International Journal of Gastrointestinal Intervention

journal homepage: www.ijgii.org

Review Article

Recent update of therapeutic application of peroral cholangioscopy

Yun Nah Lee*

ABSTRACT

Despite advancements in endoscopic retrograde cholangiopancreatography (ERCP), direct endoscopic visualization of the biliary tree by cholangioscopy is required to improve the diagnosis and treatment of the underlying disease. Although several types of peroral cholangioscopy (POC) systems are available, single-operator cholangioscopy (SOC) has been widely used for interventions in the biliary system. The first SOC was SpyGlass direct visualization system (Boston Scientific, Natick, MA, USA) expanded to a digital version of the SOC (SpyGlass DS; Boston Scientific). More recently, single-operator direct POC using an ultra-slim upper endoscope has been proposed. The remarkable developments in POC and available specialized accessories continue to improve therapeutic procedure of the biliary diseases. POC allows the visualization of bile duct stone and guide wire placement across difficult strictures and selective cannulation of the intrahepatic and cystic ducts. It is also demonstrating its utility in investigational applications such as intraductal ablation therapy for bile duct tumors, removal of foreign body in the bile duct and evaluation of hemobilia.

Keywords: Cholangioscopy; Lithotripsy; Photodynamic therapy; Radiofrequency ablation

Introduction

Endoscopic retrograde cholangiopancreatography (ERCP) is a standard diagnostic and therapeutic procedure for biliary diseases. However, cholangiography alone has limitations for the management of some clinical situations. Cholangioscopy is a useful tool to overcome these limitations of ERCP allowing direct endoscopic visualization of biliary tree. Peroral cholangioscopy (POC) is traditionally only conducted using a mother-baby scope system. However, routine clinical application of this system has been restricted because of their fragility and requirement of the participation of two skilled endoscopists using 2 endoscopic systems.[1,2] Subsequently, POC systems operated by single-operator have been introduced to overcome drawbacks of a mother-baby scope system. The first single-operator cholangioscopy (SOC) was SpyGlass direct visualization system (Boston Scientific, Natick, MA, USA) expanded to a digital version of the SOC (SpyGlass DS; Boston Scientific). More recently, single-operator direct POC using a conventional ultra-slim upper endoscope has been proposed. The remarkable developments in POC, such as image quality, technical convenience, and available specialized accessories, continue to improve real time diagnosis and therapeutic procedure of the biliary diseases. This review summarizes the role of POC in the therapeutic applications of biliary diseases with a focus on SOC.

Instruments and Procedure

SpyGlass direct visualization system

SpyGlass direct visualization system was introduced as a SOC technique in 2007. The first version of SpyGlass system (referred to as 'SpyGlass Legacy') is composed of a reusable 0.77-mm diameter optical probe (6,000-pixel image with 70° field of view) and a disposable 10-Fr delivery catheter (SpyScvope; Boston Scientific). The delivery catheter has a fourway deflected steering, a 1.2-mm accessory channel, a 0.9-mm channel for the optical probe, and 2 dedicated 0.6-mm irrigation channels, which enables continuous water irrigation for clear image. However, SpyGlass Legacy has several limitations. The image quality was suboptimal, image stability was poor because of interference from blood and mucus, and manipulation of the catheter was challenging because of lack of coordination between the directional control dial movements and optical fiber visualization.[3]

In 2015, a digital version of SOC (SpyGlass DS; Boston Sci-

Digestive Disease Center and Research Institute, Department of Internal Medicine, Soon Chun Hyang University School of Medicine, Bucheon, Korea
Received July 8, 2021; Accepted July 14, 2021
* Corresponding author. Digestive Disease Center, Soon Chun Hyang University Bucheon Hospital, Soon Chun Hyang University School of Medicine, 170 Jomaru-ro, Wonmi-gu, Bucheon 14584, Korea.
E-mail address: yunnah@schmc.ac.kr (Y.N. Lee).

pISSN 2636-0004 eISSN 2636-0012 https://doi.org/10.18528/ijgii210039

entific) was introduced. The system consists of a fully integrated SpyScope Digital System Access and Delivery Catheter and a fully-disposable system to eliminate probe reprocessing. The integrated digital sensor provides superior imaging, greater resolution, and a 110° field of view. The insertion tube contains 1 working channel (1.2-mm diameter) for accessory devices and aspiration, 2 channels for irrigation, 2 optical fibers to transmit illumination from the controller, and wiring to transmit video signals to the controller. In addition, SpyGlass DS is easy to set up and the tapered distal end enables easy entering of the common bile duct (CBD)—using a free-hand technique or over a guidewire.[4] Accessories for use with both the legacy and the SpyGlass DS systems include an intraductal mini-biopsy forceps (SpyBite; Boston Scientific). Recently, the next version of the SpyGlass DS system (SpyGlass DS version 2.0) has been released. It is expected to provide improved diagnostic and therapeutic capabilities using fourfold higher image resolution and optimized light emitting diode (LED) illumination.

Direct peroral cholangiosocpy

During the direct POC, ultra-slim upper endoscope is directly inserted into the bile duct through the papilla. The ultra-slim endoscope was originally designed for use in pediatric patients and transnasal applications. Direct POC can be performed only after a large previous endoscopic sphincterotomy and/or sphincteroplasty, because the outer diameters are 5 to 6 mm, and the diameter of the CBD is usually > 8 mm. Ultra-slim endoscopes have working channels ranging from 2.0 to 2.2 mm which allow to extend interventional procedures, including for tissue sampling, and it permits the use of 5-Fr instruments. In addition, this system provides high-quality endoscopic imaging with the ease of performance of enhanced endoscopy by using narrow-band imaging or i-SCAN.[1,4,5]

However, advancement of an ultra-slim endoscope into the biliary tree has been a major limitation to the performance of direct POC because of acute angulation of biliary tree from second part of the duodenal lumen. Several specialized accessories and techniques are used to advance an ultra-slim endoscope into the proximal CBD.[1,6–8] Although these accessories have improved the success rate of direct POC, it was still time-consuming and technically difficult to perform.[9] Recently, a prototype multibending (MB) ultra-slim endoscope was introduced as a dedicated cholangioscope to overcome the technical difficulties of direct POC. The MB endoscope is a modified ultra-slim endoscope that can be inserted directly into the bile duct without using device assistance ("free-hand"). It has 2 bending sections and the outer diameters of the distal end and shaft of an MB endoscope are 4.9 mm and 7.0 mm, respectively, to improve pushability of the endoscope and to minimize loop formation in the stomach. The MB endoscope revealed a higher technical success rate than the conventional ultra-slim endoscope in free-hand biliary insertion of the endoscope for direct POC (89.1% vs 30.4%; $P < 0.001$).[10]

Therapeutic Applications

Intraductal lithotripsy for difficult bile duct stones

Management of difficult bile duct stones is most popular application of POC. Standard endoscopic stone-removal techniques, including mechanical lithotripsy, fails in 10%–15% of patients.[11] Intracorporeal lithotripsy, such as electrohydraulic lithotripsy (EHL) or laser lithotripsy (LL) is a main treatment option for difficult bile duct stones. POC enables to conduct EHL or LL (Fig. 1) under direct visual control for safe and precise targeting during fragmentation. In a meta-analysis of 35 studies with 1,762 participants, POC with intraductal lithotripsy showed an overall stone fragmentation success of 91.2% with an average of 1.3 lithotripsy sessions performed. Complete single session fragmentation success was 76.9%. There was no difference in overall fragmentation rate or adverse events; however, LL was associated with a higher single-session fragmentation rate and shorter procedure time compared with EHL.[12]

In randomized controlled trials (RCTs), SOC-guided lithotripsy was compared with conventional endoscopic therapies for management of difficult bile duct stone. SpyGlass DVS-guided LL achieved a higher endoscopic clearance rate than conventional therapy only (93% vs 67%; $P = 0.009$).[13] Mechanical lithotripsy had also a significantly lower stone clearance rate in the first session compared with SpyGlass DS-guided LL (63% vs 100%; $P < 0.01$).[14] Similarly, SpyGlass DS-guided LL showed a higher treatment success (93.9%) than in the large balloon sphincteroplasty (LBS) group (72.7%; $P = 0.021$) in a recent RCT.[15]

Although SOC-guided lithotripsy is effective and feasible procedure, it is considered to have several limitations in terms of cost, complexity and procedure time.[16] Buxbaum et al[13] reported mean procedure time of the SOC-guided LL (120.7 ± 40.2 minutes) was significantly longer than that of the conventional therapy (120.7

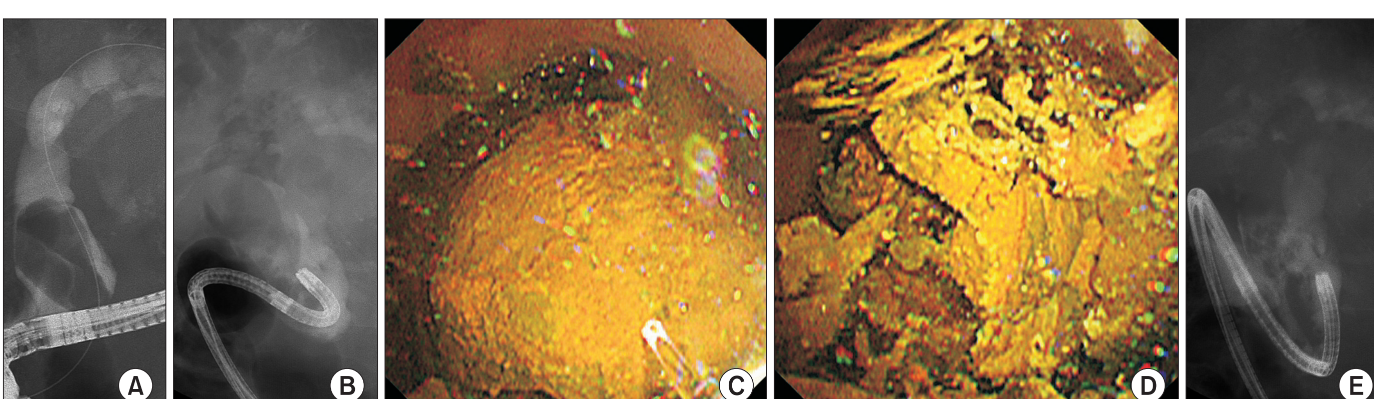

Fig. 1. Direct peroral cholangioscopy by using a multibending ultra-slim endoscope in a patient with a huge stone in the common bile duct (CBD). Cholangiograms (A) show a huge stone in the CBD and (B) a multibending endoscope located in CBD without device assistance. (C) Cholangioscopic view of a CBD stone with laser lithotripsy probe. (D) Cholangioscopy and (E) cholangiograms show the fragmented stones after lithotripsy.

vs 81.2 minutes, $P = 0.0008$). In contrast, overall treatment cost was reported as no significant difference between SOC-guided LL and LBS in previous study.[15] However, there is little data available. Therefore, POC-guided lithotripsy is recommended in patients with difficult CBD stones who have failed removal of stones by conventional endoscopic methods.[2,15]

Another advantage of POC-guided lithotripsy is a potential to reduce radiation exposure of patients and endoscopist. In a previous study, radiation exposure of patients was significantly higher in the mechanical lithotripsy group than in the LL group (40,745 vs 20,989 mGycm^2; $P = 0.04$).[14] And, a prospective study evaluating stone removal for noncomplex bile duct stone using SpyGlass DS in radiation-free setting reported that all cases achieved successful fluoroscopy-free biliary cannulation and stone extraction. Fluoroscopy was needed in only 5% cases to confirm stone clearance.[17]

Intraductal ablation therapy for bile duct tumors

POC provides visual guidance for effective and safe ablation therapy of intraductal biliary tumor. POC may be useful for determining the extent of tumor and the appropriate location of the ablation catheter. In addition, it allows to evaluate effectiveness, remnant intraductal tumor, or recurrence after ablation therapy.[1]

Endobiliary radiofrequency ablation (RFA) for malignant biliary stricture (MBS) has been reported to contribute to obtaining longer stent patency or survival.[18–21] However, endobiliary RFA under ERCP guidance has been associated with a high adverse event rate. A recent study evaluated the feasibility and safety of the RFA procedure using SpyGlass DS. In 12 patients with bile duct cancer, POC was performed before and after RFA, and endobiliary RFA was also applied under POC guidance. POC-guided RFA was technically successful in all patients and one adverse event (post-procedure cholangitis) was developed.[22] Photodynamic therapy (PDT) also can be performed under POC guidance. Choi et al[23] reported the feasibility and safety of direct POC-guided PDT (Fig. 2) in 9 patients with inoperable extrahepatic cholangiocarcinoma.

Selective guidewire placement for complex biliary stricture or cystic duct

POC facilitates selective guidewire placement into the complicated biliary stricture or cystic duct (Fig. 3) that is difficult to

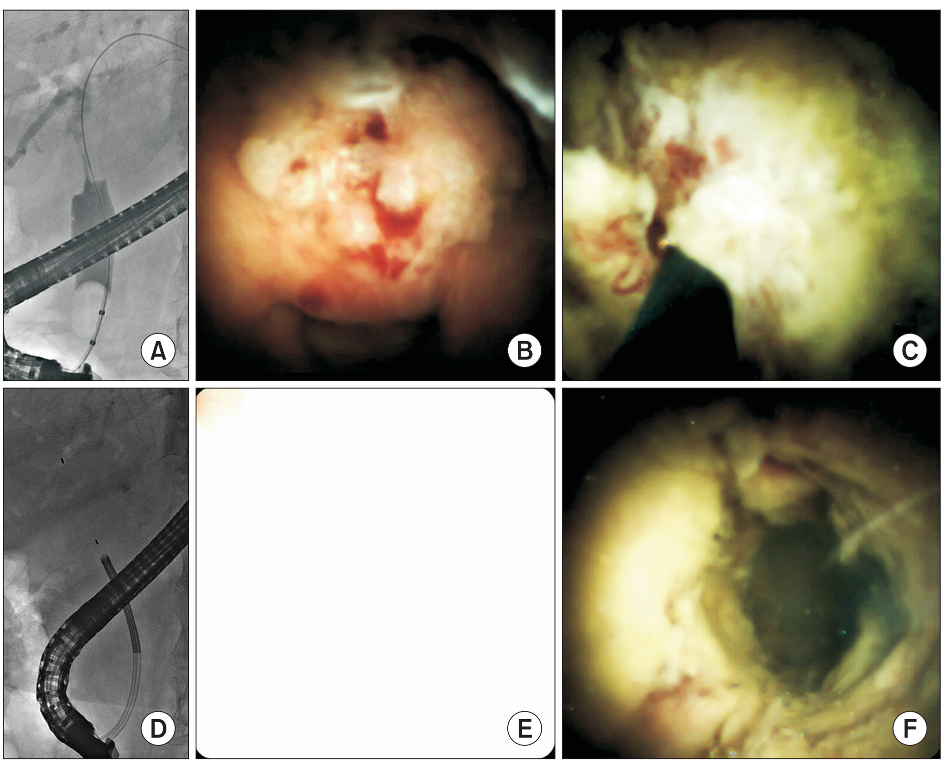

Fig. 2. Peroral cholangioscopy-guided photodynamic therapy by using the SpyGlass digital system. (A) Cholangiogram shows a stricture of the proximal common bile duct. (B, C) Cholangioscopic images show a stricture with irregular tortuous vessels at the site of the proximal biliary stricture. (D) Cholangiogram shows the photodynamic therapy catheter placed across the neoplastic stricture. (E) Cholangioscopic appearance during lighting. (F) Cholangioscopic view 2 weeks after photodynamic therapy reveals diffuse necrosis and improvement of stricture.

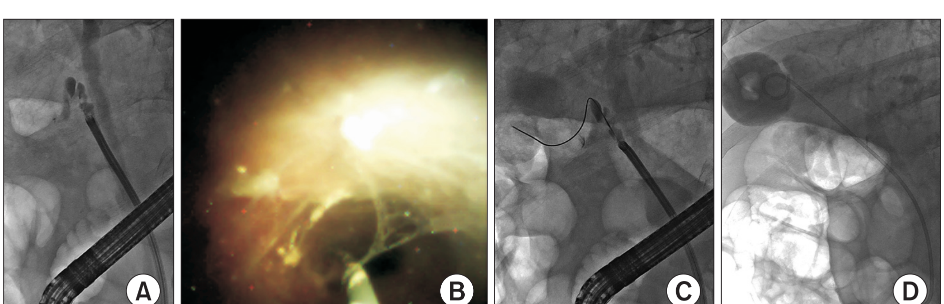

Fig. 3. Peroral cholangioscopy (POC)-guided cystic duct cannulation after failure of fluoroscopic guidance by using the SpyGlass digital system (DS). (A) Cholangiogram shows SpyGlass DS located close to the cystic duct opening. Guide wire advanced into the cystic duct under (B) POC and (C) fluoroscopic guidance. (D) Cholangiogram shows a 7-Fr, 15-cm double-pigtail stent placed between the gallbladder and duodenum.

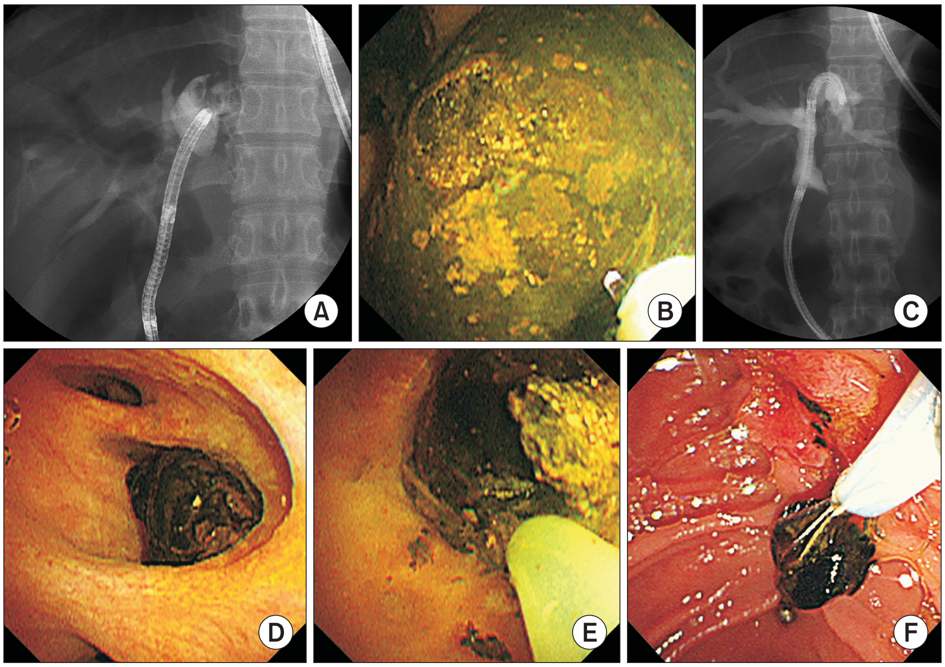

Fig. 4. Direct peroral cholangioscopy (POC)-guided stone removal by using a multibending ultra-slim endoscope after laser lithotripsy. (A) Cholangiogram shows stones in the left intrahepatic duct (IHD) and a multibending endoscope located in IHD without device assistance. (B) Cholangioscopic view of IHD stone with laser lithotripsy probe. (C) Cholangiogram shows no filling defect in the left IHD after stone removal. (D) Cholangioscopic view of small residual stones detected by direct POC. (E, F) Cholangioscopic view shows IHD stone extraction into the duodenum using a 5-Fr basket catheter under direct endoscopic visualization.

approach by only conventional fluoroscopy. In previous study, SpyGlass DS-guided guidewire placement across complex biliary stricture was tried in 30 procedures of 23 patients with previously failed conventional guidewire placement. It was successful in 21 of 30 procedures (70%).[24]

POC-guided direct biliary drainage

The 2.0 to 2.2 mm working channel of an ultra-slim endoscope enable direct stent placement with a 5 to 6 Fr diameter stent after selective guidewire placement.[6,10,25] During the direct POC, biliary stenting is possible to prevent cholangitis without exchanging the endoscope for a duodenoscope.

Other indications

Small bile duct stones which were missed by conventional ERCP can be founded and removed under POC using baskets or other accessories (Fig. 4).[26] In addition, POC has been described to successfully retrieve proximally migrated biliary stents or bile duct foreign body.[27,28] Hemobilia could also be diagnosed and managed successfully by POC.[29]

Conclusions

With the development of more advanced cholangioscopic system, POC is becoming increasingly utilized as an effective tool for patients with biliary diseases. Therapeutic applications of POC for biliary lesions is also expanded owing to continuing advances in specialized endoscopes and available dedicated accessories. Nevertheless, current POC systems are still required improvement in terms of technical difficulty, diameter of working channel, available devices and cost.

Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

ORCID

Yun Nah Lee, https://orcid.org/0000-0001-5588-784X

References

1. Moon JH, Terheggen G, Choi HJ, Neuhaus H. Peroral cholangioscopy: diagnostic and therapeutic applications. *Gastroenterology.* 2013;144:276-82.
2. Ishida Y, Itoi T, Okabe Y. Current status and future perspective in cholangiopancreatoscopy. *Curr Treat Options Gastroenterol.* 2019;17:327-41.
3. Navaneethan U, Hasan MK, Kommaraju K, Zhu X, Hebert-Magee S, Hawes RH, et al. Digital, single-operator cholangiopancreatoscopy in the diagnosis and management of pancreatobiliary disorders: a multicenter clinical experience (with video). *Gastrointest Endosc.* 2016;84:649-55.
4. ASGE Technology Committee, Komanduri S, Thosani N, Abu Dayyeh BK, Aslanian HR, Enestvedt BK, et al. Cholangiopancreatoscopy. *Gastrointest Endosc.* 2016;84:209-21.
5. Lee YN, Moon JH, Choi HJ, Lee TH, Choi MH, Cha SW, et al. Direct peroral cholangioscopy for diagnosis of bile duct lesions using an I-SCAN ultraslim endoscope: a pilot study. *Endoscopy.* 2017;49:675-81.
6. Lee YN, Moon JH, Choi HJ, Kim HS, Choi MH, Kim DC, et al. A newly modified access balloon catheter for direct peroral cholangioscopy by using an ultraslim upper endoscope (with videos). *Gastrointest Endosc.* 2016;83:240-7.
7. Moon JH, Ko BM, Choi HJ, Hong SJ, Cheon YK, Cho YD, et al. Intraductal balloon-guided direct peroral cholangioscopy with an ultraslim upper endoscope (with videos). *Gastrointest Endosc.* 2009;70:297-302.
8. Choi HJ, Moon JH, Ko BM, Hong SJ, Koo HC, Cheon YK, et al. Overtube-balloon-assisted direct peroral cholangioscopy by using an ultra-slim upper endoscope (with videos). *Gastrointest Endosc.* 2009;69:935-40.
9. Ishida Y, Itoi T, Okabe Y. Types of peroral cholangioscopy: how to choose the most suitable type of cholangioscopy. *Curr Treat Options Gastroenterol.* 2016;14:210-9.
10. Lee YN, Moon JH, Lee TH, Choi HJ, Itoi T, Beyna T, et al. Prospective randomized trial of a new multibending versus conventional ultra-slim endoscope for peroral cholangioscopy without device or endoscope assistance (with video). *Gastrointest Endosc.* 2020;91:92-101.
11. McHenry L, Lehman G. Difficult bile duct stones. *Curr Treat Options Gastroenterol.* 2006;9:123-32.
12. McCarty TR, Gulati R, Rustagi T. Efficacy and safety of peroral cholangioscopy with intraductal lithotripsy for difficult biliary stones: a systematic review and meta-analysis. *Endoscopy.* 2021;53:110-22.
13. Buxbaum J, Sahakian A, Ko C, Jayaram P, Lane C, Yu CY, et al. Randomized trial of cholangioscopy-guided laser lithotripsy versus conventional therapy for large bile duct stones (with videos). *Gastrointest Endosc.* 2018;87:1050-60.
14. Angsuwatcharakon P, Kulpatcharapong S, Ridtitid W, Boonmee C, Piyachaturawat P, Kongkam P, et al. Digital cholangioscopy-guided laser versus mechanical lithotripsy for large bile duct stone removal after failed papillary large-balloon dilation: a randomized study. *Endoscopy.* 2019;51:1066-73.
15. Bang JY, Sutton B, Navaneethan U, Hawes R, Varadarajulu S. Efficacy of single-

operator cholangioscopy-guided lithotripsy compared with large balloon sphincteroplasty in management of difficult bile duct stones in a randomized trial. *Clin Gastroenterol Hepatol.* 2020;18:2349-56.e3.
16. Yasuda I, Itoi T. Recent advances in endoscopic management of difficult bile duct stones. *Dig Endosc.* 2013;25:376-85.
17. Barakat MT, Girotra M, Choudhary A, Huang RJ, Sethi S, Banerjee S. A prospective evaluation of radiation-free direct solitary cholangioscopy for the management of choledocholithiasis. *Gastrointest Endosc.* 2018;87:584-9.e1.
18. Steel AW, Postgate AJ, Khorsandi S, Nicholls J, Jiao L, Vlavianos P, et al. Endoscopically applied radiofrequency ablation appears to be safe in the treatment of malignant biliary obstruction. *Gastrointest Endosc.* 2011;73:149-53.
19. Dolak W, Schreiber F, Schwaighofer H, Gschwantler M, Plieschnegger W, Ziachehabi A, et al. Endoscopic radiofrequency ablation for malignant biliary obstruction: a nationwide retrospective study of 84 consecutive applications. *Surg Endosc.* 2014;28:854-60.
20. Strand DS, Cosgrove ND, Patrie JT, Cox DG, Bauer TW, Adams RB, et al. ERCP-directed radiofrequency ablation and photodynamic therapy are associated with comparable survival in the treatment of unresectable cholangiocarcinoma. *Gastrointest Endosc.* 2014;80:794-804.
21. Yang J, Wang J, Zhou H, Zhou Y, Wang Y, Jin H, et al. Efficacy and safety of endoscopic radiofrequency ablation for unresectable extrahepatic cholangiocarcinoma: a randomized trial. *Endoscopy.* 2018;50:751-60.
22. Ogura T, Onda S, Sano T, Takagi W, Okuda A, Miyano A, et al. Evaluation of the safety of endoscopic radiofrequency ablation for malignant biliary stricture using a digital peroral cholangioscope (with videos). *Dig Endosc.* 2017;29:712-7.
23. Choi HJ, Moon JH, Ko BM, Min SK, Song AR, Lee TH, et al. Clinical feasibility of direct peroral cholangioscopy-guided photodynamic therapy for inoperable cholangiocarcinoma performed by using an ultra-slim upper endoscope (with videos). *Gastrointest Endosc.* 2011;73:808-13.
24. Bokemeyer A, Gross D, Brückner M, Nowacki T, Bettenworth D, Schmidt H, et al. Digital single-operator cholangioscopy: a useful tool for selective guidewire placements across complex biliary strictures. *Surg Endosc.* 2019;33:731-7.
25. Waxman I, Chennat J, Konda V. Peroral direct cholangioscopic-guided selective intrahepatic duct stent placement with an ultraslim endoscope. *Gastrointest Endosc.* 2010;71:875-8.
26. Lee YN, Moon JH, Choi HJ, Min SK, Kim HI, Lee TH, et al. Direct peroral cholangioscopy using an ultraslim upper endoscope for management of residual stones after mechanical lithotripsy for retained common bile duct stones. *Endoscopy.* 2012;44:819-24.
27. Sejpal DV, Vamadevan AS, Trindade AJ. Removal of an embedded, migrated plastic biliary stent with the use of cholangioscopy. *Gastrointest Endosc.* 2015;81:1482-3.
28. Ransibrahmanakul K, Hasyagar C, Prindiville T. Removal of bile duct foreign body by using spyglass and spybite. *Clin Gastroenterol Hepatol.* 2010;8:e9.
29. Sum Foong K, Lee A, Kudakachira S, Ramberan H. Hemobilia from biliary angiodysplasia diagnosed with cholangioscopy. *ACG Case Rep J.* 2016;3:e132.