Sphincter of Oddi dysfunction: SOD after EPISOD, Now what do we do?

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Director of Endoscopy
Yale School
February in Connecticut
What is sphincter of Oddi dysfunction?

“A riddle in a mystery wrapped inside an enigma”

John Baillie
Desiderando fare uno studio comparativo sulla influenza che la bile poteva esercitare sulla digestione quando essa si versasse comunemente nell'intestino, o altrimenti si obbligasse a sversarsi in modo non interrotto nella stomaco, e fosse consigliato dal mio amico professore Marconcini, ad esprimere la citofilia. Provando così l'animale del verme della bile, obbligava quest'ultima (almeno io la credere allora) a versarsi, via via che si formava, nello intestino, nel modo inteso che, collo svolgere la famosa colonno-gastrica (prima legatoria del colonno), io l'obbligavo a versarsi comunemente nella stomaco. I due casi mi parvero allora assolutamente comparabili, per cui operai tra casi di questa estirpazione che, come ognuno sa, venne eseguita dallo Zamboncari sin dal tempo di Galileo e per consiglio di quest'ultimo. Ottenni facilmente la guarigione, ricorrendo negli animali così operati vari fatti degni di nota, dei quali mi occupò a parte. Quello che però devo riferire, non solo perché al collega direttamente dal tema di cui ora mi occupo, ma...
Papillary Stenosis: Definition

• Benign noncalculous obstruction to flow of pancreatic juice or bile through the pancreaticobiliary duodenal junction (Sph. of Oddi) which may present with pain, pancreatitis, and/or cholestasis
Relationship Between the Papillary Sphincters of the Common and Pancreatic Ducts with the Duodenal Wall
Type 1 Sphincter of Oddi dysfunction
SOD Clinical Features

- Usually female; CCX; 25-50 years old
- Pancreaticobiliary type pain
- Epigastric, RUQ, LUQ
- Radiation to back, scapulæ, R shoulder
- Worse after meals; nocturnal; codeine, acid peptic Rx – no help
Classification of Biliary Sphincter disease

**Type I:** All of the following:
- Recurrent biliary pain
- Liver test elevations (AST or ALT) on two separate occasions (2x upper limit of normal) with resolution in between
- Dilated common bile duct (11 mm)

**Type II:** Recurrent biliary pain plus 1 of the above criteria

**Type III:** Biliary type pain only
Medical Rx of SOD

- Low fat diet
- Anticholinergics
- Nitrates
- Ca channel blockers
- Antidepressants
- Analgesics (avoid narcotics)
Complications of Biliary Sphincterotomy (MESH study)

- 2347 patients underwent Biliary ES
- 229 (9.8%) had complications
- Deaths 2.3 % (ERCP related 0.4%)
- Complications in 21.7% SOD vs 8.2% in non SOD patients
- Severe complications > in SOD (3.7% vs 1.3%)

Non-invasive tests of biliary SOD

CBD

- Hepatobiliary Scintigraphy ± CCK, Morphine
- Fatty Meal Sonography

PD

- EUS + Secretin
- MRCP + Secretin
Sphincter of Oddi Manometry
Sphincter of Oddi Manometry-Profile
SO Pressure
< 40 mmHg

5

12

SO Pressure
> 40 mmHg

5

18

4 Year
Follow-Up

SHAM

ES

SHAM

ES

Poor

Fair

Good

(*p<.005)
## RCT comparing ES, S-ES and SSP (with or without CCX)- Results

<table>
<thead>
<tr>
<th>Therapy</th>
<th>FU (yrs)</th>
<th>Mean Pain Score</th>
<th># Hosp. Days/Mo.</th>
<th>% Pts. Imp.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Pre-Rx</td>
<td>Post-Rx</td>
<td>Pre-Rx</td>
</tr>
<tr>
<td>ES (n=19)</td>
<td>2.9</td>
<td>9.2</td>
<td>3.9*</td>
<td>.85</td>
</tr>
<tr>
<td>S-ES (n=17)</td>
<td>2.0</td>
<td>9.4</td>
<td>6.7</td>
<td>.87</td>
</tr>
<tr>
<td>SSp ± CCx (n=16)</td>
<td>3.1</td>
<td>9.4</td>
<td>3.3*</td>
<td>.94</td>
</tr>
</tbody>
</table>

* *p<.04; *p=.002; ***p=.02, ES and SSp + CCx vs. S-ES
EPISOD

Evaluating Predictors and Interventions in Sphincter of Oddi Dysfunction
“SOD III” (pain only)

Post-cholecystectomy pain with
- normal liver labs and
- normal bile duct size (<10mm)
The problem of SOD III

- Results of ERCP/sphincterotomy unimpressive
  - *Unblinded cohort studies, one tiny RCT*
- Manometry is unproven as a predictor
- Risks are substantial
  - *Pancreatitis rate at least 15%. Perforations occur*
  - *Slippery slope of more procedures, and surgery*
Goals for EPISOD

• Which, if any, patients respond to biliary and/or pancreatic sphincterotomy?

• Are there clinical predictors of outcomes?
  – pain pattern, reason for cholecystectomy and response to it, presence of other functional GI disorders, psychological status

• Is manometry predictive?
EPISOD Study sites

Virginia Mason Medical Center, Seattle, KOZAREK

University of Minnesota, FREEMAN

Indiana University, FOGEL

Yale, JAMIDAR

Midwest Therapeutic Endoscopy Consultants, St. Louis, ALIPERTI

Methodist Dallas Medical Center, TARNASKY

MUSC, Charleston, ROMAGNUOLO
EPISOD criteria

- Post-cholecystectomy (>3 m), aged 18-65
- Severe biliary pain
- No prior pancreatitis or sphincter treatment
- Normal EGD and scans, bile duct <10mm
- Labs (any time <6 months)
  - Transaminases < 3xULN
  - Alk phos, Amylase, Lipase <2xULN
- No daily narcotics or severe depression
Baseline characteristics
(Brawman-Mintzer Am J Gastro 2014)

- 92% female, mean age 38
- Less psychologically distressed than expected
  - 9% anxiety, 7.5% depression, 17% trauma
- 34% had IBS
- 26% had taken narcotics in prior month
- 38% on anti-depressants
Methods

- ERCP with manometry of both sphincters
- Randomized 2:1 sphincterotomy vs sham irrespective of manometry results
- Those randomized to sphincterotomy with elevated pancreatic pressures were re-randomized to biliary or dual sphincterotomy
- Temporary stent (all patients) to reduce pancreatitis
Primary outcome

<table>
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<tr>
<th>Treatment</th>
<th>Number</th>
<th>Success</th>
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</thead>
<tbody>
<tr>
<td>Sphincterotomy</td>
<td>141</td>
<td>31 (23%)</td>
</tr>
<tr>
<td>Sham</td>
<td>73</td>
<td>26 (37%)</td>
</tr>
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</table>
Outcome in patients with PSH

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Number</th>
<th>Success</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biliary sphincterotomy</td>
<td>51</td>
<td>10 (20%)</td>
</tr>
<tr>
<td>Dual sphincterotomy</td>
<td>47</td>
<td>14 (30%)</td>
</tr>
<tr>
<td>Overall sham</td>
<td>73</td>
<td>26 (37%)</td>
</tr>
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Manometry not predictive

<table>
<thead>
<tr>
<th>Manometry</th>
<th>Sphincterotomy success</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Biliary</td>
</tr>
<tr>
<td>Biliary</td>
<td>Pancreatic</td>
</tr>
<tr>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>-</td>
<td>+</td>
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<td>+</td>
<td>-</td>
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<tr>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>33%</td>
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Factors predicting success/failure?

- Manometry
- No clinical feature predicted outcome
  - pain daily or not, presence of IBS, minor lab abnormalities, psyche/anxiety status, reason for cholecystectomy and response to it
Questions/limitations

• Excluded too many people?
  – *Those least likely to benefit (eg narcotics)*

• Success criteria too strict?
  – *Same with 50% pain reduction, allow narcs*

• Sham arm (ERCP/manometry/stent)
  – *Therapeutic?*
  – *Needed a no-touch arm?*
EPISOD conclusions

- Many subjects improved initially regardless of treatment allocation
- At one year, sphincterotomy was not superior to sham treatment
- Manometry did not predict primary outcome
- Significant risks even with experts
- Alternative approaches are needed for these challenging patients
Goodbye SOD types I, II, III

- Type III doesn’t exist
- Type I can be diagnosed as stones or stenosis by EUS
- Leaving “Suspected SOD” based on
  - Biliary type pain
  - Abnormal liver labs and/or dilating bile duct
- More studies needed
EPISOD Reaction

CLINICAL OPINION

EPISOD puts an end to sphincter of Oddi dysfunction type III

Jeffrey D. Mosko, Ram Chuttani
Beth Israel Deaconess Medical Center and Harvard Medical School, Boston, MA, USA

ENDOSCOPIC SPHINCTEROTOMY FOR SPHINCTER OF ODDI DYSFUNCTION:
INEFFICACIOUS THERAPY FOR A FICTIONS DISEASE
SOD Advocacy Alert: The American Gastroenterological Association (AGA) refused to pull the damaging article, “Endoscopic Sphincterotomy for Sphincter of Oddi Dysfunction: Inefficacious Therapy for a Fictitious Disease" from circulation. The SODAE Network had formally requested the article be removed as the title alone promotes a discord between gastroenterologists and their patients; and infers that every type of SOD is fictitious. Although we are disappointed, the AGA has encouraged we send a "Letter to the Editor" regarding this matter, which will be sent next week. More details to follow.
Sphincter of Oddi Dysfunction: Still Alive?

September 19, 2014

Glen A. Lehman, MD

Indiana University Department of Medicine
EPISOD-other considerations

- Around 3000 publications the last 150 years or so
- ? Adequate Pancreatic Sphincterotomies
- Is it fair to label patients that require retreatments as failures
- IBS 34% of cohort
- Hawthorere effect
- What are “normal SO pressures”
What do we do with Type 111 patients now?

Cure sometimes, treat often, comfort always.

Hippocrates
What do we do with Type 111 patients now?

• Consider other diagnosis
  – *Chronic functional abdominal pain*
  – *Visceral hypersensitivity*
  – *Narcotic Bowel Syndrome*
  – *Chronic pancreatitis*
  – *Irritable Bowel Syndrome*
What do we do with Type 111 patients?

- **DO NOT DO ERCP !!!!**
- Many desperate patients, referral for SOM is end of the road
- Long term pain management not a great option
- Trial of medical therapy i.e, low fat diet, antispasmodics, acid suppressive therapy etc
- Support and reassurance
- ? Role for Botox injections
The Course: Yale vs. Harvard, Southampton Princess Hotel Hotel Bermuda. April 17 and 18, 2015
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