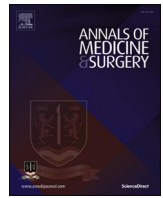


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Current grading of gall bladder cholecystitis and management guidelines: Is it sufficient?

Cholecystitis is a commonly seen biliary disease [1]. Pathophysiology varies, but is often due to an obstructing stone at the level of the cystic duct. Gallbladder contraction against this persistent obstruction leads to local inflammation with bacterial overgrowth, and gallbladder wall edema. Progressive edema leads to venous congestion, and necrosis with perforation. With full disease progression, empyema of the gallbladder, gangrenous cholecystitis, acute emphysematous cholecystitis may develop. Ultrasound may serve as confirmatory imaging which can show gallstones, gallbladder wall thickening, pericholecystic fluid, or a sonographic Murphy's sign. Equivocal findings can be investigated further using CT or a hepatobiliary iminodiacetic acid (HIDA) scan. Current literature advocates for early laparoscopic cholecystectomy (defined as laparoscopic cholecystectomy within 24–96 hours of hospital admission) as this has been shown to result in shorter hospital length of stay, less major complications, but no difference in conversion to open procedures compared to delayed laparoscopic cholecystectomy [2,3]. Several guidelines have been introduced into practice for assessing acute cholecystitis severity. The three most commonly used are The Parkland Grading Scale for Cholecystitis (PGS), The Tokyo Guidelines 2018 for Acute Cholecystitis, and The American Association for the Surgery of Trauma - Emergency General Surgery (AAST EGS) score for acute cholecystitis.

The PGS grades cholecystitis on a scale of 1–5 based on intraoperative gallbladder findings in order to predict operative difficulty. Grading also helps predict the need for conversion to an open operation, calling for more experienced help sooner, predict patient outcomes, assist with justifying a complex laparoscopic case for surgical resident logging, and improve surgeon reimbursement [4,5]. Grade 1 correlates with a normal appearing gall bladder without adhesions. Grade 2 correlates with minor adhesions at the neck of the gallbladder. Grade 3 correlates with the presence of hyperemia, pericholecystic fluid, adhesions to the body of the body of the gallbladder, or a distended gallbladder. Grade 4 correlates with adhesions obscuring the majority of the gallbladder or a grade 1-3 with abnormal liver anatomy, intrahepatic gallbladder, or an impacted stone. Grade 5 correlates to perforation, necrosis, or the inability to visualize the gallbladder because of adhesions (Table 1).

The Tokyo Guidelines for acute cholecystitis are intended for use in guiding management of early or delayed laparoscopic cholecystectomy as well as potential gallbladder drainage [6]. Once a patient has achieved a suspected diagnosis of acute cholecystitis, severity grading on a scale of I through III is determined based on specific clinical and laboratory findings (Table 2). With this grading severity, patients are stratified into optimal management of their suspected acute cholecystitis.

The AAST EGS for acute cholecystitis is an anatomically based severity grading system for acute cholecystitis with grades varying from I to V [7]. Grade I correlates to a localized gallbladder inflammation. Grade II correlates to a distended gallbladder with purulence or hydrops, necrosis/gangrene of the wall without iatrogenic perforation. Grade III correlates to a noniatrogenic perforation with bile in the right upper quadrant. Grade IV correlates to a pericholecystic abscess, bilioenteric fistula, and gallstone ileus. Grade V correlates to a Grade IV with generalized peritonitis (Table 3).

The PGS and AAST grading scales include mainly intraoperative factors for grading while the Tokyo Guidelines focus more on preoperative factors. Further modifications to the above grading systems can allow for improved inclusion for all types of patients who present with acute cholecystitis. Intraoperatively, distorted anatomy due to significant inflammation can pose a challenge to the operating surgeon. Elkbuli et al. document a case of severe empyema of the gallbladder [8]. While preoperatively the patient had a clinical exam, laboratory values, and imaging consistent with acute cholecystitis, the intraoperative anatomy was unexpected (Fig. 1). Ultimately, the patient's cholecystectomy was able to be performed laparoscopically and the patient was discharged on postoperative day 3 without complications. Another case by Elkbuli et al. report an enormous gangrenous gallbladder presenting as chronic acid reflux symptoms [9]. The preoperative imaging was suggestive of the large size of the gallbladder; however, it was difficult to stratify the best approach for removal of the gallbladder (Figs. 2 and 3). This patient's gallbladder was successfully removed laparoscopically despite previous reports of "giant" gallbladders requiring open removal.

These two cases highlight the limitations in current grading systems, particularly in the context of gallbladder size. We propose modifications to the PGS to include not only abnormal anatomy but instances of distorted gallbladder anatomy due to inflammation and/or the large to giant size in order to account for the increased associated complications with these presentations (Table 4). Both distorted gallbladder anatomy and giant gallbladder size can make laparoscopic cholecystectomy a challenge, and thus warrant contribution to overall clinical grade. While the PGS, Tokyo Guidelines, and AAST grading scales are validated grading scales for acute cholecystitis, additional modifications can further characterize different types of acute cholecystitis to better guide patient management and predict outcomes in the postoperative setting.

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Table 1
Parkland grading scale for cholecystitis.

Cholecystitis Severity Grade	Description of Severity	Management
1	Normal appearing gallbladder (“robin’s egg blue”) No adhesions present Completely normal gallbladder	Typical acute or acute on chronic cholecystitis. Laparoscopic Cholecystectomy feasible. Relatively low; operating room time, bile leak rate, length of stay, and conversion rate.
2	Minor adhesions at neck, otherwise normal gallbladder Adhesions restricted to the neck or lower of the gallbladder	Typical acute or acute on chronic cholecystitis. Laparoscopic Cholecystectomy feasible. Relatively low; operating room time, bile leak rate, length of stay, and conversion rate.
3	Presence of ANY of the following: Hyperemia, pericholecystic fluid, adhesions to the body, distended gallbladder	Higher risk of operative difficulties compared to grades 1 and 2. Laparoscopic cholecystectomy feasible but impact on operative time and complications not predictable.
4	Presence of ANY of the following: Adhesions obscuring majority of gallbladder Grade I-III with abnormal liver anatomy, intrahepatic gallbladder, or impacted stone (Mirizzi)	Higher risk of operative difficulties compared to grades 1 and 2. Laparoscopic cholecystectomy feasibility is unclear and impact on operative time and complications not predictable.
5	Presence of ANY of the following: Perforation, necrosis, inability to visualize the gallbladder due to adhesions	High risk for longer operative time, increased operative difficulty, and increased post-operative complication rate compared to lower grades. Gangrenous cholecystitis likely. High concern for conversion to open.

Table 2
Tokyo Guidelines 2018 severity grade for acute cholecystitis.

Grade III (severe) acute cholecystitis
<p>“Grade III” acute cholecystitis is associated with dysfunction of any one of the following organs/systems:</p> <ol style="list-style-type: none"> 1. Cardiovascular dysfunction: hypotension requiring treatment with dopamine ≥ 5 $\mu\text{g}/\text{kg}$ per min, or any dose of norepinephrine 2. Neurological dysfunction: decreased level of consciousness 3. Respiratory dysfunction: $\text{PaO}_2/\text{FiO}_2$ ratio < 300 4. Renal dysfunction: oliguria, creatinine > 2.0 mg/dl 5. Hepatic dysfunction: $\text{PT-INR} > 1.5$ 6. Hematological dysfunction: platelet count $< 100,000/\text{mm}^3$ <p>Impact: High rates of intraoperative bile duct injury, gangrenous/emphysematous cholecystitis, conversion from laparoscopic to open approach, 30-day mortality, and length of stay. In most situations, patients should avoid going to the operating room and early pre-operative drainage procedure (transhepatic, percutaneous cholecystostomy, etc.) attempted instead.</p> <p>Grade II (moderate) acute cholecystitis</p> <p>“Grade II” acute cholecystitis is associated with any one of the following conditions:</p> <ol style="list-style-type: none"> 1. Elevated WBC count ($> 18,000/\text{mm}^3$) 2. Palpable tender mass in the right upper abdominal quadrant 3. Duration of complaints > 72 h^a 4. Marked local inflammation (gangrenous cholecystitis, pericholecystic abscess, hepatic abscess, biliary peritonitis, emphysematous cholecystitis) <p>Impact: Moderate rates of intraoperative complications, conversion from laparoscopic to open approach, and length of stay. 30 day mortality not significantly higher than grade 1. Early cholecystectomy is feasible but may be challenging if proper resources for adequate management (instruments, assistants, etc.) are not available. In such cases, consider early drainage procedure to bridge until of necessary resources attained.</p> <p>Grade I (mild) acute cholecystitis</p> <p>“Grade I” acute cholecystitis does not meet the criteria of “Grade III” or “Grade II” acute cholecystitis. It can also be defined as acute cholecystitis in a healthy patient with no organ dysfunction and mild inflammatory changes in the gallbladder, making cholecystectomy a safe and low-risk operative procedure</p> <p>Impact: Low relative risk of intraoperative complications, prolonged length of stay, and 30-day mortality. Rates of conversion from laparoscopic to open approach significantly lower than Grade III. Early cholecystectomy can be sought in most cases.</p>

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Table 3
AAST EGS grade descriptions of acute cholecystitis severity.

Grade	Description	Imaging	Operative	Management
Grade I	Localized gallbladder inflammation	Wall thickening, pericholecystic fluid, nonvisualization of the gallbladder	Localized inflammatory changes	Laparoscopic cholecystectomy with low risk of conversion to open.
Grade II	Distended gallbladder with purulence or hydrops, necrosis/gangrene of wall noted without iatrogenic perforation	Above plus air in the gallbladder lumen, wall or biliary tree	Distended gallbladder with pus/hydrops, nonperforated wall necrosis/gangrene	Laparoscopic cholecystectomy with low risk of conversion to open.
Grade III	Noniatrogenic perforation with bile located to RUQ	Extraluminal fluid collection limited to RUQ	Noniatrogenic gallbladder wall perforation with bile limited to RUQ	Laparoscopic cholecystectomy with risk of conversion to open. Consider percutaneous, cholecystostomy, if severe comorbidities.
Grade IV	Pericholecystic abscess, bilioenteric fistula, gallstone ileus	RUQ abscess, bilioenteric fistula, gallstone ileus	Pericholecystic abscess, bilioenteric fistula, gallstone ileus	Laparoscopic cholecystectomy with high probability of conversion to open. Consider open cholecystectomy initially. Consider percutaneous cholecystostomy if severe comorbidities.
Grade V	Grade IV disease but with generalized peritonitis	Free intraperitoneal fluid	Above with generalized peritonitis	Laparoscopic cholecystectomy with high probability of conversion to open. Consider open cholecystectomy initially. Consider percutaneous cholecystostomy if severe comorbidities.

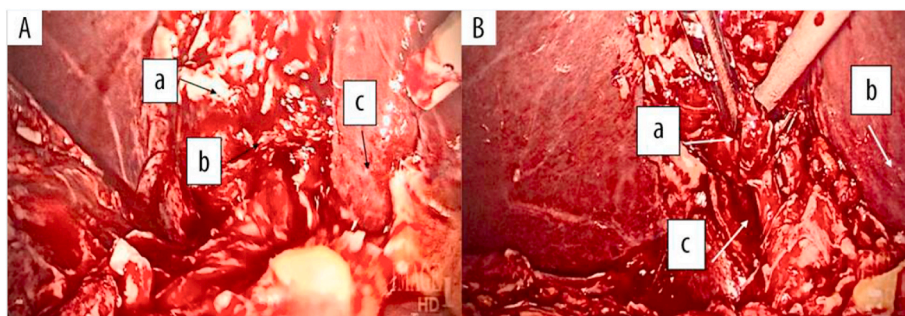


Fig. 1. (A) Laparoscopic imaging of the gallbladder showing suppurative inflammation and unrecognizable views/anatomy of the gallbladder. Gallbladder infundibulum (a), medial edge of liver (b), cystic duct (c). (B) Laparoscopic imaging of the gallbladder showing suppurative inflammation and unrecognizable views of the gallbladder. Pus (a), distorted gallbladder anatomy (b), medial edge of liver (c).

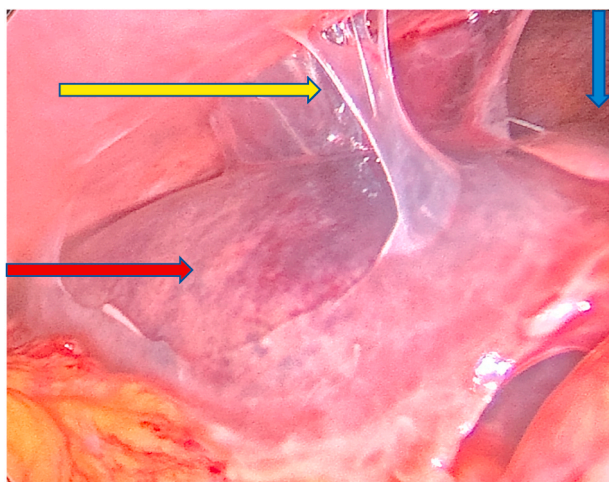


Fig. 2. Intraoperative findings of a gangrenous and necrotic gallbladder with adhesions to the anterior abdominal wall (yellow arrow pointing to the gallbladder, red arrow pointing to adhesions, blue arrow pointing to the edge of the liver). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

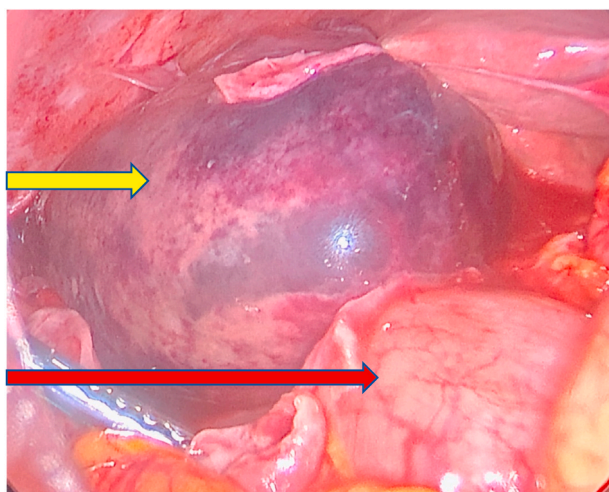


Fig. 3. Intraoperative findings of a gangrenous and necrotic gallbladder seen extending over the distal stomach causing mass effect (yellow arrow pointing to gallbladder, red arrow pointing to stomach). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

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 Manuscript preparation: Adel Elkbuli, Kyle Kinslow, Evander Meneses, Mark McKenney, Dessy Boneva.
 Critical revision of manuscript: Adel Elkbuli, Kyle Kinslow, Evander Meneses, Mark McKenney, Dessy Boneva.
 All authors read and approved the final manuscript

Ethical approval

Patient Informed written consent has been obtained and all identifying information was omitted.

Table 4
 Modified Parkland grading scale for cholecystitis accounting for uncommon presentations of acute cholecystitis.

Cholecystitis Severity Grade	Description of Severity
1	Normal appearing gallbladder (“robin’s egg blue”) No adhesions present
2	Completely normal gallbladder Minor adhesions at neck, otherwise normal gallbladder
3	Adhesions restricted to the neck or lower of the gallbladder Presence of ANY of the following: Hyperemia, pericholecystic fluid, adhesions to the body, distended gallbladder
4	Presence of ANY of the following: Adhesions obscuring majority of gallbladder Grade I-III with abnormal liver anatomy, intrahepatic gallbladder, or impacted stone (Mirizzi) Large gallbladder (>10 × 5cm)
5	Presence of ANY of the following: Perforation, necrosis, inability to visualize the gallbladder due to adhesions Distorted anatomy causing difficulty obtaining critical view of safety

Guarantor

The Guarantor is the one or more people who accept full responsibility for the work and/or the conduct of the study, had access to the data, and controlled the decision to publish. Please note that providing a guarantor is compulsory.

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Conflicts of interests

Authors declare no competing interests.

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