# Early versus delayed same-admission laparoscopic cholecystectomy for acute cholecystitis in elderly patients with comorbidities

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**BACKGROUND:** The optimal timing of same-admission laparoscopic cholecystectomy (LC) for acute cholecystitis (AC) in elderly patients, especially those with significant comorbidities, is not clear.

**METHODS:** This is a National Surgical Quality Improvement Program study, which included patients older than 65 years undergoing LC for AC. Patients with choledocholithiasis were excluded. Patients were divided into two subgroups as follows: no significant comorbidities (American Society of Anesthesiologists [ASA] score ≤ 2) and significant comorbidities (ASA score > 2). Patients undergoing LC within 24 hours of admission (early LC) were compared with patients undergoing LC later than 24 hours after admission (delayed LC), using univariable and multivariable regression analyses.

**RESULTS:** A total of 4,011 patients were included in the study. Early LC was performed in 38.0% and delayed LC in 62.0% of the patients. Regression analysis identified early LC as an independent predictor for shorter anesthesia time and postoperative length of stay, overall and in the subgroup with an ASA score greater than 2.

**CONCLUSION:** Early, within 24 hours of admission, LC for AC in patients older than 65 years with significant comorbidities is associated with shorter postoperative stay and no increase in postoperative complications or conversion to open cholecystectomy. (*J Trauma Acute Care Surg*. 2015;78: 801–807. Copyright © 2015 Wolters Kluwer Health, Inc. All rights reserved.)

**LEVEL OF EVIDENCE:** Therapeutic study, level IV.

**KEY WORDS:** Acute cholecystitis; same-admission laparoscopic cholecystectomy; elderly patients; comorbidities.

The optimal time of laparoscopic cholecystectomy (LC) for acute cholecystitis (AC) has been a controversial issue. Earlier studies suggested that initial conservative management with antibiotics, followed by interval elective cholecystectomy, was associated with reduced complications and conversion rates. However, several studies challenged this concept and suggested that same-admission LC for AC is associated with better outcomes.[1–4] Early LC (ELC) is currently the recommended treatment for AC according to the published guidelines of the Society of American Gastrointestinal and Endoscopic Surgeons[5] and the Society of Surgery of the Alimentary Tract.[6] More recent studies have also suggested that delaying cholecystectomy during the same admission increases hospital stay without any outcome benefits.[7–9] The optimal timing of same-admission LC for AC in elderly patients, especially those with significant comorbidities, has not been studied. The purpose of the present study was to study the effect of timing of same-admission LC in patients older than 65 years, with or without significant comorbidities.

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## PATIENTS AND METHODS

### Patient Selection

This is a retrospective cohort study using the American College of Surgeons (ACS) National Surgical Quality Improvement Program (NSQIP) database and included the period 2005 to 2010. The NSQIP database collects clinical data, including preoperative risk factors, intraoperative variables, as well as postoperative mortality and morbidity outcomes for patients undergoing surgical procedures. The ACS provides training and ongoing education and conducts audits to ensure data reliability. The NSQIP database contains Health Insurance Portability and Accountability Act (HIPAA) deidentified data of participating hospitals.[10]

All patients older than 65 years undergoing LC for AC were extracted from the NSQIP database. Patients with AC and concurrent common bile duct stones (choledocholithiasis [CDL]) or those treated only with cholecystostomy tubes were excluded. The study patients were divided into two comorbidity categories according to their American Society of Anesthesiologists (ASA) physical status classification score:[11] no significant comorbidities (ASA score ≤ 2) and significant comorbidities (ASA score > 2).

Patients undergoing LC for AC on hospital Day 0 (within 24 hours) after hospital admission (ELC group) were compared with patients undergoing LC for AC after hospital Day 0 but during the same hospital stay (delayed LC [DLC] group).

### Outcome Parameters

Outcome parameters included 30-day mortality and morbidity, duration of anesthesia and operation, conversion to open cholecystectomy (OC), as well as total hospital length of stay

(LOS) and postoperative LOS. The following complications were recorded: superficial incisional surgical site infection (SSI), deep incisional SSI, organ space SSI, pneumonia, unplanned postoperative reintubation, failed extubation (mechanically assisted ventilation > 48 hours postoperatively), progressive renal failure (rise in creatinine > 2 mg/dL from preoperative value without requirement for dialysis), acute renal failure (requirement for renal replacement therapy postoperatively in patients not requiring dialysis preoperatively), urinary tract infection, cerebrovascular accident, cardiac arrest, myocardial infarction, bleeding postoperatively requiring blood transfusion (up to 72 hours postoperatively), venous thrombosis, pulmonary embolism (PE), sepsis, and septic shock. Specific details and definitions of the analyzed complications are available at the ACS NSQIP Web page.[10]

Outcome parameters were analyzed in the overall cohort from 2005 to 2010. Changes in operative characteristics (including the number of ELC performed), the LOS, and the 30-day mortality during the study period from 2005 to 2010 were analyzed separately.

## Statistical Analysis

Normal distribution of continuous variables was assessed using histograms, skewness, and the Shapiro-Wilk test.

Analysis over time was performed using Kruskal-Wallis test for continuous variables and Pearson's $\chi^2$ test for categorical variables.

Univariable analysis was performed for all included variables. Continuous variables were compared using Mann-Whitney U-test. Categorical variables were analyzed using Fisher's exact test. Results were reported as numbers and percentages or medians and interquartile ranges. A p-value smaller than 0.05 was considered statistically significant.

The effect of ELC on postoperative outcome parameters was adjusted in multivariable regression analyses. Significant variables of the univariable analysis were included as dependent variables in logistic or linear regression models. Clinically important predictor variables (sex, age, body mass index [BMI], ASA score, wound contamination or infection, operating surgeon (attending or resident), nicotine abuse, alcohol abuse, sepsis at admission, and septic shock at admission) were correlated with dependent variables using Spearman's correlation coefficient and Fisher's exact test, as appropriate, and entered in regression models if the p-value was smaller than 0.1. Regression analyses were performed using the enter method. Not normally distributed dependent variables were $\log_{10}$-transformed for linear regression analyses. The regression coefficient (RC) and 95% confidence

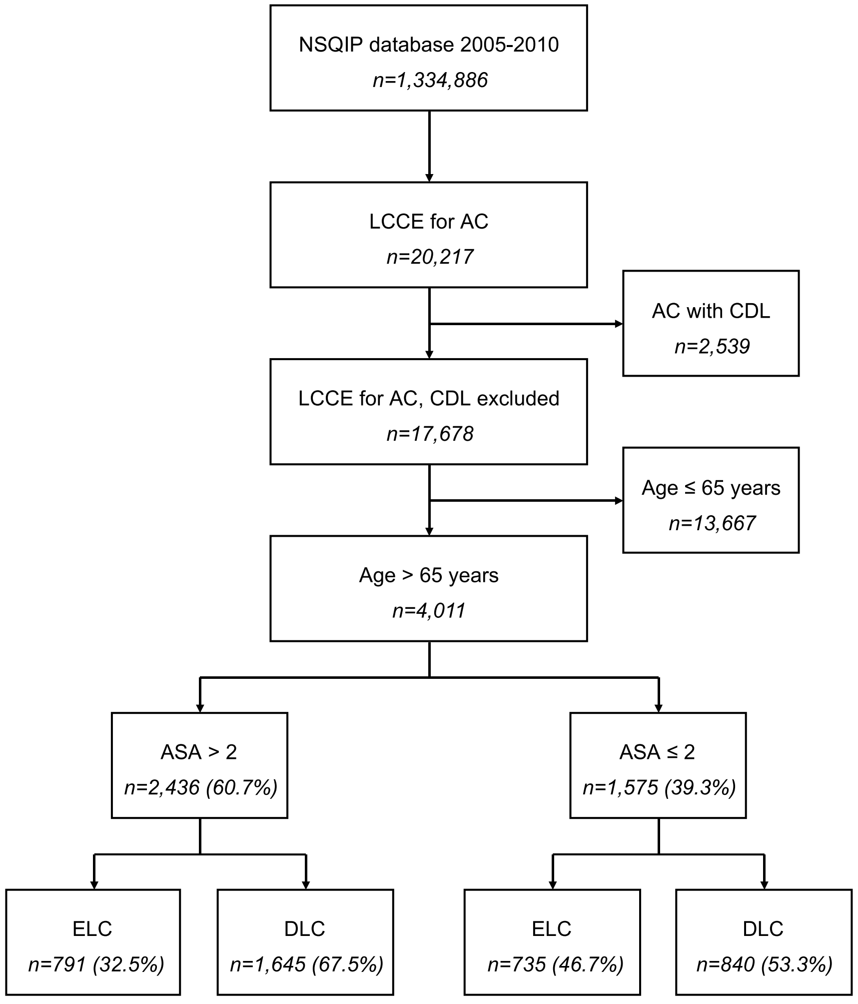


**Figure 1.** Cases Extracted from ACS NSQIP Database.

**TABLE 1.** Operative Characteristic, Mortality, and LOS Over Time

| | 2005 | 2006 | 2007 | 2008 | 2009 | 2010 | *p* |
|---|---|---|---|---|---|---|---|
| ELC | 83 (59.7) | 424 (62.2) | 408 (62.8) | 416 (61.9) | 555 (62.6) | 599 (61.0) | 0.958* |
| Anesthesia time, min** | 126 (66) | 120 (56) | 121 (56) | 116 (52) | 112 (51) | 115 (53) | **0.001**† |
| Operation time, min** | 87 (59) | 74 (48) | 75 (48) | 70 (43) | 59 (45) | 71 (43) | **<0.001**† |
| 30-d mortality | 1 (0.7) | 13 (1.9) | 10 (1.5) | 6 (0.9) | 14 (1.6) | 14 (1.4) | 0.681* |
| Total LOS, d** | 4.0 (4.0) | 4.0 (4.0) | 3.0 (4.0) | 3.0 (4.0) | 3.0 (4.0) | 3.0 (3.0) | 0.129† |
| Postoperative LOS, d** | 2.0 (3.0) | 2.0 (3.0) | 2.0 (3.0) | 2.0 (3.0) | 2.0 (3.0) | 2.0 (2.0) | 0.091† |

*Pearson's $\chi^2$ test.
**Values are presented as mean (interquartile range).
†Kruskal-Wallis test.
Values are presented as n (%) unless indicated otherwise.

intervals (CIs) were then back-transformed to the original scale. Interactions of ELC with other predictor variables were assessed with separate regression analyses. Significant interactions ($p < 0.05$) were entered in regression models as interaction terms. Continuous interaction variables were dichotomized at the median for ease of interpretation. To reduce multicolinearity, continuous predictor variables were centered at the mean for regression analyses. The degree of multicolinearity between predictor variables was assessed using the variance inflation factor (VIF). A VIF lower than 5 was assumed to exclude significant colinearity. Results were reported as odds ratio (OR) and 95% CI or RC and 95% CI. Regression model performance was assessed using $\chi^2$ goodness of fit, Snell's $R^2$, and Nagelkerke $R^2$ for logistic regression and analysis of variance, $R^2$, and adjusted $R^2$ for linear regression.

All statistical analysis was performed using SPSS Statistics (SPSS, IBM Corporation, Armonk, NY).

## RESULTS

Extracted cases from the NSQIP database are outlined in Figure 1. ELC was less frequently performed compared with DLC in all comorbidity categories. The difference between patients undergoing ELC or DLC was less pronounced in patients with ASA scores of 2 or lower (Fig. 1).

The proportion of ELC versus DLC, 30-day mortality, total hospital LOS, and postoperative LOS did not significantly change during the study period from 2005 to 2010. However, anesthesia and operative time decreased during the study period (Table 1).

In the DLC group, the median time to operation was 2 days (interquartile range, 2) in all patients included and also 2 days (interquartile range, 3) in patients with ASA scores greater than 2.

Univariable analysis of baseline characteristics revealed significant differences between the ELC and the DLC group. Patients undergoing ELC were younger, had lower ASA scores, had lower wound classification scores, and were less likely to have systemic inflammatory response syndrome, sepsis, or septic shock at hospital admission when compared with patients undergoing DLC (Table 2).

Results of univariable analysis for outcome parameters are listed in Table 3. Overall, ELC was significantly associated with fewer overall complications, a lower incidence of PE, reduced 30-day mortality, shorter anesthesia and operative time, and shorter total and postoperative stay. In patients with major comorbidities (ASA scores > 2), ELC was significantly associated with fewer complications overall, reduced mortality, shorter anesthesia and operative time, and shorter total and postoperative stay (Table 3).

Significant interactions of ELC with other predictor variables were identified in the following regression models for all patients included: anesthesia time (wound contamination/infection [$p$ = 0.018]), operative time (sex [$p$ = 0.020], wound contamination/infection [$p$ = 0.041]), total hospital LOS (wound contamination/infection [$p$ = <0.001], ASA score [$p$ = <0.001]), and postoperative LOS (wound contamination/infection [$p$ = 0.013], ASA score [$p$ = <0.001], age [$p$ = 0.036]) (Table 4). In regression models for the patient subgroup with major comorbidities, the following significant interactions of ELC with other predictor variables were found: anesthesia time (ASA score [$p$ = 0.046]), total hospital LOS (wound contamination/infection

**TABLE 2.** Baseline Characteristics at Hospital Admission, All Patients Older Than 65 Years

| | ELC Group (Hospital Day 0) (n = 1,526) | DLC Group (After hospital Day 0) (n = 2,485) | *p** |
|---|---|---|---|
| Age, y** | 74.0 (10.0) | 76.0 (12.0) | **<0.001**† |
| Sex, male/female | 722/798 (47.5/52.5) | 1,227/1,252 (49.5/50.5) | 0.228 |
| BMI, kg/m**2 | 27.5 (7.0) | 27.7 (7.0) | 0.941† |
| ASA score** | 3.0 (1.0)‡ | 3.0 (1.0)‡ | **<0.001**† |
| ASA score > 2 | 791 (51.8) | 1,645 (66.2) | **<0.001** |
| Wound classification% | 2.0 (1.0) | 3.0 (1.0) | **<0.001**† |
| Wound contaminated/infected | 636 (41.7) | 1,318 (53.0) | **<0.001** |
| Nicotine abuse | 89 (5.9) | 156 (6.3) | 0.588 |
| Ethanol abuse | 25 (1.6) | 41 (1.7) | 1.000 |
| Systemic inflammatory response syndrome | 193 (12.6) | 592 (23.8) | **<0.001** |
| Sepsis | 27 (1.8) | 154 (6.2) | **<0.001** |
| Septic shock | 5 (0.3) | 27 (1.1) | **0.009** |

*Fisher's exact text unless indicated otherwise.
**Values are presented as median (interquartile range).
†Mann-Whitney U-test.
‡Mean (SD), ELC group, 2.54 (0.607); mean (SD), DLC group, 2.75 (0.635).
Values are presented as n (%) unless indicated otherwise.
Wound classification: 1 to 4 number scale (1, clean; 2, clean-contaminated; 3, contaminated; 4, infected).

**TABLE 3.** ELC Versus DLC for AC

| | ELC (Hospital Day 0) (n = 1,526) | DLC (After Hospital Day 0) (n = 2,485) | $p$* | | ELC (Hospital Day 0) (n = 1,526) | DLC (After Hospital Day 0) (n = 2,485) | $p$* |
|---|---|---|---|---|---|---|---|
| SSI superficial | | | | Blood transfusion | | | |
| ASA overall | 17 (1.1) | 19 (0.8) | 0.301 | ASA overall | 14 (0.9) | 21 (0.8) | 0.862 |
| ASA score > 2 | 12 (1.5) | 14 (0.9) | 0.144 | ASA score > 2 | 9 (1.1) | 18 (1.1) | 1.000 |
| SSI deep | | | | Venous thrombosis | | | |
| ASA overall | 1 (0.1) | 4 (0.2) | 0.323 | ASA overall | 4 (0.3) | 13 (0.5) | 0.317 |
| ASA score > 2 | 0 (0.0) | 3 (0.2) | 0.556 | ASA score > 2 | 2 (0.3) | 12 (0.7) | 0.250 |
| SSI organ space | | | | PE | | | |
| ASA overall | 17 (1.3) | 20 (1.0) | 0.313 | ASA overall | 0 (0.0) | 9 (0.4) | **0.016** |
| ASA score > 2 | 7 (1.1) | 12 (0.9) | 0.633 | ASA score > 2 | 0 (0.0) | 33 (2.0) | 0.332 |
| Pneumonia | | | | Sepsis | | | |
| ASA overall | 15 (1.0) | 35 (1.4) | 0.305 | ASA overall | 19 (1.2) | 46 (1.9) | 0.157 |
| ASA score > 2 | 11 (1.4) | 25 (1.5) | 0.860 | ASA score > 2 | 11 (1.4) | 33 (2.0) | 0.332 |
| Unplanned intubation | | | | Septic shock | | | |
| ASA overall | 17 (1.1) | 45 (1.8) | 0.088 | ASA overall | 13 (0.9) | 26 (1.0) | 0.621 |
| ASA score > 2 | 14 (1.8) | 40 (2.4) | 0.378 | ASA score > 2 | 11 (1.4) | 22 (1.3) | 1.000 |
| Ventilator > 48 h | | | | Complication overall | | | |
| ASA overall | 9 (0.6) | 28 (1.1) | 0.091 | ASA overall | 109 (8.5) | 247 (11.8) | **0.006** |
| ASA score > 2 | 7 (0.9) | 27 (1.6) | 0.195 | ASA score > 2 | 73 (10.9) | 199 (14.3) | **0.037** |
| Progressive renal failure | | | | Conversion to OC | | | |
| ASA overall | 4 (0.3) | 18 (0.7) | 0.076 | ASA overall | 5 (0.3) | 4 (0.2) | 0.314 |
| ASA score > 2 | 4 (0.5) | 17 (1.0) | 0.244 | ASA score > 2 | 2 (0.3) | 3 (0.2) | 0.662 |
| Acute renal failure | | | | 30-day mortality | | | |
| ASA overall | 5 (0.3) | 16 (0.6) | 0.259 | ASA overall | 12 (0.8) | 46 (1.9) | **0.006** |
| ASA score > 2 | 5 (0.6) | 16 (1.0) | 0.488 | ASA score > 2 | 10 (1.3) | 44 (2.7) | **0.027** |
| Urinary tract infection | | | | Anesthesia time, min** | | | |
| ASA overall | 15 (1.0) | 43 (1.7) | 0.057 | ASA overall | 115 (53) | 118 (55) | **<0.001**† |
| ASA score > 2 | 12 (1.5) | 32 (1.9) | 0.519 | ASA score > 2 | 116 (63) | 120 (57) | **<0.001**† |
| Cerebrovascular accident | | | | Operation time, min** | | | |
| ASA overall | 3 (0.2) | 8 (0.3) | 0.549 | ASA overall | 71 (45) | 72 (47) | **0.037**† |
| ASA score > 2 | 3 (0.4) | 8 (0.5) | 1.000 | ASA score > 2 | 71 (46) | 74 (48) | **0.021**† |
| Myocardial infarction | | | | LOS, d** | | | |
| ASA overall | 8 (0.5) | 14 (0.6) | 1.000 | ASA overall | 1.0 (2.0) | 5.0 (4.0) | **<0.001**† |
| ASA score > 2 | 6 (0.8) | 11 (0.7) | 0.799 | ASA score > 2 | 2.0 (2.0) | 6.0 (5.0) | **<0.001**† |
| Cardiac arrest | | | | Postoperative LOS, d** | | | |
| ASA overall | 4 (0.3) | 14 (0.6) | 0.225 | ASA overall | 1.0 (2.0) | 2.0 (3.0) | **<0.001**† |
| ASA score > 2 | 3 (0.4) | 13 (0.8) | 0.294 | ASA score > 2 | 2.0 (2.0) | 3.0 (3.0) | **<0.001**† |

*Fisher's exact test unless indicated otherwise.
**Values are presented as medians (interquartile range).
†Mann-Whitney U-test.
Univariable analysis. Values are presented as n (%) unless indicated otherwise.

[$p$ = <0.001]), and postoperative LOS (wound contamination/infection [$p$ = 0.021]) (Table 5).

No significant colinearity was detected between the predictor variables of the regression models. The VIF was smaller than 3 for all regression models.

In all patients included, multivariable regression analysis adjusting for patient-, disease-, and procedure-related factors revealed a significant association of ELC with shorter anesthesia and operative time, shorter total hospital stay, and shorter postoperative stay (Table 4).

In the patient subgroup of older than 65 years with major comorbidities, multivariable regression analysis revealed a significant association of ELC with shorter anesthesia time, shorter total hospital stay, and shorter postoperative stay (Table 5).

Thirty-day mortality and complications overall did not differ significantly between the ELC and DLC group with regression analysis, both in all patients included and the subgroup of patients with major comorbidities (Tables 4 and 5). Both the logistic and linear regression models fit the data well. $\chi^2$ goodness-of-fit tests and $F$ ratios were statistically significant (all p-values < 0.001). Results of the model performance analysis are outlined in Table 6.

## DISCUSSION

AC is the most common emergency surgical condition in the elderly. Performing emergency surgery in this group of patients, especially in the presence of major comorbidities, is often associated with increased morbidity and mortality. LC for AC in elderly patients is associated with more complications and higher mortality when compared with younger patients.[12–14] A recent Danish retrospective study identified age as an independent predictor for worse outcome after cholecystectomy.[15] Kuwabara et al.,[16] in a large retrospective study including 2,552 patients older than 60 years with cholecystitis, showed a significantly increased risk for OC with advanced age.

**TABLE 4.** Adjusted Effect of ELC on Outcomes in Patients Older Than 65 Years

| | Adjusted OR | 95% CI | p |
|---|---|---|---|
| 30-d mortality*[1] | | | |
| ELC | 0.591 | 0.291 to 1.200 | 0.146 |
| Complications overall*[2] | | | |
| ELC | 0.916 | 0.715 to 1.173 | 0.487 |
| | **Adjusted RC** | **95% CI** | **p** |
| Anesthesia time**[3] | | | |
| ELC, reference group† | −0.043 | −0.070 to −0.014 | **0.003** |
| ELC, wound contaminated/infected | −0.002 | −0.033 to 0.029 | 0.885 |
| Operation time**[4] | | | |
| ELC, reference group† | −0.060 | −0.103 to −0.016 | **0.009** |
| ELC, male sex | 0.002 | −0.048 to 0.056 | 0.927 |
| ELC, wound contaminated/infected | −0.018 | −0.069 to 0.035 | 0.498 |
| Hospital LOS**[5] | | | |
| ELC, reference group† | −0.643 | −0.665 to −0.621 | **<0.001** |
| ELC, wound contaminated/infected | −0.512 | −0.543 to −0.480 | **<0.001** |
| ELC, ASA score > 3 | −0.694 | −0.745 to −0.632 | **<0.001** |
| Postoperative LOS**[6] | | | |
| ELC, reference group† | −0.213 | −0.276 to −0.145 | **<0.001** |
| ELC, wound contaminated/infected | −0.102 | −0.175 to −0.022 | 0.014 |
| ELC, ASA score > 3 | −0.390 | −0.507 to −0.245 | **<0.001** |
| ELC, age > 75 y | −0.287 | −0.347 to −0.222 | **<0.001** |

*Logistic regression.
**Linear regression.
†ELC reference group: female sex, resident operating surgeon, wound not contaminated/infected, no sepsis, age of 75 years or younger, ASA score of 3 or lower.
[1]Adjusted for wound contamination/infection, attending operating surgeon, nicotine abuse, septic shock, age, BMI, and ASA score. No interaction of ELC with other predictor variables.
[2]Adjusted for wound contamination/infection, sepsis, septic shock, age, and ASA score. No interaction of ELC with other predictor variables.
[3]Adjusted for sex, wound contamination/infection, attending operating surgeon, sepsis, age, BMI, and ASA score. Interaction of ELC with wound contamination/infection.
[4]Adjusted for sex, wound contamination/infection, attending operating surgeon, ethanol abuse, sepsis, BMI, and ASA score. Interaction of ELC with sex and wound contamination/infection.
[5]Adjusted for sex, wound contamination/infection, sepsis, septic shock, age, and ASA score. Interaction of ELC with wound contamination/infection and ASA score.
[6]Adjusted for sex, wound contamination/infection, sepsis, septic shock, age, and ASA score. Interaction of ELC with wound contamination/infection, ASA score, and age.
In the multivariable regression analysis, all continuous variables centered at the mean to reduce multicolinearity. Interactions of ELC with other predictor variables entered into the regression analysis as interaction terms.

**TABLE 5.** Adjusted Effect of ELC on Outcomes in Patients Older Than 65 Years With ASA Scores Greater Than 2

| | Adjusted OR | 95% CI | p |
|---|---|---|---|
| 30-d mortality*[1] | | | |
| ELC | 0.532 | 0.245 to 1.157 | 0.111 |
| Complications overall*[2] | | | |
| ELC | 0.877 | 0.653 to 1.178 | 0.877 |
| | **Adjusted RC** | **95% CI** | **p** |
| Anesthesia time**[3] | | | |
| ELC, reference group† | **−0.053** | **−0.081 to −0.024** | **<0.001** |
| ASA score > 3 | 0.025 | −0.064 to 0.123 | 0.592 |
| Operation time**[4] | | | |
| ELC | −0.029 | −0.0678 to 0.010 | 0.139 |
| Hospital LOS**[5] | | | |
| ELC, reference group† | **−0.671** | **−0.697 to −0.642** | **<0.001** |
| ELC, wound contaminated/infected | **−0.539** | **−0.577 to −0.497** | **<0.001** |
| Postoperative LOS**[6] | | | |
| ELC, reference group† | **−0.310** | **−0.373 to −0.241** | **<0.001** |
| ELC, wound contaminated/infected | **−0.191** | **−0.268 to −0.107** | **<0.001** |

*Logistic regression.
**Linear regression.
†ELC reference group: female sex, resident operating surgeon, wound not contaminated/infected, no sepsis, age of 75 years or younger, ASA score of 3 or lower.
[1]Adjusted for wound contamination/infection, attending operating surgeon, nicotine abuse, septic shock, age, BMI, and ASA score. No interaction of ELC with other predictor variables.
[2]Adjusted for wound contamination/infection, sepsis, septic shock, age, and ASA score. No interaction of ELC with other predictor variables.
[3]Adjusted for sex, wound contamination/infection, attending operating surgeon, sepsis, BMI, and ASA score. Interaction of ELC with ASA score.
[4]Adjusted for sex, wound contamination/infection, attending operating surgeon, sepsis, BMI, and ASA score. No interaction of ELC with other predictor variables.
[5]Adjusted for wound contamination/infection, attending operating surgeon, sepsis, septic shock, age, BMI, and ASA score. Interaction of ELC with wound contamination/infection and ASA score.
[6]Adjusted for wound contamination/infection, sepsis, septic shock, age, BMI, and ASA score. Interaction of ELC with wound contamination/infection.
In the multivariable regression analysis, all continuous variables centered at the mean to reduce multicolinearity. Interactions of ELC with other predictor variables entered in the regression analysis as interaction terms.

In the general population, new evidence has challenged the longstanding practice of initial conservative management followed by interval elective cholecystectomy in patients with AC presenting with duration of symptoms over 3 days. Large studies have shown convincingly that same-admission LC for AC is associated with outcomes better than those of interval elective cholecystectomy. In a recent multicenter randomized control trial where patients were treated with either ELC within 24 hours or antibiotic treatment with DLC, those undergoing ELC had significantly fewer complications and a shorter hospital stay.[7]

The optimal initial management of elderly patients with AC, especially those with serious comorbid conditions, is not clear. There has been a widespread practice among surgeons to manage elderly patients with AC nonoperatively during the initial hospitalization, followed by elective interval LC. Cull et al.,[17] in an analysis of 806 patients older than 65 years with AC, reported that 48% were selected for delayed cholecystectomy. However, there is no evidence that such a policy is

**TABLE 6.** Performance of Regression Models

| | Logistic Regression | | | | |
|---|---|---|---|---|---|
| | $\chi^2$ Goodness of Fit | | | Cox and Snell $R^2$ | Nagelkerke $R^2$ |
| | $\chi^2$ | *df* | *p* | | |
| 30-d mortality | | | | | |
| ASA overall | 91.362 | 8 | <0.001 | 0.024 | 0.169 |
| ASA score > 2 | 62.040 | 8 | <0.001 | 0.026 | 0.139 |
| Complications overall | | | | | |
| ASA overall | 121.901 | 6 | <0.001 | 0.035 | 0.072 |
| ASA score > 2 | 64.941 | 6 | <0.001 | 0.031 | 0.057 |
| | **Linear Regression** | | | | |
| | **Analysis of Variance** | | | | |
| | ***F* Ratio** | ***df*** | ***p*** | **$R^2$** | **Adjusted $R^2$** |
| Anesthesia time | | | | | |
| ASA overall | 67.494 | 9 | <0.001 | 0.137 | 0.135 |
| ASA score > 2 | 46.580 | 8 | <0.001 | 0.138 | 0.135 |
| Operation time | | | | | |
| ASA overall | 52.962 | 10 | <0.001 | 0.122 | 0.119 |
| ASA score > 2 | 51.864 | 6 | <0.001 | 0.118 | 0.116 |
| Hospital LOS | | | | | |
| ASA overall | 257.371 | 9 | <0.001 | 0.385 | 0.383 |
| ASA score > 2 | 145.724 | 9 | <0.001 | 0.373 | 0.370 |
| Postoperative LOS | | | | | |
| ASA overall | 68.665 | 10 | <0.001 | 0.158 | 0.156 |
| ASA score > 2 | 51.667 | 8 | <0.001 | 0.159 | 0.156 |

associated with improved outcomes. Cull et al.[17] showed that delayed cholecystectomy was significantly associated with recurrent episodes of pancreatitis, cholecystitis, and cholangitis, while waiting for cholecystectomy. Another retrospective cohort study of patients older than 65 years with AC reported that cholecystectomy was not performed on the initial hospitalization in 25% cases, leading to gallstone-related readmission in 38% of these patients.[18]

In the general population, the timing of same-admission cholecystectomy is undergoing major changes, with emphasis on operation within 24 hours of admission. There is strong evidence that ELC, within 24 hours of admission, is safe and is associated with reduced hospital stay. Brooks et al.,[8] in an NSQIP analysis of 5,268 patients who underwent emergency cholecystectomy within 7 days of hospital admission for AC, showed that patients who underwent operation later in the course of admission were more likely to require an open procedure and have significantly longer hospital stay. Similar findings were shown for the subgroup of high-risk patients.

Similar results were reported by other recent studies, including two meta-analyses[2,3] and a large randomized trial by Gutt et al.[7] Another retrospective cohort study by Banz et al.,[9] including 4,113 cases from a laparoscopy-specific database, investigated the effect of different time points of LC for AC on outcome and reported a significant increase in postoperative complications associated with DLC.

The optimal timing of same-admission cholecystectomy in elderly patients, especially those with significant comorbidities, is not clear. There is evidence that in the general population, patients with AC and diabetes mellitus may benefit from early same-admission operation. In a recent NSQIP study, 144 patients with AC and diabetes were matched with 432 patients without diabetes. Delaying cholecystectomy for more than 24 hours after admission in patients with diabetes was associated with significantly higher odds of developing SSIs and a longer hospital stay.[19] However, the issue with elderly patients, especially those with comorbid conditions, is more complicated. Elderly patients may need volume and antibiotic resuscitation as well as stabilization of their comorbid medical conditions before surgery. In contrast, delaying the definitive control of the source of infection may be counterproductive.

The current study aimed to identify the optimal time of same-admission LC for AC in patients older than 65 years and in the subgroup of patients with major associated comorbidities. Choledocholithiasis is present in approximately 10% of patients with acute calculous cholecystitis.[20,21] Since this condition may complicate the timing of surgical management and outcomes, these patients were excluded from the analysis.

Univariable analysis in the present study showed that patients undergoing ELC (within 24 hours of admission) had a significantly lower overall mortality and complication rate, lower incidence of PE, and shorter anesthesia time, operative time, total hospital stay, and postoperative stay compared with patients undergoing delayed, same-admission LC. In the subgroup of patients with major comorbidities (ASA score > 2), ELC was associated with a significantly lower overall mortality and complication rate and shorter anesthesia time, operative time, total hospital stay, and postoperative stay when compared with delayed same-admission LC.

On regression analysis, the timing of same-admission LC did not have any significant effect on survival or complications, although there was a strong trend toward lower mortality in the early operation group.

In both all patients included and the patient subgroup with major comorbidities, ELC was independently associated with significantly shorter anesthesia time, total hospital stay, and postoperative stay. In all patients included, ELC was also significantly associated with a reduced operative time. The shorter total hospital stay and postoperative stay in patients selected for ELC has potential to lower hospital costs[22] and the risk for hospital-acquired infections.[23,24] Prolonged anesthesia and operative time is associated with increased complications.[25–29] The reduced anesthesia and operative time thus may potentially reduce postoperative complications, although the adjusted effect of ELC on anesthesia and operative time was small (Tables 4 and 5).

Another interesting finding was that the conversion rate to OC did not differ significantly between the ELC and the DLC group. This is in agreement with the findings in a randomized trial by Gutt et al.,[7] which included patients of all ages. However, Banz et al.,[9] in a study including patients of all ages, found a significantly decreased conversion rate to OC when ELC was performed.

Interestingly, both ELC and DLC procedures were associated with similar rates of postoperative sepsis and septic shock, despite the higher preoperative rates in the DLC group. This suggests that aggressive resuscitation and stabilization followed by operation may be achieved within 24 hours, and early removal of the source of sepsis may reduce the risk of postoperative systemic sepsis. This hypothesis should be tested in a prospective, randomized study of patients with AC and age greater than 65 years, which includes significant comorbid conditions and severe systemic sepsis.

Finally, this study has several limitations. Although the study is based on NSQIP, which is a high-quality database maintained, audited for data reliability, and strongly supported by the ACS, it has the usual limitations of retrospective studies. Furthermore, the comparison of the ELC and DLC groups may be confounded by a selection bias despite the adjustment for multiple patient-, disease-, and surgery-related factors in multivariable regression analysis. To address these limitations, a prospective randomized analysis of the optimal timing for LC in patients with AC older than 65 years is warranted.

## CONCLUSION

ELC, within 24 hours of admission, for AC in patients older than 65 years, including those with significant comorbidities, is associated with shorter total hospital stay and postoperative stay without increasing postoperative complications, mortality, or conversion to OC when compared with delayed same-admission LC.

### AUTHORSHIP

D.D., E.B., and T.H. provided the study design. T.H. and E.B. performed the data collection. T.H. and E.B. performed the literature search. T.H., E.B., and D.D. performed the data analysis. T.H., E.B., D.D., K.I., and L.L. performed the data interpretation. T.H., and D.D. wrote the manuscript. K.I. and L.L. performed the critical revision.

### DISCLOSURE

The authors declare no conflicts of interest.

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