

CASE REPORT

Usefulness of measuring hepatic functional volume using technetium-99m galactosyl serum albumin scintigraphy in hilar bile duct carcinoma

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Abstract

This case involved a 75-year-old woman with obstructive jaundice, who was diagnosed with hilar bile duct carcinoma. After endoscopic retrograde biliary drainage, total bilirubin level was normalized. The indocyanine green test retention rate at 15 min (ICGR15) was 26%. The liver uptake ratio (LHL15) by technetium-99m galactosyl human serum albumin (^{99m}Tc -GSA) liver scintigraphy was 0.87. Left hepatectomy was scheduled by CT volumetry. However, biliary drainage was insufficient and the functional liver volume showed functional deterioration of the left liver. After percutaneous transhepatic biliary drainage, future remnant liver volume by ^{99m}Tc -GSA liver scintigraphy changed to 52% from 42%, and ICGR15 and LHL15 were improved to 16% and 0.914, respectively. Scheduled left hepatectomy was performed following the results of functional liver volume. The measurement of functional volume by ^{99m}Tc -GSA liver scintigraphy provides useful information with respect to segmental liver function for deciding operative indications.

Keywords: Bile duct carcinoma• Technetium-99m galactosyl human serum albumin liver scintigraphy• Functional liver volume• Biliary obstruction• Operative indication

Introduction

The frequency of postoperative hepatic failure in hilar bile duct carcinoma has markedly decreased in recent years with improved perioperative management (1-4). Child-Pugh classification or indocyanine green (ICG) test is classically used to define the indications for radical operations (5). However, in cases involving hepatectomy for bile duct carcinomas, these criteria have limitations because of increased total bilirubin levels or poor ICG results due to biliary obstruction. Furthermore, it is necessary to evaluate segmental liver function in case of biliary or vascular obstructions (6). Asialoglyco-protein receptors on hepatocytes are a sign of functional liver cells (7). Using technetium-99m galactosyl human serum albumin ($^{99m}\text{Tc-GSA}$) liver scintigraphy, functional hepatic volume in a separate lobe of the liver can also be measured by applying single-photon emission computed tomography (SPECT). Liver volume represents useful information to define the most appropriate operative course, and is usually measured by computed tomography (3-5, 8). Based on our previous report, we hypothesized that the measurement of liver uptake by $^{99m}\text{Tc-GSA}$ scintigraphy closely reflects the activity of hepatocytes (9). Therefore, dynamic alteration in the functional area of the injured liver by biliary obstruction compared to the recovered liver could be more clearly observed compared to morphological images on computed tomography. We herein report a hilar bile duct carcinoma patient with biliary obstruction, in whom measurement of functional liver volume was considered very useful in deciding operative indications.

Evaluation of liver functions for hepatectomy

The permitted volume of liver to be resected was determined preoperatively on the basis of ICGR15 using Takasaki's formula (10). Estimated resected liver volume was measured by CT volumetry (8). Liver uptake ratio at 15 min (LHL15) by ^{99m}Tc -GSA scintigraphy and serum hyaluronic acid level were also examined preoperatively, along with ICGR15 and other functional liver parameters (11).

Morphological volume using contrast CT was measured by Workstation at our institute using Ziostation version 1.1.x (Ziosoft Inc., Redwood City, CA, USA), and actual areas without tumors and large vessels in each liver area were measured. With respect to ^{99m}Tc GSA liver scintigraphy, all patients received 3 mg (185 MBq) of ^{99m}Tc -GSA (Nihon Medi-Physics, Nishinomiya, Japan). Sequential abdominal digital images were acquired from an on-line nuclear data processor at 30 s/frame for the first 16 min after injection. SPECT images were acquired after the dynamic study (11) and transaxial SPECT images were reconstructed using Ziostation software as well. The liver area was determined by the CT image, which was simultaneously examined with liver scintigraphy.

Case report

A 75-year-old woman presented with obstructive jaundice. Nodular-type bile duct carcinoma was identified at the hepatic hilum (Fig. 1). Left hepatectomy with resection of the caudate lobe and extrahepatic bile duct was planned because a tumor dominantly infiltrated the left hepatic duct. The intrahepatic bile duct was slightly dilated. Endoscopic retrograde biliary stent was placed to reduce jaundice at a previous hospital and total bilirubin level recovered to 1.0 mg/dL at the time of administration at our institute. Other conventional parameters of liver function were mildly deteriorated. ICGR15 and K value were 26% and 0.083, respectively. HH15 (uptake ratio of the heart at 15 min to that at 3 min) and LHL15 by ^{99m}Tc -GSA liver scintigraphy were 0.599 and 0.874, respectively, which showed moderate deterioration. Table 2 shows liver volume and functional liver volume in the right and left liver, respectively. Functional liver volume by GSA volumetry in the right liver was remarkably deteriorated in comparison with that in the left liver (Fig. 2), which was different from the results obtained by CT volumetry. Permitted resected liver volume by Takasaki's formula was 49%. These evaluations allow the scheduled hepatectomy by CT volumetry but not by GSA volumetry. From the result obtained by GSA volumetry, DIC-CT was performed because no increase of total bilirubin and insufficient biliary were observed (Fig. 3). Therefore, percutaneous transhepatic biliary drainage (PTBD) in the right liver was performed. At 2 weeks after PTBD, the results of conventional liver function tests were unchanged but the results of ICGR15, HH15 and LHL15 were remarkably improved to 16%, 0.550, and 0.914, respectively. Furthermore, functional liver volume in the right liver was improved to 481 cm³ in comparison with that before PTBD (Table 1 and Fig. 4). Permitted resected liver volume was increased by 62% and the estimated resected liver volume was 48% as determined by GSA volumetry. Eventually, scheduled left hepatectomy was performed on day 20 after PTBD. The postoperative course was uneventful

and the maximum total bilirubin level was increased to 1.8 mg/dL at day 1 and total liver functions were improved at day 7.

Discussion

^{99m}Tc-GSA liver scintigraphy has been used in patients with liver disease as a reliable test to assess hepatic functional reserves, because this uptake reflects the number of live hepatic cells (12, 13). We have previously reported the clinical significance of ^{99m}Tc-GSA scintigraphy in liver disease patients who underwent hepatic resection (9, 11). This test often showed divergent results compared with conventional liver functional tests or ICG test in patients with chronic hepatitis or icteric liver (11, 14). Our preliminary study showed that ^{99m}Tc-GSA liver scintigraphy was more reliable for the evaluation of liver function in this situation and this imaging showed differences in functional area in each section of the liver (9, 11). The atrophy or damage of areas of liver caused by biliary obstruction may contribute to a result of poor liver function for the whole liver and, therefore, evaluation of separate liver functions in injured and healthy liver (i.e., future remnant liver) is necessary to decide operative indications and the extent of hepatectomy. Although ICG concentration in drained bile juice also showed functional differences in the separate parts of the liver as determined by Uesaka et al. (6), preoperative biliary drainage is not always possible in bile duct carcinoma patients and this test cannot be routinely performed. Application of ^{99m}Tc-GSA scintigraphy seems likely to address the limitations of this problem.

In the present case, serum bilirubin level was improved even with inappropriate biliary drainage. At the time of placement of the endoscopic biliary drainage tube, the physician judged that the tip of the tube was placed in the right hepatic duct beyond the area of tumor involvement; however, in fact, the tube was placed in the bile duct of segment 4. Nevertheless, the ICG test showed moderately deteriorated liver function and the permitted resected liver volume by Takasaki's formula¹⁴ was equivalent to the estimated resected liver volume by CT volumetry in this case. By applying Nagino's method for evaluation as the index of (*ICG K-value (disappearance rate) × future remnant volume (%) of the liver*)(1, 6, 15), an index over

0.05 was used as the criteria for major hepatectomy in the Nagoya series, which has the highest number of hepatectomies for hilar bile duct carcinomas in the world. By applying this criteria, the indication for hemi-hepatectomy was borderline in the present case. If this information alone had been applied to decide the operative indication, scheduled left hepatectomy might have been undertaken and the diseased liver would have remained when the reevaluation of the extent of tumor involvement was not performed. Poor postoperative course of hepatic function or hepatic failure may have occurred. After biliary drainage in the right liver was performed upon noticing the inappropriate biliary drainage, uptake of GSA liver scintigraphy in the right liver was dramatically improved in 2 weeks and the ICG test results were also improved. Biliary congestion might lead to severe damage to not only sinusoidal cells but also rendering hepatocytes susceptible to ischemic/reperfusion injury (16). After decompression of biliary pressure by adequate drainage in the present case, the impaired hepatocytes with reserved potential might reversibly recover for 2 weeks. The significance of this improvement in the uptake area has not been fully clarified yet, namely, whether each liver cell had recovered or the number of active liver cells was increased.

In tests of ^{99m}Tc -GSA scintigraphy, previous reports showed that LHL15, HH15, and maximal removal rate are reliable as non-invasive methods for evaluating hepatic functional reserves without blood sampling (17, 18). In 1996, our group started to analyze ^{99m}Tc -GSA scintigraphy preoperatively and, since 2004, a combination of ICGR15, GSA scintigraphy and measurement of serum hyaluronic acid has been applied for operative indication on the basis of retrospective analysis for 8 years (9, 11, 19). As a result, the postoperative morbidity has been improved recently (data has been submitted). In our preliminary analysis, the result by GSA scintigraphy provided a much better reflection of clinical outcomes after hepatectomy than ICGR15 (11). To the best of our knowledge, the usefulness of ^{99m}Tc -GSA scintigraphy has not been fully examined in hilar bile duct carcinoma patients with biliary obstruction or portal vein

embolization (PVE). We recently reported representative cases showing the usefulness of GSA scintigraphy (20). In these cases, GSA scintigraphy closely reflected the improvement of non-embolized liver after PVE. Measurement of functional hepatic volume by ^{99m}Tc -GSA scintigraphy was well correlated with regeneration after PVE in comparison with morphological liver volume (data has been submitted). From these findings, measuring functional liver volume by ^{99m}Tc -GSA scintigraphy is considered useful to accurately evaluate the functional liver. In the present case, we hypothesized that the drained right liver exhibited an improvement in liver function by the result of GSA scintigraphy, which must have led to the good postoperative outcome. Several reports have shown that a lower level of ^{99m}Tc -GSA clearance is associated with post-hepatectomy complications (17, 18, 21). Functional hepatic volume would also be useful for predicting post-hepatectomy complications. We will continue to pursue the application of GSA liver scintigraphy using the advantages of this method to decide the appropriate operative procedure and to prevent postoperative complications in hepatic resection.

In conclusion, we have demonstrated the usefulness of measuring functional volume by ^{99m}Tc -GSA scintigraphy to evaluate separate liver function in a case of hilar bile duct carcinoma. Functional volume as estimated by ^{99m}Tc -GSA is apparently decreased in the liver with insufficient biliary drainage compared with that estimated by CT volumetry.

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Table 1

Changes in morphological (CT) and functional liver volume (GSA) before and after the PTBD in the right and left liver

	Right liver	Left liver
CT volumetry	468 cm ³ (52%)	432 cm ³ (48%)
GSA volumetry	317→481 cm ³ (+164 cm ³) (42→52%)	435→440 cm ³ (+5 cm ³) (58→48%)

FIGURE LEGENDS

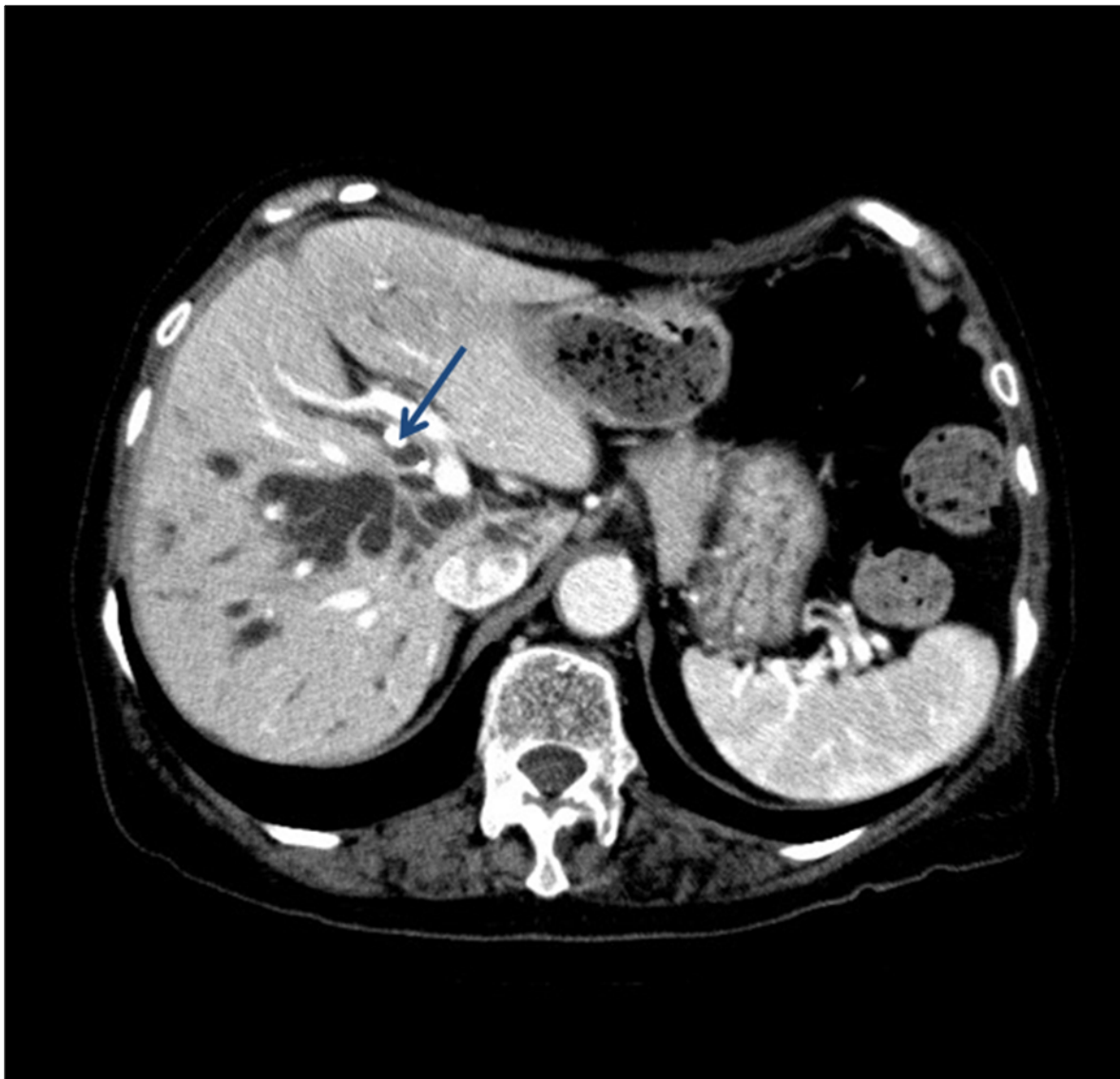


Fig. 1 The enhanced CT shows a hilar bile duct carcinoma and a drainage tube (arrow).

Intrahepatic bile duct in the right liver was mildly dilated.

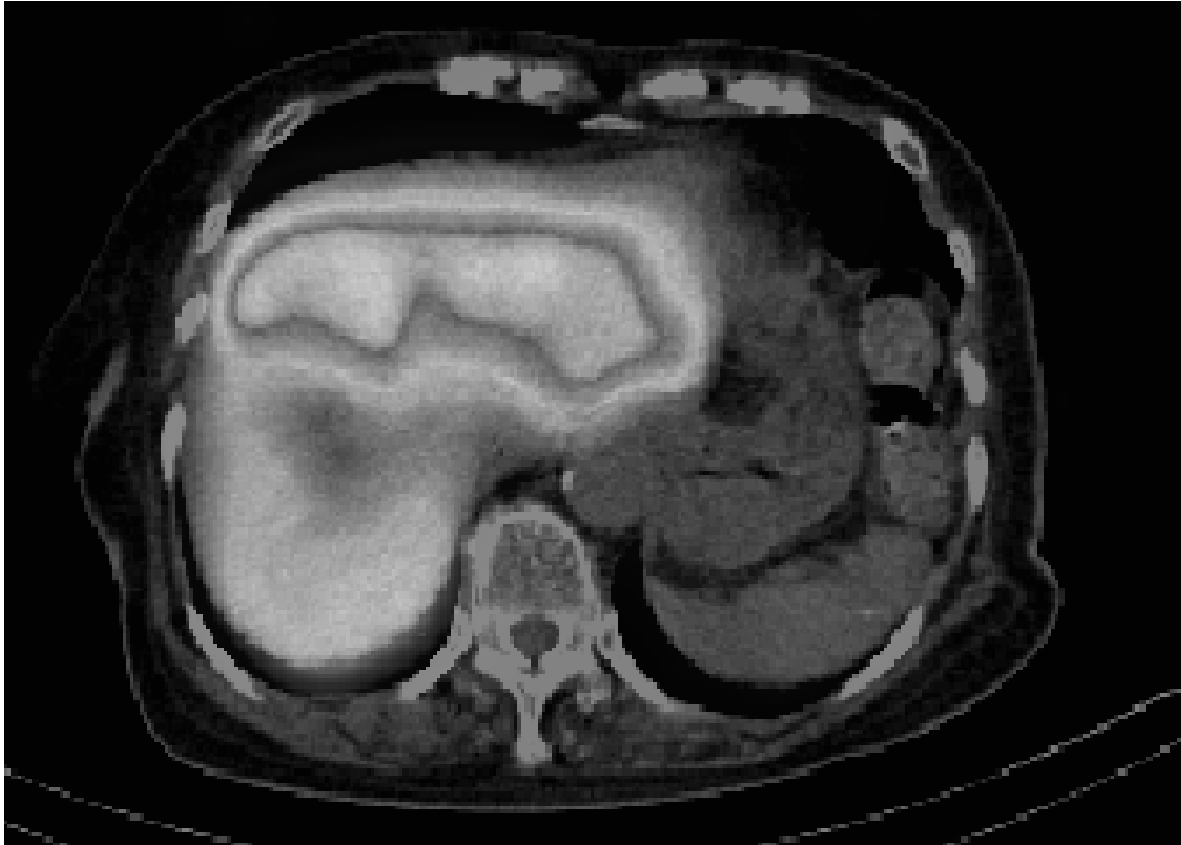


Fig. 2 Transaxial SPECT images for calculating functional volume by ^{99m}Tc -GSA scintigraphy before PTBD were obtained and measurement of hepatic volume in separate areas of the liver was performed. Arrow indicates deteriorated right liver.

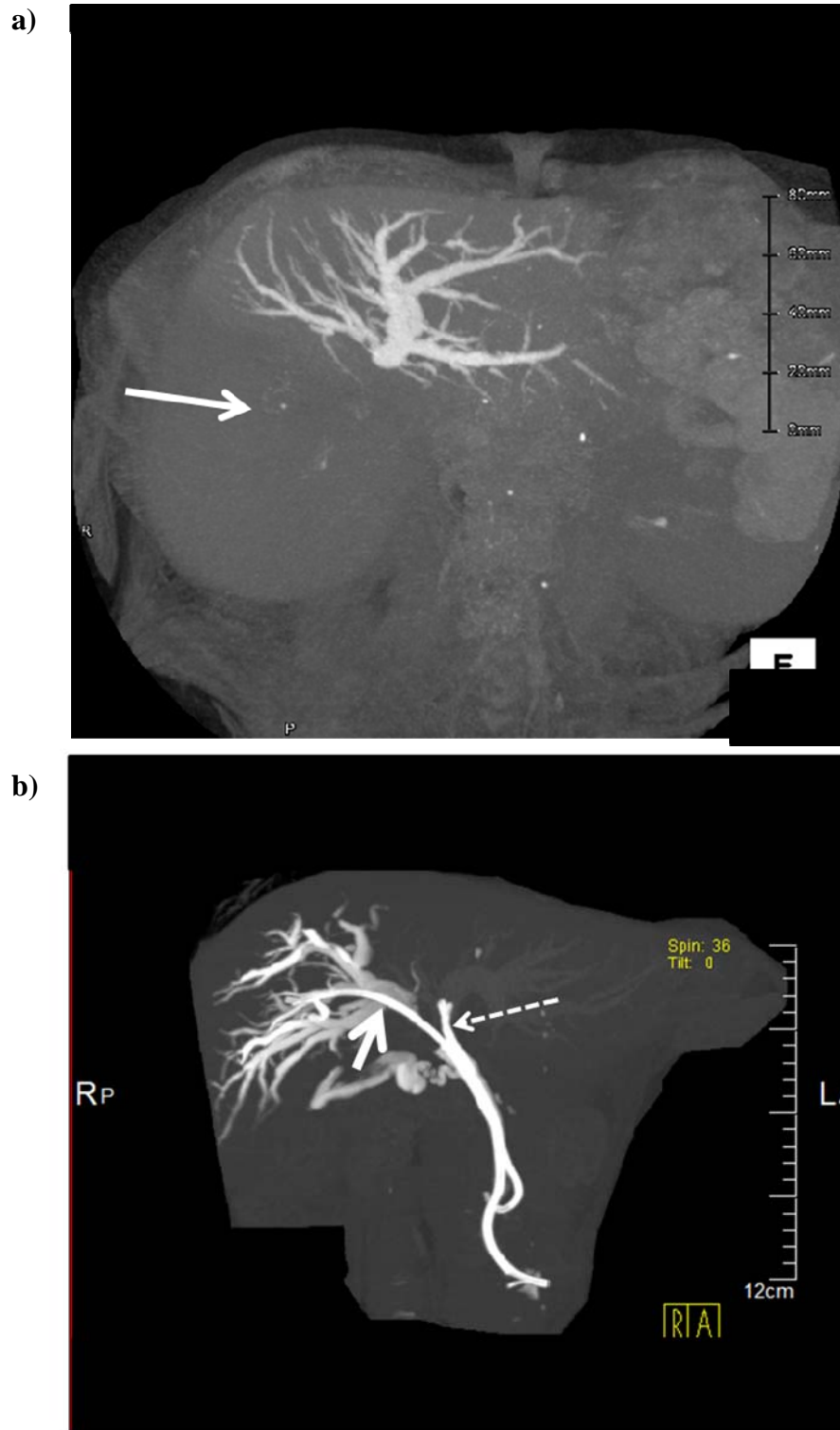


Fig 3 a) Drip infusion cholangiography shows no enhancement of the bile duct in the right liver (arrow). b) At the time of cholangiography by percutaneous transhepatic biliary drainage (large arrow), X-ray showed inadequate placement of tip of the endoscopic retrograde biliary drainage tube (dotted arrow).



Fig. 4 Transaxial SPECT images for calculating functional volume by ^{99m}Tc -GSA scintigraphy on day 14 after PTBD. Arrow indicates recovered right liver.