Clinical Infectious Diseases

IDSA GUIDELINES

2024 Clinical Practice Guideline Update by the Infectious Diseases Society of America on Complicated Intra-abdominal Infections: Risk Assessment in Adults and Children

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This paper is part of a clinical practice guideline update on the risk assessment, diagnostic imaging, and microbiological evaluation of complicated intra-abdominal infections in adults, children, and pregnant people, developed by the Infectious Diseases Society of America. In this paper, the panel provides a recommendation for risk stratification according to severity of illness score. The panel's recommendation is based on evidence derived from systematic literature reviews and adheres to a standardized methodology for rating the certainty of evidence and strength of recommendation according to the GRADE (Grading of Recommendations, Assessment, Development, and Evaluation) approach.

Keywords. intra-abdominal infection; risk assessment; risk stratification; severity of illness; guideline.

In adults and children with complicated intra-abdominal infection, which severity of illness score for risk stratification calculated within 24 hours of hospital or intensive care unit (ICU) admission best predicts 30-day or in-hospital mortality?

Recommendation: Risk stratification according to severity of illness is important for management of complicated intra-abdominal infection. For adults with complicated intra-abdominal infection, if a severity of illness score is used, the panel suggests APACHE II (Acute Physiology Age Chronic Health Evaluation II) as the preferred severity of illness score for risk stratification within 24 hours of hospitalization or ICU admission *(conditional recommendation, low certainty of evidence).*

Remarks:

- Because the WSES (World Society of Emergency Surgery) Sepsis Severity Score is specific to complicated intra-abdominal infection and performs well, it is an acceptable alternative to APACHE II for adults with complicated intra-abdominal infection.
- No severity of illness scoring system specific to complicated intra-abdominal infection can be recommended to guide management of pediatric patients with complicated intra-abdominal infection at present.

This paper is part of a clinical practice guideline update on the risk assessment, diagnostic imaging, and microbiological

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evaluation of complicated intra-abdominal infections in adults, children, and pregnant people, developed by the Infectious Diseases Society of America [1–7]. Here, the guideline panel provides a recommendation for risk stratification in adults with complicated intra-abdominal infection, according to severity of illness as determined by a scoring system. This recommendation replaces previous statements in the last iteration of this guideline [8].

A complicated intra-abdominal infection extends beyond the hollow viscus of origin into the peritoneal space and is associated with either abscess formation or peritonitis; this term is not meant to describe the infection's severity or anatomy. An uncomplicated intra-abdominal infection involves intramural inflammation of the gastrointestinal tract and has a substantial probability of progressing to complicated infection if not adequately treated.

This recommendation is intended for use by healthcare professionals who care for patients with suspected intra-abdominal infections.

METHODS

The panel's recommendation is based on evidence derived from systematic literature reviews and adheres to a standardized methodology for rating the certainty of evidence and strength of recommendation according to the GRADE (Grading of Recommendations Assessment, Development, and Evaluation) approach (Supplementary Figure 1) [9]. The recommendation has been endorsed by the European Society of Clinical Microbiology and Infectious Diseases (ESCMID) and the Pediatric Infectious Diseases Society (PIDS). Strong recommendations are made when the recommended course of action would apply to most people with few exceptions. Conditional recommendations are made when the suggested course of action would apply to the majority of people with many exceptions and shared decision making is important.

A comprehensive literature search (through October 2022) was conducted as part of a systematic review. Key eligibility criteria at both the topic and clinical question levels guided the search and selection of studies. For the clinical question addressed here, the panel considered patients with complicated intra-abdominal infection who received a scoring tool to assess risk. Studies reporting on 30-day or in-hospital mortality that referenced adjusted, multivariate analyses were included. Refer to the full list of eligibility criteria in the Supplementary Material.

Odds ratios, hazard ratios, and/or risk ratios or area under the receiver operating characteristic (ROC) curve and 95% confidence intervals (CIs) were generated for each scoring tool using random effects meta-analysis of pooled results [10]. Included studies underwent critical appraisal according to the GRADE approach, and then an assessment of benefits and harms of care options informed the recommendation [9, 11]. Details of the systematic review and guideline development processes are available in the Supplementary Material.

SUMMARY OF EVIDENCE

Severity of illness assessment can be helpful in risk stratification and for choosing treatment strategies for patients with complicated intra-abdominal infection. Although several severity of illness scoring tools have been studied in patients with complicated intra-abdominal infection, none had been subjected to a rigorous systematic review and meta-analysis.

Severity of Illness Scoring Systems for Complicated Intra-abdominal Infection

Over 20 different severity of illness scoring systems have been reported in the studies found. The 4 most common scoring systems were all disease-nonspecific and included: APACHE II [12], SOFA (Sequential Organ Failure Assessment) [13], SAPS II (Simplified Acute Physiology Score II) [14], and ASA (American Society of Anesthesiologists) [15]. APACHE II was introduced in 1985 to reflect both premorbid factors such as patient age and chronic medical conditions, as well as acute changes in 12 physiologic parameters [12]. SOFA was introduced in 1996 to assess patients with sepsis-associated multiple organ failure or dysfunction in critical care units [13]. The score is based on 6 different organ systems (respiratory, cardiovascular, hepatic, coagulation, renal, and neurological) but does not include age and chronic health or comorbidities. SAPS II was introduced in 1993 based on logistic regression modeling of a North American/European multicenter study of adult ICU patients [14]. Scoring was based on 12 physiologic variables, age, type of hospital admission, and 3 variables related to underlying disease. ASA was originally developed in 1941 to assess anesthetic risks but was later found to also be useful for assessing surgical risks [15]. These 4 scoring systems were selected for systematic review and meta-analyses (Supplementary Table 1). Only 5 of the severity scoring systems were disease-specific and validated for patients with different complicated intra-abdominal infections: Peptic Ulcer Perforation score (PULP) [16, 17]; WSES Sepsis Severity score for patients with complicated intra-abdominal infection [18]; and Ranson [19], Glasgow, and BISAP (Bedside Index of Severity in Acute Pancreatitis) [20] for acute necrotizing pancreatitis. The WSES Sepsis Severity score was derived in Europe from 6 clinical determinants found to be independent predictors of hospital mortality among patients with complicated intra-abdominal infection (clinical condition of the patient on admission with either severe sepsis or shock, healthcare-associated infection, gastrointestinal origin of infection, delayed initial intervention >24 hours, age >70 years, and presence of immunosuppression) [18]. This scoring tool was also included for further analysis because it was specifically

developed for mortality prediction in all patients with complicated intra-abdominal infection (Supplementary Table 1). All other scoring systems were developed primarily for patients managed in ICUs not necessarily with complicated intra-abdominal infection.

Mortality Risk by Different Severity Scoring Systems

The performance of each severity of illness scoring system was compared by their odds ratio (OR), hazard ratio (HR), risk ratio (RR), or ROC (AUC) for mortality prediction. APACHE II was the most common independent prognostic factor for 30-day mortality identified by multivariate analyses (10 of 13 studies [21–33]), followed by SOFA (9 of 11 studies [33–43]), SAPS II (5 of 5 studies [35, 42, 44–46]), and ASA (4 of 7 studies [16, 25, 32, 36, 37, 47, 48]. For each scoring system, forest plots of the odds or other risk ratios and AUCs are shown in Supplementary Figures 2–6.

The ability of each severity scoring system to discriminate between patients who died or did not from complicated intra-abdominal infection was quantitated by the concordance I-statistic, also known as ROC or area under the receiver operating characteristic (AUC) curve [49]. The ROC ranges from 0.5 (no discriminative ability) to 1 (perfect discriminative ability). Values from 0.7–0.8 are considered acceptable, 0.8–0.9 as excellent, and <0.6 as poor. The available pooled ROC of these scoring systems is shown in Supplementary Figures 2–6. All 4 disease-non-specific scoring systems performed well since their pooled AUC values were close to 0.8. APACHE II and SOFA had the best discriminative power (pooled AUC of 0.81 and 0.75, respectively) [23, 27, 32, 42, 50–53]. ROC data were reported by only 1 study each for SAPS II (AUC 0.83), ASA (0.70), and WSES Sepsis Severity Score (0.83) [42, 54, 55].

The evidence underpinning this recommendation is of low certainty due to study risk of bias concerns (according to QUIPS assessment; Supplementary Tables 2a–e) [56, 57]; inconsistency of results for the APACHE II studies, specifically; imprecision; and suspected publication bias due to reporting statistically significant risk factors only (Supplementary Table 3).

Other Independent Risk Factors for Mortality

A total of 36 other independent risk factors besides severity of illness scores were identified from 34 studies (Supplementary Table 4) [16–18, 21, 22, 24, 26, 28, 31, 34, 35, 39, 42, 44–47, 53, 58–72]. Where more than 1 study identified the same risk factor, the pooled OR and 95% CI was reported and only if statistically significant. These risk factors were categorized into (a) non-modifiable (16 factors) and (b) potentially modifiable (20 factors). Among the latter, presence of renal (10 studies), cardiovascular (5 studies) or respiratory (4 studies) dysfunction, sepsis (3 studies) or shock (5 studies), inadequate source control (3 studies), delayed (>24 hours) source control (5 studies), and inappropriate antimicrobial therapy (5 studies) were the statistically significant independent mortality risk factors in adult patients with complicated intra-abdominal infection.

RATIONALE FOR RECOMMENDATION

APACHE II was chosen over other severity of illness scoring systems for risk assessment of patients with complicated intra-abdominal infection because: (a) even though this tool is disease-non-specific, it has been rigorously tested in patients with complicated intra-abdominal infection and variable severity of illness; (b) it appears to be valid independent of the source or site of infection; (c) it has acceptable discriminative power as determined by ROC assessment; (d) in a retrospective study of 544 patients with complicated intra-abdominal infection, after multivariate analysis of 37 variables, it was found to be 1 of 6 independent predictors for mortality, whereas SOFA was not [33]; (e) it is relatively easy to calculate for all patients within 24 hours of hospital admission, and a user-friendly calculator is available online (http://www.globalrph.com/apacheii.htm).

SOFA was not selected for 3 reasons: (a) SOFA was developed originally to sequentially assess the degree of multiple organ failure in critically ill patients with sepsis, but is not suitable for categorizing patients with low-moderate severity without sepsis or organ failure within 24 hours of hospital admission; (b) SOFA was not intended to indicate the success or failure of interventions or to influence medical management [13]; (c) SOFA assesses the dysfunction of six organ systems (respiratory, cardiovascular, neurologic, renal, hepatic, coagulation) but does not take into consideration age and chronic health or comorbidities, which are important components of APACHE II. Although SAPS II performed well, it was evaluated in 5 studies with more limited study populations. Additionally, only 1 study reported ROC data for discriminative power. Similarly, ASA was evaluated in 7 studies and was found to be an independent predictor for mortality in only 4. ASA is also less precise and subject to inter-observer bias compared to other severity scoring systems [73]. WSES Sepsis Severity Score, the only disease-specific scoring tool for complicated intra-abdominal infection, also performed well; however, only moderately ill patients were included in these studies. This scoring system was developed and validated based on findings of a large multicenter study of patients with complicated intra-abdominal infection spanning 54 countries worldwide [18], and then validated in two single-center prospective studies from the United Arab Emirates (multivariate model) [74] and Kenya (univariate model) [75]. Importantly, the overall mortality in these studies was relatively low, ranging from 1% to 12.8% (mean 9.1%), and the most common complicated intra-abdominal infections included in these studies were perforated

appendicitis or duodenal perforation. It is unclear if the WSES sepsis severity score is generalizable to more seriously ill patients.

At present, no specific risk stratification scheme can be recommended to guide management of pediatric patients with complicated intra-abdominal infection. Although some scoring systems, including PRISM (Pediatric Risk of Mortality) [76], PIM (Pediatric Index of Mortality) [77], and PELOD-2 (Pediatric Logistic Organ Dysfunction-2) [78] have been validated for children admitted to pediatric intensive care units (PICUs), they are primarily used as tools for quality assessment and performance measures of PICUs. Their utility as a tool to guide individual patient management in disease-specific conditions such as complicated intra-abdominal infection both inside and outside of the PICU setting remains unclear.

IMPLEMENTATION CONSIDERATIONS

Risk stratification based on severity of illness is an important predictor of mortality in patients with complicated intra-abdominal infection and can guide appropriate therapy and urgency of source control. It is best to determine risk as early as possible, preferably within 24 hours of hospital admission. Risk groups based on APACHE II scores can be categorized into "low" (0–10), "intermediate" (11–15), and "high" (>15), with predicted mortality of 20%–30% in the "intermediate" risk group and ∼50% in the "high" risk group in patients with complicated intra-abdominal infection [49]. It is equally important to identify other independent risk factors for mortality not captured by APACHE II in "low" risk patients.

RESEARCH NEEDS

Just prior to publication, a new pediatric sepsis score was published, the Phoenix Sepsis Score [79, 80]. The score has been validated in pediatric emergency department, inpatient, and ICU settings. Future studies applying the Phoenix Sepsis Score, PRISM, PIM, and PELOD-2 to intra-abdominal infection specifically would be very helpful. Additionally, further validation of the WSES Sepsis Severity Score in more critically ill patients would be beneficial.

Supplementary Data

Supplementary Materials are available at *Clinical Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Notes

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Dr Robert Bonomo is chair of the panel. Drs Anthony Chow and Robert Bonomo served as clinical leads for the questions addressed in this manuscript. All panelists assisted with conception and design of the analysis, interpretation of data, drafting and revising the recommendations and manuscript, and final approval of the recommendations and manuscript to be published. Jennifer Loveless, lead methodologist, and Katelyn Donnelly, methodologist, were responsible for project management, designing and performing the data analyses, and leading the panel according to the GRADE process.

Additional information. More detailed information on the analysis and development of recommendations is available in the Supplementary Material.

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