
Positive Predictive Value of Cholescintigraphy in Common Bile Duct Obstruction

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Technetium-99m DISIDA imaging was employed in 400 patients to differentiate obstruction of the common bile duct from medical and other surgical causes of hyperbilirubinemia. Sequential anterior images demonstrated variable degrees of liver uptake, yet there was no evidence of intrabiliary or extrabiliary radioactivity for at least 4 hr after injection in 25 patients. Twenty-three patients were surgically documented to have complete obstruction of the common bile duct. One patient had hepatitis, and another had sickle cell crisis without bile duct obstruction. The remaining patients had either partial or no obstruction of the common bile duct. We conclude that the presence of liver uptake without evident biliary excretion by 4 hr on cholescintigraphy is highly sensitive and predictive of total obstruction of the common bile duct.

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Clinical interest in hepatobiliary scintigraphy has increased in recent years. This is largely attributable to the advent and availability of a variety of iminodiacetic acid (IDA) derivatives labeled with technetium-99m (^{99m}Tc). Such radiopharmaceuticals readily evaluate both biliary patency and integrity. To date, scintigraphic findings demonstrating nonvisualization of gallbladder, common bile duct, and intestinal activities have been considered to be inconclusive, indicating an uncertainty as to whether a medical or a surgical disease caused the nonvisualization. Several reports have termed as "indeterminate" sequential hepatobiliary images which demonstrate no biliary activity, because such images fail to differentiate between primary hepatocellular dysfunction and primary biliary tract obstruction with secondary hepatocytic dysfunction (1-4).

The purpose of this retrospective study was to determine the positive predictive value of hepatobiliary scintigraphy at 4 hr for diagnosing total biliary obstruction, given findings of sequential images lacking biliary or intestinal visualization and using only one of many available bilirubin analogs. It was not the purpose of our study to evaluate partial biliary obstruction.

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Technetium-99m diisopropyl-iminodiacetic acid (disofenin[†], DISIDA) has been reported to provide meaningful images in patients with moderate to severe hyperbilirubinemia and possibly to differentiate biliary obstruction from hepatocellular disease (5). We wanted to study a large population of patients, using exclusively [^{99m}Tc]DISIDA as a positive predictor of total biliary obstruction. Technetium-99m DISIDA has been suggested as the optimal imaging agent for the evaluation of the biliary tract in patients with high serum bilirubin levels (6-8), but this observation has been challenged by others (9). In any event, [^{99m}Tc]DISIDA is the only IDA radiopharmaceutical currently available for use outside of investigational purposes.

MATERIALS AND METHODS

We analyzed the results of 400 adult patients studied exclusively with [^{99m}Tc]DISIDA at the University of Texas Health Science Center, San Antonio (UTH-SCSA) and at the University of South Alabama Medical Center (USAMC). The technique at both institutions was identical: after the i.v. injection of 8-9 mCi [^{99m}Tc]DISIDA, images were acquired at 10, 15, 30, 45, and 60 min, and at longer intervals thereafter, until gallbladder and/or intestinal activity was demonstrated or a minimum of 4 hr had elapsed. All patients had been fasting for a minimum of 3-4 hr prior to the study, and

no patient with a positive study was receiving parenteral nutrition at the time of imaging.

For our specific interest, we identified those studies which demonstrated concurrent nonvisualization of gallbladder, biliary tract, and intestinal activities after 4 hr of imaging. The hospital records of those patients with positive studies were reviewed for surgical or medical findings which could explain the image pattern. Where available, SGOT, SGPT, total and direct bilirubin, and serum amylase levels were recorded. Relevant surgical or medical discharge diagnoses were obtained.

RESULTS

From 400 patients, we identified 25 patients in whom hepatobiliary studies demonstrated nonvisualization of gallbladder, biliary tract, and intestinal activity after 4 hr of imaging (Fig. 1). Despite encouragement to image beyond 4 hr, only five patients were available for imaging at 20–24 hr; in those five patients, the scintigraphic pattern was identical to the findings demonstrated at 4 hr. Twenty-three of the remaining 25 pa-

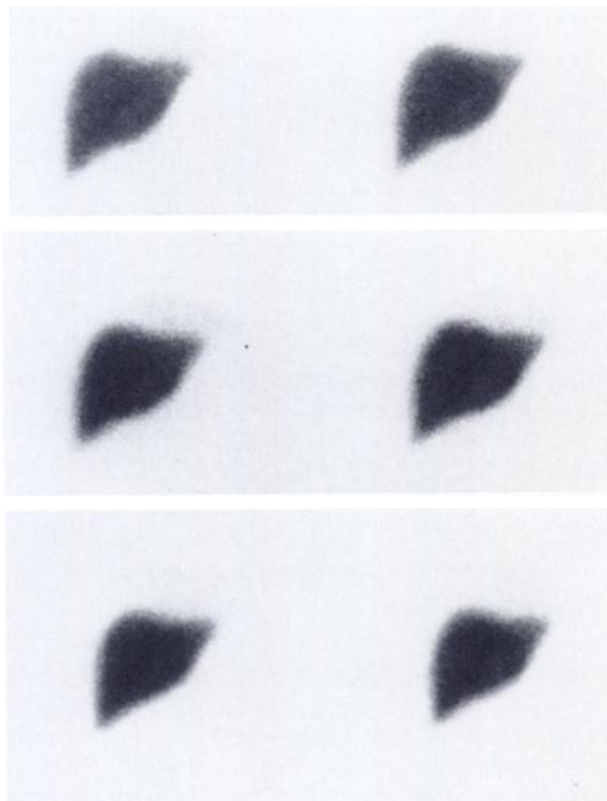


FIGURE 1
Selected anterior hepatobiliary images. Top: 10 and 15 min. Middle: 1 and 2 hr. Bottom: 3 and 4 hr. Prompt hepatic uptake as demonstrated by absence of background activity. No evidence of intrabiliary nor extrahepatic activity. This pattern has been found to be highly predictive of total obstruction of common bile duct

tients had surgically documented evidence of total obstruction of the common bile duct. Fourteen other patients demonstrated intestinal activity between 2 and 4 hr. Although it was not the primary purpose of our study, we determined that eight of these 14 patients had surgically documented choledocholithiasis, with partial biliary obstruction. In all other patients, activity was seen in the intestine prior to 2 hr, a finding incompatible with total biliary obstruction.

The sensitivity of the study for total obstruction of the common bile duct was 100%, the specificity 99.5%, and the positive predictive value 92.0% (23 of 25 patients) (Table 1). Two false-positive studies were encountered in this population, and the incidence of choledocholithiasis was 7.8% (31 of 400 patients).

False-Positive Studies

One patient, a 27-yr-old woman with a clinical diagnosis of hepatitis, yielded a false-positive study. In spite of an only moderately elevated total bilirubin (9.4 mg/dl) obtained on the same day as the scintigraphic study, there was scintigraphic evidence of total biliary obstruction. Because of the markedly elevated SGOT (4,580 IU/l) and SGPT (2480 IU/l), she was treated for hepatitis, and the diagnosis was confirmed by serology.

The other patient with a false-positive study was a 22-yr-old man who was imaged during a sickle cell crisis, when he had a total bilirubin of 27 mg/dl, in excess of the level reported (24.5 mg/dl) in which [^{99m}Tc]DISIDA has been shown to be effective (8). Because of his markedly elevated total bilirubin, imaging was extended to 6 hr, which yielded identical findings to those seen at 4 hr. He was taken to surgery based on the scintigraphic findings and subsequent ultrasonic impression of cholelithiasis and patent common duct, both confirmed at surgery. This patient has the highest total bilirubin of any patient in our experience with hepatobiliary scintigraphy.

TABLE 1
Results of Cholescintigraphy in 400 Jaundiced Patients*

Item	No. patients with nonvisualization of bile ducts and intestinal activity at 4 hr	No. patients with visualization of bile ducts and intestinal activity at 4 hr
No. patients with total common bile duct obstruction	23	0
No. patients with partial or no common bile duct obstruction	2	375

*Sensitivity = $23/23 + 0 = 100\%$; Specificity = $375/375 + 2 = 99.5\%$; Positive predictive value = $23/23 + 2 = 92\%$.

DISCUSSION

Differentiation of surgical from medical hyperbilirubinemia has not always been possible with ^{99m}Tc -labeled iminodiacetic acid derivatives prior to the widespread availability and use of DISIDA (8). Matzen et al. reported that [^{99m}Tc]HIDA was not useful in separating medical from surgical jaundice (10). The differentiation of hepatocellular disease from biliary tract obstruction using [^{99m}Tc]PIPIDA has also proved difficult; when the total bilirubin concentration exceeds 15 mg/dl or high body background consistent with poor liver function is present, [^{99m}Tc]PIPIDA scintigraphy tends to be nondiagnostic for the specific pattern which we evaluated (11). In fact, the UTHSCSA population had been previously evaluated with [^{99m}Tc]PIPIDA as a possible presumptive indicator of biliary obstruction; in 116 patients, we concluded that [^{99m}Tc]PIPIDA was not particularly useful in distinguishing diffuse hepatocellular disease from total biliary obstruction (12). Since no clear antagonism exists between bilirubin and any of the IDA compounds in the excretory pathway, the functional state of the hepatocyte determines how the radiopharmaceutical is processed, a sequence not always predictable by serum bilirubin levels alone (13). Our patient, whose total bilirubin measured 27 mg/dl (caused by a sickle cell crisis), demonstrated prompt hepatic uptake with no discernible blood-pool activity after 10 min, yet a patent common bile duct was observed surgically and by intraoperative cholangiography.

Severe hepatocyte dysfunction has been reported to produce no intestinal radioactivity through 24 hr with [^{99m}Tc]diethyl IDA (3,14). On the other hand, Huang et al. investigating the nonvisualization of the common bile duct with [^{99m}Tc]HIDA up to 24 hr, concluded that this scintigraphic pattern specifically indicates common bile duct obstruction (15). The inability of transhepatic contrast media to concentrate in the biliary tract has been experimentally explained by Burgener and his colleagues: distal hepatocytic diffuse pressure was exceeded by intrabiliary static pressure; hence, no flow occurred from the hepatocytes into the biliary system (16). Finally, using both [^{99m}Tc]diethyl IDA and [^{99m}Tc]DISIDA, Kuni et al. reported that patients with cholestasis along with secondary hepatocyte dysfunction demonstrate biliary transit times much longer than those seen in patients with hepatocyte disease but without evidence of obstruction (17). In the latter report, imaging was continued in some cases for up to 24 hr.

Whereas hepatic uptake without visualization of the biliary system and bowel after 4 hr of imaging was reported to indicate obstruction, using ^{99m}Tc -labeled HIDA, PIPIDA, and DISIDA, no indication of which radiopharmaceutical was used in specific cases was provided (18). Using [^{99m}Tc]diethyl IDA, with imaging

up to 24 hr if necessary, Pauwels and his colleagues reported that the overall accuracy of differentiating hepatocellular and obstruction jaundice was 90%; the incidence of true-positive (mechanical obstruction) scans decreased from 93% for total bilirubin below 10 mg/dl to 83% for bilirubin between 10–20 mg/dl; above 20 mg/dl, the true-positive rate fell to 25% (19). Ching and his colleagues have also reported their results in differentiating hepatocellular disease from total biliary obstruction (20). They reported 100% sensitivity and 100% specificity in 17 patients imaged through 24 hr, but only two patients had total biliary obstruction. One of the patients, with a total bilirubin of 38.5 mg/dl and studied with [^{99m}Tc]HIDA, demonstrated intestinal activity at 19 hr. In addition, the overall results were an admixture from studies using [^{99m}Tc]HIDA, [^{99m}Tc]diethyl IDA, and [^{99m}Tc]BIDA. Zeman and his colleagues reported their results of hepatobiliary scintigraphy in early biliary obstruction, using [^{99m}Tc]disofenin exclusively (21). However, the only three patients with indeterminate examinations (total bilirubins of 12, 18, and 20 mg/dl, respectively), were deleted from their results. Finally, Scott et al. reported that hepatobiliary scintigraphy was completely unable to distinguish medical from surgical jaundice (22). Yet their patients received only 2.0–2.5 mCi of [^{99m}Tc]HIDA, and there was no documentation showing that any patient was imaged longer than 1 hr.

Clinically, a test that reliably differentiates primary hepatocellular disease from total biliary obstruction with secondary hepatocyte dysfunction would be of considerable clinical value. We believe that hepatobiliary scintigraphy using [^{99m}Tc]DISIDA as a predictor of total biliary obstruction provides an accurate differentiation if images are acquired through 4 hr in those patients in whom no evidence of intrabiliary or extra-biliary activity is demonstrated on earlier images. Terminating the study prior to 4 hr significantly increases the number of false-positive studies.

FOOTNOTE

† Du Pont Company, No. Billerica, MA (disofenin).

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