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A retrospective comparative cohort study

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AIM: *Aim of this study was to evaluate whether timing of laparoscopy lasting longer than two hours before converting to open surgery can worsen the postoperative course during laparoscopic cholecystectomy (LC) for acute cholecystitis (AC).*
MATERIALS AND METHODS: *Medical records of 1,161 patients who underwent urgent laparoscopic cholecystectomy for AC during the period 2001-2017 were retrospectively analyzed. A conversion to open surgery was performed in 70 (6%) patients. Among these, two groups of patients were identified: group 1 (n=51; 73%) included patients who underwent laparotomy within 2 hours from the beginning of the operation, and group 2 (n=19; 27%) included patients who underwent conversion to open surgery after more than 2 hours of laparoscopy. Patients were analyzed for demographic data and comorbidities. Major outcome measures were mortality, morbidity and length of stay. A p value < 0.05 was considered significant.*
RESULTS: *Reasons for conversion to open surgery included severe inflammation (46%), visceral adhesions (27%), inability to manage common bile duct stones (17%), intolerance to pneumoperitoneum (7%) and the presence of a cholecystoduodenal fistula (1%). By comparing these groups, no significant differences were noted regarding overall morbidity (29% vs 42%, p=0.31), mortality (2% vs 5%, p=0.46) and mean postoperative length of stay (8.7 vs 8.2 days, p=0.75). Major postoperative complications (grade III-V according to Clavien and Dindo classification) were significantly more frequent in group 2 (p=0.03).*
CONCLUSIONS: *When approaching AC laparoscopically, the decision to convert to open surgery within two hours may prevent the occurrence of major postoperative complications. Early conversion does not seem to affect the mortality and length of hospital stay.*

KEY WORDS: Acute Cholecystitis, Conversion, Laparoscopy

Introduction

Laparoscopic cholecystectomy (LC) is by now considered the standard approach for acute cholecystitis (AC) [1–3]. Conversion to open surgery may be required in case of difficult intraoperative settings. In this setting, the conversion rates reported in different published case series range from 1.5% to 19% [4-6]. In a wide range of surgical procedures, a growing body of evidence suggests that a prolonged operative duration is associated with adverse outcomes including surgical site infections, increased venous thromboembolic events, and a longer hospital stay [7-12].
The time spent in laparoscopy before deciding to convert to open surgery can lengthen the overall duration

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of the operation and may represent a considerable risk factor for a worse outcome. A reasonably early decision to convert to open surgery could significantly shorten the operative time and give some medical advantages to the patients. So far, there are no published data proving that a shorter duration of a laparoscopic procedure may significantly influence the postoperative outcomes of patients undergoing laparoscopic surgery for AC.
The aim of this study was to evaluate whether timing of laparoscopy lasting longer than two hours before converting to open surgery can worsen the postoperative course during laparoscopic cholecystectomy (LC) for acute cholecystitis (AC).

Materials and Methods

We reviewed our database containing prospectively collected data on 1,161 patients who underwent laparoscopic cholecystectomy at the Emergency Surgery Unit of the University of Pisa for acute cholecystitis during the period 2001-2017. The policy of the Unit was early treatment of the patients with acute cholecystitis, that is within 72 hours from the onset of symptoms, as in accordance with the guidelines reported in the literature [13]. This study was designed and reported as per Strengthening the Reporting of Cohort Studies in Surgery (STROCSS) criteria [14].

Surgical Procedure

In the operating theater, a pneumoperitoneum was established by inserting a Veress needle at the umbilicus or using Hasson's open technique when requested. CO_2 insufflation pressure was maintained at 14 mmHg. A standard laparoscopic procedure was carried out after the placement of four ports, with the first 12-mm port placed at the umbilical site and the other three 5-mm ports placed under direct vision in the sub-xifoid area, in the epigastrium and in the right flank. Bi-polar Maryland forceps were used for tissue dissection. Intraoperative cholangiography (IOC) was routinely performed, unless the cystic duct was not patent. When common bile duct stones were identified during IOC, clearance of the common bile duct was attempted via transcystic approach, if the stones were small and located distally to the outlet of the cystic duct into the common duct, or via choledochotomy, if the size of the biliary stones was larger than the caliber of the cystic duct. In case of conversion, the abdomen was entered through a right subcostal incision. These patients were divided into two groups, depending on the time elapsed between the beginning of the laparoscopy and the conversion, time interval that was set at a cut-off value of two hours. This cut-off value was chosen according to the exiguous data reported in the literature as matter of discussion. Patients in group 1 (G1) underwent early conversion surgery, whereas patients in group 2 (G2) underwent conversion surgery after more than two hours.

Definitions and Parameters

The following independent parameters were analyzed: age, gender, Body Mass Index (BMI), American Society of Anesthesiologists (ASA) score, the severity grade of patients' comorbidities according to the Charlson-Age Comorbidity Index (CaCI index) (Fig. 1) [15], the grade of AC according to the American Association for the Surgery of Trauma (AAST) grading system for Emergency General Surgery Conditions (Fig. 2) [16], rate of gangrenous acute cholecystitis, rate of acute pancreatitis, reasons for conversion, occurrence of CBD stone and type of CBD stone clearance performed. Main outcome measures were: overall operative time, operative time before conversion, hospital stay, morbidity according to Clavien and Dindo classification [17] and mortality.

Statistical Analysis

For the statistical analysis, XL-STAT software (Addinsoft, NY- USA) was used. Quantitative data are expressed as mean± standard deviation (SD), qualitative data were elaborated as frequency and percentage. A comparison between groups was made by the Mann-Whitney *U* test and the Student *t* test for quantitative and by Fisher's exact test and Chi-square test for qualitative variables. A p value <0.05 was considered as statistically significant.

Fig. 1 - *Charlson Age-Comorbidity (CACI) index* [31]

Score	Medical conditions
6	AIDS (Acquired Immunodeficiency Syndrome
	Metastatic solid tumor
3	Moderate or severe liver disease
2	Any non-metastatic solid tumor
	Malignant lymphomaLeukemia
	Diabetes with end organ damage
	Moderate or severe renal disease
	Hemiplegia
1	Diabetes without end organ damage
	Mild liver disease
	Ulcer disease
	Connective tissue disease
	Chronic pulmonary disease
	Dementia
	Cerebrovascular disease
	Peripheral vascular disease
	Congestive heart failure
	Myocardial infarction

Note: Each decade of age ≥ 50 years is equivalent to a 1 point increase in comorbidity.

Fig. 2 - *AAST grading for Acute Cholecystitis* [14]

AAST Grade	Description	Clinical Criteria	Imaging Criteria (CT/US/HIDA findings)	Operative Criteria	Pathologic Criteria
I	Acute cholecystitis	Right upper quadrant (RUQ) or epigastric pain; Murphy's Sign; leukocytosis	Wall thickening; distention; gallstones or sludge; pericholecystic fluid; non-visualization of gallbladder (GB) on hepatobiliary iminodiacetic acid (HIDA) scan	Inflammatory changes localized to GB; wall thickening; distention; gallstones	Acute inflammatory changes in the GB wall without necrosis or pus
II	GB empyema or gangrenous cholecystitis or emphysematous cholecystitis	RUQ or epigastric pain; Murphy's Sign; leukocytosis	Above, plus air in GB lumen, wall or in the biliary tree; focal mucosal defects without frank perforation	Distended GB with pus or hydrops; necrosis or gangrene of wall; not perforated	Above, plus pus in the GB lumen; necrosis of GB wall; intramural abscess; epithelial sloughing; no perforation
III	GB perforation with local contamination	Localized peritonitis in RUQ	HIDA with focal transmural defect, extraluminal fluid collection or radiotracer but limited to RUQ	Perforated GB wall (non-iatrogenic) with bile outside the GB but limited to RUQ	Necrosis with perforation of the GB wall (non-iatrogenic)
IV	GB perforation with perichole-cystic abscess or gastrointestinal fistula	Localized peritonitis at multiple locations; abdominal distention with symptoms of bowel obstruction	Abscess in RUQ outside GB; bilio-enteric fistula; gallstone ileus	Pericholecystic abscess; bilio-enteric fistula; gallstone ileus	Necrosis with perforation of the GB wall (non-iatrogenic)
V	GB perforation with generalized peritonitis	Above, with generalized peritonitis	Free intra-peritoneal bile	Above, plus generalized peritonitis	Necrosis with perforation of the GB wall (non-iatrogenic)

Results

Seventy out 1,161 patients who underwent laparoscopic approach for AC had conversion to open surgery (6%). Overall, 46 patients (66%) were male with a male to female ratio of 2:1 (Table I). The median age at diagnosis was 68.9 years (±13.8 years). Mean BMI was 25.9 Kg/m^2 (±4.5 Kg/m^2). In 28 cases (40%), ASA score was ≥ 3. The Charlson Age-Comorbidity Index (CACI) score was ≥ 4 in 37 patients (53%). AAST score was I in 36 (51%), II in 27 (38%), III in 2 (3%), IV in 2 (3%) and V in 4 (5%). Three patients (4%) presented with AC complicated by mild acute pancreatitis. Intraoperatively, 24 patients (34%) were found to have a gangrenous cholecystitis (Table I).

Fifty one of these (73%) had conversion within two

TABLE I - *Patients' general and clinical characteristics*

	Overrall patients N = 70	G1 N= 51 (73%)	G2 N=19 (27%)	*p*
Median Age (Years) (± Sd)	68.9 (± 13.8)	70.9 (± 13.3)	63.5 (± 13.9)	0.04
Gender:				
Male (%)	46 (66)	32 (63)	14 (74)	0.56
Female (%)	24 (34)	19 (37)	5 (26)	
Average Bmi (Kg/M^2) (± Sd)	25.9 (± 4.5)	25.5 (± 4.5)	27.7 (± 3.9)	0.09
Asa Score ≥ 3 (%)	28 (40)	25 (49)	3 (16)	0.01
Caci score ≥ 4 (%)	37 (53)	14 (20)	5 (7)	0.93
Aast score (%) I36 (51)	25 (49)	11 (58)	0.56	
Ii	27 (38)	20 (39)	6 (31)	
III	2 (3)	2 (4)	0	
IV	2 (3)	2 (4)	0	
V	4 (5)	2 (4)	2 (11)	
Gangrenous AC (%)	24 (34)	20 (38)	4 (21)	0.15
Acute Pancreatitis (%)	3 (4)	2 (4)	1 (5)	0.80

Table II - *Intraoperative findings*

	Overall patients N=70	G1 N= 51 (73%)	G2 N=19 (27%)	*P*
Reasons For Conversion (%)				
– Severe pericholecystic inflammation	32 (46)	24 (47)	8 (42)	0.01
– Tenacious adhesions	20 (29)	18 (35)	2 (10)	
– Inability to remove biliary stones	12 (17)	4 (8)	8 (42)	
– Intollerance to pneumoperitoneum	5 (7)	4 (8)	1 (6)	
– Cholecystoduodenal fistula	1 (1)		1(2)	0
Mean operative time (Min) (± SD)	190.3 (± 65.1)	172.5 (± 49.8)	237.8 (± 81.8)	0.007
Mean conversion time (Min) (± SD)	80.9 (± 53.3)	59.8 (± 28.4)	166.7 (± 29.6)	0.0001
Intraoperative choledocholithiasis (%)	24 (34)	15 (29)	9 (47%)	0.15
Type of common bile duct clearance (%)				0.51
– Transcystic	10 (14)	7 (14)	3 (16)	
– Transcholedocotomy	13(19)	8 (16)	5 (26)	
– Biliodigestive anastomosis	1 (1)	0	1 (5)	
Mean post-operative stay (Days) (± Sd)	8.6 (± 7.3)	8.7 (± 8.2)	8.2 (± 4)	0.75

Table III - *Postoperative outcomes*

	Overall patients N=70	G1 N= 51 (73%)	G2 N=19 (27%)	*P*
Overall morbidity rate (%)	23 (33)	15 (29)	8 (42)	0.31
– Type of postoperative complications (%):				0.19
– Postoperative ileus (Grade I*)	1 (4)	1 (7)	0	
– Pleural effusion (Grade II*)	3 (13)	1 (7)	2 (25)	
– Pulmonary infection (Grade II*)	1 (4)	1 (7)	0	
– Anemia (Grade II*)	2 (9)	2 (14)	0	
– Brain stroke (Grade II*)	1 (4)	1 (7)	0	
– Hyperpyrexia (Grade II*)	1 (4)	0	1 (12)	
– Transient hyperbilirubinemia (Grade II*)	1 (4)	1 (7)	0	
– Pulmonary embolism (Grade II*)	1 (4)	1 (7)	0	
– Cardiac arrhythmia (Grade II*)	3 (13)	3 (20)	0	
– Bile leak, treated with percutaneous drainage (Grade IIIa*)	2 (9)	1 (7)	1 (12)	
– Surgical site infection (Grade IIIa*)	3 (13)	2 (14)	1 (12)	
– Bile leak treated with ERCP (Grade IIIb*)	1(4)	0	1 (12)	
– Retained abdominal drain (Grade IIIb*)	1 (4)	0	1 (12)	
– Acute respiratory failure (Grade V*)	2 (9)	1 (7)	1 (12)	
Major Postoperative Complications Rate (Clavien-Dindo > II) (%)				0.03
Clavien-Dindo IIIa	5 (22)	3 (20)	2 (25)	
Clavien-Dindo IIIb	2 (9)	0	2 (25)	
Clavien-Dindo V	2 (9)	1 (7)	1 (12)	
Mortality Rate (%)	2 (3)	1 (2)	1 (5)	0.46

*According to Clavien and Dindo classification [15]

hours (G1) and the remaining 19 (27%) underwent conversion to open surgery after more than two hours (G2). The reasons for conversion included severe inflammation with impossibility to properly identify the critical view of safety (32 patients, 46%), adhesions not amenable to laparoscopic procedure (20 patients, 29%), inability to remove stones from the common bile duct (12 patients, 17%), patient's intolerance to pneumoperitoneum (5 patients, 7%), and the presence of a cholecystoduodenal fistula (1 patient, 1%) (Table II).

On avarage, the overall operative time was 190.3 minutes (± 65.1 min), and the time spent before the conversion was 80.9 min (± 53.3 min). The post-operative hospital stay was 8.6 days (± 7.3 days). Two deaths were recorded (3%). The overall morbidity rate was 33%, including 9 patients which developed a complication with a severity grade higher than II according to the Clavien and Dindo classification (Table III).

By groups comparison, patients in G1 were significantly older (70.9 ± 13.3 yr. in G1 *vs.* 63.5 ± 13.9 yr. in

G2; *p=0.04*) and had a higher proportion of an ASA score >2 (49% *vs.* 16%; *p=0.01*) in respect to patients in G2. No significant differences were noted regarding gender distribution, BMI, CACI index, AAST grade of acute cholecystitis, associated acute pancreatitis, and occurrence of gangrenous cholecystitis.

The reason that led to conversion made the groups differ from each other significantly. CBD stones were more frequently detected in G1 patients, but difference was not statistically significant. Also, the procedures employed to clear the bile duct were substantially similar for both groups. Two patients (one in each group) died postoperatively due to acute respiratory failure. Morbidity rate (29% G1, 42% G2) and length of hospital stay (mean 8.7 days, G1; mean 8.2 days, G2) did not differ significantly, but the occurrence of a major complication (Clavien-Dindo classification score > 2) was significantly higher in G2 (63% *vs* 27%; *p=0.03*).

Discussion

In this analysis, we noted that those patients who underwent conversion to open surgery after two hours have greater odds of major complications. To our knowledge, this has been the first cohort study to assess the impact of the operative duration before conversion on the post-operative course following a laparoscopic approach to acute cholecystitis.

Literature is lacking of studies focusing on the possible effects on patients' outcomes of the length of time before conversion to laparoscopic cholecystectomy, but it is well recognized that a longer operative duration is a critical factor that influences the post-operative course of patients who underwent surgery. The rate of conversion reported in this study (6%) is substantially in line with the literature [4-6,18]. The causes of conversions included severe inflammation, tenacious adhesions, impossibility to obtain an effective clearance of the CBD from stones, intolerance to pneumoperitoneum and cholecystoenteric fistula.

The identification of the critical view of safety (CVS) is mandatory to avoid common bile duct injuries [19,20]. Tenacious adhesions and inflammation may however prevent a proper identification of the critical anatomical elements during the dissection. Furthermore, the presence of tenacious adhesions in the duodenum, the liver, the omentum and even to the abdominal wall as a result of previous upper abdominal surgery, may render the critical view of safety inaccessible [21]. In severe forms of AC, the risk of biliary injury could be increased as the cystic duct may become foreshortened or the gallbladder tenaciously adherent to the common bile duct [22]. In this scenario, also dissection can be challenging due to a thickened and friable gallbladder wall and dense scarring. For all these reasons, a delay to surgery exceeding 72 hours from the onset of symptoms in patients with acute cholecystitis is believed to increase the risk of having to perform conversion [23].

Associated choledocolithiasis is present from 7.7% to 14% of patients with AC. In our unit, we follow the policy to offer a one-stage management for AC associated with common bile duct stones. When possible, the common bile duct clearance is performed laparoscopically. One randomized study [24] and one meta-analysis [25] have stated that a single-stage management has a lesser morbidity and a higher success rate. In some cases, it may happen that clearance of the common bile duct results ineffective or unavailable both laparoscopically and through intraoperative ERCP, and this may solicit the surgeon to move towards an open surgery management of the common bile duct stones.

During laparoscopy, respiratory mechanics and gas exchange are impaired because of pneumoperitoneum and lung atelectasis. Pneumoperitoneum could worsen the cardio-vascular circulation, increasing the heart rate and blood pressure [26,27]. Although many drugs and new systems of mechanical ventilation have been used over the years to control pulmonary and hemodynamic changes in patients with severe comorbidities, penumoperitonum cannot be maintained in a small group of patients. For this reason, the only way to stabilize the patients is to remove the pneumoperitoneum, convert to open surgery and try to speed up the surgical procedure.

A cholecystoduodenal fistula is not so easy to diagnose and it is usually recognized only during laparoscopic cholecystectomy [28]. A recent study of Li et al. on a large cohort of patients demonstrated a rate of 0.27% of cholecystoenteric fistula in patients undergoing LC for gallbladder lithiasis. 79.3% of them were represented by a cholecystoduodenal fistula. They reported an 82.8% of success rate of the laparoscopic treatment with a conversion rate of 17.2%, mainly related to bleeding, difficulty in intestinal suturing and inflammation around the gallbladder. They stated that the laparoscopic management of the cholecystoduodenal fistula could be tedious and hazardous and should be performed only by experienced surgeons in clear anatomical situations [29].

In this analysis, we found that the mean age and ASA score ≥ 3 were significantly higher in G1 (p = 0.04 and p = 0.01, respectively). It can be speculated that elderly age and a higher ASA score were considered by the surgeons as relevant factors to decide for an earlier conversion to open surgery. Nevertheless, the other general characteristics of the patients (male/female ratio, BMI, CACI index ≥ 4, the AAST score classification's distribution, rate of gangrenous AC and acute pancreatitis) were substantially similar. In their review, Lawnders et al identified as a difficult procedure an intervention lasting over 60 minutes. Increased BMI, decreased age, male gender, increased ASA, and abnormal liver function tests were considered as valuable predictors for a difficult LC procedure. Furthermore, they showed that an increase in difficult procedures exposes the surgeons and the hospital to a higher workload [30].

The present study has several limitations. This was not a randomized controlled study and thus has limitations that are intrinsic in retrospective studies. Secondly, the choose of a cut-off value of 2 hours can be seen as a matter of debate: there is no evidence in the literature that 2 hours may represent a critical factor for a conversion to open surgery. Finally, the small cohort of the analyzed patients could not allow certain conclusions.

Conclusions

Our study suggests that the longer the time is before considering a conversion to open surgery, the higher is the rate of postoperative major complications. Surgeons should be aware that several complications are related with a longer time of operation. Anesthesia, pneumoperitoneum, surgical manipulation during a longer laparoscopic time could be the cause of postoperative drawbacks. Conversion should not be considered as a technical failure, but rather a better surgical strategy for the patient. The decision to move to a laparotomy should be taken as soon as the surgeon understands the complexity of the operative field and this applies especially to the inexperienced surgeons.

Riassunto

Premessa: In letteratura, non vi sono studi che valutino la correlazione tra il tempo che trascorre prima di convertire l'intervento in open nei pazienti sottoposti a laparoscopia per colecistite acuta (CA) e l'insorgenza di complicazioni postoperatorie. Questo studio ha lo scopo di valutare se una conversione a chirurgia open dopo più di due ore durante colecistectomia laparoscopica per colecistite acuta possa peggiorare il decorso postoperatorio dei pazienti operati.
Materiali e Metodi: Abbiamo valutato in maniera retrospettiva le cartelle cliniche di 1.161 pazienti sottoposti a colecistectomia laparoscopica per CA durante il periodo 2001-2017. In 70 pazienti (6%), è stato necessario convertire l'intervento in open. Tra questi, sono stati identificati due gruppi di pazienti: il gruppo 1 (n = 51; 73%), che includeva pazienti sottoposti a laparotomia entro 2 ore dall'inizio dell'operazione, e il gruppo 2 (n = 19; 27%), che comprendeva pazienti sottoposti a conversione dopo più di 2 ore di laparoscopia. I pazienti sono stati quindi analizzati per dati demografici e comorbidità. Mortalità, morbilità e durata media della degenza postoperatoria sono stati i principali outcome analizzati. Un valore $p < 0,05$ è stato considerato significativo.
Risultati: Le ragioni per cui è stato necessario convertire l'intervento in open sono state: grave infiammazione (46%), aderenze viscerali (27%), incapacità di rimuovere calcoli del dotto biliare comune (17%), intolleranza allo pneumoperitoneo (7%) e presenza di una fistola coledocoduodenale (1%). Confrontando questi gruppi, non sono state osservate differenze significative per quanto riguarda la morbilità complessiva (29% vs 42%, p = 0,31), mortalità (2% vs 5%, p = 0,46) e durata media della degenza postoperatoria (8,2 vs 8,2 giorni, p = 0.75). Le complicanze maggiori postoperatorie (grado III-V secondo la classificazione di Clavien - Dindo) erano tuttavia significativamente più numerose nel gruppo 2 (p = 0,03).
Conclusioni: Durante la colecistectomia laparoscopica per colecistite acuta, la decisione di convertire l'intervento in open entro due ore può impedire il verificarsi di importanti complicanze postoperatorie. La conversione anticipata non sembra tuttavia influenzare la mortalità e la durata della degenza ospedaliera post-operatoria.

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