is the commonest cause of gastroparesis, it is not the only one, so the possibility of gastric emptying delay should always be considered, even when a cause is not apparent. So ubiquitous are narcotic analgesics that "narcotic bowel" is a common cause of gastrointestinal motility upset. Some radiologists decline to perform radioisotope gastric emptying studies in patients taking around-the-clock narcotics, so likely are they to have an abnormal result. Narcotic analgesia may also affect SOM. Once more likely causes of abdominal pain are identified, no more than 25% of patients referred with "possible SOD" remain candidates for this diagnosis. Inevitably, the other 75% of patients are frustrated, disbelieving, and often angry that the label they have been given—and the treatment they were promised by optimistic, and sometime desperate, referring physicians and other providers—has suddenly evaporated. My institution has a neuromuscular center to which I can refer some of these unhappy and often tortured individuals—those with motility upset—for additional work-up and management, but because there is typically a waiting list of months for an appointment, I usually start the assessment myself. If not done already, esophagogastroduodenoscopy (with biopsies for *Helicobacter pylori*) and cross-sectional abdominal imaging (eg, CT) are appropriate for longstanding abdominal pain, whether it is intermittent or constant. If gastroparesis seems a possibility, a solid-phase, radioisotope, gastric-emptying study is next. If Carnett's sign is positive, and/or very localized chest wall or abdominal pain is identified during physical examination, I offer the patient a pain clinic referral for trigger-point injection (as described above).

SOD with an Intact Gallbladder?

A perennial question in the biliary clinic is, can SOD occur in patients who still have their gallbladder? There is a paucity of data on this subject. Several studies have shown an apparent correlation between gallbladder stones and SOD [5, 6], but few ERCP endoscopists will offer patients with cholelithiasis ERCP for SOM. Where doubt exists about the origin of biliary-type pain, the patient is usually advised to undergo cholecystectomy first. I personally do not offer patients with an intact gallbladder ERCP for SOM or empiric biliary sphincterotomy. SOD is a cause of idiopathic, recurrent, acute pancreatitis in a small number of patients. However, because biliary microlithiasis is a far more common cause, pancreatic sphincter dysfunction is usually not diagnosed until the gallbladder has been "removed from the equation." Gallbladder dyskinesia is considered part of a spectrum of gallbladder and biliary motility disturbance. Patients who have pre-cholecystectomy "biliary" pain, but negative imaging for gallstones or chronic cholecystitis, often have their gallbladders removed for a low gallbladder ejection fraction on a cholecystokinin (CCK)-stimulated hepatobiliary iminodiacetic acid (HIDA) study (normal ≥ 65%). It is a common, but incorrect, assumption that when cholecystectomy fails to cure this pain, SOD is the likely explanation. Most (around 80%) such patients have type III SOD, and therefore are statistically unlikely to have elevated SO pressures that would benefit from biliary sphincterotomy. I dislike the term "type III SOD" when applied to patients who are unlikely to have anything wrong with their SO. This diagnosis should be reserved for patients with disturbance of the SO proved by

manometric studies. Type III SOD patients do not like to have this diagnosis, to which they cling tightly, withdrawn and replaced by a less exotic, but more likely, one, such as visceral hypersensitivity or chest wall pain syndrome.

ERCP in SOD: Not a Benign Procedure, and No Guarantee of Cure

Before patients undergo ERCP for SOM, they must understand the risks and benefits of the procedure. Young women with normal diameter bile ducts and normal liver function tests (LFTs) (ie, type III SOD) are at highest risk from ERCP. In several large, prospective studies of ERCP complications, the post-ERCP pancreatitis (PEP) rate in such patients was in the range of 20% to more than 40% [7, 8]. Placing a prophylactic pancreatic duct stent was shown to reduce this risk [9, 10•], and I routinely perform this procedure (when possible) in type III patients having SOM. Patients with type I SOD have greater than 90% likelihood of symptomatic improvement from biliary sphincterotomy, regardless of the pressure readings, so we perform biliary sphincterotomy without prior manometry (SOM) [2]. Type II SOD patients (typical pain plus dilated bile duct *or* abnormal LFTs ×2, but not both) have about 50% to 70% chance of symptomatic benefit from sphincterotomy *if* SO pressure is elevated. In type II patients with normal SO pressure, the benefit falls to about 30%. Type III SOD patients (pain only) with elevated SO pressure have only about 20% to 30% chance of benefit from sphincterotomy; without elevated pressure, the benefit is less than 20%.

Recent data suggest that pharmacologic prophylaxis against PEP may be achieved with nonsteroidal anti-inflammatory drugs (NSAIDs) administered before or after the procedure [11, 12•]. However, such chemoprevention with NSAIDs has yet to be widely adopted. Pharmacologic intervention for PEP has been studied since the mid-1980s, when a German group reported that nitrates sprayed sublingually appeared to relax the SO [13]. Transdermal nitrates, calcium channel-blocking drugs, somatostatin and its synthetic analog, octreotide, the protease inhibitor, gabexate, and intrapapillary *Botulinum* toxin have all been touted as pharmacologic means to reduce the risk of PEP. Unfortunately, none of these has stood the test of time. Since 2003, the placement of small caliber (≤ 5 French gauge) plastic pancreatic duct stents was shown in multiple studies to be a reliable way for preventing severe (necrotizing) pancreatitis, if placed early in the procedure (ie, before significant instrumentation) [14, 15]. A fascinating newcomer in the PEP pharmacoprophylaxis area is *vardenafil*, a phosphodiesterase type 5′-inhibitor, which is marketed for erectile dysfunction in men. In a small preliminary study, vardenafil appeared to offer protection against PEP [16]. Further studies with this and other related drugs for erectile dysfunction are awaited with interest [17].

Is a Second "Look" at SO Pressure Worthwhile?

A question that is often posed about SOM is, how well does SOM reflect a patient's actual pressure measurements on a day-to-day basis? After all, the pressure values obtained during SOM represent only a 5- to 10-minute "snapshot" of that individual's lifetime SO activity. How sensitive and specific *is* SOM? There are certainly false-negative results. Khashab et al. [18] retrospectively reviewed a 13-year experience of SOM in 5,352 patients who had diagnostic procedures for SOD. Of this group, 1,037 patients had normal studies: 30 (27 female) patients underwent repeat ERCP with SOM for persistent symptoms, with a mean interval between the two ERCPs of 493 days. From this group of repeat SOM patients, 18 of 30 had abnormal results. The investigators concluded that repeat ERCP and SOM appear to be justified in a subset of patients with persistent, debilitating symptoms and a high index of suspicion for SOD.

Water-Perfused Versus Solid-State Pressure Catheters

The time-honored way to measure SO pressure has been with a manometry catheter employing the Arndorfer water-perfusion system (Arndorfer Medical Specialties, Greendale, WI). Sterile water perfused through several tiny holes arrayed along the catheter tip provides the means of detecting sphincter pressure. The entire system, including the temperamental pressure transducers, requires almost daily maintenance by a dedicated technician or nurse to ensure accurate and reproducible results. The water-perfusion system served a generation of ERCP endoscopists well, but many of these devices are now ready for retirement and are being replaced by a new generation of solid-state pressure transducers. These are usually linked to dedicated computer software that offers instant analysis of readings and an easy way to store data. A solid-state ERCP catheter and a conventional water-perfused device were recently compared directly, and no differences were detected in their ability to detect normal and abnormal SO pressures [19]. It seems likely that water-perfused manometry systems will become extinct in the near future.

Alternatives to SOM?

In view of the risk of pancreatitis from ERCP, there has been increasing interest in noninvasive imaging tests to

predict SO pressures. The two current contenders are the CCK-HIDA scans and secretin-stimulated magnetic resonance cholangiopancreatography (ss-MRCP). Some studies claim good correlation between (liver) hilum-to-duodenum time during CCK-HIDA scans in the postcholecystectomy patient. In the past year or so, I have started seeing patients referred for consideration of ERCP and biliary sphincterotomy based on confident diagnoses of SOD by CCK-HIDA scans. When the Indiana University ERCP group recently compared ss-MRCP and ERCP, they found that in patients with suspected SOD, ss-ERCP failed to predict the results of SO manometry [20]. A British study that set out to show ss-MRCP could diagnose biliary SOD fared no better [21]. MRCP as a way to reliably diagnose SOD is not ready for "prime time."

Are Type I SOD and Biliary Microlithiasis the Same Disorder?

This intriguing possibility has been made moot by Elmi and Silverman [22], who retrospectively studied prospective data from a trial of endoscopic sphincterotomy in 17 symptomatic patients, nine with biliary microlithiasis and eight with type I SOD by Milwaukee criteria. When follow-up examination was done at a median of only 9 weeks postsphincterotomy, about two thirds of each group had sustained symptomatic benefit. What this says about biliary microlithiasis is uncertain, but with this condition being diagnosed increasingly by endoscopic ultrasound, a larger prospective study with much longer follow-up is certainly justified.

Conclusions

Is there light at the end of the tunnel? Having monitored the comings and goings across the SOD "landscape" for 25 years, I find myself no closer to understanding this disorder. The Believers believe, and the Cynics disbelieve. Authors across the spectrum of SOD belief have written eloquently—even passionately—in defense of their positions [23]. One thing is certain: many patients with pre- and postcholecystectomy right upper quadrant and chest wall pain are in need of help. As a subspecialty group, gastroenterologists have not met this challenge head-on. As a result, we lack a rational, multidisciplinary approach to the investigation and management of these complaints. A US-based, prospective, randomized, multicenter trial of endoscopic therapy for SOD is currently in progress (coordinated from the Medical University of South Carolina in Charleston, SC, and funded by the National Institutes of Health). Perhaps it will answer the all-important question: is endotherapy helpful in type II and type III SOD? I predict that little difference will be found between type II and type III SOD patients, a subset of whom appears to benefit from endoscopic sphincterotomy. Perhaps a new classification will emerge, based on more solid data than tiny "blips" on the LFT "radar screen" and millimeter differences in bile duct diameter. We tritely say that "no one has ever died from SOD," but the sad truth is that we lack data on the long-term outcome of SOD therapy. Experts see others' failures, the so-called "bouncing balls," patients who drift from specialist unit to specialist unit, accumulating ERCPs and sphincterotomies, stents and celiac blocks. I suspect that most such patients give up on gastroenterologists, and seek symptomatic relief elsewhere. As a subset of irritable bowel syndrome, gallbladder and biliary disorders lag a long way behind in research funding and publications. However, perhaps it's not too late to grab this particular bull by the horns. In 2002, a National Institutes of Health consensus conference challenged the ERCP community to replace our long-cherished empiricism with science [24]. SOD is begging for more science.

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References

Papers of particular interest, published recently, have been highlighted as:
- Of importance

1. Geenen JE, Hogan WJ, Dodds WJ, et al.: The efficacy of endoscopic sphincterotomy after cholecystectomy in patients with sphincter-of-Oddi dysfunction. N Engl J Med 1989, 320: 82–87.
2. Toouli J: Sphincter of Oddi: function, dysfunction, and its management. J Gastroenterol Hepatol 2009, 24(Suppl 3):S57–S62.
3. Behar J, Corazziari E, Guelrud M, et al.: Functional gallbladder and sphincter of Oddi disorders. Gastroenterology 2006, 130:1498–1509.
4. Rome Foundation: Rome III diagnostic questionnaires. Available at http://www.romecriteria.org/questionnaires/. Accessed February 2010.
5. Ruffolo TA, Sherman S, Lehman, et al.: Gallbladder ejection fraction and its relationship to sphincter of Oddi dysfunction. Dig Dis Sci 1994, 39:289–292.
6. Choudhry U, Ruffolo T, Jamidar P, et al.: Sphincter of Oddi dysfunction in patients with intact gallbladder: therapeutic response to endoscopic sphincterotomy. Gastrointest Endosc 1993; 39:492–495.
7. Freeman ML, Guda NM: Prevention of post-ERCP pancreatitis: a comprehensive review. Gastrointest Endosc 2004, 59:845–864.
8. Freeman ML: Post-ERCP pancreatitis: patient and technique-related risk factors. JOP 2002, 3:169–176.
9. Saad AM, Fogel EL, McHenry L, et al.: Pancreatic duct stent placement prevents post-ERCP pancreatitis in patients with suspected sphincter of Oddi dysfunction but normal manometry results. Gastrointest Endosc 2008, 67:255–261.

10. • Freeman ML: Pancreatic stents for prevention of post-endoscopic retrograde cholangiopancreatography pancreatitis. Clin Gastroenterol Hepatol 2007, 5:1354–1365. *This article describes the role of pancreatic stents in the prevention of post-ERCP pancreatitis, as discussed by the pioneer in the field*.
11. Senol A, Saritas U, Demirkan H: Efficacy of intramuscular diclofenac and fluid replacement in prevention of post-ERCP pancreatitis. World J Gastroenterol 2009, 15:3999–4004.
12. • Elmunzer BJ, Waljee AK, Elta GH, et al.: A meta-analysis of rectal NSAIDs in the prevention of post-ERCP pancreatitis. Gut 2008, 57:1262–1267. *This article presents a meta-analysis of four prospective studies appearing to show that NSAIDs may significantly reduce the risk of post-ERCP pancreatitis*.
13. Staritz M, Poralla T, Dormeyer HH, et al.: Endoscopic removal of common bile duct stones through the intact papilla after medical sphincter dilation. Gastroenterology 1985, 88:1807–1811.
14. Madácsy L, Kurucsai G, Fejes R, et al, Prophylactic pancreas stenting followed by needle-knife fistulotomy in patients with sphincter of Oddi dysfunction and difficult cannulation: new method to prevent post-ERCP pancreatitis. Dig Endosc 2009, 21:8–13.
15. Freeman ML: Pancreatic stents for prevention of post-endoscopic retrograde cholangiopancreatography pancreatitis. Clin Gastroenterol Hepatol 2007, 5:1354–1365.
16. Cheon YK, Cho YD, Moon JH, et al.: Effects of vardenafil, a phosphodiesterase type-5 inhibitor, on sphincter of Oddi motility in patients with suspected biliary sphincter of Oddi dysfunction. Gastrointest Endosc 2009, 69:1111–1116.
17. Affronti J: Levitra for sphincter of Oddi dysfunction? Are you kidding? Gastrointest Endosc 2009, 69:1117–1119.
18. Khashab MA, Watkins JL, McHenry Jr L, et al.: Frequency of sphincter of Oddi dysfunction in patients with previously normal sphincter of Oddi manometry studies. Endoscopy 2009 (Epub ahead of print).
19. Draganov PV, Kowalczyk L, Forsmark CE: Prospective trial comparing solid-state catheter and water-perfusion triple-lumen catheter for sphincter of Oddi manometry done at the time of ERCP. Gastrointest Endosc 2009, 70:92–95.
20. Aisen AM, Sherman S, Jennings SG, et al.: Comparison of secretin-stimulated magnetic resonance pancreatography and manometry results in patients with suspected sphincter of Oddi dysfunction. Acad Radiol 2008, 15:601–609.
21. Baillie J, Kimberly J: Prospective comparison of secretin-stimulated MRCP with manometry in the diagnosis of sphincter of Oddi dysfunction types II and III. Gut 2007, 56:742–744.
22. Elmi F, Silverman WB: biliary sphincter of Oddi dysfunction type I versus occult biliary microlithiasis in post-cholecystectomy patients: are they both part of the same clinical entity? Dig Dis Sci 2009 (Epub ahead of print).
23. Sphincter of Oddi dysfunction (SOD). Available at http://sphincter-of-odii-sod.blogspot.com. Accessed February 2010.
24. Cohen S, Bacon B, 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.