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Percutaneous Endoscopic Holmium Laser Lithotripsy for Management of Complicated Biliary Calculi
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ABSTRACT

Background and Objectives: Advances in endoscopic techniques have transformed the management of urolithiasis. We sought to evaluate the role of such urological interventions for the treatment of complex biliary calculi.

Methods: We conducted a retrospective review of all patients (n=9) undergoing percutaneous holmium laser lithotripsy for complicated biliary calculi over a 4-year period (12/2003 to 12/2007). All previously failed standard techniques include ERCP with sphincterotomy (n=6), PTHC (n=7), or both of these. Access to the biliary system was obtained via an existing percutaneous transhepatic catheter or T-tube tracts. Endoscopic holmium laser lithotripsy was performed via a flexible cystoscope or ureteroscope. Stone clearance was confirmed intra- and postoperatively. A percutaneous transhepatic drain was left indwelling for follow-up imaging.

Results: Mean patient age was 65.6 years (range, 38 to 92). Total stone burden ranged from 1.7 cm to 5 cm. All 9 patients had stones located in the CBD, with 2 patients also having additional stones within the hepatic ducts. All 9 patients (100%) were visually stone-free after one endoscopic procedure. No major perioperative complications occurred. Mean length of stay was 2.4 days. At a mean radiological follow-up of 5.4 months (range, 0.5 to 21), no stone recurrence was noted.

Conclusions: Percutaneous endoscopic holmium laser lithotripsy is a minimally invasive alternative to open salvage surgery for complex biliary calculi refractory to standard approaches. This treatment is both safe and efficacious. Success depends on a multidisciplinary approach.

Key Words: Biliary calculi, Holmium laser, Endoscopic, Lithotripsy.

INTRODUCTION

Gallstone disease is a common and costly health problem in the Western world. In the United States alone, the incidence rate for cholelithiasis is 10% to 20%, and over 600,000 cholecystectomies are performed annually. The disease course may be complicated by the presence of stones within the common bile duct (CBD), or choledocholithiasis.1 Although choledocholithiasis is typically due to infectious causes in Asian populations, most cases in the West develop as a secondary result of calculi originating in the gallbladder or stones resulting from benign strictures, sclerosing cholangitis, choleodochal cysts, or malignant biliary tumors.2 In fact, secondary choledocholithiasis complicates between 10% and 15% of cases of cholelithiasis in the United States.1,3

The goal of treatment is to clear obstructing biliary calculi by using the minimum number of procedures with the lowest risk of morbidity. Currently, most biliary calculi are successfully removed either at the time of laparoscopic cholecystectomy or pre- or postoperatively with endoscopic retrograde cholangiopancreatography (ERCP) or transhepatic cholangiography (PTHC).4,5 Infrequently, these approaches fail and traditional open salvage procedures such as open CBD exploration are required to extract retained biliary stones. Patients with complex biliary calculi pose a unique challenge, particularly because they are often debilitated with multiple comorbidities.

Technologies well proven for the treatment of urinary calculi may prove useful in managing complicated biliary calculi. More specifically, holmium:yttrium aluminum garnet laser (Ho:YAG) lithotripsy is a safe and effective minimally invasive technique that has revolutionized the management of urolithiasis. The purpose of this study was to evaluate our preliminary experience with holmium:YAG...
laser lithotripsy in the management of complicated biliary tract calculi.

MATERIALS AND METHODS

Between December 2003 and December 2007, 9 patients (4 men, 5 women) were referred to the Urology service for management of biliary calculi refractory to standard techniques. Patient demographic and clinical data are summarized in Table 1. Mean age was 65.6 years (range, 38 to 92). Two patients had CBD and hepatic stones following orthotopic liver transplantation. Two patients had retained CBD stones after cholecystectomy. Two patients presented initially with obstructive hyperbilirubinemia due to CBD calculi. One patient had undergone multiple prior ERCPs and even open exploration for a CBD stone. One patient had a CBD stone following a Whipple procedure and hepatojejunostomy. Lastly, one patient had multiple hepatic and CBD calculi secondary to primary sclerosing cholangitis (PSC). All 9 patients had previously failed ERCP with sphincterotomy\textsuperscript{6} or PTHC,\textsuperscript{7} or both, with attempted stone extraction. These standard techniques had failed due to inaccessibility, large stone burdens, anatomic abnormalities, or all of these. Urological intervention was chosen as an alternative to an open salvage surgical procedure. Percutaneous transhepatic endoscopic stone manipulation was performed as a combined procedure between the Interventional Radiology (AC and LM) and Urology (PN and KO) departments.

All patients had stones located in the CBD, with 2 patients also having additional stones within the hepatic ducts. Five patients presented with multiple stones while 4 patients had solitary stones. Total stone burden ranged from 1.7 cm to 5 cm. All patients had an existing percutaneous transhepatic drain (8 Fr to 14 Fr) in place from 2 days to 15 years prior to endoscopic intervention. The tracts were sequentially dilated under fluoroscopic guidance to between 14 Fr and 20 Fr to accommodate either a flexible cystoscope (6) or ureteroscope (3). Lithotripsy was performed under direct endoscopic vision by using a holmium laser ranging in size from 200 μm to 500 μm, depending on stone burden, stone location, and choice of endoscope (cystoscope versus ureteroscope). Laser frequency ranged between 6 Hz and 10 Hz, generating 0.6 joules to 1.0 joules of energy. Stone fragments and debris were either flushed into the duodenum (9) or basket extracted (3) from the biliary tree (Figure 1), or both. In one case, multiple stones were small enough to basket

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (yrs)</th>
<th>Sex</th>
<th>Indication</th>
<th>Stone Location†</th>
<th>Prior Intervention(s)†</th>
<th># Stones</th>
<th>Stone Burden (cm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>78</td>
<td>F</td>
<td>s/p Whipple with hepatojejunostomy</td>
<td>CBD</td>
<td>PTHC</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>2</td>
<td>79</td>
<td>F</td>
<td>Large CBD calculi, stricture</td>
<td>CBD</td>
<td>ERCP, PTHC</td>
<td>Multiple</td>
<td>1.7*</td>
</tr>
<tr>
<td>3</td>
<td>56</td>
<td>F</td>
<td>s/p Orthotopic liver transplant</td>
<td>Hepatic, CBD</td>
<td>ERCP, PTHC</td>
<td>Multiple</td>
<td>4.5</td>
</tr>
<tr>
<td>4</td>
<td>68</td>
<td>M</td>
<td>CBD stenosis s/p cholecystectomy</td>
<td>CBD</td>
<td>PTHC (multiple)</td>
<td>3</td>
<td>4.5</td>
</tr>
<tr>
<td>5</td>
<td>69</td>
<td>M</td>
<td>Retained CBD calculi s/p cholecystectomy</td>
<td>CBD</td>
<td>ERCP (2), PTHC</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>6</td>
<td>38</td>
<td>M</td>
<td>s/p Orthotopic liver transplant</td>
<td>CBD</td>
<td>PTHC</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>7</td>
<td>52</td>
<td>M</td>
<td>Primary sclerosing cholangitis</td>
<td>Hepatic, CBD</td>
<td>ERCP, PTHC</td>
<td>Multiple</td>
<td>5</td>
</tr>
<tr>
<td>8</td>
<td>58</td>
<td>F</td>
<td>Large CBD calculus</td>
<td>CBD</td>
<td>ERCP (multiple), open CBDE</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>9</td>
<td>92</td>
<td>F</td>
<td>Large CBD calculus, stricture</td>
<td>CBD</td>
<td>ERCP (multiple), PTHC (multiple)</td>
<td>1</td>
<td>2.3</td>
</tr>
</tbody>
</table>

*Denotes size of largest calculus.
†CBD = Common bile duct, ERCP = endoscopic retrograde cholangiopancreatography, PTHC = transhepatic cholangiography.
extract with a tipless Nitinol basket, obviating the need for laser lithotripsy.

Following endoscopic stone treatment, all patients had antegrade passage of a Fogarty balloon over a guide wire into the duodenum to expel any remaining CBD calculi. Finally, endoscopic inspection of the biliary system was performed to verify that no stone fragments remained. At the conclusion of the procedure, a percutaneous transhepatic drain (12 Fr to 14 Fr) was left indwelling for follow-up cholangiography.

Success was defined as symptom relief, “stone-free” status of the biliary tree on final endoscopic inspection, and lack of residual stone fragments visualized on follow-up imaging, including antegrade cholangiography, computed tomography (CT) scans, or both (Figure 2).

RESULTS
All 9 (100%) patients were visually “stone-free” at the conclusion of one percutaneous transhepatic endoscopic procedure. Importantly, postprocedure endoscopic inspection of the CBD also showed no evidence of mucosal injury. At a mean radiological follow-up of 5.4 months (range, 0.5 to 21), there was no evidence of stone recurrence. Of the total 9 patients, 4 (44.4%) were drain-free and another 4 (44.4%) tolerated capping of their biliary drain. One patient necessitated persistent postoperative biliary drainage secondary to CBD stenosis following cholecystectomy. At last follow-up, cholangioplasty was aborted due to the patient experiencing oxygen desaturation and coding during cholangiography.

The majority of patients were discharged from the hospital 24 hours to 48 hours after lithotripsy (mean LOS 2.4 days). Two patients had extended hospital stays of 7 days after surgery secondary to comorbid conditions, not associated with the surgical procedure itself. No major perioperative complications occurred. However, one patient with a history of recurrent cholangitis expired 4 weeks postoperatively due to sepsis. As aforementioned, a second patient coded from narcosis during follow-up cholangiography 2 weeks postoperatively. This patient recovered uneventfully without adverse sequelae. Lastly, a third patient developed urinary retention following the procedure.

DISCUSSION
The majority of CBD stones are managed endoscopically with sphincterotomy and stone extraction (with or without fragmentation), performed before or after laparoscopic cholecystectomy. Alternatively, laparoscopic CBD exploration and stone extraction may be performed at the time of cholecystectomy. In a review of the literature, the reported median success rate for sphincterotomy is ap-
proximately 92% (range, 79 to 98), median complication rate 8% (range, 2% to 24%), and mortality rate 1% (range, 0% to 6%). Similarly, laparoscopic CBD exploration results in bile duct clearance rates >90% in 70% of reports, with a median retained stone rate of 5% (range, 0% to 19%). The median complication rate is 8% (range, 2% to 17%) and the mortality rate is 1% (range, 0% to 5%).

Finally, open CBD exploration is typically reserved for patients who are not candidates for endoscopic or laparoscopic procedures. However, open exploration is not fraught without associated morbidity. In a recent study by Livingston et al., complication rates for open CBD exploration rose from 3.4% in 1993 to an alarmingly high 17.4% in 2001, possibly due to decreasing open surgeon experience in the laparoscopic era.

While advances in endoscopy and laparoscopy have transformed the management of choledocholithiasis, advances in urological techniques have similarly revolutionized the treatment of urolithiasis over the past several decades. Stones that were previously managed with open surgery, shock wave lithotripsy, or “blind” fluoroscopic basketing can now be directly accessed endoscopically and treated with laser lithotripsy. This is now possible due to the miniaturization of flexible endoscopes and the widespread availability of the holmium laser. The holmium laser is a small contact lithotrite (20 μm to 1000 μm) that effectively fragments urinary stones with minimal stone retropulsion and subsequent collateral damage to surrounding tissue. Additionally, the flexible composition of the laser fibers provides little impedance to the deflection of ureteroscopes, thereby facilitating access to the entire urinary system. Moreover, the holmium laser is capable of fragmenting even the hardest stones that are oftentimes resistant to other lithotrites.

The success of holmium laser lithotripsy in the management of urinary calculi has led several investigators to apply this technology to complex biliary calculi resistant to standard treatments. A few case reports have demonstrated the clinical efficacy of the holmium laser using percutaneous access techniques in patients with complicated bile duct stones. Tarman et al. documented the utility of intracorporeal lithotripsy in a case of intrahepatic biliary stones. Monga et al. described a complex case of biliary obstruction that developed 7 years following a Roux-en-Y choledochojjunostomy. The holmium laser was used to completely fragment the stones via the percutaneous transhepatic route. Several small series have further validated the usefulness of holmium laser lithotripsy for the treatment of difficult biliary calculi. Das et al. effectively managed 4 patients who presented with sepsis associated with stones in the gallbladder (n = 2) or bile duct (n = 2). In a series of 3 patients, Teichman et al. documented successful clearance of difficult CBD stones using the holmium laser in a single therapeutic setting. Of note, no complications developed, and all patients remained free of recurrence during a 6-month follow-up period.

Subsequently, Ponsky et al. reviewed their experience with 14 patients who were treated with contemporary “urologic” intervention for refractory pancreaticobiliary calculi. Five of these patients underwent percutaneous...
Most recently, Hazey et al\textsuperscript{13} retrospectively reviewed 13 open bile duct exploration or hepatic resection. No major complications occurred. No patient required primary and secondary intrahepatic calculi, respectively.\textsuperscript{15} and 2.6 procedures (range, 1 to 10) for those with primary intrahepatic calculi and 14 patients had secondary intrahepatic calculi. Complete stone clearance was accomplished in all patients after an average of 3.9 (range, 1 to 15) and 2.6 procedures (range, 1 to 10) for those with primary and secondary intrahepatic calculi, respectively. No major complications occurred. No patient required open bile duct exploration or hepatic resection.

Shamamian and Grasso\textsuperscript{2} reported a much larger series of 36 patients with complex intrahepatic biliary calculi treated with percutaneous endoscopic holmium laser lithotripsy. In their study, 22 patients of Asian descent had primary intrahepatic calculi and 14 patients had secondary intrahepatic calculi. Complete stone clearance was accomplished in all patients after an average of 3.9 (range, 1 to 15) and 2.6 procedures (range, 1 to 10) for those with primary and secondary intrahepatic calculi, respectively. No major complications occurred. No patient required open bile duct exploration or hepatic resection.

Most recently, Hazey et al\textsuperscript{13} retrospectively reviewed 13 non-Asian patients with complex secondary biliary calculi treated percutaneously using holmium laser lithotripsy. Mean age was 69 years, and 3 of the 13 patients were treated solely as outpatients. Stone clearance required an average of 1.6 treatments per patient, and no patient underwent greater than 3 treatments. Of note, 8 of the 13 patients required only a single holmium laser treatment to clear their calculi. Average length of percutaneous access was 108 days. Notably, only one patient developed pain and required hospital admission. Based on their experience, the authors concluded that holmium laser ablation is safe and efficacious for biliary calculi but may require prolonged biliary access and several procedures.

Our cohort of patients had large, complex biliary calculi that were effectively managed endoscopically through the coordinated efforts of the Interventional Radiology and Urology teams. Consistent with prior studies, we report a uniformly high success rate in a single therapeutic setting despite failed prior attempts at stone extraction. Compared with most kidney stones, we found biliary calculi to fragment easily with the holmium laser at low power settings.

Although we did not analyze stone fragments to determine composition, several authors have reported adequate fragmentation regardless of stone composition. Shamamian and Grasso\textsuperscript{2} noted that the holmium laser was capable of delivering sufficient energy to fragment stones containing mixed combinations of cholesterol, calcium bilirubinate, and mixed bile pigments.

As we have gained increasing experience with these cases, several technical points warrant discussion. First, the use of a flexible cystoscope compared with a flexible ureteroscope allows for better maneuverability in what can be a complex and capacious biliary system. In addition, improved cystoscopic visualization is important when targeting stones in a system filled with bile. The cystoscope allows for the passage of larger instruments, specifically the use of larger 500-μm holmium laser fibers for laser lithotripsy. However, one caveat to using the larger endoscope is the need for a larger diameter working sheath. To place a >16 Fr sheath, which is necessary to accommodate our flexible cystoscope (15 Fr), a prior percutaneous biliary tube must have been placed preoperatively for a period of at least 4 to 6 weeks. Failure to do so places the patient at risk for potential liver fracture and significant hemorrhage during tract dilation. No patients in our series had any bleeding complications secondary to sheath placement or stone manipulation. Conversely, a 12 Fr sheath may be used with the flexible ureteroscope (range, 7 Fr to 9 Fr), which is our preference for patients with a small stone burden.

Secondly, the anesthesia and operating room team must institute measures to prevent postoperative complications in this often debilitated patient population. Many patients present with recurrent cholangitis from complicated biliary calculi. Therefore, culture-specific intravenous antibiotics are given at least 24 hours before surgery and continued postoperatively while the patient is hospitalized. Additionally, at the conclusion of the case, we directly instill a fluoroquinolone antibiotic into the CBD via the working sheath.

Finally, intraductal irrigation proved to be useful in flushing stone fragments clear from the field. Because large amounts of fluid are instilled into the CBD and subsequently the duodenum, we only use warmed normal saline for irrigation to prevent hypothermia and hyponatremia. Moreover, an orogastric tube is placed at the beginning of the case to help prevent fluid overload. Collectively, these perioperative maneuvers help minimize complications during this surgical procedure.

**CONCLUSION**

Percutaneous endoscopic holmium laser lithotripsy is a safe and efficacious minimally invasive treatment option for complex biliary calculi refractory to standard modalities, which
would otherwise necessitate an open salvage surgical procedure. Though traditionally used for urological procedures, flexible endoscopes and the holmium laser are also well suited for the treatment of stones in the biliary tree. Success depends on a multidisciplinary approach.

References: