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VARIA

Therapeutic decision of laparoscopy and its benefits as a gold standard in acute cholecystectomy

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Abstract: *Background: Acute cholecystitis is the most frequent complication of cholelithiasis and counts for one third of surgical emergencies.*

Aim: The study evaluates the outcomes and limits of laparoscopic cholecystectomy in acute cholecystitis.

Materials and methods: A retrospective study was performed for 2 years, between 01.01.2016-31.12.2017 in the 2nd Surgery Department of the Sibiu County Emergency Clinical Hospital, on hospitalized patients with acute cholecystitis, who underwent surgery. The severity of acute cholecystitis was analyzed using the Tokyo Guidelines (TG13 / TG18) severity risk scale. The preoperatory evaluation of the anesthetic-surgical risk was based on American Society of Anesthesiologists Physical Status Classification (ASA PS) and Charlson Comorbidity Index (CCI) (9). Statistical analysis was performed to analyze the outcomes and limits of laparoscopic cholecystectomy and the risk factors for conversion and open surgery.

Results: Out of the 262 patients in the study group, most of the patients (61%) were diagnosed with moderate acute cholecystitis, while 67 patients (26%) were diagnosed with mild form and 34 (13%) with severe acute cholecystitis. Laparoscopic cholecystectomy was performed in 96.1% of cases with no conversion to open surgery. The postoperative complications were ligature slippage (1.9%), main bile duct injury (1.9%), postoperative hemorrhage (3.9%) and surgical site infections (2.4%), most of them being managed conservatory.

Conclusions: Laparoscopic cholecystectomy can be performed nowadays with minimal morbidity in acute cholecystitis. Knowledge of various factors predicting possible conversion helps in adequate pre-operative selection and counseling for open procedure with further reduction in the overall morbidity of laparoscopic cholecystectomy.

Keywords: *laparoscopic cholecystectomy, acute cholecystitis, risk factors, inflammation*

INTRODUCTION

Acute cholecystitis is the most frequent complication of cholelithiasis and counts for one third of surgical emergencies. Blocked stones at the level of the infundibulum or cystic duct generate inflammatory phenomena of variable intensity, from mild to severe, with organ failure and septic condition. It is considered to be the second source of complicated intra-abdominal infection (18.5%), according to the World Society of Emergency Surgery complicated intra-abdominal infections Score study [1]. Laparoscopic cholecystectomy has become the "gold standard" in treatment of biliary lithiasis due to its undeniable advantages in reducing pain and postoperative complications. However, there are still controversies regarding the management of patients with acute cholecystitis. In the early days, after the first laparoscopic

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cholecystectomy, acute cholecystitis was considered as an absolute and later, a relative contraindication for this surgery [2] due to the possible risk of increased morbidity, especially common bile duct injuries [3].

The current concept is in favor of emergency intervention in the first 72 hours after hospitalization, as there is no evidence that delaying the intervention after resolving the acute outbreak would benefit in reducing intraoperative complications, especially major biliary tract injuries, due to local fibrous remodeling [4-7]. The current guidelines recommend surgery as soon as possible because evidenced-based clinical studies confirmed that an early treatment reduces the total hospital stay and does not increase the complication or conversion rates [8].

The study evaluates the outcomes and limits of laparoscopic cholecystectomy in acute cholecystitis.

MATERIALS AND METHODS

A retrospective study was performed for 2 years, between 01.01.2016-31.12.2017 in the 2nd Surgery Department of the Sibiu County Emergency Clinical Hospital, on hospitalized patients with acute cholecystitis. The inclusion criteria were:
- hospitalization diagnosis of "Acute non-/lithiasis cholecystitis"
- histopathological confirmation of the acute character of the inflammation of the gallbladder wall;
- surgical treatment of the pathology during hospitalization.

Patients with acute biliary pathology, but who were not treated surgically, and patients who did not show acute inflammatory signs in the gallbladder were excluded.

Observation sheets and operating protocols were analyzed. The collected data documented age, sex, associated pathology, preoperative clinical and paraclinical data (hemoleukogram, fibrinogen, AST, ALT, bilirubin, amylase, INR, urea, creatinine, abdominal ultrasound), type of intervention, postoperative complications, appearance histopathological examination of the gallbladder specimen, duration of hospitalization. The severity of acute cholecystitis was analyzed using the Tokyo Guidelines (TG13 /TG18) severity risk scale. According to this classification, Grade III (severe acute cholecystitis was considered the acute cholecystitis associated with organ/system (renal, cardiovascular, hepatic, respiratory, neurologic, hematologic) dysfunction, Grade II (moderate) acute cholecystitis associates clinical signs of acute cholecystitis with white blood cells (WBC)>18000/mmc, palpable tender mass in the right upper abdominal quadrant, marked local inflammation and the onset of symptoms of more than 72 hours before presentation. Grade I (mild) acute cholecystitis is defined as acute cholecystitis which does not meet criteria for grade II or III [7, 8].

The preoperatory evaluation of the anesthetic-surgical risk was based on American Society of Anesthesiologists Physical Status Classification (ASA PS) and Charlson Comorbidity Index (CCI) [9]. Statistical analysis was performed to analyze the outcomes and limits of laparoscopic cholecystectomy and the risk factors for conversion and open surgery.

Table 1: Preoperatory evaluation of the patients in the study group: demographic data and associated comorbidities

General characteristics in the study group	
	Total (n=262)
Gender	
Female	171 (65.26%)
Male	91 (34.73%)
Age	
21 - 30 years	20 (8%)
31 – 40 years	44 (17%)
41 – 50 years	68 (26%)
51 – 60 years	47 (18%)
61 – 70 years	34 (13%)
71 – 80 years	31 (12%)
>80 years	18 (7%)
Comordibities	
Diabetes mellitus	29 (11.06%)
Hypertension	120 (45.8%)
Coronary diseases	70 (26.7%)
Valvular diseases	7 (2.6%)
Respiratory diseases	22 (8.3%)
Obesity	41 (15.6%)
Previous abdominal surgery	9 (3.4%)
CCI*	
0	107 (41%)
1	73 (28%)
2	23 (9%)
3	23 (9%)
4	16 (6%)
5	10 (4%)
≥6	10 (3%)
ASA PS**	
I	59 (22%)
II	92 (25%)
III	75 (29%)
≥IV	36 (14%)

**CCI: Charlson comorbidity index*
***ASA PS: American Society of Anesthesiologists Physical Status Classification*

RESULTS

Of the total number of patients (361) who presented at the Sibiu County Hospital, Surgery Clinic, with acute biliary pathology during the analyzed period, 262 (73%) presented inclusion criteria in the study. Demographic characteristics

of the study group (Table 1) confirm the predominance of pathology in females (65.26%), and middle adulthood (40-60 years). In 73% of cases, the presentation was late, after more than 72 hours after the onset of painful abdominal symptoms.

The main associated comorbidities were: cardiovascular disease, obesity and diabetes. Assessment of surgical anesthetic risk by calculating the Charlson comorbidity score (CCI) and placing it in the risk classes of the American Society of Anesthesiologists Physical Status Classification (ASA PS) system (Table 1).

Routine preoperative evaluation consisted of clinical evaluation, abdominal ultrasound, chest X-ray, EKG, as well as evaluation of biochemical and hematological parameters, characteristics to assess the severity of infection (hemoleukogram, fibrinogen, ESR), but also liver function (AST, ALT, bilirubin), renal (urea, creatinine), coagulation (INR). According to TG13/TG18 severity risk scale, most of the patients (61%) were diagnosed with moderate acute cholecystitis, while 67 patients (26%) were diagnosed with mild form and 34 (13%) with severe acute cholecystitis.

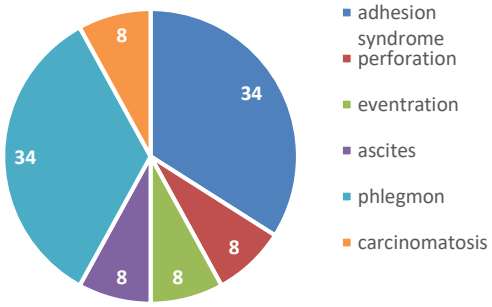
The management of acute cholecystitis was according to Tokyo Guidelines, based on the severity of symptoms, ASA and CCI index. Patients with ASA≥3 and CCI≥6 or sepsis, underwent fluid rebalance and general supportive care before surgery could be performed safely. Emergency laparoscopic cholecystectomy in the first 72-96 hours after admission was performed. Large spectrum intravenous antibiotherapy was used in all cases.

The operative moment was carefully planned after attentive clinical and paraclinical evaluation of the patient and rebalancing of associated comorbidities. Most of the patients (252; 96%) underwent laparoscopic cholecystectomy. Open surgery was used in 10 patients. There were no conversions in the study group, all intraoperative incidents and accidents were managed by laparoscopic approach.

The main reason for deciding from the beginning the classic intervention is the complex adhesion syndrome, but also the suspicion of phlegmon, representing 34% of the number of patients in this category (4 patients). Others include perforation, with biliary peritonitis, postoperative eventration, ascites and peritoneal carcinomatosis associated with colon neoplasm (1 patient each) (Figure 1).

A comparative analysis of the histopathological aspect of the gallbladder for the 2 groups in the study group (laparoscopic and classic) shows that the form of catarrhal inflammation of the gallbladder wall was 87% in the laparoscopic group and 60% in the classically operated group.

Figure 1: Factors for open cholecystectomy in the study group (percentages)



Although less frequent in the laparoscopically operated group, the presence of the difficult forms, such as gangrenous cholecystitis, piocholecystitis, pericholecystic plastron, is not a contraindication for the laparoscopic approach being successfully resolved in this way. On the other hand, the presence of peritoneal carcinomatosis, ascites, eventration, or extensive postoperative adhesions in the upper abdominal floor are absolute or relative contraindications for laparoscopy (Table 2).

Table 2: Histopathological aspects of the removed cholecyst: laparoscopic vs open cholecystectomy

Histopathological aspect of the removed cholecyst	Laparoscopic Cholecystectomy	Open Cholecytectomy
pericholecystic plastron	1 (1%)	1 (10%)
piocholecystitis	3 (1%)	0
pericholecystic fibrosis	5 (2%)	1(10%)
gangrenous cholecystitis	17 (7%)	1(10%)
hydrops	6 (2%)	1(10%)
cataral inflammatory changes	220 (87%)	6 (60%)

A particular aspect as a difficulty in surgical tactics is the association of acute cholecystitis with primary gallstones in 13 cases and angiocolitis in 2 cases.

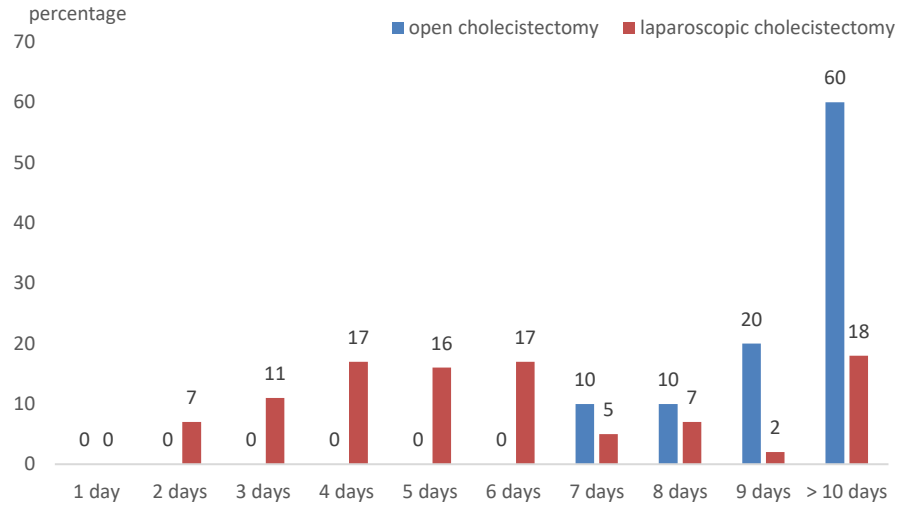
Main bile duct lithiasis resolution was achieved by ERCP, in 15% preoperatively and in 85% postoperatively.

The outcome was favorable with no complications, in most cases (88%) operated laparoscopically and in 50% of cases operated classically, which is correlated with the degree of difficulty and associated comorbidities increased in the group of 10 patients who were treated by classic cholecystectomy.

The average hospital stay was 5.7 days in the laparoscopic

group and 11.2 days in the classically operated group (Figure 2).

Figure 2: Postoperative hospital stay in open and laparoscopic cholecystectomy



The postoperative complications are presented in Tables 3 and 4. Following the study we determined the most common postoperative complications due to the surgical technique, these being: ligature slippage, main bile duct injury, postoperative hemorrhage and surgical site infections. It can be seen that the most common complication in the study is postoperative hemorrhage, caused by: either skidding of the cystic artery ligation, or by inefficient hemostasis (3.9%), followed by skidding of the cystic ligature (1.9%).

Table 3. General postoperative complications in open and laparoscopic cholecystectomy

General postoperative complications	Open cholecystectomy		Intervenție laparoscopică	
	No	*percentage*	*No*	*percentage*
Death	1	10 %	5	2 %
Stroke	0	0 %	1	1 %
Acute miocardial infarction	0	0 %	4	2 %
Malign arterial hypertension	0	0 %	2	1 %
Ascitis	1	10 %	3	1 %
Nosocomial infection	3	30 %	5	2 %
Sepsis	0	0 %	3	1 %
Others	0	0 %	6	2 %

The reasons for the skidding of the ligature are multiple and we will give some examples: the skidding of the metal clip, being the edematous and friable cyst, the skidding of the metal clip being cut to its laughter, etc. On the 3rd place, but very important due to their severity, is the damage of the main bile duct during the maneuvers (1.9%) (Tables 3, 4).

Table 4. Surgery related postoperative complications in open and laparoscopic cholecystectomy

Surgery related postoperative complications	Open cholecystectomy		Intervenție laparoscopică	
	No	*percentage*	*No*	*percentage*
Skidding of the cystic ligature	2	20 %	5	1.9 %
Lesions of the main bile duct	0	0 %	5	1.9 %
Postoperative hemmorhages	1	10 %	10	3.9 %
Surgical site infections	3	30 %	6	2.4 %

The resolution of surgical complications was done in most cases by conservative management, 2 cases requiring reintervention, 1 for postoperative hemorrhage and resolution by ERCP approach of CBP lesion.

DISCUSSION

Laparoscopic cholecystectomy has become the "gold standard", due to its undeniable advantages in reducing pain and postoperative complications, as well as the length of hospital stay. Even during the COVID-19 pandemic era, when laparoscopy was firstly regarded with extreme prudence, the general surgical opinion was that we must not step back from the achievements of modern surgery, but reinforce the

safety measure regarding the ultrafiltration of pneumoperitoneum [10].

Together with the development of anesthesia and intensive care skills and techniques, the safety limit for performing laparoscopy also increased nowadays towards the age of 80-85 years [8, 11], and even of 91 years old in our study group, if not severe ASA risk is associated. In the study group there was no case of conversion. Careful preoperative assessment of the comorbidities and attentive patient clinical evaluation is extremely important before choosing between open and laparoscopic surgery. Conversion to open surgery is associated in several studies with negative effects, including prolonged operation time and increased bleeding which is particular important in patients with increased anesthetico-surgical risk [12].

Another conclusion in the study was that the surgeons should be aware of the significant risk of severe cardiovascular acute events following both laparoscopic and open cholecystectomy, especially in cases with severe sepsis and inflammation or high risk associated comorbidities. These complications should be included in the reasonable disclosure, when the patient is informed about the procedure and the associated possible risks and complications. Informed consent process must be the base of a partnership between doctor and patient, in sharing the inherent risks associated to surgical procedures and understanding what the expectations should be [13].

The severity of local inflammatory changes is a major risk factor for intra operatory and postoperative associated complications. Hyperbilirubinemia significantly increases the likelihood of finding common duct stones in patients with acute cholecystitis, but it also occurs in patients with acute cholecystitis without common duct stones [8]. Hyperbilirubinemia is also a biomarker of intraperitoneal inflammation, along with lipopolysaccharide binding protein (LBP) and Il-6, which increase as a response of liver disfunction associated to bacterial aggression. There are evidences that Escherichia coli and Bacteroides fragilis, common pathogens of the biliary and intestinal wall, were supposed to interfere with hepatocyte microcirculation, inducing sinusoidal lesions. LPSs activate monocytes and macrophages to secrete inflammatory cytokines (tumor necrosis factor alpha (TNF-α) and IL-1, etc.) and other potent mediators [14] by an intracellular signal amplification pathway. These mediators, in turn, act on additional target cells to produce cardiovascular shock, multisystem organ failure, and septic shock [15], one of the major causes of death in intensive care units [16]. In recent studies, a raised concentration in bile but also a more pronounced immunohistochemical expression of cytokines, likeTNF-α, IL-1α, IL-6 was found in the cholecystic wall in both acute and chronic cholecystitis, which may suggest the role of these cytokines in pathogenesis of inflammation and cholelithiasis [17, 18].

Severe inflammation is associated with increased risk of main bile duct during laparoscopic dissection of gallbladder, one of the most serious complications of cholecystectomy. Recently, near infrared (NIR) fluorescence Indocyanine Green was employed in challenging cases to allow a better visualization of the biliary tree. The molecule of ICG is a polymethylic cianyne, which can be administered intravenously, with an excellent safety profile. It binds with circulating albumins and lipoproteins and is excreted into the bile almost unchanged after hepatic extraction [19]. Several studies proved the beneficial use of ICG, which may ensure the surgeon to perform LC with confidence, even in the presence of severe inflammation [20, 21].

Laparoscopic cholecystectomy can be performed nowadays with minimal morbidity in acute cholecystitis [23]. Knowledge of various factors predicting possible conversion helps in adequate pre-operative selection and counseling for open procedure [24] with further reduction in the overall morbidity of laparoscopic cholecystectomy.

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