Comparative Assessment of Three-dimensional vs. Conventional Laparoscopy in a Total Colectomy model for Ulcerative Colitis

Principal Investigator

Emre Gorgun MD

Staff, Colorectal Surgery

Cleveland Clinic Foundation

E-mail: gorgune@ccf.org

Co- PI's:

Hermann Kessler MD

Staff, Colorectal Surgery

Cleveland Clinic Foundation

E-mail: kessleh@ccf.org

Scott R. Steele MD

Staff, Chairman, Colorectal Surgery

Cleveland Clinic Foundation

E-mail: steeles3@ccf.org

Co-Investigator:

Ipek Sapci MD

Research Fellow, Colorectal Surgery

Cleveland Clinic Foundation

E-mail: sapcii@ccf.org

Sponsor Information:

Olympus Corporation of the Americas (DBA Olympus America Inc.)

3500 Corporate Parkway

P.O. Box 610

Center Valley, PA 18034

Introduction

Three-dimensional (3D) visualization technology for laparoscopy has been proposed, since the early 1990's, as a method to facilitate laparoscopic performance. However, early 3D laparoscopic technology was limited in terms of image quality, so that its use had not been implemented [1]. The latest technical developments ensure high-definition 3D visualization with the same quality that current two-dimensional (2D) systems provide.

The anticipated advantages of 3D laparoscopic visualization for the surgeon are greater accuracy and speed in manual skills, translating to decreased operative time, reduced learning curve, and superior safety [2]. It was reported that, 3D laparoscopic visualization offers significant advantages in enhancing laparoscopic performance, even in novice surgeons, comparing to the 2D systems [3-5]. We hypothesize that 3D visualization may allow surgeons to reduce the overall operating time with a rate of 10% with comparable perioperative and postoperative outcomes. The primary endpoint of this study is to determine the feasibility of the laparoscopic approach using 3D visualization in the surgical treatment of ulcerative colitis. Secondary endpoints are to determine whether 3D visualization confers benefits such as reduced operating time and intra-operative complications with comparable postoperative outcomes.

Device Description

The EXERA III Universal Platform will be used in this study, in conjunction with the ENDOEYE FLEX 3D. The ENDOEYE FLEX 3D can also be used in 2D mode, by utilizing a programmed button on the handle of the scope, or by using the 2D/3D button on the 3D Visualization Unit. The articulating tip of the ENDOEYE FLEX allows for the scope to be used in both single-site and multi-port procedures, providing critical views and allowing a bird's eye view so that the scope is out of the way of other instruments (while still capturing

the image at the surgical site). All equipment used in this trial has been cleared under 510(k) approval by the FDA, and has been on the market in the US since April 2013.

The Olympus HD 3D Laparoscopic Surgical Video System consists of the following components:

- CV-190 Processor
- CLV-190 Light Source
- 3DV-190 3D Visualization Unit
- LMD-2451MT/3G4 Sony 24" 3D Monitor
- IMH-20 Image Capture System
- UHI-4 Insufflator
- K10021611 Cart
- OL-0015-08 Tall Rollstand
- LTF-190-10-3D ENDOEYE FLEX 3D Videoscope
- 3D glasses (regular and clip-on styles)

Materials and Methods

Study Size:

Mean operating time for laparoscopic subtotal colectomy for medically refractory UC was reported longer with a comparison to open surgery in the recently published studies [6, 7].

Therefore the effort to decrease operating time in laparoscopic colectomy has gained importance. We assumed that, in order to be able to determine a 10% reduction in mean operating time, each group should include 27 patients (80% power and 5% significance).

Patients who will undergo laparoscopic total abdominal colectomy (TAC) for UC will be included in the study. All subjects will be randomized into two groups: 3D laparoscopy,

and 2D laparoscopy. Three staff surgeons (EG, HK,SS) at the department of colorectal surgery, Cleveland Clinic, Ohio will perform the procedures with 2D and 3D laparoscopy.. In total, 54 patients will be included (27 patients for each group). There will be a demonstration period in order to increase the surgeon's familiarity with the new 3D laparoscopy system, and each surgeon will perform at least one colectomy procedure before operating on study patients. One surgeon (EG) will perform all of his colectomies using a single port approach. Two surgeons (HK, SS) will perform all of their colectomies with a multiport approach.

Inclusion Criteria:

- Indication for surgery must be Ulcerative Colitis
- Patient age >18 years of ageElective procedure
- BMI between ≥ 17 and ≤ 40
- Total colectomy with end ileostomy, without proctectomy

Exclusion Criteria:

- Any preoperative diagnosis other than UC
- Patient age < 18 years old
- Emergency surgery
- (will be adjusted with adhesion scoring.)Pregnancy
- Presence of any gastrointestinal tract malignancy
- Segmental colon resections, completion proctectomy, total proctocolectomy, pouch procedures

Baseline data:

Patient demographics (age, gender, BMI), ASA score, co-morbidities, details of the current status of UC (time from diagnosis, medications, presence of dysplasia or malignancy) will be documented.

Adhesion scoring system:

With the aim of comparability of the groups, a ten-point adhesion scoring system will be adopted, modeled from Dowson et al [8]. The extent of adhesions to the incision sites and abdominal wall and severity of adhesions will be assessed. Severity of adhesions is classified as: grade 0, no adhesions; grade 1, flimsy thickness, avascular; grade 2, moderate thickness, limited vascularity; and grade 3, dense thickness, vascularized. The extent of adhesions is quantified as: 0, no adhesions; 1, mild (up to 25 per cent of total area and length of incision); 2, moderate (26–50 per cent of total area and length of incision); and 3, severe (more than 50 per cent of total area and length of incision).

Procedural data:

The procedural data that will be recorded are: name of surgeon, date of surgery, operating time, estimated blood loss, number of scope cleaning, number of scope in and out of trocar, number of scope fogging, need of conversion, reason for conversion. With the aim of underlining the technical impact of using the 3D system, intraoperative inadvertent complications such as burns, punctures, and misapplications of the energy device will be documented. Total operating time will be defined as period of time from insertion of Veress needle to last closure of the skin. Laparoscopic TAC will be evaluated in 5 stages:

1- **Take-down of ileocolic pedicle:** Following laparoscopic visualization of the liver and the rest of the abdomen to rule out metastatic or other unsuspected disease, the colonic dissection will begin with identification and takedown of the ileocolic vascular pedicle, which facilitates the exposure and preservation of the underlying second and third portions of the duodenum. This stage will start with the incision of the peritoneum covering ileocolic pedicle, and end with the completion of the ligation of ileocolic artery and vein.

2- **Mobilization of the right colon:** Attachments of the terminal ileum and ascending colon will be taken, and hepatic flexure will be mobilized. This stage will start after completion of the ileocolic pedicle takedown, and end with full mobilization of the hepatic flexure.

3- **Mobilization of the tranverse colon, takedown of the omentum and middle colic vessels:** Following complete mobilization of the right colon, this stage will be started right after taking the right edge of the omentum down in order to mobilization of transvers colon. The first three portions of the duodenum, the head of the pancreas, and the right edge of the transverse mesocolon will be identified. At this stage, it will be possible to take down the right and left branches of the middle colic artery using an energy device or, if necessary, identify and similarly take down more proximally the short trunk of the middle colic artery near the pancreas. Preservation of the omentum will be left to the discretion of the operating surgeon. The takedown of the omentum and transverse mesocolon will be continued using a tissue-sealing device from right to left until the splenic flexure is reached.

4- **Mobilization of the sigmoid and left colon, and splenic flexure takedown:** Taking down the splenic flexure by dissection of splenocolic ligament will be accepted as the onset time of this stage. Since there will be no oncologic concerns, the superior rectal artery will be preserved. The sigmoid colon will be mobilized and the sigmoidal arteries will be taken down. This stage will be completed after full mobilization of descending colon and splenic flexure.

5- **Transection of the rectum or rectosigmoid:** This stage will start with insertion of the stapler through the trocar, and end with rectal or rectosigmoid stump totally transected from the colon.

6- Identification of the ureters: Time required for identification of the ureters.

Time for each stage of the procedure will be documented separately. Postoperative complications and length of total hospital stay data will be documented.

All surgeons involved the study will have a standard eye exam containing visual acuity, color vision, stereopsis and accommodation in order to ensure standardization of evaluation of surgeon's visual satisfaction. To evaluate surgeon's subjective satisfaction with the visualization system, each surgeon will take a survey after completion of surgery. Side effects such as color rendition, visual sharpness, contrast, ghosting, eye strain, headache, dizziness, disorientation, physical discomfort, and poor visualization will be queried in the questionnaire.

Clinical data obtained from patients will be retained and entered into case report forms. These forms will be maintained on the Department of Colorectal Surgery server. Access will be restricted, and accessible by the PI, co-investigators and study coordinator approved by this protocol.

Patient Enrollment and Consent

Patients who are candidates of laparoscopic total colectomy for UC will be given a brief presentation and explanation. Printed materials regarding the study, including the Study Consent and a written explanation of the two surgical methods, will be provided to the subject at that time.

It will be made clear to prospective subjects that the purpose of an IRB approved study in this setting is to make sure the subjects rights are protected, that the new methods are being fairly described and presented, that the potential risks and alternatives are discussed, and to gather objective information regarding the two methods, as well as results and outcomes.

If an eligible patient expresses interest in the study, the Study RN/Coordinator or physician will meet/speak with the patient and thoroughly explain both the study and its consent form. All subjects will also have the opportunity to further discuss the study with their surgeon if they so desire. After all questions are answered, interested subjects will be asked to sign the IRB-approved consent form, at which time they will be enrolled. It will be made clear that in order to enter this study, subjects must be willing to receive either of the following procedures: 1) 3D laparoscopic total colectomy 2) 2D laparoscopic total colectomy.

Statistical Analysis

After obtaining informed consent for each cohort patient enrolled in the study, 2D and 3D groups will be constructed by the method of sequential randomization for each surgeon. Results will be reported in descriptive statistics and expressed as mean ± SD for continuous values. Categorical variables will be analyzed with Chi-square or Fisher exact test, whereas Wilcoxon rank sum test will be used for continuous variables. P value < 0.05 will be considered significant.

Adverse Events: Definitions and Reporting

Adverse Events (AEs) will be defined as any untoward or unfavorable medical occurrence in a human subject, including any abnormal sign, symptom, or disease, temporally associated with the subject's participation in the research, whether or not considered related to the subject's participation in the research.

Serious Adverse Events (SAEs) will be defined as any adverse event temporally associated with the subject's participation in research that meets any of the following criteria:

- results in death;
- is life-threatening;

- requires inpatient hospitalization or prolongation of existing hospitalization;
- results in a persistent or significant disability/incapacity;
- results in a congenital anomaly/birth defect; or
- any other adverse event that, based upon appropriate medical judgment,

PI will be responsible for identifying adverse events during the procedure and during the standard of care follow-up period. PI will review adverse events experienced by subjects treated at the site during the procedure and standard of care follow-up period and will record them using the adverse event (AE) Form. PI will review all adverse events, expected or unexpected, per standard medical care. PI will classify AEs and SAEs as expected or unexpected. AEs and SAEs will be reported directly to the Sponsor and IRB per local IRB reporting policy.

Device Observations

Device observations and/or malfunctions will be documented on case report forms. In the event of a suspected malfunction or device observation, Sponsor shall be contacted immediately. Sponsor will provide instructions to the investigator for returning the device, or may go to the site to investigate and resolve the problem.

Management of Data Collection

Data Recording and Case Report Forms:

All data collected under this protocol will be recorded on case report forms (CRFs). The CRFs will not include any Patient Identifiers (such as name, date of birth, address, SS number, hospital record number, etc.). Instructions for completing the CRFs include:

All entries on the CRFs will be made legibly in ink. If corrections are made to entries in the CRFs a single stroke will be drawn through them. The correct data will be inserted and the correction will be initialed and dated. Incorrect entries must not be covered with

correcting fluid, or obliterated, or made illegible in any way. A reasonable explanation must be given by the investigators and assistants for all missing data.

Monitoring Plan:

The study will be internally monitored for data integrity and accuracy. The Sponsor will have access to any internal monitoring reports generated during the study. The Sponsor will have access to case report forms, log books and signed informed consent forms to enable its own monitoring of the study.

Protocol Deviations and Modifications

No protocol modifications will be implemented prior to Sponsor approval and amendment approval from the IRB. The Sponsor and IRB (including other review boards as required for this study) will be notified of any protocol deviations.

Institutional Review Board (IRB) Approval

The principal investigator is responsible for submitting this protocol, the informed consent document, and all relevant supporting data to the IRB or Ethics Committee. IRB approval of the protocol, informed consent document, and any advertisement used to recruit study subjects must be obtained before the study may be initiated. The principal investigator is responsible for keeping the IRB advised of the progress of the study and of any changes made to the protocol as deemed appropriate, but in any case, at least once a year. The principal investigator is also responsible for notifying the IRB of any serious adverse events that occur during the study.

Confidentiality

To protect subject confidentiality, the subject's name is not to appear anywhere on the CRF's or other information provided to the sponsor. Each page should be identified with the

subject's case study number, which is comprised of a three-digit number. A Subject Log will be maintained by the Investigator to enable tracing of specific case study numbers to subjects.

References

1. Kunert W, Storz P, Kirschniak A. For 3D laparoscopy: a step toward advanced surgical navigation: how to get maximum benefit from 3D vision. Surg Endosc. 2013 Feb;27(2):696-9. doi: 10.1007/s00464-012-2468-0. Epub 2012 Jul 18.

2. Tanagho YS, Andriole GL, Paradis AG, Madison KM, Sandhu GS, Varela JE, Benway BM. 2D versus 3D visualization: impact on laparoscopic proficiency using the fundamentals of laparoscopic surgery skill set. J Laparoendosc Adv Surg Tech A. 2012 Nov;22(9):865-70. doi: 10.1089/lap.2012.0220. Epub 2012 Oct 16.

3. Storz P, Buess GF, Kunert W, Kirschniak A. 3D HD versus 2D HD: surgical task efficiency in standardised phantom tasks. Surg Endosc. 2012 May;26(5):1454-60. doi: 10.1007/s00464-011-2055-9. Epub 2011 Dec 17.

4. Smith R, Day A, Rockall T, Ballard K, Bailey M, Jourdan I. Advanced stereoscopic projection technology significantly improves novice performance of minimally invasive surgical skills. Surg Endosc. 2012 Jun;26(6):1522-7. doi: 10.1007/s00464-011-2080-8. Epub 2012 Jan 11.

5. Votanopoulos K, Brunicardi FC, Thornby J, Bellows CF. Impact of three-dimensional vision in laparoscopic training. World J Surg. 2008 Jan;32(1):110-8.

6. Telem DA, Vine AJ, Swain G, Divino CM, Salky B, Greenstein AJ, Harris M, Katz LB. Laparoscopic subtotal colectomy for medically refractory ulcerative colitis: the time has come. Surg Endosc. 2010 Jul;24(7):1616-20. doi: 10.1007/s00464-009-0819-2. Epub 2010 Mar 5.

7. Messenger DE1, Mihailovic D, MacRae HM, O'Connor BI, Victor JC, McLeod RS. Subtotal colectomy in severe ulcerative and Crohn's colitis: what benefit does the laparoscopic approach confer? Dis Colon Rectum. 2014 Dec;57(12):1349-57.