Gut, 1988, **29**, 1397–1401

Liver and biliary

Quantitative ^{99m}Tc-DISIDA scanning and endoscopic biliary manometry in sphincter of Oddi dysfunction

G M FULLARTON, A ALLAN, T HILDITCH, AND W R MURRAY

From the University Department of Surgery, Western Infirmary, Glasgow, and West of Scotland Health Boards Department of Clinical Physics and Bio-engineering, Glasgow

SUMMARY **Sphincter of Oddi (SO) dysfunction is a recognised cause of postcholecystectomy pain, but a difficult condition to diagnose, requiring endoscopic biliary manometry (EBM) to confirm sphincter motor abnormalities. We have assessed quantitative cholescintigraphy in 10 postcholecystectomy (PC) patients with clinical and manometric evidence of SO dysfunction, 10 PC patients with non-biliary type abdominal pain and 10 asymptomatic PC volunteers acting as controls to determine its value as a non-invasive screening test. Quantitative ^{99m}Tc-DISIDA scans lasted 60 minutes, activity/time curves being created by computer analysis using the entire hepatobiliary system as region-of-interest (ROI). Scintigraphic analysis demonstrated that the time in minutes to maximum counts (T_{max}) was significantly increased in the SO dysfunction group compared with the non-biliary pain group and the asymptomatic volunteers ($p<0{\cdot}001$). The per cent of biliary tracer emptied was also significantly less in the SO dysfunction group than either of the other groups at both 45 minutes ($p<0{\cdot}01$) and 60 minutes ($p<0{\cdot}02$). We conclude that quantitative cholescintigraphy may be a valuable non-invasive screening test in clinically suspected SO dysfunction.**

Postcholecystectomy pain caused by sphincter of Oddi (SO) dysfunction is a poorly understood and ill defined entity. Although functional abnormalities of the sphincter of Oddi have been suspected for many years[1–3] it is only recently with the advent of endoscopic biliary manometry (EBM) that direct evidence has accumulated confirming sphincter motor abnormalities.[4–6] Although EBM is the most definitive investigative technique available in suspected SO dysfunction it may be a technically difficult and time consuming procedure and is not widely available. Non-invasive assessment of sphincter of Oddi function in the postcholecystectomy patient using quantitative cholescintigraphy with ^{99m}Tc-DISIDA may offer a simpler method for detecting SO dysfunction.[7] Its value, however, has not yet been confirmed in patients presenting after cholecystectomy with clinical and manometric evidence of SO dysfunction.

Address for correspondence: Mr G Fullarton, Dept of Surgery, Western Infirmary, Glasgow G11 6NT.

Received for publication 4 May 1988.

Our aim was to assess the value of quantitative cholescintigraphy using ^{99m}Tc-DISIDA in patients presenting after cholecystectomy with clinical and manometric evidence of SO dysfunction.

Methods

MANOMETRIC STUDY

Over a one year period (August, 1986–87) 10 postcholecystectomy patients (eight women, median age 59 years, range 35–74) referred with clinically suspected SO dysfunction (recurrent biliary type pain, ± transient liver function test changes ± dilated bile duct at ERCP) underwent EBM before ERCP examination (group 1) (Table 1). The median time from cholecystectomy was seven years (range one to 23 years). Fourteen patients (13 women, median age 48·5 years, range 27–92) also underwent EBM and acted as our manometry control group. In this group of patients eight had common bile duct stones (all postcholecystectomy) and six had no evidence of pancreaticobiliary disease. These six patients had all

Table 1 *Clinical and radiological features of suspected sphincter of Oddi dysfunction group*

Subject	Age (yrs)	Sex	Time post cholecy-stectomy (yrs)	Biliary type pain	Transient LFT* abnormalities	Dilated CBD† (>12 mm)
MN	56	F	23	+	+	+
EM	60	F	7	+	+	+
RM	59	F	7	+	+	+
IS	74	F	3	+	+	+
MF	35	F	1	+	+	+
EB	59	F	23	+	+	+
JM	71	M	2	+	+	+
AM	73	M	1	+	+	+
AB	53	F	11	+	−	+
IB	72	F	7	+	−	−

*=liver function test; †=common bile duct.

been extensively investigated for relatively minor upper GI complaints with no abnormality being detected in the GI tract. Their symptoms were attributed to irritable bowel syndrome in five, one patient was subsequently found to have porphyria. Previous manometric studies have validated the use of patients with common bile duct stones as control subjects.[8 9]

ENDOSCOPIC BILIARY MANOMETRY TECHNIQUE

Endoscopic biliary manometry was done using an Arndorfer based capillary perfusion system with a reservoir pressure of 400 mmHg and flow rate of 0·25 ml/min of distilled water.[10] Standard polyethylene triple lumen catheters were used (Arndorfer Medical Specialties Inc, Greendale, Wisconsin, USA) with an outer diameter of 1·7 mm and inner luminal diameter of 0·5 mm. Each catheter had three side holes 2 mm apart, the most distal hole being 5 mm from the catheter tip. Catheters had eight black rings 1 mm wide at 2 mm intervals to enable the endoscopist to determine visually the depth of insertion into the sphincter of Oddi. Under study conditions this equipment gave a postocclusion pressure rise rate of 450 mmHg/s. Biliary manometry was carried out in the fasting state at time of ERCP under light diazepam sedation only (5–10 mg iv). No analgesia or smooth muscle relaxants were used. With the patient prone the manometry catheter was introduced into the common bile duct and then withdrawn at 2 mm increments until active sphincter pressure changes were noted. Sphincter pressure recordings were then taken for a further two to three minutes. The catheters position in the bile duct was confirmed by contrast injection after manometry.

ANALYSIS OF DATA

Sphincter of Oddi pressures (mmHg) were analysed as follows using duodenal lumen pressure as a reference zero: (1) Basal pressure=mean pressure at base of phasic contractions over a two minute recording period. (2) Phasic pressure=mean phasic pressure wave rise from basal pressure over a two minute recording period. (3) Frequency of phasic contractions=expressed as mean rate (c/min) over a two minute recording period.

Statistical analysis was performed using the Mann-Whitney U test and a significant difference was considered present if $p<0·05$.

SCINTIGRAPHIC STUDY

Patients

The study group consisted of 10 postcholecystectomy patients with clinical and suspected manometric evidence of SO dysfunction (group 1) as previously described. Ten postcholecystectomy patients (seven women, median age 47·0 years, range 29–66) with non-biliary type abdominal pain (group 2) and 10 asymptomatic postcholecystectomy volunteers (nine women, median age 49·5 years, range 34–64) acting as controls (group 3) were also included in the study. All patients were clinically well at time of study and routine liver function tests (serum bilirubin, alkaline phosphatase, and transaminases) were normal in all subjects before investigation. The study was approved by the local hospital Ethical Committee and all subjects gave written fully informed consent.

Scintigraphic technique

After an overnight fast 150 MBq of ^{99m}Tc-DISIDA were given at time 0. Imaging was carried out using a large field of view gamma camera (Siemens ZLC 750)

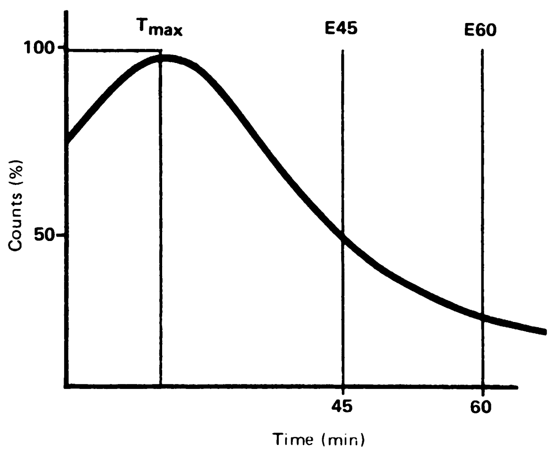

Fig. 1 *Representative activity/time curve showing parameters measured. T_{max}=time in minutes from zero to maximum counts. E45=% biliary emptying at 45 minutes and E60=% biliary emptying at 60 minutes.*

interfaced to a computer (Nodecrest Limited). Data were recorded with the subject supine under the gamma camera as a continuous series of 60 frames each of one minute duration and stored on computer disk for later analysis. Regions of interest (ROI) were drawn around the entire hepatobiliary system (liver and extrahepatic bile ducts) and activity/time curves created by computer analysis for this ROI after correction for radioactive decay. The common bile duct was also outlined as a separate ROI; however, this was often technically difficult because of duodenal overlap and preliminary analysis of this ROI revealed similar results to those of the entire hepatobiliary system. The simpler hepatobiliary ROI was therefore used throughout the study. Results for this hepatobiliary ROI were expressed as (Fig 1): (1) T_{max} (time in minutes from zero to maximum counts) reflecting hepatic uptake and early biliary clearance. (2) E45 (% biliary emptying at 45 minutes) ie activity cleared at 45 minutes as a percentage of the maximum counts in the ROI. (3) E60 (% biliary emptying at 60 minutes) ie activity cleared at 60 minutes as a percentage of the maximum counts in the ROI.

Analysis was done by staff unaware of the patient's clinical condition. For statistical evaluation of data the Kruskal Wallis analysis of variance was used. Significance was achieved at $p<0.05$. All results are given as mean standard error of mean (SE).

Results

MANOMETRY CONTROL GROUP

The manometry results for this group (n=14) are shown in Table 2. Having established our control group data we considered SO dysfunction present if SO mean basal pressure and/or phasic pressure exceeded the mean control values by >2 SD. Mild pancreatitis was induced in two patients resulting from inadvertent pancreatic duct cannulation.

SPHINCTER OF ODDI DYSFUNCTION GROUP (GROUP 1)

The manometric profiles for the 10 patients are shown in Table 2. All 10 patients had abnormalities in mean phasic pressures compared with controls ($p<0.002$). Basal pressures were also significantly raised compared with controls ($p<0.002$).

SCINTIGRAPHIC RESULTS

Results for T_{max}, E45, and E60 for groups 1, 2, and 3 are shown in Table 3. T_{max} for group 1 (SO dysfunction) patients was significantly increased when compared with group 2 (non-biliary pain) and group 3 (asymptomatic volunteers) subjects ($p<0.001$). No overlap in T_{max} values was observed between group 1 and either group 2 or 3 (Fig. 2). E45 and E60 were

Table 2 *Sphincter of Oddi pressures and frequency of phasic contractions*

	Basal (mmHg)	*Phasic (mmHg)*	*Frequency (c/min)*
Controls (n=14)	14·4 (1·2)	80·3 (3·4)	5·4 (0·5)
SO dysfunction (n=10)	28·3 (3·0)* [23·4]	143·6 (11·0)* [105·7]	6·5 (0·5) [9·2]

*p<0·002, mean (SE). Figures in square brackets indicate our upper limit of normal based on control means+2 SD.

Table 3 *Scintigraphic results*

	T_{max} *(Min)*	*E45 (%)*	*E60 (%)*
Group 1 (SO dysfunction)	25·7 (1·8)	21·7 (4·1)	37·9 (4·8)
Group 2 (non-biliary pain)	14·2 (1·0)‡	39·1 (3·2)†	50·4 (2·8)*
Group 3 (asymptomatic volunteers)	13·8 (0·8)‡	43·8 (2·8)†	56·3 (3·5)*

Mean (SE); *p<0·02, †p<0·01, ‡p<0·001.

also significantly reduced in group 1 compared with either group 2 or 3.

Group 1 patients thus exhibited characteristic ^{99m}Tc-DISIDA emptying curves with prolonged time to peak counts and slow biliary emptying compared with either group 2 or 3 patients (Figs 3 (a), (b)).

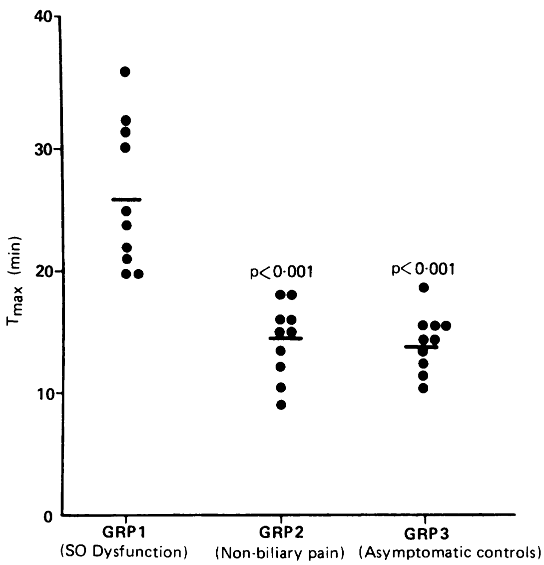

Fig. 2 *T_{max} values for group 1 (SO dysfunction) patients, group 2 (non-biliary pain) patients and group 3 (asymptomatic volunteers). Horizontal bars represent mean values.*

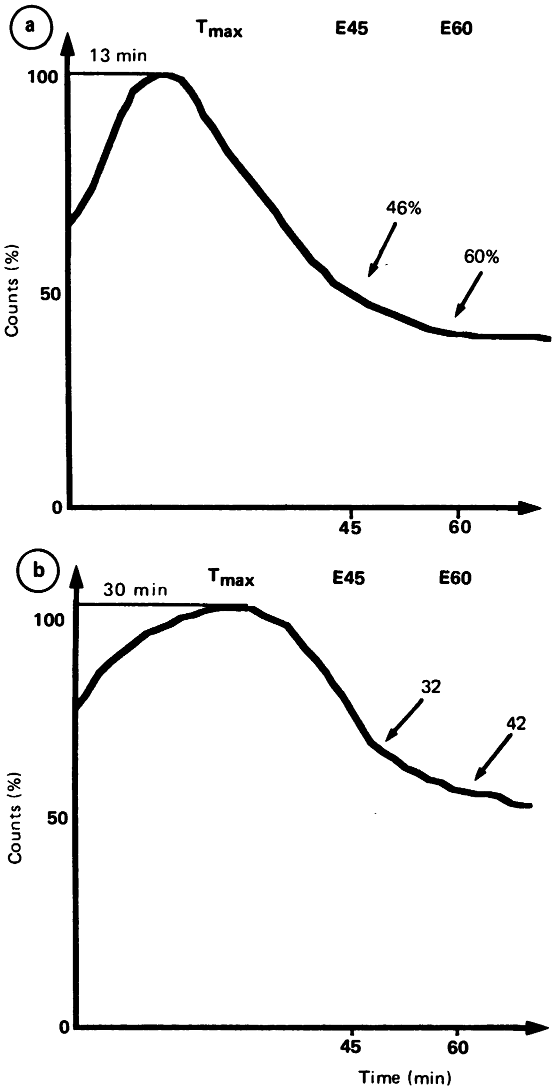

Fig. 3 (a) & (b) *Representative activity/time curves showing the differences in scintigraphic parameters between (a) asymptomatic volunteer and (b) SO dysfunction patient.*

Discussion

This study has shown that quantitative cholescintigraphy can detect alterations in Tc-DISIDA labelled bile flow in postcholecystectomy patients with clinical and manometric evidence of sphincter of Oddi (SO) dysfunction. This is in agreement with a recent study which showed the value of cholescintigraphy in patients with clinical evidence of SO dysfunction only.[7]

Postcholecystectomy pain in the absence of overt biliary or pancreatic disease is a difficult problem to resolve. Of the post-cholecystectomy patients who present with recurrent abdominal pain perhaps only 10–20% will be suffering from SO dysfunction.[11] At present EBM represents the gold standard assessment of sphincter of Oddi function despite having several inherent problems. First, the establishment of normal values is difficult. To date only three studies have published healthy volunteer SO pressures.[12–14] Subsequent studies have shown insignificant pressure differences between these normal volunteers and patients with common bile duct stones.[8,9] Second, equipment is not generally standardised with the result that published studies show widely varying results.[15] Third, EBM may be a technically difficult procedure and increases the time required for a diagnostic ERCP examination. It is clear therefore that there is a need for a more simple, non-invasive screening test with diagnostic sensitivity for SO dysfunction to select out those post-cholecystectomy patients who should be referred for EBM to confirm the diagnosis. It has been suggested that quantitative cholescintigraphy indirectly assesses SO function by allowing a dynamic assessment of bile flow across the SO.[7] In our SO dysfunction group where definite SO motor abnormalities exist it appears that cholescintigraphy does offer a sufficiently sensitive assessment of bile flow to detect even transient obstruction to flow from sphincter motor dysfunction. It is interesting to note that of the five SO dysfunction patients with the most severe manometric SO motor abnormalities (both elevated basal and phasic pressures) four of five had the most abnormal scintigraphy (four of five most prolonged T_{max} and three of five most reduced E45). There does therefore appear to be a correlation between the degree of sphincter dysfunction and the alteration in bile flow as measured by scintigraphy. This requires further study to confirm these findings. The ability of quantitative cholescintigraphy to detect transient bile duct obstruction was further illustrated by three female postcholecystectomy patients (median age 74, years range 63–76) with known choledocholithiasis and normal liver function tests who underwent DISIDA scanning. These three patients had considerably deranged scintigraphic parameters (mean SE) compared with our control group (stone group T_{max} 37·3 (5·8), E45 7·2 (5·8), E60 16·8 (3·5)).

Cholescintigraphy is simple, inexpensive and widely available and appears to offer an ideal screening test in postcholecystectomy patients with suspected SO dysfunction. T_{max} (representing the point of dynamic equilibrium between hepatic uptake and biliary emptying) appears to be the most discriminating factor in detecting SO dysfunction providing biochemical liver function tests are normal and the extrahepatic biliary tree is clear of mechanical obstruction.

We conclude that quantitative cholescintigraphy using ^{99m}Tc-DISIDA may offer a simple non-invasive method for detecting post-cholecystectomy patients with SO dysfunction.

We are grateful to Mr W Davies and Mr T Hutchinson, University Department of Anaesthetics for their technical assistance in this project and to Miss Yvonne Galbraith for typing the manuscript.

References

1 Mirizzi PL. Functional disturbance of the choledochus. *Surg Gynecol Obstet* 1942; **74:** 306–18.
2 Ryan JD, Doubilet H, Mulholland JH. Observations on biliary pancreatic dynamics in a normal human. *Gastroenterology* 1949; **13:** 1–8.
3 Nardi GL, Acosta JM. Papillitis as a cause of pancreatitis and abdominal pain. *Ann Surg* 1966; **164:** 611–21.
4 Bar-Meir S, Geenen JE, Hogan WJ, Dodds WJ, Stewart ET, Arndorfer RC. Biliary and pancreatic duct pressures measured by ERCP manometry in patients with suspected papillary stenosis. *Dig Dis Sci* 1979; **24:** 209–13.
5 Bortolotti M, Caletti GC, Brocchi E, *et al*. Endoscopic manometry in the diagnosis of the post-cholecystectomy pain syndrome. *Digestion* 1983; **28:** 153–7.
6 Toouli J, Roberts-Thomson IC, Dent J, Lee J. Manometric disorders in patients with suspected sphincter of Oddi dysfunction. *Gastroenterology* 1985; **88:** 1243–50.
7 Shaffer EA, Hershfield NB, Logan K, Kloiber R. Cholescintigraphic detection of functional obstruction of the sphincter of Oddi. *Gastroenterology* 1986; **90:** 728–33.
8 Toouli J, Geenen JE, Hogan WJ, Dodds WJ, Arndorfer RC. Sphincter of Oddi motor activity: a comparison between patients with common bile duct stones and controls. *Gastroenterology* 1982; **82:** 111–7.
9 Demasi E, Corazziari E, Habib FI, *et al*. Manometric study of the sphincter of Oddi in patients with and without common bile duct stones. *Gut* 1984; **25:** 275–8.
10 Arndorfer RC, Stef JJ, Dodds WJ, Linehan JH, Hogan WJ. Improved infusion system for intraluminal esophageal manometry. *Gastroenterology* 1977; **73:** 23–7.
11 Bar-Meir S, Halpern Z, Bardan E, Gilat T. Frequency of papillary dysfunction among cholecystectomized patients. *Hepatology* 1984; **4:** 328–30.
12 Carr-Locke DL, Gregg JA. Endoscopic manometry of pancreatic and biliary sphincter zones in man. *Dig Dis Sci* 1981; **26:** 7–15.
13 Meshkinpour H, Mollot M, Eckerling GB, Bookman L. Bile duct dyskinesia: Clinical and manometric study. *Gastroenterology* 1984; **87:** 759–62.
14 Funch-Jensen P, Kruse A, Ravnsbaek J. Endoscopic sphincter of Oddi manometry in healthy volunteers. *Scand J Gastroenterol* 1987; **22:** 243–9.
15 Lebovics E, Heier SK, Rosenthal WS. Sphincter of Oddi motility: developments in physiology and clinical application. *Am J Gastroenterol* 1986; **81:** 736–43.