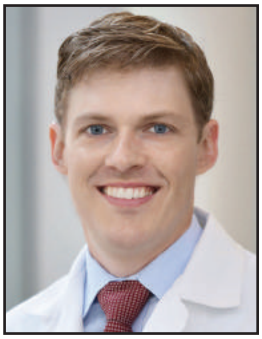
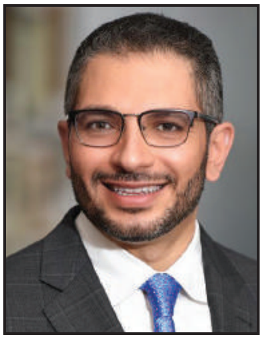
Douglas G. Adler MD, FACG, AGAF, FASGE, Series Editor

Pancreatoscopy



Robert J. Sealock



Mohamed O. Othman

Pancreatoscopy is an endoscopic procedure by which a small caliber endoscope or a catheter-based system is advanced from either the major or minor papilla into the pancreatic duct. Either system is typically advanced through a duodenoscope to allow for proper approach to the pancreatic duct orifice. We herein describe the history, technical aspects, setup, and technical success of pancreatoscopy for a variety of diagnostic and therapeutic indications.

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1. History of pancreatoscopy

The use of per oral cholangiopancreatoscopy was reported in 1975[1,2] using 10Fr endoscope under duodenoscopic visualization. The initial devices were limited to diagnostic purposes with subsequent modifications to allow for tip deflection, irrigation, and the passage of accessories namely a biopsy forcep and lithotripsy fiber. These early systems were termed "mother-daughter" as the duodenoscope served as the "mother" while the smaller "daughter" pancreatoscope was inserted through the working channel. Limitations to these early devices were that two endoscopists were required with one operating the duodenoscope and the other the pancreatoscope. The fiberoptic cable was prone to breakage given that it was housed within a small caliber device. In an early series of 50 patients undergoing pancreatoscopy, technical success was a less-than-satisfying 70%[3] and demonstrated the feasibility of examining not only normal intraductal anatomy but also those with intraductal calculi and tumors.

The mother-daughter system remained in use for over 30 years in limited clinical capacity. In 2007, a single operator cholangiopancreatoscope (SpyGlass, Boston Scientific, Natick, MA) was introduced to facilitate direct visualization of bile

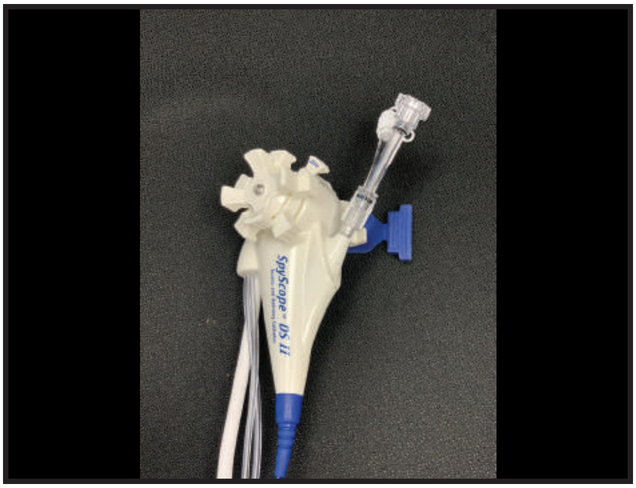


Figure 1. SpyGlass single operator cholangiopancreatoscope

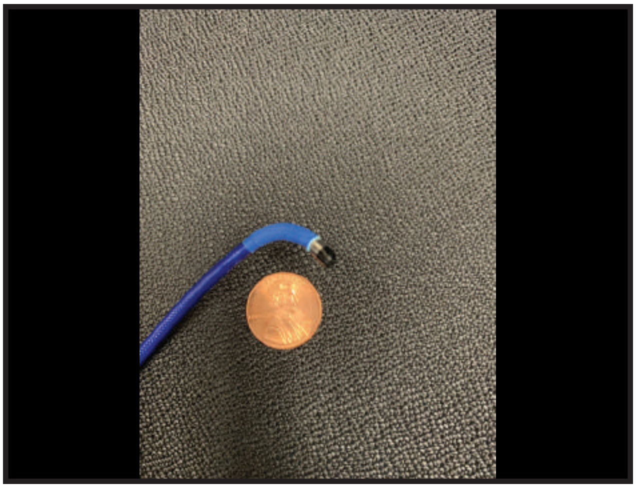


Figure 2. SpyGlass DS distal end

and pancreatic duct. This initial system contained a reusable visualization probe which was inserted through a disposable delivery catheter which also contained injection and working channels. The disposable catheter also allowed for tip deflection using a handle that was modeled after a reusable endoscope. The initial clinical feasibility study[4] was limited to biliary use but subsequent studies demonstrated technical success of this system in the evaluation and treatment of pancreatic duct pathology.

In 2015, a digital version of the SpyGlass system was introduced[5] allowing for greater visual resolution and a 60% wider field of view. At the time of this publication, there are no existing competitors to SpyGlass available in the United States, but several products are in preclinical review.

2. Setup and specifications of disposable cholangiopancreatoscope and accessories

The single operator cholangiopancreatoscope uses a sterile and steerable disposable catheter with two irrigation channels, a 1.2mm working channel, and two diodes as a light source. The handle has two control knobs, which mimic that of a standard endoscope. (Figure 1) Aspiration through the working channel is achieved by attaching an empty Luer lock syringe to the dedicated suction line. There is also tubing for irrigation that is attached to the endoscope irrigation pump. Our practice is to reduce the irrigation pressure to at least 50% to minimize the volume and pressure of fluid entering the main pancreatic duct and side branches.

The cholangiopancreatoscope is attached to a proprietary image processor. The only adjustable function via the processor is the light source brightness but rarely is manual adjustment necessary. As opposed to the mother-daughter systems, optical contrast modes such as narrow band imaging are not available. Video output options include DVI, S-video and VGA.

The working channel will accommodate any accessory equal to or smaller than 3Fr which includes most electrohydraulic lithotripsy fibers (EHL), holmium laser fibers, microforceps, and dedicated snares and baskets for the SpyGlass system. (Figure 2)

3. Performing pancreatoscopy

Amongst ERCPists with experience in pancreatography, pancreatoscopy is a straightforward extension of their endoscopic toolbox. Positioning of the patient is the same for traditional ERCP with the patient placed in either prone or supine positioning. Left lateral decubitus position makes interpretation of fluoroscopic images difficult. Endotracheal intubation should be considered given the longer duration of time needed to complete ERCP with pancreatoscopy and saline irrigation of the pancreatic duct can reflux from the second portion of the duodenum into the stomach increasing the risk of pulmonary aspiration. General endotracheal anesthesia has been associated with

Figure 3. A patient with a dilated main pancreatic duct diagnosed with main duct IPMN

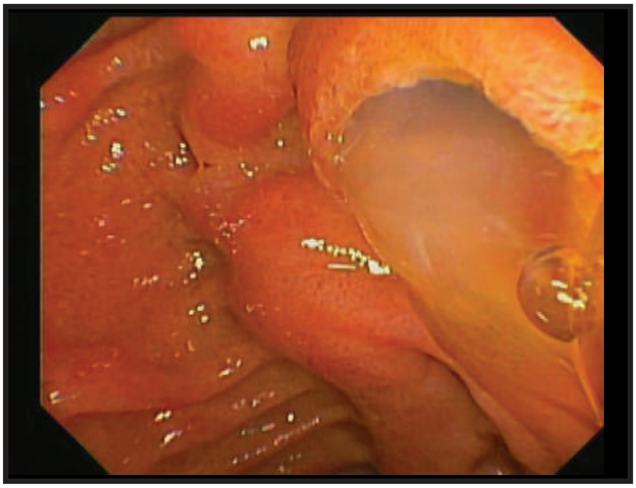


Figure 3a. Fish mouth ampulla because of a main duct IPMN

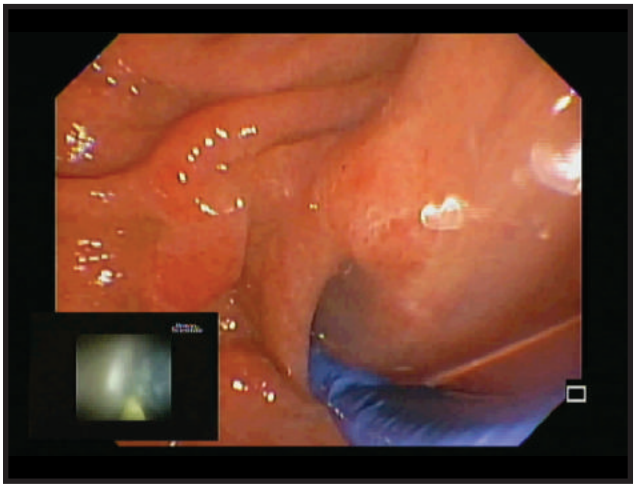


Figure 3b. Insertion of pancreatoscope through fish mouth ampulla

Figure 3c. Intraductal visualization of papillary projections and abundant mucin

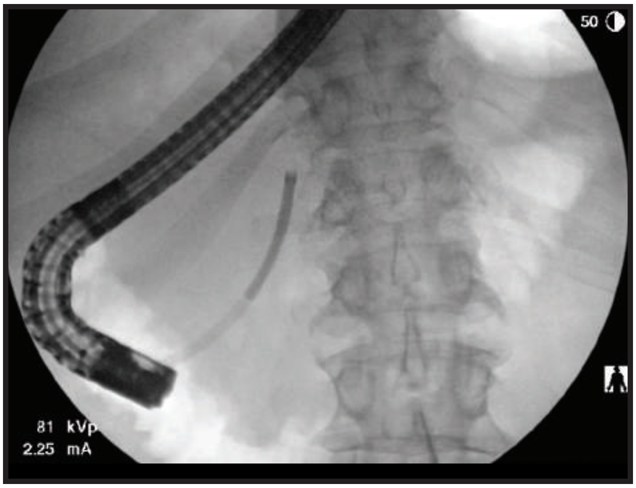
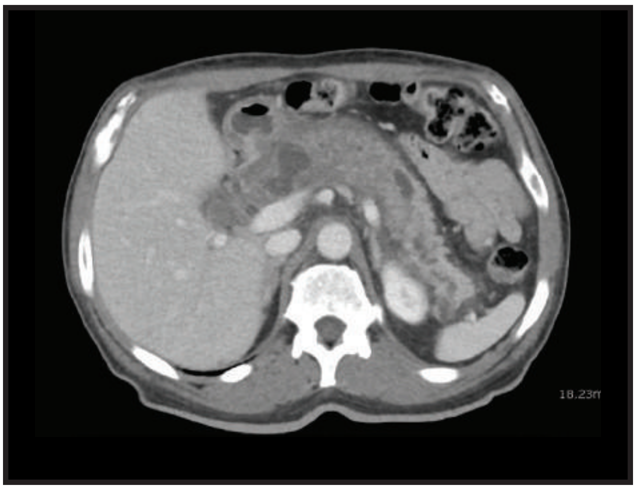


Figure 3d. Fluoroscopic image of pancreatoscope



3e. Computed Tomography of dilated main pancreatic duct in genu

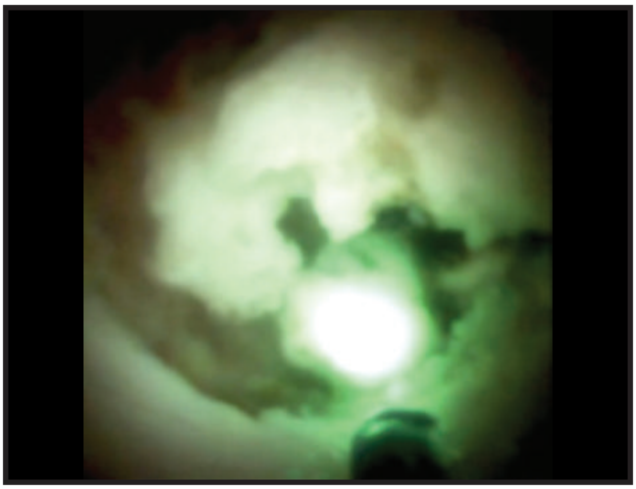


Figure 4. Lithotripsy of pancreatic duct stone

a lower rate of sedation related adverse events amongst high-risk patients undergoing ERCP.[6]

Access to the pancreatic duct is obtained via the major ampulla in most patients although reports have documented access from the minor papilla in select cases.[7-10] The choice of guidewire diameter is at the discretion of the endoscopist as the single operator cholangiopancreatoscope will accommodate up to a diameter of 0.035 inches. A 260cm length wire is acceptable in most cases, but once pancreatoscopy is complete and subsequent devices are to be used while maintaining access to the pancreatic duct, a 450cm wire must be used for device exchange. In most cases, pancreatic sphincterotomy is necessary to pass the 10Fr (3.3mm) diameter scope into the pancreatic duct however in cases of main duct intraductal papillary neoplasm (MD-IPMN) freehand cannulation without wire or sphincterotomy is feasible. (Figure 3) A minimum duct diameter of 3mm is recommended to advance the cholangiopancreatoscope through the pancreatic duct. Saline irrigation is often required to clear debris and improve endoscopic visualization. If EHL is performed, intraductal saline is required for shock wave transmission. Once pancreatoscopy is completed, our practice is to place at least a prophylactic pancreatic duct stent without leading barb for mitigation of post-ERCP pancreatitis (PEP) which can be as high as 28% of patients.[11] Rectal indomethacin is also administered unless NSAID allergy is documented.

4. Indications, technical success, and clinical outcomes for pancreatoscopy

a. Diagnostic
    i. Assessment of PD strictures
    ii. Evaluation of suspected MD-IPMN and extent of duct involvement
b. Therapeutic
    iii. Lithotripsy for PD stones (Figure 4)

Indications for pancreatoscopy mirror those of cholangiopathy and can be subdivided into diagnostic and therapeutic indications. Diagnostic applications include the assessment of pancreatic duct stricture and evaluation of suspected main duct intraductal papillary mucinous neoplasms. In addition to endoscopic visualization, pancreatic duct aspiration and directed biopsies can be obtained at the time of pancreatoscopy. (Video 1. See link below)

https://practicalgastro.com/media/Main_Duct_IPMN.mp4

Therapeutic applications include guided lithotripsy for obstructing pancreatic duct stones, ablation of pancreatic duct strictures, and assessing treatment response for intraductal radiofrequency application.

In one of the largest series of pancreatoscopy in the evaluation of benign and malignant disease of the pancreatic duct, Shah et al. evaluated 79 patients with inconclusive pancreatic duct findings based on prior CT, MRCP or EUS and found that when optical findings were combined with pancreatoscopy guided biopsy and/or aspiration sensitivity and specificity for neoplasm was 91% and 95%, respectively. Technical success was 97% and adverse events occurred in 12%. In cases with inconclusive EUS guided FNA results of lesions involving the pancreatic duct, pancreatoscopy may provide an additional benefit in evaluating for neoplastic lesions.[13,14]

Given the morbidity of total pancreatectomy, pancreatoscopy allows of precise delineation of the extent of involvement in cases of main duct IPMN thereby allowing for preservation of the uninvolved pancreas. In one of the first series to evaluate pre-operative use of cholangiopancreatoscopy, Tyberg et al. found that amongst 13 patients undergoing pre-operative pancreatoscopy for IPMN, pancreatoscopy changed surgical resection in 62% (8/13 pts) of patients.[15] In a separate series of patients with main duct IPMN who underwent pancreatoscopy followed by surgery, 95% (18/19) of the patients had a negative surgical margin. However, there was no control group of patients that did not undergo pre-operative pancreatoscopy.[16]

As stated above, therapeutic applications of pancreatoscopy are focused on the treatment of intraductal complications of chronic pancreatitis, namely visualization, fragmentation, and removal of obstructing pancreatic duct stones. The ideal candidates for pancreatic duct stone fragmentation are those with pain from obstructive pancreatitis with upstream pancreatic duct dilation. Conventional techniques of stone removal via ERCP including balloon extraction should be considered, but for multiple or stones >5mm traditional endoscopic measures may not be successful. Pancreatoscopy guided fragmentation can be achieved using an electrohydraulic lithotripsy or a holmium laser fiber which is advanced through the working channel of the pancreatoscope. Published studies have not delineated the ideal candidate but in our experience, stones located in the pancreatic head and body are more easily treated. Intraductal stones are commonly situated proximal to strictures and fluoroscopically directed dilation using small caliber balloons is often necessary to visualize and treat stones. Even if complete stone clearance is achieved, we commonly place a prophylactic small caliber pancreatic duct stent without leading barbs to mitigate the risk of post-ERCP pancreatitis.

In a multi-center retrospective study evaluating the efficacy of pancreatoscopy for intraductal stones amongst 109 patients, technical success was achieved in 90%, with a majority achieving complete stone clearance in a single session.[17] Adverse events were 10% and included 5 cases of pancreatitis and 1 main pancreatic duct perforation that was treated with stent therapy. Clinical success, defined as resolution or reduction in symptoms, was achieved in 88% but did not include a formal quality of life or pain survey. In a systemic review involving 383 patients, Saghir et al.[18] found a pooled technical and clinical success rate of 76%. When comparing EHL vs. laser lithotripsy (LL), LL achieved a higher technical and clinical success rate of 89% and 88%, respectively. Only one study out of 16 used a formal quality pre and post procedure quality of life survey to assess pain outcomes. Most studies were retrospective and single center in design.

In summary, pancreatoscopy directed therapy for intraductal stones is effective amongst experienced operators, however, randomized studies comparing pancreatoscopy to alternative therapies including extracorporeal shockwave lithotripsy or surgery are needed.

5. Troubleshooting

One of the main limitations of pancreatoscopy is the difficulty in advancing the pancreatoscope catheter into a normal sized pancreatic duct. A minimal main pancreatic duct diameter of 4-5 mm is needed to allow easier advancement of the pancreatoscope. Endoscopists should be aware of the direction of the pancreatic duct during advancement of the pancreatoscope. Using the dials of the pancreatoscope to ensure the device is aligned along the axis of the pancreatic duct is crucial for easier advancement, even if the device is advanced over a guidewire. In terms of guidewires, the device could be advanced over a 0.025-inch guidewire into the main pancreatic duct; if the endoscopist encounters difficulty in pancreatoscope advancement, using 0.035 inch guidewires could provide the tension required to advance the pancreatoscope into the pancreatic duct. During pancreatic duct lithotripsy, endoscopists could encounter difficulty advancing the lithotripsy probe outside of the pancreatoscope due to bending of the pancreatoscope catheter. In these instances, it might be easier to advance the lithotripsy probe into the pancreatoscope channel to the tip of the device while the pancreatoscope is in the duodenal lumen. After ensuring that the lithotripsy probe reached the tip of the pancreatoscope, the endoscopist should advance the device into the main pancreatic duct to start lithotripsy. It is worth mentioning that lithotripsy of pancreatic duct stones obstructing the main pancreatic duct at the head of the pancreas could be challenging due to device instability or difficulty in visualization. Endoscopists should be aware that pancreatic duct stones embedded

(continued on page 54)

(continued from page 52)

in pancreatic duct orifice may be better managed with other methods such as shock wave lithotripsy.

Future Directions

There are several prototypes of cholangio-pancretoscopes in the pipelines. It is expected that the next generation of cholangio-pancreatoscopes will have artificial intelligence capabilities which will aid in differentiating benign from malignant strictures. The working channel of the next generation cholangio-pancreatoscope will hopefully be large enough to accommodate therapeutic devices such as plastic or metal stents. Larger baskets, biopsy forceps, snare, injection needles or radiofrequency ablation probes could be advanced under direct visualization through next generation cholangio-pancreatoscopes to expedite diagnostic or therapeutic interventions.

CONCLUSION

In conclusion, pancreatoscopy is a useful diagnostic and therapeutic tool for patients with complex neoplastic and chronic conditions of the pancreatic duct with a favorable adverse event rate comparable to that of more conventional ERCP techniques. ■

Suggested Reading

- Innovations in Intraductal Endoscopy Gastrointestinal Endoscopy Clinics of North America, 2015-10-01, Volume 25, Issue 4, Pages 779-792
- De Luca L, Repici A, Koçollari A, Auriemma F, Bianchetti M, Mangiavillano B. Pancreatoscopy: An update. World J Gastrointest Endosc 2019; 11(1): 22-30 [PMID: 30705729 DOI: 10.4253/wjge.v11.i1.22]

References

1. Takekoshi T., Maruyama M., Sugiyama N., et al. Retrograde pancreatocholangioscopy. Gastrointest Endosc. 1975; 17: 678-683
2. Kawai K, Nakajima M, Akasaka Y, Shimamotu K, Murakami K. A new endoscopic method: the peroral choledocho-pancreatoscopy (author's transl). Leber Magen Darm. 1976;6:121-124.
3. Nakajima M, Akasaka Y, Yamaguchi K, Fujimoto S, Kawai K. Direct endoscopic visualization of the bile and pancreatic duct systems by peroral cholangiopancreatoscopy (PCPS). Gastrointest Endosc. 1978 May;24(4):141-5.
4. Chen YK, Pleskow DK. SpyGlass single-operator peroral cholangiopancreatoscopy system for the diagnosis and therapy of bile-duct disorders: a clinical feasibility study (with video). Gastrointest Endosc. 2007 May;65(6):832-41.
5. Navaneethan U, Hasan MK, Kommaraju K, Zhu X, Hebert-Magee S, Hawes RH, Vargo JJ, Varadarajulu S, Parsi MA. Digital, single-operator cholangiopancreatoscopy in the diagnosis and management of pancreatobiliary disorders: a multicenter clinical experience (with video). Gastrointest Endosc. 2016 Oct;84(4):649-55
6. Smith ZL, Mullady DK, Lang GD, Das KK, Hovis RM, Patel RS, Hollander TG, Elsner J, Ifune C, Kushnir VM. A randomized controlled trial evaluating general endotracheal anesthesia versus monitored anesthesia care and the incidence of sedation-related adverse events during ERCP in high-risk patients. Gastrointest Endosc. 2019 Apr;89(4):855-862.
7. Shintani S, Maehira H, Inatomi O, Tani M, Andoh A. Peroral pancreatoscopy via the minor papilla in the diagnosis of intraductal papillary mucinous neoplasm. VideoGIE. 2020 Aug 13;5(12):673-675.
8. Takeshita K, Asai S, Fujimoto N. Removal of dilated Santorini's duct stones by peroral pancreatoscopy and electrohydraulic lithotripsy through the minor papilla. Dig Endosc. 2020 Jul;32(5):e98-e99.
9. Chew EY, Varghese BT, Sealock RJ. Pancreatic duct rendezvous with pancreatoscopy through the minor papilla. VideoGIE. 2018 Feb 21;3(4):132-134.
10. Brauer BC, Chen YK, Ringold DA, Shah RJ. Peroral pancreatoscopy via the minor papilla for diagnosis and therapy of pancreatic diseases. Gastrointest Endosc. 2013 Sep;78(3):545-9.
11. van der Wiel SE, Stassen PMC, Poley JW, De Jong DM, de Jonge PJF, Bruno MJ. Pancreatoscopy-guided electrohydraulic lithotripsy for the treatment of obstructive pancreatic duct stones: a prospective consecutive case series. Gastrointest Endosc. 2022 May;95(5):905-914.e2.
12. El Hajj II, Brauer BC, Wani S, Fukami N, Attwell AR, Shah RJ. Role of per-oral pancreatoscopy in the evaluation of suspected pancreatic duct neoplasia: a 13-year U.S. single-center experience. Gastrointest Endosc. 2017 Apr;85(4):737-745.
13. Yamao K, Ohashi K, Nakamura T et al. Efficacy of peroral pancreatoscopy in the diagnosis of pancreatic diseases. Gastrointest Endosc 2003; 57: 205-209
14. Kodama T, Koshitani T, Sato H et al. Electronic pancreatoscopy for the diagnosis of pancreatic diseases. Am J Gastroenterol 2002; 97: 617-622
15. Tyberg A, Raijman I, Siddiqui A, Arnelo U, Adler DG, Xu MM, Nassani N, Sejpal DV, Kedia P, Nah Lee Y, Gress FG, Ho S, Gaidhane M, Kahaleh M. Digital Pancreaticocholangioscopy for Mapping of Pancreaticobiliary Neoplasia: Can We Alter the Surgical Resection Margin? J Clin Gastroenterol. 2019 Jan;53(1):71-75.
16. Kishimoto Y, Okano N, Ito K, Takuma K, Hara S, Iwasaki S, Yoshimoto K, Yamada Y, Watanabe K, Kimura Y, Nakagawa H, Igarashi Y. Peroral Pancreatoscopy with Videoscopy and Narrow-Band Imaging in Intraductal Papillary Mucinous Neoplasms with Dilatation of the Main Pancreatic Duct. Clin Endosc. 2022 Mar;55(2):270-278.
17. Brewer Gutierrez OI, Raijman I, Shah RJ, Elmunzer BJ, Webster GJM, Pleskow D, Sherman S, Sturgess RP, Sejpal DV, Ko C, Maurano A, Adler DG, Mullady DK, Strand DS, DiMaio CJ, Piraka C, Sharahia R, Dbouk MH, Han S, Spiceland CM, Bekkali NLH, Gabr M, Bick B, Dwyer LK, Han D, Buxbaum J, Zulli C, Cosgrove N, Wang AY, Carr-Locke D, Kerdsirichairat T, Aridi HD, Moran R, Shah S, Yang J, Sanaei O, Parsa N, Kumbhari V, Singh VK, Khashab MA. Safety and efficacy of digital single-operator pancreatoscopy for obstructing pancreatic ductal stones. Endosc Int Open. 2019 Jul;7(7):E896-E903.
18. Saghir SM, Mashiana HS, Mohan BP, Dhindsa BS, Dhaliwal A, Chandan S, Bhogal N, Bhat I, Singh S, Adler DG. Efficacy of pancreatoscopy for pancreatic duct stones: A systematic review and meta-analysis. World J Gastroenterol. 2020 Sep 14;26(34):5207-5219.