Sphincter of Oddi Dysfunction

ABSTRACT

Sphincter of Oddi dysfunction (SOD) is the stenosis or dyskinesia of biliary, pancreatic or both sphincters. Sphincter of Oddi manometry (SOM) is the gold standard for the diagnosis but rarely needed. Biliary SOD mimics CBD stone but no cause of obstruction is identified. Biliary SOD type I (papillary stenosis) is real and empiric ES is recommended without the need of SOM. Type II is true in half of the cases. Noninvasive tests or SOM may help select appropriate patients for ES. Type III is very subjective and may not be real. Response to ES is poor while the risk is high, thus, medical therapy and reassessment are preferred. Pancreatic SOD is the most controversial. ES has little and questionable benefit but with significant risks. Other more common causes of IRAP, particularly chronic pancreatitis should be ruled out before considering pancreatic SOD.


INTRODUCTION

Sphincter of Oddi dysfunction (SOD) is the stenosis or dyskinesia of biliary, pancreatic or both sphincters. It is one of the most controversial conditions in gastroenterology. There are both believers and opponents and it is difficult to discuss or debate about SOD without mood and emotion. However, the condition remains important and cannot be ignored. Recently, there have been some advances in the knowledge of SOD, thus it is worthwhile to re-appraise this condition. This article will concisely review on SOD regarding to the definition, diagnosis and management in the most (if possible) neutral way.

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- Pain builds up to a steady level
- Pain is moderate to severe, interrupts patient’s daily activities or lead to emergency room visit
- Pain not relieved by bowel movements, postural change or antacids
- Exclusion of other diseases

2. Common bile duct (CBD) dilatation $\geq$ 8 mm by ultrasonography (US).

3. Elevated liver biochemistry test (bilirubin, AST, ALT, alkaline phosphatase) $\geq$ 2 times of normal for $\geq$ 2 occasions.

Biliary SOD is subsequently classified into 3 types as the followings(1)

- Biliary SOD type I: presence of all 3 criteria
- Biliary SOD type II: presence of abdominal pain with either criterion 2 or 3
- Biliary SOD type III: presence of abdominal pain only

Pancreatic SOD

According to Rome III criteria 2006(1), pancreatic SOD is defined as:

1. Typical abdominal pain (as in biliary SOD) and
2. Elevated serum amylase or lipase

Clinical manifestations and differential diagnoses

Patients with biliary SOD type I and II present with episodic severe epigastric or RUQ pain resembling biliary pain and accompanying with dilated CBD and/or elevated LFT. Thus, the main differential diagnosis is CBD stone. However, no stone could be detected by either magnetic resonance cholangiopancreatography (MRCP), endoscopic ultrasonography (EUS) or endoscopic retrograde cholangiopancreatography (ERCP).

In biliary SOD type III, the differential diagnoses are broader and include gallstone, chronic pancreatitis, functional abdominal pain, musculoskeletal pain and abdominal wall pain.

Patients with pancreatic SOD present with idiopathic acute pancreatitis or idiopathic recurrent acute pancreatitis (IRAP). Therefore, the differential diagnoses include all causes of recurrent acute pancreatitis and idiopathic chronic pancreatitis (ICP).

Biliary SOD

So far, the gold standard for the diagnosis of biliary SOD remains sphincter of Oddi manometry (SOM). The procedure involves canulation of major papilla and manometric measurement. Detail of the procedure has been defined(2). The most accepted criteria for SOD is the basal sphincter pressure $\geq$ 40 mm Hg(3). The procedure is not without risk because 15-30% will have acute pancreatitis from the procedure(2).

Prevalence of sphincter hypertension according to the type biliary SOD and response to sphincterotomy

Not all patients diagnosed as biliary SOD by clinical criteria will have sphincter hypertension (HT) when SOM is performed. Table 1 summarizes the prevalence of sphincter HT according to type of biliary SOD and response to endoscopic sphincterotomy (ES) which is the definite treatment of SOD(4-7).

Management strategy according to the type of biliary SOD

According to Table 1, the management strategy of each type of biliary SOD seems to be as follows.

- Biliary SOD type I: the prevalence of sphincter HT and response to ES are both high. Thus, empiric ES is the preferred strategy without the need of SOM. SOD type I is believed to be the true “papillary stenosis”.
- Biliary SOD type II: the prevalence of SOD and the response to ES are in the middle. Importantly, the presence of sphincter HT impacts the response to

Table 1. Prevalence of sphincter hypertension measure by sphincter of Oddi manometry (SOM) according to type of biliary sphincter of Oddi dysfunction (SOD) and frequency of patient improvement after endoscopic sphincterotomy (ES)(4-7).

<table>
<thead>
<tr>
<th>Biliary SOD type</th>
<th>Abnormal SOM (%)</th>
<th>Improvement after ES (%)</th>
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<tbody>
<tr>
<td>I</td>
<td>75-95</td>
<td>90-95</td>
</tr>
<tr>
<td>II</td>
<td>55-65</td>
<td>50-70</td>
</tr>
<tr>
<td>III</td>
<td>25-60</td>
<td>20-30</td>
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<tr>
<td></td>
<td></td>
<td>Normal pressure</td>
</tr>
<tr>
<td></td>
<td></td>
<td>30</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&lt;10</td>
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</tbody>
</table>

High pressure | Normal pressure
ES, thus, SOM has important role in this group. Noninvasive diagnostic tests are reasonable (see below). Empiric ES can also be done in experienced hands and after discussing with the patient.

- Biliary SOD type III: the prevalence of SOD is low and the response to ES is low regardless of the presence of sphincter HT. Thus, SOM should be avoided and medical therapy may be preferred. ES may have risk more than benefit.

**Noninvasive diagnostic tests for biliary SOD**

Many noninvasive methods have been studied against the gold standard, which is SOM. Systematic reviews of the performance of each method are summarized in Table 2(6-7). All tests are far from perfect. However, hepatobiliary scintigraphy (99Tc or HIDA scan) seems to be the best candidate and may have role in patients with biliary SOD type II.

**Management other than ES**

**Medical therapy**

Medical therapy aims to relax the sphincter of Oddi in patients with sphincter dyskinesia. Thus, it may have role in biliary SOD type II-III rather than type I which is true stenosis. Studies are, however, very scarce.

<table>
<thead>
<tr>
<th>Methods</th>
<th>Measurement</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nardi test</td>
<td>Morphine-prostigmin provocative pain</td>
<td>83</td>
<td>43</td>
</tr>
<tr>
<td>Ultrasonography</td>
<td>Change of CBD diameter after fatty meals, CCK or secretin</td>
<td>21-88</td>
<td>82-100</td>
</tr>
<tr>
<td>Hepatobiliary scintigraphy</td>
<td>Duodenal appearance time</td>
<td>50-100</td>
<td>85-100</td>
</tr>
<tr>
<td>Secretin MRCP</td>
<td>Change of CBD/pancreatic duct diameter</td>
<td>37-57</td>
<td>85-100</td>
</tr>
</tbody>
</table>

CBD, common bile duct; CCK, cholecystokinin; MRCP, magnetic resonance cholangiopancreatography

**Figure 1.** Management approach to patients suspicious of biliary sphincter of Oddi dysfunction. The dash boxes indicate that they are optional; CT, computed tomography; ES, endoscopic sphincterotomy; EUS, endoscopic ultrasonography; HBS, hepatobiliary scintigraphy; LFT, liver function test; MRCP, magnetic resonance cholangiopancreatography; SOM, sphincter of Oddi manometry; US, ultrasonography (adapted from reference 1, 7)
Trimebutine and/or nitrate have been studied in a prospective case series of 59 patients. Response in biliary SOD type I, II and III are 45%, 67% and 71%, respectively.\(^8\)

Nefedipine has been studied in 2 small double-blinded placebo-controlled cross-over trials\(^9-10\) and showed response rate around 75% in patient with type II biliary SOD.

**Botulinum toxin injection**

Endoscopic injection of botulinum toxin injection has been studied in patients with type III SOD\(^11\). Response rate was 55% but those who were responded had 92% chance to respond to ES. The procedure is safe.

**Stent trial**

A short (3 months) trial of biliary stenting has been studied and shown to predict 90% response from ES if there is pain free for 3 months after stenting\(^12\). However, the complication (acute pancreatitis) can occur up to 1/3 of patients\(^13\).

**Algorithm**

Algorithm of the management of biliary SOD is shown in Figure 1.

**Pancreatic SOD**

The topic of pancreatic SOD is much more controversial than biliary SOD and has been a matter of debate for almost two decades\(^14\). The main issues of the debate are as the followings:

The supporters of pancreatic SOD demonstrated that 1/3 to 2/3 of patients with idiopathic recurrent acute pancreatitis (IRAP) have SOD diagnosed from SOM\(^14\) (basal pancreatic sphincter pressure (40 mm Hg)\(^3\)). ES could prevent RAP in some but not all patients from case series. Some patients would eventually turn to chronic pancreatitis. Thus, it is postulated that it may be due to the inadequacy of ES which may not ablate pancreatic sphincter. Therefore, dual (biliary and pancreatic) ES may be preferred.

The opponents of pancreatic SOD believe that pancreatic sphincter HT may be just a findings of early ICP because over 50% of patients with pancreatic SOD will eventually express the morphology of CP. This explains why ES could not prevent the occurrence of IRAP and stop the process toward ICP in most patients. The reason why some patients seem to respond to ES should not be concluded as the effect of ES because it has not been compared to sham procedure in a controlled trial.

**Randomized controlled trial of ES for pancreatic SOD**

Recently, there has been one (and so far the only) randomized controlled trial on ES for pancreatic SOD.\(^15\) This study was conducted by the center, which has been well-known as expert center in pancreatic SOD. Eighty-nine IRAP patients underwent SOM and 69 had pancreatic SOD while 20 had not. Sixty-nine SOD patients were then randomized to dual (36 patients) or biliary (33 patients) ES. The results showed that both dual and biliary ES group had similar rate of RAP (48%) and CP (16%) during a median follow-up of 6 years. Surprisingly, 73% of the patients still had sphincter HT despite dual ES. In 20 patients, who did not have SOD, 11 were randomized to dual ES and 9 to sham procedure. The rate of RAP was 11% with sham procedure but 27% with dual ES.

What to be concluded from this study? First, in IRAP patients without pancreatic SOD, ES is harmful than doing nothing and should be avoided. Second, in patients with pancreatic SOD, dual or biliary ES have similar effect. Third, after ES for pancreatic SOD, half will remain having RAP and 1/5 will turn to CP. Whether ES is better than doing nothing is unknown because there was no sham procedure arm in the SOD group. Finally, even after aggressive dual ES, most patients still have sphincter HT. It is unlikely that even dual ES could not destroy the sphincters\(^16\). Thus, sphincter HT may not be the cause but rather the finding of RAP (or early CP) because the problem is probably the parenchyma not the sphincter\(^16\).

**Should we search for pancreatic SOD in patients with IRAP**

Based on the information above, it is still unclear whether pancreatic SOD does exist or it is just a finding of more aggressive cases of IRAP or ICP\(^15-16\). Since SOM is not widely available, having significant risks and the benefit of ES to prevent IRAP and CP is not proven, the author does not recommend searching for pancreatic SOD in patient with IRAP until more data is available. The author is even strongly against the strategies of empiric ES in IRAP because the risk likely outweighs the benefit.

Patients with IRAP should extensively be sought for gallstone (and microlithiasis) by LFT and US, hypertriglyceridemia and hypercalcemia by blood tests,
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CONCLUSION

SOD is important but we know a little. Biliary SOD can be diagnosed by clinical grounds, LFT and imagings (MRCP/EUS) to exclude other causes of biliary obstruction. Biliary SOD type I (papillary stenosis) is real and empiric ES is recommended. Type II is real in half of the cases. Noninvasive tests or SOM may help select patients who might get benefit from ES. Type III is subjective and probably not real. Response to ES is poor but the risk is high, thus reassessment or trial of medical therapy may be preferred. Pancreatic SOD is the most equivocal condition. ES has little benefit at best but may not outweigh the risk. Other causes of IRAP, particularly ICP should be ruled out by EUS before.

REFERENCES