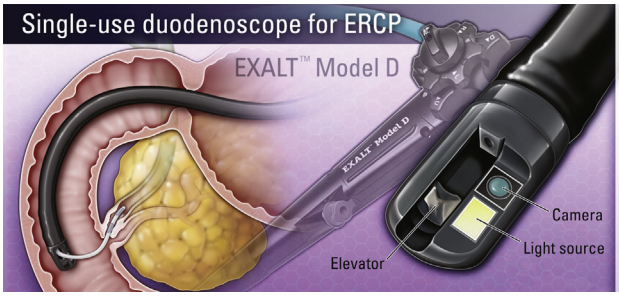
Single-use duodenoscope for ERCP performed by endoscopists with a range of experience in procedures of variable complexity CME

Adam Slivka, MD, PhD,[1] Andrew S. Ross, MD,[2] Divyesh V. Sejpal, MD, MHCDS,[3] Bret T. Petersen, MD,[4] Marco J. Bruno, MD, PhD,[5] Douglas K. Pleskow, MD,[6] V. Raman Muthusamy, MD, MAS,[7] Jennifer S. Chennat, MD,[1] Rajesh Krishnamoorthi, MD,[2] Calvin Lee, MD,[3] John A. Martin, MD,[4] Jan-Werner Poley, MD, PhD,[5] Jonah M. Cohen, MD,[8] Adarsh M. Thaker, MD,[7] Joyce A. Peetermans, PhD,[9] Matthew J. Rousseau, MS,[9] Gregory P. Tirrell, MS,[9] Richard A. Kozarek, MD[2] and the EXALT Single-use Duodenoscope Study Group

Pittsburgh, Pennsylvania; Seattle, Washington; Manhasset, New York; Rochester, Minnesota; Boston, Marlborough, Massachusetts; Los Angeles, California, USA; Rotterdam, The Netherlands

GRAPHICAL ABSTRACT



Comparison of outcomes for expert and less-expert endoscopist (N=200)

Outcome	Expert (N=160)	Less expert (N= 40)	*P* value
Procedure completed	96.3% (154/160)	97.5% (39/40)	0.999
Crossover rate	11.3% (18/160)	2.5% (1/40)	0.131
Median overall satisfaction	8.0 (160) (1.0,10.0)	8.0 (40) (4.0,10.0)	0.840
SAE rate	6.9% (11/160)	5.0% (2/40)	0.999
Median procedural completion time (min)	25.0 (158) (3.0,124.0)	28.5 (40) (4.0,125.0)	0.130
Mean number of cannulation attempts	2.8±4.0 (151) (1.0,21.0)	2.8±3.3 (36) (1.0,15.0)	0.954

Background and Aims: Expert endoscopists previously reported ERCP outcomes for the first commercialized single-use duodenoscope. We aimed to document usability of this device by endoscopists with different levels of ERCP experience.

Methods: Fourteen "expert" (>2000 lifetime ERCPs) and 5 "less-expert" endoscopists performed consecutive ERCPs in patients without altered pancreaticobiliary anatomy. Outcomes included ERCP completion for the intended indication, rate of crossover to another endoscope, device performance ratings, and serious adverse events.

Results: Two hundred ERCPs including 81 (40.5%) with high complexity (American Society for Gastrointestinal Endoscopy grades 3-4) were performed. Crossover rate (11.3% vs 2.5%, $P = .131$), ERCP completion rate (regardless of crossovers) (96.3% vs 97.5%, $P = .999$), median ERCP completion time (25.0 vs 28.5 minutes, $P = .130$), mean cannulation attempts (2.8 vs 2.8, $P = .954$), and median overall satisfaction with the single-use duodenoscope (8.0 vs 8.0 [range, 1.0-10.0], $P = .840$) were similar for expert versus less-expert endoscopists, respectively. The same metrics were similar by procedural complexity except for shorter median completion time for grades 1 to 2 versus grades 3 to 4 ($P < .001$). Serious adverse events were reported in 13 patients (6.5%).

Conclusions: In consecutive ERCPs including high complexity procedures, endoscopists with varying ERCP experience had good procedural success and reported high device performance ratings. (Clinical trial registration number: NCT04223830.) (Gastrointest Endosc 2021;94:1046-55.)

(footnotes appear on last page of article)

Duodenoscopes are classified as semicritical devices, for which the U.S. Food and Drug Administration (FDA) recommends sterilization or high-level disinfection to decrease the risk of cross-contamination.[1] Contamination with microorganisms from GI or oral origins may occur in up to 15% of reusable duodenoscopes and has been reported to be independent of device age and usage.[2] Potential cross-contamination between patients from duodenoscopes used in ERCP is most concerning for multidrug-resistant organisms (MDROs), including carbapenem-resistant *Enterobacteriaceae*, which include *Klebsiella pneumoniae*,[3] *Escherichia coli*,[4] and *Enterobacter cloacae*.[3] Rare but serious duodenoscope-associated multidrug-resistant outbreaks with carbapenem-resistant *Enterobacteriaceae* and *Pseudomonas* have been documented internationally,[5-8] even after appropriate reprocessing procedures were implemented. An FDA safety communication mentioned 3 deaths and 45 reports of patient infection tied to inadequate duodenoscope reprocessing based on medical device reports received between October 15, 2018 and March 31, 2019.[9] Because of the severity of MDRO infections[10] and high volume of ERCP procedures performed in the United States[5] and internationally,[11-14] systematic efforts to reduce duodenoscope cross-contamination and the risk of associated exogenous infection of patients are warranted.[15]

Investigations of duodenoscope cross-contamination and studies of MDRO outbreaks have shed light on cross-contamination risks and potential mechanisms of infection sources. In an April 12, 2019 safety communication, the FDA reported positive duodenoscope culture rates of 5.4% for high-concern (eg, *E coli* and *Pseudomonas aeruginosa*) organisms for 3 brands of reusable duodenoscopes after reprocessing.[9,16] A root-cause analysis of an outbreak of multidrug-resistant *K pneumoniae* infection revealed that 2 contaminated duodenoscopes led to infection/colonization rates of 35% (17/49) and 29% (7/24), respectively, in patients who had undergone ERCP over a period of 8 months.[17] This study cited miscommunication about reprocessing, undetected damaged parts, inadequate repair of duodenoscope damage, and duodenoscope design abnormalities (including forceps elevator, elevator lever, and instrumentation port sealing) as major abnormalities associated with duodenoscope-associated infection. Similarly, a 2019 review of 23 published cases (17 U.S. and 6 non-U.S. cases, including 2-35 patients each) associating confirmed (or suspected) carbapenem-resistant *Enterobacteriaceae* or MDRO infections with exposure to a duodenoscope since 2012 cited the following that may contribute to a duodenoscope remaining contaminated after reprocessing: device design; breach of recommended reprocessing guidelines (eg, inadequate manual cleaning, delayed reprocessing, or improper device storage); damage to the device; insufficient servicing, maintenance, or repair; and/or the presence of biofilms.[1] Despite modifiable issues among these risk factors, persistent contamination of reusable duodenoscopes has been documented after appropriately implemented high-level disinfection and quarantine[18,19] or sterilization,[20] rigorous field investigation after infection outbreaks,[4,21] and the availability of detailed reprocessing guidelines.[22-24] A sterile single-use endoscope has been proposed as one solution to several unresolved issues related to reprocessing and reuse of reusable endoscopes.[25]

In a preclinical bench study, expert endoscopists reported a similar performance of the single-use duodenoscope compared with 3 models of marketed reusable duodenoscopes.[26] Similarly, a clinical case series published in 2020[27] reported that expert endoscopists completed nearly all ERCPs in 60 cases with a range of complexity using the single-use duodenoscope. In December 2019, the FDA cleared the single-use duodenoscope for marketing in the United States, granting it Breakthrough Device designation.[28] In this new clinical case series, we aimed to prospectively confirm in the postmarket setting that the single-use duodenoscope can be used by expert and less-expert endoscopists to complete consecutive ERCPs of any complexity in academic medical centers. Quality control improvements based on physician feedback were made during this case series. Outcomes were compared by endoscopists' level of procedural experience and case complexity.

METHODS

Single-use duodenoscope

The device used in this clinical case series (EXALT Model D single-use duodenoscope; Boston Scientific Corporation, Marlborough, Mass, USA) is a sterile (sterility assurance level 10^{-6} or better), single-use duodenoscope designed to function similarly to currently marketed reusable duodenoscopes and intended to be used in a single procedure and then discarded. A near-final design of the device was used in previously published premarket bench[26] and clinical studies[27]; in response to expert user feedback from these studies, modifications were made to optimize device performance, most notably to the working channel design. Single-use duodenoscopes of the modified design received FDA clearance in December 2019 and gained a Conformitè Europëenne (CE) Mark in January 2020.[29] This device design was used in a bench study in January 2020 (results available on request) and in the present clinical series of 200 cases. Expert and less-expert endoscopist user feedback informed improvements to production quality control, principally to the attachment of the elevator at the tip of the duodenoscope

and to instructions related to the placement of single-use irrigation and insufflation valves on the handle of the single-use duodenoscope.

Patient population

The study plan allowed for recruitment of up to 200 adult patients scheduled for ERCP per the standard of care at 7 participating healthcare centers. Institutional Review Board approvals for the study were gained before study initiation. The study was registered in the ClinicalTrials.gov database (NCT04223830) on January 10, 2020. Recruitment and enrollment took place during 3 time periods: January to February 2020 (50 patients), May to July 2020 (50 patients), and September 2020 to February 2021 (100 patients) after delays related to the coronavirus disease 2019 pandemic. All enrolled patients provided written informed consent for study participation. Single-use duodenoscopes were provided free-of-charge to the investigational sites for use in study patients.

Consecutive eligible patients were recruited for the study on selected weekdays when participating endoscopists were performing ERCPs. Patients were eligible for inclusion if they were age ≥18 years, willing and able to comply with the study procedures and provide written informed consent to participate in the study, and scheduled for a clinically indicated ERCP or other duodenoscope-based procedure. Excluded from the study were patients with altered pancreaticobiliary anatomy; potentially vulnerable patients including, but not limited to, pregnant women; patients for whom endoscopic techniques are contraindicated; patients who were enrolled in another investigational study that would directly interfere with the current study; or patients excluded at investigator discretion.

Study interventions

Patient assessments. Data were collected at baseline/enrollment and during personal or telephone follow-up at 72 hours (±1 day) and 7 days (±2 days) after ERCP. Demographic and relevant clinical history were recorded on standard case report forms, including age, gender, relevant GI prior diagnoses (current or in last 12 months), and ERCP history (including prior sphincterotomy).

ERCP procedures. Fourteen "expert" (lifetime ERCPs >2000) and 5 "less-expert" (lifetime ERCPs ≤2000) endoscopists performed the study ERCPs. The endoscopists agreed to use the single-use duodenoscope in place of the reusable duodenoscope(s) normally used in the endoscopy unit for ERCP. Start and stop times of the procedure were recorded, and at the end of the procedure subjective feedback on performance-related attributes, American Society for Gastrointestinal Endoscopy (ASGE) grade for complexity of ERCP procedure, and all attempted or completed maneuvers during the ERCP were documented, regardless of the original indication for the procedure. Any ensuing device deficiencies were recorded and reported, even if they did not result in an adverse event (AE) or inability to complete the ERCP. Such reporting of device deficiencies was encouraged because they inform opportunities for future improvements to manufacturing quality control and/or device design. If the endoscopist was unable to perform any necessary maneuvers with the single-use device and had to cross over to use a reusable duodenoscope, the reason the procedure was not completed with the single-use device was recorded. In case of crossover, the ability to complete the ERCP maneuvers with a reusable duodenoscope was documented.

Outcomes

The outcomes for the clinical case series were the ability to complete the procedure, incidence of crossover to a reusable duodenoscope, procedure completion time in minutes, number of cannulation attempts, cannulation completion time in minutes, completion of 19 specific maneuvers, 23 device performance characteristics (Likert scale of 1 [not preferred] to 5 [comparable with reusable duodenoscope]), median overall satisfaction with the single-use duodenoscope during the procedure (Likert scale of 1 [unsatisfied] to 10 [very satisfied]), and serious AEs (SAEs) assessed at 72 hours and 7 days post-ERCP. "Difficult common bile duct cannulation" was defined by a modification of the European Society of Gastrointestinal Endoscopy definition as the presence of ≥1 of the following: more than 5 contacts with the papilla while attempting to cannulate, more than 5 minutes spent attempting to cannulate after visualization of the papilla, and at least 1 (instead of "more than 1") unintended pancreatic duct cannulation or opacification.[30]

Statistical analysis

Descriptive statistics included procedure completion rates, procedure duration, number of cannulation attempts, median overall satisfaction, and performance ratings as well as the mean, standard deviation, and range for age, crossovers, and tabulated AEs. Comparisons by duodenoscope model and by endoscopists' level of expertise were conducted for completion time and performance ratings using Wilcoxon rank-sum tests and for number of cannulation attempts using a negative binomial model. The Fisher exact test was used to compare occurrence of a crossover with a reusable duodenoscope by level of expertise or by ASGE level of case complexity. Interactions were assessed using a generalized linear model. Statistical analyses were performed using SAS 9.4 software (SAS Institute Inc, Cary, NC, USA).

RESULTS

Patient characteristics

Of 289 patients who were screened, 200 (69.2%) were enrolled after providing written informed consent to participate in the study (Fig. 1). Reasons for

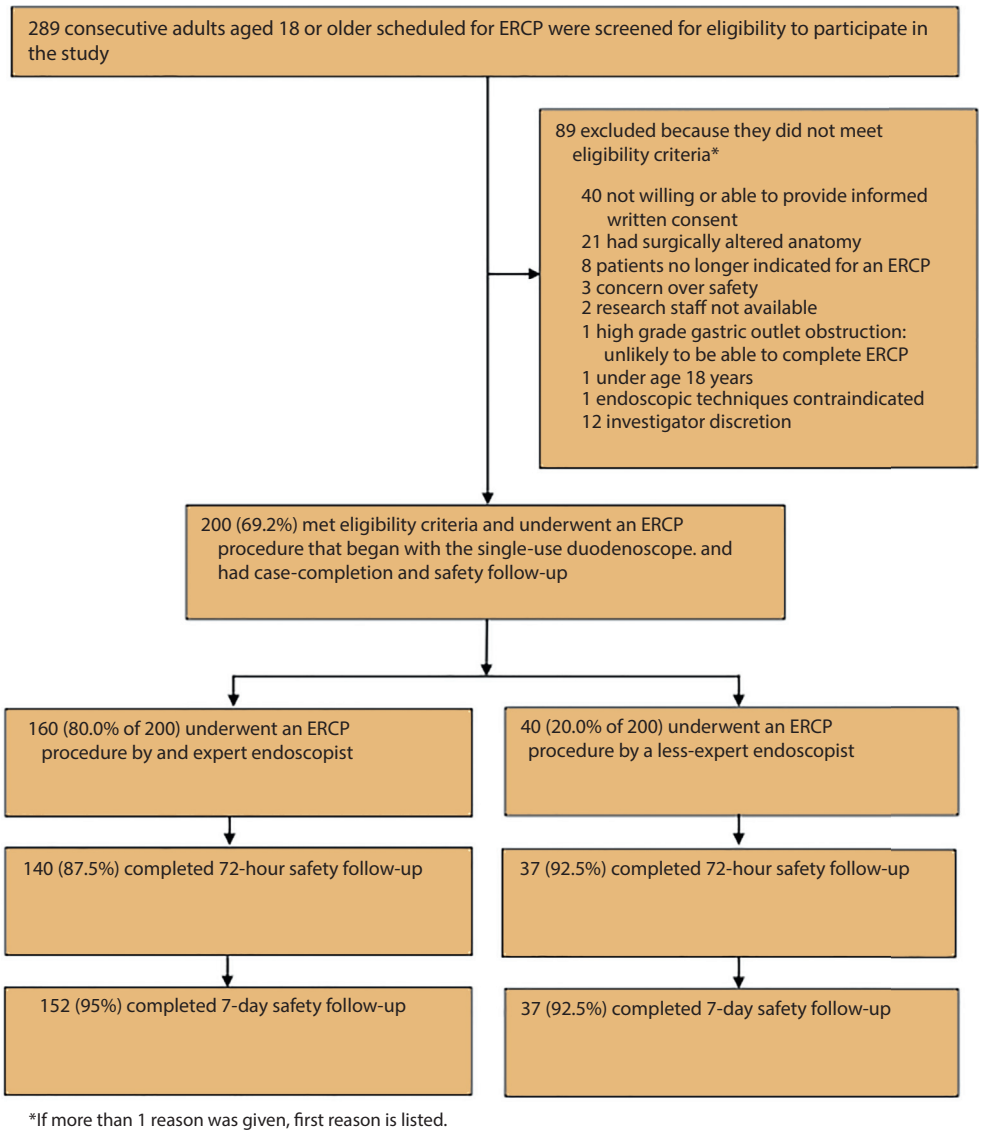


Figure 1. Patient flow through the study.

nonparticipation were unwillingness or inability to provide informed written consent (n = 40), age <18 years (1), altered anatomy (21), investigator discretion (12), no longer indicated for an ERCP (3), concern over safety (3), high-grade gastric outlet obstruction (1), and research staff not available (2).

Of the 200 patients (mean age, 62.6 years) who had an ERCP, 103 (51.5%) were women and 129 (64.5%) had a prior ERCP (Table 1). One hundred six patients (53.0%) had a prior biliary and/or pancreatic sphincterotomy. The most common GI diagnoses for patients scheduled for ERCP or other duodenoscope-based procedure were evaluation of abnormal imaging finding (75, 37.5%), biliary stones or gallstones (64, 32.0%), documented biliary or pancreatic stricture (54, 27.0%), and chronic pancreatitis (35, 17.5%). Four patients (2.0%) had a history of or current MDRO colonization.

When asked if they would have chosen to use the device to complete this case in a postmarket commercial setting and, if so, for what reason, endoscopists selected the following responses: multiple future ERCPs are anticipated (17.5%, 35/200 patients), high risk of cholangitis (12.0%, 24/200), coronavirus disease 2019 (10.5%, 21/200), current immunosuppression (10.5% (21/200), or "other" (5.5%, 11/200). In addition, 1 endoscopist wrote in "preferred standard of care" for 23 of 42 patients he treated.

Description of ERCPs

Among the 200 study cases, 19 (9.5%) included crossover from the single-use to a reusable duodenoscope; of these, 16 were reported as completed and 3 were reported as not completed using a reusable duodenoscope. In total, 7 cases (3.5%) were reported as not completed, including the 3 crossovers previously mentioned, 2 cases that

TABLE 1. Patient characteristics (n = 200)

Characteristic	Value
Age, y, mean ± standard deviation (range)	62.6 ± 14.0 (27.0-92.0)
Female	51.5 (103/200)
GI diagnoses (last 12 months)*	
Primary sclerosing cholangitis	4.0 (8/200)
Chronic pancreatitis	17.5 (35/200)
Viral hepatitis	.5 (1/200)
Hepatic or pancreatic tumor	15.5 (31/200)
Cholangiocarcinoma	7.0 (14/200)
Other GI cancer	5.0 (10/200)
Pancreatic pseudocyst	4.0 (8/200)
Bile duct stones/gallstones	32.0 (64/200)
Pancreatic stones	9.0 (18/200)
Cholangitis	13.5 (27/200)
Current immunosuppression (disease- or pharma-induced)	16.5 (31/200)
History of or current multidrug-resistant organism colonization	2.0 (4/200)
Documented biliary or pancreatic stricture	27.0 (54/200)
Documented bacterial infection	2.5 (5/200)
Documented viral infection (other than hepatitis)	.0 (0/200)
Abnormal imaging finding	37.5 (75/200)
Other	23.5 (47/200)
Prior surgical/upper endoscopic procedures	
Previous ERCPs	64.5 (129/200)
Prior biliary or pancreatic sphincterotomy	53.0 (106/200)
Prior stent placement	44.0 (88/200)
Liver transplantation	3.0 (6/200)
Other transplantation	1.5 (3/200)
Cholecystectomy	24.5 (49/200)
Sleeve gastrectomy	1.0 (2/200)
Hepatic surgery	2.0 (4/200)
Pancreatic surgery	.5 (1/200)
Other	8.0 (16/200)
Current endoscopic procedure	
Native papillae	
Native major papilla	37.5 (75/200)
Native minor papilla	10.0 (20/200)
Native major and minor papilla	40.0 (80/200)
ASGE grade for complexity of ERCP†‡	
Grade 1	10.3 (20/195)
Grade 2	48.2 (94/195)
Grade 3	30.3 (59/195)
Grade 4	11.3 (22/195)

Values are % (n/N) unless otherwise defined.
ASGE, American Society for Gastrointestinal Endoscopy.
*Each patient had 1 or more of the listed GI diagnoses; rows are not mutually exclusive.
†Denominator <200 because of 5 non-ERCP procedures that did not have an ASGE grade.
‡ASGE grade for complexity of ERCP: grade 1, deep cannulation of duct of interest, main papilla, sampling; grade 2, biliary stone extraction <10 mm, treat biliary leaks, treat extrahepatic benign and malignant strictures, placed prophylactic stents; grade 3, biliary stone extraction ≥10 mm, minor papilla cannulation in divisum and therapy, removal of internally migrated biliary stents, intraductal imaging/biopsy sampling/FNA, management of acute or recurrent pancreatitis, treat pancreatic strictures, remove pancreatic stones mobile and <5-mm, treat hilar tumors, treat benign biliary strictures hilum and above, manage suspected Sphincter of Oddi dysfunction (SOD) (with or without manometry); grade 4, remove internally migrated pancreatic stents, intraductal image-guided therapy (eg, photodynamic therapy, electrohydraulic lithotripsy), pancreatic stones impacted and/or ≥5-mm, intrahepatic stones, pseudocyst drainage/necrosectomy, ampullectomy, ERCP after Whipple or Roux-en-Y bariatric surgery.

changed to an EUS-guided procedure, and 2 aborted ERCPs that were rescheduled for ERCP at a later date. Difficult common bile duct cannulation was reported for 50 cases (25%). Advanced cannulation techniques performed included double wire in 12 (6.0%), pancreatic duct plastic stent in 11 (5.5%), precut sphincterotomy in 6 (3.0%), septotomy in 2 (1.0%), and combination bronchoscopy forceps and sphincterotome in 1 (.5%). Also reported were 4 cannulations of the minor papilla when using the single-use duodenoscope and 1 each of rendezvous/EUS-guided choledochoduodenostomy, right and left intrahepatic duct cannulation, removal of percutaneous transhepatic biliary drain, biliary sphincterotomy to facilitate pancreatic duct cannulation, and Soehendra screw catheter and balloon cannulation with 5-4-3 catheter, common bile duct cannulation after ampullectomy. In 11 cases (5.5%), cholangioscopy (Spyglass cholangioscopy system; Boston Scientific Corporation, Marlborough, Mass, USA) was performed in conjunction with the single-use duodenoscope.

Twenty different types of maneuvers were performed using the single-use duodenoscope, including sphincterotomy (biliary and pancreatic), papillectomy/ampullectomy, cannulation (common bile duct, pancreatic duct, minor papilla), mechanical lithotripsy, clearance of bile duct or pancreatic duct stones, biliary or pancreatic stent placement or removal, balloon dilation (of sphincter, biliary, or pancreatic stricture), cholangioscopy, cytology brushing, biopsy sampling, and other. For 189 of 200 patients

(94.5%), all intended maneuvers were completed using the single-use duodenoscope only. Of 721 total maneuvers attempted, 702 (97.4%) were completed using the single-use duodenoscope.

The ERCPs included all ASGE grades of complexity: grade 1 (least complex; 10.3%, 20/195), grade 2 (48.2%, 94/195), grade 3 (30.3%, 59/195), and grade 4 (most complex; 11.3%, 22/195). Median procedure completion time was 26.0 minutes (range, 3.0-125.0), including times ≤20 minutes in 69 of 195 cases (35.4%) to ≥60 minutes in 21 of 195 cases (10.8%). Fifty-one ERCPs (25.5%) were performed with the patient in the supine position, 131 (65.5%) with the patient in the prone position, 10 (5.0%) with the patient in the left lateral decubitus position, and 8 (4.0%) in which patient position was not reported.

Compared with cases with at least 1 prior sphincterotomy, cases with no prior sphincterotomy had a higher mean number of cannulation attempts (4.0 ± 4.9 vs 1.7 ± 2.0, $P < .001$) and a lower likelihood of having high complexity ($P < .001$). The baseline sphincterotomy status did not correlate with significant differences in ERCP completion rate ($P = .053$), crossover rate ($P = .636$), ERCP completion time ($P = .970$), or overall satisfaction with the single-use duodenoscope ($P = .100$).

Comparison of outcomes for expert versus less-expert endoscopists

ERCPs completed (96.3% [154/160] vs 97.5% [39/40]), median procedural completion time (25.0 vs 28.5, $P = .130$), mean number of cannulation attempts (2.8 vs 2.8, $P = .954$), crossover rate (11.3% vs 2.5%, $P = .131$), and proportion of cases with high complexity (43.6% [68/156] vs 33.4% [13/39]) were similar for expert compared with less-expert endoscopists (Table 2). On a scale of 1 (least) to 10 (most satisfied), the median rating of overall satisfaction with the performance of the single-use duodenoscope was 8.0 for both expert and less-expert endoscopists ($P = .840$).

Comparison of outcomes by ASGE grade of complexity

Median time of completion was significantly shorter for cases with ASGE grade 1 or 2 compared with those with grade 3 or 4 (19.0 vs 39.0 minutes, respectively; $P < .001$), whereas mean number of cannulation attempts (3.0 vs 2.6, $P = .401$), ERCP completion rate (98.2% [112/114] vs 96.3% [78/81], $P = .999$), and crossover rate (8.8% [10/114] vs 9.9% [8/81], $P = .806$) were similar (Table 3). The median rating of overall satisfaction with the performance of the single-use duodenoscope was 8.0 for both cases with ASGE grade 1 or 2 and cases with ASGE grade 3 or 4 ($P = .550$).

Performance characteristics and overall satisfaction

Median ratings of 5 (range, 1-5) were documented for 5 of 23 ERCP maneuvers (21.7%) tested; the 18 other median ratings were 4.0 (Table 4). Low performance scores for device attributes (at least 1 rating of 1 or 2) were documented in 6.5% of ratings (272/4189). Median overall satisfaction with the single-use duodenoscope was rated as 8.0 (range, 1-10).

Safety profiles

Of the 200 enrolled patients, 13 (6.5%) experienced 18 SAEs within 7 days postprocedure (Table 5). Five patients (2.5%) experienced a bleeding event, 3 (1.5%) experienced acute pancreatitis, 2 (1.0%) each experienced cholangitis or epigastric/abdominal pain, and 1 (.5%) each experienced choledocholithiasis, systemic inflammatory response syndrome, fever, suspected pneumonia, nausea and vomiting, or urinary tract infection. SAE rates were similar for expert versus less-expert endoscopists (6.9% [11/160] vs 5.0% [2/40], respectively; $P = .999$; Table 2) and for cases with ASGE grade 1 or 2 versus ASGE grade 3 or 4 levels of complexity (7.0% [8/114] vs 6.2% [5/81], respectively; $P = .999$; Table 3).

DISCUSSION

Academic endoscopists with both expert level and less-expert level (≤2000 lifetime ERCPs) procedural experience used a new single-use duodenoscope to complete scheduled ERCP cases across all 4 ASGE procedural complexity grades. The rate of SAEs was typical of standard ERCP practice.[31] Good technical success was achieved, with 96.5% completion of procedures including crossovers to a reusable duodenoscope in 9.5% of cases. This was higher than the crossover rates reported in a previous case series[27] using the premarket model (3.3%, n = 60) and in a postmarket randomized study[32] of the single-use duodenoscope compared with a reusable duodenoscope (4.2%, n = 48 in single-use arm).

In an effort to address the risk of duodenoscope-related infection, the FDA previously cleared duodenoscopes with disposable endcap[33] and elevator components.[34] In December 2019, the FDA cleared the first fully disposable duodenoscope, commenting that the device "represents another major step forward for improving the safety of these devices" and that "a fully disposable duodenoscope does not need to be reprocessed, eliminating the risk of potential infection due to ineffective reprocessing."[28] Although an introduction of this innovation was helpful, the expected experience level of users, coordination of use with reusable duodenoscopes, and target patient population(s) for the single-use duodenoscope have not been established. The current study shows that ERCP completion rates, AE rates, and user satisfaction ratings were similar for endoscopists with varying levels of experience in academic practices. Such findings increase the likelihood that the results are

TABLE 2. Comparison of outcomes for expert and less-expert endoscopist (n = 200)

Outcome	Expert (n = 160)	Less expert (n = 40)	*P* value
Procedure completed	96.3 (154/160)	97.5 (39/40)	.999
Crossover rate	11.3 (18/160)	2.5 (1/40)	.131
Overall satisfaction, median (n) (range)	8.0 (160) (1.0-10.0)	8.0 (40) (4.0-10.0)	.840
Serious adverse event rate	6.9 (11/160)	5.0 (2/40)	.999
Procedural completion time, min, median (n) (range)	25.0 (158) (3.0-124.0)	28.5 (40) (4.0-125.0)	.130
No. of cannulation attempts, mean ± standard deviation (n) (range)	2.8 ± 4.0 (151) (1.0-21.0)	2.8 ± 3.3 (36) (1.0-15.0)	.954
American Society for Gastrointestinal Endoscopy complexity grade of cases*			.512
Grade 1	9.0 (14/156)	15.4 (6/39)	
Grade 2	47.4 (74/156)	51.3 (20/39)	
Grade 3	32.1 (50/156)	23.1 (9/39)	
Grade 4	11.5 (18/156)	10.3 (4/39)	

Values are % (n/N) unless otherwise defined.
*Excludes 5 non-ERCP procedures that did not have an American Society for Gastrointestinal Endoscopy grade.

TABLE 3. Comparison of outcomes by American Society for Gastrointestinal Endoscopy grade of complexity (n = 195)

Outcome	Grade 1 or 2 (n = 114)	Grade 3 or 4 (n = 81)	*P* value
ERCP completed	98.2 (112/114)	96.3 (78/81)	.651
Crossover rate*	8.8 (10/114)	9.9 (8/81)	.806
Overall satisfaction, median (n) (range)	8.0 (114) (1.0-10.0)	8.0 (81) (1.0-10.0)	.550
Serious adverse event rate	7.0 (8/114)	6.2 (5/81)	.999
Procedural completion time, median (n) (range)	19.0 (112) (3.0-82.0)	39.0 (81) (11.0-125.0)	<.001
No. of cannulation attempts, mean ± standard deviation (n) (range)	3.0 ± 4.1 (109) (1.0-20.0)	2.6 ± 3.4 (78) (1.0-21.0)	.401

Values are % (n/N) unless otherwise defined.
*Excludes 1 crossover case that did not have an American Society for Gastrointestinal Endoscopy grade.

generalizable to community practices with adequate procedural expertise.

Introduction of the single-use duodenoscope into gastroenterology practice can serve an important role as a sterile equipment reserve, allowing continued performance of ERCPs while all available reusable devices are in use, while reprocessing services undergo maintenance or are off-duty, or while suspected or confirmed contaminated duodenoscopes are quarantined. For example, a 2015 report documented a multidrug-resistant *E coli* outbreak during which the endoscope reprocessing area was immediately closed, duodenoscopes were cultured and quarantined for 48 hours until negative cultures were obtained, and a full investigation was undertaken in conjunction with the local county health authority and the Centers for Disease Control and Prevention.[18] Availability of single-use duodenoscopes would enable continued care for urgent patients who could be seen at a different site until an outbreak investigation is completed.

The patient populations that could most benefit from the routine use of the single-use duodenoscope are uncertain. High-risk medical conditions represented among patients in the current study and earlier case series[27] include past or current MDRO colonization, immunosuppression, primary sclerosing cholangitis, acute cholangitis, recurrent pancreatitis, cholangiocarcinoma, pancreatic cancer, malignant liver duct tumor, biliary leak, pancreatic duct leak, and bile duct stricture. "Multiple future ERCPs are anticipated" was the top reason specified by the endoscopist-investigators as a reason to choose a single-use duodenoscope. A larger, multisite international study of the single-use duodenoscope is in planning and will allow better characterization of performance of the device among different patient groups with procedures at different ASGE levels of complexity in different practice settings.

Our study has several strengths, limitations, and considerations for study interpretation. Unlike 2 earlier studies of this single-use duodenoscope,[26,27] the current study included investigators at both expert and less-expert levels in academic gastroenterology practice. Ninety-one percent of all procedures were completed using the study instrument alone for indications

TABLE 4. Median ratings for 23 ERCP performance characteristics of the single-use duodenoscope (n = 200)

Performance characteristic	Median rating (range)*
Ease and ability to intubate the esophagus	4.0 (1.0-5.0)
Ease and ability of traversing the stomach and pylorus	4.0 (1.0-5.0)
Inadvertent slippage out of the duodenum	4.0 (1.0-5.0)
Navigation/pushability (overall from insertion to the deepest point of advancement into duodenum)	4.0 (1.0-5.0)
Predictability of range of motion	4.0 (1.0-5.0)
Suction performance	5.0 (1.0-5.0)
Ability to select short/long position as needed	4.0 (1.0-5.0)
Ease and ability to examine luminal mucosa where necessary	4.0 (1.0-5.0)
Stability of scope during cannulation of papilla	4.0 (2.0-5.0)
Elevator function	4.0 (1.0-5.0)
Ability to selectively cannulate	4.0 (1.0-5.0)
Tip control and deflection at time of cannulation	4.0 (1.0-5.0)
Ease of controlling and maintaining position during sphincterotomy	4.0 (1.0-5.0)
Position of the device in the field of view	4.0 (2.0-5.0)
Visualization/location of important landmarks on monitor	4.0 (1.0-5.0)
Maintenance of grip on wire by elevator	5.0 (1.0-5.0)
Elevator strength and ability to pass rigid device into common bile duct or pancreatic duct	4.0 (1.0-5.0)
Torquability of scope and ability to orient tip of scope in direction of push/pull	4.0 (2.0,5.0)
Ease and ability of passing ancillary devices through the channel	5.0 (1.0-5.0)
Ease and ability of advancing ancillary devices from the channel into the papilla.	5.0 (1.0-5.0)
Ease and ability to complete all ERCP-guided tasks	4.0 (1.0-5.0)
Ease and ability of duodenoscope withdrawal	5.0 (3.0-5.0)
Image quality/appearance/brightness	4.0 (1.0-5.0)

*Rating is based on a scale from 1 to 5, with 1 being "you do not prefer the performance of the EXALT duodenoscope over that of your usual reusable duodenoscope" and 5 being "performance of the EXALT duodenoscope was comparable with your experience with the reusable duodenoscope you usually use in your practice."

TABLE 5. SAEs that occurred by 7 days after ERCP (n = 200)

SAE	% (n/N patients)
All SAEs	6.5 (13/200)
Bleeding*	2.5 (5/200)
Acute pancreatitis	1.5 (3/200)
Cholangitis	1.0 (2/200)
Epigastric or abdominal pain	1.0 (2/200)
Choledocholithiasis	.5 (1/200)
Systemic inflammatory response syndrome	.5 (1/200)
Fever	.5 (1/200)
Suspected pneumonia	.5 (1/200)
Nausea and vomiting	.5 (1/200)
Urinary tract infection (*Escherichia coli*)	.5 (1/200)

Each patient had 1 or more of the listed SAEs; rows are not mutually exclusive.
SAE, Serious adverse event.
*Includes 1 post-ERCP bleed, 1 mucosal tear at the distal esophagus, 1 Mallory-Weiss tear, 1 postsphincterotomy bleed, and 1 colonic diverticular bleed.

representing all 4 ASGE grades of procedural complexity. The consecutive case series design, with a 71% overall recruitment rate among 5 sites, yielded a study population with a wide age range and the full range of procedural complexity, which should enable good generalizability of the study results to ERCP referral populations. Limitations include the lack of randomization and absence of a control group in the clinical study, which was deemed premature while endoscopists were still familiarizing themselves with the single-use duodenoscope. Because the numbers of cases in each group were small and unequal, the study findings are suggestive rather than definitive. Statistically significant differences between expert and less-expert endoscopists might have been identified in a larger study. The 7-day follow-up was appropriate to track periprocedural outcomes but not long enough to assess delayed outcomes that might have been associated with the intervention. Single-use endoscopes cannot prevent endogenous infection, which is believed to be more common than duodenoscope-related exogenous infection. Thus, the single-use duodenoscope should be recognized as a tool to eliminate interpatient transfer of microorganisms but not eliminate ERCP-related infection. Finally, some investigators participated in the development of the single-use duodenoscope[26,27] and have received research funding from the study sponsor and from manufacturers of reusable duodenoscopes. This might

have introduced bias in subjective measures of the device's performance; however, the frequency of low ratings for some duodenoscope features suggested that the investigators provided realistic feedback. In conclusion, expert and less-expert endoscopists used the first single-use duodenoscope to successfully complete almost all scheduled ERCP cases with a range of complexity and rated its function to be similar to reusable duodenoscopes.

ACKNOWLEDGMENTS

Members of the EXALT Single-use Duodenoscope Study Group are Adam Slivka, Jennifer S. Chennat, Asif Khalid, Rohit Das, Harkirat Singh, and Kishore Vipperla at University of Pittsburgh Medical Center (Pittsburgh, Pa, USA); Divyesh V. Sejpal, Calvin Lee, and Andrew Antony at North Shore University Hospital (Manhasset, NY, USA); Richard A. Kozarek, Andrew S. Ross, Jun-Ho Choi, Michael Larsen, Joanna Law, Rajesh Krishnamoorthi, and Jagpal Klair at Virginia Mason Medical Center (Seattle, Wa, USA); V. Raman Muthusamy and Adarsh Thaker at University of California, Los Angeles (Los Angeles, Calif, USA); Bret T. Petersen, John A. Martin, Barham Abu Dayyeh, Vinay Chandrasekhara, Michael Levy, and Ryan Law at Mayo Clinic (Rochester, Minn, USA); Douglas K. Pleskow at Beth Israel Deaconess Medical Center (Boston, Mass, USA); Jonah M. Cohen at Massachusetts General Hospital (Boston, Mass, USA), Marco J. Bruno and Jan-Werner Poley at Erasmus Medical Center (Rotterdam, The Netherlands); and Joyce A. Peetermans, Matthew J. Rousseau, Gregory P. Tirrell, and Jeff Insull at Boston Scientific Corporation (Marlborough, Mass, USA).

We acknowledge Boston Scientific employee Margaret Gourlay, MD, MPH, for assistance in preparation of the manuscript.

The data, analytic methods, and study materials for this study may be made available to other researchers in accordance with the Boston Scientific Data Sharing Policy (http://www.bostonscientific.com/en-US/data-sharing-requests.html).

REFERENCES

1. Muscarella LF. Use of ethylene-oxide gas sterilisation to terminate multidrug-resistant bacterial outbreaks linked to duodenoscopes. BMJ Open Gastroenterol 2019;6:e000282.
2. Rauwers AW, Voor In't Holt AF, Buijs JG, et al. Nationwide risk analysis of duodenoscope and linear echoendoscope contamination. Gastrointest Endosc 2020;92:681-91.
3. Rauwers AW, Voor In't Holt AF, Buijs JG, et al. High prevalence rate of digestive tract bacteria in duodenoscopes: a nationwide study. Gut 2018;67:1637-45.
4. Epstein L, Hunter JC, Arwady MA, et al. New Delhi metallo-beta-lactamase-producing carbapenem-resistant *Escherichia coli* associated with exposure to duodenoscopes. JAMA 2014;312:1447-55.
5. Rahman MR, Perisetti A, Coman R, et al. Duodenoscope-associated infections: update on an emerging problem. Dig Dis Sci 2019;64:1409-18.
6. Carbonne A, Thiolet JM, Fournier S, et al. Control of a multi-hospital outbreak of KPC-producing *Klebsiella pneumoniae* type 2 in France, September to October 2009. Euro Surveill 2010;15:19734.
7. Giakoupi P, Maltezou H, Polemis M, et al. KPC-2-producing *Klebsiella pneumoniae* infections in Greek hospitals are mainly due to a hyperepidemic clone. Euro Surveill 2009;14:19218.
8. Gauthier L, Dortet L, Cotellon G, et al. Diversity of carbapenemase-producing *Escherichia coli* isolates in France in 2012-2013. Antimicrob Agents Chemother 2018;62:e00266-18.
9. U.S. Food and Drug Administration. Medical devices; medical device safety; safety communications. The FDA continues to remind facilities of the importance of following duodenoscope reprocessing instructions: FDA Safety Communication (April 12, 2019). Available at: https://www.fda.gov/MedicalDevices/Safety/AlertsandNotices/ucm635828.htm.] Accessed on June 3, 2021.
10. U.S. Health and Human Services: Centers for Disease Control and Prevention. Antibiotic resistance threats in the United States, 2013 (April 2013). Available at: https://www.cdc.gov/drugresistance/threat-report-2013/pdf/ar-threats-2013-508.pdf. Accessed June 3, 2021.
11. Soreide JA, Karlsen LN, Sandblom G, et al. Endoscopic retrograde cholangiopancreatography (ERCP): lessons learned from population-based national registries: a systematic review. Surg Endosc 2019;33:1731-48.
12. Moffatt DC, Yu BN, Yie W, et al. Trends in utilization of diagnostic and therapeutic ERCP and cholecystectomy over the past 25 years: a population-based study. Gastrointest Endosc 2014;79:615-22.
13. Glomsaker T, Soreide K, Aabakken L, et al. A national audit of temporal trends in endoscopic retrograde cholangiopancreatography in Norway. Scand J Gastroenterol 2011;46:116-21.
14. Kapral C, Duller C, Wewalka F, et al. Case volume and outcome of endoscopic retrograde cholangiopancreatography: results of a nationwide Austrian benchmarking project. Endoscopy 2008;40:625-30.
15. U.S. Food and Drug Administration. Medical devices; medical device safety; safety communications. The FDA is recommending transition to duodenoscopes with innovative designs to enhance safety: FDA Safety Communication (August 29, 2019). Available at: https://www.fda.gov/medical-devices/safety-communications/fda-recommending-transition-duodenoscopes-innovative-designs-enhance-safety-fda-safety-communication. Accessed on June 3, 2021.
16. U.S. Food and Drug Administration. Medical devices; medical device safety; safety communications. The FDA provides interim results of duodenoscope reprocessing studies conducted in real-world settings: FDA Safety Communication (December 10, 2018). Available at: https://www.fda.gov/MedicalDevices/Safety/AlertsandNotices/ucm628020.htm. Accessed on June 3, 2021.
17. Rauwers AW, Troelstra A, Fluit AC, et al. Independent root-cause analysis of contributing factors, including dismantling of 2 duodenoscopes, to investigate an outbreak of multidrug-resistant *Klebsiella pneumoniae*. Gastrointest Endosc 2019;90:793-804.
18. Ross AS, Baliga C, Verma P, et al. A quarantine process for the resolution of duodenoscope-associated transmission of multidrug-resistant *Escherichia coli*. Gastrointest Endosc 2015;82:477-83.
19. Mark JA, Underberg K, Kramer RE. Results of duodenoscope culture and quarantine after manufacturer-recommended cleaning process. Gastrointest Endosc 2020;91:1328-33.
20. Naryzhny I, Silas D, Chi K. Impact of ethylene oxide gas sterilization of duodenoscopes after a carbapenem-resistant Enterobacteriaceae outbreak. Gastrointest Endosc 2016;84:259-62.
21. Wendorf KA, Kay M, Baliga C, et al. Endoscopic retrograde cholangiopancreatography-associated AmpC *Escherichia coli* outbreak. Infect Control Hosp Epidemiol 2015;36:634-42.
22. Day LW, Muthusamy VR, Collins J, et al. Multisociety guideline on reprocessing flexible GI endoscopes and accessories. Gastrointest Endosc 2021;93:11-33.

23. ASGE Quality Assurance in Endoscopy Committee; Calderwood AH, Day LW, et al. ASGE guideline for infection control during GI endoscopy. Gastrointest Endosc 2018;87:1167-79.
24. Beilenhoff U, Biering H, Blum R, et al. Reprocessing of flexible endoscopes and endoscopic accessories used in gastrointestinal endoscopy: Position statement of the European Society of Gastrointestinal Endoscopy (ESGE) and European Society of Gastroenterology Nurses and Associates (ESGENA)—update 2018. Endoscopy 2018;50:1205-34.
25. Hutfless SM, Kalloo AN. Commentary on the 2016 Multi-Society Task Force endoscope reprocessing guidelines. Gastroenterology 2017;152:494-6.
26. Ross AS, Bruno MJ, Kozarek RA, et al. Novel single-use duodenoscope compared with 3 models of reusable duodenoscopes for ERCP: a randomized bench-model comparison. Gastrointest Endosc 2020;91:396-403.
27. Muthusamy VR, Bruno MJ, Kozarek RA, et al. Clinical evaluation of a single-use duodenoscope for endoscopic retrograde cholangiopancreatography. Clin Gastroenterol Hepatol 2020;18:2108-17.
28. U.S. Food and Drug Administration. News & events; FDA newsroom; press announcements. FDA clears first fully disposable duodenoscope, eliminating the potential for infections caused by ineffective reprocessing (December 13, 2019). Available at: https://www.fda.gov/news-events/press-announcements/fda-clears-first-fully-disposable-duodenoscope-eliminating-potential-infections-caused-ineffective. Accessed on June 3, 2021.
29. FDA news. Boston Scientific gains CE Mark for single-use duodenoscope (January 24, 2020). Available at: https://www.fdanews.com/articles/195625-boston-scientific-gains-ce-mark-for-single-use-duodenoscope. Accessed June 3, 2021.
30. Testoni PA, Mariani A, Aabakken L, et al. Papillary cannulation and sphincterotomy techniques at ERCP: European Society of Gastrointestinal Endoscopy (ESGE) clinical guideline. Endoscopy 2016;48:657-83.
31. Christensen M, Matzen P, Schulze S, et al. Complications of ERCP: a prospective study. Gastrointest Endosc 2004;60:721-31.
32. Bang JY, Hawes R, Varadarajulu S. Equivalent performance of single-use and reusable duodenoscopes in a randomised trial. Gut 2021;70:838-44.
33. U.S. Food and Drug Administration. News & events; fda newsroom; press announcements. FDA clears first duodenoscope with disposable distal cap (March 26, 2018). Available at: https://www.fda.gov/news-events/press-announcements/fda-clears-first-duodenoscope-disposable-distal-cap. Accessed on June 3, 2021.
34. U.S. Food and Drug Administration. News & events; FDA newsroom; press announcements. FDA clears first duodenoscope with disposable elevator piece, reducing the number of parts needing disinfection (November 15, 2019). Available at: https://www.fda.gov/news-events/press-announcements/fda-clears-first-duodenoscope-disposable-elevator-piece-reducing-number-parts-needing-disinfection. Accessed on June 3, 2021.

Abbreviations: AE, adverse event; ASGE, American Society for Gastrointestinal Endoscopy; FDA, U.S. Food and Drug Administration; MDRO, multidrug-resistant organism; SAE, serious adverse event.

DISCLOSURE: *The following authors disclosed financial relationships: A. Slivka: Research funding from Boston Scientific Corporation and Olympus. A. S. Ross: Consultant for and research funding from Boston Scientific Corporation. D. V. Sejpal: Consultant for Boston Scientific Corporation and Olympus; research funding from Boston Scientific Corporation. B. T. Petersen: Investigator for Boston Scientific Corporation; consultant for Olympus America and Ambu. M. J. Bruno: Research funding from Boston Scientific Corporation, Cook Medical, 3M, Pentax Medical, Mylan, and InterScope; consultant for Boston Scientific Corporation, Cook Medical, and Pentax Medical. D. K. Pleskow: Consultant for and research funding from Boston Scientific Corporation; consultant for Olympus, Fuji, and Medtronic. V. R. Muthusamy: Consultant for Boston Scientific Corporation, Medtronic, Medivators, and Interpace; research funding from Boston Scientific Corporation and Medtronic; honoraria from Ethicon/Torax; stockholder in CapsoVision. J.-W. Poley: Consultant for Boston Scientific Corporation, Cook Medical, and Pentax Medical. J. M. Cohen, A. M. Thaker: Consultant for Boston Scientific Corporation. J. A. Peetermans, M. J. Rousseau, G. P. Tirrell: Full-time employees of Boston Scientific Corporation. R. A. Kozarek: Research funding from Boston Scientific Corporation. All other authors disclosed no financial relationships. Research support for this study was provided by Boston Scientific Corporation.*

See CME section, p. 1135.

Use your mobile device to scan this QR code and watch the author interview. Download a free QR code scanner by searching "QR Scanner" in your mobile device's app store.

0016-5107
https://doi.org/10.1016/j.gie.2021.06.017

Received March 12, 2021. Accepted June 18, 2021.

Current affiliations: Department of Gastroenterology, Hepatology, and Nutrition, University of Pittsburgh Medical Center, Pittsburgh, Pennsylvania, USA (1), Department of Gastroenterology, Digestive Disease Institute, Virginia Mason Medical Center, Seattle, Washington, USA (2), Division of Gastroenterology, Zucker School of Medicine at Hofstra/Northwell, North Shore University Hospital, Manhasset, New York, USA (3), Division of Gastroenterology and Hepatology, Mayo Clinic, Rochester, Minnesota, USA (4), Department of Gastroenterology and Hepatology, Erasmus Medical Center, University Medical Center, Rotterdam, The Netherlands (5), Center for Advanced Endoscopy, Division of Gastroenterology, Beth Israel Deaconess Medical Center, and Harvard Medical School, Boston, Massachusetts, USA (6), Vatche and Tamar Manoukian Division of Digestive Diseases, University of California, Los Angeles and David Geffen School of Medicine at UCLA, Los Angeles, California, USA (7), Division of Gastroenterology, Massachusetts General Hospital, and Harvard Medical School, Boston, Massachusetts, USA (8), Endoscopy Division, Boston Scientific Corporation, Marlborough, Massachusetts, USA (9).

Reprint requests: Adam Slivka, MD, PhD, University of Pittsburgh Medical Center, Division of Gastroenterology, Hepatology & Nutrition, 200 Lothrop St, Pittsburgh, PA 15213.