Comparison of sphincter of Oddi manometry, fatty meal sonography, and hepatobiliary scintigraphy in the diagnosis of sphincter of Oddi dysfunction

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Background: Sphincter of Oddi dysfunction (SOD) afflicts approximately 1% to 5% of patients after cholecystectomy. The diagnostic standard for SOD is sphincter of Oddi manometry (SOM), a technically difficult, invasive test that is frequently complicated by pancreatitis. A sensitive and accurate noninvasive imaging modality is thus needed for the diagnosis of SOD. Quantitative hepatobiliary scintigraphy (HBS) and fatty meal sonography (EMS) are frequently used for this purpose, but results vary. This study compared SOM, HBS, and EMS in the diagnosis of SOD in a large group of patients.

Methods: Three hundred four consecutive patients after cholecystectomy (38 men, 266 women, age 17-72 years) suspected to have SOD were evaluated by SOM, FMS, and HBS. SOM was considered abnormal if any of the following were observed: (1) increased basal pressure (greater than 40 mm Hg), (2) increased phasic activity with amplitude greater than 350 mm Hg, (3) frequency of contractions greater than 8 per minute, (4) greater than 50% of propagation sequences retrograde, and (5) paradoxical response to cholecystokinin. FMS was considered abnormal if ductal dilation was greater than 2 mm at 45 minutes after fatty meal ingestion. Quantitative HBS was performed with sequential images obtained every 5 minutes for 90 minutes to monitor excretion of the radionuclide. Time-to-peak, halftime, and downslope were calculated according to predetermined ranges.

Results: A diagnosis of SOD was made in 73 patients (24%) by using SOM as the reference standard. HBS was abnormal in 86 whereas EMS was abnormal in 22 patients. A true-positive result was obtained in 15 patients by EMS and 36 patients with HBS. EMS and HBS gave false-positive results, respectively, in 7 and 50 patients. Sensitivity of EMS was 21% and for HBS 49%, whereas specificities were 97% and 78%, respectively. EMS, HBS, or both were abnormal in 90% of patients with Geenen-Hogan Type I SOD, 50% with Type II, and 44% of Type III. Of the 73 patients who underwent sphincterotomy, 40 had a long-term response. Of those with SOD, 11 of 13 patients (85%) with an abnormal HBS and EMS had a good long-term response.

Conclusions: In this series, the largest reported to date, correlation of FMS and HBS with SOM in the diagnosis of SOD was poor. When HBS and EMS are used together, a slight increase in sensitivity can be expected. The accuracy of EMS and HBS in the diagnosis of SOD decreases across the spectrum from Type I to Type III SOD. EMS and HBS, nonetheless, may be of assistance in predicting long-term response to endoscopic sphincterotomy in patients with elevated sphincter of Oddi basal pressure. (Gastrointest Endosc 2001;54:697-704.)

The sphincter of Oddi (SO) is a complex muscular structure consisting of smooth muscle fibers that surround the distal common bile duct (CBD), pancreatic duct (PD), and major duodenal papilla. It is 6 to 10 mm in length and is situated almost entirely within the duodenal wall, traversing it obliquely. The SO is composed of small muscular segments, as described by Boyden.1 Three distinct sphincter segments have been identified: sphincter choledochus (surrounds distal CBD), sphincter pancreaticus (surrounds distal PD), and the sphincter ampullae (surrounds common channel of papilla). The SO is believed to regulate the flow of bile and pancreatic juice into the duodenum.

The term sphincter of Oddi dysfunction (SOD) encompasses the motility abnormalities of the SO and includes the following: (1) SO stenosis (a structural abnormality with resultant narrowing of part or all of the sphincter as a consequence of chronic inflammation or fibrosis) and (2) SO dyskinesia (intermittent functional blockage of the high pressure zone of the sphincter). SOD is suspected when a patient is seen after cholecystectomy with biliary-type pain in the absence of a structural cause. SOD dysfunction results in manometric abnormalities in patients who are seen with symptoms...
Successful SOM Previous sphincterotomy, Normal biliary tree (US, CT) Elevated amylase or lipase Previous cholecystectomy Acute recurrent pancreatitis Age ≥ 18 y Alcohol abuse

Table 1. Inclusion and exclusion criteria

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<th>Inclusion</th>
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<tr>
<td>Age &gt;18 y</td>
<td>Alcohol abuse</td>
</tr>
<tr>
<td>RUQ pain &gt;6 months</td>
<td>Chronic liver disease</td>
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<tr>
<td>Previous cholecystectomy</td>
<td>Acute recurrent pancreatitis</td>
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<tr>
<td>Normal biliary tree (US, CT)</td>
<td>Elevated amylase or lipase</td>
</tr>
<tr>
<td>Successful SOM</td>
<td>Previous sphincterotomy, biliary surgery</td>
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consistent with biliary or pancreatic ductal origin. Sphincter of Oddi manometry (SOM) is considered the standard modality for diagnosis of SOD. However, SOM is technically difficult to perform, invasive, and may be complicated by pancreatitis in 8% to 26% of patients. Furthermore, the availability of SOM is limited; the procedure is performed mainly in centers specializing in pancreatic and biliary diseases.

Quantitative hepatobiliary scintigraphy (HBS) and fatty meal sonography (FMS) may identify patients with partial bile duct obstruction, either functional or structural. FMS is a form of stress test that depends on the induction of bile flow by cholecystokinin (CCK). In the presence of partial duct obstruction, increased bile flow increases intraductal pressure and diameter proximal to the site of obstruction. FMS requires considerable operator expertise and is potentially subject to observer bias. Alternatively, HBS evaluates fasting bile flow and is not operator dependent. However, HBS is applicable only in patients who have undergone cholecystectomy. HBS and FMS are noninvasive screening tests that may be complementary in the identification of patients with partial bile duct obstruction.

The aim of this study was to accurately characterize patients with suspected isolated functional CBD obstruction after cholecystectomy by using SOM as the reference standard, and to compare these results with those of noninvasive scintigraphic and sonographic studies in the detection of SOD (Types I, II, III).

PATIENTS AND METHODS

Over a 9-year period (1987-1995), 427 patients with no history of acute pancreatitis were referred for SOM because of a suspicion of SOD. Patients presented with typical biliary colic, defined as episodic right upper quadrant pain, often associated with abnormal liver function tests. All patients had been evaluated initially by endoscopy, conventional US, and/or CT, liver function tests, and serologic tests for hepatitis viruses, when appropriate, before referral (Table 1). Ninety-two patients with gallbladder in situ were excluded. The remaining 361 consecutive patients, all of whom had previously undergone cholecystectomy, were evaluated with FMS followed by HBS and finally ERCP with biliary SOM. Patients were seen 18 months to 12 years after cholecystectomy (mean, 4.8 years).

All diagnostic studies were completed over a span of 48 hours. Patients underwent HBS and FMS followed last by ERCP with biliary SOM. HBS and FMS were performed by separate radiologists; biliary SOM by gastroenterologists without knowledge of the results of the imaging studies. Patients with bile duct stone(s) (34), stricture (6), tumor (9), advanced liver disease (3), or unsuccessful cannulation/SOM (5) were excluded. The remaining 304 patients (38 men, 266 women, mean age 46 years, range 17-72 years) underwent all 3 studies and were evaluated for response to therapy.

Seventy-three patients underwent biliary sphincterotomy because of an abnormal SOM. Sphincterotomy was performed with a traction-type papillotome (Wilson-Cook Medical, Inc. Winston-Salem, N.C.). The length of the incision was determined by the length of the intramural portion of the bile duct. Although not a primary aim, the response to sphincterotomy was rated by using an ordinal scale as follows: good (0-2), fair (3-5), and no improvement (>6). Follow-up was obtained in all patients, either during office visits or by telephone. Informed consent was obtained from all patients and the study was approved by our Institutional Review Board before patient enrollment.

FMS

FMS was performed as previously described. A standard fatty meal (Lipomul, Mead-Johnson Laboratories, Evansville, Ind.) was administered orally at 1.5 mL per kg with real-time US examinations performed before and 45 minutes after ingestion in the transverse, sagittal, and oblique planes according to which best demonstrated the proximal CBD. All examinations were performed with the same machine by the same technologist, and every effort was made to duplicate as closely as possible the scanning planes in which the CBD was best demonstrated before and after the fatty meal. Patients with a baseline CBD diameter of greater than 6 mm were included in the study. An abnormal study was defined as an increase in diameter of greater than 2 mm (at 45 mm) compared with baseline (Figs 1 and 2).

HBS

After a fast of at least 3 hours, 0.02 mg/kg of CCK was administered to each patient by intravenous infusion over 3 minutes. Fifteen minutes later, 5 mCi (185 MBq) 99MTC-DISIDA were administered intravenously. Imaging was performed in the anterior projection with a large-field gamma camera centered on the photopeak. Timed static images were obtained in a 256 × 256 matrix at 5-minute intervals up to 90 minutes. Simultaneously, dynamic imaging was performed at a rate of 1 frame per minute and stored on a computer in a 128 × 128 matrix. Regions of interest were placed over the liver parenchyma and CBD to generate time activity curves. Abnormalities were defined as time of hepatic peak (T-peak, ≥24 minutes), half-time (T 1/2, ≥30 minutes), down-
Slope (≤1.1 minutes), and percentage CBD clearances (≤78%, 90 minutes) as previously described.8,9 The static images were recorded on film for subsequent interpretation by a single radiologist (Figs. 3 and 4).

**SOM**

A polyethylene 200-cm triple-lumen catheter (Arndofer, Inc., Milwaukee, Wis.) with 3 distal side holes located 2 mm apart was used; this was continuously infused with air-free water at a rate of 0.25 mL/min with a minimally compliant hydraulic capillary infusion system as previously described.2 The manometric catheter, passed through the accessory channel of a duodenoscope, was introduced across the SO in 2-mm step increments. Correct position in the CBD was confirmed fluoroscopically by injection of a small volume of contrast medium through the manometric catheter. The catheter was then repositioned to record SO motor activity for at least 2 minutes with all 3 manometric ports. Pressure recordings were divided into 1-minute periods. SO maximal basal pressure (mm Hg) was measured at the midinspiratory phase with duodenal pressure as zero reference. Amplitude of SO contractions (mm Hg) was measured from the peak to the base of the waves with SO maximal basal pressure as zero reference. Duration of SO phasic contractions was measured from the onset of the ascending to the end of the descending limb of the wave. Frequency of SO contractions was measured as number of waves per minute. Each variable was assessed at each recording level and expressed as the average of the mean values for the 3 tracings. Patients were sedated for the procedure with standard medications with the exception of narcotic agents, which were routinely withheld.

Abnormal results were as follows: basal SO pressure of 40 mm Hg or greater, phasic wave amplitude of 300 mm

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**Figure 1.** Normal FMS study: A, Before fatty meal (time = 0) duct diameter is 3.8 mm. B, After fatty meal (time = 45 minutes), duct diameter is 4.0 mm.

**Figure 2.** Abnormal FMS study: A, Before fatty meal (time = 0) duct diameter is 3.6 mm. B, After fatty meal (time = 45 minutes) duct diameter is 5.8 mm.
Figure 3. Normal HBS study (extrahepatic duct diameter = 9 mm): A, At 10 minutes, activity is exclusively within liver. B, At 30 minutes, activity is seen within bile duct and small intestine. C, At 45 minutes, increased activity evident in small intestine. D, At 60 minutes, little activity is in bile duct with most activity in small intestine. E and F, Computer-generated activity curves for hilum, liver, and bile duct at different time intervals.
Figure 4. Abnormal HBS study (extrahepatic duct diameter = 10 mm): A, At 10 minutes, activity is seen exclusively within liver. B, At 30 minutes, activity is seen mostly within liver with little activity in hilum and bile duct, and no activity within small intestine. C, At 45 minutes, a dilated bile duct is seen with little activity within small intestine. D, At 60 minutes, most activity remains within liver and bile duct with slightly increased activity in small intestine. E and F, Computer-generated activity curves for liver, hilum, and bile duct at different time intervals.
Hg or greater, phasic wave contractions of 10 per minute or more, greater than 50% of phasic wave contractions propagated retrograde, and absence of inhibition of SO pressures after CCK administration.10

Results

SOM was successful in all patients in whom the bile duct was cannulated. Seventy-three of 304 patients had a basal SO pressure of 40 mm Hg or greater, a result that was considered a true-positive diagnosis of SOD. In contrast, HBS was abnormal in 86 of 304 patients; FMS was abnormal in only 22 of 304 patients (Table 2).

SOM results were initially compared with results of FMS (Table 3). In the 231 patients with a normal SOM, FMS demonstrated 224 true-negative and only 7 false-positive results. In the 73 patients with an abnormal SOM, FMS provided 15 true-positive diagnoses and 58 false-negative results. Sensitivity and specificity for FMS in the diagnosis of SOD were 21% and 97%, respectively, with a positive predictive value (PPV) of 68% and negative predictive value (NPV) of 79%.

SOM was next compared with results of HBS (Table 4). In the 231 patients with a normal SOM, HBS gave 181 true-negative and 50 false-positive results. In the 73 patients with an abnormal SOM, HBS demonstrated 36 true-positive and 37 false-negative results. Sensitivity and specificity of HBS for the diagnosis of SOD were 49% and 78%, respectively, with a positive predictive value (PPV) of 42% and negative predictive value (NPV) of 83%.

Last, SOM was compared with FMS plus HBS in the diagnosis of SOD. If either or both tests were abnormal, SOD was suspected. Alternatively, if both studies were normal, SOD was thought to be excluded. By using these criteria, there were 177 true-negative, 54 false-positive, 39 true-positive, and 34 false-negative results. For FMS plus HBS, sensitivity and specificity for the diagnosis of SOD were 53% and 77%, respectively, with a PPV of 42% and NPV of 84% (Table 5).

Patients with documented SOD by SOM (n = 73) were stratified based on a modified Geenen-Hogan SOD classification3 (biliary drainage time excluded) according to the presence of abnormal liver function tests and CBD diameter greater than 10 mm into Type I (all abnormalities present), II, and III (none of the abnormalities present). There were 11 patients with Type I SOD, 30 with Type II, and 32 with Type III SOD. At least 1 abnormal imaging study (HBS or FMS) was noted in 91% of patients with Type I SOD, 50% with Type II, and 44% with Type III, suggesting that the diagnostic capability of HBS and FMS imaging for SOD decreases with increasing types of SOD.

All 73 patients with SOD underwent endoscopic biliary sphincterotomy (ES). Forty of 73 patients (55%) with a diagnosis of SOD had long-term resolution of symptoms (mean, 4.8 years) after ES. The long-term response to ES in patients with SOD (n = 73) as predicted by the results of HBS and FMS is shown in Table 6. Thirty-one of 36 patients (86%) with an abnormal HBS and 13 of 15 patients (87%) with abnormal FMS had sustained responses to ES. Of the 13 patients in whom HBS and FMS were both abnormal, 11 (85%) had a sustained long-term response to ES compared with only 4 of 34 (12%) patients in whom HBS and FMS were both normal. The results of ES in patients with SOD according to the Geenen-Hogan classification are given in Table 7.

### Table 2. Comparison of SOM with FMS in the diagnosis of SOD (n = 304)

<table>
<thead>
<tr>
<th>SOM Abnormal</th>
<th>FMS Normal</th>
<th>Total</th>
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<tbody>
<tr>
<td>Abnormal</td>
<td>7</td>
<td>15</td>
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<tr>
<td>Normal</td>
<td>224</td>
<td>58</td>
</tr>
<tr>
<td>Total</td>
<td>231</td>
<td>73</td>
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### Table 3. Comparison of SOM with HBS in the diagnosis of SOD (n = 304)

<table>
<thead>
<tr>
<th>SOM Abnormal</th>
<th>HBS Normal</th>
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</thead>
<tbody>
<tr>
<td>Abnormal</td>
<td>50</td>
<td>36</td>
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<tr>
<td>Normal</td>
<td>181</td>
<td>37</td>
</tr>
<tr>
<td>Total</td>
<td>231</td>
<td>73</td>
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</table>

### Table 4. Comparison of FMS or HBS with SOM in the diagnosis of SOD (n = 304)

<table>
<thead>
<tr>
<th>FMS/HBS Abnormal</th>
<th>SOM Normal</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Abnormal</td>
<td>34</td>
<td>39</td>
</tr>
<tr>
<td>Normal</td>
<td>177</td>
<td>54</td>
</tr>
<tr>
<td>Total</td>
<td>211</td>
<td>93</td>
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</table>

### Table 5. Accuracy of FMS and HBS in the diagnosis of SOD*

<table>
<thead>
<tr>
<th>Study</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
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<tbody>
<tr>
<td>FMS</td>
<td>21%</td>
<td>97%</td>
<td>68%</td>
<td>79%</td>
</tr>
<tr>
<td>HBS</td>
<td>49%</td>
<td>78%</td>
<td>42%</td>
<td>83%</td>
</tr>
<tr>
<td>Both†</td>
<td>53%</td>
<td>77%</td>
<td>42%</td>
<td>84%</td>
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</table>

*SOM is used as the reference standard.
†Refers to either FMS or HBS being abnormal.
poor long-term response to ES, HBS and/or FMS was abnormal in only 7 (21%).

**CONCLUSIONS**

After cholecystectomy, the normal biliary tree is transformed into a single-outlet system in which intrahepatic ductal bile flows only through the bile duct into the duodenum. During contraction of the SO in a normal patient with a gallbladder, the intra-ductal pressure remains normal because the biliary system can decompress by diverting bile into the gallbladder. This organ, therefore, acts as a low-pressure reservoir. After cholecystectomy, SO contraction usually results in elevation of intraductal pressure because the reservoir effect of the gallbladder is absent. If the SO resists flow, this may cause pain and may lead to biliary stasis and ductal dilation.

There is a small subset of patients after cholecystectomy who experience attacks of biliary-type pain. Approximately 14% of these patients may have SOD as determined by SOM. Endoscopic biliary manometry has been shown to be the most sensitive method for detecting elevated choledochal sphincter pressures. The requirements for obtaining a meaningful SO pressure measurement include a cooperative patient, a skilled endoscopist, and expertise in the performance of SOM. The inherent risk of postprocedure pancreatitis further limits the applicability of SOM.

The availability of FMS and recent advances in nuclear scintigraphy of the biliary tree offer the potential for noninvasive testing of bile duct emptying. FMS is a form of a stress test that depends on the induction of increased bile flow through fat-stimulated release of CCK. HBS is not a stress test, but rather evaluates bile flow. Although these tests are technically easy to perform and noninvasive, considerable operator expertise is required to obtain meaningful results.

The present large, blinded, nonrandomized, prospective study compared 3 modalities in the diagnosis of SOD. A diagnosis of SOD was made by biliary manometry in 24% of the patients. When the results of FMS and HBS were compared with SOM, FMS had an overall sensitivity of 21%, specificity of 97%, positive predictive value of 68%, and negative predictive value of 79%. HBS had a sensitivity of 49%, specificity of 78%, positive predictive value 42%, and a negative predictive value of 83%. When the results of FMS and HBS were combined and compared with those obtained by SOM, no further improvement in the diagnosis of SOD was observed.

The strength of the present study lies in the fact that true-positive and true-negative diagnoses of SOD in patients suspected to have this disorder were documented by endoscopic biliary manometry. Of the 304 patients enrolled, 24% had an abnormal SOM and 13% had an abnormal HBS and an abnormal FMS study; 28% had only an abnormal HBS, and only 7% had an abnormal FMS.

Simeone et al. demonstrated that EMS has an 83% sensitivity and 83% specificity in the evaluation of patients with suspected biliary tract obstruction, with a negative predictive value of 92%. However, this study was not designed to evaluate patients for SOD. Thirty-four patients with a true-positive response to EMS had a final diagnosis of one of the following: choledocholithiasis, ampullary stenosis, pancreatic carcinoma, nodal metastasis, and stenosis as a result of surgery.

Simeone et al. in an earlier study found that in healthy patients the normal-diameter bile duct does
not increase in diameter after a fatty meal and that a duct that is larger than normal will return to normal diameter after stimulation by a fatty meal. With a difference of 1 mm between normal (<5 mm) and abnormal (≥6-10 mm) diameter, these investigators acknowledged that errors in interpretation may occur when the diameter changes by 1 mm. When disease was present, fatty meal ingestion induced ductal dilation in 5 patients and no response or a decrease in diameter in 5 patients. From these results it can be concluded that even in the presence of biliary obstruction, the ductal response to a fatty meal is arbitrary and nonpredictive.

Corazziari et al., in a study of 19 patients with suspected SOD that included 10 patients with SO pressures of 40 mm Hg or greater, found that HBS had a 100% specificity and 83% sensitivity when compared with SOM. Moreover, of the 12 patients with probable SOD, 2 had SO maximal basal pressures of less than 39 mm Hg, all patients had phasic wave amplitudes within the normal range, and only 2 patients had frequencies of greater than 8 per minute. Furthermore, retrograde sequences were not reported. The value of scintigraphy for discriminating normal from abnormal was problematic in this small group of patients.

Among the 73 patients in the present study with SOD as determined by SOM, 39 (53%) had an abnormal imaging result when HBS and FMS were combined (Table 7). When correlated with SOD by type, 91% of the 11 patients with Type I SOD had an abnormal imaging study when the results of HBS and FMS were considered together. As expected, the correlation was poor for types II and III SOD; 50% and 40%, respectively, of patients with these types had abnormal HBS/FMS imaging results (Table 7). Overall, therefore, HBS and FMS may complement SOM in the evaluation of patients in whom Type I SOD is suspected.

Of the 73 patients with abnormal SOM who underwent ES, 40 (55%) reported good long-term results. Of these 40 patients, 9 of 11 (82%) with Type I SOD reported a good outcome, which is consistent with our previously reported data. Twenty-two of the 30 patients (73%) with Type II and 9 of the 32 patients (28%) with Type III reported good outcomes after sphincterotomy.

When HBS and FMS are both abnormal, the response to ES is about 7 times likely to be beneficial in patients with SOM compared with patients in whom both studies are normal. In our opinion, HBS and FMS obviate SOM. However, these tests are of value in predicting response to ES in patients with Type II and III SOD. Overall, if both tests give a positive result, a good outcome for ES can be expected when compared with the predictive value of SOM alone.

The results of the present study suggest that SOM remains the most sensitive and specific test for the diagnosis of SOD and that the combination of HBS and FMS adds relatively little to the diagnosis and prediction of long-term outcome in patients in whom ES is clearly indicated. However, these noninvasive imaging studies may be of assistance in predicting long-term response to sphincterotomy, particularly in patients with Type II and III SOD. The (99m)Tc-DISIDA with morphine provocation test has been used to detect hypersensitivity and dysfunction of the SO and may also be useful as a method of noninvasive screening of patients before SOM, ES, or both.

REFERENCES