REVIEW

Endoscopic biliary stenting in irretrievable common bile duct stones: stent exchange or expectant management—tertiary-centre experience and systematic review

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Received 15 January 2015

Revised 8 April 2015

Accepted 5 May 2015

Published Online First

22 May 2015

CrossMark

To cite: Mohammed N, Pinder M, Harris K, et al. *Frontline Gastroenterology* 2016;**7**:176–186.

ABSTRACT

Introduction Conventional endoscopic duct clearance may not be possible in up to 10%–15% of common bile duct stones (CBDS). Sphincterotomy and biliary drainage by endoprosthesis have for many years been the mainstay of management in irretrievable stones. Recent years have seen the advent of sphincteroplasty or cholangioscopically-guided electrohydraulic lithotripsy (EHL) permitting duct clearance in majority of cases. However, when bile duct clearance is not possible, options include long-term stenting followed by elective stent exchange (ESE) 6–12 monthly or permanent stent insertion (PSI) in selected cases, but it is not clear which management strategy among ESE and PSI is preferable.

Methods and aims A retrospective review of all patients in Leeds Teaching Hospitals NHS Trust who underwent plastic stent insertion for biliary access for difficult CBDS from January 2006 to December 2011 was undertaken. Adult patients with irretrievable CBDS who had plastic stent insertions throughout the follow-up period were included. Patients who underwent PSI and ESE annually were retrospectively reviewed to determine the long-term outcomes. A detailed systematic review was also performed, examining the outcomes of CBDS managed with stents.

Results During the study period, 674 patients underwent 1769 biliary-stent-related procedures; of which, 246 patients met our inclusion criteria. 201 patients had subsequent duct clearance. 45 patients were, therefore, included in the final analysis, 28 of whom underwent annual ESEs and 17 PSIs. Patients in the PSI group had higher American Society of Anesthesiologists (ASA) scores compared with the ESE group. In the PSI

group, 9/17 patients presented acutely with blocked stents, 5 of whom presented within 12 months. 2/9 patients were severely ill and died within a fortnight following the repeat endoscopic retrograde cholangiopancreatography (ERCP). In the ESE group, 4/28 patients had duct clearance in subsequent ERCPs, 1/28 patient presented with a blocked stent, and no biliary-related deaths were observed. The mean numbers of ERCPs performed were 0.52 and 1.95 in the PSI and ESE groups, respectively.

Conclusions Over 50% of patients treated with long-term stenting re-presented acutely with stent blockage, though many of these were before 12 months, meaning planned stent exchange would not have affected the outcome. Duct clearance using all possible modalities is the preferred option, but where not possible, management with biliary stenting either with elective exchange or permanent stenting remains a possibility for carefully selected patients, though maybe best suited to those with limited life expectancy.

INTRODUCTION

Endoscopic retrieval of common bile duct stones (CBDS) is the preferred treatment option over surgical removal owing to its success rate and relatively low complication rates. Endoscopic sphincterotomy (ES) and stone extraction are successful in approximately 85%–90% of cases,^{1,2} but the optimum management of those patients in whom duct clearance cannot be achieved is not known. Increasing age, large or multiple stones, distal common bile duct (CBD) strictures or pathology in the periampullary region,

and surgically altered anatomy pose particular challenge to effective stone retrieval. Treatment options for difficult stones include lithotripsy (intraductal—mechanical or cholangioscopically guided electrohydraulic lithotripsy (EHL) or laser lithotripsy (LL), or extracorporeal), chemical (eg, oral ursodeoxycholate), biliary endoprosthesis (usually plastic stents) or surgery.

Biliary endoprosthesis was first introduced to achieve biliary drainage in patients with irretrievable CBDS in the elderly population. In acute situations, biliary endoprostheses play an important role in achieving biliary drainage of contaminated bile, thus, preventing complications from cholangitis, particularly after failed duct clearance.

While the majority of stones can be retrieved endoscopically, in a small number of patients, it is not possible to do so. When surgical intervention is inappropriate either due to advancing age or multiple comorbidities, or in the absence of advanced therapeutic options, the optimum endoscopic management is not clear. Options with stent management include 'elective stent exchange' (ESE) or 'permanent stent insertion' (PSI).

ESE is performed at predetermined intervals, usually either 6 or 12 monthly, the aim being to replace the stent before it becomes blocked. The interval for stent exchanges differs between centres and physicians, but generally 6–12 months is the accepted interval among many endoscopic retrograde cholangiopancreatography (ERCP) specialists. PSI is performed as a one-off procedure in elderly patients with multiple comorbidities where repeated endoscopic procedures are deemed high risk, and the management plan is expectant. In these patients, ERCP is not repeated unless the patient suffers complications with the stent (occlusion, migration or acute cholangitis). While the advantage of ESE is to maintain stent patency for a longer time, reducing the risk of cholangitis along with the possibility of duct clearance in subsequent procedures, it carries the risks and discomfort of multiple endoscopic interventions and increased costs for the healthcare provider. On the other hand, PSI offers an advantage of being a one-off procedure, but runs the risk of complications from stent blockage.

Several studies have compared the treatment modalities described above,^{3–10} but there is no clear consensus among endoscopists about the best practice when faced with this situation. Apart from one randomised controlled study,¹⁰ the rest of the data is from either prospective observational studies^{11–12} or retrospective reviews.^{3–6 13–17} The aim of our study was thus to review the outcomes of patients with irretrievable bile duct stones who have been managed by either ESE or PSI from our institution. We also conducted a systematic review of the above management options reported in the published literature.

METHODS

We conducted a retrospective review in a tertiary referral centre covering a population of approximately 800 000. During the study period, there were five hospitals making up Leeds Teaching Hospitals NHS Trust, but from 2006, all ERCP procedures were performed in a single-purpose-built room on the St James' Hospital site. This room runs nine ERCP lists per week, except when reduced by leave, carrying out an average of 880 procedures per year by five experienced endoscopists, who did not change during the study period. High volumes of complex and post-liver transplant ERCP procedures are undertaken.

This study was conducted as an audit on local practice of plastic stent insertion for difficult CBDS. The study protocol conforms to ethical guidelines of the World Medical Association Declaration of Helsinki—ethical principles for medical research.

All patients who underwent plastic stent insertion for CBDS from January 2006 to December 2011 were included. All patients were followed up until August 2013 or until their death. Since our electronic search term included the word 'stent', our data automatically excluded those patients who had had successful stone removal either by sphincterotomy or balloon sphincteroplasty, without requiring stent insertion. The remaining patients' electronic data were reviewed against the predetermined inclusion and exclusion criteria.

Patients

All patients who had plastic biliary stent insertion for irretrievable CBDS were included. Patients with biliary leak/strictures, hepatobiliary or pancreatic cancer, and those who underwent metallic stent insertion at any time during the follow-up period were excluded, even if they had plastic stent insertion earlier on in their care. Any patient with a final diagnosis other than CBDS at the end of the study period was also excluded. To rule out tertiary referral centre bias, only patients with regular follow-up at our unit were included in the final analysis.

Endoscopic procedure

All endoscopic procedures were performed by one of five experienced endoscopists using standard duodenoscopes by Olympus KeyMed (TJF-260V). Lignocaine spray (10% Xylocaine) was used for pharyngeal anaesthesia. Midazolam and fentanyl were used for sedation as felt appropriate by the operator depending on the patient's comorbidities assessed by American Society of Anaesthesiologists (ASA) status. Hyoscine-N-butylbromide was used when necessary for duodenal relaxation prior to CBD cannulation. ES was invariably performed unless absolutely contraindicated due to anatomy or coagulopathy. In later years, balloon sphincteroplasty to aid stone extraction was performed when deemed safe. Stone extraction

was performed using balloon or basket. Every attempt was made for completion of stone extraction, including use of the mechanical lithotripter if felt appropriate. If unsuccessful, a straight or double-pigtail biliary stent of either size 7 or 10 Fr (Wilson Cook) was used to achieve temporary biliary access, and a follow-up procedure was booked (usually within 3 months). Immediate complications were recorded in the endoscopy report, and in most cases, patients were observed for 24 h prior to discharge. Facilities for EHL or LL were not available at our institution during the study period.

If duct clearance is incomplete, standard practice in our institution is to place either one or two short 4–7 cm 7 Fr double-pigtail stents after sphincterotomy to achieve biliary drainage. At this juncture, a further attempt at duct clearance is planned. If at any stage, it is evident that the duct cannot be cleared, either due to stone size, anatomy or comorbidities, a decision may be taken to manage with long-term stenting. The endoscopist advises whether to assign patients to 12-monthly ESE or to expectant management. This decision is based on patient comorbidities and perceived life expectancy, and is subsequently discussed with the patient before a final decision is taken. For the purpose of this study, patients' follow-up and the number of follow-up ERCPs were calculated from the day the decision about scheduling patients for ESE or PSI was made.

Data collection and patient follow-up

Procedure-related data were obtained using endoscopy reports. Electronic patient records were reviewed for background information and outcomes. The electronic patient recording system in our institute is comprehensive, and is integrated with local healthcare providers to track any episodes of patient admission or attendances to other local hospitals.

Data were collected on urgency of the procedure, immediate success, details of endoprosthesis used, duration between the procedures and follow-up plans. Complications were recorded as intraoperative, immediate (within 24 h), short-term (within 30 days) or

long-term (within 12 months). Each patient's records were reviewed until the end of study period (August 2013) or their death. Complications were defined according to previously published criteria (bleeding (haematemesis/melena/2 g drop in the haemoglobin, with no other bleeding source on endoscopy), acute pancreatitis (new onset of abdominal pain and amylase ≥ 3 times the upper limit of normal at more than 24 h post ERCP) and cholangitis (fever $\geq 38^{\circ}\text{C}$ for more than 24 h due to biliary causes)).

Systematic review

For the systematic review, we searched PubMed, Embase and Cochrane databases. The search terms used were 'biliary stents', 'biliary endoprosthesis', 'biliary stent exchange', 'bile duct stones', 'difficult stones', 'permanent stent insertion' and 'stent exchange'. All studies showing prospective or retrospective data of long-term bile duct stenting were selected. Review topics were included if collectable data were available. Data were extracted on the number of patients in the study, type of interventions, procedure-related complications (immediate and late), concomitant choleretic therapy and stone sizes. The results from included papers were tabulated separately (tables 1–4), and where possible, the data was pooled to obtain cumulative results.

Statistics

Data collection was performed using Excel 2010 (Microsoft, Redmond, Washington, USA), and for statistical analysis, IBM SPSS Statistics V.21 (IBM, Chicago, Illinois, USA) was used. The Student's *t* test was used to compare mean values for the two groups.

RESULTS

A total of 3552 ERCP procedures for all causes were conducted between January 2006 and December 2011 in our institution. A total of 674 patients underwent 1789 stent-related ERCPs over the study period. A total of 629 patients were excluded from the study (duct clearance achieved in subsequent procedures 201, final diagnosis of hepatobiliary/pancreatic tumours 233,

Table 1 Demographic and clinical data for the patients included in the study

	ESE (exchange) group (n=28, M/F=13/15)	PSI (expectant) group (n=17, M/F=9/8)
Age	84.6 years (range 70–95)	84.6 (range 63–95)
ASA status	2.71 (range 2–3)	3.05 (range 3–4)
Total number of procedures*	45 (mean 1.95 per patient)	9 (mean: 0.52 per patient)
Follow-up*	736 months (mean 27.25 months)	603 months (mean 33.5)
Subsequent duct clearance	4 (14%)	1 (5%)
Biliary complications	1 blocked stent (3.57%)	9 blocked stents (52.9%)
Deaths (within 30 days following ERCP)	2 (non-biliary)*	2 (1 biliary sepsis)†

*After decision for long-term stent management made.

†Mean age of patients who died=84.5 years.

ASA, American Society of Anaesthesiologists; ERCP, endoscopic retrograde cholangiopancreatography; ESE, elective stent exchange; PSI, permanent stent insertion.

Table 2 Studies looking at the outcomes of LTS placement for CBDS

Author details	Study design	Total no. of patients on LTS	Mean age	Duration of follow-up of all patients (months, mean)	Late complications* (%)	Stent-related deaths (%)
Siegel JH ³ 1984, USA	Retrospective	22	77	na	0	0
Cotton PB ⁴ 1987, UK	Retrospective	17	79	39	12	0
Cairns SR ⁵ 1989, USA	Retrospective	42	83	15.9	4	0
Foutch PG ⁶ 1989, USA	Retrospective	10	77	na	10	10
Kiil J ¹⁴ 1989, Denmark	Retrospective	63	76	na	25	0
Soomers AJ ²¹ 1990, Netherlands	Retrospective	25	81	26	5	0
Caos A ²² 1990, USA	Retrospective	12	na	na	8.3	8.3
Van Steenberg W ²³ 1992, Belgium	Retrospective	23	86	23	13	0
Peters R ²⁴ 1992, UK	Retrospective	27	76	13	20	7.4
Kubota Y ¹⁸ 1994, Japan	Retrospective	9	na	24.8	11.8	0
Bergman JJ ¹³ 1995, Netherlands	Retrospective	58	83	36	40	15.5
Lauri A ²⁵ 1995, UK	Retrospective	14	83	43	7.7	0
Döbrönte Z ²⁶ 1996, Hungary	Retrospective	25	na	22.7	12	0
Chopra KB ²⁰ 1996, UK	RCT: small ES+7 Fr DPS vs large ES+extraction	43	79	20	46	0
Naranjo Rodríguez A ²⁷ 1997, Spain	Retrospective	38	na	15.2	23.7	0
Choudhuri G ²⁸ 1998, India	Retrospective	28	54	42	7.1	0
Ku MK ²⁹ 1999, Taiwan	Retrospective	12	78.4	11	8.3	0
De Palma GD ¹⁹ 2000, Italy	Retrospective	49	75.5	39	40.8	6
Hui ¹⁵ 2003, China	RCT: stent vs lithotripsy	14	76	21.9	63.2	21.1
Ang TL ¹⁶ 2006, Singapore	Retrospective	83	75.4	19	33.7	0
Slattery E ¹⁷ 2013, Ireland	Retrospective	201	80	59.6	40.3	0

*Cholangitis, jaundice, cholestasis and stent blockade/migration.

CBDS, common bile duct stones; DPS, double-pigtailed stent; ES, endoscopic sphincterotomy; LTS, long-term stenting; na, data not available; RCT, randomised controlled trial.

complicated strictures 71, biliary leak 27, post-orthotopic-liver-transplant complications (anastomotic stricture/leak) 38, tertiary-care referrals/missing information 59) (figure 1). A total of 246 patients underwent plastic stent insertion for difficult CBDS; among whom, 201 patients underwent repeat ERCPs, and duct clearance was achieved in 3–6 months' time. A total of 448 ERCPs were performed as 'temporary stenting' on these patients, with a mean number of 2.22 ERCPs per patient, to achieve duct clearance.

This left 45 patients in whom complete duct clearance was not possible over the study period, and were

therefore managed with long-term stents. This represents only 6.6% of the study population and 1.2% of the total cohort of patients who underwent ERCPs for any reason in our institution in the study period. A total of 28 patients were included in the 'exchange' group (ESE) and 17 in the 'expectant' group (PSI). Their demographic details and main results are given in table 1.

Expectant management group

In the PSI group (n=17), 62 ERCPs were performed in total. The mean age of the patients was 84.6 years, and mean ASA score was 3.05. Patients were followed

Table 3 Studies comparing the outcomes of short-term and long-term stent placements

Author	Study design	Total number of patients (ESE, PSI)	Mean age (range)	M/F	Patients in ESE group	Patients in PSI group	Mean follow-up (months)	Cholangitis (ESE) (%)	Cholangitis (PSI) (%)	Stent-related deaths (n)
Maxton DG ³⁰ 1995, UK	Retrospective	283	77 (65–94)	21/64	85	26	na	1	4	0 (ESE), 0 (PSI)
Law NM ³¹ 1996, Singapore	Retrospective	55	71 (37–89)	30/25	15	19	13	0	2	0 (ESE), 0 (PSI)
Bowrey DJ ³² 1998, UK	Retrospective	36	73 (23–89)	14/22	18	18	12.5	2	3	0 (ESE), 3 (PSI)
Chen JH ³³ 1999, Taiwan	Retrospective	19	76	6/10	3	16	34	0	3	0 (ESE), 0 (PSI)
Kochlef A ³⁴ 2011, Tunisia	Retrospective	414	68 (35–102)	12/14	16	10	na	0	3	0 (ESE), 0 (PSI)
Di Giorgio P ¹⁰ 2013, Italy	Randomised controlled trial	78	75.3 (ESE), 77.4 (PSI)	22/17 (ESE), 21/18 (PSI)	39	39	14.2 (ESE), 12.8 (PSI)	3	14	1 (ESE), 3 (PSI)

ESE, elective stent exchange; PSI, permanent stent insertion.

up for a total of 603 months (mean 33.5 months). Following the decision for expectant management, nine patients subsequently presented acutely with cholangitis/blocked stents, and a further nine ERCPs were performed (mean ERCPs=0.52 per patient). Five of the nine patients presented within 12 months (mean 132 days, range 28–313 days). Two out of the nine patients who re-presented with cholangitis were severely ill due to multiple comorbidities prior to the ERCP and stent insertion. One of them was discharged to hospice care where he died of non-biliary causes within a fortnight following the procedure. The other patient who died from a biliary cause was an 82-year-old patient with ASA score of 4, who had ongoing biliary sepsis despite a therapeutic ERCP with sphincterotomy and stent insertion, and died 16 days following the procedure. Apart from one patient aged 63 who had significant comorbidities, all other patients included in this group were >89 years of age. One patient out of nine who had re-presented with cholangitis due to blocked stent had duct clearance at the subsequent ERCP. None of the patients in this group was considered fit for general anaesthesia, cholecystectomy or bile duct exploration.

ESE group

In the ESE group (n=28), 45 ERCPs were performed after the decision to exchange stents annually was taken (mean ERCPs=1.95 per patient). The mean age of patients in this group was 84.64 years and a mean ASA score of 2.71. Patients were followed up for 736 months in total (mean 27.25). Four patients had duct clearance at subsequent ERCPs, which is significantly higher than that in PSI group (14% and 5%, respectively). Four patients underwent cholecystectomy at a later date. There were two reported deaths from non-biliary causes, but none due to biliary causes.

Complications

There were three episodes of immediate complications in the PSI group (one respiratory depression and two mild episodes of postsphincterotomy bleeding that settled without further intervention) and two episodes of mild pancreatitis managed conservatively in the ESE group. At 25 months, only 3% of patients in the ESE group and 53% of patients in PSI group had suffered at least one biliary/pancreatic complication. The complications encountered in the PSI group include cholangitis due to stent blockage (n=9). There were no stent migrations noted. The all-cause mortality was similar in both the groups.

Systematic review

Studies in the published literature are predominantly retrospective reviews of clinical practice from around the world. Earlier studies from 1980 predominantly focused on the success rate and safety of using plastic

Table 4 Studies looking at the effect of additional therapy with stent placement

Author	Study design	Purpose of study	Number of participants	Outcomes
Katsinelos P ³⁵ 2003, Greece	RCT	Stent vs stent with UDCA	49	Stone size decreased from 16–33 to 1–21 mm among patients included in the stent plus UDCA group.
Katsinelos P ³⁶ 2008, Greece	RCT	Stents with UDCA vs stent with placebo	41	No difference in stone sizes in placebo or UDCA groups.
Han ³⁷ 2009, Korea	Retrospective	Effects of stents with UDCA	28	Mean size of CBDS fell significantly from 21.6×29.5 to 12.2×20.1 mm with stenting and the use of UDCA. After biliary stenting and medication, endoscopic stone removal was successful in 92.8% of patients in a mean 1.7 subsequent ERCPs.
Lee TH ³⁸ 2011, Korea	RCT: stent vs stent with UDCA	Effects of UDCA and stent	51	Duct clearance was significantly higher in stent plus UDCA group (73.7 vs 86.4%). Stone size diminished more in stent plus UDCA group (22.58±7.61 to 14.04±6.12 mm) (20.47±3.86 to 13.31±5.12 mm).

CBDS, common bile duct stones; ERCP, endoscopic retrograde cholangiopancreatography; RCT, randomised controlled trial; UDCA, ursodeoxycholic acid.

stents in elderly patients.^{1 3–6 14} Later on, in the 1990s, when the use of biliary stents was established with a good safety profile, the research interest shifted and the long-term follow-up of patients was emerging.^{13 18 19} In these studies, efficacy of long-term stent placement was gauged by the symptom-free survival, and stent blockage, migration or cholangitis were considered as events or late complications.

Outcomes of long-term stent placements

Table 2 includes all studies looking at the follow-up data for long-term stents. The most common complications reported with the placement of long-term stents are cholangitis, cholestasis and stent blockage. An important retrospective study by Bergmann *et al*¹³ reported the outcome of 58 patients (median age 83 years) treated with permanent stents. Seventy per cent of the surviving population at 2 years were symptom free. The main complications that were reported were cholangitis (n=22) and deaths (n=9). A year later, Chopra *et al*²⁰ conducted a randomised

trial comparing use of biliary stents with the standard methods of stone extraction. There were no significant differences in the number of ERCPs performed between the groups; however, the long-term complication rate was higher in the stent group. The disease-free survival in the stent group was 64% compared with 86% in the other group at 20 months' follow-up. The largest study comes from Slattery *et al*.¹⁷ They report their experience of managing 201 patients with long-term stents alone with a mean follow-up of 59.6 months. Repeat ERCP was performed in approximately 40% of patients, but only 3% of the patients were diagnosed as cholangitis; the rest of the indications were abdominal pain, jaundice, pancreatitis, raised liver function test and stent migration. Excellent stent patency was reported at 93.5% and 81.9% at 6 months and 2 years, respectively. Among all the other studies mentioned in table 2, cholangitis emerges as the most frequently occurring complication after PSI. The reason for such a striking difference in outcomes from the study by Slattery *et al* is not entirely clear.

Figure 1 Selection process of patients into study. OLT, orthotopic liver transplant.

Long-term outcomes in ESE versus PSI

Table 3 provides a summary of all the studies comparing the stent placements in difficult CBDS with exchange versus an expectant approach. In these studies, acute cholangitis was the predominant cause of death in patients with indwelling stents. Other stent-related complications such as stent migration, jaundice and cholestasis were relatively infrequent and non-consequential. Hence, we focused our data extraction on episodes of cholangitis and death. The data from six studies mentioned in table 3 uniformly suggest that episodes of cholangitis are common in patients with expectant management. Figure 2 shows the pooled diagnostic OR and figure 3 shows the pooled positive likelihood ratio (PLR) for episodes of cholangitis in patients with PSIs. Patients with PSI were at higher risk of cholangitis with OR of 5.32

Figure 2 Pooled diagnostic OR for episodes of cholangitis in patients with permanent stent insertions (PSIs) for difficult common bile duct stones (CBDS).

(95% CI 2.23 to 12.68) and a positive likelihood of developing cholangitis of 1.89 (95% CI 1.29 to 2.77). A random effect model was used for testing both pooled OR and PLR.

Reduction in stone sizes with plastic stents and/or ursodeoxycholic acid

Stent insertion alone without any additional medical therapy has been shown to decrease the stone size and help in subsequent duct clearance.^{7 8 39} Fragmentation of stones caused by friction against the stents has been postulated. There is no consensus for the interval ERCP after initial stent placement. In one study, the effect was noted within 2 months of stent insertion,⁷ whereas in another, it was in 3–6 months.³⁹ Use of different sizes of plastic stents does not seem to influence the outcomes.^{11 29} Tables 4 and 5 show the outcomes of stents on stone sizes.

Several attempts have been made to study the outcomes of using ursodeoxycholic acid (UDCA) alone or in addition to long-term stenting in difficult CBDS^{35 37 38} (table 6). Lee *et al* in their randomised controlled trial (RCT) involving 51 patients found a 15.7% improvement in duct clearance in subsequent ERCPs when UDCA was used in addition to stent placements. The stone size reduction was 22.58 ± 7.61 to 14.04 ± 6.12 mm and 20.47 ± 3.86 to 13.31 ± 5.12 mm in stent plus UDCA and the stent-alone groups, respectively.³⁸ Han *et al*³⁷ report similar findings on reduction in stone size and subsequent duct clearance. However, in another RCT involving 41 patients,

Katsinelos *et al*³⁶ did not find any significant difference in reduction of stone sizes or fragmentation during endoscopic treatment. Interestingly, the same research group had reported a significant reduction in stone size from 16–33 to 1–21 mm among patients included in the stent plus UDCA group.

DISCUSSION

Endoscopic sphincterotomy has revolutionised the management of CBDS since its advent in 1974. In the 1980s, plastic stents were introduced to achieve biliary drainage mainly in elderly patients when conventional methods of duct clearance failed. Several studies evaluated the safety of using plastic stents in the first decade of their introduction, with follow-up ranging from 1 to 78 months. These studies report late complication rates ranging from 0% to 63%.^{3–6 14 18 21–24} Mortality related to stent placement was reported in three of these studies, which ranged from 7.4% to 10%.^{6 22 24}

A landmark study published by Bergmann *et al*¹³ in 1995 looked at the use of plastic biliary stents in 117 elderly patients with a follow-up period of 10 years (mean 3 years). In this study, 59 patients underwent temporary plastic stent insertion and 58 underwent PSIs. For all patients, a 10 Fr straight plastic stent was used. A total of 35 of 59 patients underwent repeat ERCP (the rest were managed surgically); of whom, 25 patients achieved complete duct clearance (mean 1.11 ERCP per patient). They reported a late-complication rate of 40% (predominantly cholangitis) among patients with PSI; the risk of complications

Figure 3 Pooled positive likelihood ratio (PLR) for episodes of cholangitis in patients with permanent stent insertion (PSI) for difficult common bile duct stones (CBDS).

Table 5 Studies showing the effect of stents on stone size

Author	Study design	Purpose of study	Number of participants	Outcomes
Horiuchi ⁷ 2009, Japan	Retrospective	Effects of stents on stone size	40	Median number of stones per patient fell after stent placement. Characteristically large stones became smaller and smaller stones disappeared. Duct clearance was achieved in 93% of subsequent ERCPs.
Fan Z ³⁹ 2010, China	Retrospective	Effects of stents on stone size	45	After biliary stenting for 3–6 months, bile stones disappeared or changed to sludge in 22% of patients. Median stone size decreased from 23.1 to 15.4 mm in 73% of patients. No significant change in 4% of patients.
Prachayakul V ⁹ 2013, Thailand	Retrospective	Outcomes of stents	37	Complete CBD clearance was achieved in 88% of 37 cases after initial failure to remove difficult CBDS. The average number of sessions required was 2.43 procedures.
Hong WD ⁸ 2011, China	Retrospective	Outcomes of stents	52	After biliary stenting for a mean 124 days, the mean maximal stone size decreased from 16.6 to 10.0 mm. Stone clearance at second ERCP was 94.2%.

CBD, common bile duct; CBDS, common bile duct stones; ERCP, endoscopic retrograde cholangiopancreatography.

increased proportionally with time. This study favoured the use of temporary stent insertions prior to elective surgery or repeat ERCP, but did not look at the use of periodic ESEs.

Fortunately, large majority of patients with bile duct stones can have the duct cleared endoscopically. Further attempts after stent placement with the addition of UDCA allow for successful clearance in some. In recent years, widespread adoption of balloon sphincteroplasty allows for greater duct clearance in many, though some precautions are required to avoid ductal disruption from low-lying stones.⁴⁰

In situations where duct clearance using these methods is not possible, consideration may be given to using cholangioscopically guided lithotripsy. This procedure allows the insertion of lithotripsy probe through a cholangioscope for intraductal fragmentation of the difficult stone. An ultra-slim fibre-optic cholangioscope (SpyGlass) is passed into the bile ducts through an already widened papilla (through previous sphincterotomy or sphincteroplasty). Intraductal EHL can be performed by a probe under direct vision for removal of fragmented pieces of stones. Immediate success rate has been reported between 80% and 100% in difficult CBDS with prior failed ERCPs.^{41–44} Collateral damage is avoided by direct application of the lithotripter to the stone, but accidental shock waves to the bile duct wall may cause bleeding and perforation. LL probe has an advantage of being slimmer than the EHL probe, and is beneficial for stones lodged in hepatic ducts. The results are comparable between the two in prospective studies.^{45–46}

However, LL has been shown to be superior in duct clearance compared with the extracorporeal shock wave lithotripsy in a cross-over trial.⁴⁷ While a significant step forward, cholangioscopically guided lithotripsy requires experienced ERCPists, and is not routinely available in all centres. Furthermore, it can be time-consuming and require a co-operative patient or general anaesthesia.

In our own series, only 6.6% of patients in whom a stent was initially placed could not have their duct cleared. While it may be that further attempts may have succeeded, it is the case that a small proportion of patients cannot have their duct cleared of stones either due to technical difficulties, unavailability of cholangioscopic expertise or being not suitable for an extended procedure. These patients require management with long-term stenting. Despite the data alluded to above, it remains unclear as to whether such patients should have ESE with the associated risks and inconvenience or take their chance with long-term stent placement and associated risks of cholangitis.

To the best of our knowledge, the only randomised controlled study to compare of these two approaches was from Di Giorgio *et al.*¹⁰ In this study, patients who had failed endoscopic retrieval of CBDS and deemed high risk for surgical intervention were randomly allocated to either group (n=39 each for ESE and PSI). Patients in the ESE group had frequent stent exchanges every 3 months, whereas in the PSI group, a routine 3-monthly outpatient review was arranged. Patients in the ESE group underwent additional stent

Table 6 Studies with outcome data on different stent sizes

Author	Study design	Purpose of study	Number of participants	Outcomes
Ku MK ²⁹ 1999, Taiwan	Retrospective	Use of large-calibre stents in irretrievable CBDS	12	Use of >10 Fr stents was safe with no early complications observed in 12 patients with 11 months' follow-up (median).
Jain SK ¹¹ 2000, USA	Prospective observational	Use of pigtail stents in irretrievable CBDS	22	Use of 7 Fr double-pigtail stents resulted in duct clearance in 35% and fragmentation in 20% of patients.

CBDS, common bile duct stones.

exchange procedures at an average of 4.25 procedures per patient, whereas in the PSI group, the average was 1.34 procedures per patient. There was no statistically significant difference between the success rate (stone clearance) among the two groups (61.5% in ESE group and 58.5% in PSI group); however, the complication rates were noted at 7.7% and 35.9%, respectively. In this study, the authors reported that 13 stent-exchange procedures were conducted before the scheduled 3-monthly intervention in the ESE group due to 'symptoms', but the authors have failed to include this in their analysis of complications. The ASA score for the patients in this study ranged from 3 to 4, and they were deemed unfit for surgery. Subjecting such high-risk patients to frequent repeat stent exchanges raises safety concerns, and further data are required before firm guidance can be made.

In our patient cohort, we tried to eliminate bias by excluding any patient with a final diagnosis of anything other than difficult CBDS. In the ESE group, annual exchange programme was feasible, and a small group of patients had subsequent duct clearance, while the incidence of ERCP-related complications, stent blockage and cholangitis among this group was low. On the other hand, stent-related complications were very high (52.9%) among the PSI group of patients, resulting in emergency procedures in an already high-risk group. Our stent-related complication rate was higher than that observed in the reported literature and may be due to the nature of this highly selected patient group with multiple comorbidities and high ASA scores. However, notwithstanding the higher cholangitis rate, there was only one cholangitis-related death, and deaths were not increased compared with the available literature or our elective exchange group.

It should be noted that while nine patients in the PSI group presented with cholangitis, five of these patients presented within 12 months of the index procedure (range 14–183 days) and four out of nine patients presented after 12 months (range 18–47 months). Although the numbers are small, it appears that annual stent exchanges would not have prevented five patients from presenting with cholangitis within 12 months. It is not clear why presentation with cholangitis occurred more frequently within 12 months in the PSI group than in the ESE group, but this may reflect selection bias.

Our data are consistent with that of the published literature, confirming that patients on an ESE programme have more procedures than patients managed with PSI and expectant management. However, these procedures incurred few complications as they are generally quick and straightforward. The latter approach, on the other hand, results in more acute presentations. While increased mortality has not been demonstrated in our study or the published literature, the small patient numbers do not rule this out, and it must remain a real concern.

Our study is one of the largest single-centre experiences evaluating the outcomes of these two clinical approaches, but we acknowledge a number of limitations. The retrospective design means the groups are not completely matched. We have indeed demonstrated a degree of selection bias, with higher ASA in the PSI group as would be expected. However, it would be anticipated that this would result in a higher mortality rate in this group, whereas this did not occur. Second, out of a large cohort, the final numbers of patients included were small, limiting conclusions. This is a consequence of attempts to clear the duct whenever possible.

Our view, supported by these data, is that if bile duct clearance cannot be achieved at the first sitting, a sphincterotomy and biliary stent should be inserted, and a further attempt at duct clearance be made after 2–3 months. UDCA can be considered if tolerated in the meantime. Balloon sphincteroplasty is used after sphincterotomy either at the index procedure or more commonly at the second procedure. If patients are fit enough, the second procedure will ideally be under general anaesthesia to permit a longer procedure time. In this way, only very small numbers of patients fail to have their duct cleared. Such patients can be considered for surgical duct clearance or EHL to prevent the complications of long-term stent insertion, provided it is available, and the patient is sufficiently fit.

However, in the small numbers of patients for whom this approach fails and who are not fit for lengthy procedures or anaesthesia, management with long-term stents is reasonable. The decision then as to whether to embark on annual stent exchange or PSI must be made in the light of the above data. Patients should be advised that ESE will avoid the majority of acute presentations with stent blockage, but will not completely avoid this problem and requires repeated attendances at hospital. On the other hand, PSI may result in presentation with cholangitis in approaching half of all patients, but that in the vast majority, this can be dealt with by repeat ERCP performed at that time. The final decision should be taken in conjunction with the patient and family and taking into account comorbidities and life expectancy.

CONCLUSION

We conclude that although permanent stenting has advantages of convenience, its use should be restricted to patients with low life expectancy. We found that annual stent exchanges prevent episodes of cholangitis and could be recommended in carefully selected patients. Our findings do not advocate more frequent stent exchanges in this subset of patients with heightened risk.

Contributors NM: data collection and analysis. Designing, drafting and revising the manuscript. MP: data collection. KH: intellectual input, radiological input and manuscript review.

SME: concept development, research design, data analysis, manuscript revision and providing intellectual input.

Competing interests None declared.

Provenance and peer review Not commissioned; externally peer reviewed.

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