Communication from the ASGE Technology Committee

STATUS EVALUATION REPORT

Cholangiopancreatoscopy

Prepared by: ASGE TECHNOLOGY COMMITTEE

Sri Komanduri, MD, Nirav Thosani, MD, Barham K. Abu Dayyeh, MD, MPH, Harry R. Aslanian, MD, FASGE, Brintha K. Enestvedt, MD, MBA, Michael Manfredi, MD, John T. Maple, DO, FASGE, Udayakumar Navaneethan, MD, Rahul Pannala, MD, MPH, Mansour A. Parsi, MD, FASGE, Zachary L. Smith, DO, Shelby A. Sullivan, MD, Subhas Banerjee, MD, FASGE, Chair

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The American Society for Gastrointestinal Endoscopy (ASGE) Technology Committee provides reviews of existing, new, or emerging endoscopic technologies that have an impact on the practice of GI endoscopy. Evidence-based methods are used, with a MEDLINE literature search to identify pertinent clinical studies on the topic and a MAUDE (U.S. Food and Drug Administration Center for Devices and Radiological Health) database search to identify the reported adverse events of a given technology. Both are supplemented by accessing the related articles feature of PubMed and by scrutinizing pertinent references cited by the identified studies. Controlled clinical trials are emphasized, but in many cases data from randomized controlled trials are lacking. In such cases, large case series, preliminary clinical studies, and expert opinions are used. Technical data are gathered from traditional and Web-based publications, proprietary publications, and informal communications with pertinent vendors.

Technology Status Evaluation Reports are drafted by 1 or 2 members of the ASGE Technology Committee, reviewed and edited by the committee as a whole, and approved by the Governing Board of the ASGE. When financial guidance is indicated, the most recent coding data and list prices at the time of publication are provided. For this review the MEDLINE database was searched through January 2015 for articles related to cholangioscopy and pancreatoscopy by using the key words "choledochoscopy," "cholangioscopy," cholangiopancreatoscopy," and "pancreatoscopy" paired with "bile duct stones/calculi," "intrahepatic stones/calculi," "intrahepatic biliary strictures," "percutaneous," "intraoperative," "pancreatic duct stones/calculi," "pancreatitis," "biliary disease," "primary sclerosing cholangitis," and "intraductal papillary mucinous neoplasm/tumor." Technology Status Evaluation Reports are scientific reviews provided solely for educational and informational purposes. Technology Status Evaluation Reports are not rules and should not be construed as establishing a legal standard of care or as encouraging, advocating, requiring, or discouraging any particular treatment or payment for such treatment.

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BACKGROUND

Cholangiopancreatoscopy (CP) enables direct endoscopic visualization of the biliary and pancreatic ductal systems. Cholangioscopy originated as an intraoperative procedure, performed for the localization of stones during common bile duct exploration. Cholangioscopy was subsequently used as an adjunct technique during percutaneous transhepatic cholangiography for stricture and stone visualization and treatment.[1,2-4] CP is today most commonly performed via the per-oral approach during ERCP, for managing difficult stones, and for evaluating pancreaticobiliary strictures. Traditional "mother-daughter" per-oral CP required 2 endoscopists, 1 controlling the cholangioscope, while the second controlled the duodenoscope.[5] Subsequently, a single-operator fiberoptic cholangioscope (SpyGlass; Boston Scientific, Natick, Mass) system was introduced, which removed many of the logistical difficulties inherent in requiring 2 endoscopists.[6-9] A further development has been that of direct per-oral cholangioscopy (DPOC) that uses ultrathin endoscopes capable of digital imaging.[5,10-14] The recent introduction of a digital imaging version of the single-operator cholangioscope (SpyGlass DS; Boston Scientific) together with the evolution of DPOC have significantly increased the diagnostic and therapeutic capabilities of CP.

TECHNICAL CONSIDERATIONS

Cholangioscopy usually is performed via the per-oral route, although percutaneous and surgically created routes also are feasible. Different cholangioscopy platforms accommodate these varied approaches.

TABLE 1. Cholangioscopy systems

Company	Model	Distal diameter, mm	Accessory channel, mm	Depth of field, mm	Per-oral	Working length, mm
Pentax	FCP-9P	3.1	1.2	1-50	Yes	1900
	FCN-15X	4.8	2.2	3-50	No	350
Olympus	CHF-BP30	3.1	1.2	1-50	Yes	1870
	CHF-CB30L/S	2.7	1.2	2.5-50	No	700 or 450
Boston Scientific	SpyGlass analog probe (reuse)	0.77	.9 optic channel	2-7		3000
	SpyGlass catheter (analog, single use)	3.4	1.2/0.6/0.6		Yes	2200
	SpyScope DS	3.5	1.2		Yes	2140

Dual operator mother-daughter per-oral cholangioscopy

Dedicated per-oral cholangioscopes are typically advanced to the bile duct over a guidewire through the working channel of a therapeutic duodenoscope. Reusable mother-daughter cholangioscopes incorporate a control dial for 2-way (up/down) tip deflection and have buttons for air and/or water and suction channels. The insertion tube contains an instrument channel, a coherent bundle of glass fibers that transmits the image from the objective lens system at the tip of the endoscope to the eyepiece, angulation wires for tip deflection, a channel leading to the air and/or water nozzle at the tip of the cholangioscope, and light guide illumination. The connector section is similar to that of other endoscope systems.[15] When fiberoptic cholangioscopes are used with a video adapter, the processor and light source coordinate automated gain and light control, which assists in obtaining optimal imaging. Cholangioscopes differ in their tip deflection angle, outer diameter, working channel size, field of view, and available accessories. Cholangioscopes currently available in the United States are detailed in Table 1.

Currently available instruments

Olympus. Olympus Corporation (Center Valley, Pa) currently markets 1 fiberoptic per-oral cholangioscope (CHF-BP30) with a distal diameter of 3.1 mm, a working channel of 1.2 mm, and a working length of 187 cm.

Pentax. Pentax Corporation (Montvale, NJ) currently manufactures 1 fiberoptic per-oral cholangioscope (FCP-9P) with a distal diameter of 3.1 mm, a working channel of 1.2 mm, and a working length of 190 cm.

Single-operator per-oral cholangioscopy

A dedicated, single-operator cholangioscopic system (SpyGlass; Boston Scientific Corp) is available, which overcomes some of the limitations of the dual-operator system. The single-operator cholangioscope is typically advanced over a guidewire into the bile duct through the working channel of a therapeutic duodenoscope.

The platform uses a single-operator digital cholangioscope (SpyScope DS), which is entirely disposable and has 2 components: (1) a sterile, single-use SpyScope access and delivery catheter (the cholangioscope) and (2) the SpyGlass DS digital controller (the processor). The SpyGlass cholangioscope is made up of a handle, an insertion tube, and a connection cable. The handle includes 2 articulation control knobs, which allow 4-way tip deflection, a lever to lock the control knobs in place, connectors for irrigation and aspiration, a working channel port, and a strap to attach the cholangioscope to a duodenoscope. 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. The distal end of the insertion tube incorporates a digital camera chip (charge-coupled device) for capturing video and transmitting it to the controller, elements for transmitting illumination from the controller, and the distal openings of the irrigation and working channels.

The controller is an endoscopic video imaging system that combines the functionality of a processor and a light-emitting diode light source. The controller receives video signals from the catheter, processes the video signals, and outputs video images to an attached monitor. The controller also generates and controls the illumination transmitted to the distal end of the catheter. The user interface of the controller includes a power button, a receptacle to connect the catheter connection cable, buttons to turn illumination on or off and to control the illumination intensity, and an illumination intensity indicator. The controller outputs video images to an attached monitor via digital visual interfact (DVI), video graphics array (VGA), or S-Video ports, and the user may select National Television System Committee (NTSC) or Phase Altering Line (PAL) video formats based on the geographic region of use.

TABLE 1. Continued

Angulation	Field of view, air	Image	Price, $	Processor (price) light source (price)
90/90	90	Fiberoptic	31,000	EPK1000/EPK-i5010 ($28,000-$41,000)
180/130	125	Fiberoptic	16,170	EPK1000/EPK-i5010 ($28,000-$41,000)
160/130	90	Fiberoptic	28,400	＼CV-190/CLV-190 EVIS EXERA III
120/120	75	Fiberoptic	15,000	＼CV-190/CLV-190 EVIS EXERA III
	70	Fiberoptic	4650	Camera ($19,975); light source ($10,975)
(4-way) 30/30/30/30			800	SpyGlass Light source, camera, and processor ($60,000)
240° (4-way) 60° up/down 60° left/right	120	Digital	2950	SpyGlass light source and processor ($99,500)

The previous generation of the single-operator cholangioscope system (SpyGlass Direct Visualization System) is semidisposable. The fiberoptic probe is reusable up to 10 times, whereas the rest of the cholangioscope is single-use. The insertion tube of the cholangioscope is a 3.4-mm access and/or therapeutic catheter, which allows 4-way tip deflection. The control section has 3 ports: an irrigation port that feeds into 2 0.6-mm channels, an optical probe port, and a 1.2-mm accessory channel. The reusable 6000-pixel optical probe is a collection of light fibers that surround optical fiber bundles and are incorporated into a polyimide sheath. The connector section includes a camera processor with a one-fourth-inch charge-coupled device chip, a light source, a coupler that interfaces the optical probe with the light source and video camera head, and a medical grade isolation transformer. Accessories for use with both the legacy and the new SpyGlass DS systems include an intraductal mini-biopsy forceps (SpyBite; Boston Scientific) and an irrigation pump with foot pedal and monitor, which are available through separate vendors (Table 2).

DPOC (ultraslim endoscopes)

During DPOC, ultraslim gastroscopes are directly advanced into the bile or pancreatic ducts during a standard upper endoscopy. Ultraslim gastroscopes have been well described in a previous Technology Committee document.[16] Although ultraslim gastroscopes are currently not U.S. Food and Drug Administration (FDA) approved for cholangioscopy, and direct advancement of these gastroscopes into the bile duct is technically challenging, there has been increasing use of these gastroscopes for biliary and pancreatic ductal evaluation and therapy.[17] Driving this increased utilization of ultraslim gastroscopes are the superior optics provided by digital imaging, the larger working channel for accessories, and the availability of electronic chromoendoscopy as well as the advantage of not needing to buy a separate CP platform.[18] When CP is performed, carbon dioxide or water insufflation should be used to avoid the adverse event of air embolus.[19-21]

Currently available instruments

Olympus. Olympus currently markets 3 ultraslim gastroscopes and 1 transnasal endoscope (Table 3). The gastroscopes offer narrow-band imaging, a working length of 650 to 1100 mm, and have accessory channels ranging from 2.0 to 2.2 mm.[22]

Pentax. Pentax currently markets 1 ultraslim endoscope with i-SCAN digital image processing, a working length of 1100 mm, and an accessory channel of 2.0 mm.

Fujinon. Fujinon Corporation (Wayne, Ind) currently markets 1 ultraslim endoscope and 1 transnasal endoscope. These have working lengths of 1100 mm and accessory channels of 2.0 mm.

Percutaneous and surgical cholangioscopy

These fiberoptic cholangioscopes have a larger diameter, allowing a higher number of optical fibers, resulting in better illumination, field of vision, and image resolution, and are inserted into the biliary tree via a mature percutaneous tract or at the time of surgery. Separately available eyepiece and video adapters convert the fiberoptic image to a video format.[23,24]

Currently available instruments

Olympus. Olympus offers a fiberoptic percutaneous cholangioscope (CHF-CB30L/S), which has a distal diameter of 2.7 mm and a 1.2-mm accessory channel (Table 1).

Pentax. Pentax offers a surgical cholangioscope (FCN-15X), which has an insertion diameter of 4.9 mm, working channel of 2.2 mm, and a working length of 350 mm.

Accessories for cholangioscopy

Biopsy forceps. Cholangioscopy allows for direct visualization and biopsy of biliary strictures and mass lesions. Commercially available pediatric biopsy forceps (with or without a central spike) have an outer sheath diameter

TABLE 2. Cholangioscopic accessories

Company	Accessories	Model	Price, $
Pentax			
Video camera and adapter modules for fiberscopes	PSV-4000, add-on camera	KUM98023	6000
	Anti-Moire lens, with microfocus (220 cm, reusable)	84115	1790
	For EPK-1000 video processor	PVK-1070Z	12,500
	For EPK 1000 video processor	AP-PV1	230
	For FCP-8P, FCP-9P		
	Biopsy forceps (cup diameter 1.0 mm, length 220 cm; reusable)	KS-1022CS	580
	Cleaning adapters for suction channel	OF-B103	NA
	Protective rubber inlet seal	OF-B107	NA
Olympus			
Video camera and adapter modules for fiberscopes (CV-180)	Eyepiece adapter for OES fiberscope to OTV	A10-T2	2740
	VISERA camera head, straight with Moire filter	OTV-S7H-1N	8120
	For CHF-BP30 (endoscopic)		
	Biopsy forceps (elongated cup, 4.2 mm cup opening, 230 cm length; reusable)	FB-44U-1/SO	681
	Working channel forceps and irrigation plug	MAJ-891	NA
	Cleaning adapters (Thruster MD-103)	MH-507	NA
	Cleaning brushes	BW-400V	NA
	For CHF-CB30S/L (surgical)		
	Grasping forceps for endoscope manipulation (5 mm OD)	T1079	515
		Price	
Boston Scientific	Travel cart (with 3 joint arm with clamp)	$9920	
	Light source	$23,300	
	SpyGlass video monitor	$8265	
	Irrigation pump w/footswitch 120 v	$5245	
	Ocular piece	$4650	
	Isolation transformer	$3670	
	Storage tray	$580	
	SpyBite biopsy forceps (single use)	$772	

NA, Not available; *OD*, outer diameter.

of 1.8 mm and can be used with cholangioscope and ultraslim endoscopes with an accessory channel diameter of ≥2.0 mm. The SpyBite biopsy forceps (Boston Scientific Corp) has an outer sheath diameter of 1.0 mm and a central spike and can be used with cholangioscopes with an accessory channel diameter of ≥1.2 mm.

Lithotripsy. Cholangioscopy offers the ability to visualize and provide therapy for large intraductal stones by using electrohydraulic lithotripsy (EHL) or laser lithotripsy. EHL uses a bipolar lithotripsy probe, which can discharge sparks with the aid of a generator. The EHL fibers contain coaxially insulated electrodes capable of producing sparks at the fiber tip.[25] For the 3.1-mm to 3.4-mm cholangioscopes with a 1.2-mm working channel, a 1.9F nitinol probe can be used. The EHL generator produces a series of high-voltage electrical impulses at a frequency of 1 to 20 per second with settings ranging from 50 to 100 W. EHL requires water or saline solution insufflation of the bile duct. When EHL sparks are generated in an aqueous medium, they create high-frequency pressure waves, which are absorbed by the stone and result in fragmentation.

The tip of the EHL fiber should be positioned en face with the stone while the generator's foot pedal is depressed to deliver energy. The Autolith (Nortech, Northgate Technologies Inc, Elgin, Ill) is the only EHL generator that has FDA clearance for biliary stones. The Nortech biliary EHL probe is 1.9F (0.63 mm) and is available in lengths of 250 cm and 375 cm. An alternative, more expensive technology is pulsed holmium laser lithotripsy (Lumenis Inc, San Jose, Calif). A laser beam is transmitted by a flexible quartz fiber advanced through the working channel of the cholangioscope. The laser delivery fibers are up to 4-m long and 200, 365, 550, or 1000 μm in diameter. Suggested power settings are 0.6 to 1.0 J at 6 to 10 Hz for total laser energy

TABLE 3. Ultraslim endoscopes*

Model	Angulation (degree)	Features	Shaft diameter, mm	Accessory channel diameter, mm	Working length, mm	Price, $
GIF-XP190N	210 up/90 down 100 left/100 right	NBI	5.8	2.2	1100	40,000
GIF-XP 180N	210 up/90 down 100 left/100 right	NBI	5.5	2	1100	38,500
GIF-180N	210 up/120 down	NBI	4.9	2	1100	36,800
PEF-V	180 up/130 down	N/A	5.3	2	650	25,856
EG-530N	210 up/90 down 100 left/100 right	FICE	5.9	2	1100	26,800
EG-530NP transnasal	210 up/120 down	FICE	4.9	2	1100	26,700
EG 1690K	210 up/90 down 120 left/120 right	iSCAN†	5.1	2	1100	26,500

FICE, Flexible Spectral Imaging Color Enhancement; *N/A,* not applicable; *NBI,* narrow-band imaging.
*120° field of view in all.
†Pentax proprietary image enhancement.

of 12 kJ. The application of repetitive pulses of laser energy to the stone leads to formation of a gaseous collection of ions and free electrons of high kinetic energy. This plasma rapidly expands as it absorbs the laser energy and then collapses, inducing a spherical mechanical shock wave between the laser fiber and stone for fragmentation.[26-29]

CP TECHNIQUES

Per-oral cholangioscopy can be performed by using a dual-operator or single-operator mother-daughter technique or directly with ultraslim endoscopes. In addition, cholangioscopy is occasionally performed by using a surgical or percutaneous approach.

Dual-operator mother-daughter per-oral cholangioscopy

In the per-oral technique with reusable systems, typically 2 operators are required, 1 to manage the duodenoscope, while the second manages the cholangioscope. Single operation with a specially designed external cholangioscope fixation device (ScopeDoc, Cook Medical, Bloomington, Ind) may also accomplish CP by allowing the duodenoscope to be anchored in a resting position.[30] Before the cholangioscope is advanced, sphincterotomy usually is performed. Advancing the cholangioscope over a guidewire is optional, but it reduces the need for duodenoscope elevator use to assist in advancement of the cholangioscope. Excessive elevator use may result in damage to the bending portion of the cholangioscope. The cholangioscope's control dial is kept in the unlocked position, and the duodenoscope tip should be positioned nearly flush with the papilla to optimize orientation for advancement of the cholangioscope into the bile duct. Once the cholangioscope is advanced to the target location, the guidewire may be removed to permit use of the accessory channel for irrigation and introduction of devices. In addition to operating the cholangioscope dial, the second endoscopist also advances the biopsy forceps or lithotripsy fiber for tissue acquisition and lithotripsy, respectively.[30]

Single-operator per-oral cholangioscopy

The endoscopic technique for the newer generation SpyGlass DS is similar to the analog iteration; however, the flexibility of this device facilitates improved cannulation and inspection of the distal common bile duct. In addition, the digital optics along with improved suction and irrigation abilities allow for substantially improved visualization. The control section of the SpyGlass DS is strapped just below the duodenoscope's working channel by a silicone belt. The endoscopist can use the cholangioscope's 4-way steering dials in conjunction with straightening of the bile duct by pushing in the duodenoscope to optimize duct visualization. The cholangioscope dials can be locked to further stabilize the scope position during lithotripsy or for intraductal tissue acquisition. Irrigation during the procedure is performed through a dedicated channel. Techniques to improve visualization include limiting contrast material injection before cholangioscopy, extracting contrast material with balloon sweeps if necessary, and suctioning of the debris and bile from the duct before and during installation of water or saline solution. A Y adaptor can be attached to the wire port to facilitate suctioning.

Resistance may be encountered during advancement of accessories through the cholangioscope because of the small diameter of the working channel. This typically occurs where the cholangioscope traverses the duodenoscope's elevator and can be overcome by advancing the cholangioscope with the accessory into the upstream duct, then readvancing the accessory relative to the cholangioscope or by increasing the loop of the cholangioscope within the duodenum.[31] Because blood and stone debris may reduce visualization, careful and frequent confirmation that the tip of the fiber is in the appropriate position by endoscopic

and fluoroscopic visualization is necessary to reduce duct injury or endoscope damage.[32]

For the use of the first-generation SpyGlass fiber optic system, the optical probe is preloaded onto the 10F cholangioscope catheter (SpyScope) and advanced to within a few millimeters of the catheter's bending portion to reduce the potential for damage during passage across the duodenoscope's elevator. Once the bile duct is entered with the cholangioscope catheter, the optical probe is advanced just beyond the catheter's tip to allow for duct visualization. Irrigation can be performed via a dedicated channel or via an accessory channel, but if a guidewire or EHL fiber is present, a Y adapter must be placed for coaxial irrigation to dislodge debris.

DPOC (ultraslim endoscopes)

DPOC is technically challenging and has therefore failed to achieve widespread adoption. Advancing the ultraslim gastroscope into the bile duct is difficult because of the larger outer diameter of the gastroscope and the occurrence of gastric looping as well as instability of the endoscope within the bile duct. Before introduction of an ultraslim gastroscope, a large sphincterotomy with or without papillary balloon dilation is required.[33] Various innovative techniques have been described to overcome the difficult biliary cannulation and intraductal instability inherent with DPOC. These include (1) introduction of the endoscope over a guidewire with a standard or double-balloon overtube,[13,34-36] (2) direct per-oral cholangioscopy by using a free-hand technique, (3) anchoring of the scope by using a biliary extraction balloon,[12,17,37-39] and (4) usage of a stiff stent guiding catheter designed for percutaneous use with tip deflection capability (Kautz probe).[40,41]

DPOC over a stiff guidewire with or without an overtube

In this technique, standard ERCP is performed, and a stiff guidewire is advanced into the intrahepatic ducts.[13,34,35] The duodenoscope is then exchanged over the wire, which is then backloaded onto an ultraslim endoscope by using a standard biliary catheter or extraction balloon. The ultraslim endoscope is then advanced over the catheter and wire across the ampulla into the bile duct. Subsequently, when the extraction balloon is used, it can be inflated to overcome intraductal instability. However, the guidewire and catheter may need to be removed for intraductal biopsy or lithotripsy, making it difficult to maintain a stable position within the bile duct. In addition, use of a standard or double-balloon overtube has been described in conjunction with the use of the wire to overcome the gastric loop formation that occurs with advancement of the ultraslim endoscope.[35,39,42,43]

DPOC by using a free-hand technique

After standard ERCP is performed with sphincterotomy, a forward-viewing, slim endoscope is advanced to the third portion of the duodenum. Subsequently, the endoscope is retroflexed and withdrawn slowly to engage the tip of the scope into the biliary orifice. After the tip of the endoscope is in the bile duct, the scope is then withdrawn while simultaneously turning the shaft of the endoscope in a counterclockwise direction ("J" maneuver) in order to reduce the large gastric loop. After loop reduction, the endoscope can be advanced slowly into the biliary tree.[44]

DPOC by using the balloon anchoring method

After sphincterotomy with or without papillary balloon dilation, the duodenoscope is withdrawn. The ultraslim endoscope is preloaded with a guidewire and biliary stone extraction balloon and is advanced to the ampulla. Biliary cannulation is performed by using the guidewire and extraction balloon. In order to facilitate cannulation, the ultraslim endoscope tip is deflected toward the papilla. Alternatively, the ampulla may be approached with the endoscope retroflexed as described in the previous technique.[17] Cannulation of the bile duct with the endoscope is performed by advancing the scope slowly over the wire while simultaneously pulling on the inflated balloon catheter to straighten the biliary tree. Subtle movements of the up and/or down directional knob of the endoscope may be needed. Once the endoscope is stable, the balloon is deflated.[37-39,45-48]

Percutaneous cholangioscopy

Percutaneous cholangioscopy can be performed by an endoscopist or interventional radiologist along with an assistant for guidewire, lithotripsy probe, or biopsy forceps manipulation. The cholangioscope's tip is lubricated and advanced into the biliary system through a 12F sheath placed through a preexisting mature (3-4 weeks) percutaneous tract.[49,50] After advancement to the duodenum or surgical anastomosis, the wire is removed for intraductal examination. The tract through which the sheath enters the liver predetermines the ducts that can be accessed with the cholangioscope; maneuvering to the opposite liver segment may be impossible through a single percutaneous tract.[25,51] The use of a guidewire for counter tension is optional. In case the sheath is inadvertently dislodged, the use of an intraductal safety wire or second catheter adjacent to the sheath has been reported.[52] For bilateral intrahepatic stones, a left intrahepatic duct approach has been recommended because it is easier to advance the cholangioscope from a left to a right intrahepatic duct or to the common duct. For right-sided access, a posterior rather than an anterior approach is preferred to avoid the angulations of the anterior segment.[53]

CLINICAL APPLICATIONS

Diagnostic cholangioscopy is used for the evaluation of indeterminate bile duct strictures or for equivocal findings

during fluoroscopy. Cholangioscopy allows for further characterization of biliary strictures and for mapping the extent of cholangiocarcinomas.[32,54-62] Therapeutic cholangioscopy is used for the treatment of difficult biliary stones by using intraductal lithotripsy,[2,30,31,63,64] for palliative therapy of biliary malignancies,[65,66] and for facilitation of guidewire advancement into selective intrahepatic ducts.[6]

If the less-invasive per-oral route is not feasible or fails, percutaneous cholangioscopy can be performed for the extraction of biliary stones.[1,53,67-70] An additional application for the percutaneous route is performing mapping biopsies to assess the longitudinal upstream spread of hilar cholangiocarcinoma, which aids in the determination of resectability.[59,60,71] Intraoperative cholangioscopy is occasionally used during open or laparoscopic bile duct exploration to facilitate the localization of biliary stones and to assess ductal clearance.[72-77] Although common bile duct exploration has largely been replaced by ERCP, earlier randomized controlled studies of cholangioscopy for the detection of stones indicated a 12% to 13% miss rate with cholangiography alone.[75,78,79]

EFFICACY

Biliary disease

Cholangioscopy for management of difficult common bile duct stones. Per-oral cholangioscopy with intraductal lithotripsy achieves complete clearance of difficult extrahepatic biliary stones in 71% to 100% of patients.[2,29,31,36,80-88] A large multicenter registry on the single-operator SpyGlass platform that uses EHL or laser lithotripsy demonstrated a stone clearance rate for large bile duct stones of >90%.[84] Similarly, another study demonstrated a stone clearance rate of 88.9% by using an ultraslim endoscope with EHL or laser lithotripsy.[89] Factors that decrease the success of cholangioscopy for duct clearance include surgically altered anatomy, strictures, significant ductal angulation, and impacted stones.[53,63,90,91]

For intrahepatic stones, per-oral cholangioscopy has been effective but is limited by the inability to advance the cholangioscope through intrahepatic strictures and smaller ducts. A recent study demonstrated a stone clearance rate of 64% and a recurrence rate of 21.7%.[88] Percutaneous cholangioscopy with selected use of EHL achieves initial duct clearance in 80% to 89% of patients.[53,69,88] However, high stone recurrence rates or cholangitis have been reported in 35% to 50% of cases, likely related to intrahepatic strictures and retained occult stone fragments.[53,69,88]

Cholangioscopy for indeterminate bile duct strictures. In the setting of indeterminate biliary strictures, cholangioscopy allows for direct visualization, specifically assessing for endoscopic findings suggestive of malignancy including tumor vessels (ie, irregularly dilated and tortuous vessels), intraductal nodules or masses, and papillary or villous mucosal projections.[58,70,92] Recent studies evaluating per-oral cholangioscopy have demonstrated sensitivities ranging from 88% to 100% and specificities ranging from 77% to 92% for visual assessment of malignancy at cholangioscopy.[6,32,56,92-96] For studies in which biopsy samples also were obtained, the sensitivities ranged from 48% to 100%, and specificities ranged from 55% to 100%.[6,32,56,92-95,97,98] Limited 6-month follow-up data with the fiberoptic SpyGlass system have indicated a 71% sensitivity and 100% specificity for the detection of malignancy.[6] A systematic review of studies that used the fiberoptic SpyGlass system indicated a pooled sensitivity of 66.2% for per-oral cholangioscopy-directed biopsies.[99] There are no current randomized controlled trials or long-term outcomes studies comparing efficacy of per-oral cholangioscopy versus alternative modalities for stone clearance or evaluation of indeterminate bile duct strictures. These studies are limited in applicability because of small sample sizes.

In a single cohort study of patients with known cancer, sensitivities for detecting cholangiocarcinoma by percutaneous cholangioscopy ranged from 60% to 100%.[59] Furthermore, obtaining tissue samples from the margins rather than from within strictures improved the histologic diagnosis rate of stenotic-type cholangiocarcinoma from 70% to 100%.[59] Visualization of tumor vessels alone had a sensitivity of 61% for the diagnosis of malignancy but when combined with biopsy, diagnosed 96% of cancers. The negative predictive value of tumor vessels was 100%, on the basis of a 1-year follow-up.[59]

Pancreatic disease

Pancreatoscopy generally is accomplished by using the same systems designed for cholangioscopy and is used to evaluate pancreatic duct strictures and stones. Although all cholangioscopy platforms may be used for pancreatoscopy, currently only the single-operator SpyGlass system has FDA clearance for dedicated pancreatoscopy.

Pancreatoscopy for management of difficult stones. Small case series of 6 to 44 patients have described the use of direct per-oral or intraoperative pancreatoscopy with EHL for the management of pancreatic stones. These studies have indicated complete main duct clearance rates of 100%,[100] 50%,[101] and 59%,[102] respectively, with symptom improvement in the majority of patients with complete or partial clearance. The data are hard to interpret because EHL often was combined with decompressive surgery or extracorporeal shock wave lithotripsy (ESWL).[100-103] More recently, a 10-year, single-center series on 46 patients with pancreatic stones treated with cholangioscopy by using EHL or laser lithotripsy demonstrated complete stone clearance in 70% of cases.[104]

Pancreatoscopy for evaluation of intraductal papillary mucinous neoplasms and/or pancreatic duct strictures. A study that included 115 patients with a minimum 2-year follow-up indicated that pancreatoscopy was able to diagnose 63% of pancreatic cancers, 80% of benign strictures, and 95% of intraductal papillary mucinous neoplasms (IPMNs), based on visual appearances.[105] Neoplasia assessment was based on the presence of coarse mucosa, submucosal protrusion, friability, tumor vessel, and papillary projections.[105] In distinguishing benign from malignant IPMNs, the endoscopic visualization of fish egg–like, villous, and prominent mucosal protrusions have been described to correlate with malignant lesions with a sensitivity and specificity of 68% and 87%, respectively, with lower sensitivity for branch duct IPMN compared with main duct IPMN.[106] Finally, a large retrospective series (n = 86) assessed the impact of intraoperative pancreatoscopy with biopsy during surgical resection of IPMNs. In 23.8% of patients, the initial operative plan was altered by an immediate read of pancreatoscopy direct biopsies.[107]

COMPARATIVE STUDIES

Cholangioscopy for difficult bile duct stones

There are no randomized controlled studies comparing mother-daughter to single-operator cholangioscopy for evaluation of difficult bile duct stones. However, direct comparisons of various methods of cholangioscope-assisted lithotripsy have been assessed.[108,109] In a nonrandomized comparison of 118 patients with prior failed ERCP for stone extraction who underwent ESWL followed by ERCP or per-oral cholangioscopy with EHL, similar rates of clearance were noted (79% vs 74%; $P = .1$).[110] Crossover treatments resulted in successful duct clearance in 94% of patients. In a randomized, prospective study of 60 patients, cholangioscopy-guided laser lithotripsy demonstrated a higher rate of duct clearance (97% vs 73%; $P < .05$) and a lower number of lithotripsy sessions (1.2 vs 3; $P < .001$) compared with ESWL. After crossover therapy, 59 of 60 (98%) achieved clearance.[28]

A retrospective review of 86 patients with hepatolithiasis compared EHL during percutaneous cholangioscopy with selective hepatic resection.[111] Resection was considered for unilateral stones, an atrophic lobe or segment, or suspicion for cholangiocarcinoma. Lithotripsy was considered for right-sided, bilateral, or recurrent stones and if resection was refused. Stone clearance was 96% in each group, and 30-day adverse events and 5-year survival rates were comparable. There were 3 deaths in the resection group (12%) that included 2 delayed liver failures, and 1 death (4%) from massive hemobilia and liver failure in the percutaneous transhepatic cholangiography group. Residual biliary stricture and 5-year stone recurrence rates were higher in the nonoperative group (6% vs 32%; $P < .05$).[111]

Cholangioscopy for bile duct strictures

A small, randomized comparison of mother-daughter cholangioscopy versus direct cholangioscopy with an ultraslim endoscope demonstrated similar technical success rates of 90% and 86.7%, respectively. Although mother-daughter cholangioscopy offered greater endoscope stability within the bile duct and allowed visualization of intrahepatic ducts, the ultraslim endoscope provided superior quality digital imaging, a shorter procedure time, and easier tissue acquisition because of the larger accessory channel.[112] An uncontrolled comparison of digital per-oral cholangioscopy by using ultraslim endoscopes with and without narrow-band imaging was performed in 12 consecutive patients who had indeterminate biliary strictures.[113] The 2 investigators reported a higher rate of excellent visualization of surface structures and tumor vessels with narrow-band imaging compared with white light ($P < .01$ and $< .05$, respectively), but based on the resected specimen, superficial spread of 2 of 7 cholangiocarcinomas was not detected by either method preoperatively.

In a retrospective series of cholangioscopy and virtual CT cholangiography interpreted by radiologists blinded to the endoscopic findings, no significant difference was noted for endoluminal visualization quality.[114] However, the rates for CT detection of minute papillary tumors and stones <5 mm in size were low at 30% and 25%, respectively. A single comparative study of SpyGlass-directed biopsy and brush cytology demonstrated little incremental yield for diagnosis of dysplasia or malignancy.[115] No other comparative data are available for the analog or digital iterations of the single-operator SpyGlass system.

For the investigation of dominant biliary strictures in patients with primary sclerosing cholangitis, cholangioscopic visualization increased the sensitivity for detecting malignancy from 66% to 92% (P value not significant) and specificity from 51% to 93% ($P < .001$) compared with cholangiography alone.[62] A second study evaluating patients with primary sclerosing cholangitis by using an ultraslim cholangioscope in 41 patients found stones missed by standard cholangioscopy in 30% of cases.[61]

Pancreatoscopy

There are no randomized controlled trials evaluating standard endoscopic retrograde pancreatography versus pancreatoscopy. One retrospective comparison of pancreatoscopy by using an ultraslim endoscope and SpyGlass cholangioscopy was reported in 46 patients. This study demonstrated no significant difference in stone clearance between the ultraslim endoscope versus the SpyGlass cholangioscope (68 vs 73%; $P = .519$).[104]

Several studies have compared per-oral pancreatoscopy with intraductal US, CT, EUS, and pancreatography

for distinguishing benign from malignant IPMN lesions.[106,116-121] In 2 other studies, pancreatoscopy with ductal visualization for the diagnosis of main duct IPMN lesions had a sensitivity of 67% to 100% compared with CT (16%-32%), intraductal US (56%-100%), and EUS (55%-92%).[106,117] In general, these technologies appear to be complementary rather than exclusive in the workup of IPMN. A surgical study that compared patients with intraoperative EHL and lateral pancreaticojejunostomy (n = 20) with historic control participants who underwent decompressive surgery alone (n = 85) suggested lower rates of subsequent operations (0% vs 7%; $P < .05$) for adverse events resulting from chronic pancreatitis and rehospitalization (35% vs 60%; $P < .05$) at 2 to 6 years of follow-up in the EHL-treated group.[76]

EASE OF USE AND LIMITATIONS

Per-oral reusable cholangioscopes

Although reusable cholangioscopes potentially offer cost reductions compared with platforms with single-use systems, the mother-daughter cholangioscopes have several limitations. The most difficult to overcome is the need for 2 experienced operators to complete the procedure. The ScopeDoc device (Cook Medical) allows the endoscopist to lock the mother duodenoscope in a resting position by using this fixation device around the endoscopist's waist. This then facilitates manipulation of the daughter cholangioscope. The reusable cholangioscopes are prone to damage and may have high maintenance costs. In addition, fiberoptic imaging and a small accessory channel have limited the utility of dedicated mother-daughter cholangioscopic systems.

Per-oral single-operator cholangioscopes

The main advantage of this platform is that it allows single-operator cholangioscopy. The cholangioscopes are secured to the duodenoscope, which allows simultaneous movement of the duodenoscope and cholangioscope.[7] Both generations of these cholangioscopes allow 4-way tip deflection, which may improve visualization, targeted biopsy, and accessing selective intrahepatic bile ducts. In a vendor-sponsored ex vivo study, a single operator compared 4-quadrant access, simulated biopsy, irrigation flow rates, and optical resolution between a semi-disposable cholangioscope (SpyGlass Direct Visualization System) and a reusable cholangioscope (CHF BP-30; Olympus).[7] The author reported the greater ability to access 4 quadrants for visualization and biopsy with the semidisposable cholangioscope system in all cases (odds ratio [OR] 1.7-2.94; $P < .001$).

The new generation SpyScope SpyGlass DS has substantially improved flexibility, improved steerability, improved digital visualization, and allows easier advancement of accessories. Setting up the digital SpyGlass is significantly easier than with the legacy system. The generator can be placed on top of the endoscope processor without a need for a dedicated cart and allows for a "plug and play" experience.

Although the optical probe used with the fiberoptic SpyGlass is reusable and requires reprocessing, its durability with sequential use is limited. In the presence of a lithotripsy fiber or biopsy forceps within the working channel, the dedicated irrigation channel provides higher flow rates compared with reusable cholangioscopes.[7] As with the reusable system, image quality is enhanced by irrigation with sterile saline solution or water, but the field of view is reduced when the lens is immersed in an aqueous solution because of the presence of a meniscus. The passage of the accessories can be difficult and sometimes not feasible, because the device must cross the elevator through the rigid cholangioscope.[32]

Per-oral cholangioscopy (ultraslim)

Cholangioscopy by using ultraslim endoscopes allows for improved digital imaging and avoids the need and cost of a separate platform. However, introducing the ultrathin scopes into the bile duct and maintaining stability for therapy is technically challenging.

Percutaneous and surgical cholangioscopy

Cholangioscopes designed for intraoperative or percutaneous use have larger accessory channels and therefore allow a broader array of accessory devices. Despite having only 2-way tip deflection, the shorter working length and distance to the target area improves the ability to torque the scope to allow 4-quadrant visualization. A disadvantage is that percutaneous cholangioscopy cannot be performed at the time of the initial biliary access procedure.

SAFETY

The overall rates of adverse events are higher with CP than ERCP alone (7% vs 2.9%, OR 2.5; 95% CI, 1.56-3.89).[122] Although very rare, the most serious adverse events of per-oral CP are air embolization and bile duct perforation.[46,122] Although both of these adverse events are more common with direct cholangioscopy with an ultrathin endoscope, they have also been reported with dual and single operator mother-daughter per-oral cholangioscopes.[46,122] In efforts to prevent air embolus, CO_2, or water and/or saline solution insufflation is recommended when direct cholangioscopy is performed.

A multicenter analysis of 282 patients undergoing single-operator CP demonstrated low rates of adverse events (pancreatitis 3.9%, cholangitis 1.4%, bleeding 1.4%, and perforation 0.7%).[123] Further adverse events of CP are related to the route of access, the use of directed intraductal lithotripsy, and fluid irrigation in obstructed ducts. Cholangitis also is observed more often with CP

than ERCP alone (1.0% vs 0.3%, OR 4.98; 95% CI, 1.06-19.67).[122] Per-oral cholangioscopy with and without intraductal lithotripsy has been associated with cholangitis rates of 0% to 14%,[2,6,30-32,37,86,92,102,124] hemobilia rates of 0% to 3%,[2,30,122] and a bile leak rate of 1%,[30] with the latter 2 attributable to intraductal lithotripsy. Per-oral pancreatoscopy series have reported mild postprocedural pancreatitis in 0% to 7% of patients,[104-106,117,125] with the highest rate (7%) reported when pancreatoscopy was performed in conjunction with intraductal ultrasound.[106]

In percutaneous cholangioscopy with lithotripsy, morbidity rates of 33% to 40% were noted.[64,126] In more recent large series of percutaneous cholangioscopy, infectious adverse events were noted in 8% to 35% of patients,[50,69,127] tract access was lost in 1% to 2% of patients,[127,128] and hemobilia was seen in 1% to 6% of patients,[50,69,127] with a single death from a liver laceration[129] and a single death from hemobilia with subsequent sepsis.[127]

FINANCIAL CONSIDERATIONS

There currently is no dedicated Current Procedural Terminology (CPT) code for per-oral cholangioscopy. The high capital costs for the processor, scopes, and cost of repairs must be considered before adopting this technology. Start-up costs are variable and can range from $50,000 to $90,000. Longitudinal costs, however, will depend on repairs and the durability of reusable items. The CPT code for intraoperative cholangioscopy is an add-on (47550) and must be listed with the accompanying primary procedure. For diagnostic percutaneous cholangioscopy, the code is 47552, and associated codes are as follows: with biopsy 47553, stone removal 47554, dilation 47555, or dilation with drain placement 47556. For per-oral cholangioscopy, an add-on code of 43273 should be reported with the parent ERCP code. Any reimbursement, however, is variable and payer dependent. It is important to provide a detailed indication and explanation of the procedure in the report to help the payer to review the request for extra payment and establish coverage and pricing. Payers often find it helpful to review copies of paid invoices.

FUTURE DIRECTIONS

The future of CP will be focused on improved digital endoscopes for single operator per-oral use and a wider array of accessory devices. Improvements in ease of use coupled with a reduction in costs are needed to drive further utilization of DPOC or single-operator digital CP. Further well-designed studies assessing diagnostic yield of malignancy for indeterminate strictures with optical imaging, cost-effectiveness, and comparative effectiveness of the newer cholangioscopy platforms are needed.

SUMMARY

Per-oral CP has allowed for significant improvements in diagnosis and management of biliary and pancreatic disease. Cholangioscopy with intraductal lithotripsy has become an established modality in the treatment of difficult biliary stones. Cholangioscopy increases the diagnostic yield when used in the evaluation of indeterminate biliary strictures. Pancreatoscopy is complementary to other imaging modalities in the evaluation of IPMN and treatment of pancreatic duct stones. Percutaneous cholangioscopy should be reserved for targeting inaccessible intrahepatic stones and strictures. Further advances in optics, ease of use, lower operating expenses, and improved reimbursement will permit more widespread use of CP in the future.

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Abbreviations: ASGE, American Society for Gastrointestinal Endoscopy; CP, cholangiopancreatoscopy; CPT, Current Procedural Terminology; DPOC, direct per-oral cholangioscopy; EHL, electrohydraulic lithotripsy; ESWL, extracorporeal shock wave lithotripsy; FDA, U.S. Food and Drug Administration; IPMN, intraductal papillary mucinous neoplasms.

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