Cover letter

IRB Approved Title: A Randomized Controlled Trial comparing THUNDERBEAT to the Ligasure energy device during Laparoscopic Colon Surgery

WCMC IRB Protocol #: 1403014955

IRB Initial Approval date: 06/25/2014

ClinicalTrial.gov # NCT02628093

Participating locations

Weill Cornell Medical College, New York Presbyterian Hospital
1300 York Avenue
New York, NY 10065
USA

Subsequent IRB Protocol Approved Amendments and date of approval

Amendment 006	02/08/2019
Amendment 005	11/08/2018
Amendment 002	12/05/2015

Objective

The Primary objective of this study is to compare the clinical performance (efficacy) of the new laparoscopic energy device THUNDERBEAT in performing soft tissue dissection dividing and sealing blood vessels compared to Ligasure in human subjects undergoing Laparoscopic colon and rectal surgery.

Design

Prospective randomized controlled study, with 2 groups based on the instrument used for tissue dissection and vessel ligation: Group 1 - THUNDERBEAT Group 2 – Ligasure

Methods

60 subjects with colon neoplasm or diverticulitis were randomized into one of the groups in equal chances

Inclusion

Patients that will be undergoing a Left Laparoscopic Colon Resection
Older than 18 years old
ASA 1 to 3
Elective surgeries
Patients who willingly provide informed consent

Exclusion
Morbidly obese patients (BMI >35)
Patients with acute diverticulitis
Patients with multiple previous abdominal surgeries
Patients on anticoagulants
Patients who cannot, tolerate a major surgery
Patients for whom electrosurgery is contraindicated
Patients who are pregnant
Patients who have IBD

Study Protocol
Informed consent is to be obtained prior to procedure.

After informed consent was obtained, data was collected prospectively before, during and after the surgical procedure up to 30 days after the surgery from the data of the surgical procedure.

Study Procedures:
This project will consist only of prospective data collection. No interventions will be done for research purpose. Data will be collected prospectively on:
-Patients (before, during and after surgery)

-The THUNDERBEAT and LigaSure instruments

Data will be collected on data collection sheets and entered in a password protected database
Primary Outcomes/Definitions
Overall time for dissection of the soft tissues necessary for specimen removal during colon resection, measured in minutes, from the start of colon mobilization to specimen removal from the abdominal cavity

Versatility between the two instruments
Versatility in this study is defined as: quality performance of the surgical instrument under study based on the outcome evaluation of the following variables:

Hemostasis,
Sealing ability
Cutting
Dissection
Tissues Manipulation

all measured by a score system from 1-5 in which 1 is the worst and 5 is the best and adjusted/ weighted for their importance by Coefficient of Importance with following distribution of the importance:
1. Hemostasis 27. 5 % = 0.275
2. Sealing ability 7.5 % =0.275
3. Cutting 20 % = 0.2
4. Dissection 15%= 0.15
5. Tissues Manipulation 10 % = 0.1

The two (2) instruments will be compared in terms of versatility. An average score above 3 will be considered a high versatility and score 3 and below 3 as low versatility.
Hemostasis, Sealing, Cutting, Dissection and Tissues Manipulation will be scored only by the surgeon. Hemostasis and Sealing ability will be measured on arterial vessels by surgeon and cutting, dissection and tissue manipulation will be measured on mesenteric tissue.

Secondary Outcomes

Evaluation of surgeons' experience for THUNDERBEAT or LigaSure will be measured with a survey

The design of the instrument in terms of surgical maneuvering is being evaluated via the opinion of the surgeons using an 8-item questionnaire, grading the 8 items on the scale from 1 to 10 where a score of 1 is worst and 10 is the best.

Drier surgical field -evaluation of the entire surgical field for oozing of blood or any other body fluids using a scoring system as well as video and photo documentation

Difference in the patient's outcome after laparoscopic surgery using those two devices.

Difference in operative procedure time measured in minutes from incision start time to end of surgery (placement of the last stitch during closure of abdominal incisions)

Other relevant intra and post-operative data will be collected prospectively from patients and the hospital charts prior to, during and after surgery.
This would include such outcome measures as postoperative bleeding, failure of the instrumentation to control bleeding intraoperatively or successfully dissect tissues, complications related to use of the instrument, etc.

We will compare the postoperative complication using Clavien-Dindo classification. 5
Patients will be assessed daily after surgery until discharge, at the first follow up visit within the first 30 days following surgery and at 30 days.

Statistical Considerations

Because this is a pilot randomized study, no formal sample size calculation is required. With 60 patients total and 30 in each arm, we will estimate differences in dissection time between the two groups (THUNDERBEAT and LigaSure). These estimated differences will serve as preliminary data (i.e., hypothesis-generating) for future studies.
A total of 60 patients undergoing Left Colectomy Resection will be accrued for this study. Extra 10 patients will be recruited in anticipation of a 15% withdrawal. Patients will be randomized at equal ratio to: Group 1: Using THUNDERBEAT instrument for dissection or Group 2: Using Ligasure instrument.

The primary endpoint of this study is overall time for dissection of the soft tissues necessary for specimen removal during colon resection, measured in minutes, from the start of the start of colon mobilization to specimen removal from the abdominal cavity.

Demographic, preoperative, and postoperative variables will be compared between groups by the two-sample t-test/Wilcoxon rank-sum test for continuous variables and the chi-square test/Fisher's exact test for categorical variables, as appropriate. All p-values will be two-sided with statistical significance evaluated at the 0.05 alpha level. Ninety-five percent confidence intervals will be calculated to assess the precision of the obtained estimates All analyses will be performed in JMP 10.0 (Cornell University, Ithaca, NY).

Randomization

Stratified randomization with blocking will be used in the trial. Strata are formed by the two different Instruments used during the surgical procedures: TB and LIG for both arms. Random permuted blocks within strata will be used to ensure balance between instruments. The size of a block will not be revealed during the study, only known to the biostatistician. The biostatistician will generate randomization lists before the trial starts, using the method of random permuted blocks within strata

Scientific Background

With the growing use of laparoscopic techniques for intraabdominal surgery, different surgical energy devices have been developed to shorten operative time and to lessen the need for instrument exchange. Dissection of the bowel mesentery and other soft tissues can take a significant amount of time, attributable to the need for safe and effective hemostasis. As a solution, energy-based devices are being developed that efficiently dissect the mesentery and occlude blood vessels, even larger ones up to 6-7 mm.

Three energy based methods currently used during surgical procedures for vessel ligation and dissection include monopolar electrosurgery (ME), bipolar electrosurgery (BE) and ultrasonically-activated surgery (UAS). ME results in greater amount of thermal tissue damage and intraperitoneal temperature variations when compared to UAS and BE, respectively. Bipolar electrosurgical technology has been considered as possibly a safer method for dissection and vessel ligation in laparoscopic colon and rectal surgery in particular, because electrical energy is used differently, preventing undesirable injuries.[1,2] Some studies evaluating vascular control during laparoscopic surgery between electrosurgical devices have reported that electro thermal bipolar vessel sealing has better results and effectiveness, less blood loss and a slight advantage in operating time.[3, 4] UAS devices are multi-functional and are equipped for coagulation, cutting, dissection and grasping but are only approved for use on sealing vessels up to 4-5 mm in diameter . A study comparing ultrasonic and bipolar devices in a porcine bowel mesentery model reported that UAS provides a reduced resection time with no difference in thermal bowel wall damage.[5] Amongst the current ultrasonic devices, laparoscopic dissection time in a porcine bowel mesentery model was shorter with AutoSonix and Sonosurg technology when compared to UltraCision technology.[6] Technical advances in electrosurgery and other energy sources are improving over time, becoming more powerful and efficient. A new unique laparoscopic energy device THUNDERBEAT (TB, Olympus, Japan) has been developed that delivers BOTH ultrasonically generated frictional heat energy and electrically generated bipolar energy simultaneously. This tool is also multi-functional and the surgeon will be able to coagulate (even large blood vessels), cut, and dissect during surgery and potentially reduce the need for instrument exchange. A recent study in a porcine model conducted at WCMC and presented at ACS meeting 2011, compared the versatility, bursting pressure, thermal spread, and dissection time of the new TB device in comparison to commercially available ultrasonic and bipolar energy devices: Harmonic ACE (HA, Ethicon, USA) , LigaSure V (LIG, Covidien, USA) and En Seal (EnSeal, Ethicon, USA). The study demonstrated that TB has a higher versatility compared to other instruments with faster dissection speed, similar bursting pressure, and acceptable thermal spread.[7]

References

1. Targarona EM, Balague C, Marin J, et al. Energy sources for laparoscopic colectomy: a prospective randomized comparison of conventional electrosurgery, bipolar computer-controlled electrosurgery and ultrasonic dissection. Operative outcome and costs analysis. Surg Innov 2005; 12(4):339-44.
2. Campbell PA, Cresswell AB, Frank TG, et al. Real-time thermography during energized vessel sealing and dissection. Surg Endosc 2003; 17(10):1640-5.

3. Takada M, Ichihara T, Kuroda Y. Comparative study of electrothermal bipolar vessel sealer and ultrasonic coagulating shears in laparoscopic colectomy. Surg Endosc 2005; 19(2):226-8.
4. Campagnacci R, de Sanctis A, Baldarelli M, et al. Electrothermal bipolar vessel sealing device vs. ultrasonic coagulating shears in laparoscopic colectomies: a comparative study. Surg Endosc 2007; 21(9):1526-31.
5. Bergamaschi R, Yavuz Y, Marvik R. Laparoscopic bowel resection: a comparison of three ultrasonically activated devices. JSLS 2003; 7(1):19-22.
6. Gossot D, Buess G, Cuschieri A, et al. Ultrasonic dissection for endoscopic surgery. The E.A.E.S. Technology Group. Surg Endos*c* 1999; 13(4):412-7.
7. **Milsom J,** Trencheva K, Monette S, Pavoor R, Shukla P, Ma J, Sonoda T. Evaluation of the safety, efficacy, and versatility of a new surgical energy device (THUNDERBEAT) in comparison with Harmonic ACE, LigaSure V, and EnSeal devices in a porcine model. Laparoendosc Adv Surg Tech A. 2012 May;22(4):378-86.