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Current Status and Future Perspective in Cholangiopancreatoscopy

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Abstract

Purpose of review With the rapid growth of cholangiopancreatoscopy, several platforms of cholangiopancreatoscopy have been currently available. Since the introduction of digital single-operator cholangiopancreatoscopy, there have been several reports describing its efficacy for long-standing and novel applications. The purpose of this review is to show the current status and future perspective of cholangiopancreatoscopy.
Recent findings Meta-analysis of cholangiopancreatoscopy have demonstrated good diagnostic yield for visual impression; however, it should be noted that there is no standardized classification system used for distinguishing benign from malignant lesions. In contrast, utility of tissue sampling under direct vision for cholangiopancreatic disorders is inconclusive. This could be explained by the fact that available devices (e.g., biopsy forceps) are limited by the small diameter of accessory channel. Regarding therapeutic applications, several studies demonstrated efficacy and feasibility of electrohydraulic lithotripsy or laser lithotripsy for difficult bile duct stone and pancreatic duct stone under cholangiopancreatoscopic guidance. Additionally, ablation of tumors, selective guidewire placement, retrieval of migrated stents, and anterograde cholangioscopy-guided procedure by using cholangiopancreatoscopy have been reported.
Summary The recent development of digital single-operator cholangiopancreatoscopy enables easy access to the bile duct and pancreatic duct, contributing to expanding indications for cholangiopancreatoscopy. Improvement of devices or development of innovative devices is required to overcome the remaining problems of cholangiopancreatoscopy.

Introduction

Cholangioscopy was initially described as peroral cholangioscopy (POCS) under duodenoscopic guidance in 1976 [1]. Subsequently, POCS has been developed to enable direct visualization of the inside of the biliary tree. Previously, image quality was low with the use of fiber optic system; however, a new video cholangioscope was introduced in 1999 with a high-quality digital image and a smaller scope diameter owing to improvements of very small charge-coupled devices [2]. In particular, usefulness of video POCS using a narrow-band imaging (NBI) system has been reported. POCS with NBI can provide clearer images of mucosal vessels and structures [3–5]. Peroral pancreatoscopy (POPS) was introduced and evaluated in a similar way.

Video POCS and POPS have potential for changing diagnostic or therapeutic strategy of pancreatobiliary diseases; however, these have not prevailed because of their fragility and requirement of the participation of two skilled endoscopists using two endoscopic systems. To overcome these drawbacks, direct POCS using ultra-slim upper endoscope (D-POCS) has been reported as a single-operator system [6–8]. D-POCS allows a greater variety of procedures with a larger diameter of accessory channel under excellent imaging even with an image-enhanced function system. However, scope insertion is still challenging, which avoids widespread use. Single-operator cholangioscopy consisting of disposable parts was introduced in 2007, which allowed for widespread dissemination use owing to its good maneuverability and single-operator system [9, 10]. Additionally, image quality and maneuverability has been improved in the newer generation, contributing to conversion of single-operator cholangioscopy from an advanced technique into a standard technique in clinical practice. In this article, we focus on the current status and future perspective of peroral cholangiopancreatoscopy.

Instruments and procedure

There are several platforms of currently available cholangiopancreatoscopy. It is important to understand the features of each platform as below, in an effort to select suitable cholangiopancreatoscopy.

Video cholangiopancreatoscopy

Peroral cholangiopancreatoscopy are composed of a mother duodenoscope and a baby cholangioscope. The baby scope is inserted into the bile duct through the accessory channel of a conventional therapeutic duodenoscope that acts as the mother scope. This insertion technique is called mother-baby scope insertion system (MBSS) [11]. One of a currently available video cholangiopancreatoscope as the baby scope (CHF-B260; Olympus Medical Systems, Tokyo, Japan) has a two-way angulation function, an outer diameter of 3.4 mm, and an accessory channel diameter of 1.2 mm [12, 13••]. This cholangiopancreatoscope can provide an excellent image with NBI system. Some advantages of peroral video cholangiopancreatoscopy with MBSS are as follows: (1) an excellent image is obtained, (2) the NBI system can be used, (3) insertion of the baby scope is comparatively easy, (4) the baby scope positioning in the bile duct is stable, and (5) the smaller outer diameter enables it to be used even for normal bile duct and intrahepatic bile duct [12]. In contrast, some disadvantages of video cholangiopancreatoscopy with MBSS are as follows: (1) baby scope fragility, (2) limitation of the working channel caliber, and (3) requirement of the participation of two skilled endoscopists using two endoscopic systems [12]. Peroral video cholangiopancreatoscopy with MBSS has potential for changing diagnostic and therapeutic strategies of pancreatobiliary diseases; however, it is not widely used because of these drawbacks. Given new video cholangioscope (CHF-B290; Olympus Medical Systems, Tokyo, Japan) has just launched, further development of image quality and durability is expected.

Direct video peroral cholangiopancreatoscopy

D-POCS using ultra-slim upper endoscope has been proposed as a single-operator system for direct endoscopic examination of the bile duct. The ultra-slim endoscope was originally designed for use in pediatric patients and for transnasal applications; therefore, several ultra-slim endoscopes are commercially available [12, 13••]. These ultra-slim endoscopes have a four-way angulation function and outer diameters of 5.0–5.9 mm with a 2-mm working channel, which can provide excellent images and can be used with image-enhanced function system including NBI. On the other hand, D-POCS has some disadvantages: difficulty in scope insertion to the bile duct and a larger outer diameter that limits the indications for which it can be used [12, 14, 15].

Single-operator cholangiopancreatoscopy

SpyGlass direct visualization system was introduced in 2007 and is designed for single-operator examination [9, 10]. This system was firstly composed of a reusable optical probe (SpyGlass Direct Visualization Probe; Boston Scientific Corporation, Marlborough, MA, USA) and a disposable delivery catheter (SpyScope; Boston Scientific Corporation, Marlborough, MA, USA). The delivery catheter has a four-way deflected steering, an outer diameter of 3.3 mm, and a 1.2-mm accessory channel [9]. This delivery catheter can be inserted through an accessory channel of therapeutic duodenoscope similar to MBSS; however, the four-way deflected steering makes it easier to visualize a target compared with a video cholangiopancreatoscopy. Additionally, the delivery catheter has dedicated irrigation channel, which enables continuous water irrigation for clear image. Nevertheless, this first SpyGlass direct visualization system had significant limitations related to the optical fiber system, including limited image quality and fiberoptic probe durability. This semi-disposable system is referred to as SpyGlass Legacy, because innovations in the system enabled to introduce digital single-operator cholangiopancreatoscopy: SpyGlass DS direct visualization system (SpyGlass DS), with improved image quality and better maneuverability of the catheter tip [16]. Improvement of image quality was supported by the study using a biliary tract bench model [16]. Some advantages of SpyGlass DS are as follows: (1) single-operator examination, (2) fully-disposable system, (3) four-way deflected steering, (4) dedicated irrigation channel, and (5) markedly improved image quality compared with SpyGlass Legacy [12, 16]. These advantages have brought SpyGlass DS into mainstream and widespread use, although it has some disadvantages including limited diameter of the working channel and inability of image-enhanced function systems.

Direct peroral cholangioscopy using balloon-assisted endoscope for cases with altered anatomy

Although endoscopic therapy for bile duct stone or biliary stricture with altered anatomy is still challenging, endoscopic retrograde cholangiopancreatography (ERCP)-related procedure using balloon-assisted endoscope and endoscopic ultrasonography-guided procedure have been attracting attention. Direct peroral cholangioscopy using a balloon-assisted endoscope have been reported recently, although indicated cases are limited to patients who undergo bile duct resection and pancreaticoduodenectomy with a dilated bile duct. Some reports revealed high technical success rate and feasibility of D-POCS-related procedures using double-balloon enteroscope or single-balloon enteroscope [17, 18]. The advantages of D-POCS using balloon assisted endoscopy are as follows: (1) excellent image with image-enhanced function system, (2) larger diameter of the accessory channel, and (3) endoscopic stability within the bile duct, although D-POCS using balloon-assisted endoscopy has a disadvantage including limited indication as noted above.

We reported a novel technique of direct POCS using SpyGlass DS with the overtube [19]. First, conventional balloon-assisted endoscope was inserted to the papilla or anastomotic site, and balloon dilation of papilla or anastomotic site was performed consecutively. Second, balloon-assisted endoscope was removed, leaving a guidewire in the bile duct and the overtube with inflated balloon. Third, SpyGlass DS was inserted into the bile duct over the guidewire through the overtube. This technique was named the "monorail technique," which may broaden the indication to the case with smaller bile duct compared with D-POCS using.

Clinical applications

Peroral cholangiopancreatoscopy is used for both diagnostic and therapeutic purpose. Suitable cholangiopancreatoscopy should be selected from the currently available platforms described above, according to each cases and skill of an endoscopist; however, indication of cholangiopancreatoscopy is the same as below regardless of the choice of platform.

Diagnostic application of POCS

Endoscopic visual diagnosis for biliary diseases

Osanai et al. reported good diagnostic yield of video POCS using MBSS for indeterminate biliary disease and preoperative mucosal cancerous extension: sensitivity 96.4%, specificity 80.0%, and accuracy 92.1% [20]. In addition, meta-analysis of POCS including video POCS, SpyGlass Legacy, and D-POCS also revealed good diagnostic yield for visual impression (sensitivity 93%, specificity 85%, and accuracy 89%) [21]. The results of recent studies are listed in Table 1. However, it should be noted that there is no standardized classification system used for distinguishing benign lesions from malignant lesions [5, 22]. Mounzer et al. firstly evaluated the individual video of POCS findings and reported that tortuous and dilated vessels, infiltrative stricture, polypoid mass, and the presence of fish-egg lesions were significantly associated with neoplasm [23••]. Although this study is very important and contributory to establish endoscopic classification of pancreatobiliary diseases, there is discrepancy in some of the result between this study and the previous studies. Regarding tortuous and dilated vessels, we reported that dilated and tortuous vessels were observed even in patients with IgG4-related sclerosing cholangitis [24]. Additionally, we conducted ex vivo fundamental study to reveal the difficulty in diagnosing biliary neoplasm only by the existence of abnormal vessels, highlighting the importance of evaluating the form of abnormal vessels [25].

Korrapati et al. described in the aforementioned meta-analysis that SpyGlass Legacy had a significantly reduced sensitivity for visual impression when compared with video POCS [21], whereas several reports revealed good diagnostic

Table 1. Diagnostic yield of endoscopic visual diagnosis for biliary disease

	Year	Platform	Study design	Sample size	Sensitivity	Specificity	Accuracy
Osanai et al. [20]	2013	Video	Prospective	38	96.4%	80.0%	92.1%
Korrapati et al. [21]	2015	Video, D-POCS, SpyGlass Legacy	Systematic review	–	93%	85%	89%
Navaneethan et al. [28]	2016	SpyGlass DS	Retrospective	44	90.0%	95.8%	
Ogura et al. [26]	2017	SpyGlass DS	Prospective	28	83%	89%	93%
Turowski et al. [27••]	2018	SpyGlass DS	Retrospective	99	95.5%	94.5%	
Kanno et al. [29]	2018	Video	Retrospective	56	Liver side 88% Ampullary side 100%	Liver side 83% Ampullary side 100%	Liver side 83% Ampullary side 100%
		SpyGlass DS	Retrospective	20	Liver side 58% Ampullary side 100%	Liver side 86% Ampullary side 100%	Liver side 68% Ampullary side 88%
Lenze et al. [33]	2018	SpyGlass DS	Retrospective	25	88.9%	97.6%	

yield of SpyGlass DS owing to improvement of image quality [26, 27••]. Navaneethan et al. conducted a multi-center study on SpyGlass DS and demonstrated that the sensitivity and specificity of SpyGlass DS visual impression for diagnosis of malignancy was 90% and 95.8%, respectively [28••]. In addition, Kanno et al. reported that the visual diagnosis using SpyGlass DS for tumor extension of extrahepatic cholangiocarcinoma was acceptable when compared with video POCS [29]. Improvement of image quality of SpyGlass DS obviously contributes to these results, which is supported by the retrospectively comparative study of SpyGlass Legacy and SpyGlass DS [30]. Taken together, it is conceivable that visual diagnosis of SpyGlass DS is reliable; however, it should be noted again that there is no standardized classification system of endoscopic findings of biliary diseases. Further study is required to establish endoscopic visual diagnosis.

Tissue sampling under direct vision

Aforementioned study on video POCS using MBSS also described that the definitive diagnosis of mucosal tumor extension may require a combination of visual diagnosis and biopsy under direct vision [20]. In addition, Tyberg et al. also evaluated utility of preoperative mapping biopsy using SpyGlass DS and described that it changed the surgical plan in 32 of 105 patients with cholangiocarcinoma [31•]. They uncovered the efficacy of preoperative mapping biopsy using SpyGlass DS. These results are supported by the current situation that endoscopic visual diagnosis has not been fully established. In contrast, a systematic review demonstrated the moderate sensitivity of SpyGlass Legacy-guided biopsy in the diagnosis of malignant biliary stricture (pooled sensitivity 60.1%, specificity 98.0%) [32••]. Several studies also reported moderate diagnostic yield of SpyGlass DS-guided biopsy [21, 33]. A possible explanation for these results is the fact that the same biopsy forceps (SpyBite biopsy forceps; Boston Scientific Corporation, Marlborough, MA, USA) with an outer diameter of 1.0 mm has been used since

SpyGlass Legacy was introduced, although SpyGlass system was converted from Legacy into DS. The smaller diameter of the accessory channel may be the main problem or limitation of SpyGlass DS under present circumstances that image quality of SpyGlass has been drastically improved. Based on the above results, the efficacy of tissue sampling under POCS guidance still remains inconclusive, although it should be performed as a complementary approach of visual diagnosis. The results of recent studies are shown in Table 2.

To improve diagnostic performance of tissue sampling under direct vision, Varadarajulu et al. evaluated rapid onsite evaluation (ROSE) of touch imprint cytology when SpyGlass Legacy or DS-guided biopsy was performed, suggesting that the diagnostic outcomes of SpyGlass-guided tissue sampling can be significantly improved by using ROSE of touch imprint cytology (sensitivity 100%, specificity 88.9%, accuracy 93.5%) [34]. ROSE is widely known as a good tool for improving diagnostic yield of endoscopic ultrasound (EUS)-guided tissue sampling [35, 36]. Additionally, false-negative result of cytology can be mainly attributed to insufficient material. In this regard, ROSE may be also useful for the samples obtained using SpyGlass.

As discussed so far, we recommend that diagnostic POCS should be performed for diagnosing indeterminate strictures with inconclusive result of prior tissue sampling and for evaluating tumor extension of bile duct cancer preoperatively. POCS-guided biopsy is also recommended as a complementary approach of visual diagnosis, because endoscopic visual diagnosis of biliary disorders has not been fully established.

Therapeutic applications of POCS

Treatment of difficult-to-treat biliary stone

Management of difficult biliary stones is an important application of POCS. Approximately 85–90% of bile duct stones can be extracted using conventional ERCP-related procedures [37]; however, the removal of bile duct stones may be difficult in the remaining 10–15% of patients [38]. Difficult-to-treat bile duct stone is defined as biliary stones for which various difficulties are encountered during the procedure [39]. With regard to a large or impacted stone, the utility of electrohydraulic lithotripsy (EHL) or laser lithotripsy (LL) under video POCS guidance has

Table 2. Diagnostic yield of biopsy under direct vision without visual impression for biliary disease

	Year	Platform	Study design	Sample size	Sensitivity	Specificity	Accuracy
Osanai et al. [20]	2013	Video	Prospective	35	81.5%	100%	85.7%
Korrapati et al. [21]	2015	Video, D-POCS, SpyGlass Legacy	Systematic review	–	69%	94%	79%
Navaneethan et al. [32]	2015	SpyGlass Legacy	Systematic review	–	60.1%	98.0%	
Navaneethan et al. [28]	2016	SpyGlass DS	Retrospective	44	85.0%	100%	
Ogura et al. [26]	2017	SpyGlass DS	Prospective	28	80.0%	100%	89%
Turowski et al. [27••]	2018	SpyGlass DS	Retrospective	41	57.7%	100%	
Lenze et al. [33]	2018	SpyGlass DS	Retrospective	29	62.5%	90.0%	

been reported [40–42]. Recently, several reports have evaluated the feasibility and utility of EHL or LL using SpyGlass, because video POCS with MBSS requires the excellent coordination of two skilled endoscopists and video POCS is fragile as mentioned above. Some retrospective multi-center studies revealed that technical success rates of EHL and LL using SpyGlass DS were 95–97.3% [27, 43]. These studies enrolled the cases with failed stone removal by conventional ERCP method. In addition, two randomized control trials demonstrated better stone clearance rate of LL compared with conventional ERCP-related procedure [44, 45]. Buxbaum et al. reported that stone clearance rate of the LL group was better than the conventional procedure group (93% vs. 67%), although conventional methods were allowed in the LL group [44]. Angsuwatcharakon et al. also reported that mechanical lithotripsy had a significantly lower stone clearance rate in the first session compared with LL (63% vs. 100%). In addition, LL could achieve complete stone removal in 60% of cases with failed mechanical lithotripsy [45]. Although EHL or LL using POCS is effective and feasible, these techniques are still complicated, expensive, and time consuming [39]. Therefore, indication for this procedure may be limited to the cases with unsuccessful conventional ERCP-related procedure. On the other hand, a major advantage of EHL and LL using POCS is reduction in the need for mechanical lithotripsy. Based on these findings, conventional ERCP-related procedure and EHL or LL using POCS should be used as a complementary approach to the treatment of difficult stone.

EHL and LL using SpyGlass have one more advantage to have a potential to reduce radiologic procedure. A prospective study evaluating stone removal for noncomplex bile duct stone using SpyGlass DS in radiation-free setting revealed that all cases underwent successful fluoroscopy-free biliary cannulation and stone extraction and fluoroscopy was required in only 5% cases to confirm stone clearance [46]. POCS in radiation-free setting may become a very promising procedure especially for patients with biliary disorder who are hemodynamically unstable in the intensive care unit.

Ablation of biliary tumors

Catheter-based radiofrequency ablation (RFA) under ERCP guidance has been reported to contribute to obtaining longer stent patency or survival [47–50]. However, it has been associated with a high adverse event rate, since this procedure is commonly performed under only fluoroscopic guidance [51]. A recent study demonstrated the feasibility and safety of the RFA procedure using SpyGlass DS [52]. Observation of the tumor using POCS was performed in 12 patients with bile duct cancer before and after RFA, and administration of RFA was also performed under POCS guidance. RFA was technically successful in all patients with only one patient developing post-procedure cholangitis. Although long-term outcome of biliary RFA remains to be clarified, the feasibility and safety of POCS-guided RFA may provide clinical benefit.

Selective guidewire placement for complex biliary stricture

In spite of the fact that guidewire placement is the first step of ERCP-related procedures, selective guidewire placement is sometimes difficult especially in cases with biliary stricture. Several studies reported the efficacy of POCS for selective guidewire placement as a result of a subgroup analysis [26, 32••]. Bokemeyer et al. evaluated the utility of SpyGlass DS-guided guidewire placement across complex biliary stricture in 30 procedures of 23 patients with previously failed conventional guidewire placement, revealing that selective guidewire placement was successful in 21 of 30 procedures (70%) [53]. More intensive procedure such as percutaneous treatment has to be performed if conventional ERCP-related procedures fail due to the inability of the guidewire placement; therefore, POCS-guided guidewire placement should be considered especially in the case of complex biliary stricture.

Novel application of POCS

Recently, there have been several reports describing EUS-guided anterograde intervention (EUS-AI) through a temporary fistula between the gastrointestinal tract and intrahepatic bile duct to manage biliary disease especially in patients with surgically altered anatomy [54, 55]. EUS-AI has been attracting attention as an alternative of the percutaneous procedure, because procedures using balloon-assisted endoscopy are often challenging. We reported efficacy and feasibility of POCS-assisted anterograde intervention (POCS-AI) via the created fistula, thus enabling POCS-guided lithotripsy by using EHL for the stones and selective guidewire placement across the anastomotic stricture under direct vision, even when performing EUS-AI [56]. In this procedure, the cholangioscope was inserted over the guidewire through the fistula; therefore, SpyGlass DS is suitable for this procedure due to its good maneuverability, while ultra-slim upper endoscope has been also used for this procedure in some of other reports [57]. POCS-AI is a cutting edge and promising application of POCS, although further studies with long-term follow-up are needed.

Other therapeutic application of POCS

POCS allows endoscopists easy access to the lumen of the bile duct, resulting in several reports demonstrating novel use of POCS other than described above. For example, retrieval of migrated biliary stents and hemostasis by using POCS have been reported recently in the literature [58•, 59].

Clinical application of POPS

Indication of POPS is very limited owing to the outer diameter of the scope. Specifically, both the opening of the ampulla and consecutive dilatation of main pancreatic duct from the papilla to the target area are mandatory for POPS.

Diagnosis of intraductal neoplasms of the pancreas

Several retrospective studies have recently evaluated the efficacy of SpyGlass Legacy or DS for diagnosing intraductal neoplasm, for example, intraductal papillary mucinous neoplasm. Although some of the studies demonstrated that the extent of the examination was often limited to the body or head of the pancreas, the good diagnostic yield of visual diagnosis using SpyGlass Legacy was as follows: sensitivity 87%, specificity 86%, and accuracy 87% [60•]. Additionally, 42–43.8% of cases had findings on POPS that were not seen on EUS or other imaging modalities [61, 62]. In contrast, diagnostic yield of targeting biopsy under POPS guidance was reported to be in the range 0–87%

in sensitivity [60•, 63]. Based on those findings, although utility of diagnostic POPS for intraductal neoplasms of the pancreas remains to be clarified, POPS should be considered a promising and complementary tool of diagnosing for intraductal lesions, owing to improved quality of images and maneuverability. The sample size of the previous reports is mostly small; therefore, further studies should be required.

Treatment of pancreatic duct stones using POPS

There are various treatment options for pancreatic duct stones, which include extracorporeal shock wave lithotripsy (ESWL), ERCP-related interventions, and surgery. Endoscopic treatment is less invasive and less cumbersome than ESWL or surgery; therefore, endoscopic treatment is often considered the first approach [64]. However, it is difficult to advance and use devices such as guidewire and basket catheter in the main pancreatic duct, when the stone is large or impacted in the main pancreatic duct. In these situations, endoscopic treatment of pancreatic duct stones under direct vision was one of the options. With the recent development of single-operator cholangioscopy, there have been several reports describing the efficacy of treatment of pancreatic duct stones. Ogura et al. retrospectively evaluated the utility of EHL under direct vision using SpyGlass DS, while complete stone clearance was achieved in 88.2% (18/21) of enrolled cases with only one patient developing mild pancreatitis [65]. The other reports also demonstrated high complete stone clearance rate ranging 80–85% by EHL, LL, or mechanical lithotripsy under SpyGlass DS guidance [61, 66]. A multidisciplinary approach is needed because pancreatic duct stone is inherently difficult to treat; therefore, endoscopic treatment under POCS guidance should be considered a promising alternative.

Other application of POPS

With the development of single-operator pancreatoscopy, POPS also allows endoscopists easy access to the lumen of the dilated pancreatic duct, resulting in several reports demonstrating novel use of POPS other than described above. For example, retrieval of migrated pancreatic stents, dilation of pancreatic duct stricture, laser ablation for treatment of benign, and neoplastic disorders by using POPS have been reported recently in the literature [58•, 61, 67].

Safety of cholangiopancreatoscopy

It still remains controversial whether cholangiopancreatoscopy increases the risk of adverse events. Some studies have demonstrated cholangiopancreatoscopy to be a safe procedure with low adverse event rates and no significant differences between conventional ERCP alone and cholangiopancreatoscopy [27••, 68]. In contrast, other reports have demonstrated a significantly higher overall adverse event rate with POCS and specifically a higher rate of post-procedure cholangitis [32••, 69]. Adverse events of recent reports are listed in Table 3.

Additionally, some serious and potentially fatal complications including air embolization and bile duct perforation have been reported in the previous literature [70•]. In an effort to prevent air embolism, saline or CO2 insufflation is recommended when performing cholangiopancreatoscopy [13••]. With regard to the safety of CO2 insufflation during POCS, Mukewar et al. evaluated it

Table 3. Adverse events of cholangiopancreatoscopy

	Year	Target	Platform	Procedure	Sample size	Adverse event	
Draganov et al. [68]	2011	Biliary & pancreas	SpyGlass Legacy	Diagnosis & stone management	83	4.8% (4/83)	Pancreatitis 3, sphincterotomy-related perforation 1
Sethi et al. [69]	2011	Biliary & pancreas	Video & SpyGlass Legacy	Diagnosis & stone management	402	7.0% (28/402)	Pancreatitis 9, perforation 4, cholangitis 4, others 11
Osanai et al. [20]	2013	Biliary	Video	Diagnosis & store management	87	6.9% (6/87)	Pancreatitis 4, cholangitis 2
Korrapati et al. [21]	2016	Biliary	Video, D-POCS, SpyGlass Legacy	Diagnosis & stone management	Systematic review	7% (severe AE 1%)	Pancreatitis 2%, cholangitis 4%, perforation 1%, others 3%
Navaneethan et al. [28]	2016	Biliary & pancreas	SpyGlass DS	Diagnosis tone & management	105	2.9% (3/105)	Cholangitis 2, pancreatitis 1
Tanaka et al. [58]	2016	Biliary & pancreas	SpyGlass DS	Diagnosis & many variety of therapy	26	7.7% (2/26)	Cholangitis 1, sphincterotomy-related bleeding 1
Mounzer et al. [23]	2017	Biliary & pancreas	Video	Diagnosis	96	2.1% (2/96)	Sphincterotomy-related bleeding 1, perforation 1
			SpyGlass Legacy	Diagnosis & stone management	198	1.5% (3/198)	Pancreatitis
Mizrahi et al [30]	2017	Biliary	SpyGlass DS	Diagnosis & stone management	126	1.2% (2/126)	Pancreatitis
Parbhu et al. [61]	2017	Pancreas	SpyGlass Legacy & DS	Diagnosis & stone/stricture management	41	7.3% (3/41)	Abdominal pain 2, pancreatitis 1
Hajj et al. [60]	2017	Pancreas	Video & SpyGlass Legacy	Diagnosis	102	12% (12/102) (severe AE: 5)	Pancreatitis 4, sphincterotomy-related bleeding 1
Bekkali et al. [66]	2017	Pancreas	SpyGlass Legacy & DS	Stone management	118	0%	–
Turowski et al. [27••]	2018	Biliary & pancreas	SpyGlass DS	Diagnosis & stone management	250	(33/250) (severe AE: 1)	Cholangitis 20, pancreatitis 8, bleeding: 1, perforation 1
Lenze et al. [33]	2018	Biliary	SpyGlass DS	Diagnosis & stone management	67	25.4% (17/67) (severe AE: 11)	Pancreatitis 6, cholangitis 5, bleeding: 1
Brewer et al. [43]	2018	Biliary	SpyGlass DS	Stone management	407	3.7%	
Buxbaum et al. [44]	2018	Biliary	SpyGlass Legacy	Stone management	42	9.5% (4/42)	Cholangitis 2, pancreatitis 2
Ogura et al. [65]	2018	Pancreas	SpyGlass DS	Stone management	21	4.8% (1/21)	Pancreatitis
Angsuwatcharakon et al. [45]	2019	Biliary	SpyGlass DS	Stone management	16	6%	
Bokemeyer et al. [53]	2019	Biliary	SpyGlass DS	Stricture management	30	16.7% (5/30)	Pancreatitis 2, cholangitis 2, bleeding 1
Tyberg et al. [31]	2019	Biliary & pancreas	SpyGlass DS	Diagnosis	118	2.5% (3/118)	Pancreatitis

video, video cholangiopancreatoscopy; *D-POCS*, direct peroral cholangioscopy; *AE*, adverse events in a porcine model [71]. This study showed that CO2 insufflation during POCS is safe and does not result in biliary barotrauma or vital signs instability. This is a supportive result for the above recommendation.

Conclusion

In conclusion, the recent development of single-operator cholangioscopy enables easy access to the inside of bile duct and pancreatic duct, contributing to expanding the indication of cholangiopancreatoscopy. Recently, there have been several reports describing efficacy of SpyGlass DS for long-standing or novel application with good success rate and safety. In contrast, the diagnostic yield of cholangiopancreatoscopy-guided biopsy has been reported as unsatisfactory, although tissue sampling under direct vision is still necessary because endoscopic findings of pancreatobiliary diseases is halfway through being established. Unsatisfied diagnostic yield of tissue sampling using cholangiopancreatoscopy may be partially due to small biopsy forceps, and cholangiopancreatoscopy-guided procedure inherently remains to be complicated; therefore, improvement of devices or development of innovative devices are required to overcome the remaining problems of cholangiopancreatoscopy.

Compliance with ethical standards

Conflict of interest
Yusuke Ishida declares that he has no conflict of interest. Takao Itoi declares that he has no conflict of interest. Yoshinobu Okabe declares that he has no conflict of interest.

Human and animal rights and informed consent
This article does not contain any studies with human or animal subjects performed by any of the authors.

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Papers of particular interest, published recently, have been highlighted as:

- • Of importance
- •• Of major importance

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