The Safety of Minimally Invasive and Open Cholecystectomy in Elderly Patients With Acute Cholecystitis: A Systematic Review

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Abstract

Elderly patients with acute cholecystitis (AC) often receive no surgical treatment due to a high number of comorbidities and a high risk of operations. With an increasingly aged population worldwide, this systematic review aims to review the safety of minimally invasive cholecystectomy and open cholecystectomy in this population compared to younger patients. A systematic search was conducted on PubMed, PubMed Central, and Google Scholar databases on July 2, 2022. Articles in the English language published in the last five years with free full text and involving elderly patients with AC treated with minimally invasive and open cholecystectomy were selected. Moreover, a quality assessment was carried out by using each study’s most commonly used assessment tools.

Initially, the search yielded 1,252 potentially relevant articles. After the final selection process, 11 studies were included: one cross-sectional study, eight cohort studies, one case-control study, and one systematic review with meta-analyses. These studies involved a total of 378,986 participants, with 375,625 elderly patients. In the elderly, cholecystitis severity, decreased physical status, and multiple comorbidities increase the risk of complications with cholecystectomy. In addition, the elderly had more complications, open surgery conversions, biliary tract injuries, leaks, postoperative mortality, and hospital length of stay than younger patients. Nevertheless, minimally invasive cholecystectomy is a viable treatment option for elderly patients when performing a thorough perioperative assessment.

Categories: Gastroenterology, General Surgery
Keywords: elderly patient, acute cholecystitis, open cholecystectomy, laparoscopic cholecystectomy, minimally invasive cholecystectomy

Introduction And Background

According to the 2020 Profile of Older Americans by the Administration for Community Living (ACL), the population older than 65 years accounted for 54.1 million people in 2019, representing 16% of the population in the United States [1]. As the population ages, there is a rise in the incidence, severity, and complications of gallstone diseases, along with an increase in surgical demands [2]. The specific characteristics of older patients increase the risk of complications due to surgical therapies. In addition, the heterogeneity of this group with regard to comorbidities and their diminished physical capabilities decrease their capacity to adapt and make them more susceptible to adverse outcomes [3].

Acute cholecystitis (AC) results from the obstruction of the cystic duct, typically by a gallstone, followed by gallbladder distension and bacterial or chemical inflammation. The typical symptoms of AC include right upper quadrant pain, anorexia, nausea, vomiting, and fever [4, 5]. AC usually requires rapid treatment due to the risk of potentially severe complications if left untreated. The only permanent cure for symptomatic gallstone disease is cholecystectomy. The Tokyo guidelines recommend early cholecystectomy as an adequate treatment [4].

Cholecystectomy using laparoscopy (LC) has been the operative standard of care since the late 1990s [6], and an overall reduction in operative mortality per procedure has been observed when compared with open cholecystectomy [7, 8]. However, it is still debated whether cholecystectomy should be used as the first line of treatment for AC in elderly patients. In light of this, this systematic review aims to evaluate the safety of the different surgical treatments for AC in elderly patients (>65 years) compared to younger patients.

Review

Methods

This systematic review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guideline [9].

Inclusion and Exclusion Criteria

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The studies were selected based on the participant, the intervention, and the outcome (PIO) element: participants - elderly patients with AC; intervention - laparoscopic cholecystectomy, robotic-assisted cholecystectomy, or primarily open cholecystectomy; and outcome - results of the surgery and any complication reported. Other inclusion criteria were English language articles published in the last five years with free full text available. The exclusion criteria were conference papers, abstracts, guidelines, case reports, and any studies that did not involve AC.

Search Strategy

A systematic search of the current literature was conducted on PubMed, PubMed Central (PMC), and Google Scholar databases by two independent authors; the last day of inquiry on all the databases was July 2, 2022. The search terms used were 'Minimally invasive cholecystectomy' OR 'Laparoscopic cholecystectomy' OR 'robotic-assisted cholecystectomy' and 'Open cholecystectomy' and 'Acute cholecystitis' and 'elderly patient' individually or in combination. All the search terms used for this review are shown in Table 1.

![Table 1: The strategy for conducting bibliographic searches in databases and the corresponding filters](https://example.com/table1.png)

The references of all the articles were grouped and organized in alphabetic order using Excel 2021. Then, two authors removed the duplicates, they also reviewed the titles and abstracts independently and excluded any irrelevant articles. Then the complete articles of the studies identified were retrieved and reviewed. The investigators decided to exclude conference papers, abstracts, guidelines, and case reports due to the lack of analysis required for this study. They included the sole systematic review conducted in the field so far.

Risk of Bias in Individual Studies

The remaining full articles were assessed by two independent authors for quality assessment and risk bias using different tools depending on the type of study: cross-sectional studies, Joanna Briggs Institute (JBI) critical appraisal checklist; cohort and case-control studies, the Newcastle–Ottawa Scale (NOS); systematic review and meta-analyses, assessment of multiple systematic reviews 2 (AMSTAR 2) [10-12]. The assessment tools had their criteria and different scoring. When the tool scores “YES,” "PARTIAL YES,” or ‘1,’ a point is given. When “2” is indicated, two points are given. A minimum of 70% score for each assessment tool was accepted (Table 2).
| JBI | Cross-sectional | Eight items: (1) Were the criteria for inclusion in the sample clearly defined? (2) Were the study subjects and the setting described in detail? (3) Was the exposure measured validly and reliably? (4) Were objective, standard criteria used to measure the outcome? (5) Were confounding factors identified? (6) Were strategies to deal with confounding factors stated? (7) Were the outcomes measured validly and reliably? (8) Were appropriate statistical analyses used? | 8 | Bass et al., 2021 [10] |
| NOS | Cohort | Eight items: (1) Representation of the exposed cohort. (2) Selection of the non-exposed cohort. (3) Ascertainment of exposure. (4) Demonstration that outcome of interest was not present at the start of the study. (5) Comparison of cohorts based on the design or analysis. (6) Assessment of outcome. (7) Were follow-up long enough for outcomes to occur? (8) Adequacy of follow-up of cohorts. Scoring was done by placing a point on each category. Scored as 0, 1, 2. *Maximum of two points are allotted in this category. | 9 | Xu et al., 2022 [22] |

| AMSTAR 2: assessment of multiple systematic reviews 2 | 16 | Kamarajah et al., 2018 [14] |

| NOS | Case-control | Eight items: (1) Is the case-definition adequate? (2) Representativeness of the cases. (3) Selection of controls. (4) Definition of controls. (5) Comparability of cases and controls based on the design and analysis. (6) Ascertainment of exposure. (7) The same method of ascertainment for cases and controls. (8) No response rate. Scoring was done by placing a point on each category. Scored as 0, 1, 2. *Maximum of two points are allotted in this category. | 9 | Kamarajah et al., 2018 [14] |

| NOS | Case-control | Eight items: (1) Did the review authors explain their selection of the study designs for inclusion in the review? (2) Did the review authors perform study selection in duplicate? (3) Did the review authors perform data extraction in duplicate? (4) Did the review authors provide a list of excluded studies and justify the exclusion? (5) Did the review authors describe the included studies adequately? (6) Did the review authors use a satisfactory technique for assessing the risk of bias (RoB) in individual studies included in the review? (7) Did the review authors provide on the sources of funding for the studies included in the review? (8) If meta-analysis was justified, did the review authors use appropriate methods for the statistical combination of results? (9) If a meta-analysis was performed, did the review authors assess the potential impact of RoB in individual studies on the results of the meta-analysis or other evidence synthesis? (10) Did the review authors account for RoB in individual studies when interpreting the review results? (11) Did the review authors provide a satisfactory explanation for and discussion of any heterogeneity observed in the review results? (12) If they performed quantitative synthesis, did the review authors carry out an adequate investigation of publication bias (small study bias) and discuss its likely impact on the results of the review? (13) Did the review authors report any potential sources of conflict of interest, including any funding they received for conducting the review? Scored on NOS 9 and 10. A partial tick was considered as a point. | 12 | Shin et al., 2018 [15] |

### Table 2: Evaluation of the quality of each type of study

| JBI | Joanna Briggs Institute; NOS: Newcastle-Ottawa Scale; AMSTAR 2: assessment of multiple systematic reviews 2; RoB: risk of bias | 2022 Montenegro et al. Cureus 14(11): e31170. DOI 10.7759/cureus.31170 | 3 of 15 |

### Data Collection and Analysis

Two authors extracted the data independently. Due to the varying measures of observer variability between the studies, such as heterogeneity of participants, intervention, and outcome measures, this systematic review describes these studies based on their outcomes in a narrative synthesis. Complete articles were analyzed and tabulated into a table. The data collected for each study include first author, year of publication, study type, country of origin, number of patients, the definition of elderly or age ranges, indications of surgery, type of surgery, preoperative evaluation of the anesthetic-surgical risk based on the American Society of Anesthesiology Physical Status (ASA PS), comorbidity, and the results.

### Study Outcome

The outcomes analyzed were the overall complications reported, the rate of conversion to open surgery, bile leaks and biliary tract postoperative mortality, and hospital stay duration.

### Results

#### Evaluation of Study Selection and Quality

The database search yielded a total of 1,252 potentially relevant titles. Google Scholar automatically deleted...
one title. The removal of duplicates was also done, with 952 records retained. A total of 50 articles remained when the titles and abstracts of these records were screened based on this review’s PIO elements and eligibility criteria; these articles were retrieved, and conference papers, abstracts, guidelines, and case reports were excluded (18 articles). Finally, the quality assessment for each article was done, and 11 studies with a score of greater than 70% were accepted for the review. These included one cross-sectional study, eight cohort studies, one case-control study, and one systematic review with meta-analyses. No other resources were added. We followed the PRISMA 2020 guidelines for screening and study selection. Figure 1 shows the PRISMA flow diagram illustrating the process [9].

Each study was evaluated with the appropriate quality assessment tool for each study type, and the results were tabulated. For example, the only cross-sectional study in the review was assessed using the JBI tool. This study scored 7/8, with item 6 recorded as ‘NO’ because the strategies to deal with confounding factors were not stated. This information is shown in Table 3 below.

| First author, year | Item 1 | Item 2 | Item 3 | Item 4 | Item 5 | Item 6 | Item 7 | Item 8 |
|-------------------|--------|--------|--------|--------|--------|--------|--------|--------|
| Bass et al. 2021  | Y      | Y      | Y      | Y      | Y      | N      | Y      | Y      |

NOS tool was used in assessing all the cohort studies, and most of the accepted cohort studies had a score of ‘1’ for each item; two studies used multiple controls for the confounding factor in the analysis scoring ‘2’ in item 5. Most studies fail to assess the adequacy of the follow-ups, scoring 0 in item 8. One study that scored 6 (<70% of quality) was excluded from the review. The summary of the assessment is presented in...
Table 4.

The case-control study was assessed using the NOS tool, and the accepted study had a score of ‘1’ for each item, with a total of 8/9 (Table 5).

Table 5: Result summary of coding manual for the case-control study by review authors

One study was a systematic review with meta-analysis. Upon scoring using AMSTAR 2 tool, the accepted reviews had ‘NO’ in items 3 and ‘Partial Yes’ in items 4 and 8. These items discussed the explanation of the selection of the study designs, literature search, and studies description, respectively, as presented in Table 6.

Table 6: Summary of the critical appraisal for the systematic review and meta-analysis by review authors

Y: yes; PY: partial yes; N: no

Study Characteristics

The key traits of the cohorts, case-control study, cross-sectional analyses, and the systematic review with meta-analysis in the review are presented in chronological order in Tables 7-8, respectively. The studies included 378,986 participants, with 44,655 receiving conservative treatment alone, 334,239 receiving laparoscopic cholecystectomy, 92 receiving primary open cholecystectomy, and 59,350 having to be converted to open cholecystectomy. Four of the 11 studies included in the review focused on treating elderly patients, and seven compared treatments for young and elderly patients.
| Year | Country | Patients | Age Group 1 | Age Group 2 | Key Findings |
|------|---------|----------|-------------|-------------|--------------|
| 2018 | Kingdom | 473,000  | 60 years    | >80 years   | Laparoscopic approach rate of 59% in the percutaneous cholecystectomy (30%, NRI) |
| 2019 | Brazil  | 1,065    | 60 years    | >80 years   | Relative risk reduction in 30-day mortality of 94% |

**Glazi et al., 2018**
- Turkey
- 665 patients
- Two groups: <60 years and >60 years of age
- Underwent surgery when they were experiencing Acute Cholecystitis (AC)
- ASA scores for most patients were I (38%) and II (27.7%)
- Hypertension in 110 (19.3%), diabetes mellitus in 61 (9.2%), chronic obstructive pulmonary disease in 53 (8.6%), and congestive heart failure in 41 (6.6%) were the most prevalent concomitant diseases
- elderly group had a significantly higher ASA score than the younger group
- Analysis of variables shown statistically significant in elderly individuals
- Elderly patients may also receive LC without risk
- Complication and conversion rates were comparable across age groups when adequate preoperative assessment and therapy were carried out
- Diabetic patients over 50 can safely undergo LC if a comprehensive preoperative evaluation of their health and an elective procedure is carried out

**Lucenti et al., 2018**
- Italy
- 703 patients
- Two groups: > 75 years old with 121 patients (17%) and < 60 years old (83%)
- Acute cholecystitis admitted through the emergency room
- ASA score indicates that elderly patients in the elderly group - Primary OC in both groups; three patients
- Cardiovascular illness (20% vs. 11%), lung disease (23% vs. 7%), and diabetes (19% vs. 11%) were all more prevalent and statistically significant in elderly individuals
- Elderly patients with mild-to-moderate acute cholecystitis respond well to medical-pressive cholecystostomy

**Shen et al., 2018**
- Korea
- 265 patients
- Three groups: Group A (<60 years old), group B (from 60 to 79 years old), and group C (>79 years old)
- - LC: 194 patients in group A; 70 in group B, and 21 in group C
- Elderly patients (Group B) had statistically significantly higher ASA scores than group A
- The underlying diseases of the patients varied significantly depending on the age group
- Poor physical condition (ASA III-IV), rather than age per se, limited the therapeutic options available to older AC patients
- The severity of the disease (Grade III AC) and/or poor physical condition (ASA III-IV), rather than age per se, limited the therapeutic options available to older AC patients
- In elderly individuals with Grade I–II AC, LC can be successfully conducted safely. When Grade III AC, there is a substantial risk of mortality and death, necessitating a customized treatment plan

**Giacardi et al., 2019**
- Spain
- 348 patients
- Two groups: those under the median age (85.4 years) and those over that age (85.4 years)
- Antibiotics only: 81 patients in Group A and 11% in Group B; 72 patients in Group A and 18% in Group B
- The ASA score indicates that older participants tend to be at higher risk
- The elderly can undergo LC with acceptable rates of morbidity and mortality. When elderly patients have LC, it takes longer to complete the procedure, and they are more likely to develop acute cholecystitis, correct it open cholecystectomy, and experience postoperative problems. Age is less of a protective factor for LC than the severity of gallbladder disease

**Olmos et al., 2019**
- Italy
- 245 patients
- Two groups: group A (<60 years old) and group B (>60 years old)
- Primary OC: Group A (54%); Group B (37%); 52 patients were from Group A and 32 from Group B
- Diabetes was present in 104 patients (38%); 52 patients were from Group A and 52 from Group B
- The elderly can undergo LC with acceptable rates of morbidity and mortality. When elderly patients have LC, it takes longer to complete the procedure, and they are more likely to develop acute cholecystitis, correct it open cholecystectomy, and experience postoperative problems. Age is less of a protective factor for LC than the severity of gallbladder disease

**Cazetta et al., 2020**
- Brazil
- 1,065 patients
- Two groups: elderly (85 years) and younger (<60 years of age)
- Acute and chronic cholecystitis: LC: 26% (50% of the patients were older, and 39% were younger) in the younger group, there were more patients with ASA I in the elderly group, NR
- The elderly can undergo LC with acceptable rates of morbidity and mortality. When elderly patients have LC, it takes longer to complete the procedure, and they are more likely to develop acute cholecystitis, correct it open cholecystectomy, and experience postoperative problems. Age is less of a protective factor for LC than the severity of gallbladder disease
The cut-off ages utilized to designate elderly populations varied significantly, with age 60 (n=3 studies), 65 (n=5 studies), 70 (n=1 research), 75 (n=1 study), and 80 (n=5 studies) being the most common. The features and outcomes of the studies were described using the age groups established by each study. There were a total of 375,623 elderly patients in the 11 studies. The systematic review and meta-analysis was the study with a significant population of 326,517 elderly patients (>60 years old) receiving laparoscopic cholecystectomy. Also, this study mainly emphasized the perioperative results of the surgery. In contrast, the rest of the studies reported the patients' physical status with aging was supported by the linear-by-linear association test, which revealed that there were substantially fewer patients in group C compared to groups A and B with ASA PS I and significantly more patients with ASA PS II.

The critical variable affecting the unfavorable result of LC is the elderly was the level of systemic inflammation. Diabetes was linked to higher surgical and systemic postoperative morbidity among complications, while acute and chronic renal insufficiency were linked to a higher risk of cardiovascular problems. With proper perioperative care, elderly patients can significantly benefit from a minimally invasive procedure's advantages, which include a lower risk of postoperative complications and a shorter hospital stay.

### TABLE 7: Main characteristics of the cohort studies included in the review

| First author, year | Study Type | Country of origin | Patient number | Age ranges | Indications for surgery | Type of treatment | ASA PS | Comorbidity | Results and key points |
|--------------------|------------|-------------------|----------------|------------|-------------------------|------------------|-------|-------------|----------------------|
| Bass et al., 2021 | Cohort     | Romania           | 837            | ≥80 years  | N/A                     | LC               | NR    | CCI         | Three groups: Group A: 119 (60.5%) Group B: 99 (58.5%) Group C: 31 (37.3%) Group D: 26 (16.5%); CCI: Group A: 1.5 (8%) Group B: 1.5 (8%) Group C: 0.8 (6%) Group D: 0.4 (2.5%); The incidence of acute cardiac insufficiency at admission increased with age. In addition, serious complications between decompensation in the context of systemic inflammation and acute renal insufficiency were more frequent in patients with ASA PS II. The cut-off ages utilized to designate elderly populations varied significantly, with age 60 (n=3 studies), 65 (n=5 studies), 70 (n=1 research), 75 (n=1 study), and 80 (n=5 studies) being the most common. The features and outcomes of the studies were described using the age groups established by each study. There were a total of 375,623 elderly patients in the 11 studies. | N/A                        |

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### TABLE 8: Main characteristics of the cross-sectional study, case-control study, and systematic review and meta-analysis included in the review

| First author, year | Study Type | Country of origin | Patient number | Age ranges | Indications for surgery | Type of treatment | ASA PS | Comorbidity | Results and key points |
|--------------------|------------|-------------------|----------------|------------|-------------------------|------------------|-------|-------------|----------------------|
| Xu et al., 2022    | Case-Control | China           | 66            | >65 years  | N/A                     | LC               | NR    | CCI         | Elderly individuals with AC who receive early LC treatment benefit from postoperative functional rehabilitation and experience minimal effects on their energy metabolism. Early LC treatment is superior to LC treatment administered after 48 hours because it causes less severe stress reactions, has lower infection rates, less intraoperative complication, improved liver function, and has a lower incidence of problems. | N/A                        |

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### TABLE 9: Main characteristics of the cohort studies included in the review

| First author, year | Study Type | Country of origin | Patient number | Age ranges | Indications for surgery | Type of treatment | ASA PS | Comorbidity | Results and key points |
|--------------------|------------|-------------------|----------------|------------|-------------------------|------------------|-------|-------------|----------------------|
| Seo et al., 2021   | Cohort     | South Korea       | 333            | 45-60 years| N/A                     | LC               | NR    | CCI         | The variables determinants of outcomes, the statistical significance, the critical variable affecting the unfavorable result of LC is the elderly was the level of systemic inflammation. Diabetes was linked to higher surgical and systemic postoperative morbidity among complications, while acute and chronic renal insufficiency were linked to a higher risk of cardiovascular problems. With proper perioperative care, elderly patients can significantly benefit from a minimally invasive procedure's advantages, which include a lower risk of postoperative complications and a shorter hospital stay. | N/A                        |
## Outcomes

The authors analyzed all the studies in search of the overall complications reported, the rate of conversion to open surgery, bile leaks and biliary tract injury, postoperative mortality, and length of hospital stay. Unfortunately, some of the secondary results were not reported due to the different methods used in the study design. The resumed studies’ outcomes are presented in Table 9.

| First | Outcomes addressed | Conversion to open surgery | Postoperative mortality | Length of hospital stay |
|-------|--------------------|----------------------------|------------------------|------------------------|
| author, year | Overall complications | | | |
| Wiggins et al., 2019 | The overall 30-day mortality was 15.2% (9, 29), of which the conservation surgery group had 4, 400 deaths, emergency cholecystectomy 3, 69, and postoperative cholecystectomy 190. Near the end of the study period, the overall 30-day mortality was 15.2% (9, 29) | Several patients (2.1%) suffered bile duct injury, and biliary leakage was reported in 47 (2.1%) | Elderly patients undergoing cholecystectomy have a mortality rate of 11.8% | Near the end of the study period. The overall 30-day mortality was 15.2% (9, 29). |
| Goccia et al., 2019 | Forty-seven patients (7.1%) experienced postoperative complications, and these were statistically significantly higher in the age group >60 years | Five cases of biliary tract injury were noted (0.8%). Three (0.1%) of these patients were over 70. Biliary leakage was reported in 10 patients, and the most common complication was in the elderly group with eight patients (7%) | The overall 30-day mortality was 15.2% (9, 29) | Near the end of the study period. The overall 30-day mortality was 15.2% (9, 29) |
| Lucas et al., 2019 | The perioperative morbidity and mortality rates for elderly patients were 17% and 3%, respectively, but these rates were better for non-elderly patients at 8% and 1%, respectively | Three cases had biliary tract injury, one (0.8%) of these patients was over 70. Biliary leakage was reported in 10 patients, the most common complication was in the elderly group with eight patients (7%) | The overall 30-day mortality was 15.2% (9, 29) | Near the end of the study period. The overall 30-day mortality was 15.2% (9, 29) |
| Shi et al., 2019 | Eight of the 114 patients in group A, seven of the 70 in group B, and one of the 20 in group C required open conversion. Conversion to open cholecystectomy was not statistically significant. Common bile duct injury was present in three cases, one patient from each age group. In addition, biliary leakage was reported in two (2%) patients of group B | The mortality rate in group A was 5.4% (2 cases of postoperative mortality and 3 cases of postoperative morbidity). The mortality rate in group B was 11.8% (two cases of postoperative mortality and 9 cases of postoperative morbidity). The mortality rate in group C was 12.5%. Eight of the 114 patients in group A required open surgery. Group A had two (11.8%) deaths, and group B had one (5.0%) death. Group C had one (6.2%) death. Grade I-II AC: No deaths in group A and morbidity was minimal in both operated and non-operated patients (1.3% vs. 0.7%). In addition, patients with bile duct injury did not. Grade III AC: One main bile duct injury was reported. Three cases had biliary tract injury, one (0.8%) of these patients was over 70. Biliary leakage was reported in 10 patients, the most common complication was in the elderly group with eight patients (7%) | Hospital stays in group A, between 5.0 and 11.5 days in non-operated and from 5.0 to 10.4 days in the operated group. In comparison, group B was between 6.7 and 12.1 days in non-operated and from 7.5 to 11.4 days in operated patients. | Near the end of the study period. The overall 30-day mortality was 15.2% (9, 29) |
| Goccia et al., 2019 | Grade A-4: No deaths in group A and morbidity was not reported in both operated and non-operated patients (12.5% vs. 8.2%). Group B had overall death and more significant complications when they underwent surgery (20% vs. 8.8%). Grade B-4: Severe complications were more frequent in group B patients who underwent surgery than in those who did not (30% versus 50%, respectively), and death was very high (1.4%) in the patients that underwent surgery, compared to 20.6% in those who did not. In group B, the proportion of deaths and severe complications was similar | The overall postoperative mortality rate in group A was 4.8%. There were no discernible variations across the age groups | Hospital stays in group A, between 5.0 and 11.5 days in non-operated and from 5.0 to 10.4 days in the operated group. In comparison, group B was between 6.7 and 12.1 days in non-operated and from 7.5 to 11.4 days in operated patients. | Near the end of the study period. The overall 30-day mortality was 15.2% (9, 29) |
| Cobian et al., 2019 | Eight of the 114 patients in group A, seven of the 70 in group B, and one in Group C required open surgery. Conversion to open cholecystectomy was not statistically significant. Common bile duct injury was present in three cases, one patient from each age group. In addition, biliary leakage was reported in two (2%) patients of group B | The overall postoperative mortality rate in group A was 4.8%. There were no discernible variations across the age groups | Hospital stays in group A, between 5.0 and 11.5 days in non-operated and from 5.0 to 10.4 days in the operated group. In comparison, group B was between 6.7 and 12.1 days in non-operated and from 7.5 to 11.4 days in operated patients. | Near the end of the study period. The overall 30-day mortality was 15.2% (9, 29) |
| Cobian et al., 2019 | Eight of the 114 patients in group A, seven of the 70 in group B, and one in Group C required open surgery. Conversion to open cholecystectomy was not statistically significant. Common bile duct injury was present in three cases, one patient from each age group. In addition, biliary leakage was reported in two (2%) patients of group B | The overall postoperative mortality rate in group A was 4.8%. There were no discernible variations across the age groups | Hospital stays in group A, between 5.0 and 11.5 days in non-operated and from 5.0 to 10.4 days in the operated group. In comparison, group B was between 6.7 and 12.1 days in non-operated and from 7.5 to 11.4 days in operated patients. | Near the end of the study period. The overall 30-day mortality was 15.2% (9, 29) |
| Cobian et al., 2020 | Eight of the 114 patients in group A, seven of the 70 in group B, and one in Group C required open surgery. Conversion to open cholecystectomy was not statistically significant. Common bile duct injury was present in three cases, one patient from each age group. In addition, biliary leakage was reported in two (2%) patients of group B | The overall postoperative mortality rate in group A was 4.8%. There were no discernible variations across the age groups | Hospital stays in group A, between 5.0 and 11.5 days in non-operated and from 5.0 to 10.4 days in the operated group. In comparison, group B was between 6.7 and 12.1 days in non-operated and from 7.5 to 11.4 days in operated patients. | Near the end of the study period. The overall 30-day mortality was 15.2% (9, 29) |
| Saito et al., 2021 | Similar rates of intraoperative complications were observed in both groups, but the rate of postoperative complications was lower in the older group (12.2% vs. 6.7%) than in the younger group. Postoperative mortality was significantly higher in the elderly too. | The overall postoperative mortality rate in group A was 4.8%. There were no discernible variations across the age groups | Hospital stays in group A, between 5.0 and 11.5 days in non-operated and from 5.0 to 10.4 days in the operated group. In comparison, group B was between 6.7 and 12.1 days in non-operated and from 7.5 to 11.4 days in operated patients. | Near the end of the study period. The overall 30-day mortality was 15.2% (9, 29) |
| Saito et al., 2021 | Similar rates of intraoperative complications were observed in both groups, but the rate of postoperative complications was lower in the older group (12.2% vs. 6.7%) than in the younger group. Postoperative mortality was significantly higher in the elderly too. | The overall postoperative mortality rate in group A was 4.8%. There were no discernible variations across the age groups | Hospital stays in group A, between 5.0 and 11.5 days in non-operated and from 5.0 to 10.4 days in the operated group. In comparison, group B was between 6.7 and 12.1 days in non-operated and from 7.5 to 11.4 days in operated patients. | Near the end of the study period. The overall 30-day mortality was 15.2% (9, 29) |
| Bae et al., 2021 | Patients over 65 reported greater postoperative complications than younger patients. Statistically, the difference was not significant (29.6% vs. 10.1%, p < 0.05). Nineteen patients (5.6%) were transferred to the ICU during their hospital stay, and 12 patients (3.4%) suffered bile duct injury. | The overall postoperative mortality rate in group A was 4.8%. There were no discernible variations across the age groups | Hospital stays in group A, between 5.0 and 11.5 days in non-operated and from 5.0 to 10.4 days in the operated group. In comparison, group B was between 6.7 and 12.1 days in non-operated and from 7.5 to 11.4 days in operated patients. | Near the end of the study period. The overall 30-day mortality was 15.2% (9, 29) |
TABLE 9: Outcomes addressed by the included articles

- NR: not reported; AC: acute cholecystitis; LC: laparoscopic cholecystectomy; OC: open cholecystectomy; ASA PS: American Society of Anesthesiologists Physical Status Classification; CCI: Charlson Comorbidity Index; ICU: intensive care unit; LOS: length of hospital stay

Discussion

AC in the elderly is becoming more prevalent as the population ages. However, while patients’ general health improves as they age, having comorbid conditions makes choosing a treatment more difficult. This systematic study evaluates the safety of minimally invasive cholecystectomy and open cholecystectomy in this population compared to younger patients.

The likelihood of a patient undergoing a cholecystectomy after presenting with symptomatic gallstone disease as AC decreases with age [22]. This was shown by Wiggins et al., where only 7.5% of the elderly patients had a cholecystectomy, and the majority of patients (89.7%) had conservative treatment [14]. Also, Escartín et al. reported increased use of conservative treatment with increased age [18]. However, the rest of the studies did not note differences in the treatment received.

When comparing the type of surgery, half of the studies reported a laparoscopic procedure as the preferred course of treatment [15,17,20,22,23]. In contrast, in the rest of the studies, the number of open approaches was minimum. Due to this, a proper comparison between the open and laparoscopic procedures could not be made because the open procedure was not a first-line surgical treatment option regardless of the patient’s age [15,16,18,19,21]. Furthermore, none of the studies uses robotic-assisted cholecystectomy.

In the case of preoperative physical status (ASA), elderly patients have higher score distribution; this was reported by Serban et al. and supported by the linear-by-linear association test [21]. Furthermore, ASA III and higher were more significant in the elderly group in most studies, showing an increased surgical risk. However, according to the same research, surgery is safe if an adequate preoperative assessment is performed on the elderly [15,15–21].

Elderly patients have a higher burden of comorbidity when compared to their younger counterparts, which results in a higher frequency of complications [26]. This is evidenced by a significantly higher CCI in elderly groups [15,14]. Cardiovascular illness, lung disease, and diabetes were the most prevalent concomitant diseases [15–18]. Consequently, Wiggins et al. reported fewer comorbidities in patients who underwent emergency cholecystectomy [14].

Overall Complications

In general, an increase in age has been substantially linked to higher risks of surgical complications. Most of the studies in this review reported an increase in overall complications associated with the increasing age of the patients. However, the age of cut-off varies in the studies. For example, Serban et al. reported an increased rate of postoperative complications in patients over 50 and an increase in age-related cardiovascular postoperative complications [21]. In the same way, Bass et al. and Kamarajah et al. reported higher postoperative problems in patients over 65 [15,23]. However, Escartín et al. reported increased complications with the increase in AC severity. Serious complications are more frequent in patients with grade III AC, independent of the treatment [18]. Also, Loozen et al. discovered that severe AC was linked to higher comorbidity [16].

Conversion to Open Surgery

The probability of converting to an open cholecystectomy rose considerably with age. This was consistently reported by the majority of the studies [15,15,16,19,20]. These results contrast with the study conducted by Shin et al., where no significant differences in conversion rate were discovered [17]. Also, the effect of
advancing age on conversion to open cholecystectomy was documented in 53 studies with 59,173 patients, forming part of the systematic review and meta-analysis by Kamarajah et al. [23]. This result is consistent with the literature, which shows that advanced age increases the risk of converting to an open procedure [27].

**Bile Leaks and Biliary Tract Injury**

There was a significant correlation between age and bile leakage [15,16,19]. Similarly, Kamarajah et al. reported that the effect of aging on bile leakage was documented in 30 studies involving 42,765 patients [23]. In the same way, biliary tract injury was reported more frequently in elderly patients [15,16]. However, Shin et al. did not find a difference in the incidence of biliary tract injury between old and young groups [17].

**Postoperative Mortality**

Aging was substantially linked to higher postoperative mortality rates [15,16,18-20]. Likewise, Kamarajah et al. reported that the effect of aging on postoperative mortality was observed in 30 studies with 78,404 patients [23]. Moreover, Wiggins et al. stated that in the case of elderly patients undergoing emergency cholecystectomy, the mortality rate can be as high as 11.6%. However, one of the major flaws of this research was that it did not consider the associated comorbidities and their impact on the outcomes [14]. In contrast with these findings, Antonioiu et al. discovered that mortality was 1.0% for the laparoscopic approach and 4.4% for the open approach in a meta-analysis of 11 studies published between 1993 and 2011 involving 101,559 patients aged 65 years or older (48,195 treated laparoscopically and 53,364 by open cholecystectomy) [28].

**Length of Hospital Stay**

In most studies, a more extended hospital stay was substantially correlated with older age [15-18,23]. However, Coelho et al. reported no difference in the length of hospital stays between the elderly and the younger group [20]. On the other hand, Serban et al. expressed that laparoscopic cholecystectomy produces better results than open cholecystectomy in terms of shorter postoperative and overall hospital stays [21], whereas Xu et al. showed that early LC in elderly patients with AC leads to shorter hospital stays after surgery [22].

**Overall Outcomes**

In elderly patients with mild to moderate AC, minimally invasive therapy appears to be a practical and effective therapeutic option. Conservative treatment is deemed ineffective based on existing research [14,18,29,30]. Comorbidities, however, should be kept in mind since they may complicate the procedure and the postoperative recovery period [15,16,18,19,21]. Complication and conversion rates are comparable across age groups when adequate preoperative assessment and therapy are carried out [17]. The severity of the disease (grade III AC), poor physical condition, and/or comorbidities rather than age per se can limit the therapeutic options available to older AC patients [15,18,20,21]. Also, reduced readmission rates and one-year mortality are two potential advantages of emergency cholecystectomy in very elderly patients reported [14]. However, Kamarajah et al., in their meta-analysis of 99 studies, support prior assumptions that older patients undergoing cholecystectomy face increased risks and reported a seven-fold rise in perioperative mortality, which rises to 10-fold in patients over the age of 80 years. Furthermore, they recommended surgery selection on a patient-by-patient basis [23].

**Limitations**

This review restricted the included studies to those in the English language and those with a full-text published in three databases between 2018 and 2022. Gray literature and other databases were not used. In addition, the majority of the studies that the search yielded were cohort studies. Furthermore, the review was limited by the heterogeneity of the studies. For example, the studies vary in patient age, preoperative evaluations, and treatment options. No randomized controlled clinical trials (RCTs) or studies involving robotic-assisted cholecystectomy in the elderly with AC were found.

There was no extensive follow-up in the patients; most of the studies focused on the immediate postoperative results instead of preoperative management. Therefore, we recommend observational studies with longer follow-ups after surgery and adequate preoperative preparations as well as RCTs to find out which procedures or treatments provide the most significant benefits to elderly patients.

**Conclusions**

The studies included in this review demonstrate that in the elderly, compared with younger patients, the surgical treatment of AC is a challenging decision. The severity of this condition, the diminished physical status, and multiple comorbidities increase the risk of operative and postoperative complications in the older group of patients. Even though there is no consensus on the surgical treatment of AC in elderly patients, the laparoscopic approach is the preferred procedure for cholecystectomies. It can be safely performed in older patients and the conservative approach is not recommended.

The overall complications, open surgery conversions, biliary tract injury, leaks, postoperative mortality, and hospital length of stay increase considerably with age. Nevertheless, minimally invasive cholecystectomy is a feasible treatment option for elderly patients suffering from mild to moderate AC when a comprehensive perioperative assessment is conducted. Most complications reported in old patients who underwent
cholecystectomy were related to the burden of comorbidities and cholecystitis severity than to the age or surgical procedure. That being the case, a thorough optimization of elderly patients with severe cholecystitis or severe comorbidities is required to determine the optimal treatment. Furthermore, extensive observational studies and RCTs need to be conducted and guidelines regarding associated diseases, physiological status, and age have to be devised and published.

Additional Information

Disclosures

Conflicts of interest: In compliance with the ICMJE uniform disclosure form, all authors declare the following: Payment/services info: All authors have declared that no financial support was received from any organization for the submitted work. Financial relationships: All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. Other relationships: All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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