



RAPID COMMUNICATION

Timing of laparoscopic cholecystectomy for acute cholecystitis: A prospective non randomized study

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Abstract

AIM: To study the timing of laparoscopic cholecystectomy for patients with acute cholecystitis.

METHODS: Between January 2002 and December 2005, all American Society of Anesthesiologists classification (ASA) I, II and III patients with acute cholecystitis were treated laparoscopically during the urgent (index) admission. The patients were divided into three groups according to the timing of surgery: (1) within the first 3 d, (2) between 4 and 7 d and (3) beyond 7 d from the onset of symptoms. The impact of timing on the conversion rate, morbidity and postoperative hospital stay was studied.

RESULTS: One hundred and twenty-nine patients underwent laparoscopic cholecystectomy for acute cholecystitis during the index admission. Thirty six were assigned to group 1, 58 to group 2, and 35 to group 3. The conversion rate and morbidity for the whole cohort of patients were 4.6% and 10.8%, respectively. There was no significant difference in the conversion rate, morbidity and postoperative hospital stay between the three groups.

CONCLUSION: Laparoscopic cholecystectomy for acute cholecystitis during the index admission is safe, regardless of the time elapsed from the onset of symptoms. This policy can result in an overall shorter hospitalization.

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Key words: Acute cholecystitis; Laparoscopic cholecy-

INTRODUCTION

Laparoscopic cholecystectomy (LC) has been established as the treatment of choice for the management of acute cholecystitis (AC), despite initial reservations, regarding the impact of this policy on the conversion rate and morbidity^[1]. Several prospective randomized trials^[2-4] suggest the superiority of early (within 72 h) over the delayed (after a few weeks interval) intervention. This 72 h limit, however, is difficult to be kept in many cases for a variety of reasons, referring to both patients and physicians. On the other hand, there is a paucity of solid data as to what happens in the period after this 72 h time frame. The speculation of a worse outcome, when attempting LC for AC during the urgent admission beyond this very early phase, is experience rather than evidence-based.

In our daily practice, we have realized that only a small number of patients with AC are managed surgically within this "gold window" of 72 h from the onset of symptoms. If the remaining majority of patients with AC are managed conservatively with interval cholecystectomy to follow, then an increased total hospitalization and subsequently increased cost can be expected. Furthermore, the subgroup of patients who do not respond to conservative treatment, as well as those who relapse while awaiting an interval cholecystectomy should be considered^[5]. For these reasons, we have adopted a policy of performing a LC during the initial emergency/urgent admission for "all comers" with AC, regardless of time delay between its onset of symptoms and surgery.

In view of this policy, we examined prospectively the impact of the duration of symptoms on mortality, morbidity, conversion rate and postoperative hospital stay in patients who underwent LC for AC during the urgent (index) admission.

MATERIALS AND METHODS

Subjects

Between January 2002 and December 2005, all American Society of Anesthesiologists classification (ASA) I, II and III patients admitted or referred to our unit with AC under the care of one consultant surgeon (GT) with a special interest in HPB and laparoscopic surgery, were treated with LC during the index admission, regardless of the time elapsed from the onset of symptoms. ASA IV patients were usually offered ultrasound-guided percutaneous cholecystectomy and therefore, were excluded from the study. Patients were considered having AC when they had five out of the following six positive criteria: persistent right upper quadrant pain, temperature > 37.5°C, WBC > 10 × 10⁹/L, positive Murphy's sign, presence of gallstones on ultrasound in combination with wall thickening and/or fluid at the gallbladder fossa. The diagnosis of AC was confirmed by intraoperative findings and pathologic specimens. Patients with strong evidence of concomitant common bile duct (CBD) stones were not excluded from the study, but were treated initially with preoperative endoscopic retrograde cholangiopancreatography (ERCP), sphincterotomy and CBD clearance, followed by LC after an interval of at least 24 h, in order to assure that no ERCP-related complication occurred. Patients with suspicion of CBD stones had preoperative MRCP, and if stones were detected, they were treated as above. Intraoperative cholangiogram was not performed in any of the cases. There were no other selection criteria and every effort was made to operate on all the patients as soon as theatre time was available, provided that any concomitant medical problem was previously dealt with. The latter resulted sometimes in what is called in the literature "physician delay"^[6]. Laparoscopic cholecystectomy was attempted in all cases under general anesthesia. The usual four-trocar technique was used (10 mm umbilical, 10 mm subxiphoid, 5 mm subcostal midclavicular line, 5 mm anterior axillary line) but additional trocar was used as necessary. The gallbladder was aspirated in most of the cases in order to be grasped, and dissection of the Calot's triangle structures was always performed close to the gallbladder wall. Retrograde dissection was only exceptionally performed, when in doubt about the triangle's structures after the initial dissection.

Methods

The patients were divided in three groups according to the time between onset of symptoms and operation: (1) within 3 d (early group), (2) between 4 to 7 d (intermediate group) and (3) ≥ 8 d (delayed group). All data including demographics, preoperative, operative findings and postoperative information were collected prospectively into a computerized database. The episode of AC was considered simple (oedematous, hydrops) or complicated (emphyema, gangrenous, emphysematous, concomitant choledocholithiasis or pancreatitis). The aim of the study was to detect the impact of the time elapsed from onset of symptoms to operation on the conversion rate, 30-d mortality, 30-d morbidity with special attention to bile duct injury incidence and length of postoperative hospital stay.

Table 1 Impact of delay in laparoscopic cholecystectomy on outcomes

Outcome	I: ≤ 3 d (n = 36)	II: 4-7 d (n = 58)	III: ≥ 8 d (n = 35)	P
Conversion rate	1 (2.8%)	2 (3.4%)	3 (8.5%)	NS
Mortality	0	0	0	NS
Morbidity	3 (8.3%)	6 (10.3%)	5 (14.2%)	NS
Postop hospital stay	2 (1-6) d	2 (1-14) d	2 (1-35) d	NS

NS: no significant difference.

Statistical analysis

Statistical analysis was performed using the Arcus Quickstat biomedical statistical package (Research Solutions, UK) with the median values for continuous variables presented with range in parentheses. Fisher's exact test and Mann Whitney U test were used as appropriate to compare the groups to each other. $P < 0.05$ (two-tailed test) was considered statistically significant.

RESULTS

One hundred and twenty-nine patients underwent LC for AC during the index admission according to the protocol. During the same period some 453 elective laparoscopic cholecystectomies were performed by the same team. Thirty-six of the patients with acute cholecystitis (28%) had their operation within the first 3 d from the onset of their illness, 58 patients (45%) between 4 to 7 d and the other 35 patients (27%) after the first week. None of our patients had a more than 48 h delay due to unavailability of theatre space. Any other delay from the onset of symptoms to operation was attributed to either patients' delayed presentation/referral to our unit or to concomitant medical problems needing to be addressed preoperatively. Special mention should be made of a subgroup of patients with AC whose surgery was delayed due to the intake of anti-coagulants or more often anti-platelet agents, due to the dramatically increased use of these drugs during the last decade.

The impact of timing of LC on outcomes is shown in Table 1. Although the conversion rate was somewhat higher in the "delayed" group, this difference was not significant when this group was compared to either the "early" ($P = 0.35$, Fisher's exact test) or the "intermediate" group ($P = 0.36$, Fisher's exact test). Similarly, there was no significant difference in mortality, morbidity and postoperative hospital stay between the three groups of patients. Interestingly, this was noted despite the fact that a significantly higher number of complicated cases of AC were found among patients of the "intermediate" group, compared to those who underwent earlier operations. This was also reflected on the operative time difference between the groups (Table 2). No major bile duct injuries occurred. Four cases had bile leak, two in the "intermediate" group and two in the "delayed" group. The first was attributed to the gallbladder fossa, the second from an avulsed cystic duct and the remaining two from a friable cystic stump.

The first case eased spontaneously after 48 h, the other three cases with bile leak were treated successfully with ERCP, sphincterotomy and stenting of the common bile duct. Other complications and their treatment are shown in Table 3.

DISCUSSION

Acute cholecystitis which is generally found in approximately 20% of all admissions for gallstone disease^[7] is no longer considered a contraindication for laparoscopic cholecystectomy. In fact, urgent LC is now considered the optimal treatment of patients with AC^[1]. Early LC has been proven superior to delayed interval LC in most of the prospective randomized trials. It results in a shorter hospital stay and a shorter recuperation time while the conversion rate and morbidity remain similar with or even lower than delayed interval LC^[2-4]. How early is “early” is not clear in the literature, as this parameter has not been effectively tested in controlled randomized trials. All these prospective randomized trials comparing early and delayed interval LC, refer to the first 48-72 h for the early group, making this group somewhat highly selected. In daily practice very few patients are able to have surgical treatment during this short period of time, due to either patient or/and physician delay^[6]. Very often patients present with delay or they are referred with delay by their physicians. Others suffer from co-morbidities needing consultation with other specialties preoperatively, while some require other intervention preoperatively, i.e. ERCP. A significant number of patients take oral anti-coagulants or anti-platelet agents requiring reversing before surgery. For all these reasons many patients in reality cannot have surgery within this time frame. In the present series some 72% of patients with acute cholecystitis were treated surgically during the index admission beyond the 72 h boundary, which is not very different from the reported experience by other authors^[8-10]. There were no solid data regarding the optimal policy for this large group of patients treated outside this 72 h boundary. To our knowledge, there is only one small prospective randomized trial designed to address this issue^[11]. Chandler *et al*^[11] found that there is no difference in the conversion rate or morbidity between the early group (n : 21, surgery as soon as theatre schedule allowed) and the delayed group (n : 22, surgery during the index admission, after resolution of symptoms or failure to resolve on 5 d course of conservative treatment). Results from other comparative non-randomized trials of early and delayed LC during the urgent admission for AC are rather conflicting and most of these however indicate a higher conversion rate for the delayed group, but no difference in morbidity^[6,8,9,12-14]. The definition of the so called “early” group among trials is also confusing. Some trials define early group counting from the time of admission or diagnosis rather than the time of onset of symptoms. This could be sometimes misleading, as the onset time of episode could differ significantly from the time of admission. We believe that counting from the onset of symptoms is more representative of the reality. Furthermore, all the studies were designed by using a boundary either of 48, 72 or 96 h from either onset of symptoms or time of admission, in order

Table 2 Demographic and perioperative characteristics of patients with acute cholecystitis

Characteristic	I: ≤ 3 d (n = 36)	II: 4-7 d (n = 58)	III: ≥ 8 d (n = 35)
Male / Female	15/21	19/39	16/19
Age (median)	55 (19-76) yr	65 (24-87) yr ^b	62 (30-81) yr ^a
ASA (I/II/III)	18/13/5	23/25/10	14/15/6
Complicated cholecystitis	9	34 ^b	15
Preoperative ERCP	2	10	8 ^a
Spillage	21	39	18
Drain use	17	32	19
Operative time	55 (35-90) min	62.5 (25-120) min	72.5 (35-120) min ^a

^a $P < 0.05$, ^b $P < 0.01$ vs group I.

to compare the two groups of population. They included invariably patients who had surgery within the first 7 d for comparison. In our study, the patients were divided into three groups, including those who were treated surgically during the index admission even beyond one week from the onset of their illness.

Our findings are in accordance with previous studies, suggesting the safety of early LC for AC. The present study, however, does not support the findings of earlier reports, regarding the rising conversion rate, when LC for AC is performed after 72 h^[6,12,15]. Our data have shown that the timing of cholecystectomy does not influence the conversion rate, as recently shown by others^[8,10]. This is probably attributed to the very low conversion rate in the whole group of our patients, making any differences between the subgroups insignificant. Our total conversion rate of 4.6% for LC in AC is one of the lowest in the literature and only slightly higher than that in our team's experience with elective LC for the same period (~1%). Even one week after the onset of symptoms there was nothing to suggest increased risk with regards to the conversion rate and morbidity; this has never been challenged before. Another issue of concern in laparoscopic treatment of AC is the presumed increased risk of bile duct injury when the procedure is performed beyond the early edematous phase of the first 48-72 h. Our data do not support this traditional belief, as there was no major bile duct injury in any of the patients. It is possible that the majority of patients with AC who are deferred for interval LC because they are outside this “early window of chance” are faced with a “difficult” elective cholecystectomy after few weeks^[16]. Waiting for the gallbladder to “cool down” allows maturation of acute inflammation, neovascularization, fibrosis, and contraction, making the dissection more difficult, as it has been proposed by others^[9]. While inflammation in the early stages may not necessarily involve Calot's triangle structures, chronic inflammation may scar and distort it, making dissection in this critical area more difficult and prone to bile duct injuries.

In conclusion, our data show that LC for AC during the index admission is safe and associated with a low morbidity and a low conversion rate. These findings refer not only to those patients who undergo surgical treatment very

Table 3 Complications and their treatment

Group 1: ≤ 3 d (n = 36)	Group 2: 4-7 d (n = 58)	Group 3: ≥ 8 d (n = 35)
(1) Subhepatic collection Laparoscopic drainage	(2) Bile leaks ERCP and CBD stent Spontaneous closure at 48 h	(2) Bile leaks ERCP and CBD stent
(1) Bleeding Laparotomy d 1	(1) Subhepatic collections Percutaneous CT guided drainage Laparotomy after failed percutaneous	(1) Bleeding from drain site Drain removal
(1) Wound infection (converted) Wound opening	(1) Re-admission at postop day 15 with cholangitis ERCP & sphincterotomy (1) Chest infection Antibiotics, physiotherapy	(1) Severe pancreatitis ICU admission (1) Readmission at postop d 6 with DVT Heparin

Complications are presented with parentheses to indicate the number of patients suffered the complication; under the complication line the way of management for each case (without numbers) is presented.

early, but also to those treated after the window of the first 3 or 7 d from the onset of symptoms. Further prospective randomized trials focusing on this particular question are required to validate these results. However, it appears reasonable to state that in units with expertise in laparoscopic surgery, every effort should be made to operate on all patients with AC during the index admission as soon as diagnosis is made and co-morbidities are dealt with, regardless of the time delay from the onset of symptoms. This policy is safe, not associated with a higher conversion rate or morbidity and results in an overall shorter hospitalization by avoiding re-admissions.

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