World J Surg (2017) 41:1762–1768
DOI 10.1007/s00268-017-3928-4

ORIGINAL SCIENTIFIC REPORT

Delayed Laparoscopic Cholecystectomy for Acute Calculous Cholecystitis: Is it Time for a Change?

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Published online: 1 March 2017

Abstract

Background Our aim was to evaluate the advantages and limitations of delayed laparoscopic cholecystectomy (LC) in a tertiary center.

Materials and methods A retrospective analysis of all patients admitted to our institution with acute calculous cholecystitis (ACC) between January 2003 and December of 2012 was performed. Data collected included patient demographics and comorbidities, presenting symptoms, laboratory findings, imaging results, length of stay (LOS), time to surgery, and surgical complications.

Results A total of 1078 patients were admitted with ACC. There were 593 females (55%), and the mean age was 57 ± 0.6 years. Mean LOS at initial admission, re-admission until surgery, and following surgery was 7.9 ± 0.2, 1.5 ± 0.1, and 3.4 ± 0.2 days, respectively. Percutaneous cholecystostomy (PC) tube was inserted in 24% of the patients. Only 640 (59%) patients eventually underwent LC. Mean time to surgery was 97 ± 9.8 days, and 16.4% of patients were readmitted in this time period resulting in a mean total LOS of 10.6 ± 0.2 days. Conversion rate to open surgery was 5.8% and bile duct injury occurred in 1.1%. Postoperative complications occurred in 9.8% of the patients, and 30-day mortality was 0.6%. Patients with more severe inflammation according to Tokyo Criteria grade were more likely to undergo PC, were more likely to be readmitted while waiting for LC, and also had more postoperative complications.

Conclusions Delayed LC is associated with significant loss of follow-up, long LOS, and higher than expected use of PC. Conversion rates are lower than in the literature while rates of bile duct injury and mortality are comparable. We believe these data as well as the available literature are sufficient to change our hospital policy regarding the surgical treatment of ACC from delayed to early same admission surgery in appropriate cases.

Introduction

Acute calculus cholecystitis (ACC) is one of the most common diseases in general surgery [1]. Gallstones are present in up to 15% of the adult population and 4% of these patients become symptomatic every year [2]. More than half a million cholecystectomies are performed in the USA each year, and almost all are due to symptomatic cholelithiasis [3].

ACC is caused by initial sterile inflammation as a result of cystic duct obstruction, followed by secondary bacterial

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infiltration. Clinical symptoms include right upper quadrant abdominal pain, fever, nausea, and vomiting. Right upper quadrant tenderness is noted in physical examination. Laboratory findings include elevated white cell count and C-reactive protein. Ultrasonography can support the diagnosis by demonstrating a distended gallbladder filled with gallstones, increased thickness of the gallbladder wall or pericystic fluid [4].

In young healthy individuals, laparoscopic cholecystectomy (LC) is the treatment of choice [5]. There are two main approaches to the timing of LC. The early LC approach is to perform the operation within the first days after the initial presentation of symptoms. In the delayed approach, LC is performed as an elective procedure several weeks following a conservative treatment with a course of intravenous antibiotics [2]. There is more and more evidence supporting that early LC has some advantages namely shorter LOS and decreased hospital costs. [6–9] Percutaneous cholecystostomy (PC) is reserved as a salvage procedure in patients too moribund to undergo cholecystectomy or in patients in which conservative treatment with antibiotics has failed [5]. This procedure is associated with several complications including longer hospitalization, more readmissions, and increased 30-day morbidity and mortality rates [10–13]. Ideally PC should be followed by cholecystectomy in those who are able to undergo the procedure.

Some unresolved issues regarding the timing of cholecystectomy still remain. Most trials have shown improved cost and decreased LOS [6–9]. Some trials showed increased morbidity with delayed LC mostly due to biliary disease while patients await surgery [6]. Previous reports did not find differences in bile duct injury and mortality between early and delayed LC [2]. Additional issues that have not been thoroughly investigated include loss to follow-up and the extent of PC use during the cool down period. We hypothesized that loss to follow-up would be a minor problem and that PC would be used on a minority of patients.

At the Department of Surgery at Hadassah-Hebrew University Medical Center delayed cholecystectomy is practiced due to logistical constraints. Our hospital is geared toward performing cholecystectomies as elective and not as acute care procedures. Performing early LC would require a change in both the logistics and the infrastructure of the hospital. Over the years, delayed LC has proved to be associated with low complication rate and satisfactory outcomes. The aim of this study is to evaluate the advantages and limitations of delayed LC and compare our results to existing literature on the outcomes of early cholecystectomy.

Materials and methods

Approval by the institutional review board (IRB) at Hadassah-Hebrew University Medical Center was obtained prior to data collection. We retrospectively reviewed the charts of all patients admitted to our institution with ACC between January 1, 2003, and December 31, 2012. Identification of these patients was done according to the International Statistical Classification of Diseases and Related Health Problems (ICD-9), and ACC was defined according to the Tokyo criteria [4].

Recorded data included: patient demographics, clinical presentation, and laboratory tests of the index admission. Patient demographics included age, gender, comorbidities, prior biliary symptoms, and previous surgical history. Clinical presentation included positive findings on physical examination, concurrent cholangitis or pancreatitis and relevant sonographic findings. Laboratory results included, total and direct bilirubin, serum amylase, aspartate and alanine aminotransferase, alkaline phosphatase, gamma glutamyl transpeptidase, serum creatinine, and white blood cell count (WBC). All patients were classified according to the severity of cholecystitis according to the Tokyo Criteria [4].

Additionally, we recorded information regarding hospitalization, interventions of PC and surgery as well as loss to follow-up. Hospitalization information included, length of stay (LOS) calculated as a sum of all admissions, number of hospitalizations, and number of admissions to the emergency department (ED).

LC was conducted with the widely accepted four-port technique. Surgery was performed by 12 experienced, attending surgeons, who had performed at least 300 previous cholecystectomies. Surgical variables recorded were: time to surgery, operative time, conversion to open surgery, and intraoperative complications. Postoperative course was examined for complications within 30 days of surgery, biliary related complications, need for endoscopic retrograde cholangiopancreatography (ERCP), readmissions to the ED, hospital readmissions, and mortality.

Statistical analysis

To identify differences between the groups, univariate analysis with Chi-square and *t* test were used as appropriate. Statistical calculations were completed using statistical software SPSS version 20 (SPSS, Inc., Chicago, Il), and a p value <0.05 was considered to represent statistical significance for all comparisons. Data are presented as the median or mean $\pm$ standard error of mean, as appropriate.

Table 1 Comparison of patients according to Tokyo cholecystitis grade

Variable	Grade I (N = 690, 64%)	Grade II (N = 325, 30%)	Grade III (N = 63, 6%)	*p* value *(significant)
Age (years)	55.6 ± 0.74	57.1 ± 1.11	73.7 ± 1.59	<0.001*
Gender (% females)	55.7%	53.5%	55.6%	0.800
Cholecystostomy (%)	14.5%	36.0%	61.9%	<0.001*
Surgery (%)	57.8%	64.9%	30.2%	<0.001*
Mean time to surgery (days)	90.2 ± 8.82	108 ± 16.1	115 ± 12.8	0.575
Readmissions (%)	7.97%	14.7%	15.9%	<0.0015*
Mean operative time (minutes)	117 ± 5.46	115 ± 3.98	150 ± 14.6	0.460
Conversion (%)	4.76%	7.58%	5.26%	0.360
Bile duct injury (%)	0.50%	2.37%	0%	0.100
Postoperative complications	8.02%	13.3%	21.1%	0.035*

Results

During the study period, 1078 patients were admitted to our institution with the diagnosis of ACC. Of the entire cohort, there were 593 females (55%) and the mean age was 57 ± 0.6. Mean body mass index (BMI) was 27.9 ± 0.1.

Eight hundred and forty (78%) patients underwent ultrasonography upon admission. Other patients were either diagnosed clinically or by aid of computed tomography. Common sonographic findings included: cholelithiasis (82%), wall thickening (80%), pericystic fluid (29%), and positive sonographic Murphy's sign (13%).

Mean LOS at index admission was 7.9 ± 0.2 days. While awaiting delayed surgery, 18.2% of patients returned to the ED and 16.4% were readmitted resulting in an additional mean LOS of 1.5 ± 0.1 days. The patients who were readmitted were older (60.6 ± 2.12 vs. 51.8 ± 0.75 years), more often had renal failure (12.2 vs. 2.20%), had higher Tokyo Criteria grade (see Table 1), had a longer index admission (8.4 ± 0.47 vs. 6.99 ± 0.20 days), and were more likely to require PC (65.3 vs. 22.1%). Mean LOS following delayed cholecystectomy was 3.4 ± 0.2 days. The cumulative LOS from index admissions to discharge following delayed cholecystectomy was 10.6 ± 0.2 days (Fig. 1).

Of the entire cohort, 256 patients (24%) required insertion of a PC tube during their index admission and the data for this group was recently published [13]. As opposed to the entire cohort, these patients were more often male (54 vs. 45%, $p < 0.005$) and were significantly older (67.4 ± 0.9 vs. 53 ± 0.7 years, $p < 0.005$). This group

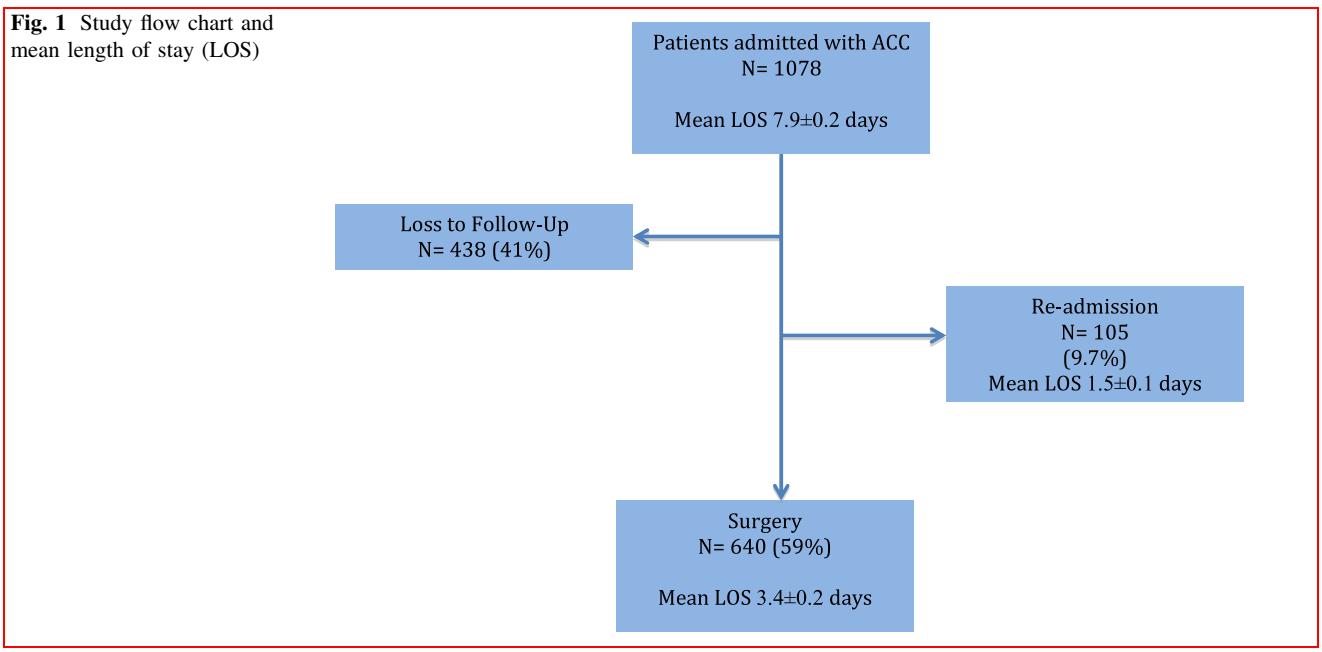

Fig. 1 Study flow chart and mean length of stay (LOS)

Table 2 Summary of randomized controlled studies (with over 30 patients in each arm) and meta-analyses comparing early versus delayed cholecystectomy

Study/ Year	Design	Early cholecystectomy					Delayed cholecystectomy				
		Number of patients	Overall LOS (days)	Conversion to open surgery	Bile duct injury	Mortality	Number of patients	Overall LOS (days)	Conversion to open surgery	Bile duct injury	Mortality
Lo et al. [15]	RCT	45	6.0	11.1%	0%	0%	41	11.0	22.0%	2.4%	0%
Lai et al. [17]	RCT	53	7.6	20.8%	0%	0%	51	11.6	21.6%	0%	0%
Johansson et al. [18]	RCT	74	5.0	31.1%	0%	0%	71	8.0	28.2%	1.4%	0%
Macafee et al. [21]	RCT	36	6.0	2.8%	N/A	N/A	36	6.0	2.8%	N/A	N/A
Gutt et al. [8]	RCT	304	5.4	9.9%	N/A	0.3%	314	10.0	10.5%	N/A	0.3%
Saber et al. [19]	RCT	61	2.4	4.9%	N/A	N/A	59	5.7	1.7%	N/A	N/A
Gurasamy et al. [2]	Meta-analysis	244	6.1	19.7%	0.4%	0%	244	9.0	22.1%	0.6%	0%
Wu et al. [20]	Meta-analysis	809	4.8	12.0%	0.7%	0.3%	816	8.3	13.1%	0.7%	0.3%

had more comorbidities including HTN, DM, CRF, CAD, COPD, dialysis, cirrhosis, and atrial fibrillation. These patients experienced more complications including: 14% accidental ejection of the PC tube, 11% reinsertion of a PC, and 5% peri-tubal leakage. Additionally, 8.2% of patients with PC were readmitted to the ED and 4.7% were readmitted.

Only 640 (59%) patients eventually underwent cholecystectomy at our institution (Fig. 1). Mean time from index admission to surgery was 97 ± 9.8 days. In this time period, 16.4% of patients required readmissions for a mean of 1.5 ± 0.1 days. Laparoscopy was the initial surgical approach in 98% of the cases, and conversion rate to open surgery was 5.8%. Mean operative time was 117 ± 4 min. Drains were utilized in 22.6% of cases as per surgeons' discretion.

Intra- or postoperative bleeding occurred in 3.6%, superficial surgical site infection (SSI) in 2% and deep SSI in 4%. Bile leak from the cystic duct was noted in 3.8%, and common bile duct (CBD) injury was identified in 1.1% of cases. These included two cases of side injury to the common bile duct (type D injury) and five cases of common bile duct transection (type E injury). Thirty-two patients (4.7%) required ERCP after surgery and of these 7 suffered from post-ERCP pancreatitis. Mean LOS following surgery was 3.4 ± 0.2 days. Eighteen percent of patients were referred to the ED during the first 90 days following surgery, and 10.2% of these patients were readmitted. Thirty-day mortality following surgery was 0.6% (four patients), and the cause of postoperative death in all cases was attributed to septic shock most likely due to bile leakage.

Significant differences were identified when comparing patients according to the Tokyo grading of cholecystitis severity (Table 1). Patients with Tokyo grade 3 were older, more often required PC insertion, were less likely to undergo surgery, had more readmissions while awaiting surgery, and had more postoperative complications (Table 1). There was no statistically significant difference between the groups in terms of gender, time to surgery, operative time, or conversion to open surgery rate. Although not significantly different, the rate of bile duct injury was higher for grade 2 patients as compared to grade 1.

Discussion

Despite the growing body of evidence of the advantages of early LC for ACC, our institution practices the delayed LC approach. This is mostly due to logistical limitations influenced primarily by operating room availability, high volume of trauma patients, and understaffed OR. Our data present some limitations of this approach. The delayed approach is associated with considerable loss to follow-up, as well as liberal use of PC particularly in patients with

Tokyo grade 3 cholecystitis. While waiting for surgery, a significant minority was readmitted to the hospital with biliary tract disease or with PC tube complications. More severe cases of cholecystitis were more likely to be readmitted. The overall rate of conversion to open surgery was low. Length of stay, bile duct injuries, and mortality were comparable to previous reports in the literature.

The first drawback of the delayed approach is the higher than expected use of PC at initial admission. Nearly a quarter of our patients (24%) required the insertion of PC. and this was frequently associated with tube related complications. Moreover, we have recently demonstrated that PC is associated with increased perioperative complications including bile duct injury, bleeding, and SSI [13]. PC has been recognized as a definitive procedure for ACC in a selective group of old and high-risk patients [14].

Another obvious and striking shortcoming of the delayed approach is loss to follow-up. Four hundred and thirty-eight patients (41%) were not operated on at our institution. It is encouraging to think that by simply changing hospital policy in favor of early LC, we could nearly double the volume of LC at our institution. Poor adherence to discharge recommendations, suboptimal follow-up, and limited operating room slots are the primary reasons for the length of time between initial admission and surgery. Although our team recommends cholecystectomy six weeks after the initial hospitalization, mean time to surgery in the cohort was nearly 14 weeks.

Several studies have demonstrated that early LC is associated with a significantly shorter LOS as compared to delayed LC [2, 8, 15–20]. Our cumulative LOS in this study was 10.6 ± 0.2 days and compares somewhat favorably to other studies on delayed LC. [2, 8, 15, 17–21] This can be explained by the high loss of follow-up rate where a significant portion of our cohort did not undergo surgery and therefore did not require an additional admission for this purpose.

Additionally, 16.4% of patients were readmitted due to gallstone-related disease from the time of index admission and while awaiting their elective delayed cholecystectomy. All these admissions and related health care cost would have been avoided if the early approach to surgery were implemented at our institution.

This is not to say the delayed LC does not have some advantages namely low conversion rate of 5.8% for our cohort. Previous randomized controlled trials have shown a conversion rate between 3 and 30% for LC due to ACC (Table 2) [8, 15–19, 21]. Meta-analyses have demonstrated the conversion rate to be between 12 and 22% (Table 2) [2, 20]. It is possible that the long time between ACC admission and surgery allowed sufficient convalescence for the anatomy to be more easily identifiable. A low conversion rate is one of the advantages pointed out by the delayed LC advocates. The rate of bile duct injury in this study was comparable to the high side of reports in the literature at 1.1%. Strikingly the rate of bile duct injury for patients with Tokyo grade 1 was only 0.5% as compared to 2.4% for grade 2 patients (not significant). A mortality rate of 0.6% was also comparable to previous published reports [20, 22, 23]. Intraoperative cholangiography and selective use of subtotal cholecystectomy were not routinely performed. It is possible that judicious utilization of these techniques could reduce rates of bile duct injury.

All patients were divided into three grades of cholecystitis severity according to the Tokyo Criteria. Patients with grade 3 cholecystitis were older. Over 60% of these patients underwent cholecystostomy. Only 30% of these patients eventually underwent cholecystectomy, and when they did they experienced more complications. It is inferred that cholecystostomy was used as a definitive procedure in significant subset of Tokyo grade 3 patients. There was no statistically significant difference in the groups in terms of operative time, conversion and bile duct injury, although the degree of inflammation in the index admission must have been quite different. This could support the theory that delayed cholecystectomy may be beneficial in cooling the pericholecystic inflammation until surgery and may contribute to better recognition of the anatomy.

In the beginning of the laparoscopic era in the early 1990s, several studies demonstrated high conversion and complication rate in LC for ACC and advocated delayed cholecystectomy [6, 24]. In some centers at that time acute inflammation was even considered, a contraindication to LC [25]. More recently, randomized controlled trials (RCT) and meta-analyses have shown that early LC is superior to delayed LC in terms of LOS and hospital costs. Early LC has been found to be associated with lower morbidity in one RCT, but the opposite was demonstrated in another RCT [6–9]. Following these studies, early cholecystectomy has been gaining worldwide acceptance as the preferred surgical approach for ACC. Despite this consensus, many institutions across the globe still practice delayed cholecystectomy due to a variety of causes including, among others, infrastructure difficulties and financial constraints [26]. Additionally, there is still a question regarding how long it is safe to wait from the onset of symptoms to surgery in the acute setting. Initially, the inflammation edema guides the surgical planes but afterword fibrosis sets in. Several studies have suggested that operating after 72 h from the onset of symptoms, the so-called golden time period is reasonable and has acceptable outcomes [8, 26, 27]. Our experience described in this study and the published literature supports a change of our treatment algorithm to early LC. We hope this study influences other centers that still practice delayed LC to do the same.

This study has several limitations. This study is retrospective and subject to biases including possible selection bias. It has also been shown that prospective collection of complications is more accurate than retrospectively doing so [28]. This article is a description of a cohort of patients and there is no comparison between groups, and we did compare our experience to published results in the literature. Additionally, 41% of patients were loss to follow-up and we lack any information regarding their possible admissions at other medical centers or any surgical outcomes. This study only focuses on patients diagnosed and treated as ACC. Patients with biliary colic are not the focus of this study and were not included.

Conclusions

The aim of this study is to describe our experience with the delayed LC approach over a period of ten years and to critically evaluate it. This approach is associated with significant loss to follow-up, long LOS, and higher than expected use of PC. Conversion rates are low and rates of bile duct injury and perioperative mortality are comparable to previous reports in the literature. These data and published literature support a change in the management paradigm of ACC at our center to early LC and requires the establishment of acute surgical care infrastructure.

Compliance with ethical standards

Conflict of interest All the authors have no conflict of interest related to the manuscript and did not receive grants for the work involved.

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