Endoscopic balloon dilatation versus endoscopic sphincterotomy for the removal of bile duct stones: a prospective randomised trial

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Background: Endoscopic balloon dilatation (EBD) of the sphincter of Oddi has been proposed as an alternative therapy with possible advantages, as compared with endoscopic sphincterotomy (ES), for removal of bile duct stones.

Patients and methods: In a randomised study, we compared the efficacy and complication rate of the two techniques in 202 patients with common bile duct stones. Patients were followed up for 12 months.

Results: A total of 103 patients were randomised to the EBD group and 99 to the ES group. Overall duct clearance was 87.1% and did not differ between the two groups (EBD 87.4%; ES 86.9%). The complication rate at 24 hours was 6.8% in the EBD group and 3.0% in the ES group (NS). Complications during follow up were 11.7% and 15.2% respectively (NS). A multivariate logistic regression analysis showed only the size of the largest stone to be predictive of success for either technique.

Conclusion: Endoscopic balloon dilatation offers no significant advantage over the well established technique of endoscopic sphincterotomy for the removal of bile duct stones.

PATIENTS AND METHODS

Patients

Two hundred and two consecutive patients, aged 18 years or older, referred to the endoscopy unit of the Chelsea and Westminster Hospital from 1 January 1995 to 31 July 1999 for endoscopic retrograde cholangiopancreatography (ERCP) and shown on the initial cholangiogram to have bile duct stones, were included in the study. Patients with a liver parenchyma or bile duct malignancy were excluded.

Written informed consent was obtained for the study from each patient suspected on clinical information to have bile duct stones and the study was approved by the hospital ethics committee. Patients were randomised when CBD stones were identified, using table random sampling numbers in numbered sealed envelopes.

On randomisation, the following data were recorded: presenting symptoms (biliary pain, jaundice, acute pancreatitis, acute cholangitis); history of previous cholecystectomy or other biliary intervention; and routine laboratory values obtained in the last 24 hours (full blood count, prothrombin time, serum urea, creatinine and electrolytes, routine liver function tests, and serum amylase).

After initial diagnostic ERCP the diameter of the CBD, the number of stones, and the size of the largest one were recorded. At 24 hours post ERCP, patients were examined by the referring doctor and the occurrence of acute pancreatitis, bleeding, acute cholangitis, perforation, or any other complication was recorded. Acute pancreatitis episodes were classified as mild, moderate, or severe if the patient had to stay in hospital for less than four days, 4–10 days, or more than 10 days, respectively.

Patients were then followed up in outpatient clinics at one, three, six, and 12 months, and questioned with regards to biliary related symptoms or complications. Every effort was made to follow up the patients. If patients were referred from other hospitals, letters were written to the referring doctors or to the patient’s GP. Attempts were also made to contact the patient over the telephone.

Abbreviations: EBD, endoscopic balloon dilatation; ES, endoscopic sphincterotomy; SO, sphincter of Oddi; RCT, randomised controlled trial; ERCP, endoscopic retrograde cholangiopancreatography; CBD, common bile duct.
Primary end points were success or failure to clear the ducts and the complication rate related to each procedure. The number of attempts needed to clear the duct was recorded.

**Methods**

After cannulation of the CBD, an initial cholangiogram was taken and the diameter of the CBD at its most dilated part, as well as the size and number of existing stones, was assessed, in comparison with the diameter of the shaft of the endoscope. An over the wire endoscopic sphincterotomy or papillary dilatation was performed and cutting current was mainly used for ES to minimise the risk of pancreatic duct damage. For EBD, a 3 cm long, 10 mm in diameter dilating balloon was used. The balloon was inflated to a pressure of 12 Atm for 30 seconds. The balloon was then deflated and the papilla observed for the result. If there was no free bile flow from an obviously enlarged papillary opening, the procedure was repeated again until papillary dilatation was satisfactory. Stones were extracted using extraction balloons or baskets, depending on their size. A balloon occlusion cholangiogram was obtained at the end of the procedure to ensure complete stone removal.

Mechanical lithotripsy (Lithocrush, Olympus) was used within the study when the operator considered that the size of the stone precluded successful duct clearance. However, a policy was adopted whereby in patients with moderate/severe acute cholangitis, acute pancreatitis, or severe comorbid illness, mechanical lithotripsy was deferred to avoid prolonging the procedure or exposing the patient to excessive trauma. In these patients and in any other in whom drainage was not achieved, a pigtail Teflon stent was inserted to avoid stone impaction and the procedure was repeated in 2–4 weeks.

If cannulation of the CBD was not possible, a small precut sphincterotomy was performed to gain access and the patient was subsequently randomised.

**Statistics**

The sample size was calculated using a two tailed test criterion for analysis. The aim of the study was to achieve a 50% difference in the complication rates between ES and EBD (from 10% to 5%). The sample size was calculated to achieve a statistical significance of 95% (α=0.05) and for the study to have a power of 80% (β=0.2). Analysis of the data was performed on an intention to treat basis.

Univariate logistic regression analysis was carried out to determine the likelihood of success following removal of gall stones for the variables studied. Using conservative p value cut off, factors which were associated in univariate analysis (p<0.02) were selected for building a multivariate model.

The same statistical analysis was repeated after the 31 patients who required precut sphincterotomy for access into the CBD to be gained were excluded.

**RESULTS**

A total of 202 patients were included in the study: 103 patients (male/female ratio 25/78; mean age 60.8 years (95% confidence interval (CI) 56.8–64.7)) were randomised to EBD and 99 (male/female ratio 35/64; mean age 61.9 years (95% CI 58.3–65.4)) to ES. Recruitment stopped as soon as the aimed number of 202 patients was reached and this accounts for the inequality in sample size between the two groups. Twenty six (32.1%) from group one and 31 (34.8%) from group two had undergone a previous cholecystectomy.

Seventy patients in total presented with acute cholangitis and 20 with acute pancreatitis. There was no difference between the two groups regarding the number of patients included in each group with acute cholangitis or acute pancreatitis which were equally distributed between the two groups (table 1).

| Table 1 Baseline characteristics of the patients in the two groups |
|------------------|------------------|
|                  | EBD             | ES              |
| n                | 103             | 99              |
| Sex (M/F)        | 25/78           | 35/64           |
| Age (y)          | 60.8 (56.8–64.7)| 61.9 (58.3–65.4)|
| Presenting with  |                 |                 |
| Acute cholangitis| 35 (34.7%)      | 35 (35.4%)      |
| Acute pancreatitis| 10 (9.7%)     | 10 (10.1%)      |

*Mean (95% confidence interval).

**EBD, endoscopic balloon dilatation; ES, endoscopic sphincterotomy.**

In the univariate logistic regression analysis, the following parameters were included: randomisation, sex, age, presentation with jaundice, acute cholangitis or acute pancreatitis, diameter of the CBD on the initial cholangiogram, and number of the stones and size of the largest one. From these, age, diameter of the CBD, and size and number of stones were significantly associated with success (table 4). Multivariate logistic regression analysis showed only the size of the largest stone to be an independent predictor of success for duct clearance. In our patients, the average CBD diameter was 12 mm, the average number of stones was two, and the average size of the stones was 10 mm. These were taken as cut off points in the statistical analysis.

| Table 2 Baseline cholangiographic characteristics of the patients |
|------------------|------------------|
|                  | EBD (No (%))     | ES (No (%))     |
| Dilated CBD (>7 mm) | 83 (80.6) | 77 (77.8) |
| No stones         | 9 (9.1)     | 65 (65.7)     |
| Debris            | 56 (54.4)   | 40 (38.8)     |
| ≤2                | 40 (38.8)   | 25 (25.3)     |
| >3                | 27 (26.2)   | 31 (31.3)     |
| Size of stones (mm) |
| ≤5                | 37 (35.9)   | 26 (26.3)     |
| 6–9               | 39 (37.9)   | 42 (42.4)     |
| ≥10               | 40 (38.8)   | 25 (25.3)     |

**EBD, endoscopic balloon dilatation; ES, endoscopic sphincterotomy; CBD, common bile duct.**

On the initial diagnostic cholangiogram, the CBD was dilated in 83 (80.6%) patients in the EBD group and in 77 (77.8%) patients in the ES group. There were no differences between the two groups with respect to the estimated size and number of stones (table 2).

Precut sphincterotomy was performed in 31 (15.3%) patients (12 in the EBD group, 19 in the ES group). Duct clearance was achieved in 176 (87.1) and failed in 26 patients (12.9%). The success rate in clearing the ducts did not differ between the two groups. After the first attempt, the success rate was 63.1% for the EBD group and 63.6% for the ES group. The final success rate was 86.4% for the EBD group and 86.9% for the ES group (table 3). A total of 143 (70.8%) patients underwent a single procedure, 42 (20.8%) two, 13 (6.9%) three, and two (1%) patients required four ERCPs.

In the univariate logistic regression analysis, the following parameters were included: randomisation, sex, age, presentation with jaundice, acute cholangitis or acute pancreatitis, diameter of the CBD on the initial cholangiogram, and number of the stones and size of the largest one. From these, age, diameter of the CBD, and size and number of stones were significantly associated with success (table 4). Multivariate logistic regression analysis showed only the size of the largest stone to be an independent predictor of success for duct clearance. In our patients, the average CBD diameter was 12 mm, the average number of stones was two, and the average size of the stones was 10 mm. These were taken as cut off points in the statistical analysis.

| Table 3 Success rate in the two groups |
|------------------|------------------|
|                  | EBD No (%)       | ES No (%)       |
| 1st ERCP         | 65 (63.1)       | 63 (63.6)       |
| Final ERCP       | 90 (87.4)       | 86 (86.9)       |

**EBD, endoscopic balloon dilatation; ES, endoscopic sphincterotomy; ERCP, endoscopic retrograde cholangiopancreatography.**
The odds ratio for success, for stones less than 10 mm in diameter, was 10.0 (95% CI 2.24–44.64; p < 0.001). Hence in 81 patients with stones ≥ 10 mm, duct clearance was achieved in 61 (75.3%) and failed in 20 (24.7%) while in 121 patients with stones < 10 mm in diameter, duct clearance was possible in 115 (95.04%) and failed only in six (4.96%).

There were no differences between the two groups when success for large stones (≥ 10 mm) only was considered. From 81 patients, 41 were allocated to the EBD group with duct clearance achieved in 29 (70.7%) and 40 were allocated to the ES group with duct clearance achieved in 30 (75%). Even when success rate for stones ≥15 mm was examined, there were no differences between the two groups (EBD group: success 8/17 = 47.1%; ES group: success 7/13 = 53.8%).

Mechanical lithotripsy was used in only seven (6.8%) patients in the EBD group and in 11 (11.1%) in the ES group. On one occasion ES was converted to EBD (in a patient with a duodenal diverticulum) and on five occasions EBD was converted to ES, resulting in clearing the ducts in all cases.

There were two cases of polya gastrectomy included in this trial, one patient allocated to each of the two groups. There was one death in this series of a 90 year old woman, who had a precut sphincterotomy performed (12 EBD, 19 ES). At 24 hours after ERCP, there were the following complications: one episode of moderate pancreatitis, one episode of acute cholangitis, and the aforementioned death in the ES group, and five episodes of pancreatitis (two mild, two moderate, one severe) and two episodes of acute cholangitis in the EBD group (table 5). No patient required surgical intervention or died as a result of the ERCP induced pancreatitis or cholangitis. There was no statistically significant difference either in the total number of complications between the two groups or between the pancreatitis cases.

Complications over a 12 month follow up occurred in 12 patients in the EBD group and in 15 patients in the ES group. From those, five in the EBD group and seven in the ES group were right upper quadrant abdominal pain without specific diagnosed aetiology. The remaining complications included residual stones (two in the EBD group and three in the ES group), lower CBD stricture (two in the ES group), acute cholecystitis (two cases in the EBD group), acute cholangitis (two in the EBD group, one in the ES group), acute pancreatitis (one case in the ES group), and one case each of perforated gall bladder and gall bladder empyema in the ES group (table 6).

In 26 patients in total (13 patients in each group) we were unable to clear the bile ducts. These included the single death in the ES group, 12 patients (five in the EBD group and seven in the ES group) who had pigtail stents inserted and subsequently underwent surgical bile duct exploration, nine patients (seven in the EBD group and two in the ES group) who had pigtail stents inserted and did not return for a repeat procedure (lost to follow up) (table 7). From the 12 patients who underwent surgical bile duct exploration, in four (three in the EBD and one in the ES group) there was a protocol violation. These patients were operated on from two days to four weeks after a single endoscopic stone removal attempt, failing to return for a repeat ERCP as requested.

Seventy seven patients (33 in the EBD group and 44 in the ES group) underwent a cholecystectomy post ERCP usually within the following month.

There was no difference between the two groups in the number of patients with incomplete follow up. At one, three, six, and 12 months, 28 (13.9%), 42 (20.8%), 47 (23.3%), and 52 (25.7%) patients were lost, respectively.

Statistical analysis was repeated after excluding patients who had a precut sphincterotomy performed (12 EBD, 19 ES).
There was no difference in the baseline characteristics of the two groups, in the success rate, or in the complication rate. Again, stone size was the only parameter predictive of success.

**DISCUSSION**

Endoscopic sphincterotomy has a proven role for the management of bile duct stones in patients with a previous cholecystectomy, acute cholangitis, and in the presence of a predicted small first major of gall stone related pancreatitis. Outside of these settings the role of endoscopic management is less well defined. This is particularly so since the introduction of laparoscopic cholecystectomy for the management of gall bladder stones. There are now well established techniques, either by the transcystic or choledochotomy approach, for laparoscopic management of bile duct stones. These techniques are demanding of technical expertise and time but do not appear to add any significant risk as compared with laparoscopic cholecystectomy combined with endoscopic sphincterotomy. Despite this evidence, the majority of patients with bile duct stones are still referred for endoscopic therapy.

The debate between these two approaches has inevitably focused attention upon the risks of the procedures, particularly ES. Clinically significant complications have been observed in 5–11% of patients undergoing sphincterotomy, the most important of which are post procedural bleeding and acute pancreatitis. Recent attention has also been paid to the potential long term complications of sphincterotomy. The risks of ES have provided an impetus towards the development of safer techniques. One approach has been to carry out balloon dilatation of the SO to a diameter of 8–10 mm using coaxial instrumentation. The most important potential advantage (as compared with sphincterotomy) was thought to be the ability of the sphincter to recover within a few weeks of dilatation. This might then prevent some of the long term risks referred to. Recently, during the preparation of this manuscript, a study comparing the long term manometric effects of ES versus EBD on the SO was published showing only partial recovery of the sphincter but a lower incidence of recurrent CBD stones, cholangitis, and pancreatitis in the EBD group was found.

Furthermore, by avoiding a cut to the sphincter the risks of post procedural bleeding might be reduced. Early anecdotal reports suggested that the risk of acute pancreatitis might be enhanced by balloon dilatation but this was not confirmed in the first major uncontrolled study of the technique. From this report it appeared that balloon dilatation was an extremely safe procedure.

The aim of the present investigation was to establish whether EBD offered any advantages both with respect to efficacy and safety as compared with ES for the management of CBD stones. Complications were assessed both in the short term and at the end of one year of follow up. The results of this study have shown the two techniques to have very comparable efficacy for bile duct clearance. With respect to complication rates, no statistically significant difference was observed between them, although particular mention should be made of the extremely low rate of complications (3%) in patients undergoing ES.

A multivariate analysis was carried out from the results of this study with the aim of identifying factors that might influence the success rate of either technique. Duct clearance only correlated with the size of the stones observed, although there was no difference in the outcome with respect to the two different approaches. This was somewhat surprising in that sphincterotomy offers the potential for larger access to the bile duct which, depending upon the size of the papillary fold, may be up to 5 mm in excess of that seen with a 10 mm balloon dilatation. Failure to observe a difference in efficacy between the two techniques cannot be attributed to the use of mechanical lithotripsy as this was infrequently applied and was similar for the two groups. This might be explained by the tendency of the larger duct stones to be brown and friable, therefore relatively easily removed irrespective of the modest differences in potential size of access. The very low complication rates observed (less than predicted at the outset of the study) precluded any meaningful statistical analysis of risk factors for complications.

There are several important differences between the present and previous published reports. The success rate for duct clearance was somewhat lower in the present study but the overall outcome was similar (after subsequent attempts were taken into account). On the other hand, the complication rate reported in this study was considerably lower at the end of the first 24 hours, as well as at the end of follow up, despite the fact that patients with acute cholangitis, as well as gall stone pancreatitis, were randomised into the present study, but excluded from other trials. It might be speculated that the initial relatively low rate of duct clearance reflects the rare use of mechanical lithotripsy, representing a low risk strategy for the management of bile duct stones in relatively high risk patients. Based on our previous experience we have a low threshold for temporary placement of a pigtail endoprosthesis following the initial sphincterotomy with the aim of minimizing the time period of the procedure, particularly in complicated cases such as acute cholangitis or gall stone pancreatitis or in the presence of severe comorbidity. This then allows the duct to be cleared in a much more controlled circumstance, a short period after recovery from the acute event. Seventy (34.7%) and 20 (9.9%) patients in total presented with acute cholangitis or acute pancreatitis, respectively. In addition, in four of 12 patients who underwent surgical bile duct exploration, the referring teams carried out the procedure in violation of the protocol—that is, they should have been re-referred for endoscopic duct clearance.

There was one death in this study which had a clear respiratory cause and this occurred in a patient with preceding decompensated pulmonary disease. Despite the comparable complication rates for the two groups, some difference might be made with respect to post procedural pancreatitis. This occurred in only one patient (1%) of those undergoing sphincterotomy, an extremely low rate for this technique. The five patients in the balloon dilatation group (4.9%) developing acute pancreatitis represents a very comparable value to that seen in a large number of previous series of ES. The observed post procedural pancreatitis rate does not approach statistical significance and therefore must be interpreted with caution. Whether there is a true difference in this complication for the two groups cannot be satisfactorily answered by this study which was structured on the basis of an anticipated complication rate considerably higher than that observed in the final outcome.

Long term complication rates have been the subject of considerable concern in a number of recent studies. The rates observed in the current trial at the end of follow up were similar to those seen elsewhere. There have been concerns about the incidence of acute cholecystitis following sphincterotomy in patients in whom there was a plan to retain the gall bladder. However, in the present study, no difference was observed between the two groups although this may be largely
explained by our policy to obtain early cholecystectomy in a high proportion of our patients. As might be predicted, the majority of complications seen were related to either retained or recurrent stones.

In conclusion, this study has confirmed similar efficacy for balloon dilatation of the SO and ES for the management of CBD stones. However, hopes that balloon dilatation might provide a safer option have not been confirmed. With respect to the short term complications, balloon dilatation was comparable with historical complication rates for ES. However, the extremely low complication rate seen with sphincterotomy throughout this study may also have minimised areas of potential risk. While cholecystectomy is the usual outcome following CBD clearance, the long term risk of sphincterotomy is unlikely to be considerably greater than the sphincter preserving balloon dilatation. There is therefore insufficient evidence from this study to recommend a move away from ES to balloon dilatation. Balloon dilatation may offer advantages in selected instances such as in the presence of papillary varices, intradiverticular papilla, and after polya gastrectomy. However, in the majority of instances ES should remain the management of choice.

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