**Biliary Tract**

Outcome of endoscopic sphincterotomy in post cholecystectomy patients with sphincter of Oddi dysfunction as predicted by manometry and quantitative choledochoscintigraphy

M Cicala, F I Habib, P Vavassori, N Pallotta, O Schillaci, G Costamagna, M P L Guarino, F Scopinaro, F Fiocca, A Torsoli, E Corazziari

**Background:** Sphincter of Oddi dysfunction is diagnosed at manometry and, after cholecystectomy, non-invasively at quantitative choledochoscintigraphy. Patients may benefit from endoscopic sphincterotomy.

**Aims:** The aim of this study was to assess the usefulness of choledochoscintigraphy compared with manometry in predicting outcome of sphincterotomy in post cholecystectomy patients with sphincter of Oddi dysfunction.

**Patients and methods:** Thirty patients with biliary-type pain complying with the Rome diagnostic criteria of sphincter of Oddi dysfunction and belonging to biliary group I and II were subjected to clinical evaluation, choledochoscintigraphic assessment of the hepatic hilum-duodenum transit time, endoscopic retrograde cholangiopancreatography, and perendoscopic manometry. Twenty two biliary group I and II patients with prolonged hepatic hilum-duodenum transit times were invited to undergo sphincterotomy. Fourteen patients underwent sphincterotomy; eight refused. Clinical and scintigraphic assessments were performed at follow up.

**Results:** Hepatic hilum-duodenum transit time was delayed in all patients with manometric evidence of sphincter of Oddi dysfunction, in all biliary group I patients and in 64% of biliary group II patients. At follow up, all patients who underwent sphincterotomy were symptom free and hepatic hilum-duodenum transit time had either normalised or significantly improved. A favourable outcome of sphincterotomy was predicted in 93% of cases at choledochoscintigraphy and in 57% at manometry.

**Conclusions:** Quantitative choledochoscintigraphy is a useful and non-invasive test to diagnose sphincter of Oddi dysfunction as well as a reliable predictor of sphincterotomy outcome in post cholecystectomy biliary group I and II patients, irrespective of clinical classification and manometric findings.

**METHODS**

A total of 140 consecutive post cholecystectomy patients referred to our centre from June 1988 to November 1998 for upper abdominal pain of suspected biliopancreatic origin underwent clinical interview and a symptom scored questionnaire, physical examination, and laboratory assessment: liver function tests, liver function tests; QC, quantitative choledochoscintigraphy; ROI, region of interest; He, heart; L peripheral liver parenchyma; BD, bile duct; D, duodenum; SO, sphincter of Oddi.

**Abbreviations:** CBD, common bile duct; ERCP, endoscopic retrograde cholangiopancreatography; ES, endoscopic sphincterotomy; F, factor; HHDT, hepatic hilum-duodenum transit time; HIDA, hepatic iminodiacetic acid; LFTs, liver function tests; QC, quantitative choledochoscintigraphy; ROI, region of interest; He, heart; L peripheral liver parenchyma; BD, bile duct; D, duodenum; SO, sphincter of Oddi.
function tests (LFTs) (serum glutamic and alanine aminotransferases, protein, alkaline phosphatase, gamma glutamyl transcpeptidase, conjugated and unconjugated bilirubin, prothrombin time), lipase, amylase, as well as ultrasound examination of the upper abdomen, upper gastrointestinal endoscopy, and endoscopic retrograde cholangiopancreatography (ERCP). Eighty-two patients presented pathological alterations (choledocholithiasis, biliary pancreatitis, chronic pancreatitis) and were excluded from the study. Of the remaining 58 patients, 30 had undergone surgery on the upper gastrointestinal tract, pancreatic alterations at ERCP. None of these patients had evidence of oesophago-gastro-duodenal disease, and duodenum (D). The selection of ROIs has been described previously. The time/activity curves obtained from L and BD are derived from ROIs with a different number of pixels, as amplitude, duration, and frequency of phasic SO pressure as the zero reference. Duration of phasic SO contractions was measured from the peak to the base of the waves and expressed as mm Hg with duodenal pressure as the zero reference. Mean basal SO pressure represented the mean of the basal pressures, recorded by the three sensors and measured on a steady baseline of at least 20 seconds. Maximal basal pressure was the highest value recorded by any one of the three sensors. The amplitude of the SO contractions was measured from the peak to the base of the waves and expressed as mm Hg with basal SO pressure as the zero reference. Duration of phasic SO contractions was measured from the onset of the ascending to the end of the descending slope of the wave. The frequency of the SO contractions was expressed as the number of waves per minute. Amplitude, duration, and frequency of phasic SO contractions were assessed at each recording level and expressed as the average of the three tracings. A maximal basal SO pressure equal to or exceeding 40 mm Hg was considered as evidence of SO dysfunction.

Acquisition and analysis of data
Definition of clinical biliary subgroupings, and of normal manometric and choledochoscintigraphic values, were established before recruitment of the patients and data were acquired in a prospective manner. Clinical, manometric, and scintigraphic data were each acquired by an independent observer unaware of the findings of the other techniques. A favourable therapeutic outcome at medium and long term follow-up was defined if patients complied with the following: (a) absence of specific symptoms and (b) normalisation of LFTs, amylase, and lipase. Intragroup changes were assessed using the Wilcoxon matched pairs signed rank test whereas the Mann-Whitney U test, 95% confidence intervals, was used for analysis of intergroup differences. The Pearson coefficient of correlation and concordance test were used to assess data relationship.

Perendoscopic manometry
Immediately before ERCP, patients were sedated with diazepam (10–20 mg intravenously). After completion of ERCP, perendoscopic manometry was performed using a 200 cm polyethylene triple lumen catheter with three distal side holes located 2 mm apart (Arndorfer Medical Specialties, Inc., Greendale, Wisconsin, USA), continuously infused with sterile bubble free water at a rate of 0.25 ml/min by a minimally compliant hydraulic capillary infusion system (Arndorfer Medical Specialties, Inc., Greendale, Wisconsin, USA). The catheter, passed through the biopsy channel of a duodenoscope (Olympus Co., TJF 100/TJF 140, Tokyo, Japan), was introduced into the CBD and withdrawn across the SO in 2 mm step increments. The catheter was then positioned to record SO motor activity for at least two minutes with all three manometric sensors. Pressure recordings were divided into, and measured over, one minute intervals. Basal SO pressure was measured at the mid inspiratory phase and expressed as mm Hg with duodenal pressure as the zero reference. Mean basal SO pressure represented the mean of the basal pressures, recorded by the three sensors and measured on a steady baseline of at least 20 seconds. Maximal basal pressure was the highest value recorded by any one of the three sensors. The amplitude of the SO contractions was measured from the peak to the base of the waves and expressed as mm Hg with basal SO pressure as the zero reference. Duration of phasic SO contractions was measured from the onset of the ascending to the end of the descending slope of the wave. The frequency of the SO contractions was expressed as the number of waves per minute. Amplitude, duration, and frequency of phasic SO contractions were assessed at each recording level and expressed as the average of the three tracings. A maximal basal SO pressure equal to or exceeding 40 mm Hg was considered as evidence of SO dysfunction.
RESULTS

The sex and age of the patients in the two biliary groups were not significantly different.

Choledochoscintigraphic data in the two groups are reported in table 1. The HHDT was prolonged in all biliary group I patients and in 14/22 (64%) biliary group II patients.

SO manometric variables in the two groups are reported in table 1. Maximal basal SO pressure was >40 mm Hg in all but one biliary group I patient; it was ≥40 mm Hg in 8/22 (36%) biliary group II patients.

Maximal basal SO pressure was directly correlated with choledochoscintigraphic values of HHDT ($r=0.77$, $p<0.001$; $k=0.7$) (fig 1). Amplitude, duration, and frequency of phasic SO contractions did not differ significantly between the two biliary groups.

No significant relationship was found between HHDT and CBD diameter or amplitude, duration, or frequency of phasic SO contractions.

HHDT was abnormally prolonged in all patients with maximal basal SO pressure ≥40 mm Hg and in 7/15 (47%) patients with a normal maximal basal SO pressure (<40 mm Hg).

Twenty two biliary group I and II patients had a prolonged (>9 minutes) HHDT and were invited to undergo ES. Eight (two from biliary group I and six from biliary group II) refused and thus 14 patients underwent ES. At medium term follow up, all 14 patients (six from biliary group I and eight from biliary group II) who underwent ES had a favourable outcome except for one biliary group II patient who was still symptomatic and showed an increased alkaline phosphatase and whose HHDT did not vary. All patients were asymptomatic and did not have LFTs, amylase, or lipase alterations at long term follow up. HHDT decreased from 13.7 (2.5) minutes (mean (SD)) pre-ES to 6.4 (2.8) minutes ($p<0.001$) post-ES at medium term follow up. At follow up, all eight patients who refused ES were still symptomatic and their HHDT did not vary (13.8 (1.8) minutes at referral, 13.0 (2.2) minutes at medium term follow up) (fig 2).

In the 14 biliary group I and II patients who underwent ES and in whom both SO manometry and QC were performed, the favourable post-ES outcome was predicted by QC in 13 patients (93%) and by manometry in eight (57%).

DISCUSSION

SO dysfunction is usually suspected in symptomatic patients who have previously undergone cholecystectomy. As symptoms have low diagnostic specificity and sensitivity, detection of SO dysfunction usually requires an extensive diagnostic workup which includes invasive examinations such as ERCP and perendoscopic manometry of the SO.

Attempts have thus been made to limit these invasive techniques to those patients who would most benefit so as to reduce the unnecessary risks of complications and the costs. Clinical clues and more available tests have been used to detect or at least to reduce the diagnostic uncertainty of SO dysfunction. The subdivision of post cholecystectomy patients into three subgroups according to an arbitrary classification based on clinical, laboratory, and endoscopic findings proved over the years to offer a simple and practical approach. Patients with biliary group I characteristics have a high probability of presenting manometric evidence of SO dysfunction, a finding confirmed by the present study which showed that the presence of the biliary I clinical characteristics predicted a favourable response to ES in 100% of those post cholecystectomy patients complying with the Rome diagnostic criteria of SO dysfunction. This finding is in agreement with previous observations reporting a favourable response after ES in patients classified as belonging to biliary group I.

It is not surprising that biliary group I patients benefit to such a high degree from sphincter bisection as the combined occurrence of dilated CBD, increased serum LFTs, and delayed contrast drainage from the CBD converge to indicate the presence of an obstruction at the SO level. On the other hand, as confirmed in the present study, a large number of biliary group II patients do not have any SO alteration at manometry and further investigations are then required to ascertain the presence of SO dysfunction.

SO manometry is the only method that can directly assess SO motor function. As expected, in the present study perendoscopic manometry, confirming previous
observations, showed that maximal basal SO pressure was frequently increased in biliary group I and less so in biliary group II. In the absence of a pathological reference marker of SO dysfunction, SO manometry has gained acceptance as the gold standard for the diagnosis of this condition as the finding of increased SO pressure has a high predictive value for a favourable response to ES. Despite the highly statistical direct correlation between the HHDT value and the manometric finding of SO dysfunction predicts a favourable outcome after ES but the reverse does not hold true as one biliary group I and five biliary group II patients with normal SO manometry benefited from ES, indicated on the basis of QC abnormalities.

The results of the present study show that the non-invasive technique of QC identified all patients with a maximal basal SO pressure of 40 mm Hg or more and all patients belonging to biliary group I. The satisfactory diagnostic agreement between QC and SO manometry reflects the highly statistical direct correlation between the HHDT value and the manometric value of maximal basal SO pressure. Despite the highly statistical correlation between HHDT and maximal basal SO pressure values, not all patients belonging to biliary group I presenting a prolonged HHDT at QC had abnormal findings at SO manometry; one patient had a maximal basal SO pressure within the normal range and one patient a borderline value of 40 mm Hg. These two patients underwent perendoscopic sphincterotomy: at follow up they became asymptomatic and QC had normalised. Also, six patients belonging to biliary group II had normal basal SO pressure and a prolonged HHDT, five of these biliary group II patients underwent ES and at follow up they became asymptomatic and showed a normal QC value.

The lack of agreement between manometry and QC findings in the individual patient could be interpreted as a drawback of either one or both techniques which necessarily offer a spot measurement of a variable which may vary over time and the values of which are acquired by the two techniques at different times.

We cannot exclude the fact however that an SO pressure of less than 40 mm Hg may still offer resistance to bile flow. The threshold of 40 mm Hg that discriminates normal from abnormal SO motor function was determined in studies which lacked control values from healthy populations. The only study performed in healthy volunteers reported that normal basal SO pressure does not exceed 30 mm Hg. Hence patients with basal SO pressure exceeding 30 mm Hg could also be considered to have SO dysfunction and would likely benefit from ES. In addition, although mean phasic SO contractions did not differ among the investigated subgroups, abnormal phasic SO motor activity may have hindered bile flow in the individual patient.

It is also possible that, in addition to basal SO pressure, other factors not detectable at perendoscopic manometry may contribute to prolong intrahepatic bile transit.

All biliary group I and II patients with prolonged HHDT were invited to undergo ES irrespective of manometric findings, and the comparison between the outcome of those who agreed with those who refused this treatment offers an indication of the extent to which QC per se, and relative to SO manometry, can predict the therapeutic effect of ES in these subgroups of patients. The results of the present study indicate that a prolonged HHDT at QC could predict a favourable response to ES, irrespective of the clinical classification into biliary group I or II.

In conclusion, within the limits of the present study, in which no attempt was made to compare randomised therapeutic groups of patients, it would appear that at least in post cholecystectomy patients belonging to biliary group II, a prolonged HHDT at QC is a better predictor of ES outcome than manometric findings.

Authors’ affiliations
M Cicola, P Vavassori, G Costamagna, M P L Guarino, DPT Gastroenterologia, Università “Campus Bio-Medico” Roma, Italy
F I Habib, N Pallotta, A Torsoli, E Corazziari, DPT Scienze Cliniche, Università “La Sapienza” Roma, Italy
O Schillaci, F Scopinaro, DPT Medicina Sperimentale, Università “La Sapienza” Roma, Italy
F Fiocco, DPT Chirurgia, Stefaniuni Università “La Sapienza” Roma, Italy

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