Double high-level disinfection versus liquid chemical sterilization for reprocessing of duodenoscopes used for ERCP: a prospective, randomized study

Mark A. Gromski[1], Marnie S. Sieber[2], Stuart Sherman[1], Douglas K. Rex[1]

[1]Division of Gastroenterology and Hepatology, Department of Medicine, Indiana University School of Medicine, Indianapolis, IN, USA

[2] Infection Prevention, IU Health, Indianapolis, IN, USA

Corresponding Author:

Mark Andrew Gromski, MD

Assistant Professor of Medicine

Indiana University School of Medicine

Division of Gastroenterology and Hepatology,

550 N. University Blvd, Suite 1634

Indianapolis, IN 46202

mgromski@iu.edu

Office Phone: 317-944-0925

Office Fax: 317-968-1265

Author Involvement:

This is the author's manuscript of the article published in final edited form as:

Gromski, M. A., Sieber, M. S., Sherman, S., & Rex, D. K. (2020). Double high-level disinfection versus liquid chemical sterilization for reprocessing of duodenoscopes used for ERCP: A prospective, randomized study. Gastrointestinal Endoscopy. https://doi.org/10.1016/j.gie.2020.07.057

MA Gromski: analysis and interpretation of data, drafting of manuscript, statistical analysis, technical support

MS Sieber: study concept and design, acquisition of data, statistical analysis, critical revision of manuscript, technical support

S Sherman: study concept and design, analysis of data, critical revision of manuscript, study supervision

DK Rex: study concept and design, analysis of data, critical revision of manuscript, study supervision

Conflicts of Interest Statement:

Dr. Douglas Rex reports that he is a consultant for Olympus Corporation, Boston Scientific, Medtronic, Aries Pharmaceutical, Braintree Laboratories, Lumendi Ltd., Norgine, Endokey, GI Supply, Covidian/Medtronic. Research support: EndoAid, Olympus Corporation, Medivators, ERBE USA Inc. Ownership interest: Satisfai Health.

Dr. Stuart Sherman reports that he is a consultant for Olympus America (Center Valley, PA), Boston Scientific (Marlborough, MA), Ambu, Inc (Columbia, MD) and Cook Endoscopy (Winston Salem, NC)

Dr. Mark Gromski reports that he is a consultant for Boston Scientific (Marlborough, MA).

None of the other authors have identified a conflict of interest related to this research.

IRB approval: This research was determined to be exempt from Institutional Review Board (IRB) approval (IRB research study #1901874607).

Conference Proceedings:

Previously presented as oral presentation at Presidential Plenary Session at ACG 2019, San Antonio, TX, October 28th, 2019.

Acknowledgments: We appreciate the work put in by our endoscopy nurses and scope cleaning technicians. We also acknowledge the efforts put in by Dr. Douglas Webb of Infectious Diseases who has helped to guide our decision-making regarding our scope surveillance protocols.

ABSTRACT

Background and Aims The potential for transmission of pathogenic organisms is a problem inherent to the current reusable duodenoscope design. Recent outbreaks of multidrug resistant pathogenic organisms transmitted via duodenoscopes has brought to light the urgency of this problem. Microbiological culturing of duodenoscopes and reprocessing with repeat high-level disinfection or liquid chemical sterilization have been offered as supplemental measures to enhance duodenoscope reprocessing by the U.S. Food and Drug Administration (FDA). This study aims to compare the efficacy of reprocessing duodenoscopes with double high-level disinfection (DHLD) versus liquid chemical sterilization (LCS).

Methods We prospectively evaluated 2 different modalities of duodenoscope reprocessing from October 23, 2017 to September 24, 2018. Eligible duodenoscopes were randomly segregated to be reprocessed by either DHLD or LCS. Duodenoscopes were randomly cultured after reprocessing for surveillance based on an internal protocol.

Results During the study time period, there were 878 postreprocessing surveillance cultures (453 in the DHLD group and 425 in the LCS group). Of all of the cultures, 17 were positive for any organism (1.9%). There was no significant difference of positive cultures when comparing the duodenoscopes undergoing DHLD (8 positive cultures, 1.8%) to duodenoscopes undergoing LCS (9 positive cultures, 2.1%, p=0.8). Both groups had 2 cultures that grew high-concern organisms (0.5% vs. 0.5%, p=1.0). No multi-drug resistant organisms (MDRO), including carbapenem-resistant enterobacteriaceae (CRE), were detected.

Conclusions DHLD and LCS both resulted in a low rate of positive cultures, both for all organisms and for high-concern organisms, but neither process completely eliminated positive cultures from duodenoscopes reprocessed with 2 different supplemental reprocessing strategies.

Background and Aims

ERCP is an invasive endoscopic procedure that provides important, often lifesaving therapy for diseases of the pancreas and biliary tracts. The potential for transmission of pathogenic organisms due to incomplete reprocessing is a problem inherent to current reusable duodenoscope design. Recent reports of multidrug resistant pathogenic organisms transmitted via duodenoscopes has brought to light the severity of this problem.[1-3] Since the first cases of potential transmission of drug resistant organisms[1, 2], the United States Food and Drug Administration (FDA) has issued a number of safety communications regarding the problem.[4] Furthermore, there have been multiple studies that have compared the effectiveness of duodenoscope reprocessing and/or suggested improvements to the process.[4-9]

In August 2015, the FDA distributed a safety communication enumerating supplemental measures to enhance duodenoscope reprocessing.[1] These 4 supplemental measures included: (1) microbiological culturing of duodenoscopes, (2) reprocessing with repeat high-level disinfection, (3) reprocessing with liquid chemical sterilization and/or (4) reprocessing with ethylene oxide (EtO) sterilization.[1]

Liquid chemical sterilization (LCS) has been proposed as an alternative to standard heat or gas/vapor/plasma sterilization for temperature sensitive medical devices such as duodenoscopes. Although unknown, there are suggestions that LCS may lead to less wear on endoscopes than standard sterilization procedures (ie, EtO sterilization). Presently, there are no prospective studies comparing LCS with double high-level disinfection (DHLD) for duodenoscope reprocessing.

The aim of this study is to compare the efficacy of reprocessing duodenoscopes used for ERCP by DHLD versus LCS by evaluating surveillance cultures obtained from duodenoscopes after

reprocessing. We hypothesized that there would be significantly fewer positive postreprocessing cultures in the LCS group compared with the DHLD group.

Methods

This study is a single-center prospective, randomized study evaluating reprocessing of duodenoscopes with either DHLD (Cantel DSD EDGE Dual Basin AER System) or LCS (Steris 1E system). The study time period was October 23, 2017 to September 24, 2018. The study was deemed exempt from IRB review by the Indiana University School of Medicine institutional review board (Study no. 1901874607) because it was considered a quality/process improvement study that did not directly impact patient care. All routinely used duodenoscopes were prospectively, randomly allocated to a reprocessing strategy (DHLD or LCS) before the initiation of the study, and then subsequently relegated to that same reprocessing strategy for the duration of the entire study period. Patients, physicians and procedural nurses were all blinded to the reprocessing strategy. The personnel involved with endoscope cleaning and the culturing process were by design not blinded to the reprocessing strategy, but were not involved in assessing study outcomes.

In the DHLD group, duodenoscopes underwent precleaning at the bedside, then were moved to the decontamination area where manual cleaning was performed followed by the automated HLD reprocessing. The Cantel system used Rapicide OPA high-level disinfectant solution. This sequence of manual cleaning followed by automated HLD was then repeated for a second reprocessing phase. In the LCS group, duodenoscopes underwent precleaning at the bedside, then were moved to the decontamination area where manual cleaning was performed followed by a single liquid chemical sterilization cycle. The Steris system used S40 sterilant concentrate.

This study was performed at a high-volume referral center for pancreatobiliary disease (IU Health, University Hospital, Indianapolis, Ind, USA). From 2014 to 2018, the ERCP volume at this center has ranged from 2,700 to 2,900 ERCP procedures per year. All duodenoscopes used are manufactured by Olympus (Olympus America, Center Valley, Pa, USA). Per usual clinical care, the endoscopist specifies the model of duodenoscope to be used for each patient. The selection of the individual duodenoscope within that model line is performed by the endoscopy nurse from available duodenoscopes within the endoscope cabinet. The endoscopy nurses for this study were blinded to the reprocessing strategy. The older model JF-130, JF-140 and TJF-140 duodenoscopes were not prospectively randomized to a cleaning strategy. All JF-130, JF-140 and TJF-140 model duodenoscopes were reprocessed with DHLD, as they are not used routinely and there is significantly more institutional experience cleaning these duodenoscopes with DHLD. Surveillance culture data for these models were collected and are reported herein.

Duodenoscopes were randomly cultured after reprocessing. There was an internal goal for the duodenoscopes to be cultured for approximately 30% of ERCPs performed per week. There was a periodic evaluation of the duodenoscope culture process and distribution of duodenoscopes and culturing by our infection prevention specialist, to ensure all duodenoscopes were subject to culturing in a relatively equitable fashion. The cultures were appropriated by sampling the duodenoscope tip, duodenoscope tip seams, and elevator recess (both with elevator up and with elevator down) by with a single sterile swab. The culturing method has previously been described.[8] Microbiology staff identified organisms by standard laboratory protocol, with antibiotic susceptibilities tested and reported upon request.

To ensure that the duodenoscopes were not contaminated during the culture appropriation process, all scopes underwent an additional single HLD cycle after the culturing protocol was

performed. All cultured duodenoscopes were quarantined until the culture results finalized. Duodenoscopes that grew low-concern or high-concern organisms were recultured and quarantined. Any duodenoscope that had positive growth on the reculture was then sent for EtO sterilization.

A high concern or potentially pathogenic organism was defined according to the Department of Health and Human Services Collaboration report on duodenoscope surveillance sampling and culturing, as "organisms that are more often associated with disease," including gram negative rods, gram positive organisms, *Enterococcus* species and yeasts.[1, 10]

Data analysis was performed using Excel (Microsoft Corporation, Redmond, Wash, USA) and SAS (SAS version 15, SAS Institute Inc, Cary, NC, USA). Sample size of 350 samples per group was calculated assuming a baseline incidence of 4.8% overall culture positive rate in the double high-level disinfection group based on a previous study from our center[8], to test for a reduction in baseline incidence positive culture of 75% in the liquid chemical sterilization group, we required 350 samples per group at a significance level of 0.05 and power of 80%. Descriptive data are reported as mean (standard deviation) or median (interquartile range; IQR) for continuous variables. Categorical variables are described using frequency (proportion). Chi-square or Fisher exact test were used for comparisons of categorical data. The Student t-test or Wilcoxon rank-sum test are used for comparisons of continuous variables, as appropriate. The level of significance is considered to be ≤ 0.05.

Results

During the study time period, 67 total duodenoscopes were clinically used that qualified for random allocation of reprocessing strategy. Of these, 48 were institutional duodenoscopes (owned by our institution) and 19 were "loaner" duodenoscopes from the manufacturer (loaned

to our institution for scopes out for repair or quarantine). Additionally, 10 institutional duodenoscopes were not eligible for random allocation (JF-130, JF-140, TJF-140), and all underwent DHLD. Table 1 describes the breakdown of the individual scope models in each group. Data are presented both including and not including the older 130 and 140 model duodenoscopes.

During the study time period, 878 post-reprocessing surveillance cultures were drawn from all duodenoscopes. There were 453 cultures drawn from the DHLD group and 425 cultures drawn from the LCS group. In total, 17 cultures returned positive for any organism (1.9% of all cultures). There were 8 positive cultures in the DHLD group and 9 positive cultures in the LCS group (1.8% vs. 2.1%, respectively, p=0.8). The organisms identified for each positive culture are described in Table 2. There was growth of a high concern or potentially pathogenic organism in 2 cultures for each group (0.4% vs. 0.5%, p=1.0). The *Klebsiella pneumoniae* and *Enterobacter cloacae* organisms were tested for antibiotic susceptibility. No multidrug resistant organisms were detected, including no carbapenem resistant *enterobacteriaceae* (CRE). There was no known transmission of organisms from a duodenoscope to a patient during the study period. One duodenoscope had a repeat positive culture of a low concern organism (LCS group) after reprocessing. This duodenoscope was sent for EtO sterilization and subsequent culture was negative. No other duodenoscopes had more than one positive culture throughout the duration of the study.

Excluding the JF-130, JF-140 and TJF-140 duodenoscope cultures, a total of 796 cultures were appropriated from the duodenoscopes eligible for randomized reprocessing. Of these, 371 cultures were in the DHLD group and 425 cultures were in the LCS group. In total, 14 cultures returned positive for any organism (1.8% of all cultures). There were 5 positive cultures in the DHLD group and 9 positive cultures in the LCS group (1.3% vs 2.1%, respectively, p=0.6).

There was growth of a high concern or potentially pathogenic organism in 2 cultures for each group (0.5% vs 0.5%, p=1.0). A total of 82 post-reprocessing surveillance cultures were drawn from the JF-130, JF-140 and TJF-140 model duodenoscopes. There was growth of 3 low-concern organisms in these cultures (3.7%). There was no growth of high-concern organisms in this group. In post-hoc analysis, the rate of positive surveillance cultures in the JF-130, JF-140 and TJF-140 group reprocessed by DHLD (3.7%) was not significantly different than the group of newer model duodenoscope group that was randomized to DHLD (1.3%, p = 0.16).

Although the time of each reprocessing procedure was not prospectively collected, post-hoc observations of the reprocessing team show that the approximate time of the DHLD reprocessing is 98 minutes (manual cleaning time 20 minutes, twice; single high-level disinfection cycle time 24 minutes, twice; drying time 10 minutes). The approximate time of the LCS reprocessing is 55 minutes (manual cleaning time 20 minutes; Single LCS cycle 25 minutes; drying time 10 minutes).

Discussion

ERCP is an important, invasive endoscopic procedure that can have significant, life-saving therapeutic consequences for the patient. The documented transmission of pathogenic organisms that subsequently caused harm in multiple patients in multiple centers around the globe revealed an infection control issue, likely related to the reusable duodenoscope design and also human and procedural factors related to reprocessing. Since the initial outbreaks have been reported, additional measures to improve duodenoscope reprocessing have been recommended by the FDA, in an effort to improve the reprocessing method.[1] In the past 5 years, our center has devoted significant time and resources to improve our reprocessing strategy. Some of the efforts before this current study have previously been reported.[8] Despite recommendations for enhanced duodenoscope reprocessing by the FDA, there had been no

prospective evaluation comparing the effectiveness of DHLD to LCS, which was the impetus of this study. Three of the 4 supplemental measures recommended by the FDA were incorporated into this current study, to attempt to determine whether one heightened reprocessing method (DHLD) was favorable to another (LCS).

In this prospective study in which the reprocessing strategy for duodenoscopes was randomized, we found that DHLD and LCS both resulted in a low rate of positive surveillance duodenoscope cultures. Additionally, there was a very low rate of high concern or potentially pathogenic organism growth. There was no difference in the rate of growth of surveillance cultures between the 2 reprocessing strategies. This study did not randomize the older models of duodenoscopes (130 and 140 series Olympus duodenoscopes). When the postreprocessing cultures of these duodenoscopes (all done with DHLD) were compared with the newer model scopes reprocessed with DHLD, there was a trend toward higher numbers of low concern organism growth, but no significant difference.

This study had an overall rate of positive culture that was lower than the overall rate of positive culture (4.9%) in the final phase of our prior published study on double high-level disinfection.[8] Nonetheless, during the final phase of that study, the percentage of high-risk positive cultures was consistent with this current study (0.3% in prior study on DHLD and 0.5% in current study in DHLD arm).[8] This comparative reduction in the growth of low risk organisms in the current study compared with the historic study may be secondary to improved training and technical performance of the scope cleaning team over time. Effective and continued training and evaluation of scope cleaning technicians and scope cleaning processes are essential to bringing the risk of transmission of pathogens by reusable duodenoscopes as low as possible.

The strengths of this study include the prospective, randomized nature comparing 2 enhanced duodenoscope reprocessing strategies. Some limitations include the following: not all duodenoscopes used throughout the study period were cultured; this was performed at a high-volume ERCP center with dedicated duodenoscope cleaning technicians, which may not be generalizable to all practices; and the possibility that the study was not powered to detect subtle differences in the reprocessing techniques. However, it is unlikely that a higher power to detect a subtle overall difference would lead to a clinically relevant result. Furthermore, we did not include a reprocessing strategy arm of single high-level disinfection. This would have required a much higher enrollment goal for 3-way statistical comparisons, and the FDA at the time of the study had recommended supplemental measures to enhance reprocessing. Thus, a single high-level disinfection group during the time of the study could be considered to have received substandard reprocessing.

Duodenoscope reprocessing costs are an important consideration, particularly in the setting of single use duodenoscopes now being available in the market. These costs were not prospectively evaluated in this study. Reprocessing strategies (including both LCS and DHLD) do include capital costs (the physical reprocessor), recurrent costs (the sterilant or reprocessing fluid, test strips, etc), training costs and labor costs (reprocessing technicians). Institutions may have variable costs due to volume and negotiated contracts. At our institution, there was not a dramatic difference in the cost between reprocessing strategies—the capital costs and the per endoscope cost for reprocessing materials were similar.

Despite the low rates of positive cultures, neither reprocessing strategy entirely eliminated the growth of high concern organisms. In a safety communication released August 2019, the FDA recommended that health care providers begin a transition to duodenoscopes with innovative designs that facilitate or eliminate the need for reprocessing.[3] The current issue with infection

control has spurred a significant amount of development into disposable components and single-use endoscopes, many of which are reaching the marketplace now.[11-14] Nevertheless, these new devices have many variables including price, availability and performance that are unknown. New developments in reusable scope reprocessing and sterilization are warranted. Optimally reprocessing reusable duodenoscopes will likely continue to be a necessity and priority for the foreseeable future. Based on our study, we do not endorse any comparative advantage of either (DHLD or LCS) enhanced reprocessing strategy over the other.

References

1. Centers for Disease C, Prevention. Notes from the Field: New Delhi metallo-beta-lactamase-producing Escherichia coli associated with endoscopic retrograde cholangiopancreatography - Illinois, 2013. MMWR Morb Mortal Wkly Rep 2014;62:1051.
2. 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.
3. Wendorf KA, Kay M, Baliga C, et al. Endoscopic retrograde cholangiopancreatography-associated AmpC Escherichia coli outbreak. Infect Control Hosp Epidemiol 2015;36:634-42.
4. Becq A, Snyder GM, Heroux R, et al. Prospective assessment of the effectiveness of standard high-level disinfection for echoendoscopes. Gastrointest Endosc 2019;89:984-989.
5. Kim S, Russell D, Mohamadnejad M, et al. Risk factors associated with the transmission of carbapenem-resistant Enterobacteriaceae via contaminated duodenoscopes. Gastrointest Endosc 2016;83:1121-9.
6. Snyder GM, Wright SB, Smithey A, et al. Randomized Comparison of 3 High-Level Disinfection and Sterilization Procedures for Duodenoscopes. Gastroenterology 2017;153:1018-1025.
7. Bartles RL, Leggett JE, Hove S, et al. A randomized trial of single versus double high-level disinfection of duodenoscopes and linear echoendoscopes using standard automated reprocessing. Gastrointest Endosc 2018;88:306-313 e2.
8. Rex DK, Sieber M, Lehman GA, et al. A double-reprocessing high-level disinfection protocol does not eliminate positive cultures from the elevators of duodenoscopes. Endoscopy 2018;50:588-596.
9. 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.
10. Department of Health and Human Services Collaboration (HHS F, CDC, ASM). Duodenoscope Surveillance Sampling and Culturing: Reducing the Risks of Infection. https://www.fda.gov/media/111081/download Last accessed December 18, 2019. .
11. Muthusamy VR, Bruno MJ, Kozarek RA, et al. Clinical evaluation of a single-use duodenoscope for endoscopic retrograde cholangiopancreatography. Clin Gastroenterol Hepatol; Epub Nov 11 2019.

12. 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.
13. Muthusamy VR, Bruno MJ, Kozarek RA, et al. Clinical evaluation of a single-use duodenoscope for endoscopic retrograde cholangiopancreatography. Clin Gastroenterol Hepatol 2019.
14. 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 2019.

Table 1: Distribution of duodenoscopes, by model, between reprocessing strategies

Duodenoscope Model	DHLD (n=44)*	LCS (n=33)**
TJF-Q180	**7**	**11**
TJF-160	**27**	**22**
JF-140	**6**	
JF-130	**3**	
TJF-140	**1**	

DHLD, Double high-level disinfection, LCS, liquid chemical sterilization
*****35 institutional duodenoscopes, 9 "loaner" duodenoscopes. The JF-140, JF-130 and TJF-140 duodenoscopes were not randomly allocated – all received DHLD.
******23 institutional duodenoscope, 10 "loaner" duodenoscopes

Table 2: Organisms detected in positive cultures from all duodenoscope reprocessing surveillance cultures

Organism	**DHLD (n=8 positive cultures)***	**LCS (n=9 positive cultures)****
Coagulase negative *Staphylococcus* spp.	**5**	**5**
Micrococcus spp.		**2**
Bacillus spp.	**2**	**3**
Streptococcus viridans		**1**
***Enterococcus* spp.**		**1**
Klebsiella pneumoniae	**1**	
Enterobacter cloacae	**1**	

spp, Species
BOLD organisms are considered high-concern organisms.
*One culture in the DHLD group had more than one organism grow in a positive culture.

**Three cultures in the LCS group had more than one organism grow in a positive culture.

Acronyms and Abbreviations:

ERCP – endoscopic retrograde cholangiopancreatography

FDA – Food and Drug Administration

EtO - Ethylene oxide

DHLD - Double high-level disinfection

LCS - Liquid chemical sterilization

CRE - carbapenem resistant enterobacteriaceae

Spp - species