

# Risk factors and clinical outcomes of laparoscopic cholecystectomy in elderly patients

Arif Atay,
Feyyaz Güngör,
Mehmet Sercan Candan,
Örgün Güneş,
Özlem Gür,
Osman Nuri Dilek

Departments of Surgery, İzmir Katip Celebi University, Faculty of Medicine, Ataturk Training and Research Hospital, İzmir, Türkiye

## ABSTRACT

**Introduction:** Significant advances in medicine have led to a prolongation of life expectancy and an increase in the rate of operations performed on the elderly. However, despite all these developments, advanced age continues to be one of the factors affecting perioperative and post-operative morbidity and mortality. Considering the increase in elderly population, it is estimated that an increasing number of elderly patients will apply for cholecystectomy in the next decade.

**Materials and Methods:** In this retrospective single-center study, the files of patients over 65 years of age who underwent laparoscopic cholecystectomy (LC) between January 2018 and February 2020 were evaluated. We divided the patients into two groups. Patients aged 65–74 as Group A, and patients aged 75 and over as Group B. Besides the clinical data of the patients, we compared inflammatory markers.

**Results:** Of the 92 patients included in the study, 35 (38.05%) were male, 57 (61.95%) were female, and the mean age was 71.72±5.06. The operation was completed laparoscopically in 85 of the patients who underwent cholecystectomy. The morbidity rate was statistically significantly higher in Group B. Furthermore, Group B stayed in hospitals more than Group A, which was statistically significant.

**Conclusion:** LC is a safe surgical method for elderly patients. However, comorbidity, length of hospital stay, and morbidity seem to be higher with advanced age. This age group should be evaluated with a multidisciplinary approach before and after surgery.

Keywords: Elderly, Geriatric surgery, Laparoscopic cholecystectomy, Outcomes, Prediction

# Introduction

Significant advances in medicine have led to a prolongation of life expectancy and an increase in the rate of operations performed on the elderly. However, despite all these developments, advanced age continues to be one of the factors affecting perioperative and post-operative morbidity and mortality.<sup>[1]</sup> Cholelithiasis is one of the most common indications for abdominal surgery. The preferred treatment procedure for symptomatic patients in the general population is laparoscopic cholecystectomy (LC). Studies on the practice of cholecystectomy in elderly patients are discussed in the literature.<sup>[2]</sup>

The prevalence of gallstones is increased in elderly pa-





tients; the prevalence in patients over 60 years of age ranges from 20% to 30%, and this rate rises to 80% in individuals over 90 years of age. However, considering the increase in the over aged patients, it is estimated that an increasing number of elderly patients will apply for cholecystectomy in the next decade.<sup>[3-4]</sup>

Some studies in the literature report higher mortality, morbidity, conventional surgical methods, and a more extended hospitalization time in elderly patients who underwent cholecystectomy. These risks lead surgeons to minimally invasive treatment methods such as endosonography-guided gallbladder drainage, cholecystostomy, or conservative treatments, which can be an alternative to cholecystectomy. However, the use of LC has been found beneficial in selected geriatric patients.<sup>[57]</sup>

This study aimed to evaluate the risk factors and clinical outcomes of patients who underwent LC in the aged and very aged patients.

## **Materials and Methods**

In this retrospective single-center study, the files of patients over 65 years of age who underwent LC between January 2018 and February 2020 were evaluated. The entire series included 92 patients in whom 85 procedures were completed laparoscopically.

The following parameters were analyzed for all patients: Age, gender, ASA score, comorbidities, pre-operative laboratory tests, results of imaging modalities, operation indications, surgical techniques, duration of surgery, hospital stay, morbidity, and mortality.

We evaluated the patients in two groups. We classified the patients aged 65–74 as Group A, and patients aged 75 and over as Group B. We performed comparative statistical analysis for the recorded data of Group A and Group B. Besides the clinical and demographic data of the patients, we compared comorbidities and the inflammatory markers (white blood cell [WBC], platelet [PLT], neutrophil-lymphocyte ratio [NLR], and platelet-lymphocyte ratio [PLR]) in pre-operative blood parameters in patient groups with and without morbidity. Furthermore, we compared the inflammatory markers (WBC, neutrophil, lymphocyte, PLT, NLR, and PLR) in pre-operative blood parameters in patient groups with laparoscopic surgery and converting open surgery.

We recorded the duration of surgery of the patients from the time of diagnosis to be <1 year and above. We divided the surgical indications into symptomatic cholelithiasis and cholelithiasis with complications. In addition, we evaluated the surgeries as emergency and elective. In both groups, we recorded the operation times as less than and above 90 min.

Ethics Committee Approval was received for this study from the Ethics Committee of Izmir Kâtip Celebi University (2021/GOKAE/0307).

### **Diagnostic Tests**

It was found that abdominal ultrasonography, triphasic computed tomography, and occasional magnetic resonance cholangiopancreatography were used as cross-sectional imaging methods.

#### Surgical Procedures

LC was performed using a standard 4-port technique by an experienced surgical team. A Veress needle was inserted, and the abdominal cavity was insufflated with the maximum insufflation pressure being 12 mmHg. All patients underwent cholecystectomy. Nasogastric tube was placed in all patients.

We used the Clavien-Dindo classification for post-operative complications. It was found that the patients were followed up with outpatient visits every 3 months in the 1<sup>st</sup> post-operative year and then every 6 months.

#### **Statistical Analysis**

We analyzed the data in IBM SPSS Statistics 25.0 statistics package program. A comparison of variables and two groups were made using the Mann-Whitney U and Chi-square test. P<0.05 was considered statistically significant.

## **Results**

Of the 92 patients included in the study, 35 (38.05%) were male, 57 (61.95%) were female, and the mean age was 71.72±5.06 (range; 65–86)/year.

In Group A and B patients, common comorbidities were hypertension and diabetes mellitus. Although the frequency of comorbidity was found to be similar in both groups, the incidence of HT in Group B was statistically significantly higher than in Group A (p=0.038).

We operated on 39 patients (62.9%) in Group A and 16 patients (53.3%) in Group B for symptomatic cholelithiasis. The most common symptoms in both groups were abdominal pain and nausea. Twenty-three (37.09%) patients in Group A and 14 (46.66%) patients in Group B were operated on for complications related to cholelithiasis. The most common complications were pancreatitis, cholecystitis, and cholangitis. Pancreatitis was observed in 14 patients and acute or chronic cholecystitis developed in 13 patients.

In both groups, five patients were operated on for acute abdomen. The majority of the patients were operated on under elective conditions in Groups A–B (91.94–83.33%). Both groups consisted of ASA 2 and 3 patients. In Group A 14 (22.6%) and Group B 5 (16.67) patients, the time from the first diagnosis to surgery was 1 year or more.

In 92 of the patients, the surgery first started laparoscopically and then turned to laparotomy in seven patients. In all cases, cholecystectomy was performed. Converting to open surgery from laparoscopy was performed in five patients because the callout triangle could not be revealed and two patients due to respiratory complications. Converting from laparoscopic surgery to open surgery was statistically significantly higher in Group B patients (p=0.035).

In the analysis of operation time and drain use, we found no statistically significant difference between the groups. Early mortality (first 30 days postoperatively) was not observed in any patient. Grades 1–2 morbidity developed in 10 patients according to the Clavien-Dindo classification. Superficial surgical site infection was the most common complication in six patients. While atelectasis developed in three patients, urinary tract infection was observed in one patient. The morbidity rate was statistically significantly higher in Group B (p=0.012). Furthermore, Group B stayed in hospitals more than Group A (p<0.001) (Table 1).

	Group A (n=62)	Group B (n=30)	р
Gender (Female)*	39 (62.9)	18 (60)	0.788ª
Age (years) <sup>4</sup>	68.82±2.50	77.73±3.47	0.685°
Comorbidity (Yes)*	48 (77.42)	24 (80)	0.778ª
DM (Yes)*	18 (29.03)	8 (26.67)	0.813ª
Hypertension (Yes)*	25 (40.32)	19 (63.33)	0.038ª
Pulmonary disease (Yes)*	6 (9.67)	2 (6.67)	>0.999ª
Cardiac disease (Yes)*	7 (11.3)	7 (23.3)	0.214ª
Renal disease (Yes)*	3 (4.83)	1 (3.33)	>0.999ª
Indication*			0.38ª
Symptomatic cholelithiasis	39 (62.9)	16 (53.3)	
Cholelithiasis complication	23 (37.09)	14 (46.66)	
The period from the first diagnosis to the operation (more than 1 year)*	14 (22.6)	5 (16.67)	0.511ª
ASA score*			0.374ª
ASA II	43 (69.4)	18 (60)	
ASA III	19 (30.6)	12 (40)	
Cholecystectomy *			0.285ª
Elective	57 (91.94)	25 (83.33)	
Urgent	5 (8.06)	5 (16.67)	
Operation time			
(more than 90 min)*	25 (40.32)	13 (43.33)	0.685ª
Drain (Yes)*	40 (64.52)	17 (56.66)	0.467ª
Laparoscopic $\rightarrow$ Open (conversion)*	2 (3.22)	5 (16.66)	0.035ª
Morbidity (Yes)*	3 (4.83)	7 (23.33)	0.012ª
Length of stay in the hospital (day)#	2 (2–3)	3 (3–4)	<0.001 <sup>b</sup>

\*; n (%),#; Median (Q1-Q3) <sup>a</sup>; Chi-square, <sup>b</sup>; Mann–Whitney U-test<sup>c</sup>; Student's t-test, 4; Mean±standard deviation.

Inflammatory markers in the pre-operative period compared with the patients completed laparoscopically and the patients converted to open surgery, it was found that WBC and PLR values were higher in the group converted to open surgery. However, no statistically significant difference was detected (Table 2). No statistically significant difference was found between groups with and without morbidity in terms of inflammatory markers. Furthermore, in the analysis of ASA scores, comorbidities, and surgical indications, we found no statistically significant difference between groups (Table 3).

Table 2. Comparison of pre-operative blood parameters in patients converting from laparoscopic surgery to open surgery

	No (n=85)	Yes (n=7)	р
Wbc# (10º/L)	6.91 (5.95-8.43)	7.39 (6.31–9.86)	0.31 <sup>b</sup>
PLT# (10 <sup>9</sup> /L)	244 (197.5–291)	281 (189–335)	0.617⁵
Neutrophil# (10º/L)	4.33 (3.43-5.36)	4.72 (3.87-6.35)	0.418 <sup>b</sup>
Lymphocyte# (10º/L)	1.95 (1.57–2.54)	1.95 (1.46–2.73)	0.606 <sup>b</sup>
PLR#	114.6 (96.4–168.24)	123.61 (93–144.1)	0.842 <sup>b</sup>
NLR#	2.13 (1.53–2.89)	2.17 (1.96–3.23)	0.664 <sup>b</sup>

#; Median (Q1-Q3), WBC: White blood cell, PLT: Platelet, NLR: Neutrophil-lymphocyte ratio, PLR: Platelet-lymphocyte ratio, <sup>b</sup>;Mann–Whitney U-test.

Table 3. Comparison of pre-operative blood parameters in groups with and without morbidity					
	No (n=82)	Yes (n=10)	р		
Wbc# (10º/L)	6.94 (5.96-8.45)	7.33 (5.13–9.11)	0.9 <sup>b</sup>		
PLT# (10º/L)	247 (195.75–289.5)	240.5 (215.25-309.5)	0.73 <sup>b</sup>		
Neutrophil# (10º/L)	4.42 (3.49-5.49)	4.52 (3.33-5.80)	0.759 <sup>b</sup>		
Lymphocyte# (10º/L)	1.96 (1.57–2.55)	1.76 (1.45–2.94)	0.787 <sup>b</sup>		
PLR#	114.35 (95.63–167.52)	135.91 (97.29–180.69)	0.634 <sup>b</sup>		
NLR#	2.12 (1.54–2.79)	2.48 (1.52-3.5)	0.514 <sup>b</sup>		
ASA score*			0.486ª		
ASA II	53 (64.63)	8 (80)			
ASA III	29 (35.37)	2 (20)			
Comorbidity (Yes)*	65 (79.27)	7 (70)	0.449ª		
DM (Yes)*	22 (29.83)	4 (40)	0.46ª		
Hypertension (Yes)*	38 (46.34)	6 (60)	0.511ª		
Pulmonary disease (Yes)*	8 (9.75)	0 (0)	0.592ª		
Cardiac disease (Yes)*	13 (15.85)	1 (10)	>0.999ª		
Renal disease (Yes)*	2 (2.43)	2 (20)	0.057ª		
The period from the first diagnosis	17 (20.73)	2 (20)	>0.999ª		
to the operation (more than 1 year)*					
Indication*			0.516ª		
Symptomatic cholelithiasis	50 (60.97)	5 (50)			
Cholelithiasis complication	32 (39.02)	5 (50)			

\*; n (%),#; Median (Q1–Q3), <sup>a</sup>; Chi-square, <sup>b</sup>; Mann–Whitney U-test, WBC: White blood cell, PLT: Platelet, NLR: Neutrophil-lymphocyte ratio, PLR: Platelet-lymphocyte ratio.

## **Discussion**

According to a classification made by the World Health Organization (WHO), the elderly between the ages of 60 and 74 and the elderly between the ages of 75 and 89 are included in the category. Some guidelines have made different definitions in the classification of the elderly. While two guidelines defined those aged 65 or beyond as the elderly, one guideline used 75 years as the cutoff for its description of the elderly. This variability in chronological age determination when describing the elderly is an issue that hinders a standard definition. In clinical studies specific to some diseases, variable definitions of the elderly are encountered.<sup>[8]</sup> In our study, among elderly patients, we evaluated the patients over 75 years old in the second group in the light of the current literature data.

In elderly patients, there has been an increase in disorders such as hypertension and pulmonary diseases, negatively affecting the outcome of surgical interventions. At the same time, these patients develop limitations in physiological functions. Accordingly, there has been an increase in post-operative complications in aged patients. <sup>[9]</sup> In our study, morbidity was higher in Group B (p=0.012). Another study by Yi et al. reported that higher ASA score did not affect operation and discharge time, but increased morbidity.<sup>[10]</sup> In our study, all of the patients had ASA II-III and more complications happened in ASA II patients. The operation duration was similar in Groups A and B, but the hospitalization duration (p<0.001) was higher in Group B. Furthermore, Tokyo guidelines do not consider advanced age as a risk factor but emphasize the severity of acute cholecystitis attacks in these patients.<sup>[11]</sup> This is in line with our study, as the majority of our patients had symptomatic cholelithiasis. Moreover the surgical time has been described by many studies as a risk factor; a cholecystectomy lasting more than 100 min increases the probability of complications by 6 times compared to a shorter duration.<sup>[12]</sup> Conversely, in our study, the duration of surgery was similar in both groups and Group B patients had a higher mean age which may explain the high rate of post-operative complications.

There is no consensus regarding the timing of cholecystectomy in elderly patients. Comorbidities presented in this population may require prior stabilization that will delay the intervention. We preferred to perform early LC for the patients as the first choice. Medical treatment and minimally invasive procedures such as percutaneous cholecystostomy are treatment modalities that can be used instead of emergency cholecystectomy in elderly patients or patients with comorbidities that protect the patient from the side effects of general anesthesia. On the other hand, randomized controlled studies comparing percutaneous cholecystostomy with LC have demonstrated the advantages of surgical treatment, such as lower complication rate and reintervention.<sup>[13,14]</sup> The laparoscopic approach is the first choice in gallbladder surgery in the current treatment. In addition, laparoscopic surgery is preferred over conventional methods due to decreased physiological reserves in elderly patients. It has been reported in the literature that patients operated with laparoscopic procedures are more comfortable in terms of pain in the postoperative period. In addition, these patients have lower hospital stays and mortality and morbidity rates.<sup>[15-17]</sup> In our study, there was no mortality, proving that LC could be safely performed.

It has been shown that the patient's age and prolonged interval between the appearance of symptoms are related to a greater probability of conversion to laparotomy.<sup>[18]</sup> In our study, the conversion to open surgery occurs in seven patients, two of them in Group A. The most reason for conversion was the inability of identifying the anatomical structures in five patients. Our conversion rate for Group A is in accordance with the literature.<sup>[19]</sup> Advanced age in Group B entails a higher risk of conversion to an open procedure. This risk was higher in the  $\geq$ 75-year-old group (p=0.035).

Some studies examining the relationship of inflammatory parameters with malignancies, inflammatory and autoimmune diseases, and their diagnosis, prognosis, and mortality. These are used to predict diagnosis and mortality in colorectal and gastric cancers, appendicitis, GIS perforations, sepsis, and the novel coronavirus disease. As a result, NLR and PLR are also part of the routine peripheral blood parameters evaluated in many laboratories. <sup>[20-22]</sup> We also compared WBC, NLR, and PLR, in pre-operative blood parameters. There was no statistical significance between these parameters between laparoscopic completed cases and open cases, and in patients with or without morbidity. The morbidities that developed in our study were recorded as levels 1 and 2 according to the Clavien-Dindo classification. In addition, we think that there is no difference in inflammatory markers because the cases with laparotomy are very few compared to the cases with laparoscopic.

Our study is limited mainly by its retrospective nature and the sample size was less than the sample sizes in the literature.

### Conclusion

LC is a safe procedure for the geriatric population. However, comorbidity, length of hospital stay, and morbidity seem to be higher with advanced age. This age group should be evaluated with a multidisciplinary approach before and after surgery.

### Disclosures

**Ethichs Committee Approval:** Ethics committee approval was received for this study from the Clinical Trials Ethics Committee of Izmir Kâtip Celebi University School of Medicine (2021/GOKAE/0307).

Peer-review: Externally peer-reviewed.

#### Conflict of Interest: None declared.

Authorship Contributions: Concept – A.A., F.G.; Design – E.Ö.G., Ö.G.; Supervision – O.N.D.; Materials – S.C., F.G.; Data collection and/or processing – Ö.G., S.C.; Analysis and/or interpretation – O.N.D., A.A.; Literature search – E.Ö.G., S.C.; Writing – A.A., Ö.G.; Critical review – O.N.D.

#### References

- Erenoglu C, Öztürk A, Uluutku H, Kurt Y, Demirbaş S, Akın L. 70 yaş ve üzerindeki hastalarda uygulanan laparoskopik kolesistektomi sonuçları. End Lap ve Minimal İnvaziv Cerrahi 2003;10:36–40.
- 2. Agrusa A, Romano G, Frazzetta G, Chianetta D, Sorce V, Di Buono G, et al. Role and outcomes of laparoscopic cholecystectomy in the elderly. Int J Surg 2014;12:37–9. [CrossRef]
- Loozen CS, van Ramshorst B, van Santvoort HC, Boerma D. Early cholecystectomy for acute cholecystitis in the elderly population: A systematic review and meta-analysis. Dig Surg 2017;34:371–9. [CrossRef]
- Pisano M, Ceresoli M, Cimbanassi S, Gurusamy K, Coccolini F, Borzellino G, et al. 2017 WSES and SICG guidelines on acute calcolous cholecystitis in elderly population. World J Emerg Surg 2019;14:10. [CrossRef]
- Irojah B, Bell T, Grim R, Martin J, Ahuja V. Are they too old for surgery? safety of cholecystectomy in superelderly patients (≥ Age 90). Perm J 2017;21:16-013. [CrossRef]
- Kamarajah SK, Karri S, Bundred JR, Evans RPT, Lin A, Kew T, et al. Perioperative outcomes after laparoscopic cholecystectomy in elderly patients: a systematic review and metaanalysis. Surg Endosc 2020;34:4727–40. [CrossRef]
- Teoh AYB, Kitano M, Itoi T, Pérez-Miranda M, Ogura T, Chan SM, et al. Endosonography-guided gallbladder drainage versus percutaneous cholecystostomy in very high-risk surgical patients with acute cholecystitis: an international randomised multicentre controlled superiority trial (DRAC 1). Gut 2020;69:1085–91. [CrossRef]
- 8. Singh S, Bajorek B. Defining 'elderly' in clinical practice

guidelines for pharmacotherapy. Pharm Pract (Granada) 2014;12:489.

- Leardi S, De Vita F, Pietroletti R, Simi M. Cholecystectomy for gallbladder disease in elderly aged 80 years and over. Hepatogastroenterology 2009;56:303–6.
- Yi NJ, Han HS, Min SK. The safety of a laparoscopic cholecystectomy in acute cholecystitis in high-risk patients older than sixty with stratification based on ASA score. Minim Invasive Ther Allied Technol 2006;15:159–64. [CrossRef]
- Yokoe M, Takada T, Strasberg SM, Solomkin JS, Mayumi T, Gomi H, et al; Tokyo Guidelines Revision Committee. TG13 diagnostic criteria and severity grading of acute cholecystitis (with videos). J Hepatobiliary Pancreat Sci 2013;20:35–46.
- Cheng H, Clymer JW, Po-Han Chen B, Sadeghirad B, Ferko NC, Cameron CG, et al. Prolonged operative duration is associated with complications: a systematic review and metaanalysis. J Surg Res 2018;229:134–44. [CrossRef]
- Loozen CS, van Santvoort HC, van Duijvendijk P, Besselink MG, Gouma DJ, Nieuwenhuijzen GA, et al. Laparoscopic cholecystectomy versus percutaneous catheter drainage for acute cholecystitis in high risk patients (CHOCOLATE): multicentre randomised clinical trial. BMJ 2018;363:k3965.
- Jang WS, Lim JU, Joo KR, Cha JM, Shin HP, Joo SH. Outcome of conservative percutaneous cholecystostomy in high-risk patients with acute cholecystitis and risk factors leading to surgery. Surg Endosc 2015;29:2359–64. [CrossRef]
- Kirshtein B, Bayme M, Bolotin A, Mizrahi S, Lantsberg L. Laparoscopic cholecystectomy for acute cholecystitis in the elderly: is it safe?. Surg Laparosc Endosc Percutan Tech 2008;18:334–9. [CrossRef]
- Polychronidis A, Botaitis S, Tsaroucha A, Tripsianis G, Bounovas A, Pitiakoudis M, et al. Laparoscopic cholecystectomy in elderly patients. J Gastrointestin Liver Dis 2008;17:309–13.
- Philip Rothman J, Burcharth J, Pommergaard HC, Viereck S, Rosenberg J. Preoperative risk factors for conversion of laparoscopic cholecystectomy to open surgery - a systematic review and meta-analysis of observational studies. Dig Surg 2016;33:414–23. [CrossRef]
- Yang TF, Guo L, Wang Q. Evaluation of preoperative risk factor for converting laparoscopic to open cholecystectomy: a meta-analysis. Hepatogastroenterology 2014;61:958–65.
- Antoniou SA, Antoniou GA, Koch OO, Pointner R, Granderath FA. Meta-analysis of laparoscopic vs open cholecystectomy in elderly patients. World J Gastroenterol 2014;20:17626–34.
- 20. Lagunas-Rangel FA. Neutrophil-to-lymphocyte ratio and lymphocyte-to-C-reactive protein ratio in patients with severe coronavirus disease 2019 (COVID-19): A meta-analysis. J Med Virol 2020;92:1733-4. [CrossRef]
- Huang Z, Fu Z, Huang W, Huang K. Prognostic value of neutrophil-to-lymphocyte ratio in sepsis: A meta-analysis. Am J Emerg Med 2020;38:641–7. [CrossRef]
- Li T, Huang A, Zhang M, Lan F, Zhou D, Wei H, et al. Increased red blood cell volume distribution width: important clinical implications in predicting gastric diseases. Clin Lab 2017;63:1199–206. [CrossRef]