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Management of acute cholecystitis in elderly (≥65 years old) patients: A retrospective study comparing early versus delayed cholecystectomy

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Abstract

Aim: Acute cholecystitis is the most common causes of acute abdomen in elderly population. This study aimed to present the early postoperative period (≤ 30 days) outcomes of elderly patients (≥ 65 years old) with acute cholecystitis who underwent early or delayed cholecystectomy.

Materials and Methods: Between January 2016 and December 2020, 74 patients aged 65 and over underwent cholecystectomy for acute cholecystitis were included in the study. The patients were divided into two groups as early (time between diagnosis and cholecystectomy 7 days or less, n= 43, 58.1%) or delayed (time between diagnosis and cholecystectomy over 7 days, n= 31, 41.9%) cholecystectomy. Demographic characteristics, preoperative laboratory and radiological findings, and perioperative data of patients were evaluated, and the groups were compared.

Results: The median age of patients was 73 (65-90) years, and 39 (52.7%) were male. Sixty-one (82.4%) patients underwent laparoscopic, 8 open (10.8%) and 5 (6.8%) conversion cholecystectomy. The rate of laparoscopic cholecystectomy was higher in the delayed group (n= 29, 93.5%) than in the early group (n= 32, 74.4%), but no statistically significant difference was detected (p=.06). The rate of open cholecystectomy was statistically significantly higher in the early group (n=8, 18.6%) than in the delayed group (n=0) (P=.017), the conversion rate was similar between the groups (p=1). There was no significant difference between the groups in terms of intraoperative complications (p=1). The length of hospital stay was statistically significantly longer in the early compared to the delayed group (5 (1-21) days and 2 (1-12) days, respectively, p< .001).

Conclusion: There was no statistical difference regarding intraoperative complications in patients underwent early or delayed cholecystectomy. We believe that the patient's clinical presentation and early or delayed cholecystectomy experience of the team are vital in determining the timing of cholecystectomy, as well as the severity of acute cholecystitis.

Introduction

Acute cholecystitis is defined as the inflammation of the gallbladder and it is usually associated with gallstones. The incidence of acute cholecystitis increases with age. Patients aged 65 and over are considered elderly, and in this population, the management of AC and the timing of cholecystectomy is still controversial [1]. Currently, life expectancy of elderly people is increasing. A study by Escartin et al [2] reported that among the 998, 34.5% (n=348) were ≥ 80 years. Therefore, the incidence of AC is high in the elderly patients. However, the treatment of AC in elderly patients is challenging because this population of patients have concomitant chronic diseases. Early cholecystectomy (EC) is generally the recommended treatment for healthy and young patients with AC. Moreover, advancements in surgical techniques and perioperative care proved that EC can be a safe method that can be performed in selected elderly patient population [3]. Despite all advancements that increase patient safety, there is still a notable risk of morbidity and mortality therefore, there is still a controversy for the treatment of AC in elderly

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patients [4].

The timing of cholecystectomy is important and main point that needs to be clarified is to determine the efficacy of timing of treatment. Therefore, the aim of the present study to evaluate the comparative results of elderly (≥65 years old) patients who underwent EC or delayed cholecystectomy (DC) for AC.

Materials and Methods

Data collection

The study was approved by the institutional review board (Inonu University Health Sciences Non-Invasive Clinical Research Ethics Committee, IRB approval no. 2022/ 364). Demographic and clinical data, including the age, gender, comorbid diseases, American Society of Anesthesiologists (ASA) score, the severity of cholecystitis, timing of the operation, type of operation, intraoperative complications, radiological and laboratory findings, need for preoperative interventional procedure, postoperative complications, duration of hospital stay and early (postoperative first 30 days) outcomes were analyzed by using hospital database. The duration of hospitalization for the delayed cholecystectomy group was calculated as sum of hospitalization during the medical therapy and the duration of postoperative hospital stay.

Study population

A total of 74 patients aged 65 years or older with AC treated in our clinic between January 2016 and December 2020 were included in this retrospective study. Only the patients who were confirmed to have acute calculous cholecystitis with clinical and radiological findings were included in the study. The patients who had incidental gall bladder cancer and also patients with acalculous cholecystitis were excluded from the evaluation. The patients were divided into two groups according to the time elapsed between diagnosis and cholecystectomy. Patients who received cholecystectomy within 7 days were included in the EC group (n=43, 58,1%); whereas those patients who received cholecystectomy over seven days were included in the DC group (n=31, 41.9%). In both two groups, the diagnosis of AC was confirmed by using clinical signs (fever, right upper quadrant pain, Murphy's sign), laboratory tests (white blood cell count, liver function tests, procalcitonin, and C-reactive protein (CRP) levels) and imaging techniques, including ultrasound (USG) or computed tomography (CT). The updated Tokyo Guidelines (TG13) was used to grade the AC severity [5]. Comorbidities were evaluated and scored via the Charlson Comorbidity Index (CCI) [6], and postoperative complications were classified according to the Clavien-Dindo classification [7].

Statistical analysis

Statistical analyses of the data were performed using the SPSS 25.0 (SPSS Inc., Chicago, IL) package program. Numerical variables were expressed as median (minimum-maximum) values, while categorical ones as frequency and percentages. The Shapiro Wilk test determined whether the assumption of normal distribution was met for the continuous variables. Regarding differences between groups, for numerical variables, the Mann-Whitney U test was used, and the chi-square test or Fisher's exact test for categorical variables. P value <0.05 was considered statistically significant.

Results

The demographics characteristics, preoperative laboratory and imaging findings, and perioperative data of the patients are summarized in Table 1. The median age of the study group was 73 (65-90) years, and 39 (52.7%) of them were male. There were no statistically significant differences in terms of age, gender, ASA class, and preoperative imaging features between the groups. The most common comorbidities were cardiac diseases in both groups, and the median CCI score was statistically significantly higher in the EC group compared to the DC group (p=0.007). The grade of severity of AC was significantly higher in the EC group (p=0.037). The rate of Grade 1 AC was approximately one-tenth in the EC group, while it was one-third in the DC group (p=0.013). In laboratory tests, only the CRP level was statistically significantly different between the groups, and it was higher in the EC group compared to the DC group (p=0.041), the other parameters didn't show any statistically significant difference. The median time between the diagnosis and cholecystectomy in the EC group was 3 (1-6) days, and it was 33 (10-102) in the DC group. Preoperative percutaneous cholecystostomy was performed on 7 (41.1%) patients, and all were in the DC group. Preoperative endoscopic retrograde cholangiopancreatography was performed more in the EC group compared to the DC group, but the difference wasn't statistically significant. Laparoscopic cholecystectomy (LC) was performed in 61 (82.4%) patients, direct open cholecystectomy was performed in 8 (10.8%) patients, and conversion cholecystectomy was performed in 5 (6.8%) patients. LC was preferred more in the DC group. About twenty percent of the patients underwent direct open cholecystectomy in the EC group, while no patients underwent direct open cholecystectomy in the DC group (p=0.017). The conversion rates of the groups were similar.

There were two intraoperative complications, one in each group (colon serosal injury in the EC group and duodenal serosal injury in the DC group) and all were fixed intraoperatively. Postoperative complications were mostly class II in the EC group, while they were mostly class I in the DC group. Six patients developed class IV or class V complications postoperatively in the EC group, and there was no patient with class IV or class V complications in the DC group. The length of hospital stay was significantly higher in the DC group (p=0.001). Only one mortality (on the sixth postoperative day, due to multi-organ failure) was observed postoperatively and the patient was in the EC group.

Discussion

This is a unique study because it has evaluated the efficacy and safety of timing of cholecystectomy in elderly patients with AC. Elderly population are liable for any physiologic stressors such as surgery because they have a reduced reserve due to associated chronic diseases [8]. The results of the present study have shown that early cholecystectomy

Table 1. Baseline characteristics, preoperative laboratory variables, and perioperative data of the study group, and EC and DC subgroups[x].

	Study group (n=74)	EC group (n=43)	DC group (n=31)	p value
Gender, male, n (%)	39 (52.7)	22 (51.2)	17 (54.8%)	0.755
Age, years	73 (65-90)	73 (66- 90)	72 (65-90)	0.908
CCI score	1 (0-4)	2 (0-4)	1 (0-3)	**0.007**
ASA class, n (%)				0.644
ASA 1	3 (4.1)	1 (2.3)	2 (6.5)	0.568
ASA 2	50 (67.6)	29 (67.4)	21 (67.7)	0.978
ASA 3	21 (28.4)	13 (30.2)	8 (25.8)	0.676
Severity of AC (TG13), n (%)				**0.037**
Grade 1	16 (21.6)	5 (11.6)	11 (35.5)	**0.013**
Grade 2	46 (62.2)	29 (67.4)	17 (54.8)	0.270
Grade 3	12 (16.2)	9 (20.9)	3 (9.7)	0.338
Preoprative imaging, n (%)				
USG	74 (100)	43 (100)	31 (100)	-
CT	69 (93.2)	40 (93)	29 (93.5)	1
Laboratory tests				
WBC (x 10^9/L)	14 (6.4-47)	14.5 (6.4- 47)	13 (10.1- 24)	0.108
CRP (mg/dl)	6.95 (3-46)	9 (3- 46)	5 (3- 28)	0.041
PCT (ng/ml)	0.9 (0-6)	1 (0.01-6)	0.6 (0-4.2)	0.202
ALT (U/L)	46 (6-489)	65 (6-489)	45 (12-173)	0.835
AST (U/L)	47.5 (9-414)	47 (9-414)	53 (14-408)	0.701
GGT (IU/L)	61.5 (15-732)	56 (15-684)	65 (21-732)	0.983
ALP (IU/L)	65 (16-336)	65 (16-336)	65 (27-317)	0.580
TB (mg/dl)	0.8 (0.2-9.1)	0.6 (0.2-5.6)	0.8 (0.3-9.1)	0.448
Time between diagnosis and cholecystectomy, days	6 (1-102)	3 (1- 6)	33 (10- 102)	**<0.001**
Operation type, n (%)				**0.037**
LC	61 (82.4)	32 (74.4)	29 (93.5)	0.060
OC	8 (10.8)	8 (18.6)	-	**0.017**
CC	5 (6.8)	3 (7)	2 (6.5)	1
Preoperative interventional procedure, n (%)				
PC	7 (9.5)	-	7 (22.6)	**0.001**
ERCP	10 (13.5)	8 (18.6)	2 (6.5)	0.177
Clavien-Dindo classification, n (%)				**0.005**
Class I	32 (43.2)	11 (25.6)	21 (67.7)	**<0.001**
Class II	33 (44.6)	25 (58.1)	8 (25.8)	**0.005**
Class IIIb	3 (4.1)	1 (2.3)	2 (6.5)	0.568
Class IVa	2 (2.7)	2 (4.7)	-	0.508
Class IVb	3 (4.1)	3 (7)	-	0.265
Class V	1 (1.4)	1 (2.3)	-	1
Duration of hospital stay, days	5.5 (1-21)	5 (1-21)	7 (4-22)	**0.001**
Intraoperative complication, n (%)	2 (2.7)	1 (2.3)	1 (3.2)	1
Mortality, n (%)	1 (1.4)	1 (2.3)	-	1

[x]: Results are expressed as median (minimum-maximum) or frequency (percentages). Significant P values are in bold. EC: Early cholecystectomy, DC: Delayed cholecystectomy, CCI: Charlson comorbidity index, ASA: American Society of Anesthesiologists, AC: Acute cholecystitis, TG13: Tokyo guidelines 2013, USG: Ultrasound, CT: Computed tomography, WBC: White blood cell, CRP: C-reactive protein, PCT: Procalcitonin, ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, GGT: Gamma-glutamyl transferase, ALP: Alkaline phosphatase, TB: Total bilirubin, LC: Laparoscopic cholecystectomy, OC: Open cholecystectomy, CC: Conversion cholecystectomy, PC: Percutaneous cholecystostomy, ERCP: Endoscopic retrograde cholangiopancreatography.

can be performed safely in elderly provided that preoperative evaluation is performed thoroughly. Although no consensus is established on the timing of the surgery, the gold standard treatment for AC is LC [9]. For determining the best time for cholecystectomy, the most crucial factors are the clinical findings and the center's experi-

ence. There are two basic approaches in the treatment of AC as EC and DC. EC is defined as LC performed within the first 7 days after the onset of symptoms, while DC is performed 6-8 weeks after conservative antibiotic therapy [9]. There may be recurrent attacks in patients scheduled for DC after a waiting period of 6-8 weeks. It was previously mentioned that emergent surgery is needed in 45% of patients whose symptoms do not regress after the first conservative treatment or who have recurrent cholecystitis attacks during the waiting period [10,11]. DC has been demonstrated not to reduce intraoperative complications; morbidity and hospital stay [12], progresses with recurrent biliary attacks at a rate of 25-61%, and has no superiority in terms of intraoperative complications. Moreover, it may lead to an increase in general morbidity due to the need for an extended hospital stay [13]. In our study, the rate of class I and class II complications was determined to be higher in the DC group. In this study, there was no significant difference regarding intraoperative complications between the EC and DC groups and this finding is consistent with the literature [14,15]. A serosal injury to the intestinal wall was detected in one patient in each group. While the incidence of bile duct injury reported in the literature was 0.26–1.2% [14-16], there were none in our study. The reason for this result may be attributed to the fact that hepatobiliary surgeons predominantly performed the operations. LC approach could have been attempted in some of the OCs' in the EC group, but our center is over anxious about injury to hepatoduodenal ligament and also the patient's safety. Therefore, the general preference of our surgeons would be to directly choose OC if patient safety or safe dissection planes would be in doubt. In addition, higher incidence of OC in the EC group may be related to the higher severity of AC in this group. In the DC group, LC was performed for all patients and no open cholecystectomy was performed, while open cholecystectomy was needed in 8 patients in the EC group. The rate of conversion to open cholecystectomy in EC and DC in the literature has been indicated to vary between 12.7-23.6% [10,17,18]. In our study, this rate was 7% in the EC group and 6.5% in the DC group which were comparable. The hospital stay was shorter in the EC group, being 5 days (1-21 days) in the EC group and 7 (4-22) in the DC group. Most of the studies in current literature support our result confirming shorter duration of hospitalization; however, some studies have reported the contrary [10,19,20]. In the study of Gomez et al [12], no difference was found in the length of hospital stay in the EC (3 days) and DC (4 days) groups. Our results show that early cholecystectomy is associated with shorter hospital stay with comparable complication rates. Therefore, our results have confirmed the safety of early cholecystectomy in elderly patients. There are only subtle changes between updated Tokyo guidelines in 2018 and the former 2013 guidelines [21]. While the Tokyo Guidelines 2018 [21] introduced some refinements to the grading system, such as incorporating radiological findings in the definition of acute cholecystitis and the addition of criteria for organ dysfunction, the overall grading system is consistent with the Tokyo Guidelines 2013. The 2018 version of the guidelines has added ultrasonography and components of systemic inflammatory response (SIRS) in grading of the system. There is a significant overlap between the severities grading between the two versions of the guidelines. In other words, the grade of the severity of acute cholecystitis is same in both versions of the guidelines 2018 [21]. Furthermore, the antibiotic therapy and timing of cholecystectomy is the main difference between the two versions of the guidelines. We have performed a retrospective analysis of the patient electronic data charts and various subjective criteria such as the components of SIRS. Our research strategy may be considered a limitation of the study. However, in terms of the severity of cholecystitis, our data is reliable and give an important message regarding the timing of surgery in a high-risk patient group.

Limitations

Our study is a retrospective study and this is the main limitation of the study. Some of the data are not readily available therefore, the technically demanding procedures, presence of signs of SIRS and other subjective parameters. Although we are the only tertiary hepatobiliary surgical center in our region, the volume of the patient is not enough.

Conclusion

In conclusion, there was no difference regarding intraoperative complications in patients who underwent EC and DC in our study. We believe that the patient's clinical presence and the EC-DC experience of the team are critical in determining the timing of cholecystectomy, in addition to the severity of AC. Multicenter randomized studies would be useful in investigating the timing of cholecystectomy.

Ethical approval

The study was approved by the institutional review board (Inonu University Health Sciences Non-Invasive Clinical Research Ethics Committee, IRB approval no. 2022/ 364).

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