January 2018

Validation Of A New Anatomic Severity Grading System For Acute Cholecystitis

Kenneth Vera

Follow this and additional works at: https://elischolar.library.yale.edu/ymtdl

Recommended Citation
Validation of a New Anatomic Severity Grading System for Acute Cholecystitis

A Thesis Submitted to the
Yale University School of Medicine
in Partial Fulfillment of the Requirements for the
Degree of Doctor of Medicine

by
Kenneth Vera

2018
ABSTRACT

VALIDATION OF A NEW ANATOMIC SEVERITY GRADING SYSTEM FOR ACUTE CHOLECYSTITIS.

Kenneth Vera B.S. and Kevin Y. Pei M.D. Section of General Surgery, Trauma, and Surgical Critical Care, Department of Surgery, Yale University School of Medicine, New Haven, CT.

The American Association for the Surgery of Trauma (AAST) established anatomic grading in 2015 to facilitate risk stratification and risk adjusted outcomes in emergency general surgery. This study validates the AAST anatomic grading system for acute cholecystitis (AC) at a tertiary, academic referral medical center.

This is a retrospective cohort study of 315 patients admitted for AC between 2013 and 2016. Cholecystitis severity was graded based on clinical, imaging, operative, and pathologic criteria in accordance with the published AAST anatomic grading scale. Grade I is acute cholecystitis, grade II is gangrenous or emphysematous cholecystitis, grade III is localized perforation, grade IV and V have regional and systemic peritonitis respectively. There was very good interrater (2 independent raters) reliability for anatomic grading, \( \kappa = 1.00, p<0.005 \).

Concordance between the AAST grade and outcomes including mortality, length of stay (LOS), ICU use, and adverse events was assessed using statistical methods. Incidence of complications, LOS, ICU use, and any adverse event increased with increasing anatomic grade. When compared to grade I disease, patients with grade II were more likely to undergo cholecystectomy (Odds Ratio 4.07 [1.93-8.56]), require ICU use (Odds Ratio 2.41 [1.31 – 4.44]) and develop a complication (Odds Ratio 2.07 [1.22 –
3.53). Grade III patients were at higher risk of adverse events (Odds Ratio 3.83 [1.34-10.94]) and ICU use (Odds Ratio 8.07 [2.43-26.80]).

In conclusion, AAST severity grading scores were independently associated with clinical outcomes in patients with AC. Despite most patients having low grade disease, complications were common. Therefore, a refinement of the scoring system for cholecystitis may be necessary for more granular prediction of outcomes at milder levels of disease.
ACKNOWLEDGEMENTS

I would like to thank Kevin Y. Pei for his support, mentorship, teaching and guidance over the course of this project. I would also like to thank the Yale General Surgery, Trauma and Surgical Critical Care section leaders Kevin Schuster and Kimberly Davis for their support as well as contributions in preparing our manuscript. I would like to thank the New England Surgical Society for allowing me the opportunity to present the findings in this thesis at their 2017 meeting. I would also like to thank the editors at *Journal of Trauma and Acute Care Surgery* for accepting a manuscript of this thesis for publication.
TABLE OF CONTENTS

Abstract ......................................................................................................................... ii
Acknowledgements ....................................................................................................... iv
Table of Contents .......................................................................................................... 1
Introduction .................................................................................................................... 2
  The AAST Scoring System ....................................................................................... 2
  Validation of the AAST Scoring System ................................................................. 4
  Introduction to Cholecystitis .................................................................................... 7
  Diagnosis of Cholecystitis ....................................................................................... 10
  Complications of Cholecystitis .............................................................................. 11
  Management of Cholecystitis ................................................................................ 12
  Statement of Purpose and Hypothesis .................................................................... 15
Methods ........................................................................................................................ 17
  Inclusion Criteria ..................................................................................................... 17
  Data Collection ........................................................................................................ 18
  AAST Grading .......................................................................................................... 20
  Statistical Analysis ................................................................................................. 21
Results ........................................................................................................................... 23
Discussion ..................................................................................................................... 29
  Imaging Scores for AAST Grade .......................................................................... 32
  Refining the AAST Scale ....................................................................................... 33
  Limitations .............................................................................................................. 34
  Future Directions ................................................................................................... 34
Conclusions .................................................................................................................. 37
References ..................................................................................................................... 38
INTRODUCTION

Surgeons routinely care for patients with acute cholecystitis (AC). The prevalence of gallstones is approximately 10-20% of US adult population and a third will develop cholecystitis. Laparoscopic cholecystectomy (LC) is one of the most common surgical procedures, but complexity and outcomes of surgery depend on disease severity. To that extent, the American Association for the Surgery of Trauma (AAST) introduced an anatomic severity grading system for emergency general surgery (EGS) diseases in 2014 (1). This objective and uniform system for quantifying anatomic severity has been proposed for use in research as well as clinical settings. Such a system facilitates standardized communication of severity in patient management, quality studies, outcome comparisons, and provider to provider discussion. The AAST anatomic severity grading system has yet to be validated to patient outcomes for many EGS diseases. The purpose of this investigation was to validate the system for a cohort of patients admitted to Yale-New Haven Hospital with AC.

The AAST Scoring System

The AAST anatomic severity grading system is based on the Organ Injury Scale (OIS) developed in the 1990’s by a designated committee within the AAST. The committee was charged with developing a set of standardized grading scales from 1-5 for traumatic injuries to internal organs based on their anatomic description. These organ-specific scales were formed from expert opinion and subsequently proposed for use in clinical research (2) and have since been validated in numerous studies following their introduction. The AAST scoring system was designed in a similar fashion in 2015. A literature review of all existing scoring systems for individual EGS diseases was
performed and a uniform grading system that can be applied to all EGS diseases was then agreed upon by expert consensus (1).

As of 2016, emergency general surgery care accounts for approximately 7% of all hospitalizations in the US. The national average cost of a hospitalization and operation for an EGS disease is $10,744 with the total number of EGS hospitalizations in the US costing over 28 billion dollars annually. These figures are projected to increase by 45% by 2060 (3). Standardization of disease severity affords the opportunity to compare outcomes from various general surgical procedures across different medical centers in the US when adjusted for comorbid conditions and disease complexity. The need for standardized assessment is particularly critical in the current era of outcome-based practice in many facets of medicine. Incorporating a uniform system for describing disease into the field of emergency general surgery may ultimately lead to improved outcomes and quality of care.

Criteria-based scoring systems have previously been developed for medical and surgical diseases including those in EGS. One notable example is the Hinchey score, a radiographic severity grading system, for diverticulitis. The very first such scale for cholecystitis was published by a group from Tokyo in 2007 and most recently revised in 2018 (4). Although these and other scales are used across the world for a range of clinical and research purposes, the AAST scale is the first to have been designed specifically for use in the field of emergency general surgery.

The AAST advocates its grading system’s wide spectrum of disease severity, its ease of use, and intuitive application. The grading system is designed to be uniformly applied across a diverse range of EGS diseases. Furthermore, it only incorporates
anatomical data into the grading scale and excludes physiological parameters or patient comorbidities (1). As the physiological severity of a disease is more often secondary to its anatomic severity, an anatomically focused grading system is better utilized when evaluating patient outcomes due to a primary disease process. This is a potential benefit of AAST over existing grading systems such as the Tokyo system.

The AAST severity scores were not only adopted from the OIS but were also based on the TNM system used for staging various types of cancers (1). Both TNM and AAST incorporate gradients from local to wide spread of disease in the range of their grading. AAST grades I and II are both limited to the organ and are associated with mild or severe abnormality, respectively. Grades III-V represent anatomical progression from localized to regional to widespread disease (5). The grading is also consistent with respect to the progression from modest to severe inflammation. The range of this scale encompasses almost the entire severity spectrum of any EGS disease. Subsequent studies validating the scale have adopted a score of 0 for “normal” findings described in pathology or imaging on retrospective review.

Validation of the AAST Scoring System

The AAST scoring system uses clinical, imaging, operative, and pathological data to grade the anatomic severity of disease on a scale from 1-5, with 5 being the most severe. In their most recent report, the AAST provides how the scale can be applied to individual EGS diseases with 16 diseases described (6). The AAST has advocated for validation studies using this system to assess its level of applicability to EGS diseases and the outcomes of patients diagnosed with and admitted for management of the disease. To date, there have been a handful of validation studies in diseases such as diverticulitis and
small bowel obstruction. These studies include both single and multi-center retrospective studies.

One of the first published studies validating the AAST scale for EGS diseases was published in 2015 (7). The study aimed to investigate the association between AAST score and patient outcomes in a retrospective cohort of 512 patients admitted with acute colonic diverticulitis at a single center. The AAST grades for colonic diverticulitis were independently associated with adverse outcomes after controlling for patient co-morbidities. Furthermore, there were no systemic differences in grade assignment between two graders. A multicenter study including a cohort of 1,105 patients with diverticulitis from 13 centers was subsequently published by the same investigative group and again demonstrated an association of disease grade with adverse outcomes and a high level of interrater reliability (8).

A recent report validated the AAST anatomic severity grading scale for appendicitis in a population of 334 patients at a single center (9). Their study showed a significant correlation between severity score and complications including length of stay (LOS) as well as conversion from a laparoscopic to open operation. Within their cohort, 11.8% of patients with AAST grade 0-2 disease developed a complication versus 54.2% of patients with grade III-V disease. This was the first report validating the AAST scoring system for predicting any outcome in appendicitis. In a single-center retrospective review of 1,099 appendectomies including at least 40 cases from each AAST severity grade, the AAST was validated to predict symptom duration, appendectomy duration, as well as cost of care (10).
Baghdadi et al published the first report validating the AAST for small bowel obstruction (11). They studied a retrospective cohort of 351 patients with partial or complete small bowel obstruction using both the original AAST scoring system and a modified version of the AAST system incorporating patient physiology and comorbidities using SIRS criteria and Charlson comorbid scores. The authors argue that physiology is an inherent part of disease, particularly in the management of patients with small bowel obstruction, and therefore should be primarily incorporated into disease assessment.

Both the AAST and modified scores showed significant associations between greater disease severity and greater inpatient complications and extended LOS. However, neither was superior in predicting these endpoints. Despite a low mortality rate in their cohort, their modified score better predicted mortality than AAST.

The Tokyo Guidelines (TG) for cholecystitis incorporates anatomical findings as well as multiple physiological parameters into its approach to diagnosis and severity assessment. As described in their 2018 revision, grade I or “mild” disease is classified as cholecystitis in a healthy patient who has no findings of organ dysfunction. Grade II or “moderate” disease is characterized as having marked inflammation of the gallbladder. Criteria for grade II disease include elevated white blood cell count, a tender and palpable right upper quadrant mass, and duration of disease for 72 hours or more. Grade III (“severe”) disease is moderate severity accompanied by evidence of organ dysfunction (4).

The TG has been studied in multiple retrospective cohorts and revised to correct limitations to its validation. Furthermore, it has evolved from a tool used in research to a guideline for management and clinical judgement based on disease severity. The
management component of the guideline recommends early cholecystectomy with adjuvant antibiotic therapy for grade I disease and conservative approaches including medical management with percutaneous cholecystostomy tube in grades II and III (4). A similar path of evolution is ideally how AAST may become usefully incorporated into the field of emergency general surgery. However, the distinction between TG and AAST grading is an important one. Only the anatomic severity of disease contributes to the AAST grade whereas the inclusion of physiologic parameters in TG may complicate its ability to compare pure primary disease across patients.

Although physiological variables are significant predictors of outcomes themselves, statistically controlling for the patient’s physiological state at admission allows the association between anatomic disease severity and patient outcomes to more accurately be analyzed. Comorbid conditions such as smoking and hypertension and social determinants of health such as ethnicity and insurance status can likewise be controlled for their effect on outcomes. Such an analysis has been consistently incorporated into published studies validating AAST scales. The AAST scoring system was designed to assess the extent to which anatomic severity predicts outcomes. It cannot be determined whether a scale incorporating physiological parameters better predicts outcomes than one based solely on anatomical severity without first validating the AAST.

Introduction to Cholecystitis

The clinical presentation of cholecystitis, including its severity and range of associated complications, can vary within a given patient population. Gallstones are by far the most common cause of cholecystitis, followed by stenosis of the biliary tract (12).
AC may be managed either medically or surgically with a laparoscopic cholecystectomy (removal of the gallbladder and its contents) being the most common operation used for treatment (13).

Pathologically, cholecystitis occurs as a result of both cystic duct obstruction and damage to the gallbladder mucosa. Gallstones may become impacted in the neck of the gallbladder of the cystic duct and cause mechanical mural irritation as the result of the gallbladder contracting against the stone. Damage to the mucosa leads to the release of phospholipases from the epithelial cells lining the gallbladder lumen. Phospholipase A catalyzes the production of lysolecithin from lecithin, a normal component of bile. Lysolecithin further irritates the epithelial lining of the gallbladder and mural distension and edema leads to epithelial vascular insufficiency. This damage leads to continued phospholipase release from damaged epithelial cells and propagates the inflammatory reaction causing AC (12). Due to the stasis of bile proximal to the obstruction at the neck of the gallbladder, its contents are more prone to a superimposed bacterial infection. Infection of the gallbladder, and uncommonly the whole biliary system, may complicate the disease although only 20% of patients with cholecystitis grow a pathogen in bile cultures (12).

The formation of gallstones is complex and involves an interplay between secretions of cholesterol into the bile, bile stasis secondary to gallbladder dysmotility, and crystal nucleation of stones. Oversaturation of bile with cholesterol and low levels of bile salts enhance stone formation. Age, female gender, obesity, oral contraceptives, parity, North American Indian ancestry, and consuming a western diet have all been found to be
associated with increased risk of gallstones in various studies. Dyslipidemia is also risk factor and more than 80% of gallstones are cholesterol based (13).

Biliary colic is a steady right upper quadrant or epigastric abdominal pain that lasts for more than 30 minutes but less than 4 hours. It is sudden in onset and usually occurs following consumption of a fatty meal. It is caused by an intermittent obstruction of the gallbladder neck or the cystic duct by gallstones during gallbladder contraction. In most instances, colic resolves during gallbladder relaxation as the stone falls back. However, sustained obstruction of the cystic duct can lead to bile stasis, gallbladder distension with mucosal and endothelial injury, and subsequent activation of inflammatory mediators leading to AC (14).

Gallstones are highly prevalent in western populations with some studies reporting prevalence rates as high as 10-15% in adult populations (15). However, some estimated 1-4% of patients with gallstones will go on to have any serious complications such as cholecystitis. Furthermore, most patients with gallstones are completely asymptomatic, with multiple studies reporting digestive symptoms in just less than 10% of populations positive for sonographic gallstones (14). However, rates of cholecystitis in this population of patients with symptomatic stones have been reported to be as high as 15% (15). Most gallstone-related complications including cholecystitis can be prevented with cholecystectomy and thus elective cholecystectomy may be indicated for patients with frequent digestive symptoms.

Acalculous cholecystitis is pathologically identical to AC but not caused by gallstones. It accounts for approximately 10% of all cases of AC and usually occurs in hospitalized patients who are critically ill (16). Pro-inflammatory conditions such as
cancers, infections, or trauma can lead to gallbladder ischemia or promote bile stasis. This can lead to gallbladder endothelial damage which initiates the same pathophysiological cascade seen in calculous cholecystitis. The clinical features of acalculous cholecystitis more often include jaundice, hyperbilirubinemia and elevation of liver transaminases. Patients with acalculous cholecystitis have been observed to have higher morbidity and mortality rates; this may be partially explained by the comorbid inflammatory process acalculous cholecystitis may present with (16).

**Diagnosis of Cholecystitis**

Understanding the diagnosis of cholecystitis is fundamental to evaluating the severity of the disease. Traditionally, the diagnosis of cholecystitis has been made based on clinical suspicion supported by lab data and confirmed with imaging findings. Clinical features of the disease include abdominal pain, nausea, vomiting, fever, Murphy’s sign (abrupt cessation of inspiratory effort due to elicited pain), and right upper quadrant or epigastric abdominal tenderness with or without guarding (12). The differential diagnosis is wide and may also include hepatitis, pancreatitis, peptic ulcer disease, gallbladder cancer, or Fitz-Hugh-Curtis syndrome.

There are no specific blood tests used to make the diagnosis of AC. However, laboratory tests can be used to support the diagnosis and/or exclude other etiologies of pain. Common tests used include white blood cell count, serum bilirubin, lipase levels, and liver transaminase levels (12).

Imaging studies used in the diagnosis include abdominal ultrasound and cholecintigraphy. Ultrasonography is the initial imaging modality of choice as it is
rapid, taking only minutes to perform, and inexpensive to use. Findings consistent with AC include gallbladder wall thickening (>4 mm), gallbladder distension, pericholecystic fluid collections, and pericholecystic fat stranding (17). A meta-analysis of 30 studies on imaging studies for gallbladder disease found the sensitivity and specificity of ultrasound for diagnosing cholecystitis to be 88% and 80%, respectively (18). A more recent meta-analysis of 57 studies found the sensitivity and specificity to be 81% and 83% respectively (17).

Cholescintigraphy, also referred to as a HIDA (Hepatobiliary Iminodiacetic) scan, may be used to aid in the diagnosis if strong clinical suspicion is present in the context of an equivocal or indeterminate ultrasound. This study traces the uptake of a technetium labeled acid administered intravenously to a patient and selectively taken up by hepatocytes before being excreted into the bile. Prolonged uptake due to cystic duct obstruction indicates a positive study. Though more sensitive and specific than an ultrasound, at 96% and 90% respectively, the HIDA scan takes hours to perform and utilizes more sophisticated personnel and equipment than ultrasound. Additionally, it provides data solely relevant to gallbladder pathology and is therefore less useful than ultrasound in examining the liver as an alternative source of right upper quadrant abdominal pain (17).

Complications of Cholecystitis

Early diagnosis and intervention of AC is important to prevent complications associated with higher morbidity and mortality. Gangrenous cholecystitis is a more severe and complicated form of the disease characterized by necrosis secondary to ischemia and prolonged inflammation of the gallbladder. Gangrenous cholecystitis is
considered grade II on the AAST scale. It is more common in patients with greater comorbidities, such as the elderly and diabetics, and patients with a delayed presentation (19).

Though uncommon, transmural perforation of the gallbladder may occur leading to localized abscess formation. This would be grade III disease in the AAST severity scale. Spillage of gallbladder contents such as pus or bile into the peritoneal cavity may cause subsequent generalized peritonitis, AAST grade IV disease. In rare cases, a biliary-enteric fistula may form between the gallbladder and small bowel. Gallstone ileus occurs when gallstones passed through a biliary-enteric fistula become lodged in the distal small bowel, most commonly the ileum, and cause obstruction. Sepsis and multiple organ dysfunction are more likely complicate the patient’s clinical status during these complications (19). Such a severe case of cholecystitis would be considered grade V on AAST.

Emphysematous cholecystitis is caused by an intramural or intraluminal infection of the gallbladder with gas producing organisms. The most commonly isolated offending pathogens include *Clostridium perfringens*, *Escherichia coli*, and *Klebsiella*. Emphysematous cholecystitis more commonly affects men, elderly, and diabetic patients. It is also associated with higher rates of perforation and a mortality rate of up to 15% (19).

**Management of Cholecystitis**

Management of cholecystitis can range from conservative to operational. Conservative approaches to the disease include a course of intravenous antibiotics.
accompanied by supportive care including intravenous fluids, pain control, and electrolyte correction. The most common pathogens covered by empiric antimicrobial therapy include gram negative rods, particularly *Escherichia coli*, and anaerobes. The laparoscopic approach to cholecystectomy is associated with decreased morbidity and mortality as well as shorter LOS. The conversion rates to open surgery are low (13).

The optimal timing of an LC following AC is still an active area of investigation. Higher complication rates following surgery in the acute setting are a concern as increased local inflammation may obscure the critical view and dissection of Calot’s triangle. Because of this concern, some surgeons elect to manage a patient medically in the acute setting and delay surgery for up to six weeks, even in an otherwise uncomplicated case (20). However, large population-based analyses and recent meta-analyses of case-control studies have shown that early LC in the acute setting is superior to delayed LC, with no differences in complication rates and shorter LOS (20, 21). However, early cholecystectomy was associated with longer operating times, presumably due to increased inflammatory changes in the acute setting. Despite the significance of these findings, these studies do not incorporate anatomic severity of disease in their analysis due to the lack of a widely adopted scale such as the AAST.

Reports using the TG severity scale also favors early cholecystectomy. A recent meta-analysis shows that early cholecystectomy can be a feasible treatment alternative to conservative management for AC in carefully selected candidates with TG grade II and III disease (22). In a separate investigate report, Loozen et al also found no statistically significant differences in conversion rates, operating time, perioperative complication rate, and 30-day mortality between patients with TG grade I and grade II cholecystitis
undergoing emergent LC (23). A separate retrospective analysis on a group of 149 patients undergoing emergent LC for AC determined that TG severity grade alone did not predict whether a patient underwent LC or percutaneous cholecystostomy tube. Those patients undergoing LC experienced longer LOS though did not experience increased morbidity or mortality (24). Another recent study did not show statistically significant differences in complication or conversion rates across TG classification although the classifications did correlate with LOS (25). While agreeing that early cholecystectomy should be more widely considered in patients with more severe disease but fewer comorbidities, these reports also recommend further stratification between grade I and grade II disease be considered in future TG revisions.

A percutaneous cholecystostomy tube (PCT) is a safe and effective intervention widely used as a bridging therapy for AC. It is essentially a catheter which drains the gallbladder contents, placed into the lumen via an ultrasound guided transhepatic approach. A PCT can provide relief of cholecystitis symptoms for up to 91% of patients undergoing the procedure (26). It is indicated in patients with severe disease, those with contraindications to general anesthesia, those who present >72 hours after symptoms onset, or patients failing medical therapy. Additionally, they are recommended for elderly patients with multiple co-morbidities who would have a higher likelihood of a safe and successful LC at some time interval following medical management and cholecystostomy placement, usually 6-8 weeks. The disadvantage of this therapy is that rates of tube dysfunction are high with up to 46% of patients experiencing some sort of dysfunction and over half of these patients requiring re-intervention (26).
In elderly patients with multiple chronic comorbidities, PCT may be the only safe feasible intervention available as the risks of surgery would outweigh the long-term benefits. Percutaneous gallbladder aspiration has been advocated as an easy to perform and less invasive alternative therapy to PCT for patients failing initial medical management. It also avoids drain-related symptoms of discomfort reported by many patients discharged with a PCT. Percutaneous aspiration has also been shown to provide comparable outcomes to PCT in retrospective studies as well as randomized controlled trials and is recommended in cases where PCT may not be available (27, 28).

Statement of Purpose and Hypothesis

The purpose of this original investigation was to retrospectively validate the AAST anatomic severity grading system using a cohort of patients admitted to a single, tertiary, high volume center with cholecystitis. A few single center studies have been published demonstrating independent associations between severity grades and outcomes in diverticulitis and appendicitis. To our knowledge and to the extent of the published literature, there has not been a similar investigation concerning the outcomes of patients with cholecystitis.

Because the AAST grading system was designed to be uniformly applied across a variety of EGS diseases, we expect to see associations like those previously reported for other EGS diseases. However, finding a lack of association with the current grading system would also be equally valuable in gaining insight into how it may be adjusted to fit the range of severity specific to cholecystitis. Given the current understanding of cholecystitis and the validation of AAST in other surgical diseases, we hypothesize that
the AAST anatomic severity grade in cholecystitis may independently predict higher likelihood of adverse clinical outcomes.
METHODS

This was a retrospective single center cohort study undertaken by Kenneth Vera, medical student, and Kevin Y. Pei MD at Yale University School of Medicine. This study was approved by the Human Investigation Committee.

Inclusion Criteria

All patients over eighteen years of age who were admitted to Yale-New Haven Hospital between August 2013 and August 2016 with a diagnosis of ‘acute cholecystitis’ (575.0 or K81.0), ‘acute on chronic cholecystitis’ (575.12 or K81.2), or ‘cholecystitis unspecified’ (575.10 or K81.9) based on ICD-9 and ICD-10 codes were included in this study. Patients were excluded if they were a pregnant, a prisoner, or had advanced directives limiting care. They were additionally excluded if they had a prior admission for AC within 90 days. In cases where a patient had multiple admissions for AC on record, the data and management from their index admission was used. Patients were excluded if their index admission made note of a recent prior admission for cholecystitis at another facility or prior admission for cholecystitis at our facility prior to 2013 as records were not available for access in these cases. Patient who were primarily admitted to a medical or surgical floor for some other condition but were subsequently admitted as an EGS consult patient were included so long as they received a new diagnosis of AC or acalculous cholecystitis (rather than a flare of known chronic cholecystitis) and were managed as such. Cases of patients in severely critical condition found to have acute acalculous cholecystitis on imaging within 24-72 hours prior to expiration were excluded.
Data Collection

Demographic data collected for each patient included their age, gender, ethnicity, and insurance status (categorized as either commercial or public). This data was collected from the electronic medical records (EMR). All other data extraction was performed by a detailed manual review of individual admission records.

The presence or absence of common co-morbidities was noted based on data in their admission notes and past diagnoses noted elsewhere on record. Our comorbidities of interest included whether a patient has is a present smoker, has diabetes, a history of progressive renal insufficiency or failure, hypertension, chronic dyspnea, or is on chronic steroids or immunosuppressant medications. Additionally, whether a patient had two or more SIRS criteria present at admission and/or was septic based on 2016 Sepsis-3 criteria was noted and counted as a comorbidity (29).

A Sequential Organ Failure Assessment (SOFA) score was calculated based on the patient’s worse physiological parameters within the initial 24 hours of admission to the emergency general surgery (EGS) service. We included this score as a covariate in our analyses to control for the effect of physiology on outcomes. Scores were calculated as described in the literature and SOFA score component data was available for all patients (30). Patients breathing on room air were calculated as having 21% FiO2. Patients documented to be on supplemental oxygen had approximate FiO2 calculated based on published conversion formulas. Approximate PaO2 was calculated from documented SaO2 from published conversion formulas (31). GCS was assumed to be 15 unless otherwise noted on documented physical exam. In cases where the patient
received an operation within the first 24 hours of admission, the worse parameters prior to surgery were used.

The outcomes of interest included LOS, whether a patient received operative management, if they had a complication while admitted, readmission within 30 days, and ICU use (defined as at least 12 hours of admission to a medical or surgical ICU). Complications of interest included surgical wound infection or disruption, acute renal failure, transfusion of blood products during admission, mechanical ventilation for more than 48 hours, and diagnosis of UTI, pneumonia, or DVT/PE during admission, septic shock requiring vasopressors, and cardiac arrest or myocardial infarction. Operative management was cholecystectomy, either index or interval, performed for the indication of AC. Mortality data was also collected and based on death being reported during the patient’s hospital stay or within 30 days after discharge if readmitted.

Specific data was additionally collected from the operative records of those patients who had surgery. This was done to better relate the surgical complexity of this cohort subset although this data is not included in statistical analysis. This data included the interval of time between presentation to the hospital and the beginning of the patient’s operation, the operation time of day and its duration, as well as the training level of the assisting surgical resident.
AAST Grading

Data extraction and disease severity grading were performed by two independent researchers. AAST grades were assigned to each patient based on clinical, operative, pathological, and imaging criteria, with a composite of four grades for each of these criteria. A detailed grading rubric adapted from the AAST’s published 2015 report is reproduced below (6). The final grade assigned was the highest of any criteria. For those patients who did not have a cholecystectomy, either index or interval, only clinical and imaging criteria were available. Grading was based on manual review of data available in the patient’s EMR including admission history and physical exam, progress notes, as well as pathology, operative and imaging reports. Pathological grades were recorded for both patients with index cholecystectomy as well as interval cholecystectomy performed within 3-12 weeks of conservative management for their index admission of AC. Interrater reliability of grade assignment was assessed using kappa coefficient with Fleiss-Cohen quadratic weights.
AAST Anatomic Severity Grading Scale as published in Shafi et al 2015.

<table>
<thead>
<tr>
<th>Grade</th>
<th>Clinical Criteria</th>
<th>Imaging Criteria</th>
<th>Operative Criteria</th>
<th>Pathological Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>RUQ or epigastric pain, Murphy sign, Leukocytosis</td>
<td>Wall thickening, distension, gallstones or sludge, pericholecystic fluid, non-visualized GB on HIDA</td>
<td>Localized inflammation, wall thickening, distension, gallstones</td>
<td>Inflammatory changes without necrosis or pus</td>
</tr>
<tr>
<td>II</td>
<td>RUQ or epigastric pain, Murphy sign, Leukocytosis</td>
<td>Air in GB lumen, wall or biliary tree. Focal mucosal defects</td>
<td>Distended GB with pus or hydrops, necrosis/gangrene of wall (non-perforated)</td>
<td>Pus in the GB lumen, wall necrosis, intramural abscess, epithelial sloughing</td>
</tr>
<tr>
<td>III</td>
<td>Localized RUQ peritonitis</td>
<td>Focal transmural defect, extraluminal fluid collection</td>
<td>Perforated GB wall, bile outside GB but limited to RUQ</td>
<td>Necrosis with perforation of the GB wall</td>
</tr>
<tr>
<td>IV</td>
<td>Multifocal peritonitis, abdominal distension, bowel obstruction symptoms</td>
<td>Abscess in RUQ outside of GB, bilioenteric fistula, gallstone ileus</td>
<td>Pericholecystic abscess, bilioenteric fistula, gallstone ileus</td>
<td>Necrosis with perforation of the GB wall</td>
</tr>
<tr>
<td>V</td>
<td>Generalized peritonitis</td>
<td>Free intraperitoneal bile</td>
<td>Generalized peritonitis</td>
<td>Necrosis with perforation of the GB wall</td>
</tr>
</tbody>
</table>

**Statistical Analysis**

Binary logistic regression analysis was used to model the associations between AAST grades and their covariate predictors with the occurrence of clinical events. AAST grade was included as an ordinate independent variable with grade I used as the reference for comparisons of other severity grades. Separate logistic regression models were made for each clinical event. C-statistic values were calculated and used for goodness-of-fit comparisons among the models.

A negative binomial regression model was used to measure the association of covariate predictor variables and AAST grade with LOS as a continuous dependent variable. To enforce normality and equal variance assumptions to the negative binomial
regression analysis, an interpretation of the original output data was performed where all data points with Standardized Pearson Residual absolute values > 2 were considered outliers and excluded from a second otherwise identical regression model. This excluded 11 data points from the original set of 315. The Akaike’s Information Criteria (AIC) and Bayesian Information Criterion (BIC) values pre- and post-outlier exclusion were used for goodness-of-fit comparison where smaller-is-better assumptions were applied to accept the new model. These were 1532 and 1569 for AIC and BIC after outlier exclusion, compared to 1667 and 1705 originally.

In all models, age and SOFA score were both continuous predictive variables while sex, race/ethnicity, public insurance status, and presence of comorbidities were nominal variables. Male sex, non-minority race/ethnicity, having commercial insurance, and having no comorbidities were the respective reference conditions. The comorbidities of interest included those described in the data collection as well as having met SIRS or sepsis criteria at admission. Statistical Analysis was performed with IBM SPSS v.22 statistical software.
RESULTS

A final set of 315 patients was included in data analysis. A breakdown of demographic, LOS and morbidity data is shown in Table 1.

Table 1: Patient Demographics and Morbidity

<table>
<thead>
<tr>
<th></th>
<th>Average age</th>
<th>Average LOS [SD]</th>
<th>Minority race/ethnicity*</th>
<th>Median LOS [IQR]</th>
<th>Female</th>
<th>ICU use</th>
<th>Commercial Insurance</th>
<th>Average ICU days [SD]</th>
<th>Government Insurance</th>
<th>SIRS or Sepsis</th>
<th>Uninsured</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average age</td>
<td>61.5</td>
<td>5.1 days [5.6]</td>
<td>32%</td>
<td>3 days [2-6]</td>
<td>55%</td>
<td>71 (22%)</td>
<td>38%</td>
<td>1 [3.47]</td>
<td>60%</td>
<td>146 (46%)</td>
<td>2%</td>
</tr>
</tbody>
</table>

*Defined as self-identifying as black or hispanic (non-white)

A breakdown of disease severity by final AAST grade is shown in Table 2. Notably, nearly 94% of cases were grade I or grade II. No cases meeting grade IV were identified and only three were identified as grade V. There was very good interrater reliability between two independent reviewers for anatomic grading, $\kappa=1.00$, $p<0.005$.

Table 2: AAST Grade Distribution

<table>
<thead>
<tr>
<th>Grade</th>
<th>Number of Patients</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>219</td>
<td>(69%)</td>
</tr>
<tr>
<td>II</td>
<td>75</td>
<td>(25%)</td>
</tr>
<tr>
<td>III</td>
<td>18</td>
<td>(5%)</td>
</tr>
<tr>
<td>IV</td>
<td>0</td>
<td>-</td>
</tr>
<tr>
<td>V</td>
<td>3</td>
<td>(1%)</td>
</tr>
</tbody>
</table>

The prevalence for each of our comorbidities of interest is shown in Table 3. The most common co-morbidities were hypertension, diabetes, and hyperlipidemia. The prevalence for each of our complications of interest is shown in Table 3. The most common complications were acute renal injury (AKI), transfusion, or readmission.
Table 3: Prevalence of the Most Common Patient Comorbidities

<table>
<thead>
<tr>
<th>Condition</th>
<th>Count</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>171</td>
<td>(54%)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>83</td>
<td>(26%)</td>
</tr>
<tr>
<td>Current smoker</td>
<td>49</td>
<td>(16%)</td>
</tr>
<tr>
<td>Steroids/immunosuppressed</td>
<td>12</td>
<td>(4%)</td>
</tr>
<tr>
<td>Coagulopathy</td>
<td>21</td>
<td>(7%)</td>
</tr>
<tr>
<td>ESRD or CKD</td>
<td>42</td>
<td>(13%)</td>
</tr>
<tr>
<td>Chronic dyspnea</td>
<td>64</td>
<td>(20%)</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>121</td>
<td>(38%)</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>59</td>
<td>(19%)</td>
</tr>
</tbody>
</table>

A breakdown of interventions for the patient cohort is shown in Table 4.

Approximately 49% of patients underwent successful LC during their admission with another 13% undergoing interval LC following medical management or a PCT.

Approximately 32% of patients did not undergo an operation either during their admission or after their discharge, the majority (75%) of this subgroup of patients were managed with PCT. Conversion from laparoscopic to open surgery was rare and occurred in 7.6% of all operative cases. In two cases, a patient had an open cholecystectomy performed during an exploratory laparotomy. Two patients, both with grade II disease, experienced either cystic duct injury or bile leak as a complication.

Table 4: Most Common Interventions

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Count</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medical management</td>
<td>26</td>
<td>8%</td>
</tr>
<tr>
<td>Laparoscopic cholecystectomy</td>
<td>153</td>
<td>49%</td>
</tr>
<tr>
<td>Percutaneous cholecystostomy</td>
<td>77</td>
<td>24%</td>
</tr>
<tr>
<td>Interval laparoscopic cholecystectomy</td>
<td>41</td>
<td>13%</td>
</tr>
<tr>
<td>Laparoscopic converted to open cholecystectomy</td>
<td>16</td>
<td>5%</td>
</tr>
<tr>
<td>Open cholecystectomy</td>
<td>2</td>
<td>&lt;1%</td>
</tr>
</tbody>
</table>
The average time from hospital presentation to time of cholecystectomy for those patients receiving LC during their index admission was 25.2 hours (standard deviation of 20.9 hours). Approximately 13% of patients underwent interval LC following medical management or a PCT. The average time from the date of admission for cholecystitis to date of cholecystectomy for those patients was 67 days (standard deviation of 45 days). Almost all of these operations involved trainees in a seven-year academic general surgery residency with the average post-graduate year of training being 4.6 years (standard deviation of 1.7 years) for the resident trainees scrubbed into the procedure.

Approximately 74% of all operations occurred between the hours of 0700 and 1700. The average operation length was 105 minutes (standard deviation of 42 minutes).

Table 5 shows the incidence of clinical events by final AAST grade. The proportional incidence of any complication, adverse event (defined as either death or readmission), ICU use, and median LOS trended upward with increasing severity grade. Note that complications in this table are listed as a composite outcome. Table 6 shows a breakdown of the complications observed. The most common complications were acute kidney injury, readmission within 30 days and receiving a blood product transfusion.

<table>
<thead>
<tr>
<th></th>
<th>Grade I</th>
<th>Grade II</th>
<th>Grade III</th>
<th>Grade V</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complications</td>
<td>70 (32%)</td>
<td>37 (49%)</td>
<td>12 (67%)</td>
<td>2 (67%)</td>
</tr>
<tr>
<td>Surgery</td>
<td>142 (65%)</td>
<td>58 (77%)</td>
<td>10 (56%)</td>
<td>2 (67%)</td>
</tr>
<tr>
<td>ICU Use</td>
<td>34 (16%)</td>
<td>23 (31%)</td>
<td>12 (67%)</td>
<td>2 (67%)</td>
</tr>
<tr>
<td>30d readmission</td>
<td>31 (14%)</td>
<td>6 (8%)</td>
<td>7 (58%)</td>
<td>2 (67%)</td>
</tr>
<tr>
<td>Median LOS (IQR)</td>
<td>3 (1-5)</td>
<td>4 (2-7)</td>
<td>6.5 (5-8)</td>
<td>11</td>
</tr>
<tr>
<td>Any adverse event</td>
<td>90 (41%)</td>
<td>39 (52%)</td>
<td>15 (83%)</td>
<td>3 (100%)</td>
</tr>
</tbody>
</table>

Table 5: AAST Grade and Clinical Events
Table 6: Most Common Complications

<table>
<thead>
<tr>
<th>Complication</th>
<th>Count</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wound infection</td>
<td>6</td>
<td>3%</td>
</tr>
<tr>
<td>Acute kidney injury</td>
<td>77</td>
<td>24%</td>
</tr>
<tr>
<td>Transfusion</td>
<td>37</td>
<td>12%</td>
</tr>
<tr>
<td>Urinary tract infection</td>
<td>24</td>
<td>8%</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>20</td>
<td>6%</td>
</tr>
<tr>
<td>Deep venous thromboembolism or pulmonary embolus</td>
<td>7</td>
<td>2%</td>
</tr>
<tr>
<td>Septic shock</td>
<td>28</td>
<td>9%</td>
</tr>
<tr>
<td>Cardiac arrest</td>
<td>16</td>
<td>5%</td>
</tr>
<tr>
<td>Mechanical ventilation</td>
<td>29</td>
<td>9%</td>
</tr>
<tr>
<td>30-day readmission</td>
<td>45</td>
<td>14%</td>
</tr>
<tr>
<td>Death</td>
<td>24</td>
<td>8%</td>
</tr>
</tbody>
</table>

Table 7 shows the association between the included covariates and clinical events reported in Odds Ratio (Incidence Risk Ratio for LOS). Age independently predicted the occurrence of a complication and the occurrence of non-operative management. Increasing age was also associated with a greater incidence of longer LOS. SOFA score independently predicted higher incidence of a complication, ICU use, non-operative management, and occurrence of an adverse event (readmission or death). The presence of any comorbidity predicted ICU use during admission. Female sex, minority race, and having public insurance were largely non-predictive of the outcomes of interest except for public insurance status predicting non-operative management.
Table 7: Association Between Clinical Events and Predictors
Reported as Odds Ratios with 95% CIs (Incidence Risk Ratios with 95% CIs for LOS)

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Complications</th>
<th>LOS</th>
<th>Surgery</th>
<th>ICU Use</th>
<th>Adverse Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>1.04 (1.02 - 1.06)*</td>
<td>1.01 (1.00 - 1.02)*</td>
<td>0.96 (0.94 - 0.97)*</td>
<td>1.02 (1.00 - 1.04)</td>
<td>1.01 (0.99 - 1.03)</td>
</tr>
<tr>
<td>Female sex</td>
<td>0.90 (0.52 - 1.57)</td>
<td>0.87 (0.67 - 1.13)</td>
<td>1.05 (0.60 - 1.84)</td>
<td>0.65 (0.33 - 1.28)</td>
<td>1.39 (0.75 - 2.57)</td>
</tr>
<tr>
<td>Minority race</td>
<td>1.83 (0.95 - 3.5)</td>
<td>1.06 (0.78 - 1.44)</td>
<td>0.89 (0.47 - 1.71)</td>
<td>1.83 (0.82 - 4.05)</td>
<td>1.93 (0.98 - 3.83)</td>
</tr>
<tr>
<td>Public insurance</td>
<td>1.18 (0.66 - 2.09)</td>
<td>1.26 (0.96 - 1.64)</td>
<td>0.55 (0.31 - 0.98)*</td>
<td>1.22 (0.60 - 2.49)</td>
<td>1.11 (0.59 - 2.09)</td>
</tr>
<tr>
<td>SOFA</td>
<td>1.73 (1.44 - 2.09)*</td>
<td>1.14 (1.07 - 1.23)*</td>
<td>0.68 (0.58 - 0.79)*</td>
<td>1.83 (1.51 - 2.21)</td>
<td>1.44 (1.24 - 1.67)*</td>
</tr>
<tr>
<td>Comorbidity</td>
<td>1.73 (0.78 - 3.80)</td>
<td>1.39 (0.98 - 1.97)</td>
<td>1.44 (0.68 - 3.09)</td>
<td>6.1 (1.3 - 28.74)*</td>
<td>1.37 (0.57 - 3.28)</td>
</tr>
<tr>
<td>C-statistic</td>
<td>0.83 (0.78 - 0.88)</td>
<td>N/A</td>
<td>0.80 (0.75 - 0.85)</td>
<td>0.88 (0.84 - 0.92)</td>
<td>0.77 (0.71 - 0.84)</td>
</tr>
</tbody>
</table>

*Statistically significant finding with p < 0.05.

Table 8 shows the risk-adjusted associations between AAST grade and the occurrence of clinical events reported as Odds Ratios (Incidence Ratio for LOS) with grade I as the reference range. Grade II disease was associated with four times the odds of operative management. Grade III disease was associated with almost four times the odds of an adverse event (readmission or death) and over eight times the odds of ICU use. Grade III disease was also associated with higher incidence of longer LOS.

Although grade V disease appeared to be associated with greater odds of complications or ICU use, these were not statistically significant. The notable width of the grade V confidence intervals is likely explained by the small size of the group in our sample. All three cases of grade V disease experienced death and the odds ratio of this grade having an adverse event is not reportable as there is no variability in the outcome.
Table 8: Risk-Adjusted Association Between AAST and Clinical Events

Reported as Odds Ratios with 95% CIs (Incidence Risk Ratios with 95% CIs for LOS)

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Grade I</th>
<th>Grade II</th>
<th>Grade III</th>
<th>Grade V</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adverse Event†</td>
<td>Ref</td>
<td>0.58 (0.26 - 1.27)</td>
<td>3.83 (1.34 - 10.94)*</td>
<td>-</td>
</tr>
<tr>
<td>Complications</td>
<td>Ref</td>
<td>1.52 (0.80 - 2.89)</td>
<td>2.22 (0.70 - 7.06)</td>
<td>3.09 (0.23 - 41.41)</td>
</tr>
<tr>
<td>Surgery</td>
<td>Ref</td>
<td>4.07 (1.93 - 8.56)*</td>
<td>1.34 (0.45 - 4.03)</td>
<td>1.02 (0.08 - 12.75)</td>
</tr>
<tr>
<td>ICU Use</td>
<td>Ref</td>
<td>1.86 (0.87 - 4.01)</td>
<td>8.07 (2.43 - 26.90)*</td>
<td>8.37 (0.65 - 107.92)</td>
</tr>
<tr>
<td>Length of Stay</td>
<td>Ref</td>
<td>1.06 (0.78 - 1.44)</td>
<td>1.73 (1.03 - 2.92)*</td>
<td>1.03 (0.60 - 1.78)</td>
</tr>
</tbody>
</table>

*Statistically significant finding with p < 0.05.
†Either death or readmission within 30 days
DISCUSSION

This is the first single-center study designed to validate the AAST severity grading system for cholecystitis. Our results show that higher grades of severity, notably grade III in our sample, is independently associated with multiple patient outcomes after controlling for covariate predictors such as age, sex, and physiological status.

A great majority of patients in our population had low grade disease with 94% percent of our population having grade I or grade II disease. Notably, there were no patients with grade IV disease included in our data set. Although the AAST scale from I-V offers a rating for a wide range of severity, our data reflect a common clinical observation that cholecystitis tends to be milder disease associated with low overall rates of mortality. This reflects the modern era where we are diagnosing and managing cholecystitis earlier with the widespread adoption of sensitive imaging techniques for diagnosis and less invasive modalities for treatment (32). The implications for AAST are that the current scale for AC may need to be modified prior to being further validated in larger samples.

Other recent studies validating AAST grading scales report a similar finding of low-grade disease being over-represented in their retrospective data sets. Savage et al reported 74% of their 512 patient cohort with diverticulitis to have had grade I or II disease (7). Hernandez et al reported 78% of their 334 patient cohort with appendicitis to have grade I or II disease (9). Shafi et al reported two thirds of their 1,105 multicenter patient cohort to have had grade I or II disease (8). Collins et al reported 91% of their 1,099 patient cohort with appendicitis to have grade I-III disease. This overrepresentation presents a potential challenge for validation of the current scales. It
has been proposed by Shafi et al that oversampling patients with severe disease, especially in multicenter studies, would better select a cohort representing the spectrum of disease severity. In our study, patients with severe disease meeting eligibility criteria were included in the analysis but it was also observed that patients with higher severity scores more often met exclusion criteria.

An alternative to oversampling patients with severe disease would be to modify the current scale such that it more discretely classifies low-grade disease while consolidating the higher grades together. As the scale is currently designed, each of the five levels of severity is distinguishable from others anatomically and a gradient of morbidity follows accordingly. For instance, gallbladder perforation is grade III by definition. Because perforation more often leads to localized abscess or peritonitis, the step up from grade II to grade III is intuitively associated with increased morbidity and mortality. However, perforation leading to peritonitis is a rare event and most of the patients in our cohort cluster in grades I and II. Increasing resolution of the grading system at this mild end of the scale may allow the AAST grading of cholecystitis to better fit the spectrum of naturally occurring disease and thus make the tool to more clinically meaningful. We expect the milder spectrum of severity seen in our patient cohort to be similar to the range of disease encountered in a larger, multicenter study. Additionally, consolidation of the high-grade scores could be considered to simplify the existing AAST system given the rarity of severe grade IV and V disease.

Interestingly, the occurrence of complications was not significantly associated with AAST grade, unlike in reports validating AAST for other EGS diseases. Although an explanation for this is not clear from our data, this endpoint may again be better
validated after inclusion of cases of higher grade severity. We assessed the same outcomes as those recorded in large database registries such as the American College of Surgeons (ACS) National Surgical Quality Improvement Project (NSQIP). Outcomes such as sepsis, deep vein thrombosis, and pneumonia may not be as applicable to low risk procedures such as LC. In general, complications arising from cholecystectomy, particularly when laparoscopic, is rare (33). The confidence interval width for the complications associations, as well as others, suggests a degree of uncertainty in our data that is yet to be resolved.

Hernandez et al argues that the AAST scoring systems would be easier validated for the mortality end-point in diseases with greater odds of death (9). Our data would agree with this theory as death was rare in our data set, only occurring in 24 of our 315 patients. Only a single death was noted in the 1,105 diverticulitis patients included in Shafi et al and therefore was not an analyzed nor validated outcome in their work (8). The higher rate of death in our smaller data set may be due to inclusion of admitted patients diagnosed with acalculous cholecystitis who have greater morbidity from other causes. Future analysis of our data would consider excluding or separating this subtype of patients, further necessitating the inclusion of high grade cases in larger samples of patients.
Imaging Scores for AAST Grade

Many of the criteria proposed in the original AAST severity scale for appendicitis rely on intraoperative and postoperative pathological findings and thus cannot be utilized pre-operatively to predict need for operative management. Validation of the AAST scale as a tool which grades severity without operative or pathological information would make the scale useful tool in a real time clinical setting where making decisions with limited information is custom. Hernandez et al therefore proposed that an imaging based AAST grade, I-AAST, be first validated (8).

The I-AAST used by Hernandez et al assigned an anatomic severity grade of I-V based on objective CT findings including the size of appendiceal thickening, presence of periappendiceal edema, free intraperitoneal fluid, or presence of a localized abscess or phlegmon. A score of 0 was to indicate an appendix which appears normal on CT. They then compared the I-AAST grade with the final AAST reported from operative and pathological findings. They found no significant mean difference between the scores and had a coefficient of repeatability of 0.9 on Bland-Altman analysis and an ordinal [kappa] coefficient of 0.73 (95% CI, 0.64-0.81) on sensitivity analysis (8). These findings support a strong correlation between I-AAST and the final AAST grades.

A similar comparison between an imaging based AAST score and the final AAST can be made for cholecystitis using ultrasound findings. Some limitations will be expected, however. Ultrasound findings in cholecystitis may be more subjective and open to interpretation than CT findings for appendicitis. There is no standard imaging severity for cholecystitis and this may perhaps be a worthy subject of future study. Anatomical parameters, such as millimeters of wall thickening, are less consistently reported in
sonographic assessments for cholecystitis. This may be because it is more difficult to accurately assess. Furthermore, the quality of ultrasound images would be expected to vary based on technique and patient factors and be less consistent than the quality of images obtained in cross section CT scanning performed for appendicitis. Nonetheless, the AAST imaging scale warrants validation for cholecystitis for the same reasons addressed by Hernandez et al in their study on appendicitis. This is a future aim of this body of work.

Refining the AAST Scale

The currently proposed AAST scores include a component of the grade based purely on clinical criteria, such as presence or absence of fever, abdominal tenderness and peritoneal signs (6). The utility of this component must be considered given that the AAST’s intention is to have an anatomically based scale for disease severity. Furthermore, the clinical component fails to consider the possible complexity of the disease presentation.

For instance, a patient who is septic from a pneumonia may develop acalculous cholecystitis secondary to the inflammation and shock associated with their respiratory disease. While their clinical criteria would meet a grade V score, their gallbladder findings on ultrasound may only meet a grade I score. This discrepancy may ultimately be overlooked as the AAST recommend final scores be the highest of the component scores. Although such a complex presentation of AC such as this would likely have increased complications associated with a higher score, these complications would not be primarily due to the patient’s gallbladder disease.
The validation of this component of the scale must then be considered separately from imaging, operative, and pathology based scores, as was done in Hernandez et al. A future analysis of clinically based AAST may be performed after first validating imaging based AAST scores with final pathological and operative grades for cholecystitis.

Excluding the clinical component of the scale entirely may be considered given that it is the most inherently subjective of the four components. Furthermore, it may prove to be an unnecessary component should the imaging based grades better correlate with the pathological grades.

Limitations

The data presented in this work is from 315 patients admitted to a single academic center over the last 3 years. A larger, multicenter population of patients with AC is still needed to make a more widely generalizable validation the AAST scale. This work is also retrospective and is subject to inherent limitations from this design. Notably, our AAST grading may be affected by information bias as we are applying a new scale to existing data on a disease. Because the records on our patients did not have the AAST scale in mind when created, the anatomical descriptions in our records must be fit to the descriptions in the scale. Misclassification of patient’s severity grade may therefore occur based on misinterpretation of descriptions. This bias may be avoided in future prospective studies which deliberately record AAST grades in patient records.

Future Directions

The refinement of our patient sample is an important future direction. The use of ICD codes is sensitive enough to capture all the cases of interest but the exclusion criteria
may not be specific enough. Excluding cases of admitted patients diagnosed with cholecystitis would allow the tool to better assess acute calculous cholecystitis. However, this exclusion would be weighed against a loss of statistical power in our whole sample and make the grading scale validations less generalizable to in-patients who often have acalculous cholecystitis. At many medical centers the same EGS service providers admit patients with cholecystitis whether they are presenting to the emergency department or admitted to the floor (32). Given a large enough sample, separate analyses between the two patient types may distinguish which AC patients the AAST is best used for and what management approaches are most appropriate.

The inclusion of two reviewers to have a comparison between two sets of AAST grades provides valuable insight into the reliability and ease of using the grading system. Future studies on the concordance of multiple reviewers’ scores would benefit in determining how precise the instrument is across providers at different medical centers and across providers and trainees with varying levels of experience. As previously mentioned, we would ideally like to validate the AAST scores based on imaging against the AAST scores based on operatory and pathological findings. Finally, we are interested in analyzing whether it’s the imaging, clinical, operative, or pathological findings which most often determine final AAST scores.

Future outcomes based research using the AAST scale may be valuable after validation of the scale to common outcomes included in this report. As previously mentioned, the timing of cholecystectomy for AC is an active area of investigation. Investigating the association between AAST grade with the difficulty, duration and timing of surgery may be valuable in identifying which patients most benefit from early
cholecystectomy. Such data may also be used to validate the AAST as a system to guide management.

The mapping of EGS disease severity from existing ICD-9 and ICD-10 codes is an important future direction for research in AAST. This involves capturing AAST severity grades from disease descriptions included in ICD billing codes. This is proposed as a very quick, automated way of categorizing disease severity in currently existing patient databases that may be performed as an alternative to manual detailed chart review such as the review described in this thesis and previous AAST validation studies. More centers with less resources would be able to grade their patients and be compared. As AAST severity-standardized outcomes comparisons across 12 centers has been published as proof-of-concept (8), a more automated way of grading patients in existing registries will be needed to gather multicenter quality improvement metrics in the future.

Utter et al has published a conceptual approach that has described how, in the language used in current ICD-10 coding descriptions, five EGS diseases can be mapped into four categories of severity, seven into three categories, and four into two categories. Furthermore, when compared to ICD-9 codes, two diseases mapped into discontinuous categories of grades. Their work suggests the resolution of current ICD codes is too limited for accurate mapping to be accomplished solely using codes. Furthermore, the increased resolution of ICD-10 codes does not comport with finer mapping of AAST severity grades. Ultimately, the ability to use ICD codes to grade disease depends on incorporating the AAST disease descriptions into the code and is not easily achieved given the current complexity in ICD coding. Nonetheless, Utter et al argues that mapping ICD codes to AAST grades is a good starting point for manual review (34).
Conclusions

Higher grades of AAST anatomic severity were independently associated with significant clinical outcomes in patients with cholecystitis. Distinctions within low grade disease were less significant than comparisons of low versus high grade disease. Enhanced granularity in the lower grades of cholecystitis may enable AAST to better predict outcomes in larger, multicenter patient samples with a wide range of disease. The continued validation of AAST will facilitate better risk stratification and quality improvement in emergency general surgery.
REFERENCES


