Lobar Decrease in ^{99m}Tc-GSA Accumulation in Hilar Cholangiocarcinoma

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Hilar cholangiocarcinoma can obstruct hepatic ducts and involve the portal veins. Both biliary stasis and decrease in portal venous flow are known to reduce ^{99m}Tc-diethylenetriamine pentaacetic acid–galactosyl human serum albumin (GSA) accumulation. The specific relationship between these pathological conditions due to hilar cholangiocarcinomas and ^{99m}Tc-GSA accumulation has never been clarified. **Methods:** Sixteen patients with hilar cholangiocarcinomas who underwent ^{99m}Tc-GSA liver scintigraphy were reviewed. The relationship between significant decrease in ^{99m}Tc-GSA accumulation and lobar biliary stasis, or decrease in the portal venous flow, was evaluated. Average counts of region of interest placed in both right and left lobes were compared in the same transaxial SPECT section. Count ratios of right and left lobes were calculated. **Results:** Significant lobar decrease in ^{99m}Tc-GSA accumulation was observed in 6 of the 16 patients. Ipsilateral portal venous stenosis or obstruction was seen in all these 6 patients, whereas ipsilateral portal venous stenosis or obstruction was seen in only 1 of the other 10 patients. Symmetric bile duct dilatation was seen in 13 patients, and asymmetric bile duct dilatation was seen in 3. Lobar decrease in ^{99m}Tc-GSA accumulation correlated well with decrease in ipsilateral portal venous flow ($P < 0.0005$). The count ratio was significantly reduced when unilateral portal venous flow decreased ($P < 0.05$). **Conclusion:** Using ^{99m}Tc-GSA liver scintigraphy, we can predict lobar decrease in ipsilateral portal venous flow and monitor hepatic functional lateralities in patients with hilar cholangiocarcinomas.

Key Words: liver; radionuclide studies; ^{99m}Tc-diethylenetriamine pentaacetic acid–galactosyl human serum albumin; hilar cholangiocarcinoma; portal vein

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In 1986, Takayasu et al. (*1*) investigated the relationship between hepatic lobar atrophy and obstruction of the portal vein or biliary stasis in 17 patients with hilar cholangiocarcinomas. Hepatic lobar atrophy correlated better with ipsilateral portal vein obstruction than with biliary stasis. The authors postulated the appearance of this phenomenon as essential in planning therapy for hilar cholangiocarcinoma.

For effective biliary decompression or safe surgery, accurate evaluation of hepatic functional reserve is necessary. Exact estimation of functional reserve in each lobe and for the entire liver is essential. Previously, we analyzed regional attenuation and signal intensity differences seen on CT and MRI by ^{99m}Tc-diethylenetriamine pentaacetic acid-galactosyl human serum albumin (GSA) (*2,3*). In these studies, regional ^{99m}Tc-GSA accumulation was reduced when regional portal venous flow decreased. This phenomenon mimicked hepatic lobar atrophy due to obstruction of the ipsilateral portal vein. Evaluation of hepatic functional distribution using ^{99m}Tc-GSA is also considered essential for planning therapy. Accumulation of this radioligand correlates with the amount of normally functioning hepatocytes and is known to be unaffected directly by biliary stasis (*4,5*). Secondary impairment of hepatocytes by biliary stasis, however, can reduce ^{99m}Tc-GSA accumulation. A case of localized decrease in ^{99m}Tc-GSA accumulation due to segmental biliary obstruction has been reported (*6*). Previously, there was a case report of lobar decrease in ^{99m}Tc-iminodiacetic acid (HIDA) uptake due to bile duct obstruction (*7*). Therefore, both biliary stasis and decrease in the portal venous flow could be causes of regional decrease in ^{99m}Tc-GSA accumulation. To our knowledge, however, there has been no detailed report clarifying the relationship of these two causative factors and ^{99m}Tc-GSA accumulation. In this study, we reviewed patients with hilar cholangiocarcinomas who had undergone ^{99m}Tc-GSA liver scintigraphy. We also investigated lateralities of hepatic functional reserve and their causes.

MATERIALS AND METHODS

Patients

From December 1992 to December 1997, 18 patients with hilar cholangiocarcinomas (10 men, 6 women; age range 47–80 y; mean age 65 y) underwent ^{99m}Tc-GSA liver scintigraphy for assessment of hepatic reserve. The results were reviewed, and 16 of those patients were included in this retrospective study. Two patients were excluded because unavailability of CT or MR images made evaluation impossible. Diagnoses were made by CT, MRI, percutaneous transhepatic cholangiography and/or endoscopic retrograde cholangiography. Diagnoses were confirmed by surgery in 7 patients and by biopsy in 3 patients. Percutaneous biliary drainage was performed in 14 patients.

Radionuclide Imaging

Patients were examined in the supine position with a dual-head, rotating gamma camera interfaced to a minicomputer (GCA7200A/

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DI; Toshiba, Tokyo, Japan). A parallel-hole, low-energy, high-resolution collimator was used. Immediately after intravenous administration of 185 MBq (5.0 mCi) ^{99m}Tc-GSA (Nihon Mediphysics, Nishinomiya, Japan), dynamic imaging was performed for 30 min. After dynamic imaging, SPECT was performed by the acquisition of 60 projection images over a 360° angle in a 128 × 128 matrix. Reconstruction for transaxial sections of 6.9 mm thickness was performed. Finally, serial sets of static planar views in the anterior, posterior, right lateral and right and left anterior oblique projections were obtained up to each preset count of 900,000.

Evaluation

Three experienced readers evaluated side by side, and consensus was obtained. The readers investigated CT and MR images and were able to make out exactly the contour of the liver and the masses. Then they evaluated ^{99m}Tc-GSA liver scintigrams (planar images and transaxial SPECT) for the presence of significant nontumorous decrease in accumulation. Decrease in the portal venous flow was defined as existing when obvious stenosis or obstruction of a portal branch was seen on angiograms. Biliary stasis was defined as existing when dilatation of the intrahepatic bile duct was recognized on CT and MR images at that time or before percutaneous drainage. When dilatation of intrahepatic bile duct was obviously predominant in one lobe, it was established that biliary stasis in the region was more severe than in the contralateral lobe, and this laterality could cause a lobar difference in ^{99m}Tc-GSA accumulation. The relationship between significant decrease in ^{99m}Tc-GSA accumulation and either lobar biliary stasis or decrease in the portal venous flow was evaluated.

As a quantitative analysis, average counts of region of interest placed in both right and left lobes were compared in the same transaxial SPECT section. Count ratios were calculated by dividing smaller average counts in one lobe by larger average counts in the other.

Statistical Analysis

The relationship between decrease in ^{99m}Tc-GSA accumulation and lobar biliary stasis or decrease in the portal venous flow was studied by the chi-square test. For comparison of count ratios, the unpaired Student t test was used. $P < 0.05$ was regarded as significant.

RESULTS

Significant lobar decrease in ^{99m}Tc-GSA accumulation was observed in 6 of 16 patients. It was seen in the right lobe in 1 patient and in the left in 5. In the remaining patients, ^{99m}Tc-GSA accumulation was homogeneous except for the sites of hepatic masses, and no interlobar accumulation difference was seen. In all the patients with lobar decrease in ^{99m}Tc-GSA accumulation, ipsilateral portal venous stenosis or obstruction was seen (Figs. 1–3). In the remaining patients, ipsilateral portal venous stenosis or obstruction was seen in only 1 patient.

Symmetric bile duct dilatation was seen in 13 patients (Figs. 1 and 2), and asymmetric bile duct dilatation was seen in 3 (Fig. 3). Of these 3, 2 cases were accompanied by ipsilateral portal vein stenosis or obstruction and 1 was not. Lobar decrease in ^{99m}Tc-GSA accumulation correlated well with decrease in ipsilateral portal venous flow ($P < 0.0005$), but did not correlate significantly with lateralities of bile duct dilatation. There was no overt correlation between lobar decrease in ^{99m}Tc-GSA accumulation and occurrence of percutaneous biliary drainage or with the sites of such drainage.

Count ratios were 0.49 ± 0.22 in cases with decreases in unilateral portal venous flow and 0.79 ± 0.21 in cases of symmetric portal venous flow. The count ratio was reduced significantly when unilateral portal venous flow decreased ($P < 0.05$).

DISCUSSION

Hilar cholangiocarcinoma originates in the wall of a bile duct and spreads along bilateral hepatic ducts. Therefore, stenosis of both right and left hepatic ducts can occur in the early stage. Hilar cholangiocarcinoma involves the portal vein less frequently than does hepatocellular carcinoma (*8*). Even with such portal vein involvement, stenosis of both right and left portal branches is unusual (*1*). In animal studies, atrophy of a corresponding lobe and hypertrophy of the contralateral lobe occurred within 2 mo after ligation of a portal branch (*9*). A similar phenomenon occurred within 2 to 3 mo after ligation of a bile duct (*10*). Both biliary stasis and decrease in the portal venous flow seem to be causes of hepatic lobar atrophy. Takayasu et al. (*1*) reported hepatic lobar atrophy caused by ipsilateral portal vein obstruction from hilar cholangiocarcinoma and discussed hepatic parenchymal changes caused by obstruction of bile ducts and/or portal veins. With 6 of 17 patients having hepatic lobar atrophy, the authors emphasized its connection with obstruction of ipsilateral portal vein, because all 6 patients had obstructed or narrowed portal veins, whereas the others did not. The authors speculated that bile duct obstruction causes ipsilateral lobar atrophy in the initial stage of hilar cholangiocarcinoma and that subsequent obstruction of the portal vein promotes further atrophic change. Hann et al. (*11*) studied cases of hepatic lobar atrophy of various causes, most of which were hilar cholangiocarcinomas. They also reported that hepatic lobar atrophy usually occurs in the setting of combined biliary and portal vein obstruction but that a significant correlation exists between hepatic lobar atrophy and ipsilateral portal vein obstruction alone. Therefore, it would seem that hepatic lobar atrophy indicates a decrease in the ipsilateral portal venous flow. But objective assessment is difficult because the exact criteria for this pathological process are not yet determined. Takayasu et al. (*1*) used the angle between the line connecting the middle hepatic vein to the inferior vena cava and the horizontal line in the frontal plane passing the inferior vena cava as one criterion. This does, however, seem a little crude, and Hann et al. (*11*) did not indicate any clear criteria for hepatic lobar atrophy.

Hepatic lobar attenuation and signal intensity differences from decrease in portal venous flow on CT and MRI have been reported in the literature (*12,13*). Precontrast CT showed hypoattenuation and T1-weighted MRI showed iso- or hypointensity, whereas T2-weighted imaging showed

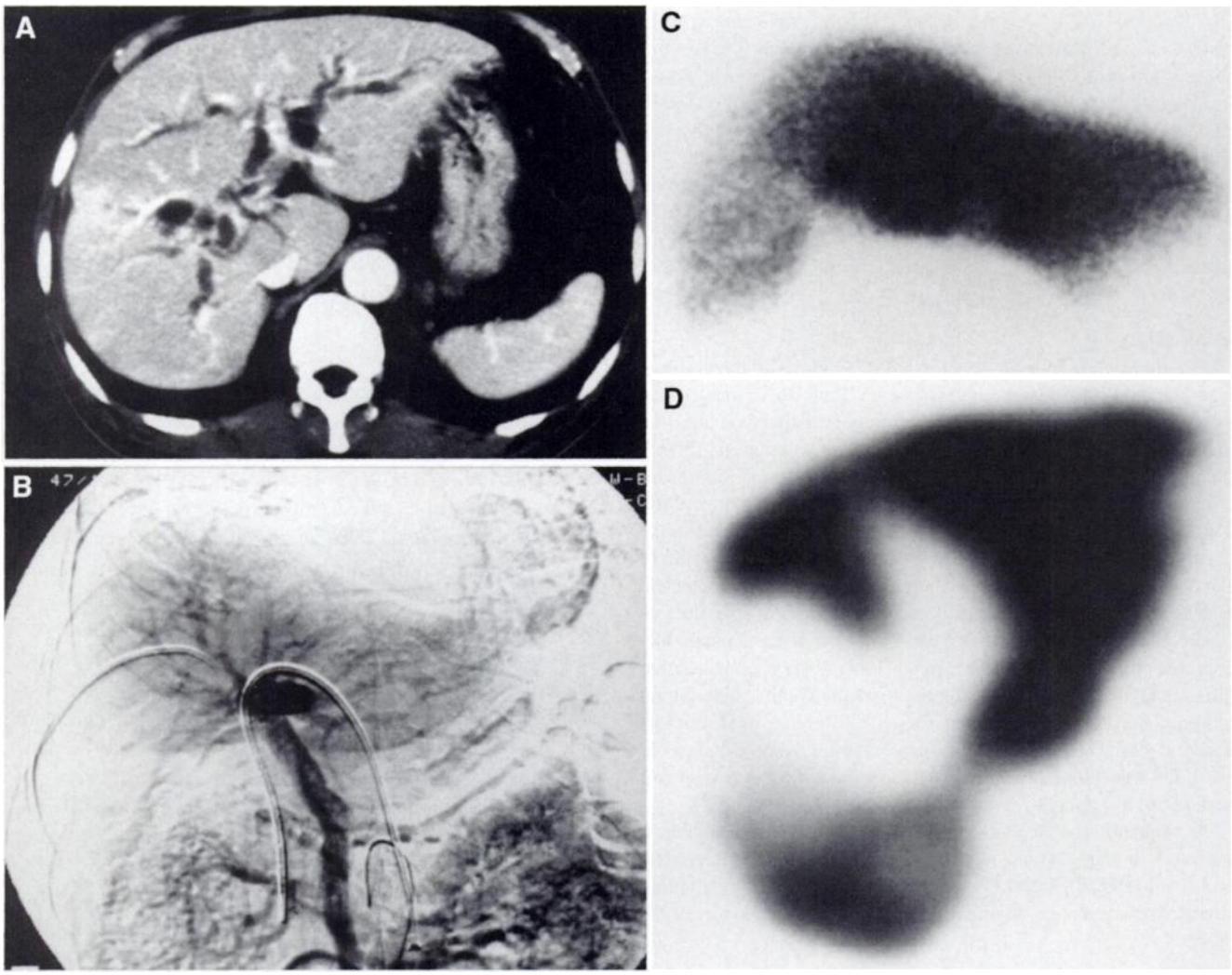

FIGURE 1. 66-y-old man with hilar cholangiocarcinoma. (A) Enhanced CT scan shows symmetric intrahepatic bile duct dilatation. Right hepatic lobe is atrophic to some degree. (B) Portogram via superior mesenteric artery shows obstruction of right portal vein. Portal venous perfusion is markedly decreased in right lobe. Right anterior oblique (C) and transaxial (D) SPECT images show obvious decrease in ^{99m}Tc-GSA accumulation in right lobe.

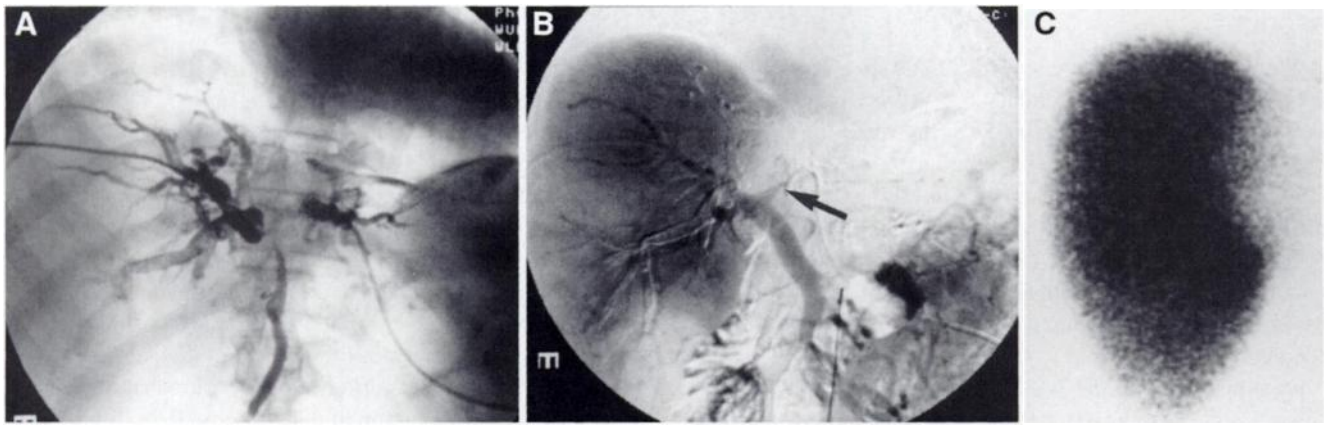

FIGURE 2. 60-y-old man with hilar cholangiocarcinoma. (A) Percutaneous transhepatic cholangiogram shows obstruction of both right and left hepatic ducts and symmetric intrahepatic bile duct dilatation. (B) Portogram via superior mesenteric artery shows severe stenosis of left portal vein (arrow) and decreased portal perfusion in left lobe. (C) Anterior view shows obvious decrease in ^{99m}Tc-GSA accumulation in left lobe.

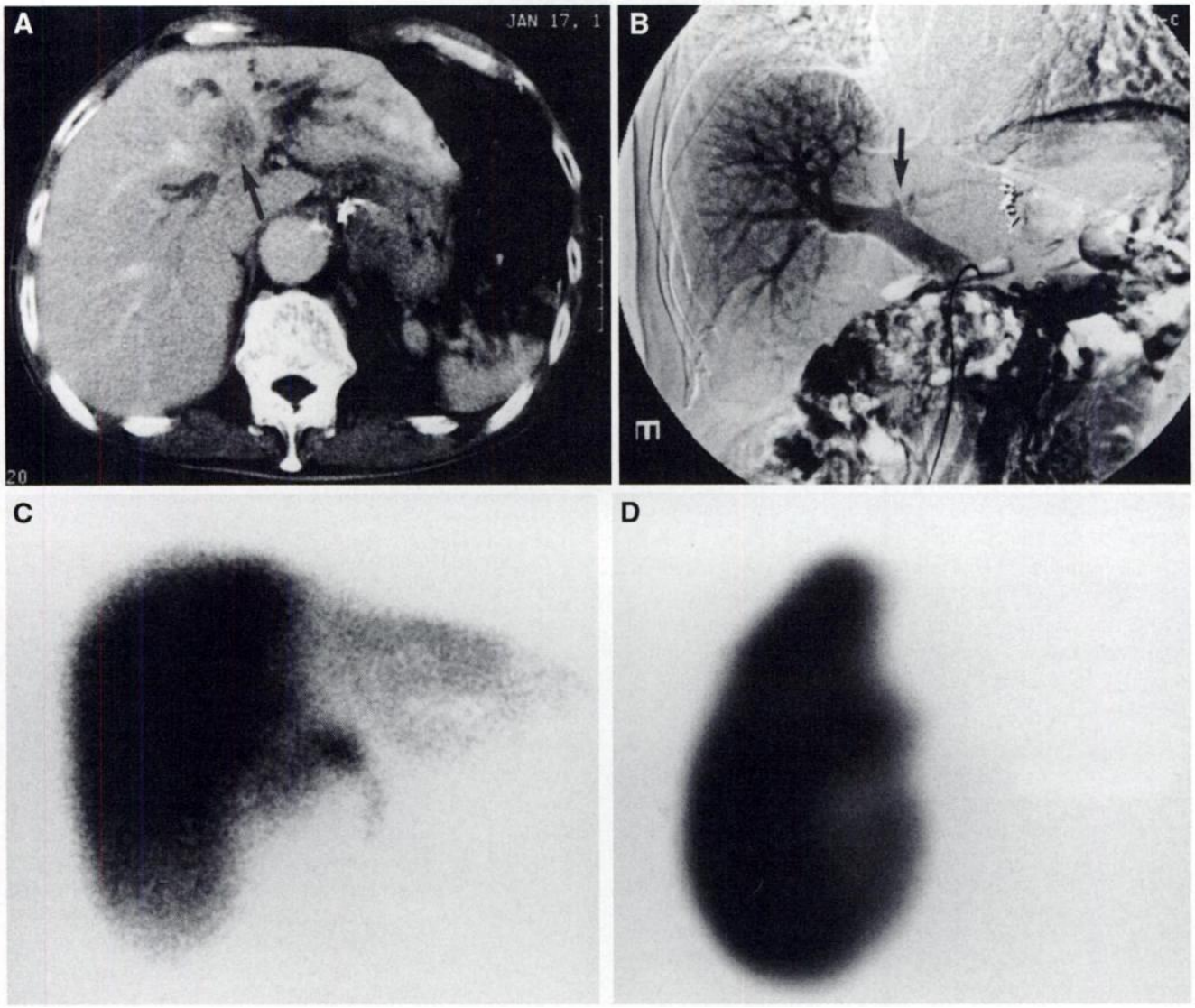

FIGURE 3. 78-y-old man with hilar cholangiocarcinoma. (A) Enhanced CT scan shows hilar mass (arrow) and dilated right and left hepatic ducts. Dilatation is asymmetric and predominant in left lobe. (B) Portogram via superior mesenteric artery shows stenosis of left portal vein (arrow) and decreased portal perfusion in left lobe. Anterior (C) and transaxial (D) SPECT images show decrease in ^{99m}Tc-GSA accumulation in left lobe. Cause of functional laterality is considered to be decreased portal perfusion in left lobe or intrahepatic biliary stasis predominant in left lobe or both.

hyperintensity in the corresponding lobe because of the occurrence of edema, depletion of hepatocytes or fibrosis. Similarly, our previous study using ^{99m}Tc-GSA proved that accumulation of this radioligand decreased when regional portal venous flow decreased (*2*). Lobar decrease in ^{99m}Tc-GSA accumulation from hilar cholangiocarcinomas that could involve the portal branches, however, has not been well documented.

In this study, lobar decrease in ^{99m}Tc-GSA accumulation correlated better with ipsilateral portal venous stenosis or obstruction than with laterality of intrahepatic biliary stasis. Obvious decrease in ^{99m}Tc-GSA accumulation in one lobe is thought to indicate ipsilateral portal vein impairment rather than interlobar laterality of biliary stasis. In these lobes, obvious atrophy was not seen. It was also thought that lobar decrease in ^{99m}Tc-GSA accumulation occurs earlier than atrophy and can detect hepatic parenchymal damage more sensitively. Moreover, lobar decrease in ^{99m}Tc-GSA accumulation is a more objective phenomenon than hepatic lobar atrophy and can be assessed quantitatively. In this study, count ratios in cases with decrease in unilateral portal venous flow were significantly smaller than in cases with homogeneous portal venous flow. We should be able to evaluate hepatic functional laterality objectively using this parameter. This type of approach was impossible with previous anatomic liver evaluations such as CT volumetry.

To achieve effective percutaneous biliary drainage, the obstruction patterns of the bile duct and its anatomic details must be well understood. This study proved that a hepatic lobe with decreased portal venous flow has less functional

reserve than the contralateral lobe. Takayasu et al. (*1*) suggested that the contralateral lobe with patent portal venous flow should be chosen for drainage for effective biliary decompression. Using ^{99m}Tc-GSA liver scintigraphy, we can determine a suitable lobe for percutaneous drainage without an invasive method such as angiography.

A quantitative approach to hepatic functional lateralities can also be significant, even in cases of potentially resectable disease. With increased knowledge of these functional lateralities, we should be able to estimate postoperative hepatic function more accurately. One should be cautious in planning an extended hepatic lobectomy that resects part of the contralateral, hyperfunctioning lobe, because most hepatic function depends on it.

CONCLUSION

^{99m}Tc-GSA liver scintigraphy in 16 patients with hilar cholangiocarcinomas was reviewed, and the relationship between hepatic functional lateralities and biliary stasis or decrease in the ipsilateral portal venous flow was studied. Lobar decrease in ^{99m}Tc-GSA accumulation was seen in 6 patients and correlated well with a decrease in ipsilateral portal venous flow. An understanding of hepatic functional lateralities by use of ^{99m}Tc-GSA would seem essential in determining therapeutic procedures for hilar cholangiocarcinomas.

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