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Original Article

# Comparison between Two Severity Classifications in Patients with Acute Cholecystitis

**Mun Jong Hyon[1], Kim Hye Song[1,*], Rim Song Il[2]**

[1]Department of Gastroentetology, Pyongsong Medical University, DEMOCRATIC PEOPLE'S REPUBLIC OF KOREA.
[2]Department of Abdominal Surgery, Pyongyang Medical University, DEMOCRATIC PEOPLE'S REPUBLIC OF KOREA.

## ABSTRACT

**Background and Aim:** Assessment severity helps clinicians to guide appropriate treatment and minimumize adverse outcome. The objective of our study was to comparison between TG13 severity system and EGS grade system for predicting clinical outcomes in acute cholecystitis. **Methods:** This is a retrospective single-center study which enrolled patients who were admitted to Pyongsong Medical University Hospital between February 2020 and October 2021. Tokyo 2013 (TG 13) severity classification and Emergency General Surgery (EGS) severity systems were validated. Clinical outcomes were mortality, postoperative complication, need for emergency surgery and hospital stay. Predictive accuracies were evaluated using Area Under the ROC Curve (AUC). **Results:** A total of 164 patients were included in the analysis (mean age of 57.4 years; 52.4% males). On the basis of EGS grade, 132 patients (80.5%), 22 patients (13.5%), 2 patients (1.2%), 4 patients (2.4%) and 4 patients (2.4%) were determined to have I, II, III, IV and V. Using TG13 grade, 113 patients (68.9%) were categorized as mild, 46 patients (28.0%) as moderate, and 5 patients (3.1%) as severe. In general, higher grades of severity were signifi cantly associated with worse clinical outcomes for all classification systems and this was more precise in TG 13 severity system. EGS severity classification was more superior to TG 13 grade system for predicting mortality (AUC 0.866 vs. 0.812, P <0.001), post-operative complication (AUC 0.848 vs. 0.799, P < 0.001) and need for surgery (AUC 0.798 vs. 0.734, P < 0.001). **Conclusion:** EGS severity classification was more superior to TG 13 grade system for predicting clinical outcomes.

**Keywords:** Acute cholecystitis, Severity classification, Comparison, EGS classification, TG13 classification.

***Correspondence:**
**Kim Hye Song**
Department of Gastroentetology, Pyongyang Medical University, DEMOCRATIC PEOPLE'S REPUBLIC OF KOREA.
Email: hs.kim0428@ryongnamsan.edu.kp

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## INTRODUCTION

Acute cholecystitis is the aucte inflammation of the gall bladder and it is classified into calculus and acalculus cholecystitis based on the presence of gallstone. The progression of acute cholecystitis varies from mild to severe form with multiple organ failure with mortality up to 0.6%.[1,2] Assessment severity helps clinicians to guide appropriate treatment and minimumize adverse outcome.[3,4]

Unlike acute pancreatitis there were few studies on severity classification in acute cholecystitis. Tokyo severity classification was first developed in 2007 and clinicians had led to revision in 2013. Now severity grading revised as the updated Tokyo Guidelines (TG13) are presented in accordance with actual clinical settings.[3,5,6]

In 2013 a new grading system for measuring anatomic severity of disease in emergency general surgery was proposed, with specific grades for eight commonly encountered gastrointestinal conditions (acute appendicitis, perforated peptic ulcer, acute divertulitis, acute cholecystitis, intestinal obstruction of small and large bowel, hernias, acute pancreatitis, and arterial ischemic bowel). These grades range from Grade I through Grade V, reflecting an escalating clinical progressionfrom mild disease limited within the organ itself to severe disease that is widespread.[7]

TG13 grading system is widely used in clinical setting and EGS is not fully validated. These two-severity classification are quite different since TG 13 assesses severity based on clinical parameters and patient's physical status whreas EGS focuses on anatomical severity of disease progress.

We hypothesized EGS may be more suitable in indivisualizing treatment levels since it reflects imaging, pathological, and operative findings of acue cholecystitis. Therefore, we aimed to compare TG13 severity system and EGS grade system for predicting clinical outcomes in acute cholecystitis.

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## MATERIALS AND METHODS

### Study Design and Data Collection

This is a retrospective single-center study which enrolled patients who were admitted to Pyongsong Medical University Hospital between February 2020 and October 2021.

### Inclusion Criteria

Patients who fulfilled TG13 diagnostic criteria were included.[5]

### Exclusion Criteria

- Biliary obstruction secondary to malignancy.
- Age younger than 17.

Baseline data included age, sex, comorbidity status as assigned by the Charlson Comorbidity Index, vital signs (blood pressure, pulse, body temperature), laboratory findings (WBC) ultrasonographic findings (gallbladder enlargement, gallbladder wall thickness, pericholecystic fluid, presence of gallstone, ascites), operative treatment (cholecystectomy, cholecystostomy), postoperative complication, in-hospital mortality and hospital stay.

The severity of postoperative complication were assessed by Clavien-dindo classification system.[9]

### Validation of Severity Classification

Severity assessment was performed in all patients using TG 13 grading system and EGS severity classification (Tables 1 and 2).

### Parameters Assessed

Clinical outcomes were mortality, postoperative complication rate, need for emergency surgery (emergency laparascopic

**Table 1: EGS grade descriptions of acute cholecystitis severity.**

| Grade | Description | Imaging | Operative |
|---|---|---|---|
| I | Localized gallbladder inflammation. | Wall thickening, pericholecystic fluid, nonvisualization of the gallbladder. | Localized inflammatory changes. |
| II | Distended gallbladder with purulence or hydrops, necrosis/gangrene of wall noted without iatrogenic perforation. | Above plus air in the gallbladder lumen, wall or biliary tree. | Distended gallbladder with pus/ hydrops, nonperforated wall necrosis/ gangrene. |
| III | Noniatrogenic perforation with bile located to RUQ. | Extraluminal fluid collection limited to RUQ. | Noniatrogenic gallbladder wall perforation with bile limited to RUQ. |
| IV | Pericholecystic abscess, bilioenteric fistula, gallstone ileus. | RUQ abscess, bilioenteric fistula, gallstone ileus. | Pericholecystic abscess, bilioenteric fistula, gallstone ileus. |
| V | IV with generalized peritonitis. | Free intraperitoneal fluid. | Above with generalized peritonitis. |

**Table 2: TG13 severity assessment for acute cholecystitis.**

| Grade | Description |
|---|---|
| III (severe) | Organ dysfunction in any one of the following systems.<br>Cardiovascular: Hypotension requiring administration of ≥5μg/kg/min of dopamine or any dose of norepinephrine.<br>Neurologic: Decreased level of consciousness.<br>Respiratory: PaO2:FIO2 <300.<br>Renal: Oliguria or Creatinine >2.0 mg/dl (>177 μmol/liter).<br>Hepatic: International normalized ratio >1.5.<br>Hematologic: Platelet count <100,000/mm3. |
| II (moderate) | Any one of the following characteristics.<br>Leukocytosis (>18,000 cells per mm3).<br>Palpable, tender mass in right upper quadrant.<br>Symptom duration >72 hr.<br>Marked local inflammation (gangrenous or emphysematous cholecystitis, pericholecystic or hepatic abscess, biliary peritonitis. |
| I (mild) | Acute cholecystitis in otherwise healthy patient with mild local inflammatory changes and without organ dysfunction.<br>Criteria for grade II or III not met. |

cholecystectomy, emergency open cholecystectomy, emergency cholecystostomy) and hospital stay.

Postoperative complications included hematoma, atrial fibrillation, iatrogenic bowel injury, sepsis, surgical site infection, small bowel obstruction, biloma, urinary retention, respiratory failure, postoperative hemorrhage, cystic stump leak, cholangitis, acute kidney injury, pneumonia, ileus, urinary tract infection and upper gastrointestinal bleeding.

### Statistical Analysis of Data

Data were analyzed using SPSS 20.0 for Windows (SPSS, Chicago, IL). Categorical variables were described using frequencies and percentages. Continuous variables were summarized using mean and SD. Pairwise testing between severity grades within a classification system was performed using Fisher exact for binary outcomes and were expressed as percentage, whereas Kruskal–Wallis tests were used for continuous outcomes and expressed as mean (the 25% percentile to the 75% percentile). The area under the receiver operating characteristic curve was used to describe the predictive value of a classification system. Comparison of AUC was perfomed using chi-square test.[10]

## RESULTS

### Patients Characteristics

A total of 164 patients were included in the analysis (mean age of 57.4 years; 52.4% males). Patient's demographic and clinical data were summarized in Table 3.

On the basis of EGS grade, 132 patients (80.5%), 22 patients (13.5%), 2 patients (1.2%), 4 patients (2.4%) and 4 patients (2.4%) were determined to have I, II, III, IV and V. Using TG13 grade, 113 patients (68.9%) were categorized as mild, 46 patients (28.0%) as moderate, and 5 patients (3.1%) as severe.

In general, higher grades of severity were associated with worse clinical outcomes for all three classification systems and this was more precise in TG 13 severity system (Tables 4 and 5).

### EGS Severity Classification

Mortality in patients with grade II was higher compared to grade I and this was not statistically significant. No death was observed in patients with grade III. However, mortality was significant increasing in patients with grade IV and V.

There was significant increase in postoperative complication rate and need for emergency surgery. Morever all patients graded more than II received emergency surgery and developed postoperative complication.

In addition, higher grades of severity were associated with increased hospital stay. However, it was only statically significant between grade I and II.

**Table 3: Patients characteristics (n=164).**

| Characteristics | Value |
|---|---|
| Calculus cholecystitis, n (%) | 101 (61.6) |
| Vital signs | |
| Systolic pressure (mmHg), $\bar{X}$±SD | 124.0±22.3 |
| Pulse ($min^{-1}$), $\bar{X}$±SD | 88.6±15.6 |
| Body temperature (>38°C), n (%) | 34 (20.7) |
| WBC ($10^9$/L), $\bar{X}$±SD | 11.9±6.0 |
| Ultrasonographic findings | |
| Gallbladder enlargement, n (%) | 145 (88.4) |
| Thickening of the gallbladder wall (5 mm or greater), n (%) | 115 (70.1) |
| Pericholecystic fluid, n (%) | 36 (22.0) |
| Ascites, n (%) | 28 (17.1) |
| Percentage of emergency surgery, n (%) | 61 (37.2%) |
| Postoperative complication type, n (%) | |
| Hematoma | 0 (0.0) |
| Iatrogenic bowel injury | 0 (0.0) |
| Sepsis | 4 (2.4) |
| Surgical site infection | 17 (10.4) |
| Small bowel obstruction | 0 (0.0) |
| Urinary retention | 0 (0.0) |
| Respiratory failure | 9 (5.5) |
| Postoperative hemorrhage | 0 (0.0) |
| Cystic stump leak | 0 (0.0) |
| Cholangitis | 0 (0.0) |
| Pneumonia | 2 (1.2) |
| Ileus | 0 (0.0) |
| Urinary retention | 1 (0.6) |
| Upper gastrointestinal bleed | 0 (0.0) |
| Atrial fibrillation | 1 (0.6) |
| Acute kidney injury | 0 (0.0) |
| Postoperative complication severity, n (%) | |
| I | 1 (0.6) |
| II | 14 (8.5) |
| III | 10 (6.1) |
| IV | 3 (1.8) |
| V | 6 (3.7) |
| Mortality, n (%) | 6 (3.7) |
| Hospital stay (days), $\bar{X}$±SD | 10.7±8.9 |

**Table 4: Distribution of clinical outcomes stratified by classification system.**

| Outcomes | Mortality, n (%) | Postoperative complication rate, n (%) | Need for emergency surgery, n (%) | Hospital stay ( $\bar{X}$±SD, days) |
|---|---|---|---|---|
| I (n=132) | 1 (0.8) | 7 (5.3) | 30 (22.7) | 8.2±5.0 |
| II (n=22) | 2 (9.1) | 11 (50.0)[a] | 21 (95.5)[a] | 20.8±11.8[a] |
| III (n=2) | 0 (0.0) | 2 (100.0)[b] | 2 (100.0) | 28.5±10.6 |
| IV (n=4) | 1 (25.0)[c] | 4 (100.0) | 4 (100.0) | 33.2±13.1 |
| V (n=4) | 2 (50.0)[d] | 4 (100.0) | 4 (100.0) | 35.0±24.0 |

a: I vs II was significant; b: II vs III was significant; c: III vs IV was significant; d: IV vs V was significant.

**Table 5: Distribution of clinical outcomes stratified by classification system.**

| Outcomes | Mortality, n (%) | Postoperative complication rate, n (%) | Need for emergency surgery, n (%) | Hospital stay ( $\bar{X}$±SD, days) |
|---|---|---|---|---|
| Mild (n=113) | 1 (0.9) | 6 (5.3) | 19 (16.8) | 7.7±6.0 |
| Moderate (n=46) | 3 (6.5) | 18 (39.1)[a] | 37 (80.4)[a] | 16.8±8.7[a] |
| Severe (n=5) | 2 (40.0)[b] | 4 (80.0)[b] | 5 (100.0) | 36.3±11.4[b] |

a: Mild vs moderate was significant; b: Moderate vs severe was significant.

**Table 6: Prediction of clinical outcomes by EGS and TG13 using ROC analysis.**

| Outcomes | EGS | TG13 |
|---|---|---|
| Mortality | 0.866 (0.680~1.052) | 0.812 (0.619~1.004) |
| Postoperative complication rate | 0.848 (0.748~0.947) | 0.799 (0.701~0.896) |
| Need for emergency surgery | 0.798 (0.721~0.875) | 0.734 (0.647~0.820) |

### TG13 Severity Classification

There was significant increase in postoperative complication rate and hospital stay for all grades. With regard to mortality, there was significant difference moderate vs severe (6.5 vs 40.0; P<0.01). Pairwise also showed increase in need for emergency surgery for all grades and it was significant between mild and moderate (16.8 vs 80.4; P<0.01).

### Comparison between Classification Systems

The AUCs for EGS was significantly higher in predicting mortality (0.866 and 0.812; P <0.001), postoperative complication rate (0.848 and 0.799; P <0.001) and need for emergency surgery (0.798 and 0.734; P < 0.001) compared with TG13 (Table 4, Figure 1).

## DISCUSSION

Recently, two new classification systems for AP have been reported and it is controversial which classification predicts clinical outcomes more accurately. EGS is a clinical, pathological, surgical grading system for acute abodominal disease including acute cholecystitis. Therefore, it might offer uniformed understanding of disease anatomic severity. TG 13 incorporates physiology and clinical status of the patient aiming to improve disease severity assessment with preoperative status, management approach, and postoperative events. It suggests various management approaches depending on disease severity: mild (grade I) receive early laparoscopic cholecystectomy, moderate (grade II) receive fluid and antimicrobial resuscitation with early or delayed cholecystectomy, and severe (grade III) disease is often associated with organ failure, which necessitates percutaneous drainage. In the present study we found the biggest propotion of patients with EGS grade, which suggests most patients with acute cholecystitis develop localized gallbladder inflammation.

In previous study 154 patients, 148 patients, 81 patients, 46 patients, 14 patients were determined to have I, II, III, IV and V grade.[11] This distribution is incordorance with our result since it did not include patients consecutively. With regard to usage of TG 13 classification, 68.9% of patients have mild grade whereas severe grade was only 3.1%. Various results have reported in several studies applying TG 13 in clinical practice. In one study 104 patients was defined as mild, 45 patients were defined as moderate and 1 was defined as severe. In the other study mild disease was determined in 83.7%, moderate in 14.2% and severe in 2.1%.

Unlike above two studies Yokose M *et al.* reported moderate disease was more prevelant than mild one. These various results

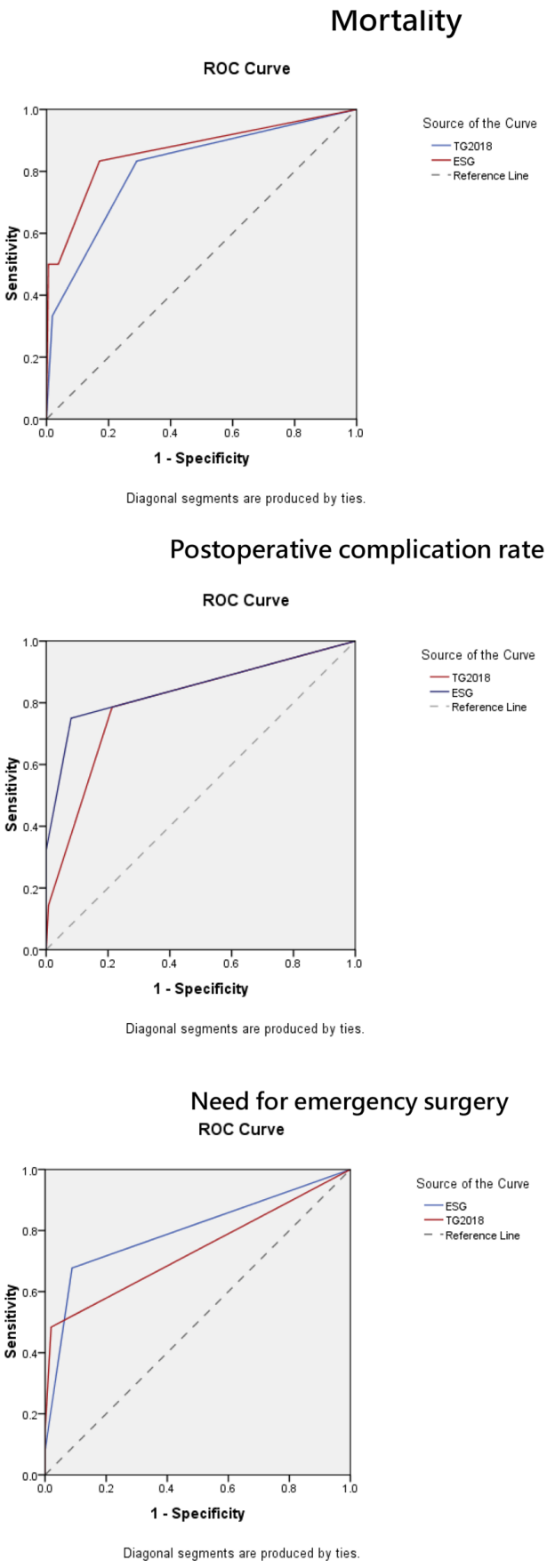


**Figure 1:** Area under the receiver operating curves comparing EGS and TG 13 for predicting clinical outcomes.

might be due to different level of institutions and capability of emergency department. In addition, increasing severity grade was associated with worse clinical outcomes, which demonstrates two severity systems accurately classify patients with various prognosis. Comparing two classifications using ROC analysis, EGS was more accurate than TG 13 for predicting mortality, postoperative complication and need for emergency surgery.

In one report EGS was better for predicting mortality (0.86 vs 0.73), complication (0.76 vs 0.63) and cholecystostomy tube utilization (0.80 vs 0.68) comparing with TG 13. This is in line with our result which demonstrates anatomic measurement of disease severity is closely with poor outcome for disease requiring emergency surgery.

## CONCLUSION

EGS severity classification was more superior to TG 13 grade system for predicting clinical outcomes.

## CONFLICT OF INTEREST

The authors declare no conflict of interest.

## ABBREVIATIONS

**TG13:** Tokyo 2013; **EGS:** Emergency General Surgery.

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