

## IDS A GUIDELINES

# 2024 Clinical Practice Guideline Update by the Infectious Diseases Society of America on Complicated Intra-abdominal Infections: Diagnostic Imaging of Suspected Acute Cholecystitis and Acute Cholangitis in Adults, Children, and Pregnant People

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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 recommendations for diagnostic imaging of suspected acute cholecystitis or acute cholangitis. The panel's recommendations are based upon evidence derived from systematic literature reviews and adhere 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.

**Key words.** intra-abdominal infection; acute cholecystitis; acute cholangitis; guideline

**In adults with suspected acute cholecystitis or acute cholangitis, should abdominal ultrasound (US) or computed tomography (CT) be obtained as the initial imaging modality?**

**In adults with suspected acute cholecystitis or acute cholangitis, if initial imaging is inconclusive, should CT, MRI (magnetic resonance imaging)/MRCP (magnetic resonance cholangiopancreatography), or HIDA (hepatobiliary iminodiacetic acid) be obtained for subsequent imaging?**

**Recommendation:** In non-pregnant adults with suspected acute cholecystitis or acute cholangitis, the panel suggests abdominal US as the initial diagnostic imaging modality (*conditional recommendation, very low certainty of evidence*).

**Remarks:**

- The diagnosis of acute cholangitis should include clinical signs (jaundice, fever, chills, and right upper quadrant [RUQ] abdominal pain), laboratory findings (indicators of

inflammation and biliary stasis), and imaging findings (biliary dilatation, or evidence of an etiology, e.g., stricture, stone, obstructing mass).

- The panel did not identify any studies assessing the accuracy of abdominal US or CT for the diagnosis of acute cholangitis and relied on indirect evidence from acute cholecystitis.
- Because acute cholecystitis and acute cholangitis are uncommon in children, evidence in children was not systematically reviewed; however, it would be reasonable to mirror the imaging pathway for adults in children.

**Recommendation:** In non-pregnant adults with suspected acute cholecystitis or acute cholangitis, if initial US is equivocal/non-diagnostic and clinical suspicion persists, the panel suggests obtaining an abdominal CT scan as subsequent imaging to diagnose acute cholecystitis or acute cholangitis (*conditional recommendation, very low certainty of evidence*).

**Remarks:**

- The diagnosis of acute cholangitis should include clinical signs (jaundice, fever, chills, and RUQ abdominal pain), laboratory findings (indicators of inflammation and biliary stasis), and imaging findings (biliary dilatation, or evidence of an etiology, e.g., stricture, stone, obstructing mass).
- CT with IV contrast is preferable and usually appropriate when CT is obtained for subsequent imaging [1].
- The panel did not identify any studies assessing the accuracy of abdominal US or CT for the diagnosis of acute cholangitis and relied on indirect evidence from acute cholecystitis.
- Because acute cholecystitis and acute cholangitis are uncommon in children, evidence in children was not systematically reviewed; however, it would be reasonable to mirror the imaging pathway for adults in children.

**Recommendation:** In non-pregnant adults with suspected acute cholecystitis, if both US and CT are equivocal/non-diagnostic and clinical suspicion persists, the panel suggests obtaining either an abdominal MRI/MRCP or hepatobiliary iminodiacetic acid (HIDA) scan as subsequent imaging to diagnose acute cholecystitis (*conditional recommendation, low certainty of evidence for HIDA, knowledge gap for MRI/MRCP*).

**Remarks:**

- If both abdominal US and CT are inconclusive but acute *cholangitis* is suspected, MRI/MRCP is a reasonable option.
- The diagnosis of acute cholangitis should include clinical signs (jaundice, fever, chills, and RUQ abdominal pain), laboratory findings (indicators of inflammation and biliary stasis), and imaging findings (biliary dilatation, or evidence of an etiology, e.g., stricture, stone, obstructing mass).

- Because acute cholecystitis and acute cholangitis are uncommon in children, evidence in children was not systematically reviewed; however, it would be reasonable to mirror the imaging pathway for adults in children.

**In pregnant people with suspected acute cholecystitis or acute cholangitis, should abdominal US or MRI be obtained as the initial imaging modality?**

**Recommendation:** In pregnant people with suspected acute cholecystitis or suspected acute cholangitis, US or MRI can be considered as the initial diagnostic imaging modality; however, the panel is unable to recommend one imaging modality versus the other (*knowledge gap*).

**Remarks:**

- The diagnosis of acute cholangitis should include clinical signs (jaundice, fever, chills, and RUQ abdominal pain), laboratory findings (indicators of inflammation and biliary stasis), and imaging findings (biliary dilatation, or evidence of an etiology, e.g., stricture, stone, obstructing mass).

## INTRODUCTION

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 [2-8]. Here, the guideline panel provides recommendations for diagnostic imaging of suspected acute cholecystitis (both acalculous and calculous) and acute cholangitis in adults and pregnant people, along with remarks for applying these recommendations in children. Recommendations are stratified by initial imaging and then subsequent imaging if initial imaging is inconclusive. These recommendations replace previous statements in the last iteration of this guideline [9].

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.

These recommendations are intended for use by healthcare professionals who care for patients with suspected intra-abdominal infections.

## METHODS

The panel's recommendations are based upon evidence derived from systematic literature reviews and adhere 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) [10]. The recommendations have 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 questions addressed here, the panel considered adults with suspected *acute* cholecystitis (calculous or acalculous) or *acute* cholangitis, gangrenous cholecystitis, and/or emphysematous cholecystitis, and excluded patients with stiffness or fibrosis only (without evidence of infection) and chronic processes. Because acute cholecystitis and acute cholangitis are uncommon in children, evidence in children was not systematically reviewed. Though uncommon, certain conditions (e.g., biliary atresia, sickle cell disease) may raise the risk of acute cholecystitis or cholangitis in children, in which case the panel felt it reasonable to mirror the imaging pathway for adults. Ultrasound, CT (including multidetector CT), MRI, MRCP, and HIDA scan were reviewed as possible imaging modalities, whereas magnetic resonance elastography (MRE), endoscopic retrograde cholangiopancreatography (ERCP), and point-of-care US (POCUS) were excluded. Though POCUS is used frequently, only studies assessing ultrasounds performed in a controlled manner and interpreted by a radiologist were included, primarily due to the variability in interpretation of POCUS. ERCP was not included because it is more invasive and is employed for both diagnostic and therapeutic purposes. Observational studies published after 2010 and randomized controlled trials were screened for inclusion. Due to a lack of studies addressing MRI, the publication date limit was expanded to include observational studies published in 2005 or thereafter for MRI only. Refer to the full list of eligibility criteria in the Supplementary Material.

Sensitivities, specificities, and corresponding 2X2 tables were plotted in RevMan based on the population and imaging study [11]. Included studies underwent critical appraisal according to the GRADE approach, and then an assessment of benefits and harms of care options informed the recommendation(s) [10, 12]. Details of the systematic review and guideline development processes are available in the Supplementary Material.

### **Summary of Evidence**

Six observational studies were identified for the analysis on whether to use US or CT as initial imaging for diagnosing acute cholecystitis in adults with suspected acute cholecystitis [13-18] (Supplementary Table 1). All included studies examined US; median sensitivity was 73% (range 32-83%) and median specificity was 83% (range 46-88%) (Supplementary Figure 2). Only 1 study reported on CT [16] which demonstrated a sensitivity of 73% and a specificity of 94%

(Supplementary Figure 3). In addition to these, another study reported a sensitivity of 88% when using either US or CT to diagnose acute cholecystitis; however, only patients with confirmed acute cholecystitis were studied (retrospectively) [19].

The panel did not find any studies to include in our analysis on whether to use US or CT as initial (or subsequent) imaging for diagnosing acute cholangitis. Instead, the panel considered the evidence on acute cholecystitis as indirect evidence for this patient population and supposed this approach appropriate since at the time of ordering initial imaging, distinguishing between suspected cholecystitis and acute cholangitis is likely challenging.

A comprehensive search was conducted and three observational studies that reviewed the diagnostic accuracy of HIDA for suspected acute cholecystitis were found [13,14,16]. Median (range) sensitivity and specificity for HIDA were 89% (85-92%) and 67% (34-86%), respectively (Supplementary Figure 4). No studies addressing MRI/MRCP in this patient population were found, even after expanding the publication date limit by an additional 5 years (2005 on).

The evidence comparing US and CT in patients with suspected acute cholecystitis is of very low certainty due to study risk of bias (according to QUADAS-2 assessment; Supplementary Table 2) [20,21], indirectness from indirect comparisons, and inconsistency of the results (Supplementary Table 3). For patients with suspected acute cholecystitis, no studies on MRI/MRCP were found, and the evidence evaluating HIDA is of low certainty due to indirectness of comparisons and inconsistency of the results (particularly for specificity) (Supplementary Table 4). The evidence comparing US and CT in patients with suspected acute cholangitis is also of very low certainty due to the reasons described above for patients with suspected acute cholecystitis, along with an additional layer of indirectness in patient populations assessed (Supplementary Table 5). No studies addressing diagnostic accuracy of imaging modalities for pregnant patients with suspected acute cholecystitis or acute cholangitis were identified. However, the panel considered evidence from non-pregnant adults, along with the balance between benefits and harms (e.g., radiation exposure) of each imaging modality. Additional analyses were performed that were considered informative but not essential to formulating the recommendation (Supplementary Tables 6-7).

### **Rationale for Recommendations**

In non-pregnant adults and children with suspected acute cholecystitis or acute cholangitis, US is suggested as the initial imaging modality over CT because it is reasonably accurate and useful in identifying gallstones, less costly, and more portable, and results are generally available in a timelier manner. Additional benefits include the avoidance of radiation exposure (particularly important for children) and contrast-associated side effects that may be encountered with CT. US is more operator-dependent than CT and may not be as accurate in obese patients, but the desirable effects of US outlined above outweigh these undesirable effects.

CT is suggested as the subsequent imaging modality for non-pregnant adults and children due to its ability to identify complications and rule out other etiologies. If additional imaging beyond US

is required, the risk-to-benefit ratio of radiation exposure for CT should be considered (particularly for children). If CT is also equivocal and acute cholecystitis, specifically, is suspected, MRI/MRCP and HIDA are both reasonable options as subsequent imaging studies beyond CT. The benefits of MRI/MRCP as compared to HIDA are that these studies provide a clearer picture of the surrounding structures and a faster time to result, in addition to being more readily available. On the other hand, HIDA is considered the gold standard for diagnosing acute cholecystitis and is far less costly than MRI/MRCP. However, a patient must fast for several hours before undergoing a HIDA scan.

In pregnant people with suspected acute cholecystitis or suspected acute cholangitis, US or MRI can be considered as the initial diagnostic imaging modality.

### **Implementation considerations**

US results may be limited by abdominal tenderness and patient obesity. For suspected acute cholecystitis in non-pregnant adults, if clinical suspicion for acute cholecystitis is high and initial US is equivocal, it may be appropriate to proceed directly from US to HIDA [22]. However, if other diagnostic possibilities are being considered for RUQ abdominal pain, it is reasonable to obtain a CT as subsequent imaging before a HIDA scan. Additionally, if complications of acute cholecystitis (e.g., biloma, intra-abdominal abscess, bile duct injury, hepatic injury, small bowel injury, infection, retained stones in the bile duct, bleeding) or acute cholangitis (e.g., hepatic abscess, portal vein thrombosis, acute biliary pancreatitis, liver failure) are suspected, CT should be obtained as subsequent imaging. CT with IV contrast is preferable and usually appropriate when CT is obtained for subsequent imaging [1].

The diagnosis of acute cholangitis should include clinical signs (jaundice, fever, chills, and RUQ abdominal pain), laboratory findings (indicators of inflammation and biliary stasis), and imaging findings (biliary dilatation, or evidence of an etiology, e.g., stricture, stone, obstructing mass).

### **Research needs**

More contemporary literature on the diagnostic accuracy of MRI/MRCP for acute cholecystitis and acute cholangitis would be very useful, especially since imaging technologies and techniques have evolved and advanced over time. Future research in pregnant women would be very informative. Head-to-head comparisons of different imaging modalities in these patient populations would also be valuable.

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

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