Laparoscopic cholecystectomy in acute cholecystitis : support for an early interval surgery

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Abstract

Background and study aims : **Although laparoscopic cholecystectomy is advocated for acute cholecystitis, debate still exists about its optimal timing. This retrospective study compares the outcome of laparoscopic cholecystectomy within versus later than 5 days of onset of symptoms in patients with acute cholecystitis.**

Patients and methods : **One hundred thirty six patients with acute cholecystitis grade I or II were included in the study and divided in two groups. Group 1 received surgery within 5 days of symptoms and group 2 received conservative therapy and delayed surgery after 6 weeks.**

Results : **Group 1 and 2 consisted of 100 and 36 patients respectively. Because of failure of conservative therapy 5 patients of group 2 had surgery before 6 weeks. The remaining 31 patients underwent surgery after 6 weeks. Preoperative ERCP was indicated in 2 and 11 patients in groups 1 and 2 respectively ($p < 0.001$). The median total hospital stay was 3.0 days for group 1 and 11.0 days for group 2 ($p < 0.001$). In terms of operation time, conversion rates, intraoperative cholangiography, postoperative ERCP, morbidity or mortality both groups were comparable ($p > 0.05$).**

Conclusion : **Laparoscopic cholecystectomy can be performed safely within 5 days after the onset of symptoms in patients with acute cholecystitis. Because of shortened total hospital stay and risk of failure of conservative therapy, early laparoscopic cholecystectomy should be favored.** (Acta gastroenterol. belg., **2014**, 77, **306-311**).

Key words : laparoscopic cholecystectomy, acute cholecystitis, conversion, operation time, ERCP, intraoperative cholangiography.

Introduction

Up to 15% of the Western adult population has gallstones, of which 1-4% becomes symptomatic each year (1). Acute cholecystitis is one of the major complications of gallstones, which is diagnosed in 10% - 35% of patients admitted for cholecystectomy (2). Until the 1980's, prospective randomized studies proved urgent open cholecystectomy beneficial for the management of acute cholecystitis in terms of reducing the morbidity rate and shortening the hospital stay in comparison with conventional conservative treatment with subsequent interval open cholecystectomy (3). With the introduction of laparoscopic cholecystectomy in 1987, the management strategy for acute cholecystitis dramatically changed. Although it seemed reasonable to apply the knowledge acquired from open gallbladder surgery to the laparoscopic technique, many authors remained rather skeptical. Early studies demonstrated early laparoscopic surgery for acute cholecystitis to be associated with a higher complication rate, a prolonged operation time and a higher rate of conversion to open surgery (4-5). Therefore, acute cholecystitis was once considered a relative contraindication for laparoscopic cholecystectomy, with a large proportion of surgeons in the early 2000s preferring to delay laparoscopic cholecystectomy for patients presenting acute gallstone-related cholecystitis (6). The accepted timing had generally been considered to be 6 weeks to 8 weeks after the onset of symptoms to allow resolution of the acute inflammation of the gallbladder (7).

The growing experience and improvement in laparoscopic skills and the several shortcomings of initial medical treatment followed by delayed laparoscopic cholecystectomy have once again swung the pendulum toward early laparoscopic cholecystectomy for the management of acute cholecystitis. Although the overall rate of biliary complications remains at least twice that of open surgery after more than two decades experience in laparoscopic cholecystectomy (8), three different meta-analyses have demonstrated that compared with delayed-interval laparoscopic cholecystectomy, early laparoscopic cholecystectomy provides benefit in terms of total hospital stay and shows no disadvantage in terms of conversion rates or postoperative complications (9-11). The aim of our study was to evaluate the results in our institution by defining early laparoscopic cholecystectomy within 5 days of symptoms. We retrospectively analyzed whether there is an increase in conversion ratio, total hospital stay, morbidity or mortality for laparoscopic cholecystectomy for acute cholecystitis "à chaud" within 5 days of symptoms, compared with delayed treatment.

Patients and methods

Patients

Over an 8-year period, ranging from January 2004 to December 2011, we retrospectively analyzed all patients in a prospectively kept database undergoing cholecystectomy in our surgical department at Ghent University Hospital, resulting in a total of 965 patients. Diagnosis

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and assessment of the severity of acute cholecystitis were performed according to the Tokyo Guidelines (12). Briefly, acute cholecystitis was diagnosed not only by clinical manifestation (Murphy's sign, upper abdominal pain, and fever) and laboratory data (elevated C-reactive protein and white blood cell counts) but also by imaging findings of ultrasonography and computed tomography (enlarged gallbladder and thickened gallbladder wall of > 4 mm). Severity was intraoperatively classified into 3 grades : grade I, mild acute cholecystitis without marked local inflammation of the gallbladder and organ dysfunction ; grade II, moderate acute cholecystitis with marked local inflammation of the gallbladder (pericholecystic abscess, hepatic abscess, gangrenous cholecystitis, and biliary peritonitis) ; and grade III, severe acute cholecystitis with organ dysfunction (cardiovascular, neurological, renal, or hematological dysfunction). Inclusion criteria were grade I and II acute cholecystitis. Patients with grade III acute cholecystitis or with suspicion of neoplastic process were excluded from this study. These criteria resulted in the inclusion of 136 patients treated for acute cholecystitis grade I or II.

The 136 patients were divided into two groups according to the timing of laparoscopic cholecystectomy from the onset of acute cholecystitis : group 1 received surgery within 5 days of onset of symptoms and group 2 received conservative therapy with delayed surgery. Of the 36 patients in group 2, five patients underwent surgery before 6 weeks because of insufficient therapeutic response to conservative therapy. The remaining 31 patients received conservative therapy and surgery after 6 weeks (Fig. 1). Conservative management consisted of analgesics, fluid replacement, antibiotics and naso-gastric-tube insertion if indicated.

Baseline patients characteristics were patients' age, American Society of Anesthesiology (ASA) classification and preoperative ERCP. Operative parameters were conversion from laparoscopic to open cholecystectomy, intraoperative cholangiography and operation time. Postoperative parameters were ERCP, the total hospital stay, short-term morbidity and mortality. Total hospital stay includes days spent in hospital during first admission for acute cholecystitis, second admission for elective cholecystectomy in patients with a delayed surgery and eventually the days spent in the hospital for recurrent cholecystitis or complications occurring during the interval period. Pathology reports were consulted to confirm the initial diagnosis.

Statistical Analyses

All statistical analyses were performed using SPSS Statistics 20 (SPSS, Chicago, IL, USA) in cooperation with the biostatistical unit of Ghent University. Since the data were not normally distributed non parametric descriptors median and range were calculated. For a continuous variable Mann-Whitney U-test was used and 95% confidence interval was calculated. In case of a categorical variable Pearson Chi square test was used and odds ratio including 95% confidence interval of the odds ratio was calculated. Odds ratio was not possible to calculate for ASA-classification, so 95% confidence interval of the p-value was calculated. A two-sided value of $p < 0.05$ was considered statistically significant.

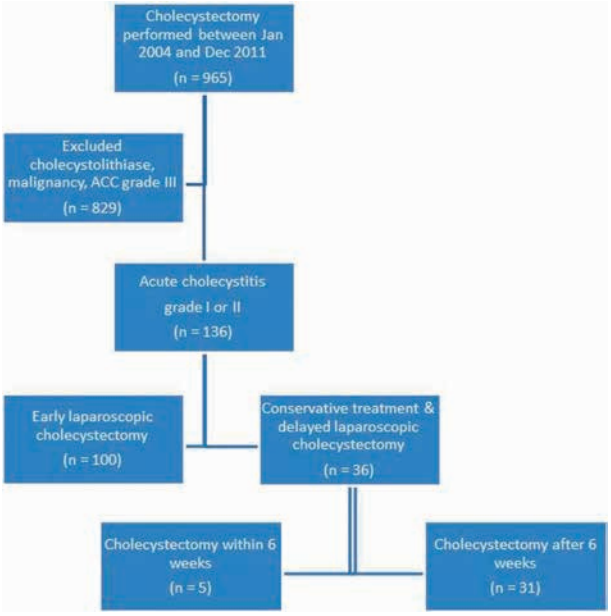

Fig. 1. — Population of patients included in the study

Results

Overall results

A total group of 136 patients was diagnosed with acute cholecystitis grade I or II. The median age was 67.0 years (range 21-94). Median ASA-classification score was 2.0 (range 1-3).The median age and ASA-classification score for each group are shown in table 1. Analyses revealed no significant difference in age distribution or ASA-classification between the study groups ($p = 0.154$ [0.09-0.22] and $p = 0.066$ [0.02-0.11] respectively). The sex distribution was 42.6% female and 57.4% male.

One hundred patients (73.5% of the total study population) underwent laparoscopic cholecystectomy within 5 days after onset of symptoms (group 1). The remaining 36 patients (26.5%) were treated with conservative therapy (group 2). Regarding the reason to choose conservative therapy 3 different reasons were identified. Fifteen patients (41.7% of group 2 patients) had a duration of symptoms longer than 5 days at the time of presentation to the surgeon. Seven patients (19.4% of group 2 patients) were treated conservatively because of other reasons : 2 patients had cardiac contra-indications for surgery, one patient was on a holiday, one patient was being treated with chemotherapy because of metastasized ovarian carcinoma, one patient was diagnosed with pericholecystitis including the head of the pancreas, one

Table 1. — **Descriptive parameters of the study groups (median and range)**

Age	Group 1 (n = 100)	65.5 (21-94)	*p = 0.154 [0.09-0.22]*
	Group 2 (n = 36)	67.5 (37-86)	
ASA-classification	Group 1 (n = 100)	2.0 (1-3)	*p = 0.066 [0.02-0.11]*
	Group 2 (n = 36)	2.0 (1-3)	

patient was initially misdiagnosed as pyelonephritis and another patient with a kidney transplant was not presented to the surgeon in the initial phase and treated conservatively by the nephrologists. The remaining 14 patients (38.9% of group 2 patients) were given antibiotics immediately at the time of presentation to the gastroenterologist, not being presented to the surgeon even though these patients did not have symptoms longer than 5 days. In 31 patients (22.8% of the total study population) laparoscopic cholecystectomy was performed after 6 weeks, while only 5 patients (3.7%) needed urgent cholecystectomy prematurely because of failure of conservative therapy.

Preoperative management

Preoperative ERCP was performed in a small group of patients (n = 13, 9.6%). The indication for this procedure was related to suspicion of choledocholithiasis with cholestasis and/or cholangitis in all cases. Preoperative ERCP in group 1 and 2 was distributed into 2 and 11 patients respectively (Table 2). The two patients of group 1 showed no signs of choledocholithiasis. Six out of eleven patients in group 2 showed common bile duct stones. One of these patients needed an urgent cholecystectomy within 6 weeks, due to renewed symptoms. All patients with bile duct stones on ERCP underwent papillotomy and extraction of the stones. Analysis showed a significant difference between the study groups regarding preoperative ERCP ($p < 0.001$, OR 21.56 [4.49-103.56]). Additional intraoperative cholangiography was performed in two patients (5.56%) of group 2, which did not reveal any signs of lithiasis. None of the 13 patients needed postoperative ERCP.

Intraoperative developments

The median operation time, including conversion, was 90.0 minutes (range 30-300) in the total study population. Looking at the separate groups, median operation time was 87.5 minutes (range 30-300) in group 1 and 91.50 minutes (range 35-285) in group 2 (Table 2). No significant difference ($p = 0.610$ [0.53-0.69]) was found when comparing operation times of both groups.

Conversion from laparoscopic to open cholecystectomy was indicated in 7.4% (n = 10) of the total study population. In group 1 conversion was performed during six operations (6.0%), while in group 2 four patients (11.1%) needed conversion (Table 2). None of the patients that had surgery before 6 weeks needed conversion. The main reason for conversion was difficulty in exposure and dissection of Calot's triangle because of adhesions and inflammation obscuring a clear anatomy. There was no significant difference between the groups concerning conversion rates ($p = 0.455$, OR 1.96 [0.52-7.38]).

Intraoperative cholangiography was performed in 19.0% (n = 26) of the total study population, respectively in 19 (19.0%) and 7 (19.4%) patients in group 1 and 2 (Table 2). The main reasons for cholangiography included preoperative laboratory rise in cholestatic parameters or unclear biliary tract anatomy. Of the 26 executed cholangiographies, only six (23.1%) revealed lithiasis of the biliary tract. Two of the seven patients in group 2 already underwent ERCP preoperatively, as mentioned above. One of the patients in group 1 needed postoperative ERCP because of inability to clear common bile duct stones intraoperatively. No significant difference was found between the study groups ($p = 1.000$, OR 1.03 [0.39-2.70]).

Table 2. — **Pre-, intra- and postoperative management**

Preoperative ERCP	Group 1 (n = 100)	2	2.0%	*p < 0.001, OR 21.56 [4.49-103.56]*
	Group 2 (n = 36)	11	30.6%	
Operation time	Group 1 (n = 100)	87.5 min	(30-300)	*p = 0.610 [0.53-0.69]*
	Group 2 (n = 36)	91.5 min	(32-285)	
Conversion	Group 1 (n = 100)	6	6.0%	*p = 0.46, OR 1.96 [0.52-7.38]*
	Group 2 (n = 36)	4	11.1%	
Intraoperative cholangiography	Group 1 (n = 100)	19	19.0%	*p = 1.000, OR 1.03 [0.39-2.70]*
	Group 2 (n = 36)	7	19.4%	
Postoperative ERCP	Group 1 (n = 100)	2	2.0%	*p = 0.608, OR 0.98 [0.95-1.01]*
	Group 2 (n = 36)	0	0.0%	

Postoperative management

In the postoperative setting, ERCP was indicated in two patients of group 1 (Table 2). No postoperative ERCP was performed in patients who received preoperative ERCP. The first patient underwent ERCP because of signs of cholestasis. This revealed papillary stenosis and common bile duct stones. A drain was left because of insufficient clearance of lithiasis and remaining stenosis. Four days later a second ERCP was done : all remaining lithiasis fragments were removed and a biliary prosthesis was left because of remaining stenosis. The second patient had an intraoperative cholangiography which showed common bile duct stones. However, since it was not possible to remove the stone intraoperatively, an ERCP with papillotomy was performed postoperatively, as mentioned earlier. All fragments were removed from the common bile duct. No significant difference was found between the study groups ($p = 0.608$, OR 0.98 [0.95-1.01]).

Complications classified according to Clavien-Dindo are shown in table 3. No significant difference was found between the groups ($p = 0.341$, OR 0.57 [0.20-1.65]). There was no mortality.

Hospital stay

Patients in group 2 had an additional median hospital stay for antibiotic therapy of 7.0 days prior to surgery. Analysis revealed a significant difference between the study groups ($p < 0.001$ [0.001-0.02]). Regarding the median postoperative hospital stay, patients of group 1 stayed 3.0 days in the hospital, while patients of group 2 only stayed 2.0 days. A significant difference was found ($p < 0.001$ [0.001-0.02]). The median total hospital stay was 3.0 and 11.0 days in group 1 and 2 respectively

Table 3. — **Complications classified by Clavien-Dindo with corresponding treatment**

Grade 1 : Any deviation from the normal postoperative course			
	Group 1 (n = 100)	1× Dysphonia	
		1× Pain left shoulder	
		1× Persisting fever for 24 hours	
		1× Trocar bleeding	
		1× Cor decompensation treated with diuretics	
Grade 2 : Complications requiring pharmacological treatment			
	Group 1 (n = 100)	3× Persisting inflammatory parameters	antibiotics
		1× Angina pectoris	isosorbide dinitrate
		1× Bile leak	conservative treatment
		1× Persisting constipation	fleet enema
	Group 2 (n = 36)	1× Pneumonia	antibiotics
		1× Urine retention	urine catheter
		1× Urine infection	antibiotics
Grade 3a : Surgical, endoscopic or radiological intervention not under general anesthesia			
	Group 1 (n = 100)	2× Cholestasis	ERCP
Grade 3b : Surgical, endoscopic or radiological intervention under general anesthesia			
	Group 1 (n = 100)	1× Small bowel perforation	surgical revision
		1× Abscess near trocar	surgical revision
		1× Abscess of the incision	surgical revision
		1× Bleeding left epigastric artery	surgical revision
	Group 2 (n = 36)	1× Drop in hemoglobin	surgical revision
Grade 4a : Life-threatening complication with ICU-care, single organ dysfunction			
	Group 1 (n = 100)	1× Acute on chronic kidney failure	ICU
		1× Respiratory problems	ICU
		1× Clotting problems with Marevan	ICU
		1× Oxygen desaturation	ICU
Grade 4b : Life-threatening complication with ICU-care, multi organ dysfunction			
		No grade 4b complications	
Grade 5 : Death of patient			
		No grade 5 complications	

Table 4. — **Hospital stay (median and range)**

Hospital stay for antibiotic therapy	Group 1 (n = 100)	0 days (0-0)	*p < 0.001 [0.001-0.02]*
	Group 2 (n = 36)	7.0 days (0-30)	
Postoperative hospital stay	Group 1 (n = 100)	3.0 days (0-39)	*p < 0.001 [0.001-0.02]*
	Group 2 (n = 36)	2.0 days (0-9)	
Total hospital stay	Group 1 (n = 100)	3.0 days (0-39)	*p < 0.001 [0.001-0.02]*
	Group 2 (n = 36)	11.0 days (0-31)	

(Table 4). These results reveal a significant difference between the groups, favoring patients who had cholecystectomy within 5 days after onset of symptoms ($p < 0.001$ [0.001-0.02]).

Discussion

The aim of this study was to determine if early laparoscopic cholecystectomy, defined as surgery within 5 days after the onset of symptoms of acute cholecystitis, can be considered as safe and effective as delayed cholecystectomy. The results show that the duration between the onset of symptoms of acute cholecystitis and the performance of laparoscopic cholecystectomy did not significantly influence almost any intraoperative or postoperative outcome, except for that of the total hospital stay. Although we could not find significant differences between early laparoscopic cholecystectomy within 5 days and the other timings of laparoscopic cholecystectomy, early laparoscopic cholecystectomy for acute cholecystitis in the patients treated in our hospital showed excellent results.

Regarding the characteristics of our study, some considerations should be made. First of all, since this is a retrospective analysis, the data might be biased and due to the low number of patients in group 2 firm conclusions cannot be drawn from these results. Thirdly, non-surgically treated patients were not analyzed in this study (for example : gallbladders that were percutaneously drained, old patients who received definitive treatment with ERCP or patients considered not fit for any intervention). And finally, patients in this study were operated by experienced hepatobiliary surgeons, so our results (relatively low conversion and complication rate) might not reflect the overall clinical practice.

The time limit for early laparoscopic cholecystectomy in our study population was surgery within 5 days of symptoms. A review of the literature of the past decade shows early laparoscopic cholecystectomy mostly defined as surgery within 3 days of symptoms. The same results however were drawn : compared with delayed-interval laparoscopic cholecystectomy, early laparoscopic cholecystectomy provided benefit in terms of total hospital stay, but not in terms of conversion rates or postoperative complications (9-11,13-16). So the use of 5 days in this study as the critical limit for early laparoscopic cholecystectomy can be considered as a fully-fledged extension of the time limit of 72 hours.

In this study, only 22 patients (61.1%) of group 2 were treated conservatively because of adequate reasons. Fifteen patients (41.7%) had a duration of symptoms longer than 5 days and 7 patients (19.4%) presented with contra-indications for surgery or other reasons making early laparoscopic cholecystectomy impossible. This implies that 38.9% (n = 14) of the patients treated conservatively could have been presented to the surgeon for early laparoscopic cholecystectomy within 5 days after the onset of symptoms. Looking more closely to the 5 patients in which conservative therapy failed, 3 of the 5 patients presented themselves after 3 to 4 days after the onset of symptoms without any contra-indications for surgery. While they were eligible for early cholecystectomy, they received conservative treatment with subsequently failure of the treatment and the need for an urgent laparoscopic cholecystectomy. In patients with no additional medical or surgical co-morbidity, early referral from both the general practitioner, specialists in internal medicine and gastroenterologists for surgical treatment should be the treatment of choice.

Concerning the preoperative management, ERCP was mostly performed in patients with delayed cholecystectomy. The indication for this procedure was related to cholestasis in all cases. One possible explanation for these results is the lack of communication between the different involved specialties, which causes patients to be seen by the surgeon after the critical limit of 5 days, making them directly group-2-patients with conservative therapy and often the need for preoperative ERCP.

There were no significant differences in morbidity between early and delayed laparoscopic cholecystectomy in low-risk patients. There were no cases of mortality in this study. In the literature the same conclusions are generally drawn (9-11,13-16). Recent studies however describe that patients operated on early base after hospital admission had significantly fewer complications than patients in whom surgery was delayed for a few days (15-16). Of the 36 patients who were treated conservatively, 13.89% patients needed cholecystectomy before 6 weeks. Although our analysis did not show any difference in outcome, other articles have reported worse outcome for these patients (17-18).

Delayed laparoscopic cholecystectomy with initial medical treatment for acute cholecystitis is associated with several shortcomings. First of all, several studies report up to 25% of patients who fail to respond to conservative treatment or develop early complications during the first admission. In more than 50% of these patients an urgent and technically demanding cholecystectomy is required (13,19). Secondly, up to 30% of the patients treated conservatively, are readmitted with recurrent symptoms and undergo an unplanned emergency cholecystectomy while waiting for their scheduled elective procedure. At last, during the early stages of acute inflammation, edematous connective tissue facilitates the dissection of the gallbladder and Calot's triangle (13). Although delayed-interval operation allows maturation of the acute inflammation, resultant fibrosis, neovascularization and contraction make the dissection technically difficult and the operation potentially hazardous (20). An increase in the duration of an operation may reflect the complexity and the technical challenges associated with the surgery, as in the case with laparoscopic cholecystectomy for acute cholecystitis. However, in this study, no significant differences could be found in operating time between the study groups.

Although the morbidity was similar, the longer post-operative stay in group 1 was related to some grade 4a complications. The total hospital stay was significantly longer in group 2 due to the initial admission for intravenous antibiotic therapy which lasted approximately one week. By extending the time limit to 5 days, the total hospital stay can be reduced in patients with acute cholecystitis who are eligible for immediate laparoscopic surgery.

Early laparoscopic cholecystectomy results in significantly shorter hospital stay and avoids the risks of failed conservative treatment. Hence, most surgeons consider early laparoscopic cholecystectomy as the optimum treatment for acute cholecystitis. This approach is well supported by the international consensus published as Tokyo Guidelines and its recent updates (12). We can only support these results with our findings.

Conclusion

This retrospective analysis shows that early laparoscopic cholecystectomy up to five days after the onset of symptoms is not associated with a higher percentage of post-operative complications, conversion to open surgery or mortality. It seems therefore as safe and effective as delayed cholecystectomy. Furthermore, the total length of hospital stay is significantly lower and there is no risk of readmissions attributable to recurrent acute cholecystitis because of the potential failure of conservative treatment. In patients with no additional medical or surgical co-morbidity, early referral from both the general practitioner and gastroenterologists for surgical treatment should be considered as the treatment of choice.

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