Sphincter of Oddi Dysfunction
A paradigm shift to come?

Paul R. Tarnasky, MD
Digestive Health Associates of TX
Methodist Dallas Medical Center

SO Dysfunction
Sphincter of Oddi Dysfunction

“She had endured much under many physicians, and had spent all that she had; and she was no better, but rather grew worse.”

Mark 5:26

SOD Challenges

• Controversial
• Frustrating for patients and doctors
• Requires careful clinical evaluation
• Technically difficult procedures
  – Cannulation and pancreatic expertise
• Potential for serious complications
• Medicolegal risk
• Paucity of good outcomes data
SOD Overview

- SO Anatomy & Physiology
- SOD Syndromes / Definitions
- Clinical Evaluation
- Pharmacologic Therapy
- Endoscopic Evaluation and Therapy
- Outcomes & Recent Results
- Techniques & Risks
- Current Recommendations

Tarnasky (Dallas, TX)

Sphincter of Oddi Anatomy

- 6-10 mm long
- Variable length of common channel
- Separate from duodenal musculature

Tarnasky (Dallas, TX)
Sphincter of Oddi

- **Functions**
  - Regulates flow into duodenum
  - Prevents reflux
  - Promotes GB filling

- **Normal Motility**
  - Basal = 10-15 mmHg
  - Frequency = 2-6/min
  - Amplitude = 50-150 mmHg

**SO Physiology**

**Stimulates**
- Morphine
- Noradrenaline
- Octreotide
- Substance P
- ?VIP
- Secretin

**Inhibits**
- Cholecystokinin
- Glucagon
- VIP
- Nitric oxide
- Nitrates
- Botulinum toxin
- Calcium channel blockers
SOD Epidemiology

- Household survey
  - ≈ 2% of women, < 1% of men
- > 85% are women
- Increased in s/p CCX (up to 14%)

SOD Clinical Syndromes

- Unexplained acute pancreatitis
- Unexplained upper abdominal pain
- Chronic acalculous cholecystitis
- Early chronic pancreatitis
- Biliary pancreatitis
- Pancreatic fistula / duct disruption
- Postoperative bile leak
SOD Clinical Syndromes

Functional Subjective Dyskinesia  →  Structural Objective Stenosis

Pain ←→ Pancreatitis

Unexplained Acute Pancreatitis

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>N</th>
<th>SOD (%)</th>
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<tbody>
<tr>
<td>Toouli</td>
<td>1985</td>
<td>28</td>
<td>15 (57)</td>
</tr>
<tr>
<td>Guelrud</td>
<td>1986</td>
<td>42</td>
<td>17 (40)</td>
</tr>
<tr>
<td>Venu</td>
<td>1989</td>
<td>116</td>
<td>17 (15)</td>
</tr>
<tr>
<td>Raddawi</td>
<td>1991</td>
<td>24</td>
<td>7  (29)</td>
</tr>
<tr>
<td>Sherman</td>
<td>1993</td>
<td>55</td>
<td>18 (33)</td>
</tr>
<tr>
<td>Coyle</td>
<td>2002</td>
<td>90</td>
<td>28 (31)</td>
</tr>
<tr>
<td>Kaw</td>
<td>2002</td>
<td>126</td>
<td>67 (53)</td>
</tr>
<tr>
<td>Mehraban</td>
<td>2011</td>
<td>358</td>
<td>173 (48)</td>
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> 70% improve after endotherapy
• PRCT in pts with URAP
• PSOM +/- BSOM
Normal SOM: Sham vs EBS
PSOD: EBS vs DES
• Prophylactic PD stents (15% PEP)
• Follow-up for > 1 year (median 78mo)
Follow-up Data

- 17% developed chronic pancreatitis during follow-up
- PSOD increased risk for RAP (4X)
- 42% underwent repeat ERCP to investigate RAP
- Residual PSOD was frequent (>75%) among those that underwent repeat ERCP

SOD and URAP Conclusions

- SOD does not cause URAP
- SOD is marker for RAP
- Endotherapy does not treat SOD
Biliary Dyskinesia

- Chronic acalculous cholecystitis
- Gallbladder dyskinesia
- Cystic duct syndrome
- Sphincter of Oddi dysfunction
  - Gallbladder in or out

Acalculous Biliary-Type Pain
SOD: Rome III Criteria Definition

Episodes of steady pain in epigastric and/or RUQ and all of following

- Lasts > 30 min
- Recurrent attacks, not daily
- Pain interrupts life or leads to encounter
- Not relieved by bowel movements
- Structural disease is excluded

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Functional Dyspepsia
weekly, > 3mo duration

- Postprandial distress syndrome
  - Postprandial fullness
  - Early satiety
  - Nausea, belching are supportive
- Epigastric pain syndrome
  - Pain or burning
  - Intermittent

Tarnasky (Dallas, TX)  Am J Gastroenterol, Vol 105, 2010
Differential Diagnosis

- **Esophageal**
  - Motility disorders, Esophagitis
- **Gastric**
  - Gastroparesis, Ulcer, Volvulus, Pyloric stenosis, Neoplasm
- **Duodenal**
  - Stricture, Ulcer, Diverticulitis, Sprue, Neoplasm
- **Bowel**
  - Stricture, Ulcer, Diverticulitis, Ischemia, Neoplasm
- **Biliary**
  - Stone, Benign stricture, Sump syndrome, Neoplasm
- **Pancreatic**
  - Pancreatitis, Neoplasm
- **Abdominal Wall Neuralgia**
- **Hepatic**
  - Steatosis, Cyst, Neoplasm

Evaluation of Suspected SOD

- **History**
- **Noninvasive options**
- **ERCP with SOM**

For Disabling Symptoms
History: When, Where, What

- When did the attacks begin?
- When do the attacks occur?
- Where is the pain?
- Where does the pain radiate?
- What is associated with the attacks?
- What has been done to investigate?
- What has been done for treatment?
- What are consequences?

Noninvasive Imaging

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SOD Therapy

- Observation
- Surgical (historical)
- Pharmacologic
- Endoscopic
  - Biliary or Dual sphincterotomy

“When there are many suggested treatments, there is no cure.”

Anton Chekhov
Pharmacologic Therapy

- Calcium channel blockers
- Nitrates
- Nitric oxide
- Botox
- Choleretic agents

Reasonable Safe ? Predictive Side-effects ? Effective

Suspected SOD Classification

Typical Pain LFT >2X nl BD >10mm

<table>
<thead>
<tr>
<th></th>
<th>I</th>
<th>II</th>
<th>III</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td></td>
<td>+</td>
<td>+</td>
<td>OR</td>
</tr>
<tr>
<td></td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

Modified from 1987 Geenen-Hogan Classification
Does G-H Type Predict SOD?

- Type I
  13-65% abnormal SOM
- Type II
  ~50% abnormal SOM
- Type III
  25-70% abnormal SOM

Sherman et al., Gastrointest Endosc 1991;86:586-190

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SOD Treatment Outcomes

- Thatcher 1987, Rolny 1993, Viceconte 1995: **Type I**
  - Biliary sphincterotomy effective ~85%
  - Independent of SOM results
- Geenen 1989, Toouli 2000: **Type II**
  - RCT of biliary sphincterotomy vs sham
  - SOM abnormal, sphincterotomy benefits ~70%
  - No benefit if SOM normal

Dilated BD Predicts Response

- Retrospective study
- 46 pts underwent EBS
- Favorable response in pts with a dilated BD and/or delayed drainage
- Response did not correlate with SOM results

Thatcher et al., Gastrointest Endosc 1987;3:91-95
LFT versus Bile Duct Size

- Retrospective
- 24 SOD II pts
- Biliary sphincterotomy
- No SOM
- 20 Abnormal LFT
- 8 Dilated bile duct

Lin et al., Am J Gastroenterol 1998;93:1833-1836

Early Type III SOD Outcomes

- Kumar 1992 (n=38)
  - 56% good to excellent after EBS
  - Retrospective, abstract only
- Sherman 1994 (n=23)
  - 62% improved after EBS C/T 30% for sham
  - RCT, abstract only
- Bozkurt 1996 (n=5)
  - 100% improved or symptom free
- Wehrmann 1996 (n=13)
  - 38% short-term benefit
  - 8% benefit after median F/U = 2.5yr
### Are G-H types II & III Different?

<table>
<thead>
<tr>
<th></th>
<th>Type II</th>
<th>Type III</th>
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<tbody>
<tr>
<td>SOD</td>
<td>21/35 (60%)</td>
<td>22/38 (55%)</td>
</tr>
<tr>
<td>Improved after biliary sphx</td>
<td>13/19 (68%)</td>
<td>9/16 (56%)</td>
</tr>
<tr>
<td>Post-ERCP pancreatitis</td>
<td>16%</td>
<td>15%</td>
</tr>
<tr>
<td>S/P CCX</td>
<td>64%</td>
<td>76%</td>
</tr>
</tbody>
</table>

Botoman et al., Gastrointest Endosc 1994; 40: 165-170

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### Treatment Outcome Predictors

- **121 pts over 3yr**
- **Daily pain in 37%**
- **Post-ERCP pancreatitis in 18%**
- **50% underwent re-intervention**

- **Good Outcomes**
  - 83% G-H I
  - 70% G-H II
  - 62% G-H III

- **Poor Outcomes**
  - **age < 40yr**
  - **Gastroparesis**
  - **Normal PSOM**
  - **Daily narcotics**

Freeman et al., J Clin Gastroenterol 2007; 41: 94-102
Sphincter of Oddi Dysfunction Type III

- Randomized controlled trial
- Sponsored by NIH
- Seven USA sites

Post-CCX pain
- Normal LFT
- Normal imaging

clinicaltrials.gov

Original Investigation

Effect of Endoscopic Sphincterotomy for Suspected Sphincter of Oddi Dysfunction on Pain-Related Disability Following Cholecystectomy

The EPISOD Randomized Clinical Trial

- Randomized 2:1 Sphincterotomy (ES):Sham
- Randomized independent of SOM
- If PSOD in ES group: randomized to biliary (EBS) alone or biliary + pancreatic sphincterotomy (DES)
- Subjects declining randomization underwent SOM-directed therapy (EPISOD2)

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EPISOD Trial Protocol

• Battery of questionnaires
  – RAPID (lost productivity due to pain)
  – Psychological disorders
• Pancreatic +/- biliary SOM
• Treatment per randomization
• Prophylactic pancreatic stenting
• Blinded follow-up for 1 year

EPISOD: Definition of Success

• < 6 days of lost productivity within last 90 days at months 9 and 12
• No re-intervention
• No narcotics

Success was very strictly defined
Pain and encounters not measured
EPISOD Trial

1584 Screened

214 Randomized

1298 Excluded

141 Sphincterotomy

73 Sham

72 EPISOD2

EPISOD Baseline Data

Sphincterotomy | Sham
---|---
Daily pain in last 30 d | 52% | 49%
Irritable bowel syndrome | 32% | 38%
Physical/Sexual Abuse | 27% | 18%
Narcotic use (last month) | 28% | 22%
Psychiatric medications | 39% | 40%

Pain in last 90d (mean) | 69 d | 69 d
Pain intensity in last 90d | 7 / 10 | 7 / 10
EPISOD Results

Figure 2. RAPID Score Distribution by Assigned Treatment Group and Visit

No. of participants:

<table>
<thead>
<tr>
<th>Month</th>
<th>Baseline</th>
<th>3</th>
<th>6</th>
<th>9</th>
<th>12</th>
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<tbody>
<tr>
<td></td>
<td>141</td>
<td>73</td>
<td>130</td>
<td>67</td>
<td>129</td>
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</table>

Tarnasky (Dallas, TX)

EPISOD Primary Outcomes

<table>
<thead>
<tr>
<th>Treatment</th>
<th>No. of Patients</th>
<th>No. (%) [95% CI] of Treatment Success</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary outcome</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sham</td>
<td>73</td>
<td>27 (37) [21.6 to 33.6]</td>
</tr>
<tr>
<td>Sphincterotomy (any)</td>
<td>141</td>
<td>32 (23) [15.8 to 29.6]</td>
</tr>
<tr>
<td>Secondary outcome</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pancreatic sphincter hypertension with biliary sphincterotomy</td>
<td>51</td>
<td>10 (20) [8.7 to 30.5]</td>
</tr>
<tr>
<td>Pancreatic sphincter hypertension with pancreatic and biliary sphincterotomy</td>
<td>47</td>
<td>14 (30) [16.7 to 42.9]</td>
</tr>
</tbody>
</table>

PEP: 11% after Sphincterotomy  
15% in Sham group

Tarnasky (Dallas, TX)
### EPISOD Treatment Success

<table>
<thead>
<tr>
<th>EPISOD</th>
<th>Sphincterotomy</th>
<th>Sham</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>23%</td>
<td>37%</td>
</tr>
<tr>
<td>PSOD</td>
<td>NA</td>
<td>37%</td>
</tr>
<tr>
<td>PSOD → EBS</td>
<td>20%</td>
<td></td>
</tr>
<tr>
<td>PSOD → DES</td>
<td>30%</td>
<td></td>
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</table>

<table>
<thead>
<tr>
<th>EPISOD2</th>
<th>No therapy</th>
<th>17%</th>
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<tbody>
<tr>
<td>EBS</td>
<td>24%</td>
<td></td>
</tr>
<tr>
<td>DES</td>
<td>31%</td>
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</tr>
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</table>

### Reasons for Failure

- Success defined too strictly
- Wrong definition of success
- Studied wrong patients
  - Chronic pain, Other functional disorder
  - Narcotic dependence
- Ineffective endoscopic treatment
- Sham actually provided treatment
- People are crazy
## SOD Conclusions

- Choose wisely
- Treat kindly
- SOD patient
- SOD doctor

## Likely SOD & Responds to ES

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Score</th>
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<tbody>
<tr>
<td>Intermittent pain</td>
<td>+1</td>
</tr>
<tr>
<td>↑ LFT w attacks</td>
<td>+3</td>
</tr>
<tr>
<td>UAP not p. divisum</td>
<td>+2</td>
</tr>
<tr>
<td>Bile duct &gt;9mm</td>
<td>+1</td>
</tr>
<tr>
<td>Age ≥ 40 yrs</td>
<td>+1</td>
</tr>
<tr>
<td>SOD HIDA =4-6</td>
<td>+1</td>
</tr>
<tr>
<td>SOD HIDA &gt;6</td>
<td>+2</td>
</tr>
<tr>
<td>CCX for stones</td>
<td>+1</td>
</tr>
<tr>
<td>Daily pain</td>
<td>-1</td>
</tr>
<tr>
<td>Positional pain</td>
<td>-3</td>
</tr>
<tr>
<td>Daily narcotics</td>
<td>-2</td>
</tr>
<tr>
<td>Other motility d/o</td>
<td>-1</td>
</tr>
<tr>
<td>Persistent ↑ LFT</td>
<td>-2</td>
</tr>
<tr>
<td>Age &lt; 40 yrs</td>
<td>-1</td>
</tr>
<tr>
<td>Chr pancreatitis</td>
<td>-2</td>
</tr>
<tr>
<td>Psychiatric dx</td>
<td>-4</td>
</tr>
<tr>
<td>CCX for ? reason</td>
<td>-1</td>
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</table>
SOD Unlikely

- Daily pain
- Positional pain
- Normal ducts
- Normal labs

ERCP Risk

Operator

Techniques

Patient

↑ Risk

↓ Risk
SOD (Risk) Management

- Expertise
- Restraint
- Consent
- Protection

SOD Management

- Pain
- Labs
- Ducts

- Sphincterotomy
- Type I
- +/- PSOM

Tarnasky (Dallas, TX)
Ideal Disease

- Benign
- Not contagious
- Genders sympathy
- Likely die from another cause
- May not need a doctor
- Known cause
- Preventable
- Limited course
- Rarely complicated
- Known cure

Is SOD an Ideal Disease?

- Benign
- Not contagious
- Genders sympathy
- Likely die from another cause
- May not need a doctor
- Unknown cause
- Not preventable
- Unlimited course
- Occasionally complicated
- No known cure