

The Significance of Functioning Gallbladder Visualization on Hepatobiliary Scintigraphy in Infants with Persistent Jaundice

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The purpose of this study was to determine whether gallbladder visualization can help exclude biliary atresia in hepatobiliary scintigraphic studies of infants with persistent jaundice. **Methods:** One hundred fifty-two infants with persistent jaundice (49 patients with a final diagnosis of biliary atresia and 103 with biliary patency) were studied using both hepatobiliary scintigraphy and abdominal sonography. Food was withheld for 4 h before the examination, and the infants were fed nothing but glucose until 6 h after the initial injection of ^{99m}Tc -disofenin or until the gallbladder was seen. If the gallbladder was seen, the infants were fed milk, and imaging was continued to observe gallbladder contractility. **Results:** In none of the 49 patients with biliary atresia could the gallbladder be seen with hepatobiliary scintigraphy, but abdominal sonography revealed 9 normal-sized gallbladders. Of the 103 patients with biliary patency, hepatobiliary scintigraphy detected the gallbladder more frequently (74%, 76/103) than did abdominal sonography (63%, 65/103). All visualized gallbladders contracted after the infants were fed milk. If we include visualization of both the gallbladder and bowel radioactivity as criteria, the specificity of biliary atresia on hepatobiliary scintigraphy increases to 86% (89/103). **Conclusion:** Gallbladders were usually visible on hepatobiliary scintigraphy of fasting patients with biliary patency. A functioning gallbladder, with or without visualization of bowel radioactivity, indicated biliary patency.

Key Words: biliary atresia; biliary patency; hepatobiliary scintigraphy; abdominal sonography

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Hepatobiliary imaging has been used to determine the patency of the biliary tract in cases of persistent neonatal jaundice and to distinguish biliary atresia from biliary patency (1–20). For the past 20 y, the most important imaging criterion of biliary patency and biliary atresia has been the presence or absence of bowel radioactivity within 24 h without impaired hepatocellular uptake of the radiotracer. With this criterion, scintigraphic diagnosis of biliary

atresia has a sensitivity of 100%. However, the specificity is not fully satisfactory (46%–88%) because studies have indicated that biliary patency may show no bowel radioactivity within that 24-h period (6–7,13,14,19). Some of the patients in these studies had fair liver uptake, but scintigraphy failed to detect bowel radioactivity. As a result, biliary atresia was erroneously diagnosed, and those patients could have been subjected to unnecessary laparotomy.

Hepatobiliary scintigraphic visualization of the gallbladder with or without bowel radioactivity has not been thoroughly investigated. Although a few reports have slightly mentioned visualization (3,7,12,14,16,17), many have not mentioned visualization at all (1,2,4–6,8–11,13,15,18,19). Most investigators think the gallbladder is rarely visible; for this reason, it has traditionally not been considered an important diagnostic parameter (20).

In some reports, researchers provided no information on whether the patients fasted before and after the initial injection of radiopharmaceutical (1,4–6,10,11,14,17,19). One report mentioned only that the patients were fed (2). The remaining reports mentioned that the patients fasted for only a short time (3,7–9,12,15,16,18). Only Cox et al. (13), like us, mentioned that the patients fasted for 4–6 h and until 4 h of scanning. However, Cox et al. did not mention gallbladder visualization. None of these investigators, with the exception of Majd et al. (3) and Jaw et al. (7), used gallbladder visualization as a second parameter, nor did any of them evaluate gallbladder contraction.

The purpose of this study was to determine whether gallbladder visualization can help exclude biliary atresia in hepatobiliary scintigraphic studies of infants with persistent jaundice. We discuss the related advantages and limitations of this approach by comparing it with abdominal sonography.

MATERIALS AND METHODS

Between January 1989 and March 1999, hepatobiliary scintigraphy and abdominal sonography were performed on 152 infants with persistent jaundice (90 boys, 62 girls; age range, 14–97 d; mean age \pm SD, 55 ± 18 d). Only the initial scans of these 152 patients were collected for data analysis. Patients with severely impaired hepatic uptake of the radiotracer and no evidence of

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bowel or gallbladder radioactivity were excluded from the study. The final diagnosis was confirmed independently through operative cholangiography and liver biopsy, through follow-up of the clinical course (for at least 6 mo), or through repetition of hepatobiliary scintigraphy a few days later.

Hepatobiliary Scintigraphy

All patients received phenobarbital orally at a dose of 5 mg/kg/d for 5 to 7 d before the examination. All studies were performed after 4 h of fasting. A venous line was established to give glucose fluids and radiotracer to the infants, who were also given oral glucose water instead of milk until the initial 6 h of scanning had been completed or until visualization of the gallbladder was confirmed. No sedation was used; infants were kept still during imaging using a pacifier and, if necessary, sandbags and tape as passive body restraints.

Patients received an intravenous injection of 37 MBq (1 mCi) ^{99m}Tc -disofenin ([[(2,6-diisopropylphenyl)carbamoyl]methyl]-imido]diacetic acid). They were imaged supine with a gamma camera (Starcam 4000XR; General Electric Medical Systems, Milwaukee, WI) having a large field of view and equipped with a low-energy high-resolution collimator. Anterior images of the abdomen were obtained for 100,000 counts at 5, 15, 30, and 45 min and at 1, 2, 3, 4, 5, 6, 7, and 8 h until intestinal radioactivity was identified with certainty. If needed, additional right lateral images were obtained to determine the presence of radioactivity in the gastrointestinal tract, abdominal skin, or right kidney. The infant's diaper was changed if it contained radioactivity from urine. If questions about possible urine contamination arose during the examination, the infant was washed thoroughly.

During imaging, if persistent radioactivity over a 2-h period in the gallbladder region was noted, the infants were fed milk and imaging was continued. If this persistent radioactivity was seen to disappear after milk feeding, we supposed that the radioactivity could indeed be attributed to the gallbladder and that the gallbladder had contracted and was functioning. If, after exclusion of radioactivity in the intestine or in the stump of the common hepatic duct, radioactivity still persisted in the gallbladder region after milk consumption, we supposed that the gallbladder had not contracted and was not functioning. We assumed that a nonfunctioning gallbladder would not indicate biliary patency. The position of radioactivity in the intestine may change over time, and radioactivity in the stump of the common hepatic duct was seen to be higher than the gallbladder and nearer the midline of the liver.

The degree of radioisotope uptake in the liver, the time of initial visualization of the gallbladder, and the presence of bowel radioactivity were recorded. If no bowel radioactivity was detected after 8 h, an additional 37 MBq (1 mCi) ^{99m}Tc -disofenin were administered intravenously, and imaging was repeated the next morning approximately 24 h after the first injection. Imaging at 24 h was performed for 10 min or 100,000 counts.

The hepatobiliary scintigraphic findings were interpreted as biliary atresia if bowel radioactivity remained absent 24 h after injection and if efficient liver uptake was relatively preserved. Efficient liver uptake was defined as rapid accumulation of radioactivity by hepatocytes and rapid disappearance (by 30 min) of radioactivity from the blood pool and background structures. The findings were interpreted as biliary patency if radioactivity was seen in the bowel.

Abdominal Sonography

Abdominal sonography was performed by a pediatric gastroenterologist or radiologist within 48 h of hepatobiliary scintigraphy. All studies were performed after at least 4 h of fasting (usually just before the expected time of the next feeding). Abdominal sonography was performed using a mechanical-sector real-time unit with 5.0- to 7.5-MHz sector transducers. During all scanning and measurements, the patients were supine and breathing as quietly as possible.

The criterion for an abdominal sonographic diagnosis of biliary atresia included either nonvisualization of the gallbladder or a gallbladder shorter than 1.5 cm. A gallbladder longer than 1.5 cm is considered normal and thought to favor biliary patency (4,8, 21-23).

RESULTS

The results of hepatobiliary scintigraphy and abdominal sonography in 152 infants with persistent jaundice are summarized in Table 1. The hepatobiliary scintigraphy performed on 49 patients in whom biliary atresia was subsequently proven showed nonvisualization of the gallbladder and lack of bowel radioactivity throughout the following 24 h despite efficient hepatic uptake. The sensitivity was 100% (49/49). However, among these patients, abdominal sonography revealed 9 normal-sized gallbladders with a sensitivity of 82% (40/49).

Among the 103 patients with a final diagnosis of biliary patency, hepatobiliary scintigraphy showed 67 to have both gallbladder and bowel radioactivity (Fig. 1), and sonography showed 46 of these 67 to have normal-sized gallbladders. Hepatobiliary scintigraphy showed 13 patients to have bowel radioactivity only (Fig. 2), and sonography showed 7 of these 13 to have normal-sized gallbladders. Hepatobiliary scintigraphy showed only the gallbladder in 9 patients (Fig. 3), and sonography showed 4 of these 9 to have normal-sized gallbladders. Hepatobiliary scintigraphy showed no gallbladder or bowel radioactivity in 14 patients (Fig. 4), and sonography showed 8 of these 14 to have normal-sized gallbladders.

TABLE 1
Results of Hepatobiliary Scintigraphy and Abdominal Sonography in Infants with Persistent Neonatal Jaundice

Final diagnosis	Hepatobiliary scintigraphy				Abdominal sonography	
	Seen			Not seen	Gallbladder of normal size	Gallbladder small or absent
	Gallbladder	Bowel	Both			
Biliary atresia (n = 49)	0	0	0	49	9	40
Biliary patency (n = 103)	9	13	67	14	65	38

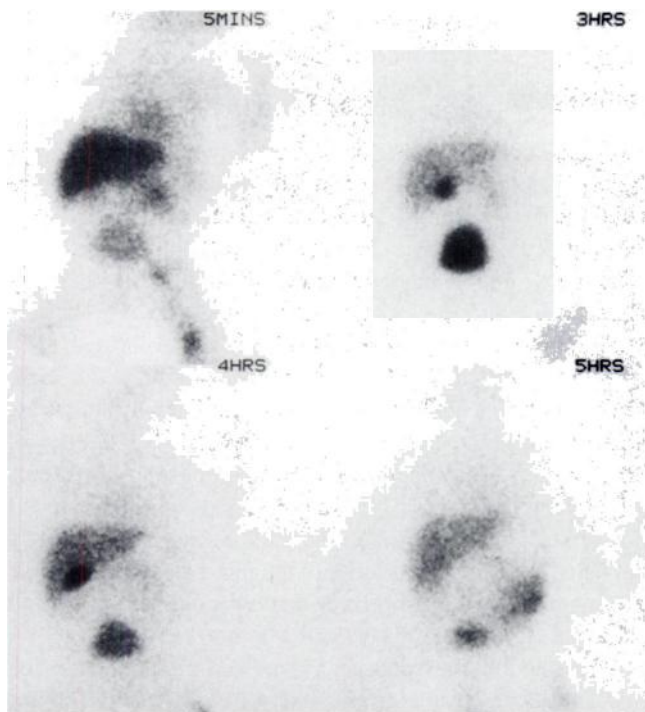


FIGURE 1. Biliary patency. Anterior image of abdomen obtained after injection of ^{99m}Tc -disofenin shows both gallbladder and bowel radioactivity. Five-hour image shows gallbladder contraction after milk ingestion.

In total, there were 15 patients whose gallbladder was seen on sonography but not on scintigraphy, and there were 26 patients whose gallbladder was seen on scintigraphy but not on sonography. Combining the scintigraphic and sonographic findings improved detection of the gallbladder to 88% (91/103) in the patients with biliary patency.

When hepatobiliary scintigraphy was performed, the average time to gallbladder visualization after tracer injection was 1.8 h (range, 15 min to 6 h). Most gallbladders were seen within 4 h (74/76), 15 within 1 h, 17 at 1 h, 30 at 2 h, 8 at 3 h, 4 at 4 h, 1 at 5 h, and 1 at 6 h. The radioactivity in all 76 gallbladders disappeared after milk ingestion, meaning that all visualized gallbladders had contracted and were functioning.

Not all the gallbladders of the infants with biliary patency were seen by hepatobiliary scintigraphy and abdominal sonography. However, hepatobiliary scintigraphy showed the gallbladders more frequently (74%, 76/103) than did abdominal sonography (63%, 65/103).

Furthermore, all the infants whose gallbladders were shown by hepatobiliary scintigraphy proved to have biliary patency. However, the presence of a normal-sized gallbladder (1.5 cm or longer) as shown by sonography in this selected group of patients was not always associated with such a diagnosis. In actuality, 9 of our 74 patients shown to have normal gallbladders did indeed have biliary atresia.

If visualization of either bowel activity or the gallbladder was used as the sole criterion, a scintigraphic diagnosis of biliary atresia was found to have a specificity of 78%

(80/103) and 74% (76/103), respectively. If visualization of both bowel activity and the gallbladder was used as the criterion, specificity increased to 86% (89/103).

DISCUSSION

Because gallbladder visualization has been shown to be significantly better in healthy adults who are fasting than in those who are not (24), visualization is likely to be better in fasting infants as well. However, in some reports, the authors did not indicate whether their patients were fasting before and after the injection of the radiotracer (1,4-6,10,11,14,17,19). In 1 study, fasting was not used (2); in others, infants fasted for only a short time (3,7-9,12,15,16,18). The authors might have avoided using lengthy fasting because they feared that the increased movement of hungry infants would affect image quality. The authors might also have believed that the gallbladder was too small to be visible and therefore not important in the diagnosis. Of course, eating would cause the gallbladder to contract to an even smaller, almost invisible size. In studies that did include fasting, it probably was of too short a duration to effectively minimize gallbladder contraction.

By establishing a venous line for glucose fluids, and by feeding glucose water to the infants, we could keep most of the infants still during imaging, allowing good image quality. Because of this venous line and glucose feeding, we could use a longer fasting time and detect the gallbladder in more patients with biliary patency (74%, 76/103) than could other authors (3,7,12,14,16,17).

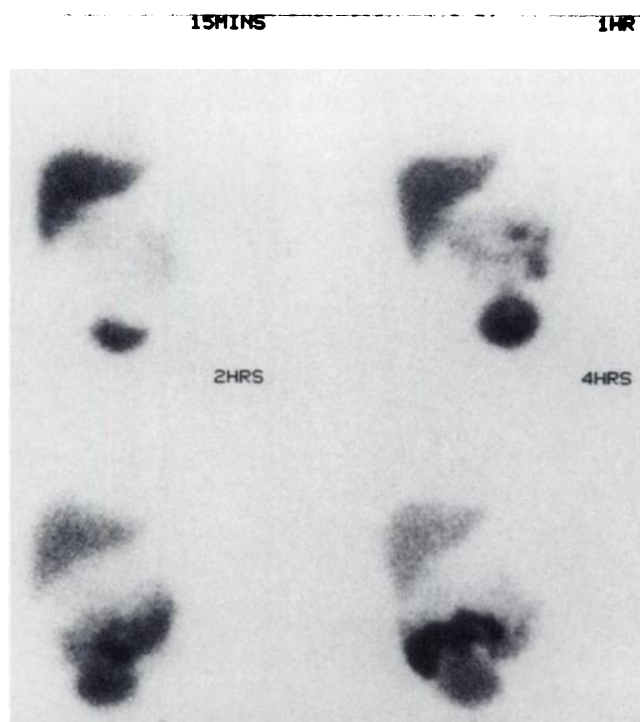


FIGURE 2. Biliary patency. Anterior image of abdomen obtained after injection of ^{99m}Tc -disofenin shows bowel radioactivity only.

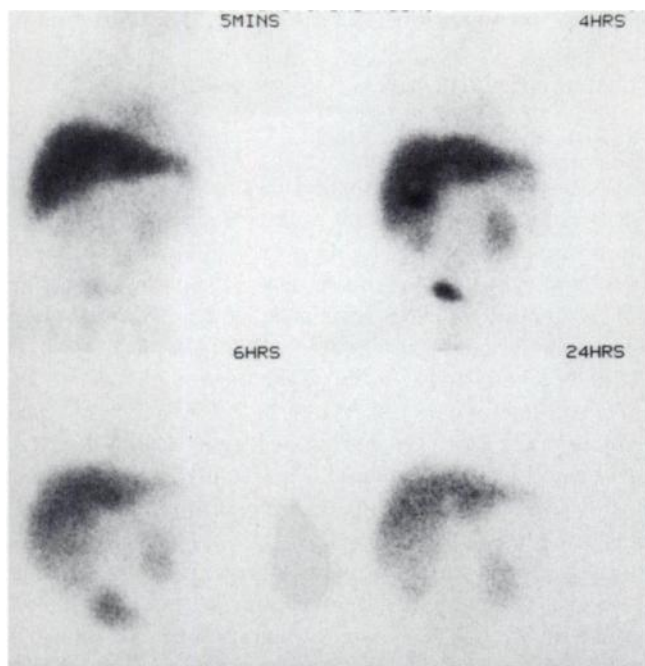


FIGURE 3. Biliary patency. Anterior image of abdomen obtained after injection of ^{99m}Tc -disofenin shows gallbladder radioactivity only. Six-hour image shows gallbladder contraction after milk ingestion.

Radioactivity in the intestine of patients who have biliary patency must not be confused with radioactivity in the stump of the common hepatic duct of patients who have biliary atresia. The position of intestinal radioactivity may change over time. Radioactivity in the stump of the common hepatic

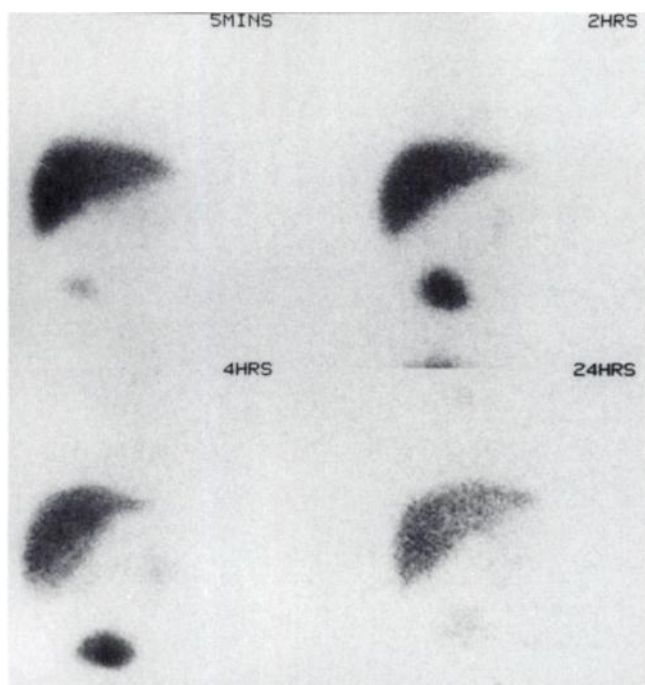


FIGURE 4. Biliary atresia. Anterior image of abdomen obtained after injection of ^{99m}Tc -disofenin shows no gallbladder or bowel radioactivity.

duct is seen as higher than the gallbladder and nearer the midline of the liver. Furthermore, radioactivity there does not disappear after feeding.

In this study, visualization of gallbladder radioactivity with hepatobiliary scintigraphy was frequent in patients with biliary patency (76/103), and all visualized gallbladders contracted after milk ingestion. All such patients were subsequently proven to have biliary patency. Therefore, a functioning gallbladder could rule out a diagnosis of biliary atresia even when bowel radioactivity was absent.

Similar to the experience of Jaw et al. (7), Tolia et al. (14), and Ben-Haim et al. (17), we had 9 patients with visualization of only the gallbladder on hepatobiliary scintigraphy. One reason could be that bile flow was slow and a small amount of radioisotope passed into the intestine of patients with liver dysfunction. If the radiotracer was concentrated in a relatively small volume in the gallbladder, it could easily be visualized. But if ejected into the relatively large volume of the intestine, the radiotracer could become too diluted to show patency of the biliary tract.

When abdominal sonography showed a gallbladder, the possibility of biliary atresia could not be excluded. Similar to other authors (8,23), we found normal-sized gallbladders (1.5 cm or longer) in our infants with biliary atresia. Although some types of biliary atresia actually preserve the gallbladder, intraoperative observation and operative cholangiography have proven these gallbladders to be either shrunk or fibrotic (24–26). These gallbladders were likely nonfunctioning and not visualized on hepatobiliary scintigraphy but still visible on sonography.

We found that lack of gallbladder visualization or, especially, bowel visualization on hepatobiliary scintigraphy was consistent with biliary atresia. All 49 of our patients with biliary atresia showed no gallbladder or bowel radioactivity, thus making hepatobiliary scintigraphy 100% accurate in diagnosing biliary atresia. However, visualization of the gallbladder or bowel on hepatobiliary scintigraphy was consistent with biliary patency. Among the 103 patients with biliary patency, scintigraphy showed 89 (86%) to have either gallbladder or bowel radioactivity.

In contrast, visualization of the gallbladder on sonography has less predictive value than scintigraphy in individual patients. In 9 patients, a normal-sized gallbladder was shown by sonography, yet biliary atresia was present. In 65 patients (63%) with biliary patency, the gallbladder was seen.

CONCLUSION

Gallbladder visualization on hepatobiliary scintigraphy is frequent in patients with biliary patency when lengthy fasting is required before and during imaging. All visualized gallbladders contracted after feeding. With or without visualization of bowel radioactivity, scintigraphic visualization of a functioning gallbladder indicates biliary patency and excludes biliary atresia. When both the presence of bowel radioactivity and the presence of gallbladder radioactivity

were used as criteria, hepatobiliary scintigraphy was highly accurate in differentiating biliary atresia from biliary patency.

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