



ORIGINAL ARTICLE / *Interventional imaging*

Percutaneous transhepatic Laser lithotripsy for intrahepatic cholelithiasis



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KEYWORDS

Hepatolithiasis;
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Holmium Laser

Abstract

Purpose: To report the technical success, complications and long-term outcomes of patients with intrahepatic cholelithiasis not amenable to endoscopic retrograde cholangiopancreatography (ERCP) who were treated with percutaneous transhepatic biliary Laser lithotripsy (PTBLL). **Patients and methods:** A retrospective review of 12 patients who underwent PTBLL for intrahepatic cholelithiasis was performed. There were 5 men and 7 women with a mean age of 46 ± 18 (SD) years (range: 23–75 years). PTBLL was performed when stone clearance using ERCP had previously failed or was not appropriate due to unfavourable anatomy or the presence of multiple stones or a large stone. Percutaneous biliary access into intrahepatic ducts was obtained if not already present and lithotripsy was performed using a HolmiumYAG 2100 nM Laser. Patients files were analyzed to determine the technical success, complications and long-term outcomes. **Results:** Eleven patients (11/12; 92%) had a history of previous hepatobiliary surgery and nine (9/12; 75%) had multiple stones confirmed on preprocedure imaging. A 100% success rate in fragmenting the target stone(s) was achieved and 11/12 patients (92%) had successful first pass extraction of target stone fragments. Two patients (2/12; 17%) required 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 (range 3–84 months).

Conclusion: For patients with intrahepatic biliary calculi not amenable to ERCP, PTBLL provides an effective and safe alternate treatment.

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Intrahepatic cholelithiasis, although uncommon, is prevalent in Asian patients and those with primary liver disease or previous hepatobiliary surgery [1,2]. Treatment of intrahepatic cholelithiasis is important to prevent biliary obstruction, cholangitis, chronic liver disease and cholangiocarcinoma [3]. In patients with normal hepatobiliary anatomy, endoscopic retrograde cholangiopancreatography (ERCP) is often the first-line treatment and commonly involves a combination of sphincterotomy, balloon dredging or dilatation, stenting and endoscopic lithotripsy [4]. However, the success rate of ERCP for patients with intrahepatic cholelithiasis is low, particularly in those with widespread or large calculi [5]. In patients with unconventional anatomy such as a Roux-en-Y anastomosis associated with liver transplantation, the success rate of ERCP is similarly low. Hepatectomy is an alternative management options for hepatolithiasis but is associated with complication rates ranging between 30 and 50% [6].

For patients with intrahepatic cholelithiasis not amenable to ERCP, minimally invasive procedures using percutaneous intrahepatic biliary access are an alternative option. Biliary drainage, balloon dredging, stricture dilatation and biliary stenting can all be performed percutaneously. Derived from urological management of genito-urinary calculi, direct visualisation of intrahepatic calculi using percutaneous cholangioscopy has led to the use of percutaneous transhepatic biliary Laser lithotripsy (PTBLL) with a holmium: yttrium aluminum garnet (YAG) Laser to treat complex cases of intrahepatic biliary calculi [7]. The safety and efficacy of this technique has been described in a number of case series, although long-term data are lacking [8–14].

The purpose of this study was to report the results of PTBLL using a holmium YAG Laser to treat complex intrahepatic cholelithiasis in patients who are unsuitable or have failed ERCP at a major tertiary liver transplant hospital.

Patients and methods

Patients

Approval was granted by the institutional review board. Clinical data of all patients who underwent PTBLL between January 1st 2010 and January 1st 2018 for intrahepatic cholelithiasis were retrospectively collected from electronic hospital records and reviewed. Patients were retrieved from the hospital radiology database which was searched using the keywords "Laser" and "lithotripsy". Reviewed records included radiology reports, discharge summaries and outpatient clinic letters. All patients who underwent PTBLL for intrahepatic biliary calculi were included. 'Intrahepatic' was defined as proximal to the confluence of the left and right hepatic ducts. This was based on preprocedural magnetic retrograde cholangiopancreatography (MRCP) which was performed in all patients unless contraindicated, in which case computed tomography (CT) cholangiogram was performed. Two patients who underwent PTBLL for cholelithiasis and choledocholithiasis were excluded from this study as these stones were extrahepatic. PTBLL was performed if stone clearance using ERCP had previously failed or was not appropriate due to large stone size, presence

of multiple stones or unfavourable anatomy (*e.g.*, previous surgical reconstruction; Fig. 1).

The final study population included 12 patients (Table 1). There were 5 men and 7 women with a mean age of 46 years \pm 18 (SD) years (median age, 44 years; IQR 27–66 years; range: 23–75 years). MRCP was performed preprocedurally in all patients (Fig. 2).

Procedure details

All procedures were performed using general anesthetic with continuous monitoring of the patient's vital signs after administration of prophylactic intravenous (IV) antibiotics (ampicillin and gentamicin; cefotaxime if these are contraindicated; piperacillin-tazobactam for patients with previous liver transplant). A pre-existing biliary drain was present in all patients but one. For the patient without a pre-existing biliary drain, percutaneous biliary access into the appropriate duct was achieved under ultrasound guidance using a 20-gauge Chiba needle with a Cook Aprima[®] access set (Cook Medical). Serial dilatation was performed so that a 23 cm 11Fr or 12Fr Britetip[®] sheath could be inserted (Cordis) and PTBLL was performed as part of the same procedure. When present, the existing drain was exchanged over a straight Amplatz[®] wire (Cook Medical) for the sheath. Indwelling biliary drain tubes were eventually removed in all patients post-lithotripsy. Median time (months) until drain tube removal was 45 days (IQR: 3.75–75 days). No patients required multiple biliary drains.

Lithotripsy was performed by an interventional radiologist in the angiography suite using a Holmium: YAG 2100 nM Laser with a 272 micrometer optical laser fiber at a pulse duration of 250–350 microseconds (10 Hz), pulse energy of 0.5–1.0 Joules and pulse power of 0.25–2.5 kilowatts. Initial Laser settings for biliary calculi are 1.0 J and 10 Hz and titrated as appropriate. This was performed under direct video visualisation of target calculi using an Olympus CHF flexible cholangioscope (Type CB30S). At the completion of the procedure, an 8–12Fr biliary drainage catheter was left in situ to maintain biliary access. Supplementary balloon cholangioplasty, balloon dredging and biliary stent insertion were undertaken at the discretion of the interventionalist. Cholangioplasty and dredging were performed using an angioplasty balloon and Fogarty[®] balloon respectively and a 10 mm \times 4 cm Niti-S covered removable metallic stent was used when biliary stenting occurred (Taewoong Medical). Balloon dilatation of the stent up to 10 mm was performed following deployment. The Fogarty balloon was dilated between 7–10 mm during cholangioplasty of biliary or anastomotic strictures. Stones were not routinely sent for biochemical microbiological analysis.

Postprocedure evaluation

Patients were routinely admitted overnight for observation following PTBLL. After discharge from hospital, patients were followed up in the outpatient clinic by gastroenterologists. The duration of long-term follow-up was recorded as the time between performance of PTBLL and the most recent outpatient clinic documentation. Prior to clinic, patients were screened for hepatic dysfunction using liver function tests. Postprocedural imaging (MRCP or CT

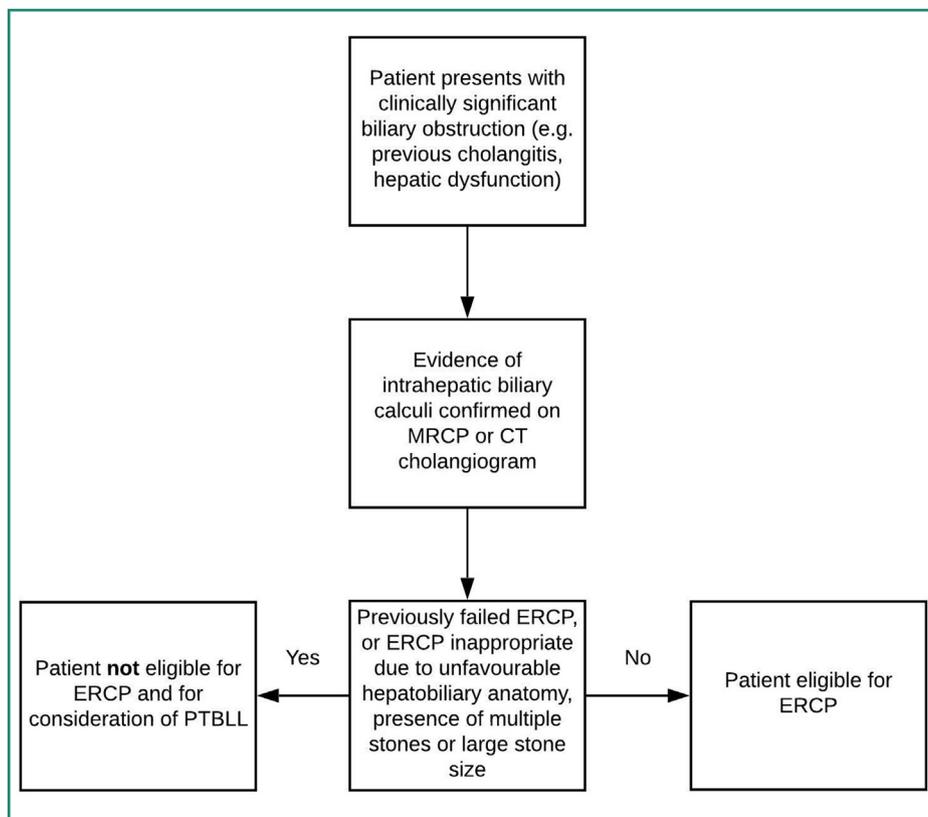


Figure 1. Flowchart shows inclusion/exclusion criteria for percutaneous transhepatic biliary Laser lithotripsy treatment (PTBLL) of intrahepatic cholelithiasis.

cholangiogram) was only performed if this result was abnormal and warranted further investigation. Stone recurrence was defined as radiological evidence of intrahepatic calculi during follow-up.

Statistical analysis

Quantitative data were reported as means and/or medians, standard deviations (SD), interquartile ranges (IQR) and ranges. Qualitative data were reported as raw numbers, proportions and percentages.

Results

Study population

Eleven patients (11/12; 92%) had a history of previous hepatobiliary surgery including liver transplantation (5/12; 42%), cholecystectomy (3/12; 25%), unspecified biliary resection/reconstruction (2/12; 17%), choledochojejunostomy (1/12; 8%), hepaticojejunostomy (1/12; 8%), hemihepatectomy (1/12; 8%), Kasai procedure (1/12; 8%) and Whipple’s procedure (1/12; 8%). Nine (9/12; 75%) patients had a history of primary liver disease including biliary atresia (4/12; 33%), primary sclerosing cholangitis (PSC) (1/12; 8%), cryptogenic cirrhosis (1/12; 8%) and acute hepatic failure of unknown cause (1/12; 8%). One patient had secondary sclerosing cholangitis after an ischemic bile duct injury following cholecystectomy.

Ten patients (10/12; 83%) underwent PTBLL for recurrent cholangitis. One patient with a history of orthotopic liver transplantation had intrahepatic calculi treated to prevent cholangitis and progression of obstructive liver disease and another suffered symptomatic biliary obstruction. Nine patients (9/12; 75%) had multiple stones or stone fragments visible on percutaneous transhepatic cholangiogram (PTC) or cholangioscopy and three had a single stone (3/12; 25%). The single stones were located in the left hepatic duct, right hepatic duct and at the biliary anastomosis in a patient with a Roux-en-Y reconstruction following liver transplantation (Fig. 3).

Procedural outcomes

Median procedure duration was 98 min (IQR: 76–124 min). In all patients the target stone(s) were able to be fragmented into smaller pieces and 11/12 patients (92%) had successful extraction of target stone fragments. The patient with incomplete fragment clearance had these cleared at a later date. Most patients required an overnight hospital admission only (8/12; 67%). Two patients (2/12; 17%) required repeat lithotripsy. One patient (1/12; 8%) underwent a further two lithotripsy treatments after recurrent intrahepatic stones were seen on later PTCs. Another patient (1/12; 8%) underwent three additional laser treatments after failed fragment extraction at their original procedure, also requiring simultaneous percutaneous lithotripsy and ERCP. Five patients received PTBLL alone (5/12; 42%) and seven patients (7/12; 58%) underwent simultaneous procedures including balloon

Table 1 Demographics and outcomes of 12 patients.

Patient #	Sex	Age (year)	Indication	Primary liver disease	Previous hepatobiliary surgery	Number of stones	Target stone fragmentation	Target stone fragment extraction	Complications	Follow-up (month)	Recurrence of stones during follow-up
1	M	55	Recurrent cholangitis	Primary sclerosing cholangitis	Cholecystectomy, choledochojejunostomy	Multiple	Yes	Yes	Hypotension	18	Nil
2	F	37	Prevention of cholangitis and progressive liver disease	Biliary atresia, hepatitis C in liver graft	OLT	Multiple	Yes	Yes	No	N/A	Data unavailable
3	F	30	Recurrent cholangitis	Biliary atresia	Kasai procedure	Multiple	Yes	Yes	No	7	Yes
4	F	70	Recurrent cholangitis	No	Whipple's procedure	Multiple	Yes	Yes	No	N/A	Data unavailable
5	M	25	Symptomatic biliary obstruction	Biliary atresia	OLT	Multiple	Yes	Yes	Presumed postprocedural cholangitis/septic shock	11	No
6	M	75	Recurrent cholangitis	Cryptogenic cirrhosis	OLT	Multiple	Yes	Yes	No	34	No
7	M	26	Recurrent cholangitis	Acute liver failure of unknown cause	OLT	Multiple	Yes	Yes	No	31	Yes

Patient #	Sex	Age (year)	Indication	Primary liver disease	Previous hepatobiliary surgery	Number of stones	Target stone fragmentation	Target stone fragment extraction	Complications	Follow-up (month)	Recurrence of stones during follow-up
8	F	50	Recurrent cholangitis	Secondary sclerosing cholangitis after ischemic bile duct injury following cholecystectomy	Hepaticojejunostomy, cholecystectomy	One	Yes	Yes	No	42	No
9	M	23	Recurrent cholangitis	Biliary atresia	OLT	One	Yes	Yes	Self-limiting fever	48	No
10	F	61	Recurrent cholangitis	No	Biliary resection/reconstruction for choledochal cyst	One	Yes	Yes	No	49	No
11	F	68	Recurrent cholangitis	No	Cholecystectomy, hemihepatectomy and biliary reconstruction (performed overseas)	Multiple	Yes	Yes	Blocked drain tube	87	Yes
12	F	35	Recurrent cholangitis	Yes – Unknown etiology	No	Multiple	Yes	No	No	Died at 24 months	N/A—Incomplete clearance

OLT: orthotopic liver transplantation; M: male; F: female.

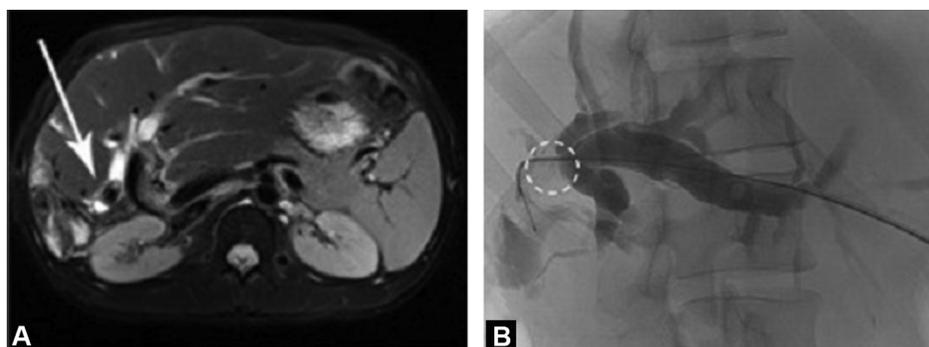


Figure 2. T2-weighted magnetic resonance image demonstrates an intrahepatic stone (arrow) just proximal to the anastomosis in a patient with a previous Roux-en-Y bypass (A); This stone was difficult to visualise on cholangiography (circle) demonstrating the challenging visibility of some intrahepatic stones on a percutaneous cholangiogram (B).

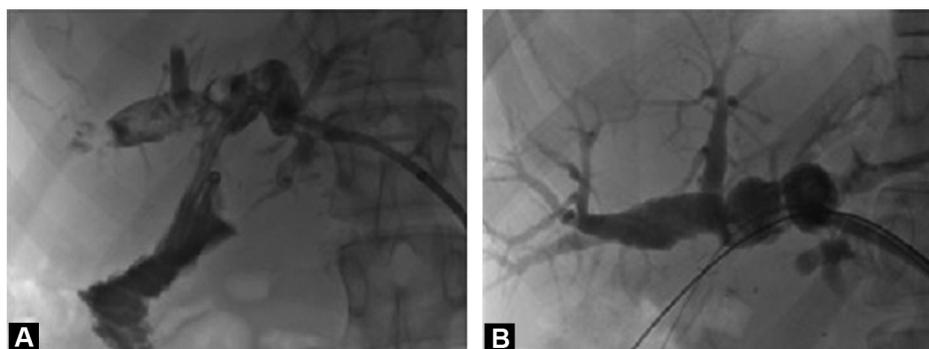


Figure 3. Intraprocedural percutaneous cholangiogram images demonstrate multiple intrahepatic biliary calculi in a patient with a Roux-en-Y anastomosis following liver transplantation (A) with almost complete stone clearance following percutaneous transhepatic biliary Laser lithotripsy (B).

dredging (6/12; 50%), balloon cholangioplasty (3/12; 25%) and biliary stenting (2/12; 17%). Some patients received a combination of these. No patients required surgery during the study period for the treatment of intrahepatic cholelithiasis.

Complications

Four patients experienced periprocedural complications (4/12; 33%). Three of these were mild complications and one was a major complication. Mild complications included asymptomatic hypotension responsive to IV hydration (1/12; 8%), self-limiting postprocedure fever (1/12; 8%) and a blocked biliary drain tube requiring replacement (1/12; 8%). One patient (1/12; 8%) had asymptomatic migration of a biliary stent into the gastrointestinal tract after percutaneous deployment which was allowed to pass through on its own.

The major complication was postprocedural sepsis (1/12; 8%) which was responsive to IV antibiotics. As a result, this patient had an unexpected prolonged hospital admission. An additional patient experienced a prolonged hospital admission after requiring a repeat PTC to assess remaining stone burden at which point their biliary drain was removed. Both of these patients were admitted for 3 days. Two patients admitted emergently with severe biliary sepsis and subsequently underwent PTBLL had complex and prolonged hospital admissions. There were no long-term sequelae from any complications. There were no periprocedural deaths.

Ten patients (10/12; 83%) had documented long-term follow-up data (median 33 months, IQR 16–48 months). Follow-up data was unavailable in two patients – one patient had complex social circumstances and a history of failing to attend clinic appointments and the other has since moved away from our region and follow-up attempts have been unsuccessful. Of the 10 patients with long-term data, 4 (4/10; 40%) had recurrence of intrahepatic calculi seen on either MRCP or PTC at a mean of 31 months (range 3–84 months). One patient died during the follow-up period at 2-years postprocedure from biliary sepsis with recurrent intrahepatic calculi.

Discussion

Our study found that PTBLL using a holmium: YAG Laser is an efficacious, safe and technically feasible treatment option for complex intrahepatic cholelithiasis in patients who are unsuitable or have failed ERCP. All target stones were able to be fragmented and stone fragments clearance rates were high. Complication rates were low and long-term stone recurrence rates were modest.

Restricted access to the biliary tree in patients with atypical anatomy makes treatment of biliary stones using ERCP difficult. Patients without a contraindication to ERCP may also have an unsuccessful procedure as impacted or widespread stones are difficult to treat endoscopically. This

was the case for the single patient in this series with no previous hepatobiliary surgery. Successful treatment of intrahepatic calculi is defined by clearance of the calculi and its fragments from biliary ducts on cholangioscopy or cholangiography at procedure completion.

Our success rate of target stone fragmentation and fragment extraction using PTBLL for intrahepatic biliary calculi are similar to previously published results and demonstrates efficacy of PTBLL in the treatment of intrahepatic cholelithiasis [9,10]. The majority of published data on PTBLL largely include patients with extrahepatic biliary calculi with only a small number of patients having concomitant or solely intrahepatic calculi [8,9,11–14]. All patients with extrahepatic stones were excluded from this study, although PTBLL can be highly effective in patients with large extrahepatic duct stones that are unresponsive to standard ERCP retrieval techniques.

In patients for whom calculus fragmentation is difficult and only partial fragmentation is possible, repeat procedures may be required. Other procedures that may be performed either simultaneously with or as an alternative to PTBLL include percutaneous transhepatic stone retrieval using forceps or a basket, balloon dredging, balloon cholangioplasty and biliary stenting. For these procedures to be successful, stones may need to be fragmented first and these are associated with their own complications [15]. Electrohydraulic lithotripsy is an alternative to laser lithotripsy but has been shown to produce inferior outcomes in patients with ureteric calculi and is more likely to cause mucosal damage [15,16]. Extracorporeal shockwave lithotripsy has previously been described but is now seldom used. Larger stones benefit most from PTBLL.

Reported rates of successful biliary calculi clearance after PTBLL are variable and only one published case series has focused solely on intrahepatic calculi [10]. This reported that an average of 3.9 procedures and 2.6 procedures were required to achieve complete stone clearance in patients with primary and secondary intrahepatic calculi respectively. Although our results may seem superior, they are not comparable as the reporting of technical success differs. We reported technical success as successful clearance of target stone fragments whereas Shamamian et al. reported on total stone clearance. The reason for this is that co-existent small stones that were thought to likely pass on their own were often left untreated. Sninsky et al. reported a successful stone clearance rate of 93% and a repeat lithotripsy procedure rate of 31% in 13 patients, with 7/13 (54%) of these having intrahepatic calculi [9].

Other series that have primarily included patients with extrahepatic calculi, but contain small numbers with intrahepatic calculi, have reported success rates between 85.7–100% [8,11,12]. One case series of 22 patients with either common bile duct (CBD) or intrahepatic cholelithiasis reported a 95% rate of successful fragmentation, however the proportion of patients with intrahepatic stones was not reported [13]. PTBLL has also shown to be successful in patients with solely CBD stones not amenable to ERCP [14].

Results from the literature suggests that PTBLL is a safe procedure and that major complication rates are low. This aligns with our experience. An advantage of using a flexible choledochoscopy via a percutaneous access sheath is direct visualization of the ducts, minimising the risk of damage to

surrounding tissues. Major potential complications include cholangitis and biliary sepsis, liver hematoma, biliary tree perforation and bleeding. However, our most significant and only major complication was postprocedural biliary sepsis. This resulted in a short hospital admission for IV administration of antibiotics and observation. Otherwise, complications were mild. Postprocedural cholangitis was the only major complication reported by Sninsky et al. and Schlatloff et al. while other published case series reported no major complications whatsoever [8,9,11–14]. The largest published case series ($n=36$) describing the use of PTBLL reported postprocedural self-limiting fever as the most common complication, however other complications included hepatic subcapsular hematoma, infection, supraventricular tachycardia and postprocedure pneumonia [10]. Reported complication rates for cholangioscopy alone range from 5–54% [17]. No published case series have reported any deaths attributable to the procedure.

Long-term data of patients with intrahepatic cholelithiasis treated with PTBLL is lacking. Our long-term stone recurrence rate is not dissimilar to those that have previously been published, with all recurrent stones in this series secondary to recurrent intrahepatic or anastomotic strictures. Shamamian et al. reported a stone recurrence rate of 14% (5/36) with a similar proportion of patients dying of liver-related disease during follow-up [10]. The lower rate of stone recurrence may be explained by the fact that most patients had primary intrahepatic stones with no underlying structural liver disease. There were also a lower proportion of patients that had undergone previous hepatobiliary reconstruction which has a known association with the development of anastomotic strictures.

Being a retrospective case series, there are likely inherent limitations such as selection bias in addition to the small patient number and cohort heterogeneity. However, large studies evaluating PTBLL for intrahepatic cholelithiasis in homogenous cohorts are unrealistic. Nevertheless, our case series suggests that percutaneous transhepatic biliary lithotripsy is an effective technique for treating intrahepatic biliary calculi yielding durable results.

In conclusion, the removal of intrahepatic calculi is important however traditional measures are not appropriate or feasible in all patients. PTBLL provides an alternative treatment option for patients unsuitable for ERCP such as those with previous hepatobiliary surgery, widespread calculi or a large calculus. Published data exploring the use of PTBLL in patients with hepatolithiasis is scarce, however the results of our study support that PTBLL is technically feasible, effective and safe with modest long-term outcomes. Further studies with more robust numbers are required to strengthen the evidence surrounding the use of PTBLL for intrahepatic calculi so that its use in clinical practice can be encouraged.

Informed consent and patient details

The authors declare that this report does not contain any personal information that could lead to the identification of the patient(s).

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Author contributions

All authors attest that they meet the current International Committee of Medical Journal Editors (ICMJE) criteria for Authorship.

Anthony Lamanna: Conceived and designed the analysis, collected the data, contributed data or analysis tools, performed the analysis, wrote the paper.

Julian Maingard: Contributed data or analysis tools, wrote the paper.

James Tai: Collected the data, contributed data or analysis tools, wrote the paper.

Dinesh Ranatunga: Performed the analysis, wrote the paper.

Mark Goodwin: Performed the analysis, wrote the paper.

Disclosure of interest

The authors declare that they have no known competing financial or personal relationships that could be viewed as influencing the work reported in this paper.

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