

# Sphincter of Oddi Dysfunction: A Survey of Current Practice in USA

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## Abstract

**Background and aims:** The role of sphincter of Oddi dysfunction (SOD) and sphincter of Oddi manometry (SOM) in patients with post-cholecystectomy pain and idiopathic recurrent acute pancreatitis (IRAP) is controversial. We sought to survey the American Gastroenterology community to define current approaches.

**Methods:** An electronic survey was sent to U.S. members of the American Society of Gastrointestinal Endoscopy (ASGE) on May 1<sup>st</sup>, 2014 to assess their approach to SOD and IRAP.

**Results:** There were 169 respondents, 54 (32%) of who worked in university hospitals and the majority (135, 80%) were endoscopic retrograde cholangiopancreatography (ERCP) providers. Utilization of magnetic retrograde cholangiopancreatography (MRCP) and endoscopic ultrasound (EUS) was significantly more often in IRAP than in SOD (69%, 72% vs 48%, 26% respectively). The majority (121, 90%) of ERCP providers perform ERCP in SOD or IRAP, although most (83, 69%) do not use SOM. Empiric biliary sphincterotomy (BS) was the dominant approach reported in patients with SOD type I (92%). Among the SOM providers, majority perform SOM directed BS in SOD type II (77%) and type III (75%). More than one-half perform SOM directed pancreatic sphincterotomy (PS) in SOD types II, III, and IRAP; less in SOD type I (33%). While less than one-third perform SOM directed dual sphincterotomy (DS) in SOD II, III, and IRAP; none in SOD type I.

**Conclusion:** This survey of ASGE members shows low utilization of sphincter manometry and mixed utilization of ERCP for SOD types II-III and IRAP. More stringent research is required to guide clinical practice.

**Keywords:** Endoscopic retrograde cholangiopancreatography; Sphincter of Oddi dysfunction; Idiopathic recurrent acute pancreatitis; Sphincter of Oddi manometry; Endoscopic sphincterotomy

**Abbreviations:** SOD: Sphincter of Oddi dysfunction; SOM: Sphincter of Oddi Manometry; BS: Biliary Sphincterotomy; RAP: Recurrent Acute Pancreatitis; IRAP: Idiopathic Recurrent Acute Pancreatitis; ACG: American College of Gastroenterology; ASGE: American Society of Gastrointestinal Endoscopy; MRCP: Magnetic Resonance Cholangiopancreatography; ERCP: Endoscopic Retrograde Cholangiopancreatography

## Introduction

Sphincter of Oddi dysfunction (SOD) has long been proposed and widely accepted as a cause of biliary pain after cholecystectomy, and of recurrent acute pancreatitis [1]. Sphincter of Oddi manometry (SOM) became popular in selected U.S. referral centers as a technique to diagnose SOD, which was defined by a basal sphincter pressure of >40mmHg [2]. Based on the manometric results, endoscopic sphincterotomy would be performed on the biliary orifice, pancreatic orifice, or both. For patients with post-cholecystectomy pain, this practice was based on three small-randomized trials showing that manometrically confirmed SOD correlated with the outcomes of biliary sphincterotomy (BS), and on many less stringent cohort studies [3,4].

SOD has been classified into three subtypes: SOD type I (dilated duct with abnormal liver tests), type II (dilated duct or abnormal liver tests), and type III (no objective abnormalities) [5]. Recurrent acute pancreatitis (RAP) is defined as two or more episodes of acute pancreatitis without any evidence of underlining chronic pancreatitis, while idiopathic recurrent acute pancreatitis (IRAP) is without a clear etiology after standard diagnostic testing [6,7]. Two recent randomized clinical trials have challenged the clinical significance of SOD, as classically defined by sphincter of Oddi manometry. The EPISOD study in patients with post-cholecystectomy pain and no objective imaging or laboratory findings (classically defined as type III SOD), first released in October 2013 at the American College of Gastroenterology (ACG) annual scientific meeting, showed that endoscopic sphincterotomy (biliary, pancreatic, or both) resulted in no greater reduction in pain-related disability than sham treatment after 12 months of follow-up.<sup>8</sup> Furthermore, the results of sphincter of Oddi manometry had no correlation with change in disability or response to sphincterotomy [8,9]. An open-label clinical trial in patients with idiopathic recurrent pancreatitis (IRAP) comparing biliary sphincterotomy with dual (biliary + pancreatic) sphincterotomy (DS) in patients with manometrically confirmed SOD of the pancreatic orifice

showed no difference in delaying the time to recurrent pancreatitis during follow-up, or in overall rates of recurrence [10]. Furthermore, empiric biliary sphincterotomy conferred no benefit among patients with normal sphincter of Oddi manometry.

In view of these uncertainties, we sought to survey the American Gastroenterology community to define current approaches to post-cholecystectomy pain and unexplained recurrent acute pancreatitis, with a particular emphasis on the utilization of ERCP and sphincter of Oddi manometry.

## Materials and Methods

### Participants

After approval by our local Institutional Review Board and the American Society of Gastrointestinal Endoscopy (ASGE), all 7,784 North American ASGE members were invited to participate. E-mail addresses for the invited subjects were obtained with permission from the ASGE.

### Survey instrument and administration

A 77-item survey was created to obtain demographic information and to assess utilization of magnetic resonance cholangiopancreatography (MRCP), endoscopic ultrasound (EUS), hepatobiliary iminodiacetic acid (HIDA) scans, and sphincter of Oddi manometry. Additionally, we queried opinions on the use of endoscopic sphincterotomy for the indications of SOD and IRAP independently. Recognizing that SOD has long been categorized into types by the presence or absence of objective findings, we asked about general attitudes regarding SOD including physician-perceived predictors that would indicate performing ERCP, and then specifically in SOD types I, II and III, and in idiopathic recurrent acute pancreatitis. For most questions, the available responses included never, sometimes, usually, always; or not applicable; definitely, probably, possibly, not helpful, uncertain; yes, sometimes, or no. For the purposes of this analysis, we considered usually and always to be yes, while sometimes and never to be no. There were only a few responses that included free text.

All members were contacted once by e-mail on May 1<sup>st</sup> 2014, approximately 6 months after the EPISOD study results were first presented at the American College of Gastroenterology (ACG) annual scientific meeting held in San Diego, California, USA. The e-mail consisted of a cover letter describing the study and an Internet link to the survey where they could complete the instrument

anonymously. The findings from the EPISOD study were not disclosed in the cover letter. De-identified responses were recorded using REDCap [11], a web-based electronic data capture application.

Utilization of advanced imaging procedures (EUS, MRCP, HIDA) was analyzed for all respondents. Responses about ERCP-specific practices were limited to those who performed ERCP, and SOM-specific practices were limited to those who performed manometry.

### Manometry catheter supplies

As a quantitative assessment of sphincter manometry utilization, we asked the company supplying almost all SOM catheters in the USA to provide data on the number supplied each quarter from January 1<sup>st</sup> 2009, to December 31<sup>st</sup>, 2015.

### Statistical analysis

SAS software version 9.3 (SAS Institute Inc, Cary, NC) was used to perform analyses. Variables were described using counts and percentages for categorical data, or means and standard deviations for continuous normal data. For the main outcome, the utilization on advanced imaging procedures, paired responses were assessed using the exact McNemar's test to account for small numbers of discordant pairs. For one of the secondary interests, the Sphincter of Oddi manometry catheter supplies, a paired Student's t-test was used to compare the average amount of catheter supplies and an interrupted time-series model was used to compare the trends of the supplies pre/post dissemination of EPISOD results. All tests were two-sided with a criterion for

statistical significance of  $p<0.05$ .

## Results

### Demographics

Of 7,784 individuals contacted, we received replies from 169 (2%) individuals spanning 39 states, 54 (32%) of whom worked in university hospitals. The majority (135, 80%) performed endoscopic retrograde cholangiopancreatography (ERCP), with a median annual number of 100 (interquartile range (IQR), 50-200).

### Utilization of advanced imaging procedures

When managing patients with suspected SOD of any type, 48% of respondents usually or always utilized MRCP, 26% EUS, and 11% HIDA scans. By comparison, MRCP and EUS were used more often when managing patients with IRAP (69% and 72% respectively), ( $p < .0001$ ).

### Attitudes to predictors

Table 1 shows the opinions of the ERCP providers ( $N=121$ ) about the features that might predict a good outcome when using ERCP in patients with suspected SOD of any type. The only apparent consensus was that most respondents believed that elevated transaminases in attacks (117, 97%) and a markedly dilated bile duct (101, 83%) were predictive of a good outcome. Conversely the majority dismissed features of a period of pain relief after cholecystectomy (34, 28%), greater pain burden (30, 25%) and mild to moderate bile duct dilation (21, 17%).

S.No	Predictors	Definitely and Probably (%)
1	Transaminases elevated with pain	97
2	Bile duct > 12 mm	83
3	Bile duct > 10-12 mm	62
4	Absence of other functional GI disorder	56
5	Pain during episodes (not daily)	55
6	No daily narcotics	50
7	Transaminases elevated at any time	49
8	Cholecystectomy was for stones	43
9	Absence of major depression or anxiety	42
10	Period of pain relief after cholecystectomy	28
11	Greater pain burden	25
12	Bile duct 8-9mm	17

Table 1: Physician-perceived predictors of response to endoscopic sphincterotomy in cases of suspected SOD. Percent ERCP providers, ranked by most favored (1-12) predictor for a good outcome after ERCP performed in patients with suspected SOD (any sub-type).

## Utilization of ERCP, Manometry and Sphincterotomy

A large majority (121, 90%) of ERCP providers perform ERCP among patients with suspected SOD of any type, including IRAP. However, most (83, 69%) do not perform sphincter manometry. Among manometry providers (38, 31%), SOM was more often utilized in the private setting as compared to the university setting (23 VS.15; p value =.27). Among sphincter manometry providers, manometry was utilized by more than half in SOD II (22, 58%) and

SOD III (24, 63%) while less in IRAP (14, 37%) and SOD I (3, 8%).

Table 2 shows data on the utilization of sphincterotomy in patients with suspected SOD and IRAP. Empiric biliary sphincterotomy (BS) was the dominant approach to patients with SOD I (92%). It was also used by a little over a third of respondents in SOD II, less in IRAP and rarely in SOD type III. Empiric pancreatic (PS) or dual sphincterotomy (DS) was used rarely (< 10%) in any context.

<b>Empiric Sphincterotomy</b>	<b>SOD I</b>	<b>SOD II</b>	<b>SOD III</b>	<b>IRAP</b>
	N = 121	N = 121	N = 121	N = 121
Biliary (BS)	111 (92%)	47 (39%)	9 (7%)	23 (19%)
Pancreatic (PS)	3 (2%)	0 (0%)	1 (1%)	7 (6%)
Dual, pancreatic and biliary (DS)	3 (2%)	2 (2%)	2 (2%)	6 (5%)
<b>SOM Directed Sphincterotomy</b>	<b>N = 3</b>	<b>N= 22</b>	<b>N = 24</b>	<b>N= 14</b>
BS only if biliary SOM (+)	1 (33%)	17 (77%)	18 (75%)	9 (64%)
PS only if pancreatic SOM (+)	1 (33%)	13 (59%)	15 (63%)	8 (57%)
DS if either SOM (+)	0 (0%)	2 (9%)	2 (8%)	1 (7%)
DS if pancreatic SOM (+)	0 (0%)	3 (14%)	5 (21%)	4 (29%)

Table 2: Utilization of sphincterotomy in SOD of any type and IRAP. All categories are not mutually exclusive and may represent a respondent with more than one response. For example, one respondent among the 121 providers who perform a specific sphincterotomy in SOD I may be represented more than once.

Among the minority of respondents who perform sphincter manometry, biliary sphincterotomy directed by SOM results was performed by a majority of respondents in SOD type II (77%) and SOD type III (75%), less in IRAP and type I SOD. In comparison, manometry directed pancreatic sphincterotomy was used by more than half of respondents in SOD type II (59%), III (63%), and IRAP (57%) and less in Type II (33%). Overall, dual sphincterotomy (DS) was performed by less than a third of respondents in SOD II, III, and IRAP, and none in SOD I.

## Manometry catheter supplies

Figure 1 show that the supply of sphincter manometry catheters has been declining steadily between 2009-2016, with a more steep decrease following the dissemination of

EPISOD results at the ACG meeting in October 2013. The mean  $\pm$  SD catheter supply was  $960 \pm 148$  per quarter before the ACG meeting and  $451 \pm 147$  following the meeting. The difference was statistically significant (p value < .0001). Using an interrupted time-series model with an interaction between the time of data collection and the release of EPISOD results, we compared the linear trend of catheter supplies prior to and after the EPISOD results were disseminated in October 2013. The quarterly catheter supplies declined to 23 (95% CI: 16, 29) before the dissemination of EPISOD study results and declined further after the dissemination of results to 50 (95% CI: 31, 69). The increased decline rate for the catheter supplies was statistically significant (27, 95% CI: 7, 47; p value=0.01).

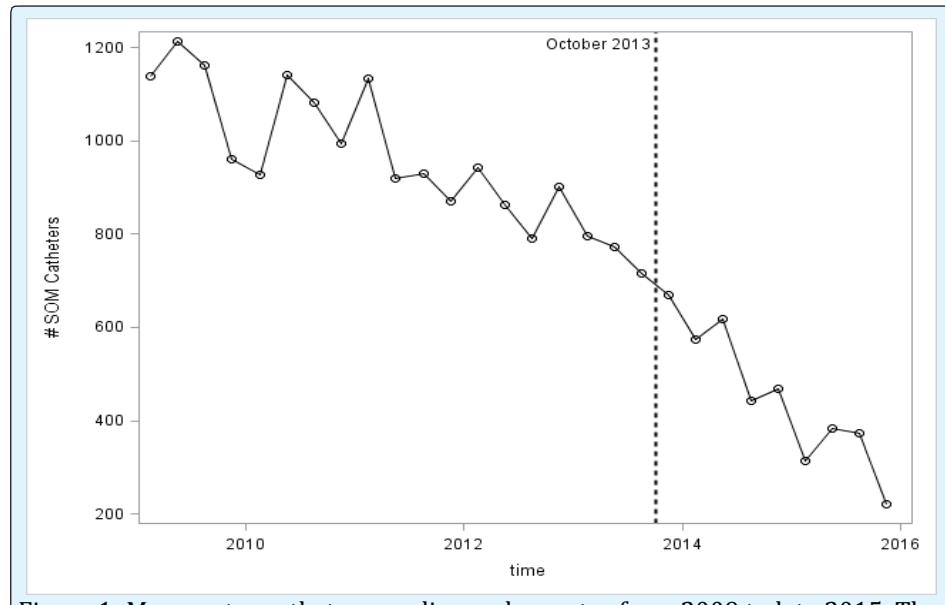


Figure 1: Manometry catheter supplies each quarter from 2009 to late 2015. The dotted vertical line represents when the EPISOD results were revealed during the annual American College of Gastroenterology (ACG) scientific meeting on October 2013.

## Discussion

This survey of ASGE members provides a snapshot of current approaches to patients with suspected SOD and unexplained recurrent acute pancreatitis. In view of the known significant risks of ERCP in these contexts, it is surprising that modern non- or less-invasive diagnostic methods are not used almost universally. When managing patients with suspected SOD in general, roughly one half of respondents used MRCP, a quarter used EUS and only 11% used dynamic biliary scanning (HIDA). Other methods for investigating sphincter function, such as secret in-stimulated EUS and MRCP results have not yet become popular in such patients [12].

Attitudes to likely predictors of benefit from intervention in SOD reflect current teaching, anecdotes, and a paucity of data, with confidence expressed only in the finding of a markedly dilated bile duct and transaminase elevation during attacks (Table 1). These features are the basis of the old classification of SOD into three subtypes [2], which themselves derive from multiple cohort studies of varied quality [3,4]. The latest iteration of the Rome consensus (Rome IV) recommends abandoning this classification [13] since "SOD I" is mainly a structural rather than functional disorder. Furthermore, the EPISOD study showed that patients classified as "SOD III" do not benefit from endoscopic sphincterotomy, and SOM does not correlate with disease course. These

findings indicate the etiology of pain in these patients is very unlikely to emerge from transient or persistent elevation in basal pressure at the sphincter of Oddi [8]. This leaves only patients with "suspected SOD" (the prior SOD II). The challenge now is to confirm whether sphincterotomy benefits those patients with suspected SOD, and to refine the predictors of any response (Table 2).

The National Institute of Health (NIH) sponsored "State of the Science" conference on ERCP in 2002 [14] and the Rome III conclusions in 2005 [1] recommended that patients with suspected SOD II and III should be referred for Sphincter of Oddi manometry. That is clearly not current practice in USA, with only 18% and 20% using it in types II and III respectively. The falling popularity of sphincter of Oddi manometry is confirmed by the progressive fall in supplies from the main manufacturer. Possible explanations for this include skepticism of its prognostic significance and the accuracy of the technique itself, reluctance to refer to a tertiary center, and perceived concern about the risks. In fact, sphincter manometry does not add to the high risks of ERCP in these patients. That sphincter manometry has any predictive value is based mainly on three small and old randomized trials (one published only in abstract) [15-17] all completed before MRCP and EUS became

widely available. Manometry has not been validated in IRAP, and the EPISOD study showed no diagnostic relevance in "SOD III".

With currently little use of manometry among ERCP providers, it is clear that the use of endoscopic sphincterotomy is based mainly on personal convictions (Table 1). Empiric biliary sphincterotomy is highly favored in SOD I, but used also by 39% in SOD II, and by 19% in IRAP. Sphincter manometry directed biliary sphincterotomies are favored by a majority among SOM users in SOD II (77%) and III (75%) and less in IRAP and SOD I.

This study has limitations. The response rate was low. While this cohort may not be a representative sample of the entire ASGE, the distribution of demographics (university based practitioners 32% and private practitioners 68%) are similar to a previously reported ASGE survey in evaluating ERCP practices [18]. Limiting the survey to ASGE members alone may have resulted in selection bias, but the majority of interventional endoscopists with interest in pancreatico-biliary disease within the USA are members of the ASGE. Population bias is also probable, as providers interested in SOD or IRAP were most likely to respond. This would suggest that our estimates of ERCP and SOM utilization may be higher than rates in general clinical practice. The declining supply of SOM catheters support the survey observations.

This survey shows that ASGE members (and their patients) are entering these clinical minefields with inadequate maps to guide them, and little consensus in practice. The results of the EPISOD study should discourage further use of ERCP in patients with post-cholecystectomy pain and no objective features (prior SOD type III). Similar stringent prospective research is essential to maximize the benefits of our interventions and to minimize the risks in patients with SOD II and IRAP.

## Author Contribution

Conception and design (Cotton, Cote); analysis and interpretation of the data (Cotton, Suarez, Pauls, Durkalski-Mauldin, Cote); drafting of the article (Cotton, Suarez); critical revision of the article for important intellectual content (Cotton, Suarez, Cote); final approval of the article (Cotton, Suarez, Pauls, Elmunzer, Durkalski-Mauldin, Coté).

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