




Original research

Outcome of long-term biliary stenting for stones in the 2010s: beware the cholecystectomised!

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ABSTRACT

Objective Endoscopic retrograde cholangiopancreatography (ERCP) is the mainstay of management for most patients with common bile duct stones (CBDS). Duct clearance at initial ERCP may not be achieved in a third of patients, many of whom may be elderly with multiple comorbidities rendering them at potentially high risk for further procedures. We aimed to quantify the rate of biliary sequelae and mortality among a large cohort undergoing a single ERCP with sphincterotomy and stent insertion without having undergone complete ductal clearance (permanent stent insertion, PSI), and to examine factors that may predispose to adverse outcomes.

Design/method Outcomes of all ERCPs undertaken on the intact papilla between February 2010 and January 2020 were distilled to identify a cohort who had undergone PSI for initially irretrievable CBDS. These were subjected to retrospective follow-up until the development of biliary sequelae, death or survival into 2023.

Results There were 2175 index ERCPs for CBDS, of whom 114 met the PSI criteria. Eleven did not survive their index hospitalisation, leaving 103 for follow-up. Of these, 25 (24%) developed late biliary sequelae, 19 (18%) required at least one further ERCP and 8 (8%) died from biliary sequelae. Adverse outcomes were found to be more common among those who had undergone cholecystectomy prior to ERCP, and those with peripapillary diverticula.

Conclusions Long-term biliary stenting following sphincterotomy remains a valid option for selected patients with initially irretrievable bile duct stones who could be at high risk from repeat procedures.

INTRODUCTION

National expectation in the UK is complete clearance of common bile duct stones (CBDS) at initial endoscopic retrograde cholangiopancreatography (ERCP)

WHAT IS ALREADY KNOWN ON THIS TOPIC

- ⇒ Bile duct clearance of stones can be achieved at initial endoscopic retrograde cholangiopancreatography (ERCP) in around two-thirds of patients.
- ⇒ Biliary stenting is sometimes chosen as sole long-term management, though late biliary sequelae are common.
- ⇒ Since the adoption of balloon extension sphincteroplasty the long-term outcomes of permanent stent insertion (PSI) have not been well studied.

WHAT THIS STUDY ADDS

- ⇒ Late biliary sequelae occur in approximately one-quarter of patients with PSI. Deaths from these causes occur in less than 10%, and the large majority die from other illnesses.
- ⇒ Adverse outcomes may be more likely in those who had cholecystectomy before ERCP and those with peripapillary diverticula.
- ⇒ Persistently raised alkaline phosphatase on liver blood testing is common but of uncertain clinical significance.
- ⇒ Repeat conventional ERCP rarely achieves complete ductal clearance in this population.

in $\geq 75\%$.¹ It appears this standard is not met in most English centres.^{2,3} A tertiary centre suggested most patients present with CBDS ≥ 10 mm in diameter {3}. This may explain why $\geq 50\%$ of ERCPs for CBDS in England are repeat procedures.²

Placement of biliary endoprosthesis following endoscopic sphincterotomy (ES), with or without balloon extension sphincteroplasty (BES) and incomplete duct clearance, is mandatory to prevent



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HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

- ⇒ Long-term biliary stenting following sphincterotomy (preferably with extension sphincteroplasty and attempted duct clearance) remains a valid option for selected patients at high risk from further procedures.
- ⇒ The risk of biliary sequelae may be higher in patients with periampullary diverticula and those who have undergone prior cholecystectomy.

stone impaction and cholangitis. Patients who are unsuitable for surgical duct exploration normally undergo further ERCP which may include mechanical lithotripsy or a direct cholangioscopic approach. The latter interventions may involve prolonged procedures, sometimes under deep sedation or general anaesthesia. Mechanical lithotripsy is becoming less commonly used, partly for fear of a trapped basket around a ductal stone.⁴ Moreover, cholangioscopy is not always successful (duct clearance in 88%) and can be followed by early complications (7%) and stone recurrence (13%).⁵ These approaches may not be appropriate for frail patients with comorbidities and potentially short life expectancy. Leaving the stent in situ (with or without periodic stent changes) is an attractive alternative strategy.

Current national guidelines recommend that patients being managed by long-term stenting for CBDS should undergo periodic repeat ERCP and stent changes or further attempts at ductal clearance,⁶ and that management with long-term stenting alone 'should be restricted to a selected group of patients with limited life expectancy and/or prohibitive surgical risk'.⁷

Descriptions of long-term stenting for CBDS go back to 1984,⁸ and have been subject of systemic reviews.^{9–10} Most cohort studies are based on small numbers and are retrospective with varying quality of follow-up duration and diligence. Mohammed *et al* termed planned permanent stent insertion for definitive management of CBDS as permanent stent insertion (PSI).¹⁰ Their series was ascertained between 2006 and 2011. We only know of one large series based on follow-up of patients undergoing PSI after 2011,¹¹ when performance of BES entered routine practice.¹² There are thus limited recent data on conservative PSI strategy to aid decision-making on further procedures. Herein we report on a series of 114 patients with CBDS managed by PSI between 2010 and 2020 within a single health board catchment area with low patient mobility and excellent portals for case ascertainment and follow-up.

METHODS

Aneurin Bevan University Health Board serves a mixed urban and rural population of 565 000 inhabiting Gwent and southeast Powys. The radiology database (RADIS II, Health Solutions Wales, Cardiff) was

interrogated to identify all patients who underwent ERCP during the 10 years between February 2010 and January 2020. In addition, we searched ERCPs performed between 1987 and January 2010 to identify and exclude those in the later dataset who had undergone a prior successful ERCP.

During the study period ERCPs were performed on two hospital sites predominantly by two gastroenterologists (MCA and MAC) and one radiologist (NDC). All relevant procedure reports on RADIS and the endoscopy reporting system (Endoscopy Management System (EMS), Medilogik, Ipswich, UK) were inspected. Patients in whom cannulation had failed were excluded unless a second procedure within days proved successful.

The following information was entered onto spreadsheets: patient hospital reference number, sex, age at index ERCP and main findings (CBDS, stricture, tumour, other). Immediate outcomes for those with CBDS were documented (complete bile duct clearance after ES+/-BES, incomplete clearance with stent deployment, or stones no longer present in the common duct). All subsequent interventions for those who underwent initial stenting for CBDS including repeat ERCP, percutaneous or surgical intervention with or without cholecystectomy were recorded. Those who did not undergo further interventions are the focus of the detailed clinical follow-up in this paper (PSI group).

Those meeting PSI criteria were reviewed as to (1) history of cholecystectomy; (2) periampullary diverticula; and (3) whether BES had been performed. Cystic duct patency, size of the largest stone, maximum bile duct diameter and single versus multiple stones were determined by review of index cholangiograms stored on RADIS.

Clinical follow-up of the PSI group was done using the Health Board clinical portal (Clinical Workstation). Hospital episodes between index ERCP and January 2023 were examined for evidence of late biliary sequelae (LBS), as well as need for unplanned repeat ERCP. LBS were defined as: (1) hospitalisation with pain and/or features of sepsis with deterioration in liver blood tests; (2) late complications of PSI (eg, delayed perforation); or (3) grossly elevated liver tests at final hospitalisation. Follow-up was until the earliest of: (1) presentation with LBS; (2) death; or (3) survival to 2023 without LBS. Progress of those who developed sequelae but had survived was also documented. Survival without LBS was recorded in months or to 2023, and presumed causes of death were documented. Finally, the most recent liver blood test results were recorded so as not to miss those dying from cholangitis masquerading as non-biliary illness. The upper limit of normal for alkaline phosphatase (ALP) in our laboratory is 130 IU/L, and for alanine transaminase (ALT) is 59 IU/L.

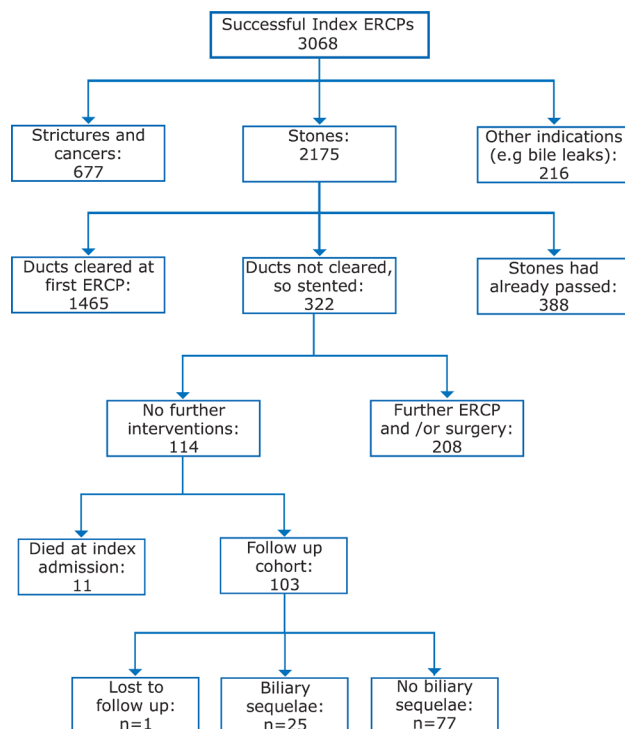


Figure 1 Flow chart of the case mix and outcomes of endoscopic retrograde cholangiopancreatography (ERCPs) performed over 10 years, demonstrating how the permanent stent insertion cohort was derived.

Differences between subgroups who developed LBS and those who did not were analysed by χ^2 testing. Our overall outcome results were tabulated with similar studies including at least 50 patients with PSI.

RESULTS

The ERCP patient population is summarised in the flow chart (figure 1). There were 3068 successful index ERCPs via intact papilla, of whom 2175 (71%) had CBDS. Of these, 114 patients had index ERCP with stenting and no further intervention for CBDS. Eleven (9%) did not survive their index hospitalisation. This left 103 PSI patients as candidates for follow-up. Their median age at index ERCP was 84 years (IQR 77–90 years).

Follow-up was median of 25 months (IQR 11–45 months). LBS occurred in 25 (24%), of whom five were managed conservatively, 19 underwent a total of 29 further ERCPs, but ductal clearance could ultimately be achieved in only four patients.

In 2023, seventy-nine patients (78%) had died, of whom 71 probably died from causes other than LBS. Of eight patients considered to have had biliary death, six died from cholangitis. Four were recorded as such on final discharge note and two others had very deranged liver tests during final hospitalisation. Another patient died from complications of a repeat ERCP, and the final patient was found to have a plastic stent with its proximal end originally inserted via the cystic duct and eventually finding its way via the gallbladder into the hepatic flexure. The eight patients dying from biliary sequelae had a median age of 81 years at their index ERCP and died at a median age of 83 years at 1.5–26 months after ERCP.

Comparison of patients developing LBS with those who did not is shown in table 1. History of cholecystectomy was more common in the LBS group, and presence of patent cystic duct and gallbladder may be protective. BES, undertaken in 30 patients, may reduce LBS risk. Indeed, those alive in 2023 were more likely to have undergone BES ($\chi^2=3.89$ ($p<0.05$)). More patients with LBS had periampullary diverticula. Only three patients with such diverticula underwent BES.

Diameter of the largest stone before sphincterotomy was median 14 mm (IQR 12–16 mm). No differences were noted in duct diameter nor stone size between the LBS and non-LBS groups. Outcomes were no different with single or multiple bile stones at index ERCP.

Twenty-four patients were alive in January 2023 after 46 months (IQR 35–70 months). Of these, four had needed further ERCP and one was managed conservatively.

Analysis of the final or latest liver blood test results from those who did not develop biliary sequelae demonstrated normal results in 46 patients and (usually mild) elevations in ALP in 30 patients (median 170 IU/L, IQR 143–208). One patient who died from myocardial infarction had an acute rise of ALT, but

Table 1 Comparison of potential protective and risk factors in patients with PSI who developed late biliary sequelae with those who did not

Factor	Biliary sequelae (n=25)	No biliary sequelae (n=77)	Difference	Possible effect
Age (years: median and IQR)	81 (75–87)	84 (78–90)	NS	
History of cholecystectomy before index ERCP	5 (20%)	5 (6%)	$\chi^2=3.89$ ($p<0.05$)	Increased risk
Patent cystic duct with gallbladder in situ	2 (11%)	21 (30%)	$\chi^2=2.56$ ($p=0.12$)	Protective
Balloon extension sphincteroplasty performed	4 (16%)	26 (34%)	$\chi^2=2.86$ ($p=0.09$)	Protective
Periampullary diverticulum present	10 (40%)	15 (19%)	$\chi^2=4.29$ ($p<0.05$)	Increased risk
Alive in January 2023	5 (20%)	19 (25%)	NS	

ERCP, endoscopic retrograde cholangiopancreatography; PSI, permanent stent insertion.

elevations in ALT were uncommon. Liver blood tests within a year of death or January 2023 were not available for four patients.

DISCUSSION

We report outcomes in a large cohort undergoing single ERCP and sphincterotomy (\pm BES), with stenting and no further interventions other than at need. Performance of index ERCP was above UK quality standards¹ (figure 1). High index CBDS clearance rate may have been aided by BES for larger stones.¹²

The main stimulus to this review was evidence that older comorbid patients with CBDS are being more often referred for ERCP.¹³ Our volume of ERCPs more than doubled from 1446 during the 10 years from February 2000 to over 4000 during the study period. Our PSI cohort had a median age of 84 years and included 25 nonagenarians. Given that such a small proportion of those needing further ERCP were able to undergo successful duct clearance by means of conventional ERCP, it is likely that complex discussions on interventions such as peroral cholangioscopy and/or mechanical lithotripsy (with their attendant risks) will become more frequent in the future.

While some argue that stents left in the duct act as a nidus for stone formation,¹⁴ others have observed high stone recurrence after duct clearance especially if the gallbladder remains.¹⁵ Herein we found that history of cholecystectomy may increase risk of LBS after PSI. Cholecystectomy histories were documented by Bergman *et al*,¹⁶ and while no relationship to LBS was shown, patient numbers were small.

Comparison of other factors potentially influencing risk of LBS after PSI identified trends towards better outcomes in those with patent cystic duct, and those who had BES in addition to sphincterotomy. Presence of periampullary diverticula may herald worse outcomes, but again numbers are small. BES was more frequently performed during the later part of the study decade. We believe that the presence of such diverticula may have prompted reluctance in performing BES; indeed, only three such patients underwent BES in this series. More recent work suggests BES is safe

in patients with periampullary diverticula.¹⁷ Another potential factor is that, in sicker patients with major comorbidity and/or limited life expectancy and those on anticoagulants and antiplatelet therapy undergoing emergency procedures, the endoscopist might have shortened the procedure in favour of small sphincterotomy and immediate PSI alone, with no attempt to remove stones.

Table 2 details cohorts of PSI patients during the last 30 years, but only our series and one from Israel¹¹ included patients undergoing index ERCP since 2011. Sbeit *et al* compared 83 patients with PSI for ≥ 6 months with a younger cohort who underwent earlier ERCP. LBS were similar in the PSI group than after planned reintervention. Their low complication rate may reflect shorter follow-up than in older reports and herein. Our LBS rate of 24% compares favourably with largest series of Slattery *et al*¹⁸ and with the cohort of Bergman *et al*.¹⁶ In the former review, patients were discharged to their referring team following index ERCP. Their end point was 'stent patency' which appears to have been defined by need for reintervention, and no data are presented on deaths from LBS. This suggests some patients were not referred again, and follow-up may have been less meticulous than herein.

Strengths of this study include complete and comprehensive clinical and radiological portals, so patients are very unlikely to have been missed. Care was taken to exclude patients who had undergone prior successful ERCP. The two hospitals deliver all ERCP services to its catchment area, eliminating referral bias, and no ERCPs are delivered in the independent sector. Patient mobility is low.¹⁹ Analysis of the 2011 National Census demonstrates that half as many people moved out of the area per year compared with the rest of Wales and in England. This enabled complete follow-up until death or January 2023 in all but one patient. An 82% bile duct clearance rate at first ERCP compares favourably with national standards and may reflect the frequent use of BES to aid removal of larger stones.

Potential limitations include the retrospective clinical assessment of older patients with non-specific illness and mild elevations of liver blood tests. This was partly overcome by reviewing details of hospitalisations and final

Table 2 Comparison of patients and outcomes in large studies of biliary stenting after sphincterotomy as sole treatment for bile duct stones since 1995

First author/ year	Method and year of first ERCP	Patients (n)	Age (years)	Follow-up duration (months)	Late biliary complications (%)	Method of follow- up	Biliary deaths
Bergman ¹⁶ (1995)	Retrospective, 1983–1988	59	Median 83	Median 36	40	Contacting referring team	9
Ang ²⁰ (2006)	Retrospective, 2002–2003	83	Mean 75	Mean 19	34	Liver blood tests, need for repeat ERCP	0
Slattery ¹⁸ (2013)	Retrospective, 1998–2008	201	Median 80	Median 60	40	Review in clinic	Not shown
Sbeit ¹¹ (2020)	Retrospective, 2013–2018	83	Average 84	Median 15	11	Case note review	Not shown
Present study	Retrospective, 2010–2020	103	Median 84 (IQR 77–90)	Median 25 (IQR 11–45)	24	Clinical portals	8

ERCP, endoscopic retrograde cholangiopancreatography.

illnesses from the clinical portal. This identified two patients who almost certainly died from LBS who had been considered to have died from other causes. We also identified 11 patients who did not survive their index ERCP hospitalisation, reflecting the potentially severely ill and comorbid characteristics of these patients. Comparison of potential factors influencing the risk of LBS is limited by small numbers, and while trends were identified, the possibility of type 1 error remains.

Our exclusion of patients who had undergone prior ERCP means the findings cannot be extrapolated to those undergoing PSI to manage a second or subsequent presentation. Bergman's series included nine patients who had undergone prior ERCP and duct clearance,¹⁶ but the numbers of such patients are not specified in the other studies set out in table 2.^{11 18 20}

In conclusion, long-term follow-up of patients undergoing single ERCP and stent insertion as sole treatment for irretrievable CBDS may inform discussions with patients and families regarding pros and cons of further ERCP with or without mechanical lithotripsy or peroral cholangioscopy. Our findings suggest that the case for repeat ERCP is strengthened by the gallbladder no longer remaining in situ, and perhaps by the presence of periampullary diverticula.

Correction notice This article has been corrected since it published Online First. The incorrect initial has been removed for author Tessa Davies.

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Contributors JA, PP, YYL, TMD and GM each reviewed a block of some 800 ERCPs undertaken during the study period to derive the study cohort and documented history, demographic data and outcomes on a spreadsheet. MCA, MAC and NDC performed the large majority of the ERCPs. All authors critically reviewed the manuscript. MCA conceived the study, supervised the data collection, conducted follow-up of the PSI cohort, wrote the first draft of the manuscript and is the guarantor of the study.

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