
A Noninvasive Test of Sphincter of Oddi Dysfunction in Postcholecystectomy Patients: The Scintigraphic Score

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The ideal noninvasive test of sphincter of Oddi dysfunction (SOD) does not exist and the diagnosis of patients with postcholecystectomy pain often relies on invasive procedures. In this paper we describe a scintigraphic test for SOD: the scintigraphic score. This score combines quantitative and visual criteria for interpretation of hepatobiliary scans. Twenty-six consecutive postcholecystectomy patients underwent hepatobiliary imaging, ERCP, and sphincter manometry. Twelve patients had SOD and 14 had normal sphincters determined by clinical findings, ERCP, and manometric studies. All patients with normal sphincter had scores of 0–4, while patients with SOD had values of 5–12 for a perfect sensitivity and specificity of 100%. Hepatobiliary scans scored in this fashion may become the noninvasive test of choice to screen postcholecystectomy patients with suspected SOD.

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Sphincter of Oddi dysfunction (SOD) is a poorly defined disorder which creates an obstacle to bile drainage from the common bile duct (CBD). Usually presenting with recurrent pain after a cholecystectomy, the obstacle is often caused by stenosis or dyskinesia of the sphincter of Oddi, conditions best identified and characterized by manometry (1).

According to estimates by Steinberg and Bar-Meir (1, 2), at least 45,000 patients in the U.S. develop postcholecystectomy pain every year. In approximately 6200, the pain is due to SOD. If manometry were employed to screen patients with postcholecystectomy pain, 7.2 studies would be performed for every case of SOD detected. This efficacy ratio may be unacceptable for a procedure that is invasive, difficult to perform and associated with significant complications, such as pancreatitis (1,3).

A need exists for a reliable noninvasive screening test to identify patients likely to have SOD and who may benefit from the more invasive manometric test.

Several techniques have been proposed for this purpose, but quantitative cholescintigraphy is probably the one most often utilized (4–7). It can identify patients with SOD by demonstrating and quantifying a significant delay in hepatic uptake and washout (Fig. 1). This ability to quantify is helpful because it allows assignment of a concrete numerical value to a physiologic function. This value can be used to compare patients, to estimate statistical significance between groups and to compare follow-up studies in the same subject. Unfortunately, quantitative cholescintigraphy has not yielded a high sensitivity consistently and is therefore not a good screening test (8). It also suffers from lack of specificity. Patients with liver dysfunction and cholestasis show results indistinguishable from those of SOD (1,4,5).

Recently, in an attempt to improve sensitivity and specificity, we amplified work done by other authors (9,10) and described a modified scintigraphic technique utilizing cholecystokinin (CCK) pretreatment and visual interpretation of hepatobiliary scintigrams (11). By using visual rather than quantitative criteria, we achieved perfect sensitivity and specificity in a small group of postcholecystectomy patients with recurrent pain and suspected SOD. In spite of the good results, visual interpretation fails to provide measurable parameters amenable to quantification.

In this paper, we propose a scoring system of CCK-stimulated hepatobiliary scintigrams that combines visual and quantitative criteria for the diagnosis of SOD. This strategy is expected to maintain the high sensitivity and specificity of visual analysis, while adding the advantages of quantification. Moreover, the presence of quantitative data to support the visual interpretation should increase the diagnostic certainty of the interpreters.

MATERIALS AND METHODS

Patient Population

Between December 1988 and December 1990, 26 consecutive postcholecystectomy patients were referred by a single gastroenterologist (ANK) for disofenin CCK-stimulated biliary imaging to search for possible SOD. Some patients had biliary pain, some had nonbiliary pain and still others were asymptomatic. Endo-

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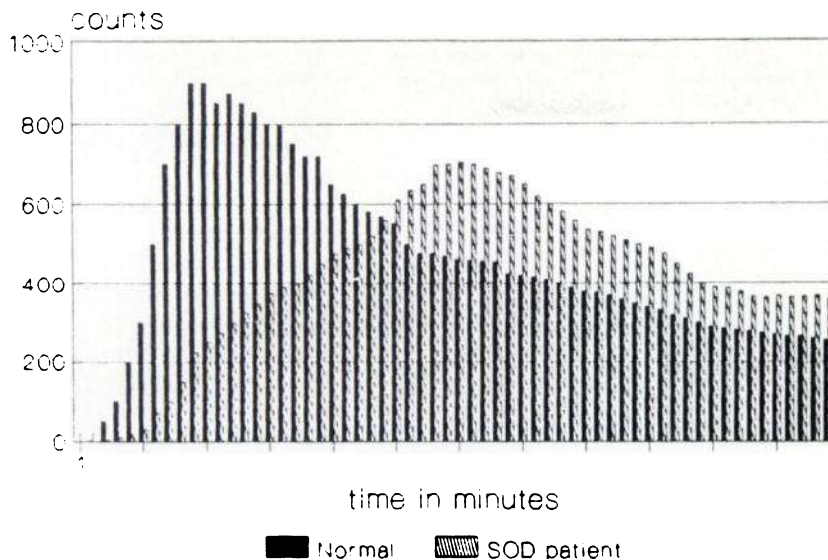


FIGURE 1. Quantitative scintigraphy in a normal subject and in a patient with SOD. Note delayed hepatic peak and washout in the SOD patient.

scopic retrograde cholangiopancreatography (ERCP) and sphincter manometry were performed in all within 48 hr of the scintigraphic study. This was designed as a prospective, double-blind study and no clinical, ERCP or manometric information were available at the time of hepatobiliary scintigraphy.

Scintigraphic Method

After a fasting period of at least 3 hr, each patient received 0.02 $\mu\text{g}/\text{kg}$ cholecystinin-8 (CCK) (Kinevac, Squibb Diagnostics, Princeton, NJ) in a 3-min intravenous infusion. Fifteen minutes later, 5 mCi (185 MBq) $^{99\text{m}}\text{Tc}$ -DISIDA (Disofenin) were administered intravenously.

Imaging was performed in the anterior projection with a large field of view gamma camera centered on the 140-keV photopeak. Timed static images were obtained in a 256×256 matrix at 3, 5, 10, 15, 30, 45 and 60 min. Simultaneously, a dynamic study was acquired at a rate of 1 frame/min and stored on computer in a 128×128 matrix.

Regions of interest (ROIs) were placed over the liver parenchyma and CBD to generate time-activity curves. From these curves we derived: (a) time of hepatic peak (T-peak) and (b) % CBD emptying, which was calculated by the equation (Fig. 2A):

$$100 \times \left(\frac{\text{Peak CBD counts}}{\text{CBD counts at 60 min/Peak CBD counts}} \right)$$

When a continuously raising curve was obtained, the 30-min value was taken as peak CBD counts.

The liver ROI was chosen in the right lobe excluding visible bile ducts; the CBD ROI was placed in the lowest portion of the CBD not affected by superimposed bowel activity (Fig. 2B).

The static images were recorded on film for subsequent visual interpretation.

Image Interpretation

Two independent observers interpreted the images and curves without knowledge of the clinical or endoscopic findings. They

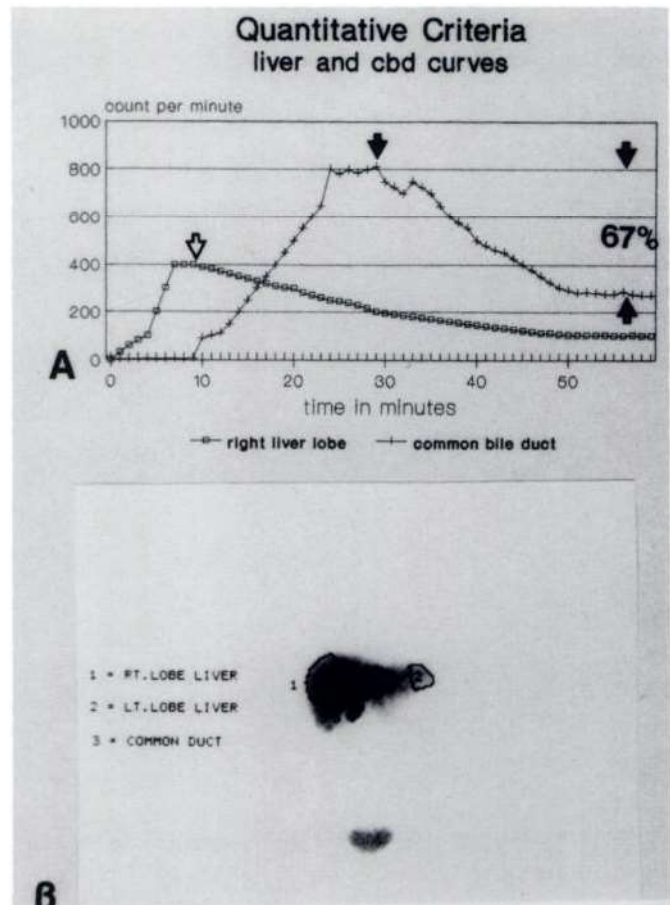


FIGURE 2. (A) Time-activity curves from liver and CBD used to calculate T-max (open arrow) and percent CBD emptying (solid arrows). (B) Placement of hepatic and CBD ROIs. Occasionally, a third ROI was placed in the left hepatic lobe, but the curve was not used in the interpretation.

TABLE 1
Criteria for Scoring Scintigrams

Criteria	Score
1. Peak Time	
a. Less than 10 min	0
b. 10 or more min	1
2. Time of Biliary Visualization	
a. Less than 15 min	0
b. 15 or more min	1
3. Prominence of Biliary Tree	
a. Not prominent	0
b. Prominent major intrahepatic ducts	1
c. Prominent small intrahepatic ducts	2
4. Bowel Visualization	
a. Less than 15 min	0
b. 15-30 min	1
c. More than 30 min	2
5. CBD Emptying	
a. By more than 50%	0
b. Less than 50%	1
c. No change	2
d. Shows increasing activity	3
6. CBD-to-Liver Ratio	
a. $CBD_{60} \leq Liver_{60}$	0
b. CBD_{60} higher than $Liver_{60}$ but lower than $Liver_{15}$	1
c. CBD_{60} higher than $Liver_{60}$ and equal to $Liver_{15}$	2
d. CBD_{60} higher than both $Liver_{60}$ and $Liver_{15}$	3

were asked to score six parameters in each study as described in Table 1. The following parameters were evaluated:

1. Time of peak liver activity. Obtained from the right lobe time-activity curve as in Figure 2A.

2. Time at which intrahepatic biliary tree was first visualized, determined from the static images (Fig. 3).
3. Prominence or dilatation of the biliary tree as determined from the static images as a subjective evaluation similar to that described by Zeman (9) and Lee (10) (Figs. 4 and 5).
4. Time at which bowel was first visualized as determined from the static images (Figs. 3-5).
5. Percent CBD emptying as calculated from the CBD curve using the equation described above (Fig. 6).
6. CBD-to-Liver ratio. This parameter was obtained from the static images by visually comparing the CBD at 60 min (CBD_{60}) to the liver parenchyma at 60 ($Liver_{60}$), and liver parenchyma at 15 min ($Liver_{15}$). This ratio represents activity retained in the CBD at the end of the study (Figs. 4 and 5).

The range of the final score varied from a minimum of 0 to a maximum of 12, the higher numbers corresponding to the slower kinetics.

Interobserver Variability

Two nuclear physicians served as observers. We accepted concurrence between the observers when the scores were identical or varied by no more than 1 point. Sensitivity, specificity and accuracy were calculated for each individual observer.

Manometric and ERCP Methods

Endoscopic biliary manometry was done with a standard triple lumen catheter (Arndorfer Medical Specialties Inc, Greendale, WI) as described by Arndorfer (12). Manometric studies were carried out in the fasting state at the time of ERCP under light sedation with diazepam. With the patient in the prone position, the catheter was introduced into the CBD and then withdrawn at 2-mm increments until active sphincter pressures were observed. Sphincter pressures were then recorded for approximately 2-3

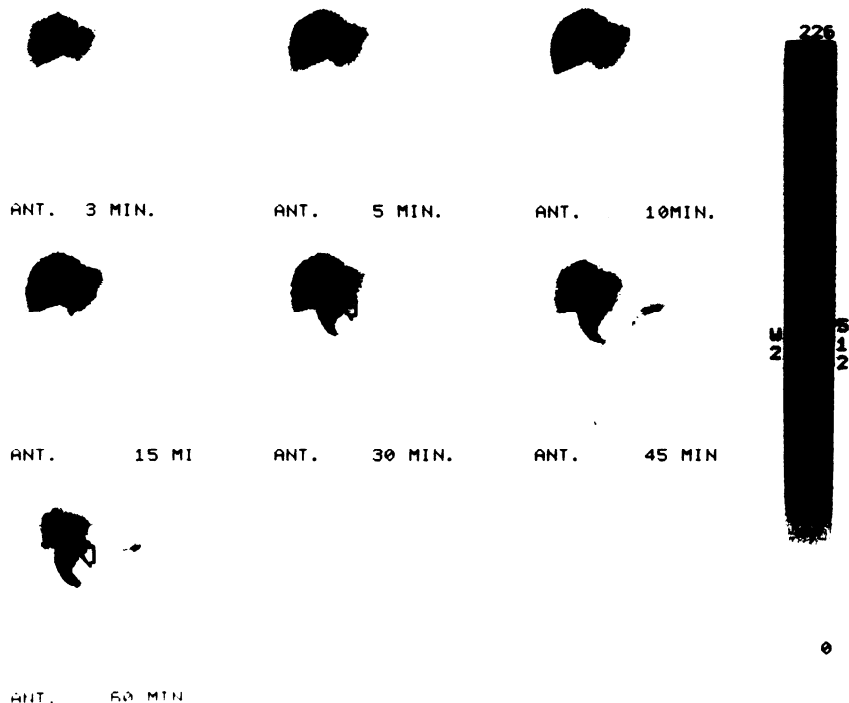


FIGURE 3. Hepatobiliary scintigram in a patient with SOD. Basal sphincter pressure: 60 mmHg. (1) Biliary tree is first visualized at 15 min. (2) CBD and intrahepatic biliary tree appear prominent in the 30-min image (this prominence is either due to true dilatation or to stasis of active bile in the ducts). The prominence persists at 45 and 60 min. (3) Bowel is first visualized at 30 min. (4) The activity in the CBD at 60 min is higher than in liver at 15 min. Notice also that activity in the CBD does not decrease between 30 and 60 min.

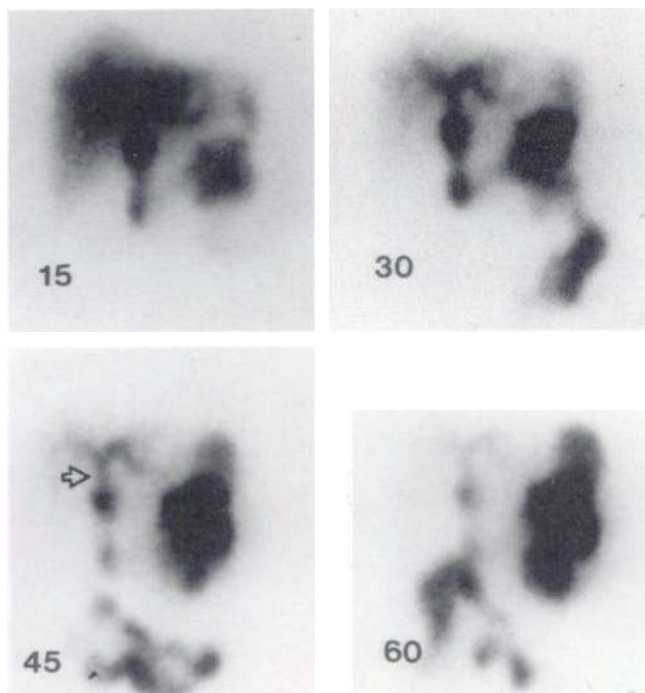


FIGURE 4. Hepatobiliary scintigram in a normal postcholecystectomy patient (sphincter pressure: 15 mmHg). (1) There is marked activity in the bowel by 15 min. Bile ducts and bowel were actually visualized in earlier images (not shown). (2) By 45–60 min, the biliary tree does not appear prominent. After 30 min, the CBD becomes progressively thinner and fainter. (3) The CBD at 60 min is slightly more active than the liver at 60 min, but much less than liver at 15 min.

min. The duodenal lumen pressure was used as a reference and the patient was considered abnormal if the basal pressure was equal or higher than 40 mmHg above the duodenum, or if a paradoxical response to CCK could be demonstrated.

The ERCP studies were performed using standard techniques, and criteria for diagnosis of SOD required: (a) CBD dilatation (>1.2 cm) and (b) delayed emptying of contrast from the CBD (>45 min). Another role of ERCP was to exclude structural biliary diseases such as CBD stones and strictures. Patients with such structural lesions were excluded from the study.

The diagnosis of SOD was made when at least one of the following criteria was met: (1) basal sphincter pressure of 40 mmHg or higher, (b) paradoxical pressure response to CCK or (c) abnormal ERCP showing both CBD dilatation and contrast retention for more than 45 min.

Informed consent was obtained from all patients after the nature of the procedures were fully explained. The protocol was approved by the Joint Committee of Clinical Investigations.

Data Analysis

Sensitivity, specificity and accuracy were calculated using standard equations (13). We used the Student's t-test to compare group means.

RESULTS

Patients with SOD

A final diagnosis of SOD was established in 12 patients. Seven had elevated basal pressure (range: 40–65 mmHg).

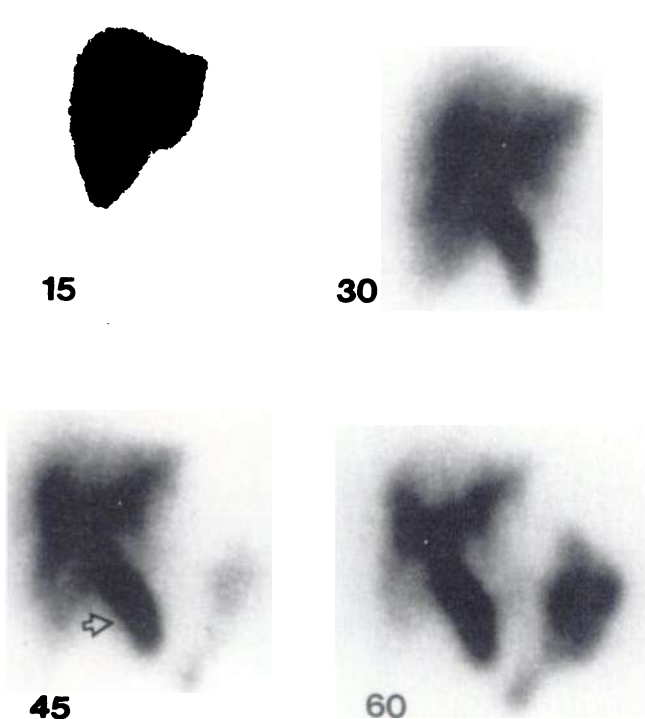


FIGURE 5. Scintigram in patient with SOD (sphincter pressure: 65 mmHg). (1) Biliary tree activity initially seen at 30 min and bowel activity at 45. (2) Biliary tree appears dilated in the 45–60-min images. (3) There is no drop in CBD activity between 30 and 60 min and CBD is more intense than the liver at 15 min.

Another three had normal basal pressure (15, 14 and 16 mmHg) but demonstrated a paradoxical response to CCK with elevation of sphincter pressure to 60, 52 and 30 mmHg, respectively.

The remaining two patients had normal basal pressures (23 and 30 mmHg) but showed both CBD dilatation and delayed contrast emptying on ERCP. Thus, the diagnosis of SOD was made without a CCK challenge. One of them had a previous sphincterotomy and presented with recurrent symptoms. Sphincter pressure may be difficult to interpret under these conditions. A papillary stricture was seen during the procedure and a second sphincterotomy was performed with excellent relief of symptoms. The second patient had been scheduled to receive somatostatin during manometry and a CCK challenge could not be given. Sphincterotomy in this patient also yielded excellent symptomatic response.

The CBD was normal in size in three patients (0.5, 0.5 and 0.8 cm), mildly dilated in another three (1.4, 1.5 and 1.5 cm) and significantly dilated in six (2–2.5 cm). These measurements were based on ERCP findings.

There were four males and eight females in the group of patients with SOD. Ages ranged from 20 to 80 yr (mean: 52) and time from cholecystectomy ranged from 1–34 yr. All had biliary-type pain.

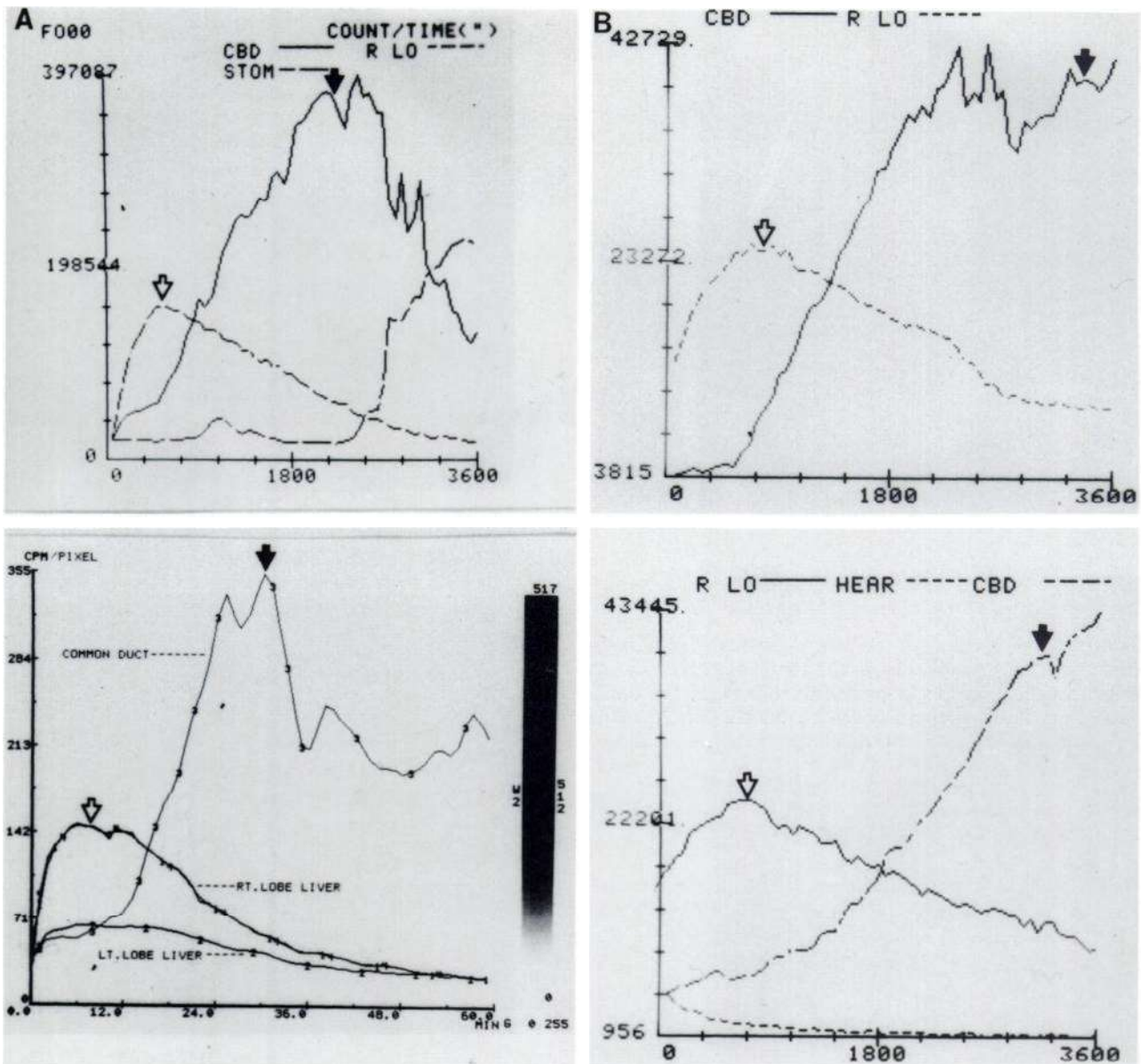


FIGURE 6. (A) CBD curves for calculation of CBD emptying. Solid arrows identify the CBD curve. (Upper) Normal curve. Notice a marked drop of CBD activity (70%) after the peak. (Lower) Abnormal curve in patient with SOD. CBD empties less than 50% after the peak. (B) CBD curves. (Upper) Abnormal curve. No CBD emptying seen after the peak. (Lower) CBD activity continuously increases in patient with severe SOD.

Patients with Normal Sphincter Pressure and No Clinical or Radiologic Evidence of SOD

Fourteen postcholecystectomy patients fell within this group (controls). All had normal basal sphincter pressure (range: 10–36 mmHg; mean: 23).

The CBD was normal in size in 11 patients (0.5–1.0 cm) and mildly dilated in 3 (1.3, 1.3 and 1.5 cm). All had normal contrast drainage from the CBD and, therefore, none met the ERCP criteria for SOD either.

Three males and 11 females comprised this group. Ages ranged from 26 to 66 yr (mean: 49) and time from cholecystectomy ranged from 1 to 24 yr. All were either asymptomatic or had a nonbiliary cause of the symptoms confirmed.

Scintigraphic Findings

The group of patients with SOD was scored from 6 to 11 by observer 1 (mean: 7.4 ± 3), and from 6 to 12 by observer 2 (mean: 8.1 ± 3) ($p = ns$). Common scintigraphic findings in these patients included: delayed hepatic peak, delayed biliary tree visualization, prominent bile ducts which remained prominent beyond 45 min, delayed bowel visualization (>15 min), poor CBD emptying retaining more than 50% of peak activity at 60 min (in many instances activity did not decrease after the peak and high CBD activity at 60 min which was equally intense or higher than liver parenchyma at 15 min (Table 2).

Patients in the control group were scored from 0 to 5 by observer 1 (mean: 1.6 ± 1.3), and from 0 to 4 by

TABLE 2
Scintigraphic Findings (Values in Controls and Abnormals)

Parameter	Controls			SOD group	
	Mean	Range	Units	Mean	Range
Liver peak	6.1	5–10	min	11.7	5–18
Biliary visualization	8.7	5–12	min	16.1	5–30
Biliary prominence*	0.4	0–3	score	2.1	1–3
Bowel visualization	11.2	5–20	min	33.3	10–60
CBD emptying	77.0	50–90	%	0.5	–100–50
CBD-to-liver ratio*	0.8	0–2	score	2.8	2–3
Scintigraphic score*	1.5	0–5	score	7.8	6–12

* Values refer to score assigned as per Table 1.

observer 2 (mean: 1.3 ± 1.3) ($p = ns$). Typical scintigraphic findings included: normal hepatic peak time, prompt biliary tree visualization, “thin” bile ducts in the 45-min image, bowel visualization before 15 min, good CBD emptying by 60 min (higher than 50%) and low CBD-to-liver ratio (Table 2).

There was no overlap of score values between the abnormal and control groups. Also, no classification errors were made by either observer. The true positive rate, true negative rate, and accuracy was 100% for both observers (Fig. 7).

Concurrence between the two observers was found in 24/26 (92%) of the cases.

Table 3 summarizes the scintigraphic findings. The range and mean values of each scintigraphic criteria are given for the control and abnormal groups. The values were calculated from the responses of both observers. For subjective criteria in which a measurement could not be made (i.e., prominence of biliary tree and CBD-to-liver ratio), the reported value is that of the score assigned as per Table 1.

Outcome

Nine patients diagnosed with SOD underwent endoscopic sphincterotomy. These included two with normal

Observer performance

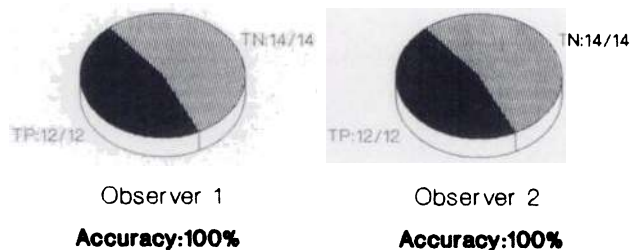


FIGURE 7. Observer performance.

TABLE 3
Sensitivity and Specificity of Individual Scintigraphic Criteria

Parameter	Sensitivity	Specificity
Liver peak	0.83	0.79
Biliary visualization	0.50	1.00
Biliary prominence	1.00	0.79
Bowel visualization	0.92	0.71
CBD emptying	1.00	0.93
CBD-to-Liver ratio	1.00	0.86
Final scintigraphic score	1.00	1.00

basal pressures described earlier, three with paradoxical CCK reponse and 4 with high basal pressures.

Symptoms disappeared or improved in seven patients who have required no further treatment. We performed post-therapy scintigrams in only 4 since the other three were followed at referring facilities. All four patients showed normalization of the scintigram (score <5).

Two patients had initial symptomatic improvement but experienced pain recurrence. For 4 and 10 mo after the initial sphincterotomy, scintigraphy showed unimproved tracer kinetics and repeat ERCP and manometry revealed re-stenosis of the sphincter. After initial success with a second sphincterotomy, their symptoms recurred and re-stenosis was reconfirmed. Surgical sphincteroplasty was then performed, resulting in complete symptomatic relief at the latest follow-up visit (9 and 12 mo, respectively). Scintigraphy after the surgical procedure was normal in both cases.

Three patients have had no endoscopic or surgical treatment. However, two have received calcium channel blockers, one with complete response (resolution of pain and weight gain) and the other with partial response. Two patients had procedure-associated pancreatitis which resolved with medical treatment. No one in the control group underwent sphincterotomy.

DISCUSSION

After a cholecystectomy, the normal biliary tree is transformed into a single-outlet system where intrahepatic ductal bile can flow only through the common duct into the duodenum. The alternate flow pathway into the gallbladder no longer exists. During contraction of the sphincter of Oddi in a normal patient, intraductal pressure remains normal because the biliary system can decompress by draining into the gallbladder. This organ acts as a pressure reservoir (14). On the other hand, sphincter contraction in a postcholecystectomy patient usually results in elevation of intraductal pressure because the reservoir effect of the gallbladder is no longer present (15). High intraductal pressure may cause pain (16), and together with a tight sphincter may lead to biliary stasis, ductal dilatation, and to delayed hepatobiliary radionuclide transit.

SOD is a disorder characterized by an abnormal sphinc-

ter pressure. This may be due to stenosis or dyskinesia and is often a cause of pain after a cholecystectomy (1).

Investigators have shown that functional outlet obstruction caused by the sphincter in this disease tends to delay hepatobiliary radionuclide transit (4-8). Hepatic tracer uptake, tracer transfer from liver to bile ducts, CBD emptying and transit to bowel are all delayed (4-11). Consequently, one may find tracer pooling within the ductal system (manifested by prominent or dilated ducts) and excess tracer retention in the CBD (11).

We have proposed a scintigraphic scoring system to diagnose SOD which takes into account all the above parameters. By incorporating all the abnormalities found in SOD, this score promised to be superior to previously used diagnostic criteria. The expectations were supported by the present study in which the score showed a perfect separation between patients with SOD and controls (sensitivity: 100%, specificity: 100%).

By combining quantitative and visual criteria, we were able to maintain the high sensitivity of visual analysis (11), while adding measurements such as %CBD emptying, T-max and scintigraphic score which provided discrete numerical values useful for comparing follow-up and post-therapy studies. Also, the interpretative confidence of the observers was reportedly improved by the quantitative data supplementing the visual assessment.

As an added benefit, visual analysis may help differentiate between diseases. Quantitative cholescintigraphy yields similar results in patients with liver dysfunction, cholestasis or SOD (1,4,5), making the differentiation dependent on clinical rather than on scintigraphic criteria (17). In our experience, the combination of prominent bile ducts and abnormal retention in the CBD (visual criteria 2 and 6) help make the differentiation because they are seen in SOD, but rarely in liver disease or cholestasis. However, this test cannot differentiate functional from structural obstruction.

One concern of all dynamic tracer studies is the potential of false-positive studies caused by low flow states. This is common in radionuclide kidney studies where delayed transit and tracer retention may be seen in dehydrated patients due to decreased urine flow. This could potentially occur also on hepatobiliary scans during states of decreased bile flow. In an attempt to prevent false-positive studies, we pretreated all patients with CCK, a substance believed to stimulate bile production (18,19). However, we did not test for CCK effect either on biliary kinetics or diagnostic accuracy of the test. Because of the short duration of CCK effect, one may consider administering the drug in a longer infusion. CCK may lower sphincter pressure and improve test specificity by enhancing biliary drainage in normal patients.

Our series is small, reflecting a low prevalence of SOD that probably occurs in only 0.8% of all postcholecystec-

tomy patients (2). However, our initial experience suggests that the proposed scoring system utilizing quantitative and visual criteria reliably identifies patients with SOD. The study is simple, safe and can be performed in virtually any nuclear medicine facility.

If the high accuracy persists as further investigation is made, this technique may provide the sensitivity and specificity necessary in a useful screening test for postcholecystectomy patients with suspected SOD.

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