Clinical Assessment of Acute Cholecystitis in Adults

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RATIONAL CLINICAL EXAMINATION REVIEW SOURCE

This is a rational clinical examination abstract, a regular feature of the *Annals'* Evidence-Based Emergency Medicine (EBEM) Series. Each features an abstract of a rational clinical examination review from the *Journal of the American Medical Association* and a commentary by an emergency physician knowledgeable in the subject area.

The source for this rational clinical examination review abstract is: RL Trowbridge, NK Rutkowski, KG Shojania. The rational clinical examination: does this patient have acute cholecystitis? *JAMA*. 2003;289:80-86. The *Annals'* EBEM editors assisted in the preparation of the abstract of this rational clinical examination review, as well as the selection of the Evidence-Based Medicine Teaching Points.

OBJECTIVE

To evaluate the effectiveness of components of medical history, physical examination, and laboratory testing to determine which patients require additional investigations to validate the presence or absence of acute cholecystitis.

DATA SOURCES

The authors used data obtained from 4 sources: a MEDLINE search from January 1966 to November 2000, the Science Citation Index, Cochrane Library, and a hand search of Index Medicus from 1950 through 1965. In addition, the MEDLINE search was repeated in July 2002 to look for relevant, recent studies. The search was conducted using the Medical Subject Headings of "acute abdomen," "abdominal pain," "cholecystitis," "cholelithiasis," "gallbladder," and "gallbladder diseases," with various combinations of text and title words related to medical history, physical examination, and diagnostic testing.

STUDY SELECTION

For inclusion, studies had to evaluate a clinical or laboratory test in adult patients with abdominal pain or suspected cholecystitis, using a control group. Furthermore, the reference standard for acute cholecystitis had to be defined on the basis of surgery and pathologic examination, radiographic imaging (hepatic iminodiacetic acid scan or abdominal ultrasound), or clinical follow-up that documented a course consistent with acute cholecystitis without an evident alternate diagnosis.

DATA EXTRACTION AND ANALYSIS

Seventeen of 195 identified studies met inclusion criteria. Twelve studies entered patients suspected of having acute cholecystitis, whereas the remaining 5 included patients with abdominal pain but did not require the specific suspicion for acute cholecystitis. Eight of the 17 studies were prospective. The published raw data were tabulated for each of the evaluated components of clinical examination and basic laboratory tests, and sensitivities were calculated from the data summaries. A random effects model was used to develop pooled likelihood ratios and confidence intervals for each component.

MAIN RESULTS

The authors note that although the precision of laboratory measures is relatively well defined, the interrater reliability of components of clinical diagnosis, including historical features and physical examination findings such as tenderness or guarding, remains unclear. Each of the 17 studies evaluated a variable number (1 to 9) of both clinical and laboratory diagnostic criteria. Selected results are summarized in the Table.

No single clinical or laboratory finding demonstrated a likelihood ratio sufficiently low to rule out or sufficiently high to rule in the diagnosis of acute cholecystitis. The authors point out that 2 confounding variables with this disease process are the elderly, in whom right upper quadrant signs are often absent, and the nonspecific presentation of acalculous cholecystitis, a disease more often observed in critically ill inpatients.

Interestingly, elevation of any one of the 3 classically elevated liver function markers only improved sensitivity to 0.70 and did not improve the likelihood ratio. Similarly, the combination of leukocytosis and fever increased specificity to 0.85 but did not appreciably affect the likelihood ratios. No other combinations of findings were evaluated.

CONCLUSIONS

The evaluation of clinical and laboratory findings to diagnose acute cholecystitis is hampered by a lack of sufficient

Table. Summary test characteristics for selected clinical and laboratory findings.

Findings	Studies, No.	Subjects, No.	Sensitivity	Specificity	+LR	–LR
Clinical						
Fever	8	1,292	0.35	0.80	1.5	0.9
Nausea	2	669	0.77	0.36	1.5	0.9
Emesis	4	1,338	0.71	0.53	1.5	0.6
RUQ pain	5	949	0.81	0.67	1.5	0.7
RUQ tenderness	4	1,001	0.77	0.54	1.6	0.4
Murphy's sign	3	565	0.65	0.87	2.8	0.5
Laboratory						
Leukocytosis >10, 000/mL	7	1,197	0.63	0.57	1.5	0.6
AP >120 U/L	4	556	0.45	0.52	0.8	1.1
Elevated AST or ALT	5	592	0.38	0.62	1.0	1.0
TB >2 mg/dL	6	674	0.45	0.63	1.3	0.9
Elevated AP, AST, or TB	1	270	0.70	0.42	1.2	0.7

ALT, Alanine aminotransferase; *AP,* alkaline phosphatase; *AST,* aspartate aminotransferase; *RUQ,* right upper quadrant; *TB,* total bilirubin.

investigation and methodologic flaws in existing literature. Future study of combinations of various findings may allow identification of patients who do not require additional testing. However, for the moment, for patients with abdominal pain suggestive of acute cholecystitis, we must rely on the clinical impression supplemented by diagnostic imaging.

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COMMENTARY: CLINICAL IMPLICATION

Acute cholecystitis is observed with an annual prevalence rate of 3% in western societies, and more than 500,000 annual cholecystectomies are performed each year in the United States.[1] Given the potential morbidity and the high rate of associated emergency department visits, the emergency physician must be comfortable with the clinical examination of possible acute cholecystitis. This methodologically rigorous review of the literature identified 17 relatively weak studies that failed to clearly identify clinical or laboratory features that confirm the presence or absence of acute cholecystitis. Although 9 of the 17 included studies were retrospective and had the limitations inherent in that study design, there was also the effect of verification (ie, "evaluation") bias. As the authors note, 12 of the included studies specifically relied on the enrollment of patients already suspected of having acute cholecystitis (eg, patients referred for ultrasonography or hepatic iminodiacetic acid scan), presumably because of positive findings on medical history and physical examination or laboratory testing. Therefore, some patients with falsely negative results on these screening tests would not be included in the study. The exclusion of false negatives would have the effect of overestimating sensitivity and underestimating specificity.

Laboratory findings performed as poorly as individual clinical findings in differentiating acute cholecystitis from other conditions. The study by Gruber et al[2] found a mean leukocyte count of 12,600/mm^3, with an SD of 4,300/mm^2 in 198 patients with cholecystitis. A range similar to that of leukocyte counts was found in 26% of patients with abdominal pain of unknown cause[2] and 43% of gastroenteritis cases.[3] Another evidence-based diagnostic review has also found the leukocyte count to be of questionable value in contributing to the diagnosis of acute appendicitis.[4]

Conversely, although the individual contributions of right upper quadrant tenderness, Murphy's sign, and elevated leukocyte count appear to be small (not nearly enough to consider them decisive), the absence of each these findings appeared to decrease the likelihood of cholecystitis more than other findings (likelihood ratio [LR]– of 0.4, 0.5, and 0.6, respectively). Emesis, right upper quadrant pain, right upper quadrant tenderness, Murphy's sign, and leukocytosis all demonstrated negative likelihood ratios below 1.0, with confidence intervals including 0.5, indicating that their absence may contribute incrementally to ruling out acute cholecystitis. Other findings failed to demonstrate utility in ruling out the disease.

Because no one clinical finding was suitably discriminative, it may be tempting to conclude that physical examination skills are of little value in diagnosing acute cholecystitis. In fact, the truth is likely to be the opposite, for a variety of reasons. Most important, no study has examined the sensitivities or LRs for combined clinical findings most likely used to develop a clinical suspicion of acute cholecystitis (eg, fever, nausea, and right upper quadrant pain). Because of the relatively small individual contribution of each finding, correct clinical assessment may require the cumulative use of multiple accurate findings, demanding more clinical acumen and skill rather than less. In addition, limited research has been conducted on the reliability of physical findings in the emergency setting. Clearly, this is an area of research need.

TAKE HOME MESSAGE

Until additional evidence emerges, physician judgment (or clinical "gestalt") will continue to be the driving force behind further diagnostic imaging studies for acute cholecystitis. Of the clinical signs tested, right upper quadrant tenderness or pain and Murphy's sign may contribute the most incrementally in helping to detect the disease, whereas absence of right-upper-quadrant pain may have the most value in terms of ruling out the disease.

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EBEM TEACHING POINT

Spectrum bias. Acute cholecystitis is thought to be part of the larger continuum of biliary tract disease and presents with nonspecific complaints. Spectrum bias occurs when there is an inadequate representation of the entire disease process or applicable disease-free states. In this case, the authors suggest the prevalence of cholecystitis in the study populations averaged 41% as opposed to the expected prevalence of 3% to 5% observed in patients with abdominal pain in an acute care setting. Thus, as in verification bias, a lower chance to detect true negatives and false positives would overestimate sensitivity and underestimate specificity when a test is applied to these study populations. The combination of these 2 types of bias must be taken into account with other limitations when the tabulated results are evaluated.[5-16]

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CORRECTION

The American Academy of Family Physicians (AAFP)-ACEP Joint Statement on Emergency Care was published incorrectly in the March 2006 issue of *Annals of Emergency Medicine*. The statement was a draft approved by the AAFP Board of Directors after negotiations with ACEP. Subsequent to the ACEP Board's adoption of the statement, the statement was rejected by AAFP's Congress in September 2005. The College regrets publication of the joint statement and apologizes for this oversight.