Revision of the AAST grading scale for acute cholecystitis with comparison to physiologic measures of severity

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Kevin M. Schuster, Rick O'Connor, Michael Cripps, Kali Kuhlenschmidt, Luis Taveras, Haytham M. Kaafarani, Majed El Hechi, Ruchir Puri, Thomas J. Schroeppel, Toby M. Enniss, Daniel C. Cullinane, Laura M. Cullinane, Suresh Agarwal, Jr, Krista Kaups, Marie Crandall, Gail Tominaga have nothing to disclose.

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Kevin M. Schuster, MD, MPH, FACS, Rick O'Connor, RN, Michael Cripps, MD, Kali Kuhlenschmidt, MD, Luis Taveras, MD, Haytham M. Kaafarani, MD, Majed El Hechi, MD, Ruchir Puri, MD, MS, FACS, Thomas J. Schroeppel, MD, MS, Toby M. Enniss, MD, FACS, Daniel C. Cullinane, MD, Laura M. Cullinane, Suresh Agarwal, Jr, MD, Krista Kaups, MD, MSC, Marie Crandall, MD, MPH, FACS, *and* **Gail Tominaga, MD, FACS**, *New Haven, Connecticut*

BACKGROUND: Grading systems for acute cholecystitis are essential to compare outcomes, improve quality, and advance research. The American Association for the Surgery of Trauma (AAST) grading system for acute cholecystitis was only moderately discriminant when predicting multiple outcomes and underperformed the Tokyo guidelines and Parkland grade. We hypothesized that through additional expert consensus, the predictive capacity of the AAST anatomic grading system could be improved.

METHODS: A modified Delphi approach was used to revise the AAST grading system. Changes were made to improve distribution of patients across grades, and additional key clinical variables were introduced. The revised version was assessed using prospectively collected data from an AAST multicenter study. Patient distribution across grades was assessed, and the revised grading system was evaluated based on predictive capacity using area under receiver operating characteristic curves for conversion from laparoscopic to an open procedure, use of a surgical "bail-out" procedure, bile leak, major complications, and discharge home. A preoperative AAST grade was defined based on preoperative, clinical, and radiologic data, and the Parkland grade was also substituted for the operative component of the AAST grade.

RESULTS: Using prospectively collected data on 861 patients with acute cholecystitis the revised version of the AAST grade has an improved distribution across all grades, both the overall grade and across each subscale. A higher AAST grade predicted each of the outcomes assessed (all $p \leq 0.01$). The revised AAST grade outperformed the original AAST grade for predicting operative outcomes and discharge disposition. Despite this improvement, the AAST grade did not outperform the Parkland grade or the Emergency Surgery Score.

CONCLUSION: The revised AAST grade and the preoperative AAST grade demonstrated improved discrimination; however, a purely anatomic grade based on chart review is unlikely to predict outcomes without addition of physiologic variables. Follow-up validation will be necessary. (*J Trauma Acute Care Surg.* 2022;92: 664–674. Copyright © 2021 American Association for the Surgery of Trauma.)

LEVEL OF EVIDENCE: Diagnostic Test or Criteria, Level IV.

KEY WORDS: Cholecystitis; grading scales; outcomes.

Acute cholecystitis is one of the most common acute surgical conditions in the United States representing over 215,000 annual hospital admissions and over $3 billion in charges.[1] Notwithstanding the generally younger age range associated with cholecystitis, it continues to carry a mortality risk that may be as high as 3.6%.[2] Acute cholecystitis is generally treated with laparoscopic cholecystectomy during the index hospitalization with an overall low risk of complications.[3] That risk, however, may be as high as 9% for major complications despite being one of the most common operations performed in the United States.[4] To optimize the care of these patients, surgeons need to be able to determine their degree of illness on presentation to the hospital. Unfortunately, models developed to date are not able to predict cholecystitis outcomes from preoperative data with high degree of certainty, unless patients present with a high degree of illness.[5] The poor predictive accuracy for the models may limit risk adjustment for nonrandomized studies comparing treatment strategies. There are only two prospective randomized studies that compare cholecystectomy with either nonoperative management of acute cholecystitis or percutaneous cholecystostomy.[6,7] Both trials were at moderate to high risk for bias and would have benefited from the ability to support the findings through highly accurate risk adjustment.[5] Accurate risk assessment would also allow future trials to be stratified based on risk and thereby reduce necessary sample size.

Understanding the severity of the cholecystitis is also valuable for informing patients, benchmarking hospital and surgeon performance and potentially determining reimbursement. We have previously compared the American Association for the Surgery of Trauma (AAST) grading scale for acute cholecystitis with the Tokyo guidelines and the Parkland grade.[8] The AAST grade performed less well than the Parkland grade but similar to the Tokyo guidelines. This was at least partially driven by a lack of dispersion of patients across grades. The widely used available grading scales also have important design limitations. Much of the Tokyo guidelines, especially Grade III relies on physiologic variables to grade disease severity, which are exclude from the AAST scale by design.[9] Similar to the AAST organ injury scales, the AAST emergency general surgery grades were designed to be pure anatomic descriptions of the diseases graded.[10] The Parkland grade is highly predictive of outcomes;

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From the Department of Surgery (K.M.S., R.O.), Yale School of Medicine New Haven, Connecticut; Department of Surgery (M.C., K.K., L.T.), University of Texas Southwestern School of Medicine, Dallas, Texas; Department of Surgery (H.M.K., M.E.H.), Massachusetts General Hospital Boston, Massachusetts; Department of Surgery (R.P., M.C.), University of Florida College of Medicine Jacksonville, Jacksonville, Florida; Department of Surgery (T.J.S.), UC Health, Colorado Springs, Colorado; Department of Surgery (T.M.E.), University of Utah, School of Medicine, Salt Lake City, Utah; Department of Surgery (D.C.C., L.M.C.), Marshfield Clinic Marshfield, Wisconsin; Department of Surgery (S.A.J.), Duke University Medical Center Durham, North Carolina; Department of Surgery (K.K.), University of California San Francisco, Fresno, Fresno; and Department of Surgery (G.T.), Scripps Memorial Hospital La Jolla, California.

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Address for reprints: Kevin M. Schuster, MD, MPH, FACS, Yale School of Medicine, 330 Cedar St, BB310 PO Box 208062 New Haven, CT 06520-8062; email: kevin.schuster@yale.edu.

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however, it can only be applied to patients undergoing cholecystectomy. Given that the central decision in managing patients with cholecystitis is often the choice between nonoperative management and operative management, preoperative grading will be essential.

The goal of disease grading should be development of the most predictive system possible. The grade should predict patient outcomes irrespective of treatment strategy, thereby informing decision making for patients presenting with acute cholecystitis. Development of the grading system is an iterative process using available data to create the next version of the system. We hypothesized that using the data from the recent cholecystitis grading validation, an expert consensus evaluation of the data would result in an improved grading system.

MATERIALS AND METHODS

Grading System Modification

Data obtained from the recent AAST cholecystitis validation study were used to identify potential predictors of outcome in acute cholecystitis.[8] All of the granular data from imaging findings, laboratory values, and clinical assessments that had any potential to be associated with outcomes were assessed. Anatomic and some physiologic factors associated with various

TABLE 1. Comparison of Imaging Findings With Outcomes

	Any Complication	Surgical Bail-Out	Conversion to Open	Bile Leak
US thick wall (>3 mm)				
Yes	34 (8.7)	12 (3.3)	19 (6.1)	6 (1.6)
No	32 (8.7)	10 (2.6)	12 (3.2)	9 (2.3)
US CBD diameter				
<5 mm	36 (7.9)	10 (2.2)	15 (3.5)	7 (1.5)
6–7 mm	11 (8.3)	5 (3.8)	6 (5.2)	2 (1.5)
8–9 mm	8 (12.9)	0 (0.0)	2 (4.1)	2 (3.2)
>9 mm	6 (15.0)	1 (2.5)	3 (8.6)	1 (2.5)
US pericholecystic fluid				
Yes	19 (9.2)	8 (4.5)	11 (6.3)	5 (2.4)
No	47 (8.5)	14 (2.7)	20 (3.9)	10 (1.8)
US GB wall air				
Yes	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
No	66 (8.8)	22 (3.2)	31 (4.6)	15 (2.0)
US CBD stone				
Yes	5 (25.0)	0 (0.0)	0 (0.0)	0 (0.0)
No	61 (8.3)	22 (3.2)	31 (4.7)	15 (0.0)
CT scan performed				
Yes	44 (12.5)	10 (3.4)	28 (9.8)	8 (2.3)
No	35 (6.9)	16 (3.3)	14 (2.9)	10 (2.0)
CT scan pericholecystic fluid				
Yes	4 (36.4)	1 (1.1)	10 (11.4)	3 (2.6)
No	40 (11.7)	9 (4.4)	18 (9.1)	5 (2.1)
CT scan perforation				
Yes	5 (26.3)	3 (20.0)	3 (25.0)	2 (10.5)
No	39 (11.7)	7 (2.5)	25 (9.2)	6 (1.8)
CT scan inflammation				
Yes	13 (9.0)	7 (6.3)	11 (10.4)	3 (2.1)
No	31 (14.9)	3 (1.6)	17 (9.5)	5 (2.4)
CT scan wall air				
Yes	0 (0.0)	1 (20.0)	0 (0.0)	0 (0.0)
No	44 (12.6)	9 (3.1)	28 (9.9)	8 (2.3)
CT lumen air				
Yes	0 (0.0)	0 (0.0)	1 (25.0)	0 (0.0)
No	44 (12.6)	10 (3.4)	27 (9.6)	8 (2.3)
CT common bile duct diameter				
<5 mm	8 (17.0)	2 (4.7)	2 (4.7)	0 (0.0)
6–7 mm	1 (10.0)	2 (25.0)	2 (25.0)	0 (0.0)
8–9 mm	2 (12.5)	4 (30.8)	4 (30.8)	0 (0.0)
>9 mm	4 (13.3)	1 (4.3)	1 (4.3)	0 (0.0)

US, ultrasound; CT, computed tomography.

complications and mortality were measured for their strength of association and applicability across multiple outcomes. Dichotomous and ordinal variables were compared at each of their levels to each outcome considered. Continuous variables were assessed for any potential inflection points as predictors of outcome. Surgical outcomes included operative time, use of fenestrated cholecystectomy or use of subtotal cholecystectomy combined as a "bail-out" procedure, conversion from laparoscopic to open, and bile leak. Major biliary injury was too infrequent to assess as an outcome in this small data set. Other outcome variables were according to the National Surgical Quality Improvement Project and based on the definitions of this program. A group of experts was drawn from the AAST Patient Assessment Committee, and the group met by video conference call to review these data. Additional information was provided to the group in the form of variables in other grading systems for cholecystitis including those predicting operative difficulty. An example of the patient data compared with the assessed outcomes, as provided to the group is presented in Table 1. These are the imaging data while clinical, operative, and pathologic findings were also presented in comparison to the same outcomes. The group continued to work through a modified Delphi approach over several subsequent emails. Using the data and the original AAST grading scale a revised AAST grade was constructed. Using the data, uncommon imaging, operative and pathologic findings were either eliminated or moved to secondary factors in determining the various subscale grade. All factors used as part of the original grade, and after careful consideration, several additional anatomic and physiologic variables directly related to biliary disease were included in the clinical, radiologic and surgical subscales of the grade where appropriate. The included factors were chosen based on both apparent importance and degree to which these variables would be universally available to a grader retrospectively reviewing a medical record. The revised grade is depicted in Figure 1.

Data Collection

Collection of the patient data was thoroughly described in our prior article.[8] Briefly eight institutions prospectively collected data for all patients admitted with acute cholecystitis. Each institution was asked to collect data on 100 patients although the final contribution of each institution varied. This number of patients was felt to be adequate based on prior acute cholecystitis scoring validation studies.[11] Patients were at least 18 years old and had the diagnosis of acute cholecystitis assigned by the admitting or consulting surgeon. This method of diagnosis was chosen due to the known inability of clinical and imaging findings to reliably make the diagnosis.[3] All of the data including clinical, laboratory, and imaging findings were collected on a granular level, for example, if available, gallbladder wall thickness was collected from each imaging study performed, and if multiple sources were present, the ultrasound measurement was used. This approach was taken for the purpose of avoiding the bias potentially introduced when a physician enters a grade based on a summation of the data. Because of the nature of the Parkland grade, this potential bias was accepted to avoid having to acquire an intraoperative photo or video for later independent grading. Approximately two-thirds of the patients had the Parkland grade captured prospectively with the remaining third abstracted retrospectively from the medical record. Concomitant pancreatitis was the only specific exclusion criteria. Major medical complications, e.g., pneumonia, acute kidney injury, and so on, were grouped as "any complication" if a complication was present, these were also summed as "total complications." These data were all entered by each participating center into the AAST data entry website maintained by World Advancement of Technology for EMS and Rescue, Inc.; San Diego, CA. These data were then downloaded from the website by the primary center, Yale School of Medicine, for analysis.

Data Analysis and Reporting

We applied the revised grading scale, as displayed in Figure 2, to the existing patient data to create revised AAST grades for each of the patients. We examined the spread of the AAST grade and the revised AAST grade for distribution across grades and across the various subscales of the grade. For each of the scoring systems, a receiver operating characteristic curve was constructed for each of the outcomes, including any major complication, bile leak, need for open conversion, and utilization of a

Grade	Description	Clinical Criteria*	Imaging Criteria (CT/US/HIDA findings)	Operative Criteria	Pathologic Criteria
I	Acute cholecystitis	Right upper quadrant or epigastric pain/tenderness	Gallbladder distention; gallstones or sludge; pericholecystic fluid; non-visualization of gallbladder (GB) on hepatobiliary iminodiacetic acid (HIDA) scan	Gallbladder with hyperemia or edema	Acute inflammatory changes in the GB wall without necrosis or pus
II	Severe but uncomplicated acute cholecystitis	Murphy's Sign	Gallbladder distention; gallstones or sludge; pericholecystic fluid; non-visualization of gallbladder (GB) on hepatobiliary iminodiacetic acid (HIDA) scan	Any anatomic anomaly (large liver, intrahepatic gallbladder, BMI > 50); severe wall thickening, omental adhesions to body or fundus of gallbladder	Above, plus severely thickened gallbladder wall
III	GB empyema or gangrenous cholecystitis or emphysematous cholecystitis	Localized peritonitis in RUQ	Above, plus ultrasound findings of gallbladder wall thickening 4mm or greater or CBD diameter 8mm or greater. Inflammatory changes on CT or MRI	Gallbladder wall with necrotic areas or purulent fluid in gallbladder.	Above plus purulent fluid in the GB lumen or necrosis of GB wall (<50%) or intramural abscess
IV	Complete GB necrosis or perforation with perichole-cystic abscess	Localized peritonitis in RUQ	Abscess in RUQ outside GB	Complete or near complete necrosis of the gallbladder wall, or contained perforation.	Necrosis of the GB wall (>= 50%)
V	GB perforation with generalized peritonitis or bilio-enteric fistula	Above, with generalized peritonitis	Free gallbladder perforation or bilio-enteric fistula	Perforated gallbladder; bilio-enteric fistula	Necrosis of the GB with non-iatrogenic perforation

*For patients with prior surgery, prior cholecystitis admission, more than 3 days of pain increase the clinical grade by one point. For patients with WBC >= 18,000, or total bilirubin > 1.3 increase the clinical grade by two points.

Figure 1. Revised AAST grading schema.

Grade	Description	Clinical Criteria	Imaging Criteria (CT/US/HIDA findings)	Operative Criteria	Pathologic Criteria
I	Acute cholecystitis	Right upper quadrant (RUQ) or epigastric pain; Murphy's Sign; leukocytosis	Wall thickening; distention; gallstones or sludge; pericholecystic fluid; non-visualization of gallbladder (GB) on hepatobiliary iminodiacetic acid (HIDA) scan	Inflammatory changes localized to GB; wall thickening; distention; gallstones	Acute inflammatory changes in the GB wall without necrosis or pus
II	GB empyema or gangrenous cholecystitis or emphysematous cholecystitis	RUQ or epigastric pain; Murphy's Sign; leukocytosis	Above, plus air in GB lumen, wall or in the biliary tree; focal mucosal defects without frank perforation	Distended GB with pus or hydrops; necrosis or gangrene of wall; not perforated	Above, plus pus in the GB lumen; necrosis of GB wall; intramural abscess; epithelial sloughing; no perforation
III	GB perforation with local contamination	Localized peritonitis in RUQ	HIDA with focal transmural defect, extraluminal fluid collection or radiotracer but limited to RUQ	Perforated GB wall (non-iatrogenic) with bile outside the GB but limited to RUQ	Necrosis with perforation of the GB wall (non-iatrogenic)
IV	GB perforation with pericholecystic abscess or gastrointestinal fistula	Localized peritonitis at multiple locations; abdominal distention with symptoms of bowel obstruction	Abscess in RUQ outside GB; bilio-enteric fistula; gallstone ileus	Pericholecystic abscess; bilio-enteric fistula; gallstone ileus	Necrosis with perforation of the GB wall (non-iatrogenic)
V	GB perforation with generalized peritonitis	Above, with generalized peritonitis	Free intra-peritoneal bile	Above, plus generalized peritonitis	Necrosis with perforation of the GB wall (non-iatrogenic)

Figure 2. Original AAST grading schema.

bail-out procedure. Area under the curve (AUC) was calculated for each receiver operating characteristic curve (ROC), and these were compared across scoring systems. Our prior evaluation of the AAST grade demonstrated better performance for the Parkland grade when this grade was acquired prospectively. Therefore, in addition to the revised AAST grade, we also examined the effect of substituting the Parkland grade for the operative subscale of the AAST grade.

The design of the AAST grades as purely anatomic may impair the predictive power with respect to patient outcomes due to the lack of clinically identifiable differences between more severely and less severely ill patients. We, therefore, also compared the revised AAST grades with the emergency surgery score (ESS) as this is a physiologic score, has only a single point of overlap with AAST grade and has been shown to predict outcomes in cholecystitis, as well as other emergency general surgery diseases.[12] Models were therefore constructed to measure the predictive power of the ESS as well as combining the ESS in models with the AAST grade and Parkland grade to determine the impact of adding more extensive physiologic and comorbidity measurements to the grading scales assessed. The preoperative AAST grade was created as the maximum of the clinical and radiologic subscales of the AAST grade. This grade would be expected to be useful to the surgeon weighing the decision to proceed with surgery or manage a patient with cholecystitis nonoperatively.

The grading scales were compared to each of the outcomes and tests for trend were conducted. We also created logistic regression models for each outcome with a single predictor of each grading scale. A complete case analysis was performed because there were no missing data. We also combined the preoperative AAST grading scales with the ESS in separate models as these data could be applied preoperatively and in patients planned for nonoperative management. For each of these models, discriminatory power was assessed by generating ROCs and calculating AUC for each of these models. The AUCs were then compared using the methods of Delong.[13] All statistical analyses were performed with R: a language and environment for statistical computing v. 4.0.0 (R Foundation for Statistical Computing; Vienna, Austria) installed packages included: lmtest, pROC, ggplot2, arsenal, DescTools, dplyr. The Yale School of Medicine Institutional Review Board and all local institutional review boards approved this study. This article was prepared in accordance with the STROBE guidelines and the completed STROBE checklist is available as a Supplemental digital content, http://links.lww.com/TA/C260.

RESULTS

Score Revision

After three rounds of modification, the grading system was completed based on anatomic variables but also with the addition of laboratory values specific to acute biliary tract disease used to adjust the clinical subscale. After modifications the AAST grading scale (Fig. 2) and the revised AAST grading scale (Fig. 1) differed in several ways. The most significant change was the movement of gallbladder perforation from Grade III to Grade IV or V. A patient was able to have a grade of IV assigned without perforation. Other differences included addition of several laboratory values to the clinical grade but rather than being associated with specific grades these are used to increment the grading scale. The presence of gallstones alone is no longer adequate for an imaging or operative Grade I. However, given the assignment of Grade I to patients with upper abdominal pain this had no impact on the number of patients that could not be graded.

Patients and Distribution Across Grades

The patient population is unchanged from the prior study. There were 861 total patients with a mean age of 51.1 and 62.7% were female. Most patients were admitted from home (94.8%) and 90% were functionally independent. The only comorbidities afflicting more than 10% of the cohort were hypertension (36.4%) and diabetes (21.3%) and 781 (90.7%) were managed

with cholecystectomy. Distributions of patients across AAST grades, the revised AAST grading scale, the Parkland grading scale, and the Tokyo guidelines are displayed in Figure 3. The revised AAST grade more closely mirrors the Tokyo guidelines and Parkland grade with a peak at Grade III and a more even distribution across grades when compared with AAST grade. The distributions of subgrades are displayed in Figure 4. The imaging subscale displays a compact distribution like the original AAST subscale, this is a result of the fact that Grade I by definition rolls up into Grade II. Imaging Grade III no longer requires perforation; however, abscesses outside of the gallbladder are rare leading to no Grade IV cases and Grade V does require imaging evidence of perforation.

Association of Grades With Outcomes and Predictive Capacity

When assessing outcomes compared against the various grading scales (Table 2), most of the grading scales demonstrated worse outcomes at the higher grades and demonstrated statistically significant trends toward worse outcomes at the higher grades. The revised AAST grade had improved distribution of complications across all grades, and this remained statistically significant. The small number of deaths resulted in highly variable predictive capacity for the various grading systems. The preoperative AAST grade or the grade with the operative and pathologic characteristics removed did not demonstrate a trend of higher grades being associated with increased risk of leak. Conversely, a near linear trend toward an increased risk of bail-out procedures and conversion to open was identified with increasing grade in both the revised AAST grade and the revised AAST preoperative grade. These trends were also more linear than the Tokyo guidelines and more spread across all grades when compared with the Parkland grade. Areas under the ROCs are presented in Table 3. Despite the spread across the grading scale, none of the scoring systems performed optimally for predicting complications. The revised AAST, however, did improve the AUC of the ESS, slightly suggesting a small benefit to adding the anatomic values. The revised AAST grade and the revised AAST preoperative grade had reasonable predictive capacity and were improved compared with the AAST grade with respect to predicting a bail-out procedure, conversion to open, and discharge home. Ability to predict complications was the same, and prediction of mortality was lower, although not statistically different. The ESS performed as good or better than the revised AAST grade suggesting the importance of physiologic parameters and chronic health conditions in determining outcomes. Adding the physiologic ESS and the anatomic revised AAST overall resulted in improved predictive capacity of the scores that approached the capacity of the Parkland grade. Substituting the Parkland grade for the operative grade within the AAST grade did not improve the predictive capacity of the AAST grade.

DISCUSSION

After a thorough revision of the AAST cholecystitis grading scale, there are many improved attributes to the revised scale. The revised AAST grade demonstrated both a more uniform and

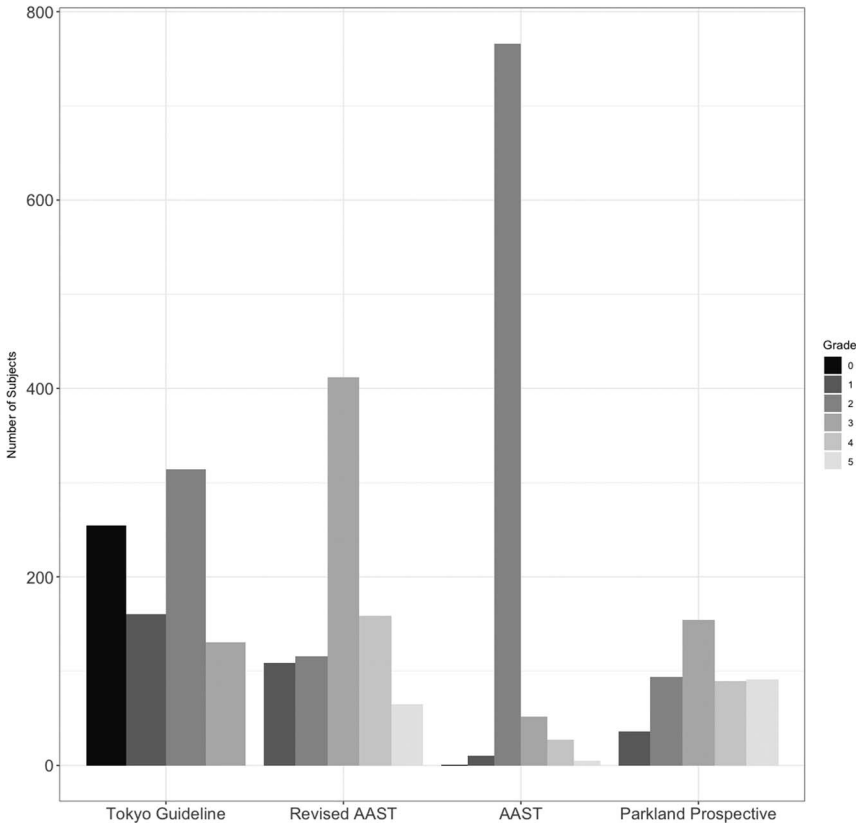

Figure 3. Grading scale distributions.

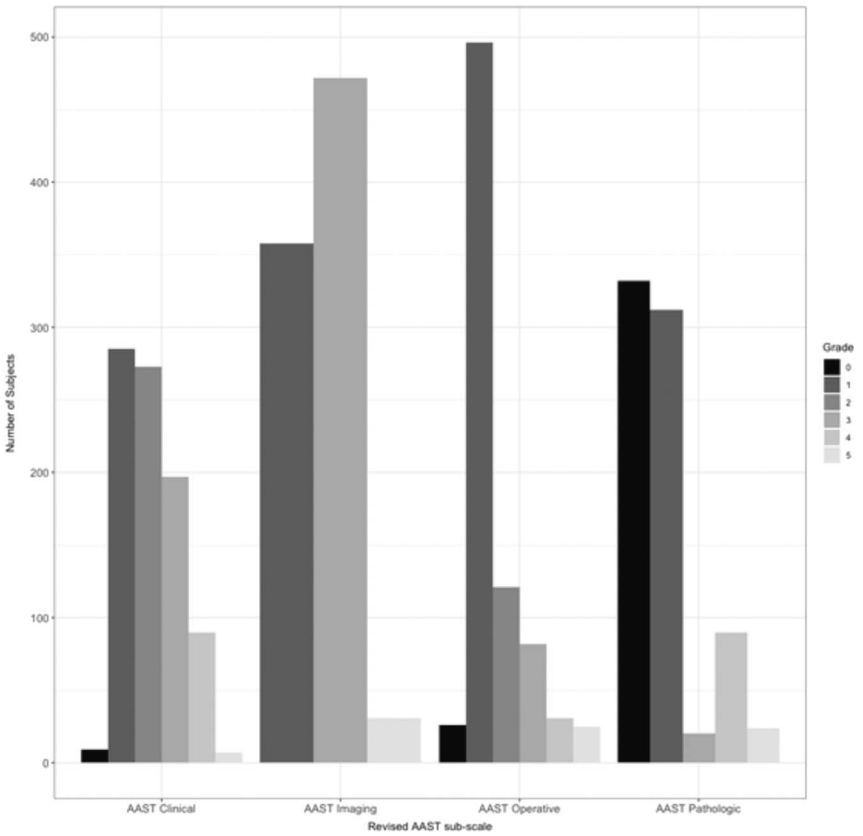

Figure 4. Revised AAST grading subscale distributions.

normal distribution across grades when compared with the original AAST grade. This more normal distribution was notable for both the overall score and the subscales within the AAST grade. This spread across grades translated into a near linear increase in risk of multiple negative outcomes as the grade increased. This was a primary goal of the revision effort and is an essential feature of any grading scale that would be expected to have predictive power. We further demonstrated that this translated into a small improvement in the predictive capacity of the score across multiple outcomes, including discharge home, conversion from laparoscopic cholecystectomy to open, need for a bail-out procedure. The predictive improvements were statistically significant for bail-out procedures, conversion to open and discharge home. Furthermore, these characteristics of the grading system carried over to the preoperatively available components of the grade, namely, a grading system composed of the clinical and imaging characteristics. Despite these improvements the revised AAST grade did not reach the performance characteristics of the Parkland grade. The Parkland grade remains as the overall best grading system across multiple outcomes. This likely reflects the prospective data collection of operative characteristics, a significant downside to this scoring system as surgeons would need to prospectively document a data point with each case. This grading approach also suffers from its partially subjective nature, and this may contribute to its improved performance. The strength of the Parkland grade relative to all other scoring systems suggests two things, first direct visual inspection of the gallbladder is more predictive than other combined measures of cholecystitis and secondarily degree of surgical difficulty has a significant impact on patient outcomes. It is uncertain if this degree of difficulty leads to increased operative trauma leading to poorer patient outcomes or if these patients would have a similar outcome distribution without surgical intervention. Regardless of the underlying mechanism the correlation between clinical and radiographic findings with those findings that increase the Parkland grade is poor. This is similarly true for the ESS where much of the score is composed of underlying medical comorbidity which, not surprisingly, does not correlate with gall bladder specific clinical and radiographic findings. Therefore, these clinical and radiographic findings are less predictive than the Parkland grade or the underlying health status of the patient.

The ideal grading system for cholecystitis will have several characteristics. Most importantly, it will predict overall patient outcome including mortality, complications, length of illness, length of hospitalization, and discharge disposition. Secondarily, it will provide surgeons with a tool to predict the need to convert to an open operation or use a bail-out surgical technique. The ability to predict this outcome is useful to both patients and surgeons as they choose cholecystectomy, percutaneous cholecystostomy, or noninterventional management of their cholecystitis. Once an ideal grading scale is implemented, it will be necessary to study it in a prospective fashion to determine if patient outcomes can be improved by using it in decision making. To date, no grading scale has been demonstrated to improve outcomes when used to guide care. This is despite the publication of at least 19 scoring systems to predict outcomes in acute cholecystitis.[14] The two

TABLE 2. Patient Outcomes Relative to Each of the Grading Scales

	AAST Revised	Revised AAST Preoperative	AAST	Tokyo Guidelines	Parkland Retrospective	Parkland Prospective
Complication, n (%)	1–7 (6.4)	1–10 (6.8)	0–1 (0)	0–21 (8.2)	1–1 (14.3)	1–0
	2–8 (6.9)	2–9 (7.9)	1–10 (0)	1–9 (5.6)	2–8 (12.5))	2–3 (3.2)
	3–34 (8.3)	3–43 (9.0)	2–61 (8.0)	2–29 (9.2)	3–12 (8.2)	3–4 (2.6)
	4–19 (11.9)	4–11 (13.1)	3–12 (23.1)	3–20 (15.3)	4–5 (12.8)	4–12 (13.5)
	5–11 (16.9)	5–6 (16.2)	4–6 (22.2)		5–4 (7.1)	5–12 (13.2)
			5–5 (0)			
	$p = 0.010$	$p = 0.044$	$p < 0.001$	$p = 0.035$	$p = 0.458$	$p < 0.001$
Death, n (%)	1–1 (0.9)	1–1 (0.7)	0–0	0–0	1–0	1–0
	2–0	2–0	1–0	1–1 (0.6)	2–1 (1.6)	2–0
	3–4 (1.0)	3–4 (0.8)	2–4 (0.5)	2–1 (0.3)	3–1 (0.7)	3–1 (0.6)
	4–1 (0.6)	4–1 (1.2)	3–0	3–4 (3.1)	4–0	4–0
	5–0	5–0	4–2 (7.4)		5–0	5–0
			5–0			
	$p = 0.791$	$p = 0.757$	$p = 0.003$	$p = 0.007$	$p = 0.824$	$p = 0.733$
Bile leak, n (%)	1–0	1–0	0–0	0–7 (2.9)	1–1 (1.4)	1–0
	2–2 (1.7)	2–5 (4.4)	1–0	1–1 (0.7)	2–0	2–0
	3–6 (1.5)	3–10 (2.1)	2–12 (1.7)	2 = 9 (3.1)	3–2 (1.4)	3–1 (0.6)
	4–5 (3.1)	4–1 (1.2)	3–5 (11.6)	3–1 (1.0)	4–2 (5.1)	4–5 (5.6)
	5–5 (7.7)	5–2 (5.4)	4–1 (4.3)		5–2 (3.6)	5–5 (5.5)
			5–0			
	$p = 0.007$	$p = 0.210$	$p = 0.007$	$p = 0.660$	$p = 0.192$	$p = 0.007$
Mean operating room time (min)	1–101	1 = 111	0–40	0–103	1–115	1–90.9
	2–119	2–110	1–86	1–123	2–88.2	2–78.3
	3–111	3–114	2–113	2–117	3–109	3–108
	4–126	4–134	3–146	3–127	4–144	4–165
	5–138	5–135	4–141		5–126	5–137
			5–121			
Bail-out procedure, n (%)	1–0	1–0	0–0	0–4 (1.6)	1–0	1–0
	2–2 (1.7)	2–2 (1.8)	1–0	1–3 (1.9)	2–0	2–0
	3–10 (2.4)	3–17 (3.6)	2–18 (2.3)	2–14 (4.5)	3–1 (0.7)	3–4 (2.6)
	4–6 (3.8)	4–3 (3.6)	3–4 (7.7)	3–5 (3.8)	4–1 (2.6)	4–8 (9.0)
	5–8 (12.3)	5–4 (10.8)	4–3 (11.1)		5–1 (1.8)	5–11 (12.1)
			5–1 (20.0)			
	$p < 0.001$	$p < 0.001$	$p < 0.001$	$p = 0.027$	$p = 0.028$	$p < 0.001$
Laparoscopic procedure converted to open, n (%)	1–1 (1.0)	1–2 (1.4)	0–0	0–8 (3.3)	1–0	1–0
	2–4 (3.5)	2–3 (2.7)	1–0	1–4 (2.7)	2–0	2–0
	3–17 (4.7)	3–27 (6.3)	2–31 (4.5)	2–20 (7.1)	3–5 (3.5)	3–0
	4–9 (6.5)	4–7 (10.6)	3–7 (18.4)	3–10 (10.4)	4–6 (16.7)	4–9 (10.1)
	5–11 (22.9)	5–3 (13.6)	4–3 (14.3)		5–8 (16.0)	5–14 (15.6)
			5–1 (50.0)			
	$p < 0.001$	$p < 0.001$	$p < 0.001$	$p = 0.002$	$p < 0.001$	$p < 0.001$

All data reported as n (%) unless otherwise noted. *p* Values based on Cochran-Armitage test for trend (one-sided, increasing).

TABLE 3. AUC Values of the Logistic Regression Models for Each of the Listed Outcomes

	AAST	Revised AAST	Revised AAST Preoperative	ESS	Revised AAST Preoperative/ ESS	Revised AAST/ESS	Revised AAST/Parkland	Parkland	Tokyo	AAST vs. Revised AAST (p)
Complications	0.599	0.582	0.561	0.670	0.670	0.675	0.601	0.720	0.568	0.986
Mortality	0.679	0.517	0.554	0.910	0.926	0.938	0.547	0.835	0.794	0.260
Bail-out procedure	0.579	0.705	0.668	0.583	0.678	0.721	0.768	0.769	0.524	0.018
Conversion to open	0.603	0.676	0.645	0.707	0.729	0.724	0.721	0.844	0.628	0.020
Bile leak	0.632	0.643	0.508	0.506	0.558	0.668	0.776	0.781	0.524	0.691
Discharge home	0.573	0.644	0.680	0.902	0.904	0.903	0.552	0.675	0.657	0.031

grading scales based on intraoperative findings have demonstrated excellent predictive capacity.[15–17] These scoring system suffer from the requirement for surgery to be applied and the above discussed need for surgeon documentation and subjectivity. Scoring systems that can be applied preoperatively have the advantage of potentially predicting outcomes and therefore can influence patient management decisions to achieve the best outcomes. Many of the grading systems, including the original and revised AAST grade, have demonstrated good capacity for predicting outcomes. These grading scales range from simple to complex however most include both anatomic, physiologic and comorbidity variables.[8,9,18] The advantage of the AAST grade is its predictive capacity while relying on only minimal physiologic criteria and no comorbidity data. It also uses only objective data points that can be easily abstracted from an electronic record with respect to the clinical and imaging domains. We have further demonstrated the potential for the AAST grade to be combined with a system focused on physiology, the ESS, to augment the predictive capacity.

All scoring systems have weaknesses, including the diagnosis of cholecystitis. The Tokyo guidelines require patients to have at least Grade I disease to be diagnosed with cholecystitis; however, the World Society of Emergency Surgery guidelines recommended against using any specific criteria and some authors have demonstrated cholecystitis to be present without achieving criteria based on the Tokyo guidelines.[3,19,20] For our study, we, therefore, chose to use surgeon diagnosis as the entry criteria. Outcomes will also be related to various patient management decisions, further complicating the validation of scoring systems. The revised Tokyo guideline is less restrictive; however, both the original and revised guideline recommended against surgery for many high-grade patients. Despite these recommendations, successful surgical treatment of high-grade patients has been demonstrated.[20,21] Other studies have demonstrated compliance with the Tokyo guidelines leads to the most cost-effective care.[22] Future studies validating grading systems should, therefore, stratify groups by treatment strategy. Given the high degree of success demonstrated by surgical management this will require focused effort to recruit patients at high risk for surgical intervention and managed without intervention or with percutaneous cholecystostomy. A single grading system or combination of systems that includes anatomic, physiologic, and comorbidity variables, as identified in our data, will likely provide the best predictive capacity. Further validation of this revised AAST grading system will be important to optimize this anatomic grading scale. Future studies should also use the revised AAST grade in a prospective fashion to dictate care decisions and determine impact on outcomes. Potential future additions to grading scale continue to be investigated and developed, including procalcitonin, leukocyte ratios, and leukocyte to albumin ratio among others.[23,24] These have all shown promise as markers for higher degrees of illness in cholecystitis; however, they have mostly been compared with existing grading scales rather than outcomes.

Limitations

Our study is a necessary step forward in the development of grading scales for acute cholecystitis. It examines several potential additions to the AAST grade and further examines predictive capacity. There are, however, important limitations that require discussion. Most importantly, we used the available data as an adjunct to revision of the AAST grade. Although the grade was modified mostly through expert input and a modified Delphi approach, the experts were provided with data that contained associations of some potential grade components with patient outcomes. Other limitations included potential missing factors included in other grading systems and potentially should be added going forward including prior abdominal surgery or possibly inflammatory markers other than leukocytosis. Patients were identified prospectively; however, the mechanism of identification varied across centers based on locally effective procedures, which had the potential to create a less than representative sample. The data were also collected retrospectively except for the Parkland grade. This creates all the potential inaccuracies associated with retrospective data collection. We reduced the risk associated with retrospective data capture by collecting very granular data, where applicable, that would be both available and quantitative. Operative grading for all scoring systems will have some inherent inaccuracy due to human failures to report or biases.

CONCLUSIONS

The revised AAST grading system as we developed is an improvement over the original system. Persistent downsides remain mostly related to the fact that the AAST grade is primarily an anatomic grading scale. These limitations can be strongly mitigated with the addition of physiologic data to the grading scale. The revised grade will require a new validation study if implementation is to be considered. Impact studies that use the revised AAST grade for clinical decision making should also be performed to demonstrate its value.

AUTHORSHIP

K.M.S. participated in the study conception, study design, data acquisition, data interpretation, article drafting, final revisions. R.O. participated in the data acquisition, data interpretation, article drafting, final revisions. M.Cripps participated in the study conception, study design, data acquisition, final revisions. K.Kuhlenschmidt participated in the data acquisition, final revisions. L.T. participated in the data acquisition, final revisions. H.M.K. participated in the study conception, study design, data acquisition, final revisions. M.H. participated in the data acquisition, final revisions. R.P. participated in the data acquisition, final revisions. T.J.S. participated in the data acquisition, final revisions. T.M.E. participated in the data acquisition, final revisions. D.C.C. participated in the data acquisition, final revisions. L.M.C. participated in the data acquisition, final revisions. S.A. participated in the data interpretation, final revisions. K.Kaups participated in the data interpretation, final revisions. M.Crandall participated in the data acquisition, final revisions. G.T. participated in the study conception, study design, data acquisition, data interpretation, final revisions.

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DISCLOSURE

The authors declare no conflicts of interest.

REFERENCES

1. Wadhwa V, Jobanputra Y, Garg SK, Patwardhan S, Mehta D, Sanaka MR. Nationwide trends of hospital admissions for acute cholecystitis in the United States. *Gastroenterol Rep (Oxf)*. 2017;5:36–42.

2. González-Castillo AM, Sancho-Insenser J, De Miguel-Palacio M, Morera-Casaponsa JR, Membrilla-Fernández E, Pons-Fragero MJ, Pera-Román M, Grande-Posa L. Mortality risk estimation in acute calculous cholecystitis: beyond the Tokyo guidelines. *World J Emerg Surg*. 2021;16:24.
3. Pisano M, Allievi N, Gurusamy K, Borzellino G, Cimbanassi S, Boerna D, Coccolini F, Tufo A, Di Martino M, Leung J, et al. 2020 World Society of Emergency Surgery updated guidelines for the diagnosis and treatment of acute calculus cholecystitis. *World J Emerg Surg*. 2020;15:61.
4. Huntington CR, Cox TC, Blair LJ, Prasad T, Lincourt AE, Heniford BT, Augenstein VA. Nationwide variation in outcomes and cost of laparoscopic procedures. *Surg Endosc*. 2016;30:934–946.
5. Tufo A, Pisano M, Ansaloni L, de Reuver P, van Laarhoven K, Davidson B, Gurusamy KS. Risk prediction in acute calculous cholecystitis: a systematic review and meta-analysis of prognostic factors and predictive models. *J Laparoendosc Adv Surg Tech A*. 2021;31:41–53.
6. Schmidt M, Søndenaa K, Vetrhus M, Berhane T, Eide GE. Long-term follow-up of a randomized controlled trial of observation versus surgery for acute cholecystitis: non-operative management is an option in some patients. *Scand J Gastroenterol*. 2011;46:1257–1262.
7. Loozen CS, van Santvoort HC, van Duijvendijk P, Besselink MG, Gouma DJ, Nieuwenhuijzen GA, Kelder JC, Donkervoort SC, van Geloven AA, Kruyt PM, et al. Laparoscopic cholecystectomy versus percutaneous catheter drainage for acute cholecystitis in high risk patients (CHOCOLATE): multicentre randomised clinical trial. *BMJ*. 2018;363:k3965.
8. Schuster KM, O'Connor R, Cripps M, Kuhlenschmidt K, Taveras L, Kaafarani HM, El Hechi M, Puri R, Mull J, Schroeppel TJ, Rodriquez J, Cullinane DC, Cullinane LM, Enniss TM, Sensenig R, Zilberman B, Crandall M, Schuster KM, O'Connor R, Cripps M, Kuhlenschmidt K, Taveras L, Kaafarani HM, El Hechi M, Puri R, Mull J, Schroeppel TJ, et al. Multicenter validation of the American Association for the Surgery of Trauma grading scale for acute cholecystitis. *J Trauma Acute Care Surg*. 2021;90:87–96.
9. Yokoe M, Hata J, Takada T, Strasberg SM, Asbun HJ, Wakabayashi G, Kozaka K, Endo I, Deziel DJ, Miura F, et al. Tokyo guidelines 2018: diagnostic criteria and severity grading of acute cholecystitis (with videos). *J Hepatobiliary Pancreat Sci*. 2018;25:41–54.
10. Tominaga GT, Staudenmayer KL, Shafi S, Schuster KM, Savage SA, Ross S, Muskat P, Mowery NT, Miller P, Inaba K, et al, American Association for the Surgery of Trauma Committee on Patient Assessment. The American Association for the Surgery of Trauma grading scale for 16 emergency general surgery conditions: disease-specific criteria characterizing anatomic severity grading. *J Trauma Acute Care Surg*. 2016;81(3):593–602.
11. Vera K, Pei KY, Schuster KM, Davis KA. Validation of a new American Association for the Surgery of Trauma (AAST) anatomic severity grading system for acute cholecystitis. *J Trauma Acute Care Surg*. 2018;84:650–654.
12. Gaitanidis A, Breen K, Naar L, Mikdad S, El Moheb M, Kongkaewpaisan N, El Hechi M, Kaafarani HMA. Performance of the emergency surgery score (ESS) across different emergency general surgery procedures. *J Surg Res*. 2021;261:152–158.
13. Zhang Y, Tang N. Confidence intervals of the difference between areas under two ROC curves in matched-pair experiments. *Stat Med*. 2020;39:2621–2638.
14. Sugrue M, Sahebally SM, Ansaloni L, Zielinski MD. Grading operative findings at laparoscopic cholecystectomy—a new scoring system. *World J Emerg Surg*. 2015;10:14.
15. Sugrue M, Coccolini F, Bucholc M, Johnston A, Contributors from WSES. Intra-operative gallbladder scoring predicts conversion of laparoscopic to open cholecystectomy: a WSES prospective collaborative study. *World J Emerg Surg*. 2019;14:12.
16. Lee W, Jang JY, Cho JK, Hong SC, Jeong CY. Does surgical difficulty relate to severity of acute cholecystitis? Validation of the parkland grading scale based on intraoperative findings. *Am J Surg*. 2020;219:637–641.
17. Madni TD, Nakonezny PA, Barrios E, Imran JB, Clark AT, Taveras L, Cunningham HB, Christie A, Eastman AL, Minshall CT, et al. Prospective validation of the Parkland Grading Scale for cholecystitis. *Am J Surg*. 2019;217(1):90–97.
18. Di Martino M, Mora-Guzmán I, Jodra VV, Dehesa AS, García DM, Ruiz RC, Nisa FG, Moreno FM, Batanero SA, Sampedro JEQ. How to predict postoperative complications after early laparoscopic cholecystectomy for acute Cholecystitis: the Chole-risk score. *J Gastrointest Surg*. 2021;25:2814–2822.
19. Yokoe M, Takada T, Strasberg SM, Solomkin JS, Mayumi T, Gomi H, Pitt HA, Garden OJ, Kiriyama S, Hata J, et al. TG13 diagnostic criteria and severity grading of acute cholecystitis (with videos). *J Hepatobiliary Pancreat Sci*. 2013;20(1):35–46.
20. Joseph B, Jehan F, Dacey M, Kulvatunyou N, Khan M, Zeeshan M, Gries L, O'Keeffe T, Riall TS. Evaluating the relevance of the 2013 Tokyo Guidelines for the diagnosis and management of cholecystitis. *J Am Coll Surg*. 2018;227:38–43.e1.
21. Takahashi N, Umemura A, Suto T, Fujiwara H, Ariyoshi Y, Nitta H, Takahara T, Hasegawa Y, Sasaki A. Aggressive laparoscopic cholecystectomy in accordance with the Tokyo guideline 2018. *JSLS*. 2021;25(1):e2020.00116.
22. Lin YN, Wu YT, Fu CY, Liao CH, Cheng CT, Wang SY, Lin BC, Hsu YP, Kang SC, Liu EH. Evaluating the advantages of treating acute cholecystitis by following the Tokyo Guidelines 2018 (TG18): a study emphasizing clinical outcomes and medical expenditures. *Surg Endosc*. 2021;6623–6632.
23. Fransvea P, Covino M, Rosa F, Puccioni C, Quero G, Cozza V, La Greca A, Franceschi F, Alfieri S, Sganga G. Role of serum procalcitonin in predicting the surgical outcomes of acute calculous cholecystitis. *Langenbeck's Arch Surg*. 2021;406:2375–2382.
24. Sato N, Kinoshita A, Imai N, Akasu T, Yokota T, Iwaku A, Koike K, Saruta M. Inflammation-based prognostic scores predict disease severity in patients with acute cholecystitis. *Eur J Gastroenterol Hepatol*. 2018;30:484–489.

DISCUSSION

NICOLE A. STASSEN, M.D. (Rochester, New York): Drs. Savage, Bulger, members and guests. Dr. Schuster and his colleagues should be lauded for their continued efforts in helping us refine the AAST cholecystectomy grading scale. The work is elegantly done. But I do have some questions.

So in your manuscript you stated that the AAST revised grading scale didn't reach the performance characteristics of the Parkland Grade. Why do you think that is?

Also, why do you think a reliable and reproducible grading scale to guide our care in cholecystitis is so difficult to produce?

The other thing you mentioned in your manuscript was that in order for patients to be included in your data set this grading criteria was surgeon diagnosis. Why utilize that rather than a more objective criteria?

And then what are your next steps? What should we all take home from this? As Dr. Richardson used to tell me, "So what?" So what do I do with this?

So I'd like to thank the AAST for the privilege of discuss this work and really, again, commend Dr. Schuster and his coauthors in continuing to deal with this vexing problem.

KEVIN M. SCHUSTER, M.D., M.P.H., F.A.C.S. (New Haven, Connecticut): Thank you, Dr. Stassen for the discussion. In terms of why the Parkland Grade works better, I think there are two issues with the Parkland Grade. One is you get a lot more information when you are in the operating room and you actually get to see the gallbladder.

The other contributing factor I believe is that the prospective grade is assigned by the surgeon and I think it's impossible to separate our biases when we see the gallbladder. Even if it doesn't quite make the criteria for a particular Parkland grade we have the tendency to say, "Oh, that's a really terrible gallbladder" and err on the side of a higher grade.

Similarly this is the reason we chose to look at granular data across the whole study because it takes out that subjective part, an investigator could not think, "I think this is a Grade 1", once they read the whole chart and see everything about

the patient. Assigning a Grade of 1 but really it's a Grade 2. And so I think that's partly why the Parkland works well, it allows for some subjectivity and biased adjustment by the surgeon.

I think the other part of it, the downside of the Parkland, is that you have to operate to get a Parkland Grade. So I think that extra subjectivity works well but, there are issues with using a grading system that requires an operation for application.

Why is it hard to grade acute cholecystitis? I think the reality is the vast majority of patients do well. Almost everybody survives, there are very few complications relative to other diseases so that's probably the biggest challenge is that despite even some of the so-called "sicker" gallbladders, if you will, everybody still does relatively well. A grading scale must be able to pick out those very few patients that do not do well, which is challenging.

Why did we choose to use a surgeon diagnosis? I think, we all know this from experience in that we see the patients that don't meet criteria based on their imaging or their clinical criteria, necessarily, but you have a suspicion that they have cholecystitis and you go to the operating room and they have a gallbladder that grades 2 or 3 on the Parkland Scale. And so I think we all see those patients and so that's why we chose surgeon diagnosis. I know the Tokyo Guidelines do have a diagnostic criteria but we felt that they were too narrow in terms of the patients that would get enrolled and we would miss a lot of patients with cholecystitis. Conversely, if patients did not have cholecystitis they would be graded in the study with a grade of zero and not impact the findings.

And finally, where do we go from here? Well, I think we have to keep working and keep making sure we make it better, to make it as best we can. I think that marrying the grading system with a physiologic scoring system is important and it will be necessary because I think that provides a lot of the predictive capacity.

We do need to be able to grade these patients and understand who is likely to do well and who is likely to not do as well for multiple reasons, one, because we have to treat the patients that we are seeing in the emergency department or on the floor but, also, because we have to answer to insurers and others that are grading our quality and they have to understand whether it was a difficult case and how to risk-adjust for these issues.

With that I will close. Thank you for your time.