

Influence of Scan and Pathologic Criteria on the Specificity of Cholescintigraphy: Concise Communication

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The influence of scan and pathological criteria on the specificity of cholescintigraphy was assessed by a prospective study of 211 patients with suspected acute cholecystitis who underwent cholescintigraphy. Sufficient data were available in all to confirm a final diagnosis. Cholescintigraphy was performed in the standard fashion using 5 mCi of Tc-99m disofenin. Sixty patients had acute cholecystitis, 64 had chronic cholecystitis, and 87 had no demonstrable gallbladder disease. As the scan and pathological criteria for acute cholecystitis were varied from strict to liberal, the sensitivity of cholescintigraphy decreased (100% to 95.3%), the specificity increased (85.1% to 98.6%), and the predictive value increased (68.4% to 96.8%). The use of strict scan and pathological criteria for acute cholecystitis obscures the advantages that accrue from such early detection of acute cholecystitis by cholescintigraphy, and thus are to be avoided. To understand the disparate opinions voiced in the literature, an appreciation is required for the effects of changes in criteria on the specificity and predictive value of cholescintigraphy.

J Nucl Med 24: 876-879, 1983

Cholescintigraphy is a sensitive tool for the detection of acute cholecystitis, and is advocated as the diagnostic screening modality of choice by several investigators (1-4). However, the role of cholescintigraphy in the clinical setting of suspected acute cholecystitis has been questioned by others, who have reported considerably lower specificities for cholescintigraphy than are desirable (5,6). Such discrepant opinions appear to ensue from differences in the methods selected by the authors in a given study. Factors such as (a) the criteria selected for confirmation of acute cholecystitis, (b) the time limit for gallbladder visualization, (c) the presence of the fasting or nonfasting state, and (d) the population studied, may have a profound influence on the cholescintigraphic results reported (7-9). The majority of the false-positive cholescintigrams reported are seen in patients with chronic cholecystitis.

Received Feb. 24, 1983; revision accepted May 9, 1983.

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To assess the influence of scan and pathological criteria upon the sensitivity, specificity, and predictive value of cholescintigraphy in patients with suspected acute cholecystitis, the following prospective study was undertaken.

METHODS

From June, 1981 to August, 1982, 211 patients with acute right upper quadrant or epigastric pain (≤ 5 days) underwent cholescintigraphy within 48 hr of hospital admission. Sufficient pathological, radiological, clinical, and/or laboratory information was available to confirm the final diagnosis in each patient.

After a minimum 2-hr fast, cholescintigraphy was performed following the intravenous injection of 5 mCi (185 MBq) of Tc-99m disofenin. Sequential 500,000-count anterior images were obtained with a standard or large-field gamma camera at 10-min intervals for 60 min. Right lateral and oblique views were obtained routinely to separate gallbladder and duodenal activity.

Delayed imaging was performed as needed until either gallbladder visualization occurred or 3–4 hr after injection had elapsed.

Cholescintigrams were given the following diagnostic designations:

- (a) *normal* if the gallbladder visualized within 1 hr of tracer injection;
- (b) *delayed* if the gallbladder visualized between 1 and 4 hr after tracer;
- (c) *persistent nonvisualization* if there were no gallbladder visualized throughout the imaging series; and
- (d) *obstructive* if—despite adequate hepatic uptake—there was no visualization of gallbladder, common bile duct, or small bowel within 4 hr of tracer injection.

In 179 of these patients, gallbladder ultrasonograms were performed with a high-resolution, real-time, sector scanner using either 3.5- or 5.0-MHz transducers having medium to long internal focusing. Patients were examined in a fasting state routinely in both supine and prone positions, and with other positions as needed.

Two basic ultrasonographic patterns were identified: (a) *normal* if the gallbladder wall was not thickened (<2 mm), echogenic foci were not present in the gallbladder lumen, and the gallbladder size was normal; and (b) *abnormal* if echogenic foci with acoustical shadowing, gallbladder wall edema, and/or pericholecystic fluid were present, indicating gallbladder disease.

Following cholecystectomy, the gallbladder specimen was examined pathologically for the presence of transmural acute inflammatory infiltrates, hemorrhagic necrosis of gallbladder wall or mucosa, gallbladder wall edema, or cystic duct obstruction.

For the reporting of initial data in the Results section, acute cholecystitis was considered present only when confirmed pathologically by the presence of either hemorrhagic necrosis of the gallbladder wall, or concomitant obstruction of the cystic duct with edema of the gallbladder wall. Chronic cholecystitis was present if: (a) the above findings of acute cholecystitis were absent, but chronic inflammatory cellular infiltrates with wall thickening was present microscopically, and/or (b) there was unequivocal sonographic demonstration of echogenic foci with acoustical shadowing, but cholecystectomy was not performed. Sonographic demonstration of gallbladder wall thickening, sludge, and/or pericholecystic fluid alone, was not considered sufficient to indicate chronic cholecystitis.

RESULTS

Pathological confirmation of gallbladder disease was obtained in 103 patients, 60 with acute and 43 with chronic cholecystitis. An additional 21 patients had sonographically demonstrated cholelithiasis with a normal cholescintigram, but did not undergo cholecystectomy

and did not have acute cholecystitis clinically. These 21 patients were classified as chronic cholecystitis.

Of the 60 patients with acute cholecystitis (prevalence 28.9%), 58 had a persistent nonvisualization cholescintigram, one had delayed gallbladder visualization at 3 hr, and one had an obstructive scan pattern with surgical confirmation of concomitant choledocholithiasis. Five of these 60 patients had acute acalculous cholecystitis, and a persistently nonvisualizing cholescintigram was obtained in each.

One hundred fifty-one patients did not have acute cholecystitis. Eighty-seven of these had a normal cholescintigram and real-time ultrasonogram, and were considered to be free of gallbladder disease. The remaining 64 patients had chronic cholecystitis with concomitant choledocholithiasis present in eight. Of these 64 patients, 44 gave normal cholescintigrams, nine showed delayed visualization, five showed persistent nonvisualization, and six showed an obstructive pattern (Table 1). Seven of the nine patients with delayed gallbladder visualization and all 11 patients with the persistent nonvisualization or obstructive patterns had surgical confirmation of chronic cholecystitis. All six patients with the obstructive scan pattern had surgical confirmation of concomitant choledocholithiasis. In two additional patients with nonobstructing choledocholithiasis, one showed a normal and the other a delayed biliary-to-bowel transit of the tracer.

If we exclude the seven patients with the obstructive scan pattern (one with acute cholecystitis, and six chronic cholecystitis patients with concomitant obstructing choledocholithiasis), 58 of 59 patients with acute cholecystitis gave a persistent-nonvisualization cholescintigram (sensitivity 98.3%). One hundred forty of 145 patients without acute cholecystitis showed normal or delayed gallbladder visualization patterns (specificity 96.5).

In this series, a persistently nonvisualizing cholescintigram had a predictive value of 92.1% for acute

TABLE 1. CHOLESCINTIGRAPHY RESULTS IN 211 PATIENTS WITH SUSPECTED ACUTE CHOLECYSTITIS

	Cholescintigraphic patterns				Total
	Nonvis.*	Delayed	Normal	Obstructive	
AC†	58	1	0	1	60
NonAC	5(5)‡	9(9)	131(44)	6(6)	151(64)

* Nonvis. = persistent nonvisualization.

† AC = acute cholecystitis; NonAC = no acute cholecystitis.

‡ The total number of each cholescintigraphic pattern is shown outside the parentheses; inside is the number of patients with chronic cholecystitis.

TABLE 2. EFFECT OF CHANGES IN ACUTE CHOLECYSTITIS CRITERIA ON SENSITIVITY AND SPECIFICITY OF CHOLESCINTIGRAPHY

Acute cholecystitis criteria		Cholescintigraphic patterns (204 patients*)		
		Nonvis.	Normal or delayed	Sens/spec.
1. Transmural acute inflammatory infiltrates	AC	49	1	98% / 90.9%
	NonAC	14	140	
2. Hemorrhagic necrosis of gallbladder wall or mucosa	AC	54	1	98.2% / 94.0%
	NonAC	9	140	
3. Criterion 2 or complete cystic duct obstruction and/or gallbladder wall edema	AC	58	1	98.3% / 96.5%
	NonAC	5	140	
4. Any criterion above, or postcholecystectomy relief of fever, pain, leukocytosis	AC	61	3	95.3% / 98.6%
	NonAC	2	138	

* Seven patients with obstructive pattern are excluded from this analysis.

Nonvis.—persistent nonvisualization.

AC—acute cholecystitis; NonAC—no acute cholecystitis.

cholecystitis, while a normal or delayed gallbladder cholescintigram had a predictive value of 99.3% for nonacute cholecystitis.

DISCUSSION

Although there are several causes of gallbladder nonvisualization in the clinical setting of acute abdominal pain, the large majority of false-positive cholescintigrams are associated with chronic cholecystitis (1,5,7-10). In this series, chronic cholecystitis accounted for all five false-positive cholescintigrams. Thus, chronic cholecystitis degrades the specificity of cholescintigraphy for the detection of acute cholecystitis. However, the magnitude of the effect varies considerably in the literature, with false-positive rates ranging from 0.6% to 27% (5-7).

Such variability appears to depend on the methods selected by the authors of a given study. The magnitude of the effect of chronic cholecystitis upon the specificity

of cholescintigraphy varies as the criteria selected for confirmation of acute cholecystitis change (Table 2). As these criteria are liberalized, the sensitivity decreases and the specificity increases as more patients with cholecystitis are considered acute rather than chronic. Similarly, as the time for gallbladder visualization is liberalized from 1 hr to 4 hr (pathological criterion for acute cholecystitis held constant), the sensitivity falls and the specificity increases (Table 3). Thus, a study demanding a strict pathological criterion for acute cholecystitis (e.g., transmural inflammatory infiltration) and requiring gallbladder visualization by 1 hr, will suggest that cholescintigraphy has a far lower specificity than a study utilizing the most liberal criteria illustrated (Table 4).

As the specificity falls in a given study, so does the predictive value of a positive test. From the data in Table 4, the predictive value of a positive test falls from 96.8% (liberal criteria) to 68.5% (strict criteria) as the number of false-positive scans increases and the number of true-positive scans decreases.

TABLE 3. EFFECT OF TIME LIMIT FOR GALLBLADDER VISUALIZATION ON SENSITIVITY AND SPECIFICITY OF CHOLESCINTIGRAPHY FOR ACUTE CHOLECYSTITIS*

Gallbladder visualization Time limit		Cholescintigraphic patterns (204 patients)		
		Nonvis. [†]	Normal or delayed	Sens/spec
1. ≤ 1 hr	AC	59	0	100% / 90.3%
	NonAC	14 [‡]	131	
2. ≤ 2½ hr	AC	59	0	100% / 93.1%
	NonAC	10 [‡]	135	
3. ≤ 4 hr	AC	58	1	98.3% / 96.5%
	NonAC	5	140	

* Criterion 3, Table 2.

[†] Nonvis = persistent nonvisualization.

[‡] Without serial images at 2, 3, and 4 hr, the precise gallbladder visualization time for seven of the nine patients with gallbladder visualization between 1-4 hr cannot be determined.

TABLE 4. EFFECT OF STRICT VERSUS LIBERAL CRITERIA FOR ACUTE CHOLECYSTITIS AND GALLBLADDER VISUALIZATION TIME ON THE SENSITIVITY AND SPECIFICITY OF CHOLESCINTIGRAPHY

		Cholescintigraphic patterns (204 patients)		
		Nonvis.*	Normal or delayed	Sens/spec
1. Strict criteria (transmural acute inflammatory infiltrates, and GB visualization \leq 1 hr)	AC	50	0	100% / 85.1%
	NonAC	23	131	
2. Liberal criteria (criterion 4, Table 2; and GB visualization \leq 4 hr)	AC	61	3	95.3% / 98.6%
	NonAC	2	138	

* Nonvis. = persistent nonvisualization.

The use of a strict pathological criterion for acute cholecystitis ignores the natural history of this condition. More than 90% of cholecystectomy specimens removed for acute cholecystitis show telltale evidence of previous inflammatory episodes of acute cholecystitis, with fibrotic, reparative processes (11). Such fibrotic, reparative processes most likely hinder the development of acute transmural inflammatory changes (Criterion 1, Table 2), and patients with acute cholecystitis superimposed on chronic cholecystitis are mislabeled as chronic cholecystitis using such a criterion.

The use of Criterion 3 (Table 2) appears most appropriate, since such an approach recognizes the natural history of acute cholecystitis discussed above, yet avoids the pitfall of labeling all syndromes of right upper quadrant pain relieved by cholecystectomy as due to acute cholecystitis. Cholescintigraphy detects cystic duct obstruction, the first step in the development of acute cholecystitis. The use of strict scan and pathologic criteria for acute cholecystitis obscures the advantages that accrue from such early detection of acute cholecystitis by cholescintigraphy, and thus is to be avoided.

REFERENCES

1. FREITAS JE, GULATI RM: Rapid evaluation of acute abdominal pain by hepatobiliary imaging. *JAMA* 244:1585-7, 1980
2. WEISSMANN HS, FRANK MS, BERSTEIN LH, et al: Rapid and accurate diagnosis of acute cholecystitis with ^{99m}Tc-HIDA cholescintigraphy. *Am J Roentgenol* 132:523-8, 1979
3. ZEMAN RK, BURRELL MI, CAHOW CE, et al: Diagnostic utility of cholescintigraphy and ultrasonography in acute cholecystitis. *Am J Surg* 141:446-51, 1981
4. MAURO MA, MCCARTNEY WH, MELMED JR: Hepatobiliary scanning with ^{99m}Tc-PIPIDA in acute cholecystitis. *Radiology* 142:193-197, 1982
5. SHUMAN WP, MACK LA, RUDD TG, et al: Evaluation of acute right upper quadrant pain: Sonography and ^{99m}Tc-PIPIDA cholescintigraphy. *Am J Roentgenol* 139:61-64, 1982
6. WORTHEN NJ, USZLER JM, FUNAMURA JL: Cholecystitis: Prospective evaluation of sonography and ^{99m}Tc-HIDA cholescintigraphy. *Am J Roentgenol* 137:973-78, 1981
7. WEISSMANN HS, SUGARMAN LA, BADIA JD, et al: Improving the specificity and accuracy of Tc-99m-IDA cholescintigraphy with delayed views. *J Nucl Med* 21:P17, 1980
8. KLINGENSMITH WC, SPITZER VM, FRITZBERG AR, et al: The normal fasting and postprandial Tc-99m diisopropyl-IDA hepatobiliary study. *J Nucl Med* 22:P7, 1981
9. PARÉ P, SHAFFER EA, ROSENTHALL L: Nonvisualization of the gallbladder by ^{99m}Tc-HIDA cholescintigraphy as evidence of cholecystitis. *Can Med Assoc J* 118:384-386, 1978
10. SHUMAN WP, GIBBS P, RUDD TG, et al: PIPIDA scintigraphy for cholecystitis: False positives in alcoholism and total parental nutrition. *Am J Roentgenol* 138:1-5, 1982
11. SCHEIN CJ: Acute cholecystitis. New York, Harper and Row, 1972, p 47

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