Outcomes of Laparoscopic Cholecystectomy in Patients 65 Years and Older

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Authors’ contributions

This work was carried out in collaboration between all authors. Authors CT and IS designed the study, wrote the protocol and wrote the first draft of the manuscript. Authors CT, IS, EK, SMD, Cem Karaali and BC managed the literature searches, analyses of the study performed the spectroscopy analysis and authors CT, IS, MO, CA and Cezmi Karaca are supervised the manuscript. All authors read and approved the final manuscript.

ABSTRACT

Aim: Laparoscopic surgery is considered to be the gold standard in gall bladder surgery and to take advantage of its benefits, the number of laparoscopic procedures carried out on elderly patients is increasing daily. The aim of this study was to determine the mortality and morbidity rates of laparoscopic cholecystectomy (LC) in a patient group over 65 years of age and to analyze the predictive factors for conversion to open surgery.

Study Design: A retrospective analysis of patients, 65 years of age and over, who had undergone laparoscopic cholecystectomy operation.

Place and Duration of Study: Tepecik Training and Research Hospital, Department of General Surgery, Izmir, Turkey between January 2012 and June 2014 in our clinic was conducted.

Methodology: A retrospective analysis of 385 patients, 65 years of age and over, who had undergone cholecystectomy operation. When excluding the patients who had open cholecystectomy or additional surgical procedures, 240 patients were included in the study. The patients were also divided into two age groups (65-74 years; 75+ years) for further analysis.

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Results: The median age of the patients was 70. The rate of conversion from laparoscopy to open surgery was 12.5% (n=30). Multivariate analysis showed the leukocytosis and pathological acute cholecystitis to be independent risk factors for conversion. A longer total hospital stay was seen in patients with inflammatory bile duct diseases (5±4 days - 3±2 days). The surgical morbidity rate was 19.6% (n= 47); the rate of systemic complication was 2.5% (n=6).

Conclusion: Inflammation related to gallstones in the biliary system is a definite risk factor for conversion to open surgery. Laparoscopic cholecystectomy, with its acceptable rates of morbidity, mortality and conversion, is a reliable surgical procedure in the 65 and over age group.

Keywords: Laparoscopic cholecystectomy; elderly; conversion; complication; mortality.

1. INTRODUCTION

As life expectancy increases in the industrial world, illnesses requiring surgical intervention have become more common in elderly patients. Gallbladder stones reach a prevalence of 20%-50% in elderly people and have emerged as the most common reason for abdominal surgery in this age group [1-3]. However, as concomitant illnesses increase at this age, surgeons are reluctant to operate on this mature group. Some studies have noted that in situations such as advanced heart failure; laparoscopic surgery can have a negative effect on the morbidity and mortality of the elderly [4-6]. Additionally, complications associated with gallbladder stones are far more common in an advanced age group than in a younger population and it has been suggested that this could cause an increase in surgical complications [7,8].

However, in this day and age, the improving opportunities afforded by intensive care and advanced life support make postoperative care safer in this age group and since the clinical picture of untreated gall bladder stones is more complex and aggressive in elderly people, surgical treatment becomes an even more important option [1,3,9,10]. Laparoscopic surgery is considered to be the gold standard in gall bladder surgery and to take advantage of its benefits, the number of laparoscopic procedures carried out on elderly patients is increasing daily.

The aim of this study was to determine the mortality and morbidity rates of laparoscopic cholecystectomy (LC) in a patient group over 65 years of age and to analyze the predictive factors for conversion to open surgery.

2. MATERIALS AND METHODS

A retrospective analysis of 385 patients, 65 years of age and over, who had undergone cholecystectomy operation between January 2012 and June 2014 in our clinic was conducted. Those patients who had open cholecystectomy or had additional surgical procedures were excluded from the study. The remaining 240 patients were all included and classified according to their original clinical diagnosis. The patients were also divided into two age groups (65-74 years; 75+ years) for further analysis.

Pre-op lab results; concomitant illnesses; American Society of Anesthesiologists (ASA) scores; pre-operative ERCP history; prophylactic and treatment antibiotics; type of operation (emergency, interval or elective); conversion to open surgery and reasons for it; reoperation; use of a drain; length of operation (operating time and anesthesia induction); total length of hospitalization and postoperative hospital stay; surgical complications and systemic complications; mortality and results of pathological specimens were all recorded. The diagnosis of ‘inflammation related to gall bladder stones in the biliary system’ was applied to patients diagnosed with acute cholecystitis, cholangitis, or pancreatitis. The operations were carried out by experienced surgeons and senior trainee surgeons under experienced supervision. In all patients, the surgical procedure was commenced in the same way with a standard four trocar laparoscopic method. The pneumoperitoneum was established using either the Veress needle or the Hasson technique. As a general approach, during dissection, the cystic artery and vein were clipped and cut after the triangle of Callot dissection.

All statistical analysis was performed using SPSS V.15.0 software. Continuous data was given as mean ± STD; categorical data was given in numbers and percentages. For continuous variables either student’s t-test or Wilcoxon was used; whichever was more suitable. Chi-square test or Fisher exact test were used for categorical variables. Significance was taken at the <0.05 level. Risk factors for conversion to open surgery were considered as univariate. Also, independent variables were determined using multivariate analysis.
3. RESULTS

The median age of the patients was 70,158 (65.8%) of whom were female. The percentage of patients over 75 years of age was 20% (n=48). 162 (67.5%) patients had at least one co-morbidity; while 72 (30%) had two or more. 22% of patients (n= 53) had been diagnosed with acute inflammatory gallstone disease (acute cholecystitis, pancreatitis, and cholangitis) in the previous six months. 37.7% of these patients (n= 20) underwent emergency cholecystectomy. LC was performed on 178 patients with symptomatic cholelithiasis; 13 patients with pancreatitis and 10 patients with choledocholithiasis; gallbladder stones or cholangitis.

In all cases diagnosed with choledocholithiasis, gallstones were removed with pre-operative ERCP (Endoscopic Retrograde Cholangiopancreatography). The rate of conversion from laparoscopy to open surgery was 12.5% (n=30). The reasons for conversion were adhesion (n=19), bleeding (n=1), Mirizzi (n=1), organ injury (n=1), anatomic variation (n=1), technical and other reasons (n=2). Conversion to open surgery was more common in patients with gall bladder diseases like acute cholecystitis, pancreatitis, and cholangitis compared to other pathologies (symptomatic cholelithiasis, etc.) (22.6%-9.6%, P = 0.011). A longer total hospital stay was seen in patients with inflammatory bile duct diseases (5±4 days - 3±2 days, P = 0.001). The median postoperative and total hospitalization durations were two and three days, respectively. Only one patient (0.4%) needed a second operation due to organ injury. The median operative duration was 105 minutes. The surgical morbidity rate was 19.6% (n= 47); the rate of systemic complication was 2.5% (n=6). The most common cause of surgical morbidity was infection in the surgical site (89.4%, n= 42). Other surgical complications were minor bleeding (n=2), biliary fistula (n=2), and organ injury (n=1). There were no cases of mortality in the study group. Pathological investigation revealed that 92.1% (n= 221) patients had chronic cholecystitis with stones; 5.8% (n= 14) had acute cholecystitis; 0.8% (n= 2) had cholelithiasis and gallbladder polyps; one patient had phlegmonous cholecystitis, one patient had gangrenous cholecystitis and one patient had a malignity of the gallbladder (intraepithelial carcinoma).

A detailed comparison of both pre-op data and surgical data in the two age groups (65-74), (75+) can be seen in Tables 1 and 2.

When examining the risk factors for conversion from laparoscopic to open surgery, using univariate analysis, the leucocyte count inflammatory gallbladder diseases (acute cholecystitis and pancreatic cholangitis) was seen as a risk factor (P = 0.032, P = 0.008). In this conversion group, the durations of the operation, post op period and the overall hospital stay were longer (P = 0.001, P = 0.001, P = 0.001); the use of third generation cephalosporin, the use of a drain, and acute cholecystitis diagnosis were also found to be greater (P = 0.001, P = 0.001, P = 0.001, respectively). Multivariate analysis showed the leukocyte count and pathological acute cholecystitis to be independent risk factors for conversion (P = 0.011, P = 0.008, respectively). These factors affecting the conversion to open surgery from laparoscopy are presented in detail in Table 3.

Patients were categorized into two groups according to their ASA scores: those with scores of 1-2 and those with 3+. In this latter group, advanced age, male gender, diagnosis of acute cholecystitis, and inflammatory gallbladder disease were more common (p=0.016, p=0.011, p=0.033, p=0.028). However, no significant difference was seen between the two groups with regard to surgical complications, rate of conversion, length of operation, post-op stay and total hospital stay(p=0.806,p=0.785, p=0.942,p=0.810,p=0.118).

4. DISCUSSION

There is an increase in the incidence of gallbladder stones and related clinical symptoms as age increases [1,3,9,11]. Research shows that 13%- 50% of the 70+ aged population and between 38%-53% of the 80+ aged population have gall bladder stones [1,12]. Because of this, LC is the most common abdominal surgery performed on patients of this age [1-3,9,11,13]. Advanced age has been considered an independent risk factor in LC, affecting both mortality and morbidity [3]. When we consider the decrease in functional reserves, increased comorbidity and the more frequent acute biliary diseases of elderly patients, we see that the current situation constitutes a serious health problem and escalation in treatment costs. Despite this, age is not seen as a contraindication for LC and so its use in even very elderly patients is increasing rapidly [11,14-16]. Furthermore, a meta-analysis consist of 101.559 patients focus on laparoscopic vs open cholecystectomy in elderly patients suggest that odds ratio were constantly in favor of...
Table 1. Preoperative status of the patients

|                                    | 65-74 age (n:192) | 75 age and over (n:48) | P value |
|------------------------------------|-------------------|------------------------|---------|
| **Age**                            | 69±3              | 78±3                   | 0.001   |
| **Gender**                         |                   |                        |         |
| Woman                              | n: 126            | n: 32                  | 0.892   |
| Man                                | n: 66             | n: 16                  |         |
| **ASA**                            |                   |                        | 0.001   |
| ≤2                                 | n: 172            | n: 32                  |         |
| >2                                 | n: 20             | n: 16                  |         |
| **Co morbidity**                   |                   |                        | 0.308   |
| None                               | n: 52             | n: 8                   |         |
| Diabetes Mellitus                  | n: 41             | n: 11                  |         |
| Cardiac Disease                    | n: 39             | n: 13                  |         |
| Hypertension                       | n: 85             | n: 29                  |         |
| COPD                               | n: 24             | n: 11                  |         |
| Neurological Disease               | n: 14             | n: 4                   |         |
| ESRF                               | n: 3              | n: 1                   |         |
| **Diagnosis**                      |                   |                        | 0.379   |
| Acute cholecystitis                | n:28              | n: 11                  |         |
| Cholelithiasis                     | n: 147            | n: 31                  |         |
| Cholelithiasis+Choledocholithiasis+cholangitis | n: 7       | n: 3                   |         |
| Biliary pancreatitis               | n:10              | n: 3                   |         |
| **Acute inflammatory gallstone diseases** |            |                        | 0.831   |
| Emergent                           | n:14              | n: 6                   |         |
| Interval                           | n:24              | n: 9                   |         |
| **Co morbidity**                   |                   |                        | 0.054   |
| None                               | n: 52             | n: 8                   |         |
| 1 co morbidity                     | n:89              | n: 19                  |         |
| 2 and over                         | n:51              | n: 21                  |         |
| ERCP (exist/none)                  | 9/183             | 6/42                   | 0.046   |
| Leukocyte                          | 8398±3037         | 9314±3300              | 0.068   |
| Haemoglobin                        | 13±1.3            | 12±1.5                 | 0.043   |
| Trombocyte                         | 249±71            | 247±68                 | 0.891   |
| Total bilirubine                   | 0.9±1.4           | 1.0±1.1                | 0.681   |
| AST                                | 48±115            | 56±121                 | 0.673   |
| ALT                                | 42±102            | 44±110                 | 0.923   |
| Amylase                            | 48±23             | 69±35                  | 0.096   |
| Creatinine                         | 1.0±0.6           | 0.9±0.3                | 0.637   |

laparoscopic surgery, in terms of mortality, morbidity, cardiac and respiratory complications [17].

The increase in the frequency of acute inflammation caused by biliary diseases in the elderly patient group is well documented [1,3,10,18]; moreover, when surgical treatment is used for the acute symptoms of biliary diseases in older patients, the rates of operative morbidity and mortality are far higher than when compared to younger patients [4,14,19]. This situation shows the strategic importance of the decision to operate and the timing of treatment in the older patient. When we evaluated the reports of our older LC patients for biliary pancreatitis and acute cholecystitis during the six months previous to their operation, we found that, although not statistically significant, the rate of inflammation amongst the 65-75 age group was 19.7% but in the 75+ age group was 31.2%. There is no consensus amongst surgeons about the timing of LC in this age group of patients; however, recent studies show that especially in the case of acute cholecystitis, operating on patients when they first present, and without delay, leads to less mortality and morbidity [20]. Haltmeier et al. [19] in a study performed on 4011 patients aged over 65, reported that although older patients suffered from higher complication and mortality rates after LC, when compared to younger patients, and that age was an independent risk factor for negative outcomes in cholecystectomy; LC could be used with safety within the first 24 hours of the patients presenting with cholecystitis. There has already been an increase in the number of older patients needing emergency surgical treatment for gallstones
In the over 65 age group, 38% of patients who do not undergo cholecystectomy when they first present with acute cholecystitis, later return to the hospital with biliary complaints [21]. In their study of a 806 strong patient group, Cull et al recorded that 48% of patients over 65 presenting with acute cholecystitis were assigned interval cholecystectomy, but while waiting for their cholecystectomy there was an increase in episodes of pancreatitis, cholecystitis and cholangitis [22]. Although in cases of acute cholecystitis and/or pancreatitis our usual clinical procedure is interval cholecystectomy, in our study we found that immediate LC was performed at first presentation in 37.7% of patients over 65 (65-75 age group:36.8%; 75+ age group:40%) who presented with acute cholecystitis, pancreatitis or cholangitis.

Conversion from LC to open surgery denies patients the benefits of laparoscopic surgery. Several current studies show that advanced age increases the likelihood of conversion to OC and is an independent risk factor for conversion. The rate of conversion in elderly patients ranges between 3% - 27% [1-3,11,23,24]. In our study, the conversion rate for over 65 year olds was 12.5%. In a large cohort group study done in Denmark, the conversion rate for patients aged between 65 and 79 was 14.6% but rose to 25.3% for patients over 80 years of age [3]. In another study, the age of 65 was seen as an independent risk factor for conversion but on comparison, the conversion rate in patients over 75 years of age rose to twice the rate of those between 65 and 74 [25,26]. Agrusa et al. [9] in their study of 1227 patients of all ages, found no difference at all between the conversion rate in older or younger age groups. They accounted for this result by underlining their use of very strong selection criteria when deciding on LC to treat gallstones diseases and their use of experienced surgeons. In our study, although the rate of conversion was higher in the 75+ age group, this difference was not statistically significant (65-75 = 11.4%; 75 += 16.6%).

| Reason to conversion | 65-74 age (n:192) | 75 age and over (n:48) | P value |
|----------------------|------------------|------------------------|---------|
| Laparoscopy          | n: 170           | n: 40                  | 0.329   |
| Conversion to open surgery | n: 22 (%12.9) | n: 8 (%20)               | 0.059   |
| Adhesions            | n: 16            | n: 3                   |
| Bleeding             | n: 0             | n: 1                   |
| Anatomic variation   | n: 1             | n: 0                   |
| Organ injury         | n: 1             | n: 0                   |
| Technical and other problems | n: 1      | n: 1                   |
| Mirizzi              | n: 0             | n: 2                   |
| Re-operation         | n: 1             | n: 0                   |
| Drain (None/Exist)   | 89/103           | 20/28                  | 0.560   |
| Operation time(min)  | 112±38           | 119±35                 | 0.243   |
| Surgical complications | %20.8            | %14.5                  | 0.806   |
| Surgical side infection | n: 35            | n: 7                   |
| Biliary fistula      | n: 2             | n: 0                   |
| Minor bleeding       | n: 2             | n: 0                   |
| Organ injury         | n: 1             | n: 0                   |
| Systemic complications | %0.25            | %0.20                  | 0.741   |
| Pulmonary            | n: 3             | n: 1                   |
| Neurological         | n: 1             | n: 0                   |
| Renal                | n: 1             | n: 0                   |
| Pathology            |                  |                        | 0.020   |
| Acute cholecystitis  | n: 7             | n:7                    |
| Flegmenous cholecystitis | n:0             | n:1                    |
| Gangrenous cholecystitis | n:1             | n:0                    |
| Chronic cholestitis | n:181            | n:40                   |
| Chronic kolesititis+polyp | n:2         | n:0                    |
| Malignancy           | n:1             | n:0                    |
| Postoperative hospital stay(day) | 2.2±1.4 (n: 192) | 2.3±1.9 (n:48)          | 0.029   |
| Total hospital stay(day) | 3.5±2.3 (n: 192) | 4.0±3.4 (n: 48)        | 0.169   |
Table 3. Factors affecting the conversion to open surgery from laparoscopy

|                        | Laparoscopy (n: 210) | Conversion from laparoscopy to open (n: 30) | Univariate P value | Multivariate P value |
|------------------------|----------------------|---------------------------------------------|--------------------|----------------------|
| **Age**                |                      |                                             |                    |                      |
| 70±4                   | 71±5                 | 0.716                                       | 0.329              |
| **Age group**          |                      |                                             |                    |                      |
| 65-74 age              | n: 170               | n: 22                                       |                    |                      |
| 75 age and over        | n: 40                | n: 8                                        | 0.918              |
| Gender (woman/man)     | 138/20               | 20/10                                       | 0.785              |
| **ASA**                |                      |                                             |                    |                      |
| ≤ 2                    | n: 179               | n: 25                                       | 0.329              |
| >2                     | n: 31                | n: 5                                        | 0.205              |
| **Comorbidities**      |                      |                                             |                    |                      |
| None                   | n: 49                | n: 11                                       |                    |                      |
| Less than 2            | n: 146               | n: 16                                       | 0.785              |
| 3 and over             | n: 15                | n: 3                                        | 0.032              |
| **Diagnosis**          |                      |                                             | 0.340              |
| Acute cholecystitis    | n: 31                | n: 8                                        | 0.032              |
| Cholelithiasis         | n: 162               | n: 16                                       | 0.066              |
| Cholelithiasis+choledocholitias | n: 8 | n: 2                                      | 0.205              |
| Biliary pancreatitis   | n: 9                 | n: 4                                        | 0.749              |
| **Acute Cholecystitis**|                      |                                             |                    |                      |
| Emergent               | n: 15                | n: 5                                        | 0.749              |
| Interval               | n: 26                | n: 7                                        | 0.008              |
| Leukocyte number       | 8380±2910            | 9986±4017                                   | 0.008              |
| Haemoglobin            | 13±1.4               | 13±1.4                                      | 0.405              |
| Trombocyte             | 248±71               | 252±69                                      | 0.790              |
| Total bilirubine       | 0.9±1.3              | 1.2±1.9                                     | 0.220              |
| AST                    | 47±114               | 72±131                                      | 0.284              |
| ALT                    | 39±97                | 70±137                                      | 0.127              |
| Amylase                | 35±27                | 69±45                                       | 0.162              |
| Creatinine             | 1.0±0.6              | 1.0±0.2                                     | 0.750              |
| Operation time (min)   | 107±29               | 161±54                                      | 0.001              |
| **Antibiotherapy**     |                      |                                             | 0.001              |
| 1. group cephalosporin | n: 191               | n: 20                                       | 0.001              |
| 3. group cephalosporin | n: 11                | n: 10                                       | 0.386              |
| Others (kinolon, tazobaktam, imipenem, cephalosporin+metronidazo) | n: 8 | n: 0                                     | 0.001              |
| ERCP ( positive)       | n: 13                | n: 2                                        | 0.920              |
| Drain (None/ Yes)      | 108/102              | 1/29                                        | 0.001              |
| **Surgical complications** |                      |                                             | 0.001              |
| Surgical side infection| n: 30                | n: 12                                       | 0.645              |
| Minor bleeding         | n: 1                 | n: 1                                        | 0.645              |
| Biliary fistula        | n: 2                 | n: 0                                        | 0.001              |
| Organ injury           | n: 1                 | n: 0                                        | 0.001              |
| **Systemic Complications** |                      |                                             | 0.741              |
| Pulmonary              | n: 3                 | n: 1                                        |                    |
| Neurological           | n: 1                 | n: 0                                        | 0.741              |
| Renal                  | n: 1                 | n: 0                                        | 0.741              |
| **Pathology**          |                      |                                             |                    |                      |
| Acute cholecystitis    | n: 8                 | n: 6                                        | 0.001              |
| Flegmenous cholecysistitis | n: 1 | n: 0                                      | 0.008              |
| Gangrenous cholecystitis | n: 0 | n: 1                                      | 0.008              |
| Chronic cholecystitis  | n: 200               | n: 21                                       | 0.001              |
| Cholelithiasis+polyp   | n: 1                 | n: 1                                        | 0.001              |
| Malignancy             | n: 0                 | n: 1                                        | 0.001              |
| Postoperative hospital stay(day) | 2±1 | 4±2                                      | 0.001              |
| Total hospital stay(day) | 3±2 | 5±2                                      | 0.001              |
In elderly patients, when preoperative risk factors for conversion to open surgery are examined, we see that a high leucocyte count and a pathological diagnosis of acute cholecystitis are independent risk factors. This is likely because as age increases, so does the effect of the biliary stones which cause inflammation in the hepatobiliary system. Genç et al attempted to determine predictive risk factors for conversion in their study of 5164 patients. They found tissue inflammation and serious adhesions in the triangle of Calot due to fibrosis to be the most common reasons for conversion. They emphasized that acute cholecystitis or a history of previous acute cholecystitis increased the surgical risk in LC and was the most common reason for conversion to OC [27]. Chandio et al. [24] found that in the 65+ age group the rate of conversion was four times greater than in the under 50 age group; he found the rate of conversion to be 10 times higher in patients with a history of acute cholecystitis and that advanced age and acute cholecystitis were independent risk factors for conversion. Polychronidis et al. [11], in a study of 2412 patients undergoing LC and comparing those under 75 years of age with those over 75, found that acute cholecystitis was the only independent risk factor for conversion and for the development of complications. In our study, the presence of acute cholecystitis and an increase of leukocytes as an indicator of inflammation were seen as independent risk factors for conversion to open surgery.

A search of the current literature shows that morbidity and mortality in elderly patients after laparoscopic cholecystectomy ranges between 5% - 26% and 0.7% to 6% respectively [4-6,11,14,16]. In our study there were no cases of mortality. Surgical morbidity was 19.5%; systemic complication rate was 2.5%. Infection of the surgical site is the most commonly seen surgical morbidity. This surgical site infection is usually concentrated near the trocar entrance beneath the xiphoid, where the gall bladder is removed from the abdomen. At our center, it is probable that this infection stems from a lack of routine endobag use while removing the gall bladder from the abdomen.

5. CONCLUSION
The results of our study act as a reminder that a history or symptoms of inflammation related to gallstones in the biliary system are a definite risk for conversion to open surgery. Also, laparoscopic cholecystectomy, with its acceptable rates of morbidity, mortality and conversion, is a reliable surgical procedure in the 65 and over age group.

CONSENT
All authors declare that written informed consent was obtained from the patient (or other approved parties) for publication of this paper and accompanying images.

ETHICAL APPROVAL
All authors hereby declare that all experiments have been examined and approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

COMPETING INTERESTS
Authors have declared that no competing interests exist.

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