Harmonic in Laparoscopic Cholecystectomy for Acute Cholecystitis (HAC)

This study is currently recruiting participants.
Verified by University of Bologna, September 2008

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<th>Sponsored by:</th>
<th>University of Bologna</th>
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<tr>
<td>Information provided by:</td>
<td>University of Bologna</td>
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<tr>
<td>ClinicalTrials.gov Identifier:</td>
<td>NCT00746850</td>
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**Purpose**

In the developmental stage of laparoscopic cholecystectomy it was considered 'unsafe' or 'technically difficult' to perform laparoscopic cholecystectomy for acute cholecystitis. With increasing experience in laparoscopic surgery, a number of centers have reported on the use of laparoscopic cholecystectomy for acute cholecystitis, suggesting that it is technically feasible but at the expense of a high conversion rate, which can be up to 35 per cent and common bile duct lesions.

The HARMONIC SCALPEL® (H) is the leading ultrasonic cutting and coagulating surgical device, offering surgeons important benefits including: minimal lateral thermal tissue damage, minimal charring and desiccation.

H technology reduces the need for ligatures with simultaneous cutting and coagulation: moreover there is not electricity to or through the patient H has a greater precision near vital structures and it produces minimal smoke with improved visibility in the surgical field.

In retrospective series LC performed with H was demonstrated feasible and effective with minimal operating time and blood loss: it was reported also a low conversion rate (3.9%).

However there are not prospective randomized controlled trials showing the advantages of H compared to MD (the commonly used electrical scalpel) in LC.

Aim of this RCT is to demonstrate that H can reduce conversion rate compared to MD in LC for AC.
### Condition | Intervention | Phase
--- | --- | ---
Cholecystitis | Procedure/Surgery: early LC within 72 hours after the diagnosis with H (Harmonic) Procedure/Surgery: early LC within 72 hours after the diagnosis with MD (Monopolar Diathermy) | N/A

**Study Type:** Interventional  
**Study Design:** Treatment, Parallel Assignment, Double Blind (Subject, Outcomes Assessor), Randomized, Active Control, Safety/Efficacy Study  
**Official Title:** Randomized, Double-Blind, Controlled Trial of Harmonic(H) Versus Monopolar Diathermy (M) for Laparoscopic Cholecystectomy (LC) for Acute Cholecystitis (AC) in Adults

**Further study details as provided by University of Bologna:**

**Primary Outcome Measure:**
- conversion rate  
  [Time Frame: 1 day]  
  [Designated as safety issue: No]
- operative time  
  [Time Frame: 1 day]  
  [Designated as safety issue: No]
- mortality  
  [Time Frame: 6-months]  
  [Designated as safety issue: Yes]
- morbidity  
  [Time Frame: 6-months]  
  [Designated as safety issue: Yes]
- hospital stay  
  [Time Frame: at discharge]  
  [Designated as safety issue: No]
- postoperative pain  
  [Time Frame: postoperatively]  
  [Designated as safety issue: No]
- return to daily activities  
  [Time Frame: 6-months]  
  [Designated as safety issue: No]

**Estimated Enrollment:** 42  
**Study Start Date:** September 2008  
**Estimated Study Completion Date:** December 2010  
**Estimated Primary Completion Date:** November 2009

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<tr>
<th>Arms</th>
<th>Assigned Interventions</th>
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| Experimental: H  
early LC within 72 hours after the diagnosis with H (Harmonic) | Procedure/Surgery: early LC within 72 hours after the diagnosis with H (Harmonic)  
early laparoscopic cholecystectomy within 72 hours after the diagnosis of acute cholecystitis with H (Harmonic scalpel) |
| Active Comparator: MD  
early LC within 72 hours after the diagnosis with MD (Monopolar Diathermy) | Procedure/Surgery: early LC within 72 hours after the diagnosis with MD (Monopolar Diathermy)  
early laparoscopic cholecystectomy within 72 hours after the diagnosis of acute cholecystitis with MD (Monopolar Diathermy) |
DESIGN

The study project is a prospective, randomized investigation. The study will be performed in the Department of Emergency Surgery St Orsola-Malpighi University Hospital (Bologna, Italy), a large teaching institutions, with the participation of all surgeons who accept to be involved in.

The patients will be divided in two groups: in the first group the patient will be submitted to early LC within 72 hours after the diagnosis with H while in the second group will be submitted to early LC within 72 hours with MD.

HOW RANDOMIZED

The randomization will be obtained through computer-generated schedule. The result of this randomization will be sealed in numbered envelopes. After cholecystitis diagnosis if the patient fulfils the inclusion criteria the responsible surgeon will ask the patient to partecipate to the study. If the patient agree, he/ she will sign the informed consent. After patient's consent the randomization will be carried out. The responsible surgeon will record the patient name (and number).

All eligible patients will be recorded.

STATISTICS

POWER CALCULATIONS:

Sample size has been calculated to reach a confidence level of 95% with a power of 80%. A sample size of 42 patients is calculated supposing that the hospital stay for LC with H the conversion rate can be reduced from 35% to 3%. The sample size will be 21 patients for each group (42 patients for the whole study). For comparison of the two groups, chi-square analysis and Fisher's exact test are used when appropriate for qualitative data, and the Student t-test (for normal variables) or the Mann Whitney U-test (for nonnormal variables) for quantitative data. For multivariate analysis the stepwise logistic regression is applied. A probability of 0.05 or less is accepted as statistically significant.

INTERVENTION

Preoperative data collected will include patient demographics and comorbid conditions (genitourinary, cardiac, pulmonary, gastrointestinal, renal, or rheumatologic) and a detailed history of symptom onset.

The procedure was performed by a surgeon that had performed at least 50 LCs. On admission, the patients were started on cefotaxime, 2 g IV every 12h, which was continued postoperatively according to NNISs score.

The standard four-trocar operative technique is used for LC for acute cholecystitis.

When the gallbladder is distended it will be first aspirated. To allow a good hold on the gallbladder larger graspers will be inserted through a 5 mm right lower port. The cystic artery and duct are clip-ligated in the MD group whereas in the H group cystic artery and duct are closed by H. In the H group the surgeon will use only H, whereas in the MD group the surgeon will use only MD. The gallbladder and intraperitoneal "dropped" stones are collected in an endoscopic bag and extracted through the umbilical cannula site, which can be extended. A closed system suction drain is left. Fascial closure is attempted only at the umbilical cannula site. The skin at all the cannula sites are closed with staples. Conversion to laparotomy will be decided by the operating surgeon and each conversion will be motivated.

Data Collection Patients’ data sheets are generated containing demographic data and preoperative, operative, and postoperative information.
Pre-operative notes concern the history of gallbladder stones, the presence of associated diseases (cardiac, hypertension, diabetes, malignancy), duration of gallbladder complaints (as an indication for the onset of the disease), finding of a palpable gallbladder, temperature, and laboratory results of WBC count, serum bilirubin, gamma GT, PCR, IL-6 and alkaline phosphatase.

Ultrasound findings are also reported. Operative data of concern are macroscopic findings (of acute cholecystitis, gangrenous cholecystitis, hydrops, and empyema of the gallbladder), the presence of small stones (< 1 cm diameter) or large bile stones (> 1 cm diameter), information regarding perforation of the gallbladder and intraperitoneally "lost" stones, reasons for conversion, and duration of surgery. Postoperative notes of interest included the use of nasogastric tubes and drains, the amount of analgesics used, (evaluation of pain with VAS score), complications, and length of hospital stay.

Complications are classified as surgical infections (wound infection, subphrenic or subhepatic abscess); noninfectious surgi-cal problems (e.g., bile duct injury, hemorrhage); remote infections (urinary or respiratory); and miscellaneous problems (e.g., atelectasis, deep vein thrombosis, AMI, CVA, etc). The collected information are entered into a database as either continuous or categorical variables for statistical analysis. Following the operative procedure, a normal sterile dressing will be applied to cover the abdomen.

A second surgical team, aware of the operative findings but not the surgical dissection instrument, then will assume the care of the patient. Postoperative care and ability to be discharged from the hospital will be determined by the second surgical team. The primary operative team will be in every moment available for emergent consultation.

Patient discharge will be based on good medical practice criteria: 1) apyrexia 2) absence of diseases requiring hospitalisation 3) return of bowel function 4) patient's compliance.

• IS THERE A PLACEBO? No
• INFORMED CONSENT TO BE SOUGHT? Yes (see: Case Report Form)
• INFORMED CONSENT FORM OR INFORMATION SHEET? Yes (see: Case Report Form).

In the informed consent form, patients will receive all the information about the study protocol, the confidential nature of personal data and will fill up a questionnaire before signing or refuse.

There will be not inconveniences caused to the patients. No incentives are planned for the patients regarding the operation or the follow-up.

All the medical informations obtained from the patients will be kept confidentially among the research scientists conducting the study.

The patients will be free to withdraw from the study, whenever they want without any obligation.

STOPPING RULES

In case of newly discovered statistically significant advantages in one group.

PRIMARY ENDPOINTS

The aim of the study is to demonstrate that H can reduce conversion rate compared to MD in LC for AC but also differences in terms of morbidity, mortality, operation time, hospital stay, postoperative pain, return to normal activity will be evaluated.

The primary endpoints of our study will be:
• To evaluate the conversion rate
• To evaluate morbidity, mortality, operation time
• To evaluate hospital stay, postoperative pain, return to normal activity

The onset of any other complications will be recorded intraoperatively, postoperatively, at discharge, at 7-days, 1-month and 6-months.

• PLANNED SUBGROUP ANALYSES? No.
• SIDE EFFECTS QUANTIFICATION? Yes There are not different side effects
• IS THERE AN ANALYSIS PLAN? Yes All the above mentioned data will be recorded in the Case Report Form (annexed to this proposal) and later stored in computer database. At the end of the study the final statistical examination will be carried out.
• ARE THERE PLANS FOR INTERIM ANALYSIS? Yes An interim statistical examination of the data will be done every 3 months during the period of patients' inclusion in the study. Then at the end of every completed follow-up period (1-month, 6-months).
• ARE THERE AN INDEPENDENT DATA-MONITORING COMITTEE? No

TYPE OF ANALYSIS

The statistical analysis will be carried out using Epi Info 2000, Version 1.1 software package (Dean AG, Arner TG, Sangam S, Sunki GG, Friedman R, Lantinga M, Zubiena JC, Sullivan KM, Smith DC. Epi Info 2000, a database and statistics program for public health professionals for use on Windows 95, 98, NT, and 2000 computers; Centers for Disease Control and Prevention, Atlanta, Georgia, USA, 2000).

INDEMNITIES SPECIFIED

No incentives are planned for the patients regarding the operation or the follow-up.

FINISHING DATE

The study will take approximately 6 months - 1 year for the inclusion period. According to the number of AC managed monthly, the duration of the inclusion period can be approximately of 1 year to reach the number of about 42 enrolled patients.

REPORTING DATE

An interim report is planned at the end of any completed follow-up period.

• IS THE STUDY CLINICALLY NECESSARY? Yes

AC is a common disease. Any improvement in this field will benefit many patients reducing morbidity, mortality, conversion rate, operation time, hospital stay, postoperative pain, return to normal activity and aesthetic result. All our patients will be informed about the study and an informed consent will be obtained. There will not be inconveniences caused to the patients. All the medical informations obtained from the patients will be kept confidentially among the research scientists conducting the study. The patients will be free to withdrawn from the study, whenever they want without any obligation.

Eligibility

Ages Eligible for Study: 18 Years and older
Genders Eligible for Study: Both
Inclusion Criteria:

- Adult patients (>18 years)
- Clinical (pain, fever > 37.5 °C, WBC > 10,000 / microL), and ultrasound evidence of cholecystitis
- ASA I-III patients
- Informed consent
- Less than 72h from the onset

Exclusion Criteria:

- Informed consent refusal
- Choledocholithiasis
- Generalized peritonitis
- Previous abdominal surgical procedures
- Patients with an intra-operative findings of different pathology will be excluded from the study
- Apache II score > 10

Contacts and Locations

Contacts

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Investigators

Study Director: Fausto Catena, M.D. PhD  S.Orsola-Malpighi University Hospital - University of Bologna
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More Information
Publications:


Responsible Party:  S.Orsola-Malpighi University Hospital (Dr. Fausto Catena MD PhD)

Study ID Numbers:  HAC Trial

Health Authority:  Italy: Ethics Committee