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Acute calculous cholecystitis: a real-life management study in a tertiary teaching hospital

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ABSTRACT

Aim: to describe the management of acute calculous cholecystitis in a tertiary teaching hospital and the outcomes obtained.

Material and methods: a retrospective single tertiary center cohort study.

Results: medical records of 487 patients were analyzed. The mean follow-up was 44.5 ± 17.0 months. Treatment alternatives were cholecystectomy (64.3%), conservative treatment (23.0%), endoscopic retrograde cholangiopancreatography (17.4%), percutaneous cholecystostomy (10.7%) and endoscopic ultrasound-guided gallbladder drainage (0.8%). Most cholecystectomies were delayed (88.8%). Recurrences occurred in 38.2% of patients. Although cholecystectomy was the therapeutic approach with the lowest recurrence rate once performed, 44.6% of patients that underwent delayed surgery had pre-surgical recurrences.

Conclusions: delayed cholecystectomy is still commonly performed, even though it is related with a high frequency of pre-surgical recurrences.

Key words: Acute calculous cholecystitis. Treatment. Cholecystectomy. Outcomes. Recurrence rate.

INTRODUCTION

Cholecystectomy is the current treatment of choice for acute calculous cholecystitis (ACC) (1). However, the surgical approach and timing of surgery are modifiable factors that can influence the results. Nowadays, early laparoscopic cholecystectomy is the preferred approach due to the multiple advantages over open and delayed cholecystectomy (OC, DC) (2,3). However, DC is still commonly used (4,5).

A high surgical risk precludes cholecystectomy in some patients, meaning that alternative management strategies are preferable. Percutaneous cholecystostomy (PC) is the current method of choice for gallbladder drainage. Although endoscopic gallbladder drainage (either transmural or transpapillary) is recognized as a suitable alternative when performed by a skilled endoscopist (6).

In summary, there is a wide range of therapeutic alternatives for ACC. The aim of this study was to describe the management options chosen in our medical area and the outcomes obtained in terms of recurrences.

PATIENTS AND METHODS

A retrospective single tertiary center cohort study was performed, which was approved by the institutional review board.

Patients

The Clinical Records Department provided a list of all patients admitted to our hospital between January 1st 2009 and December 31st 2012, with a diagnosis of cholelithiasis or other gallbladder disorders (codes 574 and 575 of the International Classification of Diseases [ICD] 9-CM). Patients with a sub-code referring specifically to ACC (574.0, 574.3, 574.6, 574.8) or acute cholecystitis (575.0) were selected.

Inclusion and exclusion criteria

The inclusion criteria were admission to our hospital during the study period with a diagnosis matching the above mentioned ICD9-CM sub-codes. The exclusion criteria included non-fulfillment of the 2013 Tokyo guidelines of the diagnostic criteria for ACC, a history of congenital or acquired biliopancreatic disease and belonging to other medical areas.

Variables and definitions

The variables used and their definitions are shown in table 1.

Data retrieval

Medical electronic records of the Emergency Department, hospital admissions and outpatient clinics were reviewed by a single researcher.

Statistical analysis

Therapeutic approach and recurrence rate (dependent variables) were assessed by univariate analysis using the Chi-square and Fisher's exact tests. Their relationship to age, ASA class, history of different comorbidities, index episode (IE) severity and therapeutic approach in the case of recurrence rate were assessed as independent variables. A statistical significance level of 0.05 was determined and the Bonferroni correction was applied whenever multiple comparisons were performed.

The Cox regression was used to identify predictors of recurrence. Predictors with a significance level < 0.20 in the univariate analysis were included in a Cox regression model using bidirectional elimination. A statistical significance level of 0.05 was determined. The PASW Statistics version 18.0 was used for the analysis.

RESULTS

Medical records of 557 patients were reviewed and 70 patients were excluded due to the different exclusion criteria. Therefore, a total of 487 subjects were included in the final analysis. The mean follow-up was 44.5 ± 17.0 months and the baseline

characteristics are shown in table 2.

Index episode treatment

The proportion of patients that underwent each type of treatment is shown in table 3. Conservative treatment and PC were significantly more frequent in patients aged ≥ 75 years (conservative: < 75: 11.0% *vs* ≥ 75: 39.3%, p < 0.001; PC: < 75: 5.3% *vs* ≥ 75: 18.0%, p < 0.001). Conservative treatment was also more common in ASA class III-IV (I-II: 17.7% *vs* III-IV: 36.2%, p < 0.001) and PC in more severe ACC cases (I: 4.4% *vs* II: 29.5% *vs* III: 25.8%, p < 0.001). In contrast, cholecystectomy was performed more frequently in patients aged < 75 years (< 75: 83.3% *vs* ≥ 75: 38.3%, p < 0.001), in ASA class I-II (I-II: 75.3% *vs* III-IV: 46.8%, p < 0.001) and in patients with prior symptomatic biliary disease (no history: 54.3% *vs* history: 69.2%, p 0.003). OC and early cholecystectomy (EC) were associated with a more severe ACC (OC: I: 19.9% *vs* II: 33.7% *vs* III: 22.6%, p 0.02; EC: I: 8.8% *vs* II: 15.9% *vs* III: 33.3%, p 0.01). The majority of EC (74.3%) were urgent and the median time between IE and DC was 4.0 (1.6-7.1) months.

Recurrences

Recurrences occurred in 38.2% of patients; 75.9% were complicated and ACC was the most frequent reason (22.0%). The median time between the IE and the first recurrence was 2.8 (1.1-8.1) months. Only the patients undergoing a single type of treatment were included in the analysis of recurrence rate according to the therapeutic approach. Due to the low number of patients that underwent endoscopic ultrasound-guided gallbladder drainage, they were excluded from the analysis. PC did not reduce recurrence rate in comparison with conservative treatment. In fact, it was associated with a higher recurrence rate (PC: 36.4% *vs* conservative: 25.0%, p 0.01). Endoscopic retrograde cholangiopancreatography (ERCP) was associated with a lower recurrence rate than PC (ERCP: 17.4% *vs* PC: 36.4%, p 0.01).

Cholecystectomized patients had fewer *postoperative* recurrences than those that underwent any of the non-surgical options (conservative: 25.0% *vs* PC: 36.4% *vs* ERCP: 17.4% *vs* cholecystectomy: 1.2%, p < 0.001). However, while none of the patients that

underwent EC had recurrences, 44.6% of those that underwent DC developed recurrences before the cholecystectomy. Multivariable analysis identified a history of ischemic heart disease and the therapeutic approach as the only predictors of recurrence (Table 4).

DISCUSSION

The most significant finding of our study was that only 35 of the 313 cholecystectomies were EC and most of them were urgent. This is despite the fact that the Tokyo guidelines advise EC as the treatment of choice for all ACC patients assessed as capable of withstanding surgery (1). This reflects a tendency to systematically defer surgery unless it is urgently required. Other studies have also reported EC rates as low as 11%, 47% or 59%, the limiting factors being the availability of surgical staff and theater space (4,5,11).

Unfortunately, this delay in surgery meant that there was an undesirably high number of recurrences before the cholecystectomy was performed. In fact, even though cholecystectomy was the therapeutic approach with the lowest recurrence rate once performed, 44.6% of patients that underwent DC suffered a recurrence before the cholecystectomy procedure. The median time between the IE and the first recurrence was around three months, while the median time between the IE and the DC was around four months. This is obviously not a good strategy. Therefore, in our opinion, EC should be performed when experienced surgeons are available. Other studies are in line with our results (3,12).

It is worth mentioning the high recurrence rate associated with PC probably resulted from the lack of long-term catheter placement. Other studies have found that the recurrence rate is reduced when the percutaneous catheter is left *in situ* after PC, in comparison to when it is removed as soon as the acute phase is over (13). Interestingly, ERCP reduced the recurrence rate. This could mean that the reduction in the biliary drainage pressure provided by endoscopic sphincterotomy may prevent recurrences (14). Although a larger prospective study would be necessary to confirm this hypothesis. A recent study has evaluated which is the best therapeutic approach in patients with coexisting cholelithiasis and choledocholithiasis (15).

With regard to the limitations of our study, some uncomplicated recurrences were probably managed exclusively in primary care and were therefore not taken into account. This could have led to an underestimation of the recurrence rate.

In conclusion, our study suggests that early cholecystectomy is the most effective therapeutic approach to prevent recurrences after an episode of ACC. Although unfortunately, DC remains the commonly performed technique.

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Table 1. Variables and definitions

Demographic data: age and sex
Medical history: ASA class (7), prior biliary problems and other comorbidities. Prior biliary problems*: – Biliary pain: any episode of right upper quadrant or epigastrium pain of high intensity, lasting under one hour, with or without nausea/vomiting or abnormal liver function tests without fulfilling the criteria used to define choledocholithiasis, ACC, acute cholangitis or acute pancreatitis – Choledocholithiasis: clear evidence of biliary sludge or stones in the bile duct showed by imaging methods, preferably including magnetic resonance imaging cholangiography, ERCP or percutaneous cholangiography – ACC: defined according to the 2013 Tokyo guidelines criteria (8) – Acute cholangitis: defined according to the 2013 Tokyo guidelines criteria (9) – Acute biliary pancreatitis: defined according to the 2012 revised Atlanta classification criteria (10)
IE: first episode of ACC treated at our hospital between 01/01/2009 and 12/31/2012
Follow-up period: time between the IE and 31/01/2015. Complete follow-up was defined as death before the end of the follow-up period, an entry in the medical electronic record after the end of the follow-up period or having been contacted by us after the end of the follow-up period
IE severity: defined as grade I, II and III according to the 2013 Tokyo criteria (8)
Therapeutic approach: conservative treatment, PC, ERCP, EUS-GBD and cholecystectomy Cholecystectomy: – EC: cholecystectomy carried out within the first seven days after diagnosis of ACC – DC: cholecystectomy carried out beyond the first seven days after diagnosis of ACC – Urgent cholecystectomy: cholecystectomy carried out within the first 48 hours of admission or labeled as “urgent” in the medical record
Recurrence: any biliary event that occurred during the follow-up period – Uncomplicated recurrence: biliary pain. Defined as in * – Complicated recurrence: ACC, choledocholithiasis, acute cholangitis and acute biliary pancreatitis. Defined as in *

Time between IE and first recurrence
Time between IE and DC

ACC: acute calculous cholecystitis; IE: index episode; PC: percutaneous cholecystectomy; ERCP: endoscopic retrograde cholangiopancreatography; EUS-GBD: endoscopic ultrasound-guided gallbladder drainage; EC: early cholecystectomy; DC: delayed cholecystectomy.

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Table 2. Baseline characteristics

	n = 487
Age, median (IQR)	71 (57-80)
Male, n (%)	279 (57.3)
ASA class, n (%)	
I	26 (5.3)
II	273 (56.1)
III	177 (36.3)
IV	11 (2.3)
Prior symptomatic biliary events, n (%)	188 (38.6)
Biliary pain, n (%)	138 (59.7)
ACC, n (%)	21 (9.1)
Choledocholithiasis, n (%)	38 (16.5)
Acute cholangitis, n (%)	11 (4.8)
Acute biliary pancreatitis, n (%)	43 (18.6)
Arterial hypertension, n (%)	283 (58.1)
Diabetes mellitus, n (%)	112 (23.0)
Dyslipidemia, n (%)	322 (66.1)
Overweight-obesity, n (%)	129 (36.6)
Cerebrovascular disease, n (%)	56 (11.5)
Ischemic heart disease, n (%)	63 (12.9)
Chronic heart failure, n (%)	49 (10.1)
Chronic obstructive pulmonary disease, n (%)	44 (9.0)
Chronic liver disease, n (%)	18 (3.7)
Chronic kidney disease, n (%)	49 (10.1)
Malignancy, n (%)	89 (18.3)
IE severity	
Grade I	365 (74.1)
Grade II	95 (19.5)
Grade III	31 (6.1)

ACC: acute calculous cholecystitis; IE: index episode.

Table 3. Index episode treatment

Therapeutic approach	*n*	*Value*
Conservative treatment, n (%)	487	112 (23.0)
PC n (%)	487	22 (4.5)
ERCP n (%)	487	32 (6.6)
EUS-GBD, n (%)	487	3 (0.6)
Cholecystectomy, n (%) LC, n (%) OC, n (%)	487	248 (50.9) 168 (34.4) 80 (16.4)
PC + ERCP, n (%)	487	4 (0.8)
PC + cholecystectomy, n (%)	487	17 (3.5)
ERCP + EUS-GBD, n (%)	487	1 (0.2)
ERCP + cholecystectomy, n (%)	487	39 (8.0)
PC + ERCP + cholecystectomy, n (%)	487	9 (1.8)

PC: percutaneous cholecystectomy; ERCP: endoscopic retrograde cholangiopancreatography; EUS-GBD: endoscopic ultrasound-guided gallbladder drainage; LC: laparoscopic cholecystectomy; OC: open cholecystectomy.

Table 4. Predictors of recurrence

	Univariate analysis		*Multivariable analysis*	
	HR (95% CI)	p	HR (95% CI)	p
Age ≥ 75 years old	1.07 (0.78-1.48)	0.67		
Female sex	0.89 (0.65-1.24)	0.51		
ASA class III-IV	1.10 (0.80-1.52)	0.57		
Diabetes mellitus	1.22 (0.86-1.73)	0.27		
Dyslipidemia	1.03 (0.73-1.45)	0.87		
Overweight-obesity	1.10 (0.76-1.59)	0.61		
Cerebrovascular disease	1.30 (0.83-2.05)	0.26		
Ischemic heart disease	1.54 (1.03-2.31)	0.04	1.39 (0.93-2.09)	0.11
Index episode severity				
Grade I	Reference			
Grade II	1.14 (0.76-1.71)	0.54		
Grade III	0.63 (0.29-1.36)	0.24		
Therapeutic approach				
Conservative treatment	Reference		Reference	
PC	1.26 (0.73-2.20)	0.41	1.24 (0.71-2.15)	0.45
ERCP	0.44 (0.23-0.87)	0.02	0.45 (0.23-0.89)	0.02
Cholecystectomy	0.04 (0.01-0.27)	0.001	0.04 (0.01-0.28)	0.001

PC: percutaneous cholecystectomy; ERCP: endoscopic retrograde cholangiopancreatography.