



Surgery

RANDOMIZED SINGLE CENTRE STUDY, SURGICAL TIMING AND CONVERSION FACTORS IN 100 CONSECUTIVE PATIENTS TREATED FOR ACUTE CHOLECYSTITIS.

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ABSTRACT

Introduction: The aim of this study is to evaluate which factors might influence the decision and the time of conversion in the laparoscopic treatment of acute cholecystitis.

Materials and methods: A monocentric retrospective study was performed on 100 patients affected by acute cholecystitis. The group A, consisting of 15 males (30%) and 35 females (70%) was treated with early laparoscopic cholecystectomy. The group B, consisting of 16 males (32%) and 34 females (68%), was undergoing delayed laparoscopic cholecystectomy approximately after 40 days.

Results: The differences between group A and group B were the incidence of laparotomic conversion (22% in the group A vs 10% in the group B) and the operating time (110' group A vs 75' group B). Time of hospitalization was shorter in patients undergone to early surgery (5 days) compared to patients undergone to delayed surgery (8,5 days). Postoperative complications rate was of 10% in group A and 6% in group B. Cases of mortality were not reported. Factors that influenced conversion to laparotomic surgery were: belonging to male sex, leukocytosis (>18000 WBC) and PCR (>20 MG/DL). In acute forms edema and tissues friability were common causes that hindered the dissection of the concerning structures. Instead, the new formed adhesions observed in patients undergone to delayed surgery has not been an obstacle to dissection.

Conclusions: Laparoscopic surgery represents gold standard in the acute cholecystitis treatment. In our experience, delayed surgery showed a lower rate of conversion and morbidity.

KEYWORDS : Cholecystitis, laparoscopy, laparotomy.**Introduction**

Acute cholecystitis is the most frequent complication in patients with cholelithiasis. The 1-2% of patients with asymptomatic gallstones and the 1-3% with mild/moderate symptoms present annually acute episodes (acute cholecystitis, acute cholangitis, severe jaundice, pancreatitis) or complications¹⁻³. Laparoscopic cholecystectomy represents the gold standard of treatment even for acute forms in which is reported a higher conversion rate.

In our UOC we evaluate, in acute cholecystitis, how the decision about timing of conversion to laparotomy and predictive factors could influence the choice of surgery.

Materials and methods

We made a study of 100 patients with acute cholecystitis undergone videolaparoscopic cholecystectomy at the U.O.C. Endocrine Surgery of the University Hospital Policlinico-Vittorio Emanuele of Catania, from January 1st 2010 to January 1st 2014. The aim of this study is to verify the precise timing and which factors could influence conversion to open cholecystectomy.

The 100 patients (31 male, 69 female) were divided in two groups A and B of 50 patients each one:

- The Group A was composed of 15 males (30%) and 35 females (70%). The average age was 53 years (range 41-76 year). The patients of this group were subjected to early laparoscopic cholecystectomy among 10 and 72 hours of hospitalization, without onset of symptoms;
- The group B was composed of 16 males (32%) and 34 females (68%). The average age was 58 years (range 45-82 year). In this group were included patients treated with delayed laparoscopic

cholecystectomy; these patients were accepted from PS and first treated with conservative medical therapy and, after approximately 40 days, with elective laparoscopic cholecystectomy.

The antibiotic prophylaxis was administrated in all patients with a single dose of third generation cephalosporin. To the first group 1 gram was administrated 30 minutes before surgery and then until 2 days after surgery. To the second group were administrated 2 gram daily (1 gram every 12h) from the first hospitalization until "cooling" of inflammatory process (4-6 days); during the second hospitalization, the same antibiotic dosage was administrated, as in the first group.

The diagnosis of acute cholecystitis was formulated by examining clinical and medical history, abdominal objectivity, laboratory data and ultrasound exam.

The enrolment criterions were:

- Age greater than 18 years
- Signs and symptoms of acute cholecystitis: epi-mesogastric pain, later moved to right upper quadrant, rear irradiation, nausea/vomit, fever, jaundice in approximately 20-30% of cases – almost always not associated with lithiasis of common bile duct – contracture in the right upper quadrant, who presented distended gallbladder, positive Murphy, generally murky peristalsis.
- Leukocytosis (12000 ≤WBC ≤22000 mm³ neutrophilia (between 80 and 92%); Alkaline phosphatase ≥200 UI/L; GPT (92-212 UI/L); GOT (179-231 UI/L); total bilirubin (1,9-3,4 mg/dL); direct bilirubin (0,60-1,3 mg/dL); PCR ≥11,5 mg/dL;
- Ultrasound showing gallbladder wall thickness greater than 4 mm, gallbladder distension, inflammatory pericholecystic liquid, positive Murphy, presence of stones in the infundibulum.

We have registered age, weigh, sex, tobacco and alcohol usage, preoperative comorbidities (diabetes mellitus, liver disease, COPD, heart disease, cancer), ASA scale, previous abdominal surgery, time between onset of symptoms and surgery (timing), operative time, hospital stay and total hospital stay.

Patients excluded from the study were those with: emphysematosis cholecystitis; Mirizzi Syndrome; ASA IV; septic shock; pregnancy; severe cardiopathy; patients entered group B after stabilization who presented resumption of symptomatology within the time between discharge and second hospitalization.

Patients affected by cirrhosis (child-Pugh C) and in therapy with oral anticoagulants derived from coumarin assigned to B group. All the remaining patients were randomized using sealed envelopes (flow Diagram). Cholecystectomy was performed by the same operator, with the same technique and working tools. Surgical times followed to perform urgency laparoscopic cholecystectomy were those developed for elective surgery. Only in a presence of a marked distension of the gallbladder was performed a puncture from outside (fig.1).

The data obtained were analysed with "statistica v.10" software.



Fig.1 – gallbladder drainage

Results

In group A, 50 patients undergone to early cholecystectomy surgery between the 10^o and the 72^o hour following the hospitalization; cholangiopancreatography RM was not performed. The mean operating time was 110 minutes (from 70 to 150 minutes). The time limit for conversion in case of intraoperative technical issues were 60-90 minutes. In the 22% of patients (11/50 of which 7 M and 4 F) was necessary to perform conversion to laparotomy; of these conversion, 6 patients had leucocytosis $\geq 18.000 \text{ mm}^3$. In 13 patients (26%) it was performed an intraoperative cholangiography with negative results, for the presence at ultrasound of minutes calculations mixed to biliary sludge. In 36 patients (72%) we had to empty the gallbladder due to the volume and thickening of the walls.

In 11 patients (80% of cases) the conversion was required because of the presence of significant edema that altered inextricably both the cystic duct and the cystic artery made, moreover, making more difficult to obtain surgical grip, the dissection of the elements of the triangle Calot, the correct identification of the adjacent structures. In one case (20%), we proceeded to conversion due to the difficulty and impossibility to locate the source of bleeding for a cystic artery laceration. After numerous attempts to isolate cystic duct and artery, it was decided to convert when reached the 50 minutes, despite the range was 60 to 90 minutes.

The mean hospital stay was 5 days (range 3-9 days). Postoperative complications appeared in 10% of cases (5/50): wound infection (1/50), atrial fibrillation (1/50), incisional hernia on the 10th day (1/50), 2 losses of about 200cc of bile per day resolved with endoscopic sphincterotomy (2/50).

The patients of Group B have been treated by delayed cholecystectomy after 40 days from acute cholecystitis; in all of them a cholangiopancreatography MRI was performed which has excluded the presence of gallstones in the common bile duct. The mean operating time was 75 minutes (range 60-125 minutes).

The conversions were 5 (10%) 2 males and 3 females: 4 cases for surgical issues in the dissection of the Calot triangle (anatomy altered by adhesions and, in only 2 cases, by fibrosclerotic tissue) and one for bleeding cystic artery lesion. The Intraoperative cholangiography was not performed in no one of the patients.

The average stay of the second hospitalization was 3,5 days (range 3-5 days); the total average hospitalization were 8,5 (first hospital stay was 5 days, range 4-8). Postoperative complications appeared in 3 cases: 1 hematoma at the point of insertion of the Hasson trocar, 1 leakage of bile, about 250cc die, resolved with endoscopic sphincterotomy, 1 suppurative infection of the laparotomy wound.

We found difficulties in the adhesion lysis between gallbladder and neighboring organs in 4% of patients in Group B, of which only 30% needed conversion. The time of conversion was similar to first group. We had no operative mortality. The histological diagnosis in all patients was: acute cholecystitis (77 pts), empyema (19pts), acute cholecystitis gangrenous (4 pts).

The average intervention time between group A and group B does not shows significant differences ($P > 0.01$). In the acute phase, males show an increased conversion rate (9/50); 5 of these have presented a leucocytosis $\geq 18.000 \text{ mm}^3$ and $\text{PCR} \geq 20 \text{ mg/dl}$.

The operating time in patients undergone to conversion was extended to 60-80 minutes. In 8 patients of group A the hospital stay was 2 days longer than in the other 3 who stayed for the same time of those undergone to laparoscopic cholecystectomy; while in group B only 1 hospitalization lasted 2 days longer.

The hospital stay was significantly longer in the second group B ($P < 0.01$) (result from the sum of two admissions).

Discussion

The 2-20% of the world population has gallstones and 15% of these develop acute cholecystitis with a mortality rate of 0-10%⁵⁻⁸.

The therapeutic approach of acute cholecystitis has been modified in recent times⁹.

The concept of "cooling" acute cholecystitis and treating it later, after the complete resolution of the acute event is a source of debates:

- 1) Every flogistic event that affects the gallbladder causes a fibrotic reaction¹⁰;
- 2) 26% of patients with acute empyetic or gangrenous cholecystitis does not respond to conservative therapy and require surgical treatment in acute phase¹⁰;

Also, a review of the literature on comparative studies on early or delayed laparoscopic cholecystectomy reveals that:

- there is no statistically significant difference in biliary tract lesions (0.5% in patients undergoing early cholecystectomy vs 1.4% delayed)¹¹;
- there is no difference in morbidity and mortality between the two groups¹¹;
- the global and post-operative hospital stays are lower in patients undergoing early cholecystectomy¹¹⁻¹⁵.
- advanced age does not preclude the indication for laparoscopic cholecystectomy¹⁶.

The Societ  FranCaise de Chirurgie Digestive¹⁷ defines early surgery less than 7 days from hospitalization and delayed after 6-12 week interval. According to other studies, the interval between admission and intervention varies from: 5 Days¹⁸, 72 hours¹⁹, 48 hours²⁰ or 24 hours²¹. In fact in the first 48 hours, the inflammation increases the parietal edema that facilitates the dissection of the gallbladder from liver bed; after this period, the inflammation induces parietal alterations (necrosis, fibrosis and parietal abscesses) and tenacious adhesions of the bowel to the surrounding structures.

Although initially it was considered a contraindication, today Laparoscopic cholecystectomy is considered the treatment of choice for acute cholecystitis (EAES Consensus Conference 2006)²²⁻²⁴.

Despite the surgeon's experience, compared to uncomplicated, today

the conversion rate in acute cholecystitis is still high (from 10% to 21.7%); the wall edema and inflammatory adhesions make difficult the identification and isolation of the structures, increasing surgical risk (hemorrhage, lesion of the main bile duct)²⁴.

Many studies have been conducted to identify the risk factors responsible for conversion: belonging to male sex²⁵⁻³², age²⁹⁻⁴², obesity³²⁻⁴⁷, previous surgeries⁴⁸, increased wall thickness of the gallbladder⁴⁹, increased CRP levels (CRP \geq 3 mg/dL), white blood cells and alkaline phosphatase⁵⁰⁻⁵⁴, onset \geq 72 hours symptoms, acute cholecystitis⁵⁹⁻⁶⁰, portal hypertension⁶¹, Mirizzi syndrome, cancer of the gallbladder⁶², and experience of the surgeon⁶³⁻⁶⁵. However, the increased CRP \geq 3 mg/dL, the duration of preoperative symptoms, the male and increased white blood cell count \geq 180.000 mm³ seems to be the most important risk factors for the conversion⁴⁴. Rattner indicates a series of laboratory factors (leukocytosis \geq 14,000/mm³, increased alkaline phosphatase) predictive of conversion laparotomy⁶⁴.

These data were confirmed by Laporte in a review of 246 patients from 4 controlled clinical trials⁶⁵⁻⁶⁶; in this study were found a series of laboratory risk factors predictive of conversion laparotomy and divided into preoperative factors (over 65 years of age, leukocytosis \geq 13.000/mm³ and gangrenous cholecystitis) and intraoperative factors (hydrosis or empyema of the gallbladder, gangrenous cholecystitis)²⁴. All these criteria are variable depending on the experience of several teams; in fact, the value of WBC oscillates between 13.000/mm³³²⁴ - 14.000/mm³³⁶⁶ and 17.000/mm³³⁵³ - 18.000/mm³³⁶⁷ and CRP \geq 20 mg/dL. These factors does not induces the surgeon to choose laparotomy, but the possibility of conversion is only determined during surgery, considering the value of these risk factors relative than absolute⁶³⁻⁶⁷. Our approach has changed, giving more value to these predictive factors.

We also considered the conversion an event to decide during the surgery if there are obvious difficulties. In our experience we have found more conversions, in Group A, due to edema, increasing the caliber of the cystic and nearby structures. Conversion to open surgery is not specifically a disadvantage for the patient but rather an act of safety to prevent complications. If the anatomy is unclear, the surgeon should never hesitate to convert⁵. The laparoscopic surgery is converted into open surgery if you encounter difficulties in organ dissection. For this reason, we placed a time limit (30-60 min) for conversion, if there is any difficulty in displaying the calot triangle. Instead, we proceed directly to open surgery if the patient has leukocytosis \geq 18,000 mm³, PCR > 20 mg/dl and fever.

Currently many surgeons believe that the incidence of laparotomy conversions, in early laparoscopic cholecystectomies, for acute cholecystitis, is greater than those performed after conservative medical treatment. These data are a source of controversy, in fact, other authors have shown a higher conversion rate in delayed surgery⁶⁷. The Société Française de Chirurgie Digestive and meta-analysis of Cochrane found no statistically significant difference in conversions between the two groups of patients. A lower incidence of laparotomy conversions is demonstrated in the early operated patients group (20.3% in patients treated immediately vs 23.6% of patients undergoing deferred treatment). The most frequent causes of laparotomy conversions are inflammation of the Calot triangle in the early surgery and post-inflammatory fibrous adhesions in delayed surgeries. In addition, during the conservative medical therapy, they may also onset of complications such as:

- Non-regression or aggravation of cholecystitis (17.5% -30%); this makes necessary in many cases (50%) an urgent surgery with a higher incidence of laparotomy conversions (45%);
- secondary common bile duct lithiasis (9.3%)⁶⁹;
- biliary pancreatitis (4.3%)⁷⁰(Tab.1).

Tab. 1 Comparison of early and delayed laparoscopic cholecystectomy

Authors	N. of patients	Percentage of conversion early VLC (gruppo A)	Percentage of conversion delayed VLC (gruppo B)	Mean days of hospitalization early VLC (gruppo A)	Mean days of hospitalization delayed VLC (gruppo B)
Lo et al ⁵	86	11%	23%	6	11
Lai et al ⁶	91	21%	24%	7,6	11,6
Chandler et al ⁷	43	24%	36%	5,5	7,1
Buffone et al 2015	100	22%	4%	5	3,5 (+5 first admission)

Conclusion

Nowadays is still a topic of discussion about acute cholecystitis treatment if to perform laparoscopic or traditional treatments. Although there is an almost univocal consent considering laparoscopic cholecystectomy as treatment of choice for acute cholecystitis, also if not all the gallbladders can be performed with this method both for the patient's general condition and for comorbidities. In these cases it is preferred undoubtedly an open access.

In relation to the results obtained from our study, we believe it is necessary to consider the predictive factors for conversion and do not hesitate to perform a traditional cholecystectomy when these are meaningful; moreover, even today, there is no agreement on early or delayed treatment and time to conversion. So, our idea is to reduce the inflammation and perform surgery after 4-6 weeks. If inflammation does not regress and there are leukocytosis \geq 18.000 mm³ and CRP \geq 20 mg/dl, open surgery is performed directly.

In our opinion it is necessary to expand the number of cases to study for data collection with national trial to test the complications and therefore patient safety.

The surgeon should never hesitate to convert when the anatomy of Calot triangle and adjacent structures is unclear.

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