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The ACTIVE study: a multicentre randomised, double-blind, controlled trial of laparoscopic versus open surgery for acute cholecystitis in adults

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20/11/2006

Registration date
21/12/2006

Last Edited
11/04/2014

Recruitment status
No longer recruiting

Overall study status
Completed

Condition category
Digestive System

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
FC111

Study information

Scientific Title

Acronym
The ACTIVE (Acute Cholecystitis Trial Invasive Versus Endoscopic)

Study objectives
In the developmental stage of Laparoscopic Cholecystectomy (LC) it was considered 'unsafe' or 'technically difficult' to perform laparoscopic cholecystectomy for acute cholecystitis. However, with increasing experience in laparoscopic surgery, a number of centres 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% and common bile duct lesions.

Several randomised studies in the early 1980s had shown that performing early open cholecystectomy (Laparotomic Cholecystectomy [LTC]) for acute cholecystitis was better than delayed cholecystectomy in terms of shorter hospital stay but both had similar operative morbidity and mortality rates. Early surgery had since gained in popularity in the late 1980s.

Routine use of the open procedure might enable more patients to have the operations during the acute phase because most surgeons are practiced in this approach. The impact of hospital stay and morbidity must also be taken into account. There is the expectation that open operation is associated with more pain and longer hospital stay.

In some trials successful laparoscopic cholecystectomy during the period of acute inflammation is associated with an earlier recovery and shorter hospital stay when compared with open cholecystectomy. Other studies did not confirm these results and the potential advantages of early laparoscopic cholecystectomy could be offset by a high conversion rate to open surgery. Moreover in these studies a similar postoperative programme to optimise recovery comparing laparoscopic and open approaches was not standardised. Many studies also do not report all eligible patients and are not double blinded.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved by the ethical Committee of the SOrsola-Malpighi Hospital, Bologna, Italy, on the 8th November 2005 (ref: 132/2005/U/Sper).

Study design
The study project is a prospective, multicentre randomised, double-blind, controlled trial.

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Acute Cholecystitis

Interventions
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 information 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.

The study will be performed in the Department of Emergency Surgery, St Orsola-Malpighi University Hospital (Bologna, Italy), a large teaching institution, and (together with other selected centres) with the participation of all surgeons who accept to be involved in the study.

On admission, the patients were started on cefotaxime, 2 g Intravenous (IV) every 12 hours, which was continued postoperatively according to National Nosocomial Infection Surveillance System (NNISS) score.

The patients will be divided in two groups:
1. Early LC within 72 hours after the diagnosis
2. Early LTC within 72 hours after the diagnosis

A surgeon that had performed at least 50 LCs will perform the procedure itself.

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. 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 will be closed with staples.

The Laparotomic (LTC) procedure is carried out with an 8 cm right subcostal incision and the traditional surgical technique with a closed system suction drain left in situ.

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-glutamyl transferase (GGT), Polymerase Chain Reaction (PCR), Interleukin-6 (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 (less than 1 cm diameter) or large bile stones (more than 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 Visual Analogue Scale [VAS] score), complications, and length of hospital stay.

Complications are classified as:
1. Surgical infections (wound infection, subphrenic or subhepatic abscess)
2. Non-infectious surgical problems (e.g., bile duct injury, haemorrhage)
3. Remote infections (urinary or respiratory)
4. Miscellaneous problems (e.g., atelectasis, deep vein thrombosis, Acute Myocardial Infarction [AMI], Cerebro-Vascular Accident [CVA], etc).

The collected information is entered into a database as either continuous or categorical variables for statistical analysis. Following the operative procedure, a large sterile dressing will be applied to cover the entire abdomen.

A second surgical team, aware of the operative findings but not the surgical access approach, will then assume the care of the patient. The second surgical team will determine postoperative care and ability to be discharged from the hospital. This second surgical team will be blinded to the surgical approach. The primary operative team will be in every moment available for emergent consultation or evaluation of the wound.

In the pre-anaesthetic holding area, baseline pain will be investigated at rest and on coughing using a pain-rating scale system: a 100 mm Visual Analogue Scale (VAS) (0 = minimal and 100 = maximal).

An investigator blinded to the study operation performed will evaluate postoperative pain intensity on returning to the Surgical Ward (zero time), and after 12 and 24 hours (± three hours). The three hours of tolerance (before or after the precise time of control) will be used in order to avoid waking the patients during the night. But during the day, if asleep, the patient will be awakened for the pain test.

At these timed intervals, the following variable will be recorded: VAS for pain at rest, and on coughing. If, at rest, VAS is more than three, the patient will be given intravenous 30 mg ketorolac. The pain tests will be also performed whenever the patient asks for additional analgesia between the timed controls, and parenteral analgesics will be administered accordingly. Every time the patient undergoes the pain test, he will be asked about the location of pain (in the surgical wound, far from the wound, everywhere or does not know). As soon as patients will begin to drink fluid instead of ketorolac 30 mg IV, they will be offered nimesulide 100 mg one tablet orally as often as necessary (maximum of two tablets daily). Orally administered analgesics will be continued in preference to parenterally administered analgesics if they will be efficacious.

After discharge, the patients will be offered nimesulide 100 mg one tablet orally as often as necessary (maximum of two tablets daily). Also parenteral and oral analgesic drug requirements will be recorded and analysed as a measure of postoperative pain. Furthermore the patient satisfaction with the analgesia provided (using a scale of poor, satisfactory, good, or excellent) will be recorded before discharge and after seven days.

Patient discharge will be based on good medical practice criteria:
1. Apyrexia
2. Absence of diseases requiring hospitalisation
3. Return of bowel function
4. Patients compliance

Intervention Type
Other

Phase
Not Specified

Primary outcome(s)
To evaluate the value of laparoscopic cholecystectomy to reduce hospital stay

Key secondary outcome(s)
1. To evaluate the value of laparoscopic cholecystectomy to reduce postoperative pain
2. To evaluate the conversion rate

Completion date
01/01/2008

Eligibility

Key inclusion criteria
1. Adult patients (more than 18 years)
2. Clinical (pain, fever more than 37.5°C, White Blood Cells (WBC) more than 10,000/microL), and ultrasound evidence of cholecystitis
3. American Surgical Association (ASA) grade I to III patients
4. Informed consent
5. Less than 72 hours from onset

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
Not Specified

Key exclusion criteria
1. Informed consent refusal
2. Choledocholithiasis
3. Generalised peritonitis
4. Previous abdominal surgical procedures
5. Patients with an intra-operative findings of different pathology will be excluded from the study
6. Apache II score more than ten

Date of first enrolment
01/01/2007

Date of final enrolment
01/01/2008

Locations

Countries of recruitment
Italy

Study participating centre
Via Lidice 4
Bologna
Italy
40139

Sponsor information

Organisation
Italian Polispecialistic Society of Young Surgeons (Italy)

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
St Orsola-Malpighi University Hospital (Italy)

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/10/2013		Yes	No