Efficacy of Hepatobiliary Imaging in Acute Abdominal Pain: Concise Communication

John E. Freitas, Darlene M. Fink-Bennett, James H. Thrall, William W. Resinger, Herminio C. Calderon, Seymour H. Mirkes, and Pradip K. Shah

University of Michigan Medical Center, Ann Arbor, Michigan and William Beaumont Hospital, Royal Oak, Michigan

To assess prospectively the usefulness of hepatobiliary imaging in acute abdominal pain (72 hr or less), 36 patients were scintigraphed after intravenous injection of 5 mCi of Tc-99m p-isopropyl-iminodiacetic acid (PIPIDA). Before the procedure, the referring physician completed Part I of a questionnaire indicating his differential diagnosis, diagnostic confidence (expressed as a percentage), and therapeutic plan. Immediately after the test, the same physician, with knowledge of the results, completed Part II of the questionnaire indicating again his differential diagnosis, diagnostic confidence, and therapeutic plan. The impact of the imaging on the physician's diagnostic confidence was expressed as a log-likelihood-ratio (LLR). The mean LLR for this series was 1.48 ± 0.93, with 33 of 36 (92%) patients demonstrating a LLR greater than 0.0. In 26 of 33 patients, a LLR greater than 1.0 was achieved; and in 11 of 36 patients, a change in the physician's therapeutic plan occurred, reflecting the considerable impact of hepatobiliary imaging on the decision-making process.

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When presented with a clinical problem, the knowledgeable physician formulates a differential diagnosis based upon the patient's history and physical examination, and from this differential diagnosis, he then selects his most likely diagnosis. The probability expressed by the physician that this diagnosis is correct is the physician's diagnostic confidence. If the physician's diagnostic confidence is not high enough to contraindicate confirmatory testing and to justify treatment, a diagnostic test is required to raise the diagnostic confidence to the level at which he is willing to treat.

Many imaging techniques are rapidly introduced as diagnostic tests and become readily accepted in clinical practice without an assessment of their true efficacy, i.e. their power to improve the physician's diagnostic confidence or his treatment plan. Although a test may be highly accurate and reliable, it may lack usefulness because it does not affect the physician's plans. Recently, several hepatobiliary tracers have been shown to be both highly sensitive and specific for the detection of acute cholecystitis in the setting of acute abdominal pain (*1–4*). From the sensitivity and specificity data reported, the post-test probability of acute cholecystitis with a normal hepatobiliary scan is only 1–2%, while the post-test probability of acute cholecystitis with an abnormal scan is usually greater than 85–90%. Such Bayesian analysis suggests that hepatobiliary imaging (HBI) in acute abdominal pain is highly reliable, but the usefulness of the test in such a setting needs confirmation in a prospective study, because retrospective analysis fails to establish the physician's pre-test diagnostic confidence and therapeutic decision (*5*). Hence, the following prospective study was undertaken.

METHODS

The study group consists of 36 consecutive patients

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For reprints contact: John E. Freitas, MD, Nuclear Medicine Dept., William Beaumont Hospital, 3601 W. 13 Mile Road, Royal Oak, MI 48072.

PART I

A

PATIENT'S NAME: REFERRING PHYSICIAN:

Hepatobiliary Scan Requisition

I.

History	Yes	No	?
Nausea			
Vomiting			
Right upper quadrant pain			
Epigastric pain			
Fatty food intolerance			
Other:			

Physical Exam	Yes	No	?
Right upper quadrant tenderness			
Murphy's sign			
Guarding			
Rebound			
Fever			
Other:			

II. What study results are now available to you? List studies:

III. A. Differential Diagnosis:

Diagnosis	Select (mark) Probability in Percentage
1. acute cholecystitis	0 —+—+—+—+— 50 —+—+—+—+— 100%
2. ulcer	0 —+—+—+—+— 50 —+—+—+—+— 100%
3. pancreatitis	0 —+—+—+—+— 50 —+—+—+—+— 100%
4. hepatitis	0 —+—+—+—+— 50 —+—+—+—+— 100%
5. appendicitis	0 —+—+—+—+— 50 —+—+—+—+— 100%
6. gastroenteritis	0 —+—+—+—+— 50 —+—+—+—+— 100%
7. other:	0 —+—+—+—+— 50 —+—+—+—+— 100%

B. Most likely Diagnosis (select No. from above) #________
Most worrisome Diagnosis (select No. from above) #________

IV. Based on present information only, what is your therapeutic choice?

____ Surgery ( )
____ Medical treatment
____ No treatment, wait and see
____ No treatment

FIG. 1. (A) Part I of questionnaire completed by referring physician before hepatobiliary imaging performed.

PART II

B

V. PIPIDA scan report

VI. A. What is your present differential diagnosis?

Diagnosis:	Select (mark) Probability in Percentage
1. acute cholecystitis	0 —+—+—+—+— 50 —+—+—+—+— 100%
2. ulcer	0 —+—+—+—+— 50 —+—+—+—+— 100%
3. pancreatitis	0 —+—+—+—+— 50 —+—+—+—+— 100%
4. hepatitis	0 —+—+—+—+— 50 —+—+—+—+— 100%
5. appendicitis	0 —+—+—+—+— 50 —+—+—+—+— 100%
6. gastroenteritis	0 —+—+—+—+— 50 —+—+—+—+— 100%
7. other:	0 —+—+—+—+— 50 —+—+—+—+— 100%

B. Most likely diagnosis (select No. from above) #________
Most worrisome diagnosis: (select No. from above) #________

VII. Your present therapeutic choice?

____ Surgery ( )
____ Medical treatment
____ No treatment, wait and see
____ No treatment

FIG. 1. (B) Part II of questionnaire completed immediately following hepatobiliary imaging.

who fulfilled the following criteria: (a) acute abdominal pain of 72 hr or less duration; (b) no history of cholecystectomy; (c) completion of Parts I and II of questionnaire by same physician; and (d) hepatobiliary imaging (HBI) within 72 hr of the onset of pain. The range for total bilirubin in the study group was 0.1–7.2 mg% (mean 2.61 ± 0.64 mg%). At the time of referral for HBI, the referring physician completed Part I of a questionnaire indicating his differential diagnosis, diagnostic confidence (expressed as a percentage), and therapeutic plan (Fig. 1A). The patient was then injected with 5 mCi of PIPIDA intravenously, and 500-kilocount anterior images were obtained at 10-min intervals for 1 hr. Right lateral and anterior oblique views were obtained as needed to differentiate gallbladder from duodenal loop. A positive hepatobiliary scan diagnostic of cystic-duct obstruction is one in which the common bile duct, but not the gallbladder, was visualized within 1 hr of tracer administration. A negative (normal) hepatobiliary scan is one in which the common bile duct and gallbladder was visualized by 1 hr after injection. If the gallbladder did not visualize by 1 hr, delayed images were not obtained routinely, since, in our experience, both chronic cholecystitis and acute acalculous cholecystitis can cause delayed visualization.

Immediately following completion of HBI, the same physician, with knowledge of the scan results, completed Part II of the questionnaire indicating again his differential diagnosis, diagnostic confidence, and therapeutic plan (Fig. 1B). The effect of HBI on the physician's diagnostic confidence was assessed by determination of the log-likelihood-ratio for each patient (5). The likelihood ratio is a statistic describing the usefulness of a given observation (in this case a positive or negative HBI) for distinguishing one entity (e.g., acute cholecystitis) from another (e.g., other causes of abdominal pain).

If the physician's diagnostic confidence of acute cholecystitis before HBI is expressed as odds (^{O}before) and the odds of AC after HBI is ^{O}after, then Bayes' theorem can be stated as LR = ^{O}after/^{O}before where LR is the likelihood ratio for the HBI study. The odds of acute cholecystitis before and after HBI were obtained from the physician's diagnostic confidence as a percentage by transforming thus:

$$\text{odds} = \frac{\%\ \text{confidence}}{100\% - \%\ \text{confidence.}}$$

To obtain a linear scale for comparison purposes, the common logarithm of the individual LR (LLR) was then determined. A LLR of 0.0 represents no change in the physician's diagnostic confidence, while the larger the LLR demonstrated, the greater the impact of HBI on the physician's diagnostic confidence.

When the most likely diagnosis before and after HBI is the same, the calculation of the LLR is straightforward. However, when the diagnosis is not the same, the

TABLE 1. FINAL DIAGNOSIS, CONFIRMATION, AND HBI OF PATIENTS WITHOUT ACUTE CHOLECYSTITIS

Pt.	Final diagnosis	Confirmation	HBI
3	Abdominal pain of unknown origin	Negative lab, radiological studies	Negative
4	Appendicitis	Appendectomy	Negative
5	Abdominal pain of unknown origin	Negative lab, radiological studies	Negative
6	Abdominal pain of unknown origin	Negative lab, radiological studies	Negative
8	Gastritis	Gastroscopy	Negative
9	Fecal impaction; dehydration	Negative lab, radiological studies	Negative
10	Chronic cholecystitis	Elective cholecystectomy (8 wk after HBI)	Negative
12	Chronic cholecystitis	Elective cholecystectomy (8 wk after HBI)	Negative
14	Ruptured ovarian cyst	Oöphorectomy	Negative
15	Adenocarcinoma of lung with liver metastases	Biopsy	Negative; focal defects present
16	Chronic cholecystitis	Cholecystectomy	Positive
17	Gastroenteritis	Negative lab, radiological studies	Negative
18	Right hydronephrosis	Nephrectomy	Negative
20	Pancreatitis, chronic cholecystitis	Cholecystectomy	Positive
21	Pelvic inflammatory disease	Pelvic findings and therapeutic response	Negative
26	Abdominal pain of unknown origin	Negative lab and clinical findings	Negative
28	Hepatitis	Laboratory findings and clinical course	Negative
31	Appendicitis	Appendectomy	Negative
32	Gastritis	Gastroscopy	Negative
33	Gastroenteritis	Negative lab, radiological studies	Negative

TABLE 2. PROBABILITY OF ACUTE CHOLECYSTITIS AND THERAPEUTIC PLAN BEFORE AND AFTER HEPATOBILIARY IMAGING WITH DERIVED LOG-LIKELIHOOD-RATIO (LLR)

	Pre-HBI		Post-HBI		
Pt.	P(AC) (%)	Therapeutic plan	P(AC) (%)	Therapeutic plan	Log LR
1	75	Medical	95	Medical	0.80
2	50	Cholecystectomy	90	Cholecystectomy	0.95
3†	90	Cholecystectomy	5	Medical	2.93
4†	70	Cholecystectomy	10	Appendectomy	1.32
5	60	Medical	1	Medical	2.17
6	80	Medical	10	Medical	1.56
7	99	Cholecystectomy	99	Cholecystectomy	0.0
8†	70	Cholecystectomy	1	Medical	2.36
9†	80	Cholecystectomy	1	Medical	2.60
10	85	Medical	50	Medical	0.74
11	85	Medical	95	Medical	0.53
12	30	Medical	1	Medical	1.63
13	95	Cholecystectomy	99	Cholecystectomy	0.72
14	10	Laparotomy	1	Laparotomy	1.04
15†	99	Cholecystectomy	1	Medical	3.99
16	99	Cholecystectomy	99	Cholecystectomy	0.0
17†	85	Cholecystectomy	1	Medical	2.75
18†	75	Cholecystectomy	1	Nephrectomy	2.47
19	80	Cholecystectomy	99	Cholecystectomy	1.39
20	90	Cholecystectomy	99	Cholecystectomy	1.04
21	30	Medical	1	Medical	1.63
22	95	Cholecystectomy	99	Cholecystectomy	0.72
23†	60	Medical	90	Cholecystectomy	0.77
24	90	Cholecystectomy	99	Cholecystectomy	1.04
25	99	Cholecystectomy	99	Cholecystectomy	0.0
26	90	Medical	15	Medical	1.71
27	80	Medical	99	Medical	1.39
28	75	Medical	1	Medical	2.47
29†	80	Medical	99	Cholecystectomy	1.39
30	90	Cholecystectomy	99	Cholecystectomy	1.04
31†	50	Cholecystectomy	1	Appendectomy	1.99
32†	80	Cholecystectomy	1	Medical	2.60
33	50	Medical	1	Medical	1.99
34	90	Cholecystectomy	99	Cholecystectomy	1.04
35	90	Cholecystectomy	99	Cholecystectomy	1.04
36	80	Cholecystectomy	99	Cholecystectomy	1.39

* AC = acute cholecystitis.

† Denotes change in therapeutic plan.

before-HBI % diagnostic confidence of the after-HBI diagnosis is inferred as equal to 100% minus the % diagnostic confidence of the original most likely diagnosis. For example, in Patient 4, Table 2, the most likely diagnoses before and after HBI are different. The before-HBI diagnosis is acute cholecystitis with a diagnostic confidence of 70%, while the after-HBI diagnosis is appendicitis with a 90% diagnostic confidence. The before-HBI percent diagnostic confidence of appendicitis is then inferred to be 30% (100% − the 70% diagnostic confidence of the original diagnosis).

All surgical specimens were given pathological examination. For the purposes of this study, acute cholecystitis was felt to exist only if hemorrhage and/or necrosis of the gallbladder wall or mucosa was found pathologically. An edematous thickened gallbladder wall with inflammatory cell infiltration was not accepted as acute cholecystitis.

RESULTS

Surgical confirmation of the final diagnosis was achieved in 24 of 36 patients; in the remaining 12 it was determined by clinical findings, radiologic procedures, or biopsy. Eighteen positive and eighteen negative scintigrams were obtained. Acute cholecystitis was confirmed surgically in 16 patients with a positive scan, including Patient 1 who was initially treated medically. In two cases (Patients 16 and 20), the scan was positive but inconsistent with the final diagnosis; pathological examination showed only chronic cholecystitis, with the cystic duct filled with debris. The final diagnosis, confirmation, and HBI findings of each of the 20 patients without acute cholecystitis are shown in Table 1.

The before- and after-HBI % diagnostic confidence of acute cholecystitis, therapeutic plan, and derived LLR for the individual patients are shown in Table 2. The LLR of 0.0, seen in three of 36 patients, indicates no change in the physician's diagnostic confidence, while greater LLRs indicate progressively increasing efficacy. In these 36 patients, acute cholecystitis was the most likely diagnosis (50% or greater diagnostic confidence) before HBI in 33; but after HBI, acute cholecystitis was still felt to be the most likely diagnosis in only 19. Eighteen of these 19 had a positive scan, whereas a normal scan was obtained in the remaining patient (Patient 10, Table 2), who was subsequently shown to have chronic cholecystitis at elective cholecystectomy 6 wk after HBI. The mean LLR was 1.48 ± 0.93, with 33 of 36 patients giving LLR > 0. The distribution of LLRs is shown in Fig. 2, with 26 of 33 patients demonstrating a LLR greater than 1.0. In 11 of 36 patients, HBI changed the physician's therapeutic decision; in these the mean LLR was 2.28 ± 0.93.

DISCUSSION

Although HBI is highly accurate in the detection of acute cholecystitis (sensitivity 100%, specificity 90% in this series), its true value in acute abdominal pain relates directly to its beneficial impact upon the physician's diagnostic confidence and therapeutic decision (*1–4*). In this prospective study of 36 patients, we have shown that HBI using PIPIDA is efficacious in the clinical setting of acute abdominal pain. Although 92% (33 of 36) of these patients were felt to have acute cholecystitis before HBI, only 53% (19 of 36) were still felt to have acute cholecystitis after HBI. Of these 33 patients, referred with a high suspicion of acute cholecystitis, a positive scan compatible with the pre-test diagnosis was obtained in 18 (mean LLR 0.83 ± 0.49), while a negative scan incompatible with the pretest diagnosis was obtained in 15 (mean LLR 2.25 ± 0.81). Thus, a negative scan is actually of threefold greater value to the physician than a positive scan.

It is often stated that, if the physician's % diagnostic confidence of acute cholecystitis is high, the probability of a false-positive clinical diagnosis is low enough to preclude confirmatory testing. Review of the before-HBI diagnostic confidence percentages for acute cholecystitis reveals 13 of 36 with 90% or greater; yet, after HBI, three of 13 (23%) were not felt to have acute cholecystitis. Both of our false-positive HBI scans (Patients 16 and 20) had before-HBI diagnostic confidence percentages of 90% or greater. These two patients show that patients with chronic cholecystitis who accumulate sufficient cystic-duct gravel or sludge to preclude gallbladder visualization present with clinical findings that are indistinguishable from those of acute cholecystitis. Such patients should not be managed any differently from those with pathologically confirmed acute cholecystitis.

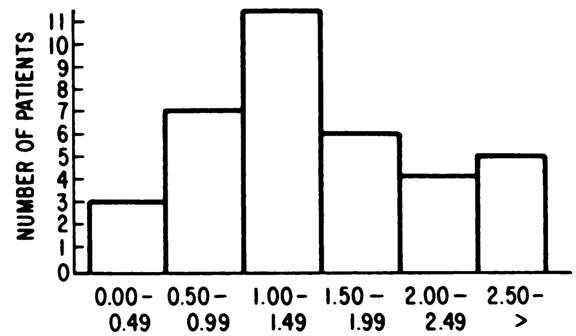

FIG. 2. Distribution of derived log-likelihood-ratio (LLR) in this series.

Although the diagnostic acumen of referring physicians varies considerably, HBI greatly influences the diagnostic confidence of most physicians (mean LLR 1.48 ± 0.93). Although such a mean LLR demonstrates the considerable influence of HBI, is this LLR statistically significant? Unfortunately, the authors know of no data to suggest a value at which the mean LLR of a series develops statistical significance. However, the change in most likely diagnosis before and after HBI is highly significant ($p < 0.01$).*

Of equal importance is the effect of HBI upon the physician's therapeutic plan. HBI changed the physician's plans correctly in 11 of 36 (30%) patients ($p < 0.01$).* In nine patients with normal HBI, the scheduled cholecystectomy was cancelled and a search promptly initiated for another cause for the patient's abdominal pain. In the remaining two patients scheduled for medical treatment, a positive hepatobiliary scan convinced the referring physician that acute cholecystitis was present and cholecystectomy was performed.

HBI is useful in the setting of acute abdominal pain, since in many patients it enhances the physician's diagnostic confidence and appropriately changes his therapeutic plan. Such efficacy should lead to reduced morbidity, mortality, and hospitalization cost. We plan a study to document cost-effectiveness of HBI in the clinical setting of acute abdominal pain.

FOOTNOTE

* Chi-square analysis 2 × 2 contingency table using Yates' correction.

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