

Use of the Tokyo Guidelines to Evaluate Acute Cholecystitis in Elderly Adults

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ABSTRACT

Background: We used the Tokyo Guidelines to evaluate outcomes of early laparoscopic cholecystectomy (ELC) among elderly patients with acute cholecystitis (AC).

Methods: We retrospectively reviewed the records of 225 patients, who were classified into 2 age groups: 172 patients were younger than 75 years, and 53 patients were 75 years or older.

Results: Presence of comorbidities, use of anticoagulant therapy, and high American Society of Anesthesiologists (ASA) class were significantly more frequent among elderly patients as compared with younger patients. In addition, severity grade was significantly higher among elderly patients than among younger patients ($p = 0.0454$). Among patients with Grade I disease, no significant differences were seen in the rates of conversion to open surgery or postoperative complications. Among patients with Grade II disease, postoperative complications were significantly more frequent among elderly patients (8.0% in younger patients vs 25% in elderly patients; $p = 0.0299$). Among elderly patients, rates of conversion to open surgery and postoperative complications did not significantly differ between the ELC group and the delayed laparoscopic cholecystectomy (DLC) group. Preoperative and total hospital stays were significantly shorter for elderly patients undergoing ELC than for elderly patients undergoing DLC.

Conclusions: ELC is a satisfactory treatment for elderly adults with the Tokyo Guidelines Grade I or II AC.

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KEYWORDS: acute cholecystitis, early laparoscopic cholecystectomy, elderly, Tokyo Guidelines

Laparoscopic cholecystectomy (LC) is now the treatment of choice for benign gall bladder disease.¹⁾ In addition, early laparoscopic cholecystectomy (ELC) for acute cholecystitis (AC) was associated with significantly lower rates of complications than early open cholecystectomy (OC).²⁾ Studies have indicated that ELC is feasible, safe, and

results in shorter total hospital stays than delayed laparoscopic cholecystectomy (DLC); however, few studies have examined the impact of ELC on outcomes among elderly patients.^{3–11)} Therefore, selection of a therapeutic strategy—such as percutaneous cholecystostomy (PC) or surgery—and determination of the optimal procedure (e.g.,

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Table 1 Severity grades, as defined by the Tokyo Guidelines

Grade	Criteria
I (Mild)	Acute cholecystitis that does not meet criteria for moderate or severe disease Mild gallbladder inflammation without organ dysfunction
II (Moderate)	Presence of any 1 of the following conditions: 1. Elevated white blood cell count ($>18000 /\text{mm}^3$) 2. Palpable tender mass in right upper abdominal quadrant 3. Duration of complaint >72 h 4. Marked local inflammation, including biliary peritonitis, pericholecystic abscess, hepatic abscess, gangrenous cholecystitis, emphysematous cholecystitis
III (Severe)	Presence of any 1 of the following conditions: 1. Cardiovascular dysfunction (hypotension requiring treatment with dopamine at ≥ 5 mg/kg/min, or any dose of dobutamine) 2. Neurologic dysfunction (decreased level of consciousness) 3. Respiratory dysfunction ($\text{PaO}_2/\text{FiO}_2$ ratio <300) 4. Renal dysfunction (oliguria; creatinine >2.0 mg/dl) 5. Hepatic dysfunction (PT-INR >1.5) 6. Hematologic dysfunction (platelet count $<100000 /\text{mm}^3$)

PT-INR: prothrombin time-international normalized ratio

OC or LC) and timing of surgery, when surgery is selected, remain controversial when treating elderly patients, as they often have associated comorbidities that could increase rates of postoperative complications and conversion to open surgery.^{5,6} Nevertheless, with advances in anesthesia, surgical technique, and postoperative care, studies have shown that ELC is safe and effective for elderly patients, and that morbidity and mortality are not increased in this population.⁷

The Tokyo Guidelines were published in 2007 (TG07) and are among the international guidelines for treating acute cholangitis and cholecystitis.¹²⁻¹⁵ A second edition was published in 2013 (TG13), but the severity classification and therapeutic strategy for AC were identical to those specified in the first edition.¹⁶⁻¹⁸ Regarding severity classification, elderly patients with acute cholangitis were assigned a more severe classification (Grade II) but, due to lack of higher-level evidence, no definition was specified for AC.^{18,19} As a therapeutic strategy for AC, the Tokyo Guidelines generally recommend ELC; however, ELC was not recommended as the definitive therapeutic strategy for Grade II patients because of operative difficulties related to the procedure.¹⁷ Furthermore, elderly patients were defined as “unusual cases” in TG07,¹⁵ and management of elderly patients with AC was excluded from TG 13.¹⁷ Therefore, TG13 does not specify a definitive therapeutic strategy for treating elderly patients. The Tokyo Guidelines have been increasingly adopted as the international guidelines for AC,²⁰ but no studies have used TG13

to analyze outcomes of elderly adults with AC. In this retrospective study, we used TG13 to evaluate ELC outcomes among elderly patients with AC.

Methods

We analyzed the medical records of 225 patients (151 men, 74 women) who underwent cholecystectomy for AC at the Department of Surgery, Toho University Ohashi Medical Center during the period from January 1998 to October 2011. Patients with common bile duct stones were excluded, and the remaining patients were classified into 2 age groups: 172 (76.4%) patients were younger than 75 years (median age, 57; range, 21-74), and 53 (23.6%) patients were 75 years or older (median age, 81; range, 75-91). Patient records were reviewed to collect demographic data, biochemical data, radiologic findings, and postoperative outcomes. A definitive diagnosis of AC was made according to TG13 criteria.¹⁸ ELC was defined as LC performed within 96 hours of symptom onset, including emergency surgery. DLC was defined as LC performed outside the period for ELC. The severity grades for AC in the Tokyo Guidelines according are shown in Table 1.¹⁸ The severity distribution of the present 225 AC cases was: Grade I (Mild), 99 cases (44.0%); Grade II (Moderate), 124 cases (55.1%); and Grade III (Severe), 2 cases (0.9%). Surgical risks were estimated using the American Society of Anesthesiologists (ASA) class, and a high ASA class was defined as an ASA class of 3 or 4. As specified in the Tokyo Guidelines, marked local inflammation was defined as presence

Table 2 Characteristics of younger and elderly patients

	Age <75 years (n = 172)	Age ≥75 years (n = 53)	p value
Sex (male/female)	122/50	29/24	0.0280
Time from onset (h)	61 ± 76	82 ± 5	0.5158
Presence of comorbidities	106	41	0.0353
Anticoagulant therapy	18	14	0.0226
ASA class 3 or 4	12	10	0.0108
Body temperature (°C)	37.3 ± 0.9	37.6 ± 0.9	0.0489
White blood cell count (/mm ³)	14233 ± 4672	14749 ± 4270	0.2770
CRP (mg/dl)	12.1 ± 10.0	14.8 ± 9.4	0.0560
Total bilirubin (mg/dl)	1.6 ± 1.3	1.6 ± 1.1	0.4714
Marked local inflammation	44	24	0.0063
Severity grade (Grade I/II/III)	82/88/2	17/36/0	0.0454

ASA: American Society of Anesthesiologists, CRP: C-reactive protein

Marked local inflammation includes biliary peritonitis, pericholecystic abscess, hepatic abscess, gangrenous cholecystitis, suppurative cholecystitis, and emphysematous cholecystitis

of severe local inflammation, including biliary peritonitis, pericholecystic abscess, hepatic abscess, gangrenous cholecystitis, suppurative cholecystitis, and emphysematous cholecystitis.¹⁸⁾ Surgical site infection (SSI) included wound infection and intra-abdominal abscess, and remote infection (RI) included pneumonia, urinary tract infection, and pseudomembranous colitis.

Statistical analysis was conducted using the χ^2 test for categorical data and the Mann-Whitney *U* test for continuous data. The results are expressed as mean ± SD. Statistical significance was defined as a p value less than 0.05. All statistical analyses were performed using SPSS for Windows, version 10.0 (SPSS Inc., Chicago, IL, USA).

Results

The characteristics of the younger and elderly patients are shown in Table 2. There was a significant difference in sex between the groups. The younger patients comprised 122 men (70.9%) and 50 women (29.1%), and the elderly patients comprised 29 men (54.7%) and 24 women (45.3%). Comorbidities, use of anticoagulant therapy, and high ASA class were significantly more common among elderly patients (61.6%, 106/172; 10.5%, 18/172; and 7.0%, 12/172, respectively, in younger patients vs 77.4%, 41/53; 26.4%, 14/53; and 18.9%, 10/53 in elderly patients; $p = 0.0353$, $p = 0.0226$, and $p = 0.0108$, respectively). Body temperature was higher and marked local inflammation was more frequent in elderly patients (37.3°C and 25.6%, 44/172 in younger patients vs 37.6°C and 45.3%, 24/53 in elderly patients; $p = 0.0489$ and $p = 0.0063$, respectively). In addition, severity grade was significantly higher among elderly pa-

tients (Grade I, 47.7%, 82 cases; Grade II, 51.2%, 88 cases; and Grade III, 1.2%, 2 cases in younger patients vs Grade I, 32.1%, 17 cases; Grade II, 67.9%, 36 cases; and Grade III, 0%, 0 cases in elderly patients; $p = 0.0454$).

Therapeutic outcomes for younger and elderly patients, by severity grade, are shown in Table 3. In the Grade I group, no significant age differences were seen in relation to type of surgery, proportion undergoing ELC, operative time, intraoperative blood loss, or rate of conversion to open surgery. In addition, the rate of postoperative complications, including SSI, did not significantly differ by age group (3.7%, 3/82 and 2.4%, 2/82 in younger patients vs 5.9%, 1/17 and 5.9%, 1/17 in elderly patients; $p = 0.8003$ and $p = 0.9812$, respectively; the values include repeat cases). An elderly patient with postoperative complications underwent delayed OC and later developed a postoperative bile leak with abdominal abscess, which was managed conservatively. Preoperative, postoperative, and total hospital stays were significantly longer for elderly patients.

In patients with Grade II disease, there were no significant age differences in type of surgery, proportion undergoing ELC, operative time, intraoperative blood loss, or rate of conversion to open surgery. However, postoperative complications, including SSI, were significantly more frequent among elderly patients (8.0%, 7/88 and 5.7%, 5/88 in younger patients vs 25%, 9/36 and 19.4%, 7/36 in elderly patients; $p = 0.0299$ and $p = 0.0433$, respectively). Among elderly patients who developed postoperative complications, there were 3 cases of early OC, 4 cases of ELC, and 2 cases of DLC. In addition, 3 of the 4 ELC cases required conversion to open surgery. Postoperative complications

Table 3 Comparison of therapeutic results between younger and elderly patients, according to severity grade

Grade I	Younger patients (n = 82)	Elderly patients (n = 17)	p value
Preoperative gallbladder drainage	10	8	0.0023
Operation (LC/OC)	75/7	13/4	0.1719
ELC	55	8	0.1991
Operative time (min)	118 ± 61	91 ± 33	0.0650
Blood loss (grams)	43 ± 91	76 ± 159	0.3668
Conversion to open surgery	7/75	0/13	0.5532
Intraoperative CBD injury	1	0	0.3816
Postoperative complications	3	1	0.8003
Surgical site infection	2 *	1 *	0.9812
Remote infection	2 *	0	0.7668
Postoperative bile leak	1 *	1 *	0.7668
Preoperative hospital stay (days)	4 ± 7	10 ± 10	0.0150
Postoperative hospital stay (days)	6 ± 3	12 ± 15	0.0019
Total hospital stay (days)	11 ± 8	23 ± 22	0.0082
Grade II	Younger patients (n = 88)	Elderly patients (n = 36)	p value
Preoperative gallbladder drainage	27	17	0.0806
Operation (LC/OC)	78/10	28/8	0.2016
ELC	51	16	0.1706
Operative time (min)	132 ± 50	122 ± 40	0.4724
Blood loss (grams)	151 ± 219	182 ± 289	0.5630
Conversion to open surgery	25/78	7/28	0.9134
Intraoperative CBD injury	1	0	0.6428
Postoperative complications	7	9	0.0229
Surgical site infection	5 *	7 *	0.0433
Remote infection	4 *	2 *	0.8234
Postoperative bile leak	2 *	0	0.8992
Preoperative hospital stay (days)	7 ± 12	8 ± 12	0.9054
Postoperative hospital stay (days)	9 ± 6	12 ± 7	0.0001
Total hospital stay (days)	16 ± 14	22 ± 13	0.0058

LC: laparoscopic cholecystectomy, OC: open cholecystectomy, ELC: early laparoscopic cholecystectomy, CBD: common bile duct

*includes repeat cases

included wound infection in 6 cases, abdominal abscess in 1 case, and pneumonia in 2 cases, but the complications were not severe and were managed conservatively. Postoperative and total hospital stays were also significantly longer for elderly patients. Among the elderly patients, there were no cases of intraoperative common bile duct (CBD) injury, regardless of severity grade, and no deaths.

The characteristics and outcomes for elderly patients undergoing LC and OC are shown in Table 4. Severity grade, time from onset of symptoms, presence of comorbidities, use of anticoagulant therapy, ASA class, operative time, and intraoperative blood loss did not significantly differ by treatment group. The rate of postoperative complications was lower in the LC group but not significantly so (LC, 14.6%, 6/41; OC, 33.3%, 4/12; $p = 0.2998$). Postoperative

and total hospital stays were significantly shorter in the LC group ($p = 0.0023$ and $p = 0.0182$, respectively).

The characteristics and outcomes for elderly patients undergoing ELC and DLC are shown in Table 5. Severity grade, time from onset of symptoms, presence of comorbidities, use of anticoagulant therapy, ASA class, operative time, and intraoperative blood loss did not significantly differ by treatment group. Rates of conversion to open surgery and postoperative complications also showed no significant differences (ELC, 8.3%, 2/24 and 16.7%, 4/24; DLC, 11.8%, 2/17 and 11.8%, 2/17; $p = 0.8655$ and $p = 0.9913$, respectively). Preoperative and total hospital stays were significantly shorter among elderly patients undergoing ELC ($p < 0.0001$ and $p < 0.0001$, respectively).

Table 4 Characteristics and outcomes of elderly patients with AC undergoing LC and OC

	LC (n = 41)	OC (n = 12)	p value
Severity grade (Grade I/II)	13/28	4/8	0.8061
Time from onset (h)	49 ± 43	69 ± 63	0.2201
Presence of comorbidities	29	12	0.0821
Anticoagulant therapy	13	2	0.5138
ASA class 3 or 4	9	1	0.5215
Operative time (min)	112 ± 40	114 ± 43	0.9913
Blood loss (grams)	157 ± 286	123 ± 141	0.1604
Postoperative complications	6	4	0.2998
Surgical site infection	6	1	0.9344
Remote infection	0	2	0.0713
Postoperative bile leak	0	1	0.5093
Preoperative hospital stay (days)	8 ± 9	12 ± 16	0.7122
Postoperative hospital stay (days)	10 ± 6	19 ± 16	0.0023
Total hospital stay (days)	19 ± 12	33 ± 24	0.0182

LC: laparoscopic cholecystectomy, OC: open cholecystectomy, AC: acute cholecystitis, ASA: American Society of Anesthesiologists

Table 5 Characteristics and outcomes of elderly patients with AC undergoing ELC and DLC

	ELC (n = 24)	DLC (n = 17)	p value
Severity grade (Grade I/II)	8/16	5/12	0.9403
Time from onset (h)	43 ± 34	59 ± 54	0.4871
Presence of comorbidities	14	12	0.6358
Anticoagulant therapy	8	6	0.8385
ASA class 3 or 4	6	3	0.8591
Operative time (min)	108 ± 40	117 ± 41	0.5023
Blood loss (grams)	205 ± 338	88 ± 178	0.1209
Conversion to open surgery	2	2	0.8655
Postoperative complications	4	2	0.9913
Surgical site infection	4	2	0.9913
Remote infection	0	0	
Postoperative bile leak	0	0	
Preoperative hospital stay (days)	1 ± 1	17 ± 9	<0.0001
Postoperative hospital stay (days)	10 ± 8	10 ± 4	0.4086
Total hospital stay (days)	12 ± 8	28 ± 11	<0.0001

ELC: early laparoscopic cholecystectomy, DLC: delayed laparoscopic cholecystectomy, AC: acute cholecystitis, ASA: American Society of Anesthesiologists

Discussion

AC is one of the most frequent abdominal emergencies among elderly adults.⁶⁾ According to the definition of the World Health Organization, an elderly case is defined as a patient aged 65 years or older.¹⁵⁾ The definition of elderly is subdivided into “early elderly (65 years and older)”, “medium elderly (75 years and older)”, and “later elderly (85 years and older)”. The present study defined elderly patients as those aged 75 years or older. A previous study

found that elderly patients had a significantly higher rate of severe local inflammation, including gangrenous cholecystitis,^{15,21)} and significantly higher rates of intraoperative and postoperative complications.²²⁾ In the present study, comorbidities, anticoagulant therapy, and high ASA class were significantly more common among elderly patients, as was marked local inflammation such as gangrenous cholecystitis. Therefore, the Tokyo Guidelines severity grades were higher for elderly patients than for younger patients. Lee et al. reported that the TG07 severity grade

for AC, particularly the proportion of patients with Grade III disease, was often higher for elderly patients.⁹⁾ In addition, Cui et al. reported that ASA score and comorbidity rates were significantly higher among elderly patients as compared with younger patients.⁴⁾ These findings suggest that elderly AC patients who are admitted to hospitals have more-severe disease, and are at higher risk, than younger patients. Therefore, an optimized therapeutic strategy is needed for elderly patients.

Unfortunately, no definitive therapeutic strategy for elderly patients with AC has been developed. Generally, physicians choose conservative management or PC for elderly patients on admission²³⁾; however, in a randomized controlled trial of high-risk patients, including elderly patients, routine PC was not superior to conservative management.²⁴⁾ Furthermore, Winbladh et al.²⁵⁾ reviewed PC versus cholecystectomy for AC in high-risk cases and noted that the 30-day mortality rate was significantly higher after PC (15.4%) as compared with early cholecystectomy (4.5%), which suggests that PC is not the definitive therapeutic strategy for elderly patients. In a recent study of elderly patients, LC during initial hospitalization was less expensive than delayed surgery, because the readmission rate due to unresolved cholecystitis or gallstone-related complications was very high after delayed surgery.²⁶⁾ These results suggest that ELC is a satisfactory therapeutic strategy, even for elderly patients.

TG13 recommends ELC for Grade I patients; however, LC is a difficult procedure for Grade II patients due to the presence of severe local inflammation.^{17, 18)} In addition, the Tokyo Guidelines do not specify a definitive therapeutic strategy for elderly patients.^{17, 18)} Previous studies have reported morbidity rates varying from 14% to 60%,^{5, 6, 8, 10, 11)} and mortality rates ranging from 1% to 10%, for elderly AC patients,^{5, 8, 10, 11)} which are relatively high rates. However, in the present study, the morbidity rate was 5.9% for Grade I patients and 25.0% for Grade II patients, and with no deaths in either grade. Ten of the present elderly patients developed postoperative complications: early OC in 3 cases, delayed OC in 1 case, ELC in 4 cases, and DLC in 2 cases. In addition, of the 6 patients who underwent LC, 3 required conversion to open surgery. Therefore, open surgery was performed for 7 of the 10 patients who developed postoperative complications. Open surgery is believed to be associated with a high risk of postoperative complications, including SSI. Our results suggest that ELC is an appropriate procedure, even for elderly patients. In-

deed, in the present study, LC, and especially ELC, significantly shortened hospital stays for elderly patients, without a significant increase in the rates of conversion or postoperative complications.

In a comparison of TG13 severity grade between younger and elderly patients, postoperative complications, including SSI, did not significantly differ among Grade I cases. However, among Grade II cases, postoperative complications, including SSI, were significantly more frequent among elderly patients. Cui et al. found no difference in intraoperative complications, except that rates of conversion and postoperative complications were significantly higher for elderly patients.⁴⁾ Among the present Grade I patients, ELC was a safe, feasible therapeutic strategy, even in elderly patients, as indicated by TG13. Among Grade II patients, postoperative complications were more frequent among elderly patients as compared with younger patients, but most patients underwent open surgery. Thus, if LC were performed completely for elderly patients, postoperative complications would be reduced.

This study was a retrospective analysis of patients treated during a 12-year period and included patients treated before and after the guidelines were published. Thus, there were several limitations. First, therapeutic strategy differed depending on operative time. Therefore, after publication of the guidelines, ELC was actively performed even for elderly patients with AC.²⁷⁾ Second, the procedures were performed by several surgeons, who were required to deal with the substantial learning curves of the procedures. Third, new surgical devices such as laparoscopic coagulation scissors have recently been introduced and used. Older age alone may not be a contraindication to ELC under appropriate clinical conditions; actively performed ELC helps reduce hospital stays and may decrease medical costs. However, because of increased morbidity rates, especially among Grade II patients, elderly patients with AC should be carefully managed, and the individual status of patients should be considered.

In conclusion, elderly patients with AC had more-severe inflammation, were in worse general condition, and had a higher TG13 severity grade on arrival and more postoperative complications, particularly those with Grade II disease. However, our findings suggest that, among elderly adults who can safely receive general anesthesia, ELC is a satisfactory therapeutic strategy for the Tokyo Guidelines Grade I and Grade II disease.

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Tokyo Guidelines に準じた高齢者急性胆嚢炎の解析

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要約

背景：急性胆嚢炎の国際版ガイドラインである Tokyo Guidelines に準じて高齢者急性胆嚢炎症例に対する早期腹腔鏡下胆嚢摘出術（early laparoscopic cholecystectomy：ELC）の検討を行ったので報告する。

対象ならびに方法：当科で経験した急性胆嚢炎症例 225 例を対象とした。75 歳未満の若年者群 172 例と 75 歳以上の高齢者群 53 例の 2 群に分けて比較検討を行った。

結果：高齢者群は若年者群と比較し併存疾患の有無，抗凝固剤内服，American Society of Anesthesiologists（ASA）分類高値例が有意に多い結果となった。さらに高齢者群では Tokyo Guidelines の重症度分類において有意に重症度が高い結果となった（ $p=0.0454$ ）。重症度が Grade I の症例は開腹移行率，術後合併症で高齢者群と若年者群との間に有意差は認めなかった。Grade II の症例において高齢者は術後合併症が有意に多い結果となった（若年者群，8.0%；高齢者群，25%； $p=0.0299$ ）。高齢者群内の比較では ELC 施行例と待機的腹腔鏡下胆嚢摘出術施行症例の間において，開腹移行率，術後合併症で有意差は認めなかった。また，術前待機期間，総入院期間は ELC 施行症例で有意な短縮を認めた。

結語：高齢者に対する ELC は有益な治療方針であると考えられた。また，急性胆嚢炎国際ガイドラインにおける Tokyo Guidelines に準じた重症度 Grade I，II の双方においても施行可能と考えられた。

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索引用語：急性胆嚢炎，早期腹腔鏡下胆嚢摘出術，高齢者，Tokyo Guidelines