Background & Aims: There are limited prospective data and long-term follow-up on cholangioscopy-directed management of difficult bile duct stones. The study objectives were to evaluate the safety and efficacy of cholangioscopy-directed lithotripsy in patients who had failed standard endoscopic retrograde cholangiopancreatography (ERCP) techniques and to determine the stone recurrence rate.

Methods: Consecutive patients with biliary stones referred for cholangioscopy after failure of conventional stone therapy were enrolled and followed prospectively.

Results: Between February 2000–October 2004, 32 consecutive patients had cholangioscopy-directed lithotripsy (30 electrohydraulic lithotripsy, 2 mechanical) after a mean of 3.3 (range, 2–14) failed ERCPs. Stones were intrahepatic (N = 8); extrahepatic (N = 18); or both (N = 6). Biliary strictures were present in 20 (63%) patients. Cholangioscopy identified additional stones not seen at ERCP in 9 (28%) patients. A mean of 1.4 lithotripsy sessions achieved complete (N = 26, 81%), partial (N = 5, 16%), or failed (N = 1, 3%) stone clearance. Follow-up was available in 28 (88%) patients for a mean of 29.2 months (95% confidence interval, 20.3–38.1 months). Stone recurrence occurred in 4 of 22 (18%) patients with complete clearance and follow-up data; 3 had primary sclerosing cholangitis. There were 2 minor periprocedural complications and 1 late complication.

Conclusions: Cholangioscopy-directed lithotripsy is a safe and effective treatment in patients who have failed standard ERCP stone removal techniques. Stone recurrence is low in patients who had complete stone clearance except in patients with primary sclerosing cholangitis. Cholangioscopy detects stones missed by cholangiography.

Patients and Methods

The study population consisted of a cohort of consecutive patients who had CP-directed lithotripsy between February 2000–October 2004 after 2 or more failed attempts at stone clearance with standard ERCP techniques. Institutional Review Board approval was obtained for prospective collection of patient data. A data collection sheet was used to record the following information: patient demographics; pertinent medical history; prior abdominal operations; prior imaging studies; prior attempts at stone extraction; details of the cholangioscopic procedure including stone characteristics, stone therapy, tissue sampling of any concomitant lesions or strictures, and complications as defined by published consensus criteria.

Methods of stone extraction included CP-directed lithotripsy (EHL and mechanical lithotripsy), conventional mechanical lithotripsy, and balloon or basket sweeping.

Abbreviations used in this paper: CP, cholangioscopy; EHL, electrohydraulic lithotripsy; ERCP, endoscopic retrograde cholangiopancreatography; ESWL, extracorporeal shock wave lithotripsy; PSC, primary sclerosing cholangitis.

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Follow-up was performed by telephone interviews, clinic visits, and chart review until death or study termination. Follow-up inquiries included clinical response to therapy, episodes of pain, cholangitis, or jaundice after CP, and any subsequent interventions for complications, stone removal, or stone recurrence including surgical or interventional radiology procedures.

**Endoscopic Retrograde Cholangiopancreatography (ERCP) Procedure**

Before introducing the cholangioscope, cholangiography was performed, and any concomitant pathology and/or stones that were identified were documented. Then conventional stone removal techniques (including extension of a pre-existing biliary sphincterotomy, when appropriate, and mechanical lithotripsy) were attempted first, and only those stones that could not be extracted by using standard ERCP techniques and stones that were missed by cholangiography and subsequently identified by CP were treated with CP-directed stone fragmentation and extraction techniques.

**Cholangioscopy Procedure**

All procedures were performed by 1 of 2 experienced endoscopists (Y.C., R.S.) assisted by an endoscopy nurse or a gastroenterology fellow. The diameter of the cholangioscopes that were used ranged from 3.1–3.4 mm with a 1.2-mm operating channel. None of the cholangioscopes that were used had a separate channel for water irrigation. The Olympus CHF BP30, CHF BP20, or BP30 (Olympus, Tokyo, Japan) non-video cholangioscope was used in 44 procedures. The Olympus CHF B160 videocholangioscope was used in 2 procedures, and the Pentax FC-P9P (Pentax Corporation, Tokyo, Japan) cholangioscope was used in 7 procedures. The Olympus videocholangioscope has a slightly smaller 2-way tip deflection (90 degrees up and down) when compared with the fiberoptic instruments (160 degrees up and 130 degrees down).

All patients received periprocedural prophylactic antibiotics, usually levofloxacin 500 mg IV or ampicillin/sulbactam 3 g IV. Postprocedure antibiotics were generally given in patients with underlying primary sclerosing cholangitis (PSC) or in patients in whom adequate biliary drainage was in doubt. After cholangiography and placement of a 0.035-inch guidewire into the desired duct, the cholangioscope was advanced through the operating channel (4.2 mm) of a standard therapeutic duodenoscope over the guidewire and into the biliary system. Sphincterotomy and/or stricture dilation was performed as needed to facilitate cholangioscope passage.

To enhance visualization and permit use of the operating channel of the cholangioscope for biopsy or EHL, the guidewire was removed. Intermittent flushing with sterile saline was performed during cholangioscope withdrawal and systematic inspection of the biliary system.

EHL was performed with the Nortech AUTOLITH system (Northgate Technologies, Inc, Elgin, IL) and a 0.8-mm nitinol fiber that during the latter half of the study was preloaded within a 1.2-mm basket sheath to facilitate passage through the cholangioscope. After a stone was identified within the bile duct, it was immersed in water by using a foot pedal–controlled irrigation pump attached to the cholangioscope. Then an EHL fiber was introduced through the working channel of the cholangioscope, with the tip positioned directly behind the stone. Shock waves generated by an electric spark (50–90 W) at the tip of the nitinol fiber were conducted via the aqueous medium to achieve stone fragmentation under visual guidance. CP-directed mechanical lithotripsy was performed with a Sengura nitinol tipless basket (3F sheath, 2.0 by 2.5 cm basket; Cook Medical, Winston-Salem, NC) introduced through the operating channel of the cholangioscope to capture and mechanically crush the stone under direct vision. Fragmented stones then were flushed out or removed with a balloon and/or basket.

**Results**

**Patient Characteristics**

Between February 2000–October 2004, thirty-two consecutive patients (21 men and 11 women; median age, 64 years; range, 18–101 years) with difficult bile duct stones were referred to University of Colorado Hospital for transpapillary CP-directed lithotripsy (EHL and/or CP-guided mechanical lithotripsy) and comprised the study group. Patient characteristics are summarized in Table 1. Fifty-seven percent of the 53 CP procedures (44 for lithotripsy, 9 for tissue sampling) were performed under general anesthesia.

**Prior Biliary Intervention**

Patients had a mean of 3.3 (range, 2–14) prior ERCPs, and one (3%) patient had a percutaneous transhepatic cholangiogram before the index CP. Six of 32 (19%) patients had prior nondiagnostic tissue sampling for indeterminate strictures. At the time of index CP, 31 of the 32 (97%) patients had a biliary sphincterotomy either before (N = 21) or during the ERCP performed in conjunction with index CP (N = 10, 8 of which were an extension of a prior sphincterotomy); 1 patient had a prior choledochoduodenostomy.

**Stone Characteristics and Treatment**

Table 2 shows stone location and characteristics, and Table 3 shows stone clearance and interventions. Forty-four CP-directed treatment sessions were performed in 32 patients for a mean of 1.4 treatment sessions (range, 1–3) per patient; an additional 9 CP procedures were performed for tissue sampling alone for a total of 53 CP procedures. Complete stone clearance was achieved in 26 of 32 patients (81%); 24 patients had EHL, and 2 other patients had CP-directed mechanical lithotripsy. Five of 32 patients (16%) had only partial stone clearance, and 1 patient (3%) had no stone clearance.

Twenty patients (63%) had a biliary stricture (8 of whom had PSC). Eighteen patients (56%) had extrahepatic stones only...
Table 2. Stone Location and Characteristics (N = 32 Patients)

<table>
<thead>
<tr>
<th>Stone location/characteristics</th>
<th>No. of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stone location</td>
<td></td>
</tr>
<tr>
<td>Intrahepatic</td>
<td>N = 8</td>
</tr>
<tr>
<td>Extrahaepatic</td>
<td>N = 18</td>
</tr>
<tr>
<td>Both</td>
<td>N = 6</td>
</tr>
<tr>
<td>Stone type</td>
<td></td>
</tr>
<tr>
<td>Pigmented</td>
<td>N = 9</td>
</tr>
<tr>
<td>Cholesterol</td>
<td>N = 6</td>
</tr>
<tr>
<td>Mixed</td>
<td>N = 12</td>
</tr>
<tr>
<td>Unknown</td>
<td>N = 5</td>
</tr>
<tr>
<td>Median stone size</td>
<td>12 mm (range, 4–27 mm)</td>
</tr>
</tbody>
</table>

Table 3. Interventions and Stone Clearance in 32 Patients Undergoing CP–Directed Lithotripsy

<table>
<thead>
<tr>
<th>Stone clearance</th>
<th>Interventions</th>
<th>No. of sessions per patient (mean)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete (N = 26, 81%)</td>
<td>N = 24 (35 sessions of EHL)</td>
<td>1.5</td>
</tr>
<tr>
<td></td>
<td>N = 2 (3 sessions of CP-directed mechanical lithotripsy)</td>
<td>1.5</td>
</tr>
<tr>
<td>Partial (N = 5, 16%)</td>
<td>N = 5 (5 sessions of EHL)²</td>
<td>1.0</td>
</tr>
<tr>
<td>Failed (N = 1, 3%)</td>
<td>N = 1 (1 failed session of EHL)²</td>
<td></td>
</tr>
<tr>
<td>Total (N = 32, 100%)</td>
<td>N = 32 (44 sessions of CP-directed therapy)</td>
<td></td>
</tr>
</tbody>
</table>

²Had PSC as well as intrahepatic stones; 2 had a prior partial gastrectomy.
²Stone in peripheral intrahepatic duct in patient with prior choledochojejunostomy; EHL fiber could not pass because of difficult angle.

Discussion

CP with EHL has been used as an adjunct to conventional ERCP techniques of stone removal. However, published data on its safety and efficacy consist mostly of retrospective studies in selected patients. There is no prospective long-term follow-up, and the stone recurrence rate is unknown after successful transpapillary CP–directed lithotripsy in patients who have failed conventional endoscopic therapy.

This prospective study consisted of a cohort of consecutive patients at a single tertiary care center who were treated with CP-directed therapy of bile duct stones after failed standard therapy. In all patients, reattempted ERCP stone extraction, including mechanical lithotripsy, at the time of the scheduled index CP procedure and excluded those patients who were successfully treated in this way. Because we only enrolled patients who had CP-directed lithotripsy, the total number of patients during the study period initially referred for CP but who underwent successful stone extraction with conventional ERCP techniques at our center was not recorded. CP-directed therapy successfully achieved complete stone clearance in most but not all patients and did not require ESWL.

Of the 32 patients in the study cohort with bile duct and/or intrahepatic stones treated with CP-directed therapy, 97% had either complete (81%) or partial (16%) stone clearance. In a large retrospective study by Arya et al, the “mother-baby” system was used to treat 94 patients during a 12-year period. The authors reported a final stone clearance rate of 90% but did not provide any information regarding stone recurrence. Most recently, Farrell et al published their experience with single-operator duodenoscope-assisted CP and EHL in 26 patients (52 CP procedures) who had failed at least 1 attempt at stone clearance by ERCP. However, the majority of failed ERCP stone extractions were performed elsewhere, and the investigators did not routinely reattempt stone removal by using conventional ERCP techniques before resorting to CP-directed EHL, as we did. Only 4 patients in their study cohort had stones proximal...
to the hepatic bifurcation and 9 patients had strictures. Moreover, neither Farrell et al nor Arya et al included patients with PSC. In contrast, our study cohort included a large number of patients with associated strictures (N = 20), PSC (N = 8), and intrahepatic stones (N = 14). Taking these differences into account, Farrell et al reported successful stone clearance in all patients, but no follow-up information was provided; in our study taking all comers, complete stone clearance was achieved in 81%. On average, only 1.4 CPs per patient were attempted for stone therapy in our study compared with an average of 2 CPs per patient in the study by Farrell et al, 23% of the patients in the study by Arya et al had 2 or more EHL sessions. Furthermore, in our study 4 of 6 patients with partial or failed stone clearance only had 1 attempt at EHL. Thus it is possible that a more aggressive approach with multiple CP lithotripsy attempts might further improve the overall success rate above that which we have reported.

Follow-up was available in 88% of patients for a mean of 29.2 months. Stone recurrence occurred in 4 (3 PSC patients, 2 of 4 with hepatolithiasis) of 22 patients (18%) who had complete clearance and follow-up. Stone recurrence rates have been reported to be around 11% after endoscopic sphincterotomy for stone extraction in 1042 patients at a mean follow-up of 7.5 years and 28% after percutaneous transhepatic EHL in 14 patients at a mean follow-up of 4.8 years. In hepatolithiasis, stone recurrence rates have been reported to be 8% in 90 patients treated with surgical CP and/or T-tube percutaneous CP and EHL at a mean follow-up of 43 months, 11% in 427 patients treated with surgical and/or non-surgical percutaneous CP at 4–10 years of follow-up, and 29.6% in 85 patients treated with surgery combined with CP and EHL at a mean follow-up of 6 years. All of these studies were retrospective. Factors contributing to stone recurrence are incompletely understood; however, one likely explanation for the high stone recurrence rates observed is that patients with stones requiring EHL have residual sludge or tiny stone fragments in the ducts as a result of lithotripsy, which then serve as a nidus for stone formation. Other authors also have suggested that gallbladder status (history of cholecystectomy, presence of gallstones), performance of lithotripsy, and pneumobilia are related to stone recurrence after biliary sphincterotomy. Other putative risk factors include associated strictures and particularly PSC (3 of 4 patients with recurrence in our series) or other underlying chronic liver disease, sphincterotomy restenosis, persistent biliary duct dilation, stone characteristics and location. Some of these factors are likely to be operative regardless of the technique used to achieve stone clearance. It is not clear whether prophylaxis with ursodeoxycholic acid and/or aggressive therapy of strictures with dilation and stenting will decrease the risk of stone recurrence.

In our study, CP inspection immediately before EHL uncovered additional stones not seen by cholangiography in 28% of patients. By comparison, Farrell et al found residual stones in 18% of 49 patients evaluated by CP immediately after successful ERCP stone extraction; the varying results are likely due to differences in the 2 study cohorts. Regardless, both of these CP studies suggest that reported stone clearance rates with only radiographic techniques likely overestimate true success rates. Similarly, an undetermined proportion of stone “recurrences” after stone clearance in some series might be attributable to missed residual stones. Much of the surgical literature also supports the fact that cholangiography misses stones that are otherwise detected by CP or intraductal ultrasound.

<table>
<thead>
<tr>
<th>Table 4. Stone Clearance in Patient Subgroups (N = 32 Patients)</th>
<th>Complete</th>
<th>Partial</th>
<th>Failed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hepatolithiasis with stricture (N = 10)</td>
<td>8 (80%)</td>
<td>2 (20%)</td>
<td></td>
</tr>
<tr>
<td>Hepatolithiasis without stricture (N = 4)</td>
<td>3 (75%)</td>
<td>1 (25%)</td>
<td></td>
</tr>
<tr>
<td>Extrahepatic stones with stricture (N = 15)</td>
<td>13 (87%)</td>
<td>2 (13%)</td>
<td></td>
</tr>
<tr>
<td>Extrahepatic stones without stricture (N = 9)</td>
<td>7 (78%)</td>
<td>2 (22%)</td>
<td></td>
</tr>
</tbody>
</table>

*6 patients overlapped subgroups because of concomitant intrahepatic and extrahepatic stones; 5 of these patients also had strictures (complete clearance in 4, partial in 1); the patient who did not have strictures and had complete stone clearance.
Missed stones, as well as strictures, are both likely contributing factors in recurrent ascending cholangitis, particularly in PSC patients. Improved identification and aggressive treatment of associated stones in patients with PSC might reduce cholangitis episodes; further investigation of this is warranted.

CP-directed basket mechanical lithotripsy is a novel technique, achieving stone capture with mechanical basket fragmentation under direct vision and complete clearance of stones in both patients in which this was attempted. In one PSC patient, multiple small stones were adherent to the bile duct wall that were previously thought to be intraductal polyps and were only identified by CP. This patient had 14 prior ERCPs at an outside institution for “surveillance.”

In our hands, only 2 procedure-related complications occurred in 53 CP procedures (3.8%; 44 lithotripsy sessions); one patient had mild cholangitis that resolved with oral antibiotics, and the other patient had mild transient hypoxia after the CP. This patient had 14 prior ERCPs at an outside institution for “surveillance.”

Refinement in scope technology permits the passage of the cholangioscope through the working channel of a standard therapeutic duodenoscope. However, CP adds significant time and additional personnel. Because of the length and complexity of these cases, 30 of 53 CP procedures in our study were performed under general anesthesia. Furthermore, fragility of the cholangioscope at its bending portion and in its optical fibers leads to costly repairs and has discouraged its widespread adoption. The relatively large (10F) shaft diameter of currently available cholangioscopes also limits access into the intrahepatic ducts for therapy of intrahepatic stones. The single case of failed CP-directed stone removal in our series was in a patient with intrahepatic stones in a peripheral duct that could not be treated by EHL as a result of a difficult angle caused by a prior choledochoduodenostomy. Difficulty retaining water in the bile ducts post-sphincterotomy for EHL therapy also presents a technical challenge. We do not advocate the use of a nasobiliary catheter for continuous irrigation because this approach is cumbersome and the catheter occasionally interferes with visualization and EHL targeting of some stones; the ideal solution is a cholangioscope with a dedicated channel for continuous fluid irrigation during EHL.

In conclusion, CP-directed stone therapy is safe and effective for management of patients with bile duct stones who have failed conventional endoscopic approaches. However, stone recurrence occurs in a subset of patients over time, probably because of underlying patient-related risk factors. CP is also a useful adjunct for confirming stone clearance and might help to distinguish residual stones from filling defects caused by air bubbles or other lesions, particularly within markedly dilated ducts and in post-sphincterotomy patients.

### References


### Table 5. Stone Recurrence Rates by Subgroup

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PSC (N = 6)</td>
<td>3 (50%)</td>
</tr>
<tr>
<td>Any stricture (N = 10)</td>
<td>4 (40%)</td>
</tr>
<tr>
<td>Extrahepatic stones only (N = 13)</td>
<td>3 (23%)</td>
</tr>
<tr>
<td>Hepatolithiasis (N = 9)</td>
<td>1 (11%)</td>
</tr>
<tr>
<td>Total (N = 22)</td>
<td>4 (18%)</td>
</tr>
</tbody>
</table>

*Patients overlapped subgroups.*


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