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Acute cholecystitis: comparing clinical outcomes with TG13 severity and intended laparoscopic versus open cholecystectomy in difficult operative cases

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Abstract

Introduction The revised Tokyo Guidelines include criteria for determining the severity of acute cholecystitis with treatment algorithms based on severity. The aim of this study was to investigate the relationship of the revised Tokyo Guidelines severity grade to clinical outcomes of cholecystectomy for acute cholecystitis.

Methods We identified 66 patients with acute cholecystitis from a prior study of difficult cholecystectomy cases. We examined the relationship between severity grade and multiple variables related to perioperative and postoperative outcomes.

Results A more severe revised Tokyo Guidelines grade was associated with a higher number of complications ($p=0.03$) and a higher severity of complications ($p=0.01$). Severity grade did not predict operative time, estimated blood loss, intensive care unit admission or length of stay. Compared to planned open cholecystectomy, intended laparoscopic cholecystectomy was associated with significantly fewer total and Clavien–Dindo grade 3 complications, fewer intensive care unit admissions, and shorter length of stay (p values range from 0.03 to <0.0001).

Conclusion In technically difficult operations for acute cholecystitis, the revised Tokyo guidelines severity grade correlates with the number and severity of complications. However, intended performance of laparoscopic cholecystectomy rather than open cholecystectomy in difficult operations predicts broader beneficial outcomes than severity grade.

Keywords Acute cholecystitis · Tokyo guidelines · Severity grade

Cholelithiasis is present in approximately 10–15% of the adult population with approximately 20% of these patients experiencing some form of symptoms [1]. Of those experiencing symptoms, 1–3% will eventually progress to acute cholecystitis (AC) [2]. The revised Tokyo Guidelines (TG13) include criteria for determining the severity of AC, with treatment algorithms based on severity and the anticipated difficulty of operative conditions [3–5]. Mild (Grade I) AC is defined as occurring without substantial organ dysfunction and not meeting either Grade II or III criteria. Moderate (Grade II) AC is defined as a WBC count > 18,000 mm, a palpable tender mass in the right upper quadrant (RUQ), a duration of symptoms greater than 72 h, or marked local inflammation (including a gangrenous, necrotic, or emphysematous gallbladder, etc.) and not meeting Grade III criteria. Severe (Grade III) AC is defined as occurring with substantial organ dysfunction with criteria included for neurological, cardiovascular, respiratory, renal, hepatic, or hematological dysfunction (Fig. 1). According to the TG13, mild AC can be treated with early cholecystectomy, moderate AC can be treated with either early cholecystectomy (in experienced hands) or delayed cholecystectomy, and severe AC is to be treated with delayed cholecystectomy [4, 5]. In North America, there are a limited number of studies assessing the validity of TG13.

It is hypothesized that increased severity grade will be associated with less favorable operative outcomes in technically difficult cases. Grade II severity, in particular, was intended to identify cases with severe gallbladder inflammation that could render operative conditions difficult [4]. The aim of this study is to investigate the relationship of TG13 severity grade, as well as intended laparoscopic

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TG 13 Criteria – Severity Grade Criteria	
Severe (Grade III)	
1. Neurological	Decreased level of consciousness
2. Cardiovascular	Hypotension requiring Dopamine > 5mcg/kg or any dose of norepinephrine
3. Respiratory	PaO2/FiO2 < 300
4. Renal	Oliguria, Cr > 2.0
5. Hepatic	PT-INR > 1.5
6. Hematological	Platelet count < 100,000
Moderate (Grade II)	
WBC > 18,000/mm^3	
Palpable tender mass in RUQ	
Duration of symptoms > 72 hours	
Signs of local inflammation (i.e. emphysematous cholecystitis, gangrenous cholecystitis, pericholecystic abscess, hepatic abscess, biliary peritonitis)	
Mild (Grade I)	
Acute cholecystitis not meeting criteria for moderate (grade II) or severe (grade III) ACC. No evidence of end organ damage or severe signs of local inflammation.	

Fig. 1 TG13 severity grade criteria

cholecystectomy (LC) versus open cholecystectomy (OC), to clinical outcomes of cholecystectomy for AC in cases that were operatively proven to be difficult for senior surgeons.

Methods

This study was approved by the Institutional Review Board at Rush University Medical Center. We identified patients from 2000 to 2012 with AC from a prior study of difficult cholecystectomy cases [6]. Cases were defined as difficult if the attending surgeon initially decided to perform an open, and not a laparoscopic, cholecystectomy based solely on the anticipated difficulty of the operation. Cases were also defined as difficult if the attending surgeon determined intraoperatively that completing the case laparoscopically would have only been possible with the additional use of laparoscopic ultrasound to help identify obscure anatomy. Patients were excluded if the decision to proceed with initial open cholecystectomy was for any other reason than the expected difficulty of the case, including Mirizzi's syndrome, suspected cancer, previous abdominal operations, pancreatitis, peritonitis, multiple comorbidities, or if the indication for an open approach was not clear. An intent-to-treat analysis was used.

The relationship between TG13 severity grade and demographic variables including age, gender, and Charlson Comorbidity Index (CCI) was examined using a Fisher exact test (gender) and Spearman correlation coefficients (age and CCI). A Fisher exact test was also used to determine the relationship between TG13 severity grade and the presence of postoperative complications. Kruskal–Wallis one-way analysis of variance was then used to determine if TG13 severity grade predicted the number or severity of

postoperative complications. Linear regressions were used to identify the relationship between TG13 grade and LOS, operative time, and estimated blood loss (EBL) while controlling for planned type of surgery (LC vs. OC). Similarly, a logistic regression was used to determine if TG13 grade could predict ICU admission while controlling for planned type of surgery. The ability of TG13 grade to predict conversion from laparoscopic to open cholecystectomy was investigated using a Wilcoxon rank sum test.

The relationship between the number of, as well the individual, TG13 Grade II criteria and the presence, number, and severity of complications was determined using Fisher exact tests and Kruskal–Wallis one-way analysis of variance. The ability for TG13 severity grade, the number of TG13 grade II criteria, and the individual grade II criteria to predict the presence of acute gangrenous/necrotic cholecystitis was assessed using Fisher exact tests and a Wilcoxon rank sum test.

To examine whether the intended type of surgery (LC vs. OC) was related to the number of Clavien–Dindo grade 3 complications, ICU admissions, or LOS, Fisher exact tests (complications and ICU admissions) and a Welch's *t* test (LOS) were utilized [7]. A Fisher exact test was used to determine the relationship between the TG13 severity and whether the patient was scheduled for LC or OC. All statistical analyses were completed using R, 3.2.0 [8]. Significance was defined as $p < 0.05$.

Results

There were 66 patients included in the study, with 37 undergoing planned open cholecystectomy (OC), 25 undergoing intended laparoscopic cholecystectomy (LC), and four that were converted from a LC to an OC. There were 32 males and 34 females ranging in age from 21 to 87 years old (median = 55.5). Subtotal cholecystectomy was performed on six patients, and four patients had percutaneous cholecystostomy tubes placed pre-operatively. Gangrenous/necrotic cholecystitis was identified grossly and histologically in 33 patients. The remaining 33 patients were found to have changes consistent with acute cholecystitis without gangrenous/necrotic changes. There were seven patients identified with Grade I AC, 52 with Grade II AC, and 7 with Grade III AC as defined by TG13. Of the 37 planned OC, 3 had Grade I AC, 29 had Grade II AC, and 5 had Grade III AC (see Table 1).

There were no significant associations between demographic variables (Age, Sex, CCI) and TG severity ($p = 0.98$, 0.67, 0.12, respectively). Additionally, a significant relationship was not found between TG13 severity and a number of perioperative variables including: LOS after cholecystectomy, operative time, EBL, or ICU admission. These findings were consistent even when controlling for OC versus LC (see Table 2).

Table 3 outlines the relationship between TG13 severity grade and the number of complications each patient had. While there were no significant differences among the three severity groups on the presence of a complication ($p = 0.09$), a higher TG13 severity grade was related to an increased number of total complications per patient ($p = 0.03$; see Table 3).

Table 4 outlines the relationship between TG13 severity grade and the severity of a complication as defined by the Clavien–Dindo scale. TG13 severity grade was associated with a higher severity of complication ($p = 0.01$; see Table 4) when each patient was represented by the highest Clavien–Dindo category of complication that occurred their case.

Within the group of patients categorized as TG Grade II acute cholecystitis, there was no significant relationship

Table 1 Planned open versus laparoscopic cholecystectomy by severity

	Tokyo Guidelines Severity		
	Grade I (Mild)	Grade II (Moderate)	Grade III (Severe)
Planned open	3	29	5
Planned lap	4	23	2

Table 2 Perioperative variables by severity of acute cholecystitis

	TG13 Severity Grade		
	Mild (Grade I)	Moderate (Grade II)	Severe (Grade III)
Estimated blood loss (mL)	65	114	57
Length of stay (days)	6.8	7.6	13
ICU admissions	0	10	4
Operative time (min)	103	142	100

Table 3 Number of patients experiencing different numbers of complications by severity of acute cholecystitis*

	Tokyo Guidelines Severity		
	Grade I (Mild)	Grade II (Moderate)	Grade III (Severe)
No complications	6	34	2
One complication	1	15	2
Two complications	0	2	2
Three complications	0	1	1

*$p = 0.03$

Table 4 Number of patients experiencing different severities of complications (Clavien–Dindo) by severity of TG13*

	Tokyo Guidelines Severity		
	Grade I (Mild)	Grade II (Moderate)	Grade III (Severe)
No complications	6	34	2
Clavien–Dindo grade 1	1	6	0
Clavien–Dindo grade 2	0	5	1
Clavien–Dindo grade 3	0	7	2
Clavien–Dindo grade 4	0	0	0
Clavien–Dindo grade 5	0	0	2

*$p = 0.01$

between the number of Grade II criteria met and the presence of a complication, the number of complications, or the severity of complications ($p = 0.35$, 0.42, 0.43, respectively). Additionally, there was no association between any individual Grade II criterion and the presence, number, or severity of complications (p values range from 0.20 to > 0.99).

No significant difference in TG13 severity grade was identified in patients that successfully completed LC and those that were converted from LC to OC ($p = 0.27$). There was no relationship between TG13 severity grade and the presence of gangrenous/necrotic AC ($p = 0.11$). However, patients with gangrenous cholecystitis were more likely than patients who did not have gangrenous cholecystitis to have an increased number of positive Grade II criteria ($p = 0.01$).

Planned LC, as compared to intended OC, was associated with significantly fewer total complications ($p = 0.02$) as well as fewer Clavien–Dindo grade 3 complications ($p = 0.03$). It was also associated with fewer ICU admissions ($p = 0.001$) and shorter LOS ($p < 0.0001$). There was no relationship between TG13 severity and whether the patient was scheduled for LC or OC ($p = 0.62$).

Discussion

Acute cholecystitis encompasses a range of potential operative conditions. The ability to pre-operatively identify factors that predict difficult operative conditions and portend increased risk for postoperative complications would be of great use to surgeons in planning the initial treatment approach and timing of operation. Our study demonstrated that, within a group of difficult operative cases, a higher TG13 severity grade correlated with an increase in the number of total complications experienced by an individual patient and the severity of those complications, though severity grade did not predict whether a patient experienced at least one complication or not. Grade II criteria alone, whether individually or in aggregate, did not serve as good predictors of complications. In contrast, for patients with Grade II AC, those meeting a higher number of Grade II criteria were more likely to have gangrenous/necrotic cholecystitis. The conversion from LC to OC was not predicted by TG13 severity grade. The total number of complications, severity of complications, LOS, and ICU admissions were observed to be increased in OC compared to LC.

There are conflicting reports in the literature in regard to the association between TG13 severity grade and complications. Wright [9] and Ambe [10], in similarly constructed retrospective single hospital studies, demonstrated a significant correlation between TG13 severity grade and postoperative complications, consistent with our findings. Alternatively, Maussoumi [11] demonstrated no association between TG13 severity and complication rates in a retrospective single hospital study, though the study excluded patients undergoing open cholecystectomy which likely restricted the range of complications experienced by patients. Our study did not demonstrate a relationship between TG13 severity grade and the need to convert from LC to OC, unlike studies completed by Asai [12], Amirthalingam [13], Ambre [10], and Wright [9]. However, given that only four patients in our study converted from LC to OC, this analysis was under powered. The low number of LC to OC conversion in our study may be attributed to the intraoperative use of laparoscopic ultrasound (LUS) which allowed for the safe identification of biliary anatomy, mitigating the need for conversion to an open approach. The presence of an increasing number of Grade II criteria could not be used to further risk stratify patients within the Grade II severity group with regard to postoperative complications but they could be used to predict the presence of gangrenous/necrotic cholecystitis. This has not been investigated in previous studies. Prior studies have demonstrated an association between increasing TG13 severity grade and increasing LOS [4, 9] and operative time [9]. No studies were found comparing ICU admissions and TG13 severity grade. While LOS, operative time, and ICU admission were not demonstrated to be correlated with TG13 severity grade in our study, LOS and ICU admission were observed to be increased in OC compared to LC. We believe this, in addition to the observed increase in complications in OC versus LC, indicates that intended LC versus OC may provide broader beneficial outcomes than TG13 severity grade does within the population of difficult operative cases.

Recently, the TG18 were released as an update to TG13. In the revised guidelines, the authors present data supporting the predictive validity of the severity criteria. They note a significant correlation between TG13 severity grade and 30 day mortality, LOS, conversion from LC to OC, and complications. While our study did find a significant association between severity grade and complications, we did not find the same relationship between severity grade and LOS and

conversion from LC to OC. We did not investigate the ability of severity grade to predict mortality as there were no 30 days mortalities in our study [13].

One of the limitations of this study is that the data were collected retrospectively, which may have biased our attribution of TG13 severity grade during chart review. The data for this study were collected from a single academic institution which potentially limits our ability to generalize our results to other patient populations. The patients selected for this study were determined by the operating surgeon to represent cases that were operatively difficult. This likely explains why our data included a majority of patients with TG13 Grade II AC as opposed to the predicted majority of Grade I AC in the general population [10, 14, 15]. An element of subjectivity, as well as surgeon experience, was likely inherent in defining what constitutes a difficulty operative cholecystectomy. The small number of Grade I and Grade III AC patients likely limited our ability to draw significant conclusions on a number of different perioperative variables. Laparoscopic ultrasound was utilized in all patients undergoing LC which may have had an influence on perioperative and postoperative outcomes in those patients (especially our low rate of conversion from LC to OC) as previous studies have demonstrated decreased morbidity in difficulty laparoscopic cholecystectomy in which laparoscopic ultrasound was utilized [6]. The use of laparoscopic ultrasounds requires consistent and repetitive use in routine cases to in order for it to reliably provide actionable information in difficult cases and its utility is user dependent.

The findings from this study suggest that the TG13 severity grades can be used to risk stratify patients undergoing cholecystectomy for AC by predicting postoperative morbidity. The utility of this is somewhat limited pre-operatively (when it would be most useful to the clinician) due to some of the TG13 criteria requiring intraoperative identification. While these results give further predictive validity to the TG13 severity grades in a U.S population, its ability to predict other peri- and postoperative outcomes (i.e., conversion to open, LOS, and ICU admission) was not observed. Our results also suggest that while severity grade can be used to risk stratify patients with regard to postoperative complications, whether a patient has a planned laparoscopic, rather than open, cholecystectomy likely predicts broader beneficial outcomes when compared to TG13 severity grade.

Author contributions All authors listed have contributed to the creation of this article in accordance with the Journal of Surgical Endoscopy's guidelines.

Compliance with ethical standards

Disclosures Justin Gerard has nothing to disclose. Daniel Deziel has nothing to disclose. Minh Luu has nothing to disclose. Jennifer Poirier has nothing to disclose.

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