NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of laser lithotripsy for difficult-to-treat bile duct stones

The flow of bile out of the liver and the gallbladder can become blocked by stones in the bile ducts. In this procedure, which is done under general anaesthesia, an endoscope is passed into the bile ducts (usually through the mouth, stomach and the small intestine). A small fibre is put through the endoscope, which emits laser light onto the stone to break it up (lithotripsy). Small pieces are removed, but small sand-like pieces may be retained and will be gradually passed through the body. This procedure usually takes 30 to 60 minutes. The aim is to break up bile duct stones that cannot be treated using conventional techniques.

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Abbreviations

Word or phrase	Abbreviation
Confidence interval	CI
Common bile duct	CBD
Digital cholangioscopy-guided laser lithotripsy	DC-LL
Digital single-operator cholangioscopy-guided laser lithotripsy	DSOC-LL
Digital single-operator cholangioscopy-guided electrohydraulic lithotripsy	DSOC-EHL
Digital single-operator video cholangioscopy-guided electrohydraulic lithotripsy	DSOVC-EHL
Digital single-operator video cholangioscopy-guided laser lithotripsy	DSOVC-LL
Electrohydraulic lithotripsy	EHL
Endoscopic retrograde cholangiopancreatography	ERCP
Endoscopic papillary large-balloon dilation	EPLBD
Extracorporeal shock wave lithotripsy	ESWL
Interquartile range	IQR
Large balloon sphincteroplasty	LBS
Laser lithotripsy	LL
Mechanical lithotripsy	ML
Odds ratio	OR
Standard deviation	SD
Single-operator cholangioscopy-guided laser lithotripsy	SOC-LL

Introduction

The National Institute for Health and Care Excellence (NICE) prepared this interventional procedure overview to help members of the interventional procedures advisory committee (IPAC) make recommendations about the safety

and efficacy of an interventional procedure. It is based on a rapid review of the medical literature and professional opinion. It should not be regarded as a definitive assessment of the procedure.

Date prepared

This overview was prepared in March 2020.

Procedure name

- Laser lithotripsy for difficult-to-treat bile duct stones

Professional societies

- Association of Upper Gastrointestinal Surgeons of Great Britain and Ireland
- British Society of Gastroenterology
- Royal College of Radiologists

Description of the procedure

Indications and current treatment

Bile duct stones which form from cholesterol or bile pigments can block the bile ducts. Difficult-to-treat bile duct stones are defined by their diameter (above 15 mm), number, unusual shape (such as barrel-shaped), location (intrahepatic or cystic duct), stone impaction, narrowing of the bile duct distal to the stone, or the anatomy of the common bile duct (sigmoid-shaped, short distal length or acute distal angulation of less than 135 degrees).

Diagnosis and management of bile duct stones is described in NICE's clinical guideline on gallstone disease. Treatments for bile duct stones include bile duct clearance and laparoscopic cholecystectomy. Conventional stone extraction involves endoscopic retrograde cholangiopancreatography and extraction from the bile ducts using balloon and basket catheters following a sphincterotomy. For difficult-to-treat bile duct stones, treatment options include temporary stenting to allow biliary drainage if the stones cannot be removed or stone fragmentation (lithotripsy).

What the procedure involves

Laser lithotripsy aims to fragment bile duct stones that cannot be treated using conventional endoscopic stone removal techniques.

This procedure is usually done using general anaesthesia and direct visualisation of the stones using an endoscope inserted into the biliary tract. A laser fibre is introduced gently through the endoscope. Once the tip of the fibre is in direct contact with the stone, a laser is focused on its surface to create a plasma bubble. This oscillates and induces cavitation with compressive waves to fragment the stone. The procedure is usually done with the endoscope passed orally and through the stomach into the duodenum. However, a percutaneous approach is also possible.

When the stone fragmentation is complete, the fragments are removed by conventional methods (such as a basket or balloon catheter). The endoscope is then removed. Any small sand-like pieces may be retained and will be gradually passed through the body. The procedure usually takes 30 to 60 minutes.

Efficacy summary

Stone fragmentation

In a systematic review of 32 studies (n=1,969 patients with retained biliary tract stones), complete stone fragmentation rates for laser lithotripsy (LL), electrohydraulic lithotripsy (EHL) and extracorporeal shock wave lithotripsy (ESWL) were 93% (394/426), 76% (176/233) and 89% (1,130/1,266) respectively (Veld 2018). The difference between groups was statistically significant ($p<0.001$). In the same review, after excluding studies without direct visualisation of the biliary system using cholangioscopy, stone fragmentation rates for LL and EHL were 92% (337/365) and 76% (176/233) respectively ($p<0.001$).

In a randomised controlled trial of 60 patients with difficult bile duct stones, complete or partial stone disintegration was reported in 97% (29/30) of patients who had LL and 87% (26/30) of patients who had ESWL (Neuhaus 1998).

Stone clearance

In the systematic review of 32 studies (n=1,969), complete ductal clearance rates were 95% (405/426) for LL, 88% (245/277) for EHL and 85% (1,070/1,266) for ESWL (Veld 2018). The difference between groups was statistically significant ($p<0.001$). In the same study, after excluding studies without direct visualisation of the biliary system using cholangioscopy, stone fragmentation rates for LL and EHL were 96% (350/365) and 88% (245/277) respectively ($p<0.001$).

In a randomised controlled trial of 66 patients with difficult CBD stones, stone clearance was reported in a statistically significantly higher proportion of patients who had single-operator cholangioscopy-guided laser lithotripsy (SOC-LL; 94% (31/33]) than patients who had large balloon sphincteroplasty (LBS) (73% [24/33], p=0.021) (Bang 2020).

In a randomised controlled trial of 32 patients with difficult bile duct stones, complete stone clearance rate in the first ERCP was statistically significantly higher in the digital cholangioscopy-guided laser lithotripsy (DC-LL) group (100% [16/16]) than the mechanical lithotripsy (ML) group (63% [10/16], p<0.01) (Angsuwatcharakon 2019).

In a randomised controlled trial of 60 patients with large bile duct stones, endoscopic stone clearance was reported in a statistically significantly higher proportion of patients who had SOC-LL (93% [39/42]) than in patients who had conventional therapy (67% (12/18], p=0.009), with an odds ratio (OR) adjusted for the covariate of previous ERCP of 8.0 (95% confidence interval [CI] 1.6 to 40.2) (Buxbaum 2018).

In the randomised controlled trial of 60 patients, complete stone clearance was reported in a statistically significantly higher proportion of patients who had LL (97% [29/30]) than patients who had ESWL (73% [22/30], p<0.001) (Neuhaus 1998).

In a non-randomised comparative study of 407 patients with difficult bile duct stones, complete ductal clearance was reported in 99% (100/101) of patients in the digital single-operator cholangioscopy-guided laser lithotripsy (DSOC-LL) group compared with 97% (296/306) of patients in the digital single-operator cholangioscopy-guided electrohydraulic lithotripsy (DSOC-EHL) group (p=0.31) (Brewer Gutierrez 2018). In the same study, complete ductal clearance in a single session was reported in 86% (87/101) by DSOC-LL compared with 75% (228/306) by DSOC-EHL (p=0.20).

In a non-randomised comparative study of 60 patients with refractory biliary stones (75 cholangioscopies), complete stone removal rate was 66% (29/44) for digital single-operator video cholangioscopy-guided laser lithotripsy (DSOVC-LL) compared with 68% (21/31) for digital single-operator video cholangioscopy-guided electrohydraulic lithotripsy (DSOVC-EHL) (p=0.868) (Bokemeyer 2020).

In a non-randomised comparative study of 89 patients with difficult bile duct stones, stone-free rate was 82% in 17 patients who had cholangioscopy-guided transpapillary LL compared with 79% in 72 patients who had fluoroscopy-guided transpapillary LL (p=0.706) (Jakobs 2007).

In a non-randomised comparative study of 93 patients with intrahepatic bile duct stones, complete stone fragmentation and intrahepatic bile duct clearance were reported in 93% (42/45) of patients who had LL compared with 85% (41/48) of patients who had traditional treatment (p=0.22) (Jiang 2013).

Hospital stays

In the randomised controlled trial of 32 patients, median length of hospital stay was 1 day for patients who had DC-LL (IQR 1 to 2.25 days) and for patients who had ML (IQR 1 to 5 days) (Angsuwatcharakon 2019).

In the non-randomised comparative study of 93 patients, mean duration of hospitalisation was 8.2 days (range 7 to 12 days) for patients in the LL group compared with 9.8 days (range 7 to 15 days) for patients in the traditional treatment group (p=0.17) (Jiang 2013).

Safety summary

Cholangitis

Cholangitis was reported in less than 1% (3/418) of patients who had LL in the systematic review of 32 studies (n=1,969) (Veld 2018). This was a statistically significantly lower proportion than in patients who had EHL (8% [17/218]) and patients who had ESWL (3% [37/1,266], p<0.001).

Cholangitis was seen in 2 patients who had SOC-LL and fatal cholangitis was seen in 1 patient who had conventional therapy in the randomised controlled trial of 60 patients (Buxbaum 2018). The 2 events in the SOC-LL group were successfully managed with intravenous hydration and antibiotics.

Cholangitis was reported in 1 patient with a percutaneous access in both LL and ESWL groups in the randomised controlled trial of 60 patients (Neuhaus 1998).

Acute cholangitis was seen in 3 patients who had LL and 6 patients who had traditional treatment in the non-randomised comparative study of 93 patients (Jiang 2013). These events were treated with antibiotics and T-tube irrigation.

Pancreatitis

Pancreatitis was reported in 2% (8/418) of patients who had LL, 1% (3/218) of patients who had EHL and 2% (21/1,266) of patients who had ESWL in the systematic review of 32 studies (n=1,969) (Veld 2018).

Mild pancreatitis was reported in 1 patient in the DC-LL group and 1 patient in the ML group in the randomised controlled trial of 32 patients (Angsuwatcharakon 2019).

Mild pancreatitis was seen in 1 patient in the SOC-LL group and moderate severity pancreatitis was reported in 1 patient in the LBS group in the randomised controlled trial of 66 patients (Bang 2020). Both cases were managed conservatively.

Pancreatitis happened in 2 patients who had SOC-LL and 1 patient who had conventional therapy in the randomised controlled trial of 60 patients (Buxbaum 2018). These events were successfully managed with intravenous hydration and antibiotics.

Mild pancreatitis was reported in 1 patient after LL and no patients after ESWL in the randomised controlled trial of 60 patients (Neuhaus 1998).

Haemobilia

Haemobilia was seen in 3% (13/418) of patients who had LL, 3% (6/218) of patients who had EHL and 3% (37/1,266) of patients who had ESWL in the systematic review of 32 studies (n=1,969) (Veld 2018).

Haemobilia happened in 2 patients during the LL procedure and no patients who had traditional treatment in the non-randomised comparative study of 93 patients (Jiang 2013). Haemobilia happened because of mucosal damage induced by laser fibre insertion. It was successfully treated by bile duct irrigation of 100 millilitre normal saline with 8 mg epinephrine.

Biliary leakage and peritonitis

Biliary leakage was reported in 3 patients who had LL and 1 patient who had EHL in the systematic review of 32 studies (n=1,969) (Veld 2018).

Bile peritonitis caused by perforation in the distal bile duct after LL was reported in 1 patient in the SOC-LL group and no patients in the LBS group in the randomised controlled trial of 66 patients (Bang 2020). This event was managed with surgical repair of the fistula.

Anecdotal and theoretical adverse events

In addition to safety outcomes reported in the literature, professional experts are asked about anecdotal adverse events (events which they have heard about) and about theoretical adverse events (events which they think might possibly occur, even if they have never happened). For this procedure, the professional expert

did not list any anecdotal adverse events, but considered bile duct damage as a theoretical adverse event.

The evidence assessed

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to LL for difficult-to-treat bile duct stones. The following databases were searched, covering the period from their start to 3 March 2020: MEDLINE, PREMEDLINE, EMBASE, Cochrane Library and other databases. Trial registries and the Internet were also searched. No language restriction was applied to the searches (see the literature search strategy). Relevant published studies identified during consultation or resolution that are published after this date may also be considered for inclusion.

The inclusion criteria shown in the following table were applied to the abstracts identified by the literature search. Where selection criteria could not be determined from the abstracts the full paper was retrieved.

Inclusion criteria for identification of relevant studies

Characteristic	Criteria
Publication type	Clinical studies were included. Emphasis was placed on identifying good quality studies. Abstracts were excluded where no clinical outcomes were reported, or where the paper was a review, editorial, or a laboratory or animal study. Conference abstracts were also excluded because of the difficulty of appraising study methodology, unless they reported specific adverse events that were not available in the published literature.
Patient	Patients with difficult-to-treat bile duct stones.
Intervention or test	LL.
Outcome	Articles were retrieved if the abstract contained information relevant to the safety or efficacy.
Language	Non-English-language articles were excluded unless they were thought to add substantively to the English-language evidence base.

List of studies included in the IP overview

This IP overview is based on 2,747 patients from 1 systematic review, 4 randomised controlled trials and 4 non-randomised comparative studies.

Other studies that were considered to be relevant to the procedure but were not included in the main summary of the key evidence are listed in the appendix.

Summary of key evidence on LL for difficult-to-treat bile duct stones

Study 1 Veld JV (2018)

Study details

Study type	**Systematic review**
Country	Included studies: US (n=8), Korea (n=7), China (n=3), Germany (n=3), India (n=3), Italy (n=2), Brazil (n=1), Canada (n=1), New Zealand (n=1), Saudi Arabia (n=1), Thailand (n=1) and UK (n=1).
Recruitment period	Literature search: 2000 to 2017
Study population and number	**n=1,969 (32 studies; 426 LL, 277 EHL and 1,266 ESWL)** Patients with retained biliary tract stones
Age and sex	Where reported, mean 47 to 76 years; 40% to 70% female
Study selection criteria	Inclusion criteria: all original studies reporting on LL, EHL and ESWL for retained intrahepatic and extrahepatic biliary tract stones, with respect to efficacy and safety; full-text articles in English. Exclusion criteria: reviews, editorials, case reports, abstracts, letters, animal studies, studies in children, cohort studies containing fewer than 5 patients, studies published before 2000, studies not written in English, studies including patients with altered upper gastrointestinal tract anatomy, solely pancreatic duct stones, and the presence of a PTC drain.
Technique	Endoscopy-assisted LL, EHL and ESWL were done but the equipment for lithotripsy methods varied among the studies.
Follow up	**Not reported**
Conflict of interest/source of funding	MAB received consulting and/or speaker fees from Acelity/KCI, LifeCell/Allergan, Bard, Gore, Johnson & Johnson, and Smith & Nephew, and research grants from Acelity, LifeCell, Bard, Mylan, Johnson & Johnson, Baxter. and IPF received consulting fees from Boston Scientific, Cook Medical, Fujifilm, Medtronic, and Olympus. JEvH received research grants from Cook Medical and Abbott, and consulting fees from Boston Scientific and Medtronic.

Analysis

Follow up issues: The paper does not describe the follow-up details including losses to follow up.

Study design issues: This systematic review evaluated the efficacy and safety of endoscopy assisted LL, EHL and ESWL in patients with retained biliary stones refractory to the conventional endoscopic or percutaneous methods. This study was done according to the preferred reporting items for systematic reviews and meta-analyses guidelines. The primary outcome was complete ductal clearance. Secondary outcomes were complete ductal clearance after the first endoscopic session,

complete stone fragmentation rate, overall morbidity, procedure-related complications, and anaesthesia related complications. Complete ductal clearance was defined as the ability to retrieve all biliary tract stones with LL, EHL and ESWL, including additional ERCP when applied. Stone fragmentation was defined as the rupture of stones by 1 of the 3 lithotripsy methods.

Two independent reviewers assessed the eligibility of titles, abstracts, and subsequently full-text articles. Discrepancies were resolved through discussion and consensus, and in cases of doubt, were resolved with the senior author. Quality assessment of the studies was done using the Oxford Centre for Evidence-Based Medicine Levels of Evidence. The Newcastle-Ottawa Quality Assessment Scale for cohort studies was used to evaluate any risk of bias. Any doubt regarding the methodological quality assessment was discussed by 2 independent reviewers.

Descriptive statistics were computed for all study variables. Sensitivity analysis was done by excluding retrospective studies and by excluding studies without direct visualisation of the biliary tract using cholangioscopy.

Study population issues: Each of the included studies was performed in a tertiary centre. Most of the studies included patients in whom conventional ERCP techniques failed to clear the bile duct. The included studies were done in various countries with different patient demographics, varying aetiologies for stone formation, and different types of stones. Multiple factors have been related to the failure of endoscopic extraction of biliary stones: size of the stone, location of the stone, stone composition, impaction, biliary strictures, and biliary anatomy. These baseline characteristics were not available for all of the included studies. Therefore, no comparison could be performed between the baseline characteristics of the study groups.

There was a lack of consensus among studies on the definition, classification, and grading of gastrointestinal procedure-related complications. No scoring system has been validated to define, classify, and grade negative outcomes of gastrointestinal procedures. Therefore, it is difficult to compare studies examining negative outcomes of gastrointestinal procedures. Although the methodological quality of the included studies was adequate, studies were mostly small and retrospective. No randomised studies were available, and no studies directly compared LL with EHL. Cholangioscopy (direct visualisation of the biliary tract) was done in some studies but not all.

Key efficacy findings

- Number of patients analysed: 1,969 (426 LL, 277 EHL and 1,266 ESWL)

Complete stone fragmentation (n=1,925):

- Complete stone fragmentation: 88.3% (1,700/1,925)
- Incomplete stone fragmentation: 11.7% (225/1,925)

Complete ductal clearance (n=1,969):

- Complete ductal clearance: 87.4% (1,720/1,969)
- Incomplete ductal clearance: 12.6% (249/1,969)

Binary logistic regression of efficacy

Lithotripsy method	%	OR	P value	95% CI
Complete stone fragmentation, n=1,925				
EHL	75.5 (176/233)	REF	<0.001	-
LL	92.5 (394/426)	3.99	<0.001	2.50 to 6.37
ESWL	89.3 (1130/1,266)	2.69	<0.001	1.09 to 3.81
Complete ductal clearance, n=1,969				
EHL	88.4 (245/277)	REF	<0.001	-
LL	95.1 (405/426)	2.529	0.002	1.42 to 4.47
ESWL	84.5 (1070/1,266)	0.71	0.10	0.48 to 1.06
Complete ductal clearance after first session, n=1,658				
EHL	65.8 (152/231)	REF	<0.001	-
LL	68.9 (215/312)	1.15	0.44	0.80 to 1.66
ESWL	31.6 (352/1,115)	0.24	<0.001	0.18 to 0.32

Sensitivity analysis of prospective studies

Lithotripsy method	%	OR	P value	95% CI	%	OR	P value	95% CI	%	OR	P value	95% CI
	Complete stone fragmentation				**Complete ductal clearance**				**Complete ductal clearance after first session**			
EHL (n=111)	82.4	REF	0.10	-	90.1	REF	<0.001	-	59.2	REF	<0.001	-
LL (n=297)	90.6	2.06	0.04	1.04 to 3.34	94.9	2.07	0.08	0.92 to 4.65	62.3	1.14	0.64	0.66 to 1.97
ESWL (n=596)	87.2	1.47	0.22	0.87 to 2.69	82.0	0.50	0.04	0.26 to 0.97	40.3	0.46	0.002	0.29 to 0.76

Sensitivity analysis after excluding studies without direct visualisation of the biliary system using cholangioscopy, n=642:

- Stone fragmentation rate: LL 92.3% (337/365) versus EHL 75.5% (176/255), p<0.001

- Ductal clearance rate: LL 95.9% (350/365) versus EHL 88.4% (245/277), p<0.001
- Complete ductal clearance within the first session: LL 71.6% (187/261) versus EHL 65.8% (152/231), p=0.34

All patients who had ESWL were excluded.

Key safety findings

Binary logistic regression of safety

Lithotripsy method	% (n)	OR	P value	95% CI	% (n)	OR	P value	95% CI	% (n)	OR	P value	95% CI
	Overall morbidity				Postprocedural complications				Anaesthesia-related complications			
EHL (n=218)	14.2	REF	0.29	-	13.8 (30)	REF	0.04	-	0.5	REF	0.01	-
LL (n=418)	10.0	0.63	0.12	0.41 to 1.11	9.6 (40)	0.66	0.11	0.40 to 1.10	0.5	1.04	0.97	0.09 to 11.57
ESWL (n=1,266)	11.2	0.76	0.20	0.50 to 1.16	8.4 (106)	0.57	0.01	0.37 to 0.88	2.8	6.35	0.07	0.87 to 46.57
Total (n=1,902)	11.3 (215)	-	-	-	9.3 (176)				0.5	REF	0.01	-

Procedure-related complications

	EHL, % (n)	LL, % (n)	ESWL, % (n)	Total, % (n)
Pancreatitis	1.4 (3)	1.9 (8)	1.7 (21)	1.7 (32)
Cholangitis*	7.8 (17)	0.7 (3)	2.9 (37)	3.0 (57)
Cholecystitis	0.5 (1)	0 (0)	0.1 (1)	0.1 (2)
Haemobilia	2.8 (6)	3.1 (13)	2.9 (37)	2.9 (56)
Abdominal pain	0 (0)	1.7 (7)	0 (0)	0.4 (7)
Fever	0 (0)	0.7 (3)	0 (0)	0.2 (3)
Bleeding	0 (0)	0 (0)	0.6 (8)	0.4 (8)
Perforation	0 (0)	0 (0)	0.2 (2)	0.1 (2)
Biliary leakage	0.5 (1)	0.7 (3)	0 (0)	0.2 (4)
Other	0.9 (2)	0.7 (3)	0 (0)	0.3 (5)

*The incidence of cholangitis was statistically significantly higher for EHL than for LL and ESWL (p<0.001).

Anaesthesia-related complications

	EHL, % (n)	LL, % (n)	ESWL, % (n)	Total, % (n)
Tachycardia	0 (0)	0.2 (1)	0 (0)	0.1 (1)
Bradycardia	0.5 (1)	0 (0)	1.3 (17)	0.9 (18)
Palpitations	0 (0)	0 (0)	0.7 (9)	0.5 (9)
Resuscitation	0 (0)	0 (0)	0.1 (1)	0.1 (1)
Nausea	0 (0)	0 (0)	0.5 (6)	0.3 (6)
Vomiting	0 (0)	0 (0)	0.2 (3)	0.2 (3)
Pneumonia	0 (0)	0.2 (1)	0 (0)	0.1 (1)

Sensitivity analysis of prospective studies

Lithotripsy method	%	OR	P value	95% CI	%	OR	P value	95% CI	%	OR	P value	95% CI
	Overall morbidity				Postprocedural complications				Anaesthesia-related complications			
EHL (n=111)	14.1	REF	0.40	-	14.1	REF	0.30	-	0	REF	>0.99	-
LL (n=297)	9.1	0.61	0.18	0.29 to 1.26	8.4	0.56	0.12	0.27 to 1.17	0.7	>0.99	>0.99	<0.001
ESWL (n=596)	10.1	0.68	0.26	0.35 to 1.33	10.1	0.68	0.26	0.35 to 1.33	0	>0.99	>0.99	<0.001

Sensitivity analysis after excluding studies without direct visualisation of the biliary system using cholangioscopy, n=642:

- Overall morbidity: LL 9.5% (34/357) versus EHL 14.2% (31/218), p=0.08

Study 2 Bang JY (2020)

Study details

Study type	**Randomised controlled trial (NCT00852072)**
Country	US (single centre)
Recruitment period	2016 to 2018
Study population and number	**n=66 (33 SOC-LL versus 33 LBS)** Patients with difficult CBD stones
Age and sex	SOC-LL: mean 72.8 years; 63.6% (21/33) female LBS: mean 63.9 years; 75.8% (25/33) female
Patient selection criteria	Inclusion criteria: patients ≥18 years who were suspected to have CBD stones on ERCP/magnetic resonance cholangiopancreatography and attempts at ductal clearance using retrieval balloons and baskets were unsuccessful at outside facilities or at the study institution. Exclusion criteria: patients with intrahepatic ductal stones, altered surgical anatomy, suspected pancreaticobiliary malignancy, pregnancy, abnormal coagulation parameters, and those on anticoagulation or antiplatelet therapy were excluded.
Technique	Patients were under general anaesthesia. SOC-LL: LL (energy settings, 1 J and 10 Hz) was done by insertion of a holmium laser probe (Lumenis, San Jose, CA) through the biopsy channel of the cholangioscope (SpyGlass DS, Boston Scientific Corp, Marlborough, MA). Lithotripsy was continued until all fragmented stones were small enough to be retrieved using a basket or balloon. When unsuccessful, retrieval was attempted using a 30-mm ML (Trapezoid, RX Wire guided Retrieval Basket, Boston Scientific). LBS: A 12- to 15-mm or 15- to 18-mm radial expansion balloon (CRE Balloon Dilation Catheter, Boston Scientific) was used. The balloon was kept inflated for 60 seconds. After deflation of the balloon, stone extraction was attempted using a retrieval balloon or basket. When assigned treatment was unsuccessful, patients had ML before crossing over to the other group.
Follow up	**6 months**
Conflict of interest/source of funding	JY Bang is a Consultant for Olympus America Inc and Boston Scientific Corporation. R Hawes is a Consultant for Boston Scientific Corp, Olympus America Inc, Covidien, Creo Medical, Nine Points Medical, and Cook Medical. S Varadarajulu is a Consultant for Boston Scientific Corp, Olympus America Inc, Covidien, and Creo Medical. The remaining authors disclose no conflicts.

Analysis

Follow-up issues: The paper states that patients were contacted via telephone at 5 days, 30 days and 6 months after the index intervention to assess for adverse events. Hospital records were reviewed in

patients who were hospitalised for the management of adverse events. No losses to follow up were reported but results did not indicate the exact follow-up time.

Study design issues: This randomised controlled trial compared the effectiveness of SOC-LL and LBS-based approached for endoscopic management of difficult bile duct stones. Difficult bile duct stones were defined as stones in which attempts at extraction after biliary sphincterotomy using a retrieval balloon and basket were unsuccessful. The main outcome was treatment success, defined as ability to clear the duct in 1 session.

Computer-generated randomisation assignments using a block randomisation method (block sizes of 4) was placed in sequentially numbered, sealed, opaque envelopes that were opened by a study coordinator intraprocedurally to determine the treatment allocation. Patients were randomised equally (1:1 allocation) to either treatment group. Given innate differences in procedural techniques, endoscopists were not blinded to the treatment allocation. Research coordinators were blinded to treatment arm.

Two-tailed sample size calculation was done based on the rate of treatment success, which was estimated at 95% for SOC-guided lithotripsy and 65% with LBS. This resulted in sample size estimation of 31 patients per group, at 80% power and type I error rate (α) of 0.05. Total sample size was set a total of 66 patients to account for 5% dropout rate.

Study population issues: Patients randomised to SOC-LL were statistically significantly older with a smaller proportion having had prior cholecystectomy compared with patients randomised to LBS (mean age, 72.8 versus 63.9 years, p=0.034; prior cholecystectomy, 42% (14/33) versus 73% (24/33), p=0.013). There was no statistically significant difference in terms of location of stone, size of largest stone, total number of stones, and ratio of stone size to extrahepatic bile duct diameter.

Key efficacy findings

- Number of patients analysed: 66

Procedure duration and clinical outcomes

	SOC-LL (n=33)	**LBS (n=33)**	**P value**
Total procedure duration, min			
Mean (standard deviation [SD])	39.2 (2.1)	37.3 (25.2)	
Median	38	27	0.379
IQR	25 to 50	15 to 58	
Range	12 to 85	5 to 88	
Treatment success, % (n)	93.9 (31)	72.7 (24)	0.021
Crossover to alternate treatment arm, % (n)	6.1 (2)[a]	27.3 (9)[b]	0.021

IP overview: Laser lithotripsy for difficult-to-treat bile duct stones

Reintervention done, % (n)	0	6.1 (2)	0.492
Total number of interventions to result in ductal clearance			
Mean (SD)	1.0 (0)	1.1 (0.4)	
Median	1	1	0.154
IQR	1 to 1	1 to 1	
Range	1 to 1	1 to 3	
1	100 (33)	93.9 (31)	0.492
2	0	3.0 (1)	
3	0	3.0(1)	

[a]Ductal clearance was reported in both patients in SOC-LL group who were crossed over to LBS.
[b]Ductal clearance was reported in 7 of 9 patients in LBS group who were crossed over to SOC-LL. In the remaining 2 patients who were crossed over to SOC-LL, complete stone removal was not reported during the index session despite crossover to SOC-LL and needed repeat interventions.

SOC-LL: No statistically significant difference was seen in the rate of ductal clearance using SOC-LL regardless of the presence or absence of a tapered bile duct (89.5% versus 100%; p=0.496).
LBS: A tapered bile duct was seen in statistically significantly more patients in whom ductal clearance failed using LBS as compared with patients in whom LBS was successful (56.3% versus 5.9%; p=0.002).

Multiple penalised logistic regression with Firth's correction examining the factors associated with treatment success

Variable	OR	95% CI	P value
Treatment arm: SOC-LL versus LBS	8.74	1.29 to 59.3	0.026
Stone location: distal versus proximal bile duct	0.90	0.14 to 5.69	0.908
Total number of stones: 1 versus ≥2 stones	1.68	0.26 to 10.6	0.584
Size of largest stone: <15 mm versus ≥15 mm	1.28	0.19 to 8.78	0.801
Ratio of stone size to extrahepatic bile duct diameter: ≤1.0 versus >1.0	28.8	1.21 to 687.6	0.038
Presence of tapered bile duct: No versus Yes	26.9	1.29 to 558.2	0.034
Prior ERCP for stone removal: Yes versus No	1.35	0.18 to 9.88	0.769

Key safety findings

Adverse events: SOC-LL 9.1% (3/33) versus LBS 3.0% (1/33), p=0.613

SOC-LL:

- Cricopharyngeal perforation: n=1. Before SOC-LL, the patient had suctioning of the oropharynx using a rigid probe and hence the precise reason for adverse event was unclear.
- Bile peritonitis caused by perforation in the distal bile duct after LL: n=1. This event was managed with surgical repair of the fistula.
- Mild post-ERCP pancreatitis: n=1. This event was managed conservatively.

LBS: moderate severity post-ERCP pancreatitis: n=1. This event was managed conservatively.

Study 3 Angsuwatcharakon P (2019)

Study details

Study type	**Randomised controlled trial (TCTR20171121001)**
Country	Thailand (2 centres)
Recruitment period	Not reported
Study population and number	n=32 (16 DC-LL versus 16 ML) Patients with difficult bile duct stones
Age and sex	DC-LL: mean 62.7 years; 56.3% (9/16) female ML: mean 63.1 years; 68.8% (11/16) female
Patient selection criteria	Inclusion criteria: patients aged >18 years with bile duct stones that were not cleared by endoscopic sphincterotomy and endoscopic papillary large-balloon dilation (EPLBD) or were not amenable to EPLBD because of a tapering CBD. Exclusion criteria: pregnancy, uncorrected coagulopathy (platelet count <50000 /millilitre or international normalised ratio >1.5), unstable vital signs, and surgically altered anatomy (Billroth II or Roux-en-Y).
Technique	DC-LL: digital cholangioscope (SpyGlass DS; Boston Scientific) was used. LL was done by insertion of a 365µm holmium laser probe (Dornier Medilas H Solvo; Dornier MedTech, Wessling, Germany) through the biopsy channel of the cholangioscope. Laser energy settings were 2 J energy and 10Hz frequency (20W). The crossover method was done if the randomised method could not be started within 20 minutes by the selected technique.
Follow up	**6 months**
Conflict of interest/source of funding	None

Analysis

Follow-up issues: The paper states that patients were admitted for a 24-hour observation period to check for any post-ERCP complications. Patients were then followed up at the outpatient department at 1 and 4 weeks and at 6 months. No losses to follow up were described. One patient who had a failed ML and then was crossed over to DC-LL had a total stone clearance time including LL that was longer than 120 minutes, and therefore data from this patient were censored.

Study design issues: This randomised controlled trial compared the efficacy of DC-LL with that of ML in patients with large bile duct stones that were not amenable to EPLBD or were not successfully treated by EPLBD. The primary outcome of the study was stone clearance rate within the first session of the randomised method. Secondary outcomes were procedure time, stone clearance time, radiation exposure, procedure-related adverse events, and length of hospital stay of the first ERCP session. The study was reported according to the Consolidated Standards of Reporting Trials.

In terms of randomisation, if stone removal failed, an envelope containing a computer-generated randomisation code, in blocks of 4 and a 1:1 ratio, was disclosed for the lithotripsy method. In the case of a tapering CBD, EPLBD was not done and the randomisation process was started directly after a complete biliary sphincterotomy. Three experienced endoscopists done these procedures in the study. Sample size calculation was based on pilot data from the study centre, with success rates being 90% for LL and 45% for ML. A total of 32 patients randomised in a 1:1 ratio provided 80% power to detect this difference at a 2-sided significance level of 5%.

Study population issues: In each group, 15 patients had large stones and 1 had floating stones. There was no statistically significant difference between groups in terms of age, gender, prior sphincterotomy, CBD diameter, number of stones, type of stones and size of CRE balloon.

Key efficacy findings

- Number of patients analysed: 32

Procedure time and clinical outcomes

	DC-LL (n=16)	**ML (n=16)**	**P value**
Complete stone clearance by selected technique, % (n)	100 (16)	62.5 (10)[a]	<0.01
Complete clearance after crossover to other technique in 1 single ERCP session, % (n)	N/A	81.3 (13)	N/A
Procedure time, mean (SD), minutes	66 (28)	83 (46)	0.23
Stone clearance time, mean (SD), minutes	39 (23)	53 (41)	0.26
Fluoroscopic time, mean (SD), minutes	11:12 (7:30)	21:27 (12:17)	<0.01
Cumulative DAP, mean (SD), mGycm2	20988.8 (14851)	40744.5 (24661.7)	0.04
Patients needing >1 ERCP session for stone clearance, % (n)	0 (0)	18.8 (3)	0.23
Length of hospitalisation, median (IQR), days	1 (1 to 2.25)	1 (1 to 5)	0.27

[a]In 6 patients, ML was considered a failure because the procedure time was longer than 120 minutes (defined as the maximum allowable procedure time for stone clearance, n=1) or there was disintegration failure (defined as the randomised method could not be started within 20 minutes by the selected technique, n=5).

6-month follow up: no recurrent cholangitis or evidence of recurrent BCD stones in both groups.

Key safety findings

Post-ERCP complications, % (n)

	DS-LL (n=16)	ML (n=16)	P value
Complications	6.3 (1)	12.5 (2)	0.76
Mild sphincterotomy bleeding	0	6.3 (1)[b]	
Mild pancreatitis	6.3 (1)	6.3 (1)	

[b]This event was successfully treated with diluted adrenaline injection and did not need blood transfusion.

Study 4 Buxbaum J (2018)

Study details

Study type	**Randomised controlled trial (NCT01759979)**
Country	US (2 centres)
Recruitment period	2013 to 2016
Study population and number	**n=60 (42 SOC-LL versus 18 conventional therapy)** Patients with large bile duct stones
Age and sex	SOC-LL: mean 51.6 years; 69.1% (29/42) female Conventional: mean 42.6 years; 66.7% (12/18)
Patient selection criteria	Inclusion criteria: adult patients with an extrahepatic (common bile or common hepatic) duct stone greater than 1 cm in diameter based on ultrasonography, computed tomography, magnetic resonance imaging or previous ERCP. Exclusion criteria: patients with a history of pancreaticobiliary malignancy or bile duct diversion surgery; age less than 18 years; or who were pregnant, incarcerated or lacked capacity to give informed consent.
Technique	SOC-LL: a single operator disposable cholangioscope with a reusable fibreoptic probe (Boston Scientific, Natick, Mass) was used to target LL. A coherent VersaPulse holmium LL system (Lumenis, San Jose, Calif) was used to deliver continuous (non-interval) laser therapy at 10 W power (1 J energy, 10 Hz frequency). Conventional therapy: techniques included baskets for ML, papillary dilation and balloon extraction to facilitate stone removal, and in some cases simply balloon or basket (non-lithotripsy) extraction without papillary dilation. In both groups, additional endoscopic procedure (same method) or bile duct surgery might be done based on the judgment of the attending endoscopist.
Follow up	**Not reported**
Conflict of interest/source of funding	JB received consultancy fees from Olympus and a research grant from Covidien. All other authors disclosed no financial relationships relevant to this publication.

Analysis

Follow-up issues: The paper does not describe follow-up periods and losses to follow up.

Study design issues: This randomised controlled trial determined whether cholangioscopy-guided LL improves clearance of large bile duct stones compared with conventional approaches. The primary endpoint was successful endoscopic clearance of bile duct stones with the assigned method. Other efficacy endpoints included procedure time, fluoroscopy time and number of procedures. Predefined procedure adverse events assessed included post-ERCP pancreatitis, cholangitis, bleeding, and perforation as defined by the Cotton Consensus criterion.

Immediately before ERCP, patients were randomised in a 2:1 ratio to cholangioscopy-guided LL versus conventional therapy only. The randomisation schedule was computer generated by an individual uninvolved in the conduct of the study. The allocation assignments were concealed. Randomisation was stratified based on whether or not the procedure was a first or repeat ERCP. Patients were blinded to the treatment group. The experienced endoscopists done ERCP, LL and conventional therapy in this study.

For sample size, a total of 60 would show a statistically significant difference (with α=0.05, 80% power and 2:1 allocation ratio) assuming a 20% difference in endoscopic clearance with the assigned method. Based on historical data, it was estimated 70% clearance of large >1 cm stones using conventional ERCP methods and 90% clearance for cholangioscopy-guided stone therapy.

Study population issues: Baseline characteristics were similar in the study groups although patients in the SOC-LL group tended to be older (p=0.03) and have more comorbidities (p=0.18). Previous ERCP within the past 3 months had been done in 31 patients (74%) in the SOC-LL and in 13 patients (72%) in the conventional therapy group. Multiple stones were present in 12 patients (67%) in the conventional therapy group and 25 patients (59%) in the SOC-LL group.

Key efficacy findings

- Number of patients analysed: 60

Procedure characteristics and clinical outcomes

	SOC-LL (n=42)	**Conventional therapy (n=18)**	**OR (95% CI)**
Endoscopic stone clearance, % (n)[a]	92.9 (39)	66.7 (12)	8.0 (1.6 to 40.2)
Number of procedures, % (n)			
1	28.6 (12)	38.9 (7)	Base outcome
2	50.0 (21)	50.0 (9)	1.4 (0.4 to 4.6)
≥3	21.4 (9)	11.1 (2)	2.6 (0.4 to 15.8)
ML	50.0 (21)	66.7 (12)	0.5 (0.2 to 1.6)
Papillary dilation, % (n)	14.3 (6)	44.4 (8)	0.2 (0.1 to 0.7)
Basket impaction with rescue lithotripsy, % (n)	9.5 (4)	22.2 (4)	0.4 (0.1 to 1.7)
Procedure time (minutes), mean (SD)[b]	120.7 (40.5)	81.2 (49.3)	38.8 (16.7 to 60.8)
Fluoroscopy time (minutes), mean (SD)	9.1 (6.1 to 14.0)	11 (5.1 to 13.5)	1.1 (0.7 to 1.7)

[a]p=0.009
[b]p=0.0008, which remained statistically significant after adjusting for age and comorbidities (p=0.0014).

All adjusted for covariate of previous ERCP. The 9 patients for whom ERCP for stone clearance was not successful had surgical CBD exploration with stone removal. Multivariate regression analysis adjusting for the 2 independent baseline variables with p<0.20 on univariable comparison of the study groups (age and comorbidities) showed consistent results: OR=8.7; 95% CI 1.1 to 69.7.

Sensitivity analysis

	SOC-LL (n=42)	Conventional therapy (n=18)	OR (95% CI)
Previous ERCP, % (n)	**74 (31)**	**72 (13)**	
Endoscopic stone clearance, % (n)	90 (28)	54 (7)	8.0 (1.6 to 40.2)
Procedure time (minutes), mean (SD)	129.7 (46.8)	98.5 (39.8)	31.1 (3.2 to 59.1)
No previous ERCP, % (n)	**26 (11)**	**28 (5)**	
Procedure time (minutes), mean (SD)	95.4 (31.8)	36.2 (7.5)	59.2 (26.3 to 92.0)

Endoscopic clearance was successful in both cases with brown stones (both in the conventional therapy group) versus 82.7% (48/58) with cholesterol stones (p=0.69). Controlling for stone type did not affect the increased endoscopic clearance with cholangioscopic versus conventional therapy (adjusted OR=8.7; 95% CI 1.8 to 41.4).

Duct diameter did not predict successful endoscopic clearance. When duct diameter was included as a covariate, the significantly higher odds of endoscopic stone clearance for cholangioscopic versus conventional therapy remained at a similar level (adjusted OR=8.7; 95% CI 1.7 to 45.4). When the number of study ERCP procedures was introduced as a covariate, the odds of endoscopic stone clearance with cholangioscopic versus conventional therapy also did not change materially (adjusted OR=9.3; 95% CI 1.7 to 50.5).

Key safety findings

	SOC-LL (n=42)	Conventional therapy (n=18)	OR (95% CI)
Adverse events, % (n)	9.5 (4)	11.1 (2)	0.8 (0.1 to 5.0)
Cholangitis, n	2	1	
Post-ERCP pancreatitis	2	1	

One patient developed fatal post procedure cholangitis after conventional therapy only; the other adverse events were successfully managed with intravenous hydration and antibiotics.

Sensitivity analysis: One (6.3%) of the 16 patients who had not had previous ERCP developed post-ERCP pancreatitis, whereas 5 (11.4%) of the 44 patients with previous ERCP developed adverse events.

Study 5 Neuhaus H (1998)

Study details

Study type	**Randomised controlled trial**
Country	Germany (single centre)
Recruitment period	Not reported
Study population and number	**n=60 (30 LL versus 30 ESWL)** Patients with difficult bile duct stones
Age and sex	LL: Mean 71 years; 60% (18/30) female ESWL: Mean 70 years; 57% (17/30) female
Patient selection criteria	Inclusion criteria: bile duct stones not amenable to standard endoscopic procedures including attempted ML caused by stone impaction or an inaccessible main duodenal papilla. Exclusion criteria: specifically being referred for LL after previous failure of ESWL; refused any lithotripsy procedure or surgery.
Technique	Patients were sedated with midazolam or propofol with the addition of meperidine when necessary. Pulse oximetry was used routinely. Antibiotics were administered prophylactically for percutaneous transhepatic interventions. LL was done using a rhodamine 6G, flashlamp-pumped dye laser with automatic stone recognition (Lithognost; Baasel Lasertech, Starnberg, Germany). A 3.4 mm miniscope (CHF-BP 30; Olympus, Tokyo, Japan) inserted through a standard therapeutic duodenoscope (TJF 100 and TJF 130; Olympus), while A 4.9 mm or 3.7 mm choledochoscope (CHF-P20 and XCHF-37 prototype, both from Olympus) were used for the percutaneous approach. LL was continued until the fragment size seemed to be less than 10 mm or exhaustion of the patient because of a prolonged procedure. A maximum of 2 additional sessions was allowed in case of a failed or incomplete stone disintegration. In both groups, the crossover method was done if the randomised method failed bile duct clearance.
Follow up	**30 days**
Conflict of interest/source of funding	Not reported

Analysis

Follow-up issues: The paper states that patients were assessed for at least 2 days after the procedure. Further follow up was by telephone interviews with all discharged patients to inquire about symptoms or complications within 30 days of the final procedure. There was no information relating to losses to follow up.

Study design issues: This randomised controlled study compared the efficacy and safety of ESWL and intracorporeal LL with automatic stone recognition in patients with difficult bile duct stones. This study also evaluated the role of crossover therapy in case of failure of 1 method.

Patients were randomly assigned to intracorporeal LL or ESWL on a computer-generated schedule by opening of sealed envelopes after establishment of endoscopic or percutaneous biliary drainage.

Study population issues: The baseline characteristics of both cohorts were similar. There were no statistically significant differences in age, sex, risk factors, serum bilirubin level, number, diameter and location of stones, the proportion of patients with gallbladder in situ, jaundice, cholangitis, and biliary pain, and approaches to stones (a peroral route was used in 33 patients and a percutaneous access was used in 27 patients). LL was done under fluoroscopic control in 2 patients with easily accessible stones and cholangioscopic guidance in 28 patients.

Key efficacy findings

- Number of patients analysed: 60

Procedure characteristics and clinical outcomes

	LL (n=30)	ESWL (n=30)	P value
No. of sessions, mean (SD)	1.2 (0.4)	2.3 (0.9)	
Duration of a single session (minutes), mean (SD)	54 (34)	63 (13)	
Total no. of pulses per patients	7,882 (7,854)	1,4578 (16,715)	
Fluoroscopic control of lithotripsy	2	30	
Endoscopic control of lithotripsy	28		
No. of interrupted laser pulses, mean (SD)	2,026 (2,383)		
Diameter of fragments			
≤10 mm	27	18	
11 to 15 mm	2	4	
>15 mm		4	
No fragmentation	1	4	
No. of lithotripsy and endoscopy sessions, mean (SD)	1.2 (0.4)	3.0 (1.3)	<0.001
Bile duct clearance	29	22	<0.05
Days since first lithotripsy, mean (SD)	0.9 (2.3)	3.9 (3.5)	<0.001
Failure			
Partial bile duct clearance		5	
Unchanged findings	1	3	
Failure of retrograde approach	1	4	
Failure of percutaneous approach		4	

Crossover therapy:

- ESWL succeeded in the single patient in whom peroral LL had failed.
- IN a mean number of 1.4±0.3 procedures of LL, there was bile duct clearance in 7 of 8 patients in whom ESWL had failed.

Key safety findings

There were no significant differences in number and type of adverse effects between the LL and ESWL groups. Exhaustion of a patient after a lengthy or painful procedure caused interruption of treatment in 5 patients treated by ESWL and 4 treated by LL.

Complications, n

	LL	ESWL
Cholangitis with a percutaneous access[a]	1	1
Mild pancreatitis	1	
Transient haemobilia through the percutaneous catheter		1
Respiratory failure[b]		1
Minor cardia arrhythmias[c]		2

[a]Successfully managed by exchange of catheters and intravenous antibiotics.

[b]This event happened during ESWL and needed resuscitation with intubation and temporary artificial respiration with rapid recovery.

[c]These events happened during ESWL but these were not clinically significant.

Crossover therapy: No severe adverse effects were seen during or after crossover therapy. There was no 30-day mortality.

Study 6 Brewer Gutierrez OI (2018)

Study details

Study type	**Non-randomised controlled study (retrospective)**
Country	US (19 centres), UK (2 centres) and Korea (1 centre)
Recruitment period	2015 to 2016
Study population and number	**n=407 (101 DSOC-LL versus 306 DSOC-EHL)** Patients with difficult bile duct stones
Age and sex	Mean 64.2 years; 60% (246/407) female
Study selection criteria	Inclusion criteria: adult patients (>18 years) who had DSOC using either LL or EHL for the management of difficult bile duct stones, which were defined as large (>15 mm), multiple (>3), intrahepatic duct/cystic duct stones or impacted stones, and those with Mirizzi syndrome or any associated CBD anatomic abnormality, such as stricture below the stone or duodenal diverticula and patients with altered anatomy. Exclusion criteria: patients were treated with other types of cholangioscopes.
Technique	Difficult bile duct stones were treated by DSOC (Spyglass DS, Boston Scientific) with LL or EHL LL: The Versa-Pulse P20, Slim line 365 mm fibre holmium laser (holmium: yttrium-aluminum-garnet; Lumenis Inc, San Jose, CA) was used with power settings of 20 W (2.5 J X 8 Hz), in bursts of no more than 5 seconds. EHL (AUTOLITH, Northgate Technologies Inc, Elgin, IL): shock waves were delivered in brief pulses, which range from a single discharge to continuous firing, until the stone is fragmented. The power setting ranged between 50% and 100% and delivered over 1 to 2 seconds. During the DSOC procedure, 92% of patients had antibiotic prophylaxis.
Follow up	**Median 83.5 days (interquartile range [IQR], 33 to 155 days)**
Conflict of interest/source of funding	IR is a consultant and speaker for Boston Scientific and Covidien; and co-owner of EndoRx. RT has received financial support from Boston Scientific to attend scientific meetings. SS is a consultant for Boston Scientific. RJS is consultant for Cook and for Boston Scientific. WW is a consultant for Boston Scientific and Abbvie. DGA is a consultant for Boston Scientific. VK is a consultant for Boston Scientific. AYW has received research support from Cook Medical. KK is a speaker for Boston Scientific; and a consultant for Olympus. VK is a consultant for Cook Medical. CJD is a consultant for Boston Scientific. BP is a consultant for Boston Scientific. GJMW is a consultant for Boston Scientific. SK is a consultant for Cook Medical and Boston Scientific. MAK is a consultant for Boston Scientific and Olympus. The remaining authors disclose no conflicts.

Analysis

Follow-up issues: This paper describes that follow-up time was recorded in 63.6% (259/407) of patients.

Study design issues: This retrospective, international, multicentre study assessed technical success, defined as bile duct clearance, in a large cohort of patients with difficult biliary stones. This study also assessed the safety of DSOC either with LL or with EHL and to compare the effectiveness of LL with EHL. The safety was defined by the rate and severity of adverse events as graded per the American Society for Gastrointestinal Endoscopy lexicon (mild, moderate, severe, fatal). Other outcomes included number of LL/EHL sessions needed to clear the bile duct; the need for other therapies; incomplete stone removal or stone recurrence after the duct was declared clear; and addition to procedure time. Univariate and multivariable analyses were done to identify factors associated with technical failure and the need for more than 1 DSOC-LL or -EHL session to clear the bile duct.

Study population issues: At baseline, there were (statistically significant) differences between the 2 groups as shown in the table below.

	Total (n=407)	DSOC-LL (n=101)	DSOC-EHL (n=306)	P value
Symptoms (>1), % (n)				
Abdominal pain	48.8 (166)	57.4 (58)	35.3 (108)	<0.001
Jaundice	40.8 (166)	13.9 (14)	49.7 (152)	<0.001
Cholangitis	16.9 (69)	9.9 (10)	19.3 (59)	0.03
Pancreatitis	1.5 (6)	1 (1)	1.6 (5)	1
Others	11.8 (48)	29.7 (30)	5.9 (18)	<0.001
Prior ERCP with failed stone extraction, % (n)	85.7 (349)	77.3 (78)	88.5 (271)	0.005
Prior interventions for stone removal (>1), % (n)				
Sphincterotomy	62.6 (253)	46.5 (47)	67.3 (206)	<0.001
Papillary balloon dilation	0.5 (2)	0	0.6 (5)	1
Sphincterotomy+papillary balloon dilation	17.2 (70)	16.8 (17)	17.3 (53)	0.91
Balloon extraction	73.2 (298)	45.5 (46)	82.3 (252)	<0.001
Retrieval basket	22.8 (93)	32.7 (33)	19.6 (60)	0.007
ML	24.8 (101)	34.6 (35)	21.6 (66)	0.008
LL	1.7 (7)	3 (3)	1.3 (4)	0.37
EHL	7.6 (31)	0	10.1 (31)	<0.001
Indwelling biliary stent, % (n)	75.9 (309)	56.4 (57)	82.3 (252)	<0.001

Key efficacy findings

- Number of patients analysed: 407 (101 DSOC-LL versus 306 DSOC-EHL)

Stone and procedure characteristics

	Total (n=407)	DSOC-LL (n=101)	DSOC-EHL (n=306)	P value

CBD size, mm (mean±SD)	15.1±5.95	18.3±6.98	14.2±5.24	<0.001
Stone locations, % (n)				<0.001
CBD	59.7 (243)	71.3 (72)	55.9 (171)	
CHD	9.6 (39)	10.9 (11)	9.1 (28)	
Cystic duct	11.3 (46)	10.9 (11)	14.4 (44)	
IHD	15.2 (62)	8.9 (9)	17.3 (53)	
Hilar	1.5 (6)	0	2 (6)	
More than 1 location	2.7 (11)	6.9 (7)	1.3 (4)	
Stone size, mm (mean±SD)	16.01±7.14	16.24±7.10	15.93±7.17	0.71
Stone number, % (n)				0.60
1	41.3 (168)	40.6 (41)	41.5 (127)	
2 to 3	4.9 (20)	3 (3)	5.6 (17)	
>3	53.8 (219)	56.4 (57)	52.9 (162)	
Stone impaction, % (n)	38.1 (155)	32.7 (33)	39.9 (122)	0.20
Stone proximal to a stricture, % (n)	19.7 (80)	28.7 (29)	16.7 (51)	0.008
Difficult cannulation/anatomy, % (n)[b]	14 (57)	24.7 (25)	10.5 (32)	<0.001
Mirizzi syndrome, % (n)	8.6 (35)	2 (2)	10.8 (33)	0.004
Devices used for stone extraction after lithotripsy, % (n)				0.03
Extraction balloon	81.8 (328)	86.1 (87)	80.3 (241)	
Retrieval basket	8.2 (33)	5 (5)	9.3 (28)	
Extraction balloon and basket	6.5 (26)	8.9 (9)	5.7 (17)	
Other	3.5 (14)	0	4.7 (14)	
Stent placed, % (n)	30.2 (123)	30.7 (31)	30.1 (92)	0.90
Plastic	86.2 (106)	90.3 (28)	84.8 (78)	
Metallic	13.8 (17)	9.7 (3)	15.2 (14)	
Procedure time, min (mean±SD)	67±34.9	49.9±32.4	73.9±33.5	<0.001

[a]Presence of duodenal diverticula, altered anatomy

Clinical outcomes:

	Total (n=407)	DSOC-LL (n=101)	DSOC-EHL (n=306)	P value
Technical success (complete bile duct clearance), % (n)	97.3 (396)	99.0 (100)	96.7 (296)	0.31
Sessions of LL/EHL to clean the bile duct, % (n)				0.20
1	77.4 (315)[b]	86.1 (87)	74.5 (228)	
>1	19.9 (81)	12.9 (13)	22.2 (68)	
N/A	2.7 (11)	1 (1)	3.3 (10)	

No. of LL/EHL sessions to clear bile duct, median (range)	1 (1 to 4)	1 (1 to 4)	1 (1 to 4)	0.12
ERCPs for additional therapy (remove stents, treat strictures), % (n)	33.7 (137)	32.7 (33)	34 (104)	0.21
Need for ESWL, % (n)	0.5 (2)	1 (1)	0.3 (1)	0.44
Need for surgery, % (n)	2.0 (8)	0	2.6 (8)	0.21
Need for ESWL and surgery, % (n)	0.2 (1)	0	0.3 (1)	1
No. of patients followed up, % (n)	63.6 (259)	31.7 (32)	74.2 (227)	<0.001
Total follow up, d (median) (IQR)	83.5 (33 to 155)	86 (32 to 129)	84 (34 to 151)	0.65
Incomplete stone removal/occult stones, % (n)	6.6 (17)	3.1 (1)	7 (16)	0.07
Management of stone recurrence (n=17) (>1 technique/device used), % (n)				
DSOC with LL/EHL	29.4 (5)	0	31.2 (5)	0.34
Balloon/basket	64.7 (11)	100 (1)	62.5 (10)	0.20
ML	23.5 (4)	0	25 (4)	0.58
ESWL	11.8 (2)	100 (1)	6.2 (1)	0.44
Surgery	5.9 (1)	0	6.2 (1)	1

[b]Of 315 patients, 31 (9.8%) had the gallbladder in situ at the time of the procedure, and a stent was placed (83.9% plastic stents).

Of patients needing surgery, 6 had Mirizzi syndrome and had cholecystectomy with cystic duct stone removal and CBD repair over a tube. The bile duct had not cleared in 1 patient with 2 EHL/LL sessions and a stent was placed; the patient then developed gallstone ileus and had a laparotomy, enterotomy, and removal of gallstone and CBD stones. One patient had intrahepatic stones and had hepatectomy with stone removal (segments 2, 3, 6 and 7). The patient who needed ESWL and

surgery had a retained cystic duct stone in the context of prior cholecystectomy and had a laparoscopy with stone removal.

Recurrence: Incomplete stone clearance/occult stones after a median follow up of 56 days (IQR, 38.5 to 154 days) after reported stone clearance: 6.5% (17/259)

Management of incomplete stone removal:

- Extraction balloon: 64.7% (n=11)
- Repeat DSOC with LL/EHL: 29.4% (n=5)
- ML: 23.5% (n=4)
- ESWL: 11.8% (n=2)
- Surgery: 5.9% (n=1)

Predictors of outcomes:

Difficult anatomy or cannulation was the only predictor that was statistically significantly associated with technical failure on univariable analysis (OR, 3.70; 95% CI 1.05 to 13.1; p=0.04). This association remained statistically significant after multivariable adjustment (adjusted OR, 5.18; 95% CI 1.26 to 21.2; p=0.02).

Prior failed ERCP (OR, 2.85; 95% CI 1.10 to 7.39; p=0.03), more than 1 prior ERCP attempt (OR, 3.77; 95% CI 1.41 to 10.1; p<0.008), and duration of the index DSOC-LL/EHL procedure (OR, 1.02; 95% CI 1.01 to 1.03; p<0.001) were associated with the need for more than 1 DSOC-LL/EHL session on univariable analysis. On multivariate analysis, and after adjusting for potential confounders, only duration of the index procedure (adjusted OR, 1.02; 95% CI 1.01 to 1.03; p<0.001) was a statistically significant predictor of the need for more than 1 DSOC-LL/EHL session.

Key safety findings

Adverse event rates were not statistically significantly different between LL (5%) and EHL (3.3%; p<0.54).

Adverse events: 15 patients (3.7% based on 407 patients)

- Cholangitis: n=6
- Pancreatitis: n=1
- Bleeding: n=1

- Transient bacteraemia: n=1
- Bile duct perforation: n=1
- Abdominal pain: n=5

These were rated as mild (n=10; 66.7%), moderate (n=3; 20%), and severe (n=2; 13.3%), as per American Society for Gastrointestinal Endoscopy lexicon. All patients, including the ones with adverse event rated as moderate and severe, had conservative treatment with intravenous fluids, pain medication, and antibiotics. Bile duct perforation was treated endoscopically with a fully covered self-expandable metal stent in 1 patient. The 2 patients with severe adverse events had cholangitis and were managed with intravenous antibiotics.

Study 7 Bokemeyer A (2020)

Study details

Study type	**Non-randomised controlled study (retrospective)**
Country	Germany (2 centres)
Recruitment period	2015 to 2018
Study population and number	**n=60 (75 cholangioscopies; 44 DSOVC-LL versus 31 DSOVC-EHL)** Patients with refractory biliary stones
Age and sex	Median 66 years; 51.7% (31/60) female
Study selection criteria	Inclusion criteria: all patients ≥ 18 years of age who had a DSOVC-based biliary stone treatment using LL or EHL after conventional endoscopic methods had failed. These methods included standard methods such as stone extraction with baskets and/or balloon catheters. EPLBD, ML or both were routinely done for difficult stones.
Technique	All patients had prophylactic antibiotic treatment. CO2 insufflation was used during the examination. The cholangioscope (DSOVC; Boston Scientific, Marlborough, MA, U.S.) was inserted into the biliary duct in a freehand or guidewire-assisted method. For LL, a Versa-Pulse P20 (Lumenis, Yokneam, Israel) or an Auriga XL 50 W (Starmedtec, Starnberg, Germany) holmium laser was used with Slim line 365 micromillimetre optical fibre. For EHL, a bipolar lithotripsy 1.9 F or 2.4 F catheter probe was used (Autolith Touch, Boston Scientific, Marlborough, MA, U.S. or Walz Elektronik GmbH, Rohrdorf, Germany) with saline solution irrigation controlled over a dedicated irrigation pump. After stone fragmentation, conventional ERC-based techniques were used to extract the remaining fragments. After incomplete biliary stone removal, plastic endoprostheses were regularly placed into the biliary duct.
Follow up	**Not reported**
Conflict of interest/source of funding	HU received honoraria for lectures from Falk Foundation; TB received honoraria for consultancy and lectures from Boston Scientific and Olympus; HN received honoraria for consultancy and lectures from Boston Scientific and Olympus. The remaining authors had no conflicts of interest or financial ties to disclose.

Analysis

Follow-up issues: The paper describes that patients were followed up throughout their hospital stay and only 1 patient was lost to follow up.

Study design issues: This retrospective, multicentre study evaluated the efficacy and safety of DSOVCs with LL or EHL to treat difficult biliary stones even in cases with a previous failure of conventional endoscopic methods. The primary endpoint was to evaluate the stone removal rate per procedure and per patient. Additionally, the per-procedure-based efficacy of LL compared with EHL to treat biliary stones was analysed. Baseline data were not compared between DSOVC-LL and

DSOVC-EHL groups and safety outcomes were not separated. All examinations were done by highly experienced endoscopists.

Study population issues: An endoscopic papillotomy was done or had been previously done before the DSOVC procedure. Of a total of 422 DSOVCs, 75 cholangioscopies were solely done for treating difficult biliary stones using LL or EHL, including 60 initial examinations and 15 repeated DSOVCs. In terms of stone locations, 36% of the biliary stones were located intrahepatic and 64% were located extrahepatic, of which CBD stones were the most frequent (70.8%) followed by hilar stones (18.8%) and cystic duct stones (10.4%).

Key efficacy findings

- Number of patients analysed: 60 (75 cholangioscopies; 44 DSOVC-LL versus 31 DSOVC-EHL)

Procedure characteristics and clinical outcomes

- Median-treated biliary stone number: 1 (IQR 1 to 2)
- Median stone size: 20 mm (IQR 10 to 25 mm)
- Complete stone removal: 66.7% (50/75)
- Incomplete stone removal: 33.3% (25/75)
  - Partial stone removal: 30.7% (23/75)
  - Non-significant stone removal: 2.7% (2/75)

Clinical outcomes: DSOVC-LL versus DSOVC-EHL

	DSOVC-LL (n=44)	DSOVC-EHL (n=31)	P value
Complete stone removal	65.9% (n=29)	67.7% (n=21)	0.868
Incomplete stone removal	34.1% (n=15)	32.3% (n=10)	
Partial stone removal	29.5% (n=13)	32.3% (n=10)	
Non-significant stone removal	4.5% (n=2)	0%	

Stone removal rate after the initial procedure: 45 patients (75%) had a complete stone removal, while 15 patients (25%) had an incomplete stone removal: of these, 9 (60%) needed a second DSOVC, 5 (33.3%) needed an additional follow-up ERC using standard techniques to successfully remove all remaining minor stone fragments and 1 patient (6.7%) with remaining stones, despite being symptom free, decided against another examination.

Treatment success per patient: 95% (57/60)

- Single DSOVC: n=50
- 2 DSOVCs: n=4
- At least 3 DSOVCs: n=3

Treatment failure per patient: 5% (3/60)

Key safety findings

Adverse events: 16% (12/75)

- Cholangitis: 10.7% (8/75), including Grade 1 n=5; Grade 2 n=3; Grade 3 n=1
- Pancreatitis: 5.3% (4/75), including Grade 1 n=2; Grade 2 n=2; Grade 3 n=0
- Bleeding: 0%
- Adverse events after initial examination: 10% (6/60)
- Adverse events after repeated examinations: 40% (6/15)
- Suspected prolonged hospital day due to adverse events, median: 3 days (IQR 2 to 4 days)

Adverse events were statistically significantly less frequent in patients with initial examinations than in patients with repeated examinations (10% versus 40%; p=0.005). All cases of DSOVC-related side effects were treated successfully by conservative therapeutic approaches and no mortalities occurred due to procedure related adverse events. Only 1 patient needed to stay in hospital for more than 10 days because of a procedure-related cholangitis (1.3%); however, the patient could be successfully discharged later.

Study 8 Jakobs R (2007)

Study details

Study type	**Non-randomised comparative study**
Country	Germany (single centre)
Recruitment period	1992 to 2002
Study population and number	n=89 (17 LL transpapillary cholangioscopic versus 72 LL transpapillary fluoroscopic) Patients with difficult bile duct stones
Age and sex	Mean 66 years: 66% (59/89) female
Patient selection criteria	Inclusion criteria: patients who had difficult bile duct stones were treated with LL by ERCP but not via a percutaneous transhepatic approach.
Technique	Patients were sedated with midazolam and/or demerol. A xenon lamp Rhodaniun GG dye-laser (Lithognost; Care Baasel Laser-technik, Starnberg, Germany) with integrated stone-tissue recognising system was used for lithotripsy (wavelength 594 nm; impulse length=2.5 ms; maximal impulse energy=150 mJ). In cases of cholangioscopic control through the transpapillary route, the laser glass fibre (core diameter 200 nm to 300 nm) was placed through the working channel of a babyscope and positioned against the stone under direct view. In the other cases, during an ERCP, the laser glass fibre was positioned at the stone under fluoroscopic guidance through a balloon catheter or a cannula.
Follow up	**Not reported**
Conflict of interest/source of funding	Not reported

Analysis

Follow-up issues: This paper does not state follow-up periods and losses to follow up.

Study design issues: This study compared the results of LL with a stone-tissue recognising system, when guided by fluoroscopy only or by cholangioscopy.

Study population issues: An endoscopic papillotomy with ML was first attempted in all 89 patients. Unsuccessful ESWL and EHL were also done before LL in 35% and 26% of patients respectively. For stone characteristics, 29 patients had 1 stone and 60 had 2 or more stones; stone size was 22 mm (range 9 to 40 mm); 41% of patients had bile duct stenosis.

This study was included in Veld et al. (2018).

Key efficacy findings

- Number of patients analysed: 89

Procedure characteristics and clinical outcomes

	LL transpapillary cholangioscopic (n=17)	LL transpapillary fluoroscopic (n=72)	P value
Median number of impulses	1,800	4,335	0.005
Stone free after LL	82.4%	79.2%	0.706
Stone free after all endoscopic procedures	100%	94.4%	0.458

In cases with stone above a bile duct stricture, cholangioscopic control was more effective than the fluoroscopic one (64.7% versus 31.9%, p=0.007). In cases of stones situated in the distal duct, fluoroscopic guidance was more often used (p=0.002), while in cases of intrahepatic stones, the use of cholangioscopic control was more frequent (p=0.006).

Other analysed factors such as stone diameter, stone number, bile duct size had no influence in the way of laser employment or the resulting stone-free state.

Key safety findings

No laser-therapy related complications were reported in either group.

Study 9 Jiang ZJ (2013)

Study details

Study type	**Non-randomised comparative study (retrospective)**
Country	China (single centre)
Recruitment period	2009 to 2012
Study population and number	**n=93 (45 LL versus 48 traditional method)** Patients with intrahepatic bile duct stones
Age and sex	LL: Mean 53 years; 58% (26/45) female Traditional method: mean 56 years; 52% (25/48) female
Patient selection criteria	Not reported
Technique	LL with or without hepatectomy: Laser pulses of 1.2 microsecond were applied at a repetition rate of 10-15 Hz. A choledochoscope (CHF type P10; Olympus, Tokyo, Japan) was used, a 280 μm flexible fibre was inserted into the working channel of the choledochoscope. Laser wavelengths of 532 nm and 1064 nm as a double pulse was applied with pulse energy of 120 mJ, with the energy being increased to 160 mJ if needed. All patients were routinely placed a T-tube in the CBD. The T-tube was removed in 2 months later if the stones were not found in the intrahepatic bile duct. The traditional methods included forceps and irrigation lithotripsy, choledochoscopic basket catheter lithotomy and hepatectomy.
Follow up	**LL: mean 19 months (range 1 to 40 months)** **Traditional method: mean 43 months (range 41 to 46 months)**
Conflict of interest/source of funding	No benefits in any form have been received or will be received from a commercial party related directly or indirectly to the subject of this article. This study was supported by grants from the Foundation for Innovative Research Groups of the National Natural Science Foundation of China (81121002) and Zhejiang Provincial Natural Science Foundation (Y2100498).

Analysis

Follow-up issues: The paper states that patients were followed up for examinations which included T-tube cholangiography, ultrasonography and laboratory tests, and these examinations were done every 3 months.

Study design issues: This study described the operative choledochoscopic Frequency-Doubled Double pulse Nd:YAG (FREDDY) LL combined with or without hepatectomy for the management of intrahepatic bile duct stones.

Stones detected in the intrahepatic bile duct within 3

months after therapies were considered as residual stones. The occurrence of any operative complications was assessed by patient visit or telephone interview.

Study population issues: At baseline, all patients had more than 1 stone. Biliary cirrhosis was in 18% (8/45) in the LL group and 19% (9/48) in the traditional method group. Biliary stricture presented in 38% (17/45) and 40% (19/48) respectively.

Key efficacy findings

- Number of patients analysed: 93
- In the 45 patients who had choledochoscopic FREDDY LL, 12 had hepatectomy. In the 48 patients who had traditional treatment, 18 had hepatectomy.

Procedure characteristics and clinical outcomes

	LL	Traditional method	P value
Mean procedure time (range, minutes)	112±8.08 (95 to 137)	145±13.07 (106 to 185)	0.01
Clearance rate of stones (%, n)	93.3 (42)[a]	85.4 (41)	0.22
Mean hospitalisation time (range, days)	8.2±1.22 (7 to 12)	9.8±1.63 (7 to 15)	0.17

[a]3 patients had a failed procedure because stones were impacted in the bilateral bile duct and associated with bile duct stricture and biliary cirrhosis.

No recurrence of stones during follow-up period was found in the LL group.

Key safety findings

Complications of LL versus traditional treatment: 11.1% (n=5) versus 22.9% (n=11), p=0.13

	LL	Traditional method
Haemobilia, n	2[b]	
Acute cholangitis, n	3[c]	6[C]
Intraoperative haemorrhage, n		3[d]
Leakage, n		1[e]

[b]During the operation, haemobilia occurred in 2 patients because of mucosal damage induced by insertion of the laser fibre and was successfully treated by bile duct irrigation of 100 millilitre normal saline with 8 mg epinephrine.
[c]These events were treated by administration of antibiotics and T-tube irrigation.
[d]These events were because of forceps injury and were treated by bile duct irrigation of 100 millilitre normal saline with 8 mg epinephrine.

[e]This event was managed by intraperitoneal drainage.

Traditional method group: 1 patient died of liver failure because of liver cirrhosis and intraoperative lithotomy for a long time on the seventh day after surgery.

Validity and generalisability of the studies

- Studies were done in various countries but only 2 studies included UK data.
- Although Jakobs (2007) was included in Veld et al. (2018), the total sample of 2,747 patients was derived from removing duplications.
- Only 1 study (Jiang 2013) included patients who had intrahepatic stones only.
- Where reported, the mean age ranged from 43 to 76 years and more than 50% were female in most of the studies. The follow-up period ranged from 1 month to 40 months.
- There was variation in the samples relating to aetiologies for stone formation, stone characteristics, previous procedures, additional interventions and procedure techniques.
- Four randomised controlled trials were included but no trials that directly compared LL with EHL.
- For efficacy, evidence on the recurrence rate of stones after LL is lacking.

Existing assessments of this procedure

The American Society for Gastrointestinal Endoscopy (ASGE) guideline on the role of endoscope in the evaluation and management of choledocholithiasis was published in 2019. ASGE recommended that “for patients with difficult and large choledocholithiasis ASGE suggest intraductal therapy (cholangioscopy and fluoroscopically guided laser and EHL) or conventional therapy with papillary dilation. The choice of therapy may be impacted by local expertise, cost, and patient and physical preferences (conditional recommendation, very low quality of evidence)”. This recommendation was based on 182 studies (123 studies of conventional therapy, 57 cohort studies of intraductal therapy, and a single randomised trial that compared the 2 approaches).

The European Society of Gastrointestinal Endoscopy (ESGE) guideline on endoscopic management of CBD stones was published in 2019. ESGE recommended that “the use of cholangioscopy-assisted intraluminal lithotripsy (electrohydraulic or laser) as an effective and safe treatment of difficult bile duct stones (strong recommendation, moderate quality evidence). ESGE suggested that the type of cholangioscopy and lithotripsy should depend on local availability and experience (weak recommendation, low quality evidence)”. This recommend

was based on 1 randomised controlled trial, 4 prospective observational studies and 1 meta-analysis (33 studies)

The British Society of Gastroenterology published the guideline on the management of common bile duct stones in 2008 and then updated in 2016. The updated guideline recommended that “cholangioscopy-guided EHL or LL be considered when other endoscopic treatment options fail to achieve duct clearance (low-quality evidence, strong recommendation)”. This recommendation was based on 6 studies.

Related NICE guidance

Below is a list of NICE guidance related to this procedure.

Interventional procedures

- Single-incision laparoscopic cholecystectomy. NICE interventional procedures guidance 508 (2014). Available from https://www.nice.org.uk/guidance/ipg508

NICE guidelines

- Gallstone disease: diagnosis and management NICE clinical guideline 188 (2014). Available from https://www.nice.org.uk/guidance/cg188

Additional information considered by IPAC

Professional experts’ opinions

Expert advice was sought from consultants who have been nominated or ratified by their professional Society or Royal College. The advice received is their individual opinion and is not intended to represent the view of the society. The advice provided by professional experts, in the form of the completed questionnaires, is normally published in full on the NICE website during public consultation, except in circumstances but not limited to, where comments are considered voluminous, or publication would be unlawful or inappropriate. One professional expert questionnaire for LL for difficult-to-treat bile duct stones was submitted and can be found on the NICE website.

Patient commentators’ opinions

NICE’s Public Involvement Programme was unable to gather patient commentary for this procedure.

Company engagement

A structured information request was sent to 1 company who manufacture a potentially relevant device for use in this procedure. NICE received a completed submission. This was considered by the IP team and any relevant points have been taken into consideration when preparing this overview.

References

1. Veld JV, van Huijgevoort NCM, Boermeester MA et al. (2018) A systematic review of advanced endoscopy-assisted lithotripsy for retained biliary tract stones: laser, electrohydraulic or extracorporeal shock wave. Endoscopy 50(9): 896-909
2. Bang JY, Sutton B, Navaneethan U et al. (2020) Efficacy of single-operator cholangioscopy-guided lithotripsy compared with large balloon sphincteroplasty in management of difficult bile duct stones in a randomised trial. Clinical gastroenterology and hepatology: the official clinical practice journal of the American Gastroenterological Association
3. Angsuwatcharakon P, Kulpatcharapong S, Ridtitid W et al. (2019) Digital cholangioscopy-guided laser versus mechanical lithotripsy for large bile duct stone removal after failed papillary large-balloon dilation: A randomized study. Endoscopy 51(11): 1066-73
4. Buxbaum J, Sahakian A, Ko C et al. (2018) Randomised trial of cholangioscopy-guided laser lithotripsy versus conventional therapy for large bile duct stones (with videos). Gastrointestinal endoscopy 87(4): 1050-60
5. Neuhaus H, Zillinger C, Born P et al. (1998) Randomised study of intracorporeal laser lithotripsy versus extracorporeal shock-wave lithotripsy for difficult bile duct stones. Gastrointestinal endoscopy 47(5): 327-34
6. Brewer Gutierrez OI, Bekkali NLH, Raijman I et al. (2018) Efficacy and safety of digital single-operator cholangioscopy for difficult biliary stones. Clinical gastroenterology and hepatology: the official clinical practice journal of the American Gastroenterological Association 16(6): 918-26e1
7. Bokemeyer A, Gerges C, Lang D et al. (2020) Digital single-operator video cholangioscopy in treating refractory biliary stones: a multicentre observational study. Surgical Endoscopy 34: 1914-22
8. Jakobs R, Pererira-Lima JC, Schuch AW et al. (2007) Endoscopic laser lithotripsy for complicated bile duct stones. Is cholangioscopic guidance necessary? Arq Gastroenterol 44(2): 137-40
9. Jiang ZJ, Chen Y, Wang WL et al. (2013) Management hepatolithiasis with operative choledochoscopic FREDDY laser lithotripsy combined with or without hepatectomy. Hepatobiliary & pancreatic diseases international: HBPD INT 12(2): 160-4
10. Buxbaum JL, Abbas Fehmi SM, Sultan S et al. (2019) ASGE guideline on the role of endoscopy in the evaluation and management of choledocholithiasis. Gastrointestinal Endoscopy 89(6): 1075

11. Manes G, Paspatis G, Aabakken L et al. (2019) Endoscopic management of common bile duct stones: European Society of Gastrointestinal Endoscopy (ESGE) guideline. Endoscopy 51(5): 472-91

12. Williams E, Beckingham I, El Sayed G et al. (2017) Updated guideline on the management of common bile duct stones (CBDS). Gut 66(5): 76582

Literature search strategy

Databases	Date searched	Version/files
Cochrane Database of Systematic Reviews – CDSR (Cochrane Library)	03/03/2020	Issue 3 of 12, March 2020
Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane Library)	03/03/2020	Issue 3 of 12, March 2020
HTA database (CRD website)	03/03/2020	
MEDLINE (Ovid)	03/03/2020	1946 to March 02, 2020
MEDLINE In-Process (Ovid) & MEDLINE ePubs ahead of print (Ovid)	03/03/2020	1946 to March 02, 2020
EMBASE (Ovid)	03/03/2020	1974 to 2020 Week 09

Trial sources searched

- Clinicaltrials.gov
- ISRCTN
- WHO International Clinical Trials Registry

Websites searched

- National Institute for Health and Care Excellence (NICE)
- NHS England
- Food and Drug Administration (FDA) - MAUDE database
- Australian Safety and Efficacy Register of New Interventional Procedures – Surgical (ASERNIP – S)
- Australia and New Zealand Horizon Scanning Network (ANZHSN)
- General internet search

The following search strategy was used to identify papers in MEDLINE. A similar strategy was used to identify papers in other databases.

Literature search strategy

Number	Search term
1	Lithotripsy/
2	Lithotripsy, Laser/
3	((electro-hydraul* or electro hydraul* or Electrohydraul* or laser*) adj4 lithotrip*).tw.

4	EHL.tw.
5	cholangioscop*.tw.
6	biliary* tract* endoscop*.tw.
7	or/1-6
8	Biliary Tract/
9	biliary tract*.tw
10	8 or 9
11	Calculi/
12	(Calculi* or stone*).tw.
13	11 or 12 (5
14	10 and 13
15	cholelithiasis/ or cholecystolithiasis/ or choledocholithiasis/ or gallstones/
16	((Biliar* or bile-duct or blie duct) adj4 (stone* or calcul* or colic*)).tw
17	Lithiasis/
18	lithias*.tw
19	stone* format*.tw
20	(cholelit* or cholecystolit* or choledocholit* or gallstone* or gall stone*).tw
21	CPDS.tw.
22	or/14-21
23	7 and 22
24	Holmium laser systems.tw.
25	33.tw.
26	24 or 25
27	23 or 26
28	Animals/ not Humans/
29	27 not 28
30	limit 29 to ed=20010101-20200331
31	limit 30 to English language

Appendix

The following table outlines the studies that are considered potentially relevant to the IP overview but were not included in the summary of the key evidence. It is by no means an exhaustive list of potentially relevant studies.

Additional papers identified

Article	Number of patients/follow up	Direction of conclusions	Reasons for non-inclusion in table 2
Ang TL and Kwek ABE (2019) Safety and efficacy of SpyGlass cholangiopancreatoscopy in routine clinical practice in a regional Singapore hospital. Singapore medical journal 60(10): 538-44	Case series n=47 (mean 63 years; 44.7% [21/47] female) LL n=28	Among the 28 patients with CBD stones, stone fragmentation was successfully started by LL in all cases and complete stone extraction in 26 (92.9%) patients.	Studies with a larger sample and/or better design are included in table 2.
Bark K, Gamblin TC, Zuckerman R et al. (2009) Operative choledochoscopic laser lithotripsy for impacted intrahepatic gallstones: a novel surgical approach. Surg Endosc 23: 221-4	Case series n=5 (mean 70.1 years)	The combination of a surgical enterotomy, biliary endoscopy, and LL provides a novel approach to treat patients with large intrahepatic stones who are not candidates for or have failed ERCP	Studies with a larger sample and/or better design are included in table 2.
Bhandari S, Bathini R, Sharma A et al. (2016) Percutaneous endoscopic management of intrahepatic stones in patients with altered biliary anatomy: A case series. Indian J Gastroenterol 35: 143-6	Case series n=5 (mean 30 years; 20% [1/5] female)	All patients had percutaneous biliary drainage followed by cholangioscopy-guided LL. Crushed stones were pushed across the anastomotic site using basket or balloon and ductal clearance was reported. Good stone pulverisation could be reported in 5 patients (100 %). Complete ductal clearance could be reported in all patients (100 %).	Studies with a larger sample and/or better design are included in table 2.
Bhandari S and Maydeo A (2015) Endoscopic management of radio-opaque bile duct stones. Indian journal of gastroenterology : official journal of the Indian Society of Gastroenterology 34(6): 458-62	Case series n=15 (mean 75 years; 47% [7/15] female) LL n=8	Cholangioscopy guided LL was done in 8 patients (53.34 %) with successful pulverization of RO BDS (100 %).	Studies with a larger sample and/or better design are included in table 2.

Bhandari S, Sharma A, Bathini R et al. (2016) Fracture of basket within the bile duct during Soehendra rescue lithotripsy, extracted after cholangioscope-guided laser lithotripsy. Gastrointestinal endoscopy 83(4): 835-6	Case report n=1 (80 years; female)	Spyglass (Boston Scientific) cholangioscopy-guided Holmium LL was done, and the impacted stone was fragmented.	This is a single case report.
Bratcher J (2009) Choledochoscopy-assisted intraductal shock wave lithotripsy. Gastrointestinal endoscopy clinics of North America 19: 587-96	Review	Efficacy of LL ranges from 80% to more than 90%, and most patients remained stone-free during follow-up evaluation. The presence of biliary strictures and low body mass index were significant risk factors for stone recurrence.	Review article
Brown NG, Camilo J, Nordstrom E et al. (2018) Advanced ERCP techniques for the extraction of complex biliary stones: a single referral centre's 12-year experience. Scandinavian journal of gastroenterology 53: 626631	Non-randomised comparative study n=349 POC with EHL/LL n=46	Complete clearance at the index ERCP was higher in the EPLBD group (89.7%; 35/39) vs. the POC with EHL/LL group (60.9%; 28/46) or the ML group (79.7%; 67/84), p=0.014.	Clinical outcomes for EHL and LL are not separated.
Buxbaum J (2013) Modern management of common bile duct stones. Gastrointestinal endoscopy clinics of North America 23: 251-76	Review	Intraductal laser and EHL may be used to fragment most large bile duct stones, and their use will likely become more widespread with the introduction of single-operator cholangioscopes.	Review article
Caddy GR and Tham TCK (2006) Symptoms, diagnosis and endoscopic management of common bile duct stones. Best practice & research clinical gastroenterology 20: 1085-101	Review	Lithotripsy including LL and EHL are confined to specialised centres and the evidence for their use is based on small studies.	Review article
Cerna VS, Figueroa CA, Mugruza TR et al. (2017) Diagnostic and therapeutic cholangioscopy in biliary diseases: a prospective study in Peru. Rev Gastroenterol Peru 37: 329-34	Case series n=39 (mean 55 years; 74% [29/39] female)	Success rate of complete removal of difficult stones was 65.3%, there was one complication. Two laser sessions were needed in 4 of the 17 patients who obtained complete removal of the stones. The visual impression accuracy of lesions in the bile duct to determine malignancy coincided in all cases	Studies with a larger sample and/or better design are included in table 2.

		with the final diagnosis of the patient.	
Cho J, Buxbaum J, Sahakian AB (2018) Balloon overtube-assisted cholangioscopy and laser lithotripsy of large bile duct stones. VideoGIE 3(7): 217-9	Case report N=1 (86 years; woman)	Large bile duct stones can be successfully managed with balloon enteroscopy-assisted ERCP. Use of the balloon overtube allows for direct cholangioscopy over a guidewire allowing for intraductal lithotripsy to be done.	This is a single case report.
Cho YD, Cheon YK, Moon JH et al. (2009) Clinical role of frequency-doubled double-pulsed yttrium aluminum garnet laser technology for removing difficult bile duct stones (with videos). Gastrointestinal endoscopy 70(4): 684-9	Case series n=52 (mean 65.4 years; 62% [32/52] female)	Of the 52 patients treated via the transpapillary route, there was complete stone removal in 48 patients (92.3%). The complete removal of stones needed a mean of 1.4 (range 1-2) endoscopic sessions. The rate of complications related to LL was 23% (acute pancreatitis, 3 cases; transient haemobilia, 8 cases; acute cholangitis, 1 case).	Studies with a larger sample and/or better design are included in table 2.
Choi HJ, Moon JH, Ko BM et al. (2009) Overtube-balloon-assisted direct peroral cholangioscopy by using an ultra-slim upper endoscope (with videos). Gastrointestinal endoscopy 69(4): 935-40	Case series n=12 (mean 69.1 years; 67% [8/12] female)	LL was successfully done in 1 patient. No procedure-related complication occurred.	Studies with a larger sample and/or better design are included in table 2.
Copelan A and Kapoor BS (2015) Choledocholithiasis: Diagnosis and Management. Techniques in vascular and interventional radiology 18(4): 244-55	Review	Evidence showed that percutaneous transhepatic endoscopic biliary holmium LL could be used to treat complicated biliary stones.	Review article
Cremer A and Arvanitakis M (2016) Diagnosis and management of bile stone disease and its complications. Minerva gastroenterological e dietologica 62: 103-29	Review	Outcomes with LL were similar to those with EHL. Bile duct clearance rates of 88% to 97% have been reported.	Review article
Day A, Sayegh ME, Kastner C et al. (2009) The use of holmium laser technology for the treatment of refractory common bile duct stones, with a short review of the relevant literature. Surgical innovation 16(2): 169-72	Case report n=1	Holmium laser provides an alternative and realistic treatment option for difficult CBD stones.	Studies with a larger sample and/or better design are included in table 2.

Deal AK, Murthy S, Wason S. et al. (2016) Percutaneous transhepatic holmium laser lithotripsy of a large common bile duct stone. Radiology Case Reports 11(4): 361-4	Case report n=1 (58 years; female)	Holmium LL was done with successful fragmentation of the stone and clearance of the obstruction, without complication.	This is a single case report.
Di Mitri R and Mocciaro F (2017) Single-operator holmium laser lithotripsy under direct peroral cholangioscopy using an ultra-slim upper endoscope in a patient with a large stone in the common bile duct. The Turkish journal of gastroenterology : the official journal of Turkish Society of Gastroenterology 28(6): 505-9	Case report n=1 (86 years; female)	Lithotripsy with laser was done under direct view, and the stone was fragmented. All fragments were removed using a retrieval balloon. No complication was seen during the procedure.	This is a single case report.
Doshi B, Yasuda I, Ryozawa S et al. (2018) Current endoscopic strategies for managing large bile duct stones. Digestive endoscopy 30: 59-66	Review	If the CBD stone is >3 cm or if the stone to CBD diameter ratio is >1.0, then cholangioscopy with EHL or LL is likely to be better at stone extraction than ML alone.	Review article
Easler JJ and Sherman S (2015) Endoscopic retrograde cholangiopancreatography for the management of common bile duct stones and gallstone pancreatitis. Gastrointestinal endoscopy clinics of North America 25: 657-75	Review	Electrohydraulic and laser intraductal lithotripsy with the assistance of cholangioscopy is now emerging as a standard of care intervention for large, complex stone burden.	Review article
Franzini TAP, Moura RN and de Moura EGH (2016) Advances in therapeutic cholangioscopy. Gastroenterology research and practice. Gastroenterology research and practice 2016	Review	The effectiveness of EHL and LL is similar in terms of stone fragmentation rates, but LL seems to be more expensive and needs more time.	Review article
Frossard JL and Morel PM (2010) Detection and management of bile duct stones. Gastrointestinal endoscopy 72: 808-16	Review	Stone clearance after EHL or LL with or without additional ERC varies from 77% to 90% after failure of conventional endoscopic fragmentation of BDSs	Review article
Ghersi S, Fuccio L, Bassi M et al. (2015) Current status of peroral cholangioscopy in biliary tract diseases. World journal of gastrointestinal endoscopy 7: 510-7	Review	Several studies have reported high success rates in clearing the bile ducts of stones after a cholangioscopic EHL or LL, ranging from 80% to 100%; these results frequently occur in only 1	Review article

		session. For intrahepatic stones, the thinner LL probe is generally preferred to the EHL probe, whereas the EHL is the most widely used technique, particularly with the SpyGlass system, because of the dedicated irrigation channel providing the flowing water that is needed to perform the EHL.	
Gokcen K, Atabey M, Gokcen P et al. (2017) Laparoscopy-assisted micropercutaneous choledocholithotripsy with holmium laser in a cholecystectomized patient: An initial report. Wideochirurgia I Inne Techniki Maloinwazyjne 12(4): 443-7	Case report n=1 (60 years; female)	Laparoscopy-assisted micropercutaneous choledocholithotripsy with holmium laser was used to treat a cholecystectomised patient and the patient was discharged without any complications.	This is a single case report.
Hammoudi N, Brieau B, Barret M. et al. (2018) Mirizzi's syndrome in Roux-en-Y bypass patient successfully treated with cholangioscopically-guided laser lithotripsy via percutaneous gastrostomy. Endoscopy International Open 6(7): e826-e9	Case report n=1 (59 years; female)	Intracorporeal LL was used to treat a patient with difficult bile duct stone. At the end of the procedure, the main biliary tract and the cystic stump were completely empty of any stone residue and biliary drainage was complete with diffuse pneumobilia.	This is a single case report.
Hazey JW, McCreary M, Guy G et al. (2007) Efficacy of percutaneous treatment of biliary tract calculi using the holmium:YAG laser. Surgical endoscopy 21(7): 1180-3	Case series n=13 (mean 69 years; 46% [6/13] female)	The use of PTHC with holmium:YAG laser ablation is safe and efficacious but needs prolonged biliary access and often multiple procedures to ensure clearance of all calculi.	Studies with a larger sample and/or better design are included in table 2.
Healy K, Chamsuddin A, Spivey J et al. (2009) Percutaneous endoscopic holmium laser lithotripsy for management of complicated biliary calculi. JSLS : Journal of the Society of Laparoendoscopic Surgeons 13(2): 184-9	Case series n=9 (mean 65.6 years; 56% [5/9] female)	All 9 patients (100%) were visually stone-free after one endoscopic procedure. No major perioperative complications occurred. Percutaneous endoscopic holmium LL was both safe and efficacious.	Studies with a larger sample and/or better design are included in table 2.
Hochberger J, Tex S, Maiss J et al. (2003) Management of difficult common bile duct stones. Gastrointestinal	Review	ESWL, EHL, and LL yield similar success rates of 80% to 95% and may be used complementarily in	Review article

endoscopy clinics of North America 13: 623-34		endoscopic centres. EHL is rarely used because of its high potential for tissue damage and bleeding.	
Ierardi AM, Fontana F, Petrillo M et al. (2013) Percutaneous transhepatic endoscopic holmium laser lithotripsy for intrahepatic and choledochal biliary stones. International journal of surgery 11: S36-S39	Case series n=10 (mean 76.6 years; 30% [3/10] female)	Technical success rate was 100%. The overall clinical success rate was 100%. No patients had additional procedures for retained stones or developed de novo strictures or other complications related to the procedure. Hospital stay was no more than 4 days after the procedure.	Studies with a larger sample and/or better design are included in table 2.
Jakobs R, Hartmann D, Kudis V et al. (2006) Risk factors for symptomatic stone recurrence after transpapillary laser lithotripsy for difficult bile duct stones using a laser with a stone recognition system. European journal of gastroenterology& hepatology 18(5): 469-73	Case series n=80 (median 65.8 years; 71.8% [51/80] female)	The median period between LL and recurrence was 40 months. The presence of a bile duct stenosis (p=0.032) and a body-mass index below 25 (p=0.025) were statistically significantly associated with an increased risk for stone recurrence.	Studies with a larger sample and/or better design are included in table 2.
Jalali F, Roorda AK and Sundaram U (2011) Biliary stone extraction techniques: old and new. Practical gastroenterology 35: 17-46	Review	Intracorporeal EHL or LL can be attempted under direct choledochoscopic visualisation. The laser lithotripters are far too expensive to encourage widespread implementation and therefore EHL has been used more frequently.	Review article
Jin P, Jing WT, Zhan WP et al. (2019) Efficacy and safety of laparoscopic holmium laser lithotripsy in the treatment of complicated biliary calculus: A PRISMA-compliant systematic reviews and meta-analysis. Medicine 98(4): e14286	Systematic review and meta-analysis n=5 studies (541 patients; mean 46 to 58 years; 51% [277/541] female)	Compared with LBDE, LHLL was associated with shorter operative time (WMD=-40.04, p<0.001) and lower estimated blood loss (WMD=-56.42, p<0.001), lesser duration of hospitalisation (WMD=-3.93, p<0.001) and lower rate of residual stone (OR=0.13, p<0.001). There was no statistically significant differences in bile leakage (OR=0.48, p=0.23) and haemobilia (OR=0.49, 0.41).	LL was used but surgical technique was involved so this study presented a different approach.

Jones T, Musawi JA, Navaratne L et al. (2019) Holmium laser lithotripsy improves the rate of successful transcystic laparoscopic common bile duct exploration. Langenbeck's archives of surgery 404: 985-92	Non-randomised comparative study n=179 (median 56 years; 66.5% [119/179] female) LABEL n=36 versus LCBDE n=143	LABEL is an effective adjunct to LCBDE that can increase the rate of successful transcystic approach but is associated with an increased risk of major complications, though none specifically attributable to the laser itself.	Studies with a larger sample and/or better design are included in table 2.
Katanuma A, Maguchi H, Osanai M et al. (2010) Endoscopic treatment of difficult common bile duct stones. Digestive endoscopy 22: S90-S97	Review	Although sufficient efficacy can be obtained with laser fragmentation, there are disadvantages (more than 1 treatment session is necessary, 2 experienced endoscopists are needed, the equipment is expensive and preparations are time-consuming.	Review article
Kedia P and Tarnasky PR (2019) Endoscopic management of complex biliary stone disease. Gastrointestinal endoscopy clinics of North America 29: 257-75	Review	Evidence shows that index and overall biliary clearance was 77.4% (74.5% EHL and 86.1% LL) and 97.3% (96.7% EHL and 99% LL) of patients. The severe and overall AE rate was 0.5% and 3.7%.	Review article
Kim HI, Moon JH, Choi HJ et al. (2011) Holmium laser lithotripsy under direct peroral cholangioscopy by using an ultra-slim upper endoscope for patients with retained bile duct stones (with video). Gastrointestinal endoscopy 74(5):1127-32	Case series n=13 (mean 66 years; 46% [6/13] female)	Holmium LL under direct POC by using an ultra-slim endoscope was successful in 11 of 13 patients (84.6%). Although direct POC was successful, holmium LL failed in 2 patients because of inaccurate targeting of the laser fibre to stones. There were no procedure-related complications except one case of mild pancreatitis.	Studies with a larger sample and/or better design are included in table 2.
Kim TH, Oh HJ, Choi CS et al. (2008) Clinical usefulness of transpapillary removal of common bile duct stones by frequency doubled double pulse Nd:YAG laser. World journal of gastroenterology 14(18): 2863-6	Case series n=17 (mean 67.8 years; 59% [10/17] female)	There was bile duct clearance in 15 of 17 patients (88%). The mean number of treatment sessions was 1.7±0.6. Endoscopic stone removal could not be done in 2 patients (7%). Adverse effects were noted in 3 patients	Studies with a larger sample and/or better design are included in table 2.

		(haemobilia, pancreatitis, and cholangitis).	
Korrapati P, Ciolino J, Wani S et al. (2016) The efficacy of peroral cholangioscopy for difficult bile duct stones and indeterminate structures: a systematic review and meta-analysis. Endoscopy International Open 04: E263-E75	Systematic review and meta-analysis n=49 studies	The overall estimated stone clearance rate was 88% (95% CI 85% to 91%). The accuracy of POC was 89% (95% CI 84% to 93%) for making a visual diagnosis and 79% (95% CI 74% to 84%) for making a histological diagnosis. The estimated overall adverse event rate was 7% (95 % CI 6% to 9%).	The outcomes for LL are not reported separately.
Kudaravalli P, Aslam B and Gabr M (2018) A review of lithotripsy applications in gastroenterology. Practical gastroenterology 42: 50-9	Review	Lithotripsy is used for various gastrointestinal conditions and EHL is 1 of the commonly used lithotripsy methods in gastroenterology.	Review article
Laing PJ and Adler DG (2013) Difficult bile duct stones: a review of current endoscopic treatments. Practical gastroenterology 37: 10-26	Review	LL has been shown to have good overall outcomes for treating refractory stones. Complications include pancreatitis, cholangitis, duct trauma, haemobilia, fever and pain.	Review article
Lamanna A, Maingard J, Tai J et al. (2019) Percutaneous transhepatic laser lithotripsy for intrahepatic cholelithiasis. Diagnostic and Interventional Imaging 100: 793-800	Case series n=12 (mean 46 years; 58% [7/12] female)	A 100% success rate in fragmenting the target stone(s) was reported and 11/12 patients (92%) had successful first pass extraction of target stone fragments. Two patients (2/12; 17%) needed repeat lithotripsy. One patient (1/12; 8%) experienced a major complication in the form of cholangitis. Of patients with long-term follow up, 4/10 (40%) had recurrence of intrahepatic calculi with a mean time interval of 31 months.	Studies with a larger sample and/or better design are included in table 2.
Lee SI, Lim BH, Heo WG et al. (2016) Successful Removal of a Large Common Bile Duct Stone by Using Direct Peroral Cholangioscopy and Laser Lithotripsy in a Patient with Severe Kyphosis. Clinical endoscopy 49(4): 395-8	Case report n=1 (75 years; female)	Holmium LL under peroral cholangioscopy was done by using an ultra slim endoscope, and the large stone in the CBD was successfully fragmented and removed without complications.	This is a single case report.

Lee SK and Kim MH (2009) Updates in the treatment of gallstones. Expert review of gastroenterology & hepatology 3(6): 649-60	Review	The success rate of bile duct stone clearance with LL has been reported to range from 64 to 97%.	Review article
Lee JE, Moon JH, Choi HJ et al. (2010) Endoscopic treatment of difficult bile duct stones by using a double-lumen basket for laser lithotripsy--a case series. Endoscopy 42(2):169-72	Case series n=14 (range 50 to 83 years; 57% [8/14] female)	Stones were successfully fragmented in 13 of 14 patients, and 13 patients eventually became stone-free. ML was applied in 2 patients with biliary strictures. Minor complications were noted in 3 patients, including transient haemobilia in 1 patient.	Studies with a larger sample and/or better design are included in table 2.
Lee TY, Cheon YK, Choe WH et al. (2012) Direct cholangioscopy-based holmium laser lithotripsy of difficult bile duct stones by using an ultrathin upper endoscope without a separate biliary irrigating catheter. Photomedicine and laser surgery 30(1): 31-6	Case series n=10 (mean 63.3 years; 40% [4/10] female)	The overall success rate of bile duct clearance was 90% (9 of 10 patients) and the mean number of treatment sessions was 1.2 (range 1 to 2). ML was done to complete stone removal in 1 patient (10%) who had a distal CBD stricture. One patient experienced mild cholangitis following LL.	Studies with a larger sample and/or better design are included in table 2.
Lei J, Wang J, Li Q et al. (2016) Laparoscopic Transcystic Common Bile Duct Exploration: T-Shaped Incision of Cystic Duct with FREDDY Laser Lithotripsy. Journal of laparoendoscopic & advanced surgical techniques. Part A 26(8): 646-51	Case series n=32 (mean 54.9 years; 59% [19/32] female)	The modified LTCBDE with a T-shaped incision of the cystic duct and FREDDY LL is a safe and effective means of managing gallstones concomitant with large or impacted CBD stones.	Studies with a larger sample and/or better design are included in table 2.
Lerardi AM, Fontana F, Petrillo M et al. (2013) Percutaneous transhepatic endoscopic holmium laser lithotripsy for intrahepatic and choledochal biliary stones. International Journal of Surgery 11: S36-S39	Case series n=10 (mean 76.6 years; 30% [3/10] female)	Complicated or large biliary calculi can be treated successfully using percutaneous transhepatic endoscopic holmium LL. In selected patients, this approach should become the first choice of treatment after other treatments are rejected.	Studies with a larger sample and/or better design are included in table 2.
Liu J, Jin L, Zhang Z (2016) Laparoscopic Transcystic Treatment Biliary Calculi by Laser Lithotripsy. JSLS : Journal of the Society of Laparoendoscopic Surgeons 20(4)	Case series n=89 (mean 52.4 years; 46% [41/89] female)	Application of laparoscopy and the ultrathin choledochoscope in combination with dual-band, dual-pulse LL via a transcystic approach is a	Studies with a larger sample and/or better design are included in table 2.

		safe, feasible, and highly effective technique for treating gallbladder and biliary tract calculi, especially those that are difficult to extract.	
Liu R, Zhang B and Liu D (2018) Peroral cholangioscopy-guided laser lithotripsy to teat regional hepatolithiasis without stricture. Digestive Endoscopy 30: 537-8	Case report n=1 (23 years; female)	Lithotripsy was carried out using holmium laser under the guidance of SpyGlass. Proximal ducts were then seen. The stone fragments were removed using balloon and basket. Clinical outcomes were satisfactory. No evidence of intrahepatic stones was seen on follow-up MRCP 1 month later	This is a single case report.
Liu F, Jin ZD, Zou DW et al. (2011) Efficacy and safety of endoscopic biliary lithotripsy using FREDDY laser with a radiopaque mark under fluoroscopic guidance. Endoscopy 43(10):918-21	Case series n=30 (mean 62.2 years)	Complete bile duct clearance was reported in 27 of the 30 patients (90 %). Adverse events were noted in 2 patients, who both developed acute mild pancreatitis.	Studies with a larger sample and/or better design are included in table 2.
Lv S, Fang Z, Wang A et al. (2017) Choledochoscopic holmium laser lithotripsy for difficult bile duct stones. Journal of laparoendoscopic & advancedsurgical techniques. Part A 27(1): 24-7	Case series n=28	Complete stone clearance was obtained in 24 patients; small numbers of residual stones in the left or right hepatic duct were found in 4 patients. No severe complications such as haemobilia and bile duct injuries occurred.	Studies with a larger sample and/or better design are included in table 2.
Maggi U, Paone G, Lauro R et al. (2016) Holmium Intraductal Laser Lithotripsy of Biliary Stones in Liver Grafts. Transplantation proceedings 48(2): 380-2	Case series n=390 Biliary stones n=14	When usual treatments are unsuccessful and biliary stones are large, their fragmentation and treatment could be done with holmium intraductal LL, a promising procedure after LT.	Studies with a larger sample and/or better design are included in table 2.
Maydeo A, Kwek BEA, Bhandari S et al. (2011) Single-operator cholangioscopy-guided laser lithotripsy in patients with difficult biliary and pancreatic ductal stones (with videos). Gastrointestinal endoscopy 74(6): 1308-14	Case series n=64 (mean 48 years; 44% [27/62] female)	Fifty of 60 patients (83.3%) had complete biliary duct clearance after a single session; 10 patients needed an additional session. All pancreatic duct stones were fragmented in a single session. Complications were mild and were encountered in 13.5% of patients; fever (n=3), transient	Studies with a larger sample and/or better design are included in table 2.

		abdominal pain (n=4), and biliary stricture (n=1).	
Maydeo AP, Rerknimitr R, Lau JY et al. (2019) Cholangioscopy-guided lithotripsy for difficult bile duct stone clearance in s single sessions of ERCP: results from a large multinational registry demonstrate high success rates. Endoscopy 51: 922-9	Case series (registry) n=156 (median 62 years; 61% [95/156] female) LL n=117	POCS-guided lithotripsy is highly effective for clearance of difficult bile duct stones in a single procedure and successfully salvages most prior treatment failures. It may also be considered first-line therapy for patients with difficult choledocholithiasis to avoid serial procedures.	Limited outcomes for LL are reported and studies with a larger sample and/or better design are included in table 2.
McHenry L and Lehman G (2006) Difficult bile duct stones. Current treatment options in gastroenterology 9: 123132	Review	A stone-free state was accomplished in 72% (range 64% to 97%) of patients, which is lower than the compiled results for EHL (85%). Complications with pulsed dye LL, including haemobilia and fever/cholangitis, occurred in 7% of patients, compared with 9% in EHL.	Review article
Moon JH, Choi HJ and Ko BM (2011) Therapeutic role of direct peroral cholangioscopy using an ultra-slim upper endoscope. J Hepatobiliary Pancreat Sci 18: 350-6	Review	Evidence shows that the overall success rate of bile duct clearance by lithotripsy (EHL or LL) under direct POC by a single endoscopist was 88.9%, with an average of 1.6 treatment sessions per patient. No procedure-related complications were seen.	Review article
Moon JH, Ko BM, Choi HJ et al. (2009) Direct peroral cholangioscopy using an ultra-slim upper endoscope for the treatment of retained bile duct stones. J Hepatobiliary Pancreat Sci 18:350–6	Case series n=18 (mean 66.5 years; 61% [11/18] female)	The overall success rate of bile duct clearance by lithotripsy under direct POC by a single endoscopist was 88.9 % (16/18). Stone fragmentation under direct POC was successfully done in 9 patients using EHL and in 7 patients using LL. Procedure-related complications were not seen.	Studies with a larger sample and/or better design are included in table 2.
Mori A, Ohashi N, Nozaki M et al. (2012) Feasibility of duodenal balloon-assisted direct cholangioscopy with an	Case series	DBA-DC appears to be sufficiently feasible and may be useful as an alternative technique in	Studies with a larger sample and/or better

ultrathin upper endoscope. Endoscopy 44(11): 1037-44	n=40 (mean 76 years; 38% [15/40] female) LL n=3	cases that elude successful diagnosis and/or therapy with conventional ERCP.	design are included in table 2.
Muzio S, Cassini P, Martino V et al. (2008) Transcystic video laparoscopy for choledocholithiasis with holmium: YAG laser lithotripsy. A case report.Chirurgia italiana 60(1): 119-23	Case report n=1 (65 years; male)	Holmium: YAG LL was found to be a valuable aid in reducing the percentage of choledochotomies when calculi are too large to be retrieved from the CBD with normal graspers.	This is a single case report.
Nakai Y, Sato T, Hakuta R et al. (2020) Management of difficult bile duct stones by large balloon, cholangioscopy, enteroscopy and endosonography. Gut and Liver 14: 297-305	Review	Evidence shows that in general LL had a higher complete ductal clearance rate than EHL. The adverse event rate was significantly lower in LL than in EHL.	Review article
Navarro-Sanchez A, Ashrafian H, Segura-Sampedro JJ et al. (2017) LABEL procedure: Laser-Assisted Bile duct Exploration by Laparoendoscopy for choledocholithiasis: improving surgical outcomes and reducing technical failure. Surgical endoscopy 31(5): 2103-8	Case series n=18 (mean 53 years; 44% [8/18] female)	Choledocholithiasis was successfully treated in 18 patients using laparoscopic holmium LL (transcystically in 14 patients). There was 1 failure where a CBD stricture prevented the scope reaching the stone. Two medical complications were recorded (Clavien–Dindo I and II). There were no mortalities or re-interventions.	Studies with a larger sample and/or better design are included in table 2.
Neuhaus H (2003) Endoscopic and percutaneous treatment of difficult bile duct stones. Endoscopy 35:31-4	Review	There were comparable success rates of about 80%with retrograde pulsed dye laser lithotripsy in smaller series.	Review article
Nezami N, Benchetrit L, Latich I. et al. (2019) Cholangiolithiasis postliver transplantation: Successful treatment utilizing percutaneous transhepatic cholangioscopy and laser lithotripsy. Radiology Case Reports 14(12): 1459-66	Case report n=1 (29 years; male)	Percutaneous transhepatic cholangioscopy and choledochoscopy with LL is a minimally invasive and efficient technique for removal of intra- and extrahepatic bile duct stones postliver transplantation	This is a single case report.
Ni ZK, Jin HM, Li XW et al. (2018) Combination of electronic choledochoscopy and holmium laser lithotripsy for complicated biliary calculus treatment: A New	Case series n=20 (mean 61 years; 65% [13/20] female)	The clearance rate of stone was 18/20 (90%). No mortality existed in this study; however, 1 patient developed acute pancreatitis. The	Studies with a larger sample and/or better design are included in table 2.

Exploration. Surgical laparoscopy, endoscopy & percutaneous techniques 28(3):e68-e73		combination of holmium LL and electronic choledochoscopy for complicated biliary calculi is safe, reliable, and minimally invasive and has low residual stone rate.	
Patel SN, Rosenkranz L, Hooks B et al. (2014) Holmium-yttrium aluminum garnet laser lithotripsy in the treatment of biliary calculi using single-operator cholangioscopy: a multicenter experience (with video). Gastrointestinal endoscopy 79(2): 344-8	Case series n=69 (median 60 years; 62% [43/69] female)	SOC-guided Ho:YAG lithotripsy is a safe and effective treatment for patients with difficult to manage biliary stones.	Studies with a larger sample and/or better design are included in table 2.
Petersson U; Johansen D, Montgomery A (2015) Laparoscopic transcystic laser lithotripsy for common bile duct stone clearance. Surgical laparoscopy, endoscopy &percutaneous techniques 25(1): 33-6	Case series n=8 (mean 52 years; 38% [3/8] female)	Duct clearance was reported in all (n=8) patients as a single-stage procedure, although 1 had to be converted to open surgery. Median operation time was 225 minutes and hospital stay was 2 days. There was no postoperative morbidity or mortality	Studies with a larger sample and/or better design are included in table 2.
Pohl J and Ell C (2011) Direct transnasal cholangioscopy with ultraslim endoscopes: a one-step intraductal balloon-guided approach. Gastrointestinal endoscopy 74(2): 309-16	Case series n=25 (mean 73 years; 32% [8/25] female) LL n=1	One-step TNC with an ultraslim endoscope allows direct visual examination and therapeutic intervention in the bile ducts in most patients with biliary disease. However, development of further accessory instruments will be needed to improve the success rate.	Studies with a larger sample and/or better design are included in table 2.
Polite NM, Brown R and Braveman J (2013) The use of laser lithotripsy status post cholecystostomy tube placement without interval cholecystectomy for calculous cholecystitis in a patient unfit for general anaesthesia. Surg Laparosc Endosc Percutan Tech 23:e229-e231	Case report n=1 (70 years; female)	On postoperative day 1, her hepatic function panel was within normal limits. Upon 1-year follow-up evaluation, the patient remains on ursodiol and has had no biliary complications or recurrent symptoms. The site of the cholecystostomy tube tract has healed without difficulty.	This is a single case report.
Prinz C, Weber A, Goecke S et al. (2014) A new peroral mother-baby endoscope	Case series	Giant or intrahepatic bile duct stones were treated by visually guided LL and	Studies with a larger sample and/or better

system for biliary tract disorders. World journal of gastrointestinal endoscopy 6(1):20-6	n=76 (mean 63 years; 53% [40/76] female) LL n=9	were subsequently successfully removed. Most of the stones were cleared in 1 session. Four patients had to have a second POCS to remove the remaining stones and to determine the absence of further stones.	design are included in table 2.
Raijman I (2000) Intracorporeal lithotripsy in the management of biliary stone disease. Seminars in laparoscopic surgery 7: 295-301	Review	The efficacy of LL is between 85% and 95% and main reasons for failure include inappropriate target contact and equipment malfunction.	Review article
Ray AA, Davies ET, Duvdevani M et al. (2008) The management of treatment-resistant biliary calculi using percutaneous endourologic techniques. Can J Surg 52: 407-12	Case series n=19 (mean 69.3 years; 74% [14/19] female)	Evidence showed that use of the Ho:YAG laser was both safe and effective in the treatment of choledocholithiasis. All patients but 1 were stone-free when the laser was used (92.3%).	Studies with a larger sample and/or better design are included in table 2.
Rosenkranz L, Patel SN and Kahaleh M (2012) Endoscopic retrograde cholangiopancreatography for stone burden in the bile and pancreatic ducts. Gastrointestinal endoscopy clinics of North America 22: 435-50	Review	Evidence showed holmium to be effective in 90% to 100% of patients for stone fragmentation, and an average of 1.5 sessions were needed to clear the ducts, with complication rates ranging from 4% to 13%.	Review article
Rosin D, Brasesco O, Rosenthal RJ (2000) A review of technical and clinical aspects of biliary laser lithotripsy. Journal of clinical laser medicine & surgery 18(6): 301-7	Review	Recent technical advances have made the use of laser energy for fragmentation of biliary calculi possible. It is a valid option for treatment of "difficult" stones, when other methods have failed or as a primary treatment in certain situations. The technical complexity and the high cost limit its use for specialised centres.	Review article
Sauer BG, Cerefice M, Swartz DC et al. (2013) Safety and efficacy of laser lithotripsy for complicated biliary stones using direct choledochoscopy. Digestive diseases and sciences 58(1): 253-6	Case series n=20 (mean 61 years; 70% [14/20] female)	Most (18/20, 90%) had final clearance after a mean of 1.4±0.8 (29 total) laser sessions and a mean of 1.9±0.8 (38 total) ERCP sessions. Five complications occurred: 2 patients needed postprocedure	Studies with a larger sample and/or better design are included in table 2.

		admission for pain and 3 patients had bile leaks. All bile leaks were minor and resolved after biliary stenting.	
Schatloff O, Rimon U, Garniek A et al. (2009) Percutaneous transhepatic lithotripsy with the holmium: YAG laser for the treatment of refractory biliary lithiasis. Surgical laparoscopy, endoscopy & percutaneous techniques 19(2): 106-9	Case series n=14 (mean 63.6 years; 57% [8/14] female)	Percutaneous choledochoscopy with holmium LL is a safe and effective minimally invasive technique to treat complex biliary stone disease and may preclude high-risk open biliary tract surgery.	Studies with a larger sample and/or better design are included in table 2.
Schlesinger NH, Svenningsen P, Frevert S et al. (2015) Percutaneous yttrium aluminum garnet-laser lithotripsy of intrahepatic stones and casts after liver transplantation. Liver transplantation : official publication of the American Association for the Study of Liver Diseases and the International Liver Transplantation Society 21(6): 831-7	Case series n=18	In all but 1 patient (17/18 or 94%), it was technically feasible to clear all BDSs with a mean of 1.3 sessions. PTCSL was unsuccessful in 1 patient because of multiple stones impacting the bile ducts bilaterally; 17% had early complications (Clavien II). All biliary casts were successfully cleared; 39% had total remission; 61% needed additional interventions in the form of percutaneous transhepatic cholangiography and dilation (17%), re-PTCSL (11%), self-expandable metallic stents (22%), or hepaticojejunostomy (6%); and 22% eventually had retransplantation. Non-anastomotic strictures were significantly associated with treatment failure.	Studies with a larger sample and/or better design are included in table 2.
Seelhoff A, Schumacher B and Neuhaus H (2011) Single operator peroral cholangioscopic guided therapy of bile duct stones. J Hepatobiliary Pancreat Sci 18: 346-349	Review	First clinical data show a high stone clearance rate of single operator guided SpyGlass lithotripsy in patients with previous failure of conventional endoscopic therapy.	Review article
Shamamian P and Grasso M (2004) Management of complex biliary tract calculi with a holmium laser. Journal of gastrointestinal surgery : official journal of the Society	Case series n=36 (64% [23/36] female)	Complete stone clearance needed an average of 3.9 procedures (range 1 to 15) for patients with primary intrahepatic	Studies with a larger sample and/or better design are included in table 2.

for Surgery of the Alimentary Tract 8(2): 191-9		calculi and 2.6 procedures (range 1 to 10) for patients with secondary intrahepatic calculi regardless of stone composition. No patient needed hepatic resection and no complications or deaths were attributed to the holmium laser.	
Shim CS (2010) How should biliary stones be managed? Gut and Liver 4: 161-72	Review	Lithotripsy is a relatively safe and effective treatment for selected difficult bile duct stones. Treatment of difficult biliary stones is generally accomplished using a multimodal approach, with mechanical and/or shock-wave lithotripsy (EHL and LL or ESWL).	Review article
Sninsky BC, Sehgal PD, Hinshaw L et al. (2014) Expanding endourology for biliary stone disease: the efficacy of intracorporeal lithotripsy on refractory biliary calculi. Journal of Endourology 28: 877-80	Case series n=13 (mean 52 years; 23% [3/13] female) LL=5	Evidence showed III to be effective in treating refractory biliary calculi and no follow-up procedures were needed.	Studies with a larger sample and/or better design are included in table 2.
Stefanidis G, Christodoulou C, Manolakopoulos S et al. (2012) Endoscopic extraction of large common bile duct stones: A review article. World journal of gastrointestinal endoscopy 4: 167-79	Review	EHL and LL yield similar success rates and may be used complementarily in referral centres.	Review article
Takayama S (2009) Percutaneous laser lithotripsy for gallbladder and common bile duct stones. Surgical laparoscopy, endoscopy & percutaneous techniques 19(4): e135-7	Case report n=1 (52 years; male)	The result was successful non-operative treatment of a patient with Mirizzi syndrome involving a CBD stone, using LL via a cholangiofiber scope. This case suggests that LL is a feasible optional treatment method for severe cholecystitis patients having a percutaneous drainage tube.	This is a single case report.
Takeshi O and Higuchi K (2016) A review of treatment options for bile duct stones. Expert review of	Review	ESWL or the laser in EHL should be considered for bile duct stones over 25 mm in diameter. POCS has	Review article

gastroenterololyg & hepatology 10: 1271-8		improved, and digital single-operator cholangioscopy may offer improved technical success rates for LL or EHL under POCS. Prospective evaluations are warranted.	
Teichman JM, Schwesinger W H, Lackner J et al. (2001) Holmium: YAG laser lithotripsy for gallstones. A preliminary report. Surgical endoscopy 15(9): 1034-7	Case series n=3 (mean 44 years; 100% male)	All of the stones were cleared successfully in a single therapeutic setting. No complications developed, and all patients remained free of recurrence during a 6-month follow-up period.	Studies with a larger sample and/or better design are included in table 2.
Tellez-Avila FI et al. (2016) Percutaneous laser application using the SpyGlass system in a patient with intrahepatic lithiasis, liver cirrhosis and surgically altered anatomy. Endoscopy 48: E49-E50	Case report n=1 (35 years; woman)	The SpyGlass system was used and LL was applied, with the stone fragments being removed in an antegrade fashion using the balloon of a biliary extraction catheter. On follow-up MRCP, no evidence of intrahepatic stones was seen.	This is a single case report.
Tellez-Avila FI, Pattel S, Duarte-Medrano G et al. (2017) A challenging case of giant biliary stones in a patient with situs inversus totalis: conventional ERCP combined with intraductal cholangioscopy and laser lithotripsy. Endoscopy49(10): e248-e249	Case report n=1 (65 years; male)	Intraductal cholangioscopy using the SpyGlass DS system and LL were done successfully. A fully covered, biliary, self-expandable metal stent was placed across the stenosis in the distal bile duct. Fragmentation of the large stones was noted, and the patient was asymptomatic 6 weeks later.	This is a single case report.
Trikudanathan G, Arain MA, Attam R et al. (2014) Advances in the endoscopic management of common bile duct stones. Nature reviews: Gastroenterology & Hepatology 11: 535544	Review	Cholangioscopically directed electrohydraulic and LL enables fragmentation of refractory stones.	Review article
Trikudanathan G, Navaneethan U and Parsi MA (2013) Endoscopic management of difficult common bile duct stones. World J Gastroenterol 19: 165-73	Review	Ductal clearance can be safely achieved with peroral cholangioscopy guided laser or EHL in most cases where other endoscopic treatment modalities have failed.	Review article
Turowski F, Hugle U, Dormann A et al. (2018)	Case series	SOC-guided lithotripsy was done in 54 patients	Studies with a larger sample

Diagnostic and therapeutic single-operator cholangiopancreatoscopy with SpyGlassDS™: results of a multicentre retrospective cohort study. Surgical endoscopy 32: 3981-8	n=250 (4 LL)	(75 procedures) and EHL or LL was used for the treatment of large bile duct stones.	and/or better design are included in table 2.
Uchiyama K, Onishi H, Tani M et al. (2002) Indication and procedure for treatment of hepatolithiasis. Arch Surg 137: 149-53	Case series n=89 (median 56.9 years; 52% [46/89] female) LL n=3	In PTCSL procedures, favourable results have been obtained using the Ho:YAG laser for fracturing intrahepatic stones.	Studies with a larger sample and/or better design are included in table 2.
Wang W, Shi X, Jin Z et al.(2017) Endoscopic laser lithotripsy and lithotomy through the lumen-apposing metal stent for a giant gallstone after EUS gallbladder drainage. VideoGIE2(5): 112-5	case report n=1 (65 years; female)	Endoscopic LL and lithotomy is safe and feasible for gallstones through the LAMS. This may be an effective alternative treatment for patients who are not suitable for open surgery.	This is a single case report.
Watson RR, Parsi MA, Aslanian HR et al. (2018) Biliary and pancreatic lithotripsy devices. Gastrointest Endosc 3: 329-38	Review	EHL and LL are effective at ductal clearance when conventional techniques are unsuccessful, although they usually need direct visualisation of the stone by the use of cholangiopancreatoscopy and are often limited to referral centres.	Review article
Wong JC, Lam SF and Lau JY (2015) Novel use of an optical fiber in triple-lumen catheter for percutaneous choledochoscopy and holmium: yttrium aluminum garnet laser lithotripsy of intrahepatic bile duct stones. Gastrointestinal endoscopy, 82: 171	Case report n=1 (85 years; male)	Under direct visualisation, the intrahepatic stones were fragmented with holmium:YAG laser (1.0 J at 10 Hz). The stone fragments were removed by ERCP with use of an extraction balloon and basket. A cholangiogram by PTBD 1 week later showed complete clearance of the intrahepatic stones.	This is a single case report.
Wong JCT, Tang RSY, Teoh AYB et al. (2017) Efficacy and safety of novel digital single-operator peroral cholangioscopy-guided laser lithotripsy for complicated biliary stones. Endoscopy International Open 5(1): e54-e58	Case series n=17 (median 76 years; 41% [7/17] female)	Post lithotripsy, 2 patients developed cholangitis and 1 patient with underlying COPD developed respiratory distress, all resolved with conservative management. There were no haemobilia,	Studies with a larger sample and/or better design are included in table 2.

		perforations, pancreatitis nor any deaths	
Wong JC, Wong MN, Lam KL et al. (2015) Second-generation peroral cholangioscopy and holmium:YAG laser lithotripsy for rescue of impacted biliary stone extraction basket. Gastrointestinal endoscopy, 83: 837-8	Case report n=1 (79 years; male)	The impacted basket and the captured stone were targeted for LL under direct visualisation. Stone fragmentation by using 1.2 kJ was seen under real time. The impacted basket was then successfully pulled from the CBD. Residual stone fragments were removed by a mechanical lithotripter without adverse events.	This is a single case report.
Xia HT, Liu Y, Jiang H et al. (2018) A novel laparoscopic transcystic approach using an ultrathin choledochoscope and holmium laser lithotripsy in the management of cholecystocholedocholithiasis: An appraisal of their safety and efficacy. American journal of surgery 215(4): 631-5	Case series n=126 (mean 46.1 years; 52% [66/126] female)	LC+LTCBDE was done successfully in 118 of 126 patients, with a surgical success rate of 94%. An ultrathin choledochoscope was used in 75 (64%) patients, and holmium lithotripsy was done in 38 (32%) patients. The stone clearance rate was 99% (117/118). No significant complications occurred. One hundred (85%) patients had excellent and 13 (11%) had good outcomes for an overall success rate (excellent plus good) of 96%.	Studies with a larger sample and/or better design are included in table 2.
Yasuda I and Itoi T (2013) Recent advanced in endoscopic management of difficult bile duct stones. Digestive endoscopy 25: 376-85	Review	Large bile duct stones are typically treated by ML. However, if this fails, LL or EHL is carried out under the guidance of conventional mother-baby cholangioscopy. In cases of altered anatomy, it is often difficult to reach the papilla; in such cases, a percutaneous transhepatic approach, such as EHL or LL under percutaneous transhepatic cholangioscopy, can be a treatment option.	Review article