Annals of Nuclear Medicine Vol. 17, No. 1, 61–67, 2003

^{99m}Tc-GSA liver dynamic SPECT for the preoperative assessment of hepatectomy

Katashi SATOH,* Yuka YAMAMOTO,* Yoshihiro NISHIYAMA,*
Hisao WAKABAYASHI** and Motoomi OHKAWA*

*Department of Radiology and **First Department of Surgery,
Faculty of Medicine, Kagawa Medical University

Objective: The purpose of the present study was to devise a predictive index to predict residual liver function before hepatic resection, using technetium-99m diethylenetriamine-penta-acetic acid-galactosyl human serum albumin (^{99m}Tc-GSA) liver dynamic single photon emission computed tomography (SPECT). ***Methods:*** Fifty-seven patients with liver disease underwent liver dynamic SPECT with ^{99m}Tc-GSA. Dynamic SPECT was performed to obtain the k-value according to the accumulation curve after injection of ^{99m}Tc-GSA. The k-value is a mathematical reflection of the rate of disappearance of the circulating radiotracer as it is accumulated into the hepatocytes. We devised an original predictive residual index (PRI) by combining k-value with liver volume (V) and functional liver volume (FV). Correlation between these parameters and results of liver function tests and the grade of liver disease severity was analyzed. We investigated retrospectively the correlation between PRI and post-operative patient prognosis. ***Results:*** The k-value slightly correlated with indocyanine green clearance test at 15 mins, bilirubin level and hepaplastin test. FV and V did not correlate with liver function tests. Post-operative complications were observed in 5 patients. The PRI of these patients was below 0.37. When PRI was above 0.38, no patient had hepatic failure. ***Conclusions:*** When PRI is above 0.38, there is a low probability of hepatic failure after hepatectomy. The PRI is useful in preoperative prediction of post-hepatectomy residual liver function in patients with liver disease.

Key words: liver cancer, ^{99m}Tc-GSA, dynamic SPECT, liver function, predictive index

INTRODUCTION

THE INCIDENCE of post-operative morbidity and death following resection of hepatocellular carcinoma is higher than that after resection for colorectal liver metastasis because of the poor hepatic functional reserve resulting from co-existing chronic liver disease.[1–6] Therefore, the appropriate selection of patients for hepatic resection, using a reliable predictor of operative risk, is important in the management of patients with hepatocellular carcinoma.[4]

In general, the risks associated with partial hepatectomy have been estimated from the results of liver function tests including serum bilirubin, serum albumin, indocyanine green (ICG) clearance test and prothrombin time.[7] Although the ICG retention rate at 15 minutes after intravenous administration (ICG R15) is widely used to assess hepatic functional reserve, discrepancies between ICG R15 values and histologic liver findings are occasionally seen.[8–10] These differences are thought to depend mainly on the hepatic blood supply and the intrahepatic/extrahepatic shunt. Hence, a more reliable method for the quantitative assessment of hepatic function and functional reserve needs to be developed.

Technetium-99m diethylenetriamine-penta-acetic acid-galactosyl human serum albumin (^{99m}Tc-GSA) has

Received September 20, 2002, revision accepted December 16, 2002.

For reprint contact: Katashi Satoh, M.D., Department of Radiology, Faculty of Medicine, Kagawa Medical University, 1750–1 Ikenobe, Miki-cho, Kita-gun, Kagawa 761–0793, JAPAN.

E-mail: satoh@kms.ac.jp

recently been developed as a receptor-binding ligand that specifically binds to asialoglycoprotein receptors (ASGP-R) on the hepatocyte cell membrane.[11] It provides valuable information for the receptor density that also directly reflects the functional hepatocyte mass.[12–14] Especially, single photon emission computed tomography (SPECT) with ^{99m}Tc-GSA provides direct measurement of functional volume of the liver.[15] Therefore, ^{99m}Tc-GSA uptake and functional volume as measured by SPECT are expected to yield comprehensive evaluation of liver function in relation to individual hepatocyte function and the number of hepatocytes.[16] However, only a few clinical reports have dealt with regional hepatic function estimation using dynamic SPECT with ^{99m}Tc-GSA.[17,18]

The purpose of the present study was: 1) to investigate correlation between liver function using dynamic SPECT with ^{99m}Tc-GSA and standard biochemical liver function tests; and 2) to devise a predictive index that will describe the post-operative liver function/status, using liver dynamic SPECT with ^{99m}Tc-GSA.

MATERIALS AND METHODS

Patients

There were 57 patients (34 males, 23 females) aged 35–73 years who underwent ^{99m}Tc-GSA liver scintigraphy using dynamic SPECT within 2 weeks prior to the operation. The primary diseases of the patients were: hepatocellular carcinoma (n = 33), cholangiocellular carcinoma (n = 9), gall bladder cancer with liver invasion (n = 7) and metastatic liver cancer (n = 8). The clinical stage of disease, based on the General Rules for the Clinical and Pathological Staging of Primary Liver Cancer,[19] was stage I in 34 patients and stage II in 23 patients. The range of resection was as follows: subsegmental in 9 patients, a single segment in 10, two segments in 18 and three segments in 20. After the purpose of the study had been explained, each patient gave his or her informed consent.

Imaging

A dual head SPECT (RC 2600I, Hitachi, Tokyo, Japan) with a low energy high resolution parallel hole collimator was used for the dynamic SPECT. The term "dynamic SPECT" means the repeat and rapid SPECTs. ^{99m}Tc-GSA (3 mg, 185 MBq, Nihon Medi-Physics, Nishinomiya, Japan) was administered via an antecubital vein with the patient in the supine position on SPECT bed. This compound was approved for general use in Japan. Imaging was commenced immediately post-injection, with the patient's arms folded over the head. Each rotation consisted of 180° turn in 64 steps in a 64 × 64 matrix. Thirty-five continuous rotations were performed at a rate of 35 seconds per rotation. The SPECT field of view was included the whole liver. A Shepp and Logan filter was used for image reconstruction, and smoothing was performed at nine points before and after image reconstruction. The matrix size for image acquisition was 64 × 64, with a pixel size of 0.54 cm. The slice thickness for image reconstruction was 1.08 cm or a thickness of 2 pixels.

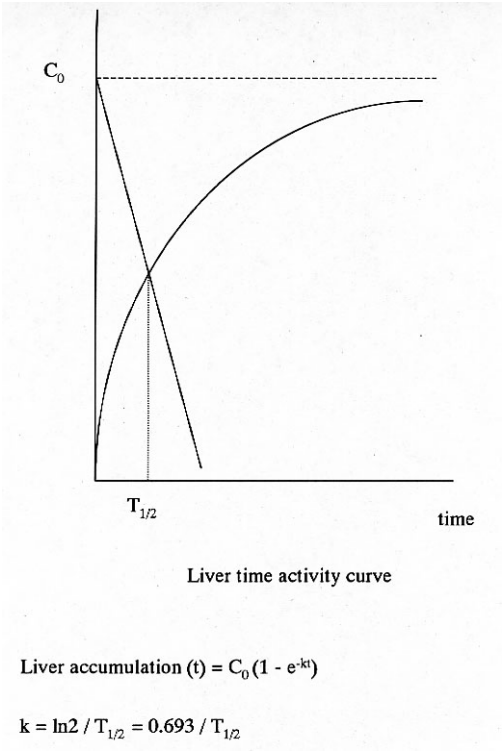


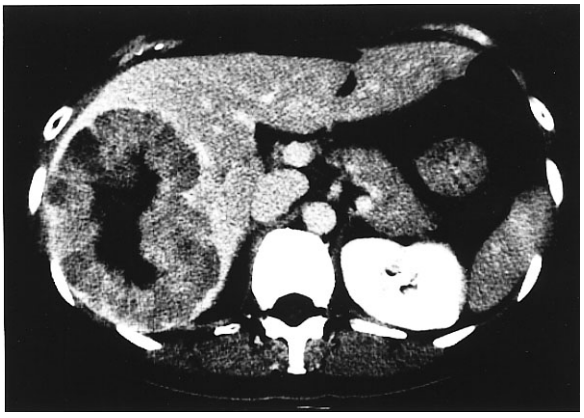
Fig. 1 Schema of accumulation curve analysis. The liver time activity curve of one voxel in a slice on continuous SPECT image. The liver time activity curve was subtracted from plateau value to create the new time activity curve. The new time activity curve was converted to logarithmic function and k-value was calculated from the downward slope.

Calculation of the liver volume (V)

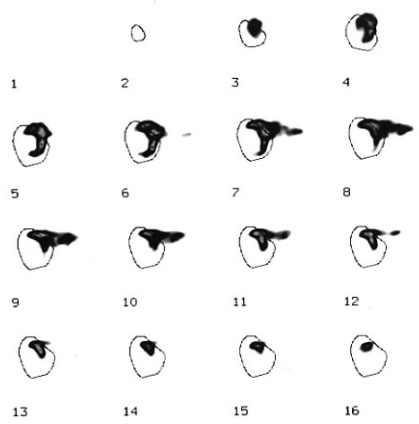
Reconstructed images of the same slice in the final five rotations were summed, and the maximum counts in each voxel (2 slices: 0.54 cm × 0.54 cm × 1.08 cm) were determined. The thickness of each voxel for which the count was above 54% of the maximum was estimated to be 1.08 cm. The area under 54% of the maximum was regarded as background. The value of 54% was determined from a previous phantom study in our laboratory.[20] The phantom was filled with 1,200 m*l* of water containing 112 MBq ^{99m}Tc-GSA and subjected to dynamic SPECT. There was a good correlation between the volume calculated from SPECT and the true volume.

Calculation of the functional liver volume (FV)

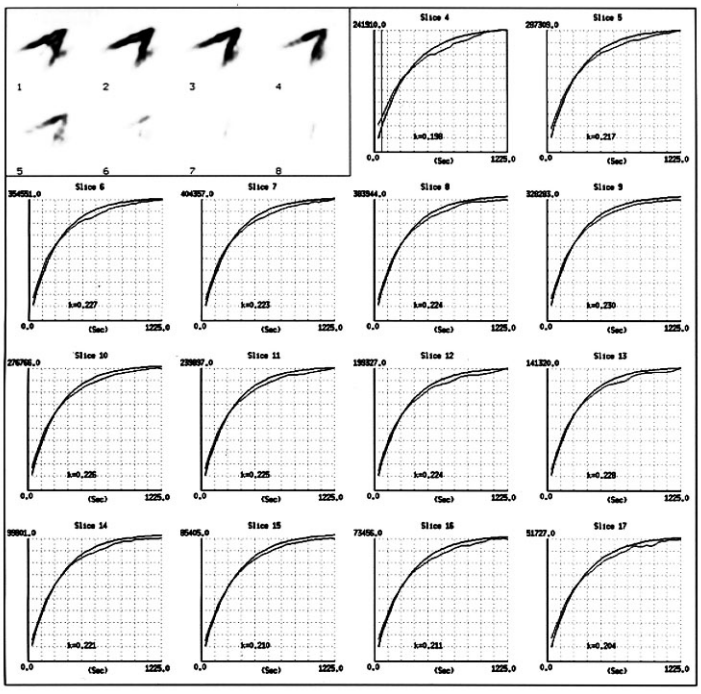
Reconstruction of images was done as described above for calculation of liver volume. The thickness of each voxel for which the count was above 80% of the maximum was estimated to be 1.08 cm, and that of each voxel for which the count was from 54% to 80% of maximum was estimated according to the accumulated counts. The



a



b



c

* Functional Volume & K Value *

Slice	FV	Fv	K	V	v
1	0.00	0.00	0.000	0.00	0.00
2	2.23	1.28	0.000	16.63	10.34
3	38.51	13.49	0.120	67.88	25.62
4	73.77	25.41	0.190	115.52	40.46
5	87.49	33.97	0.201	136.20	54.84
6	105.82	44.41	0.239	177.11	88.10
7	123.89	62.58	0.216	195.09	104.74
8	118.55	66.12	0.209	187.90	106.98
9	100.86	59.20	0.221	166.32	98.44
10	85.09	45.63	0.224	138.90	76.87
11	72.12	32.91	0.239	120.02	62.93
12	57.34	20.37	0.245	102.49	46.75
13	39.91	7.54	0.258	74.62	26.07
14	29.96	2.97	0.254	50.35	9.44
15	24.84	1.43	0.254	44.50	5.39
16	20.64	0.30	0.277	41.36	1.35
17	15.26	0.00	0.000	28.77	0.00
18	6.08	0.00	0.000	17.08	0.00
19	0.04	0.00	0.000	0.45	0.00
20	0.00	0.00	0.000	0.00	0.00
	1002.40	417.61	0.221	1681.17	758.33

RESI. INDEX : 0.430
Normal K : 0.21

d

Fig. 2 Process of obtaining the predictive residual index (PRI) in one patient. The patient had hepatocellular carcinoma (HCC) with liver cirrhosis (clinical stage II based on the General Rules for the Clinical and Pathological Staging of Primary Liver Cancer). (a) The computed tomography (CT) image shows HCC in the right lobe of the liver. (b) The right lobectomy of the liver was planned. Planned incision lines were drawn on each SPECT image by reference to the CT images. (c) The curves corresponding to each slice show the fit between the accumulation curve and the disappearance curve from the blood. (d) Values of FV, Fv, k, V and v for each SPECT image: FV = entire functional liver volume; Fv = planned residual functional liver volume; k = k value in the planned residual liver; V = entire geographical liver volume; v = planned geographical residual liver volume. The PRI was estimated as follow:

$PRI = \Sigma (k_i \times Fv_i)/k_n \times FV = (0.120 \times 13.49 + 0.190 \times 25.41 + 0.201 \times 33.97 + 0.239 \times 44.41 + 0.216 \times 62.58 + 0.209 \times 66.12 + 0.221 \times 59.20 + 0.224 \times 45.63 + 0.239 \times 32.91 + 0.245 \times 20.37 + 0.258 \times 7.54 + 0.254 \times 2.97 + 0.254 \times 1.43 + 0.277 \times 0.30)/0.21 \times 1002.40 = 0.43$

In this patient, the clinical course after right lobectomy of the liver showed no complications.

area under 54% of the maximum was regarded as background. The values of 54% and 80% were determined from the same phantom study mentioned above.[20]

Calculation of the k-value

Using 35 images obtained in the same position over 35 rotations, ^{99m}Tc-GSA accumulation curves were generated for each slice, and the level of plateau activity of each

Table 1 Correlation between ^{99m}Tc-GSA parameters and biochemical liver function tests

Liver function test	V		FV		k	
	r	p	r	p	r	p
ICG R15	−0.037	0.796	−0.187	0.181	−0.422	0.002
Bilirubin	0.179	0.185	0.177	0.387	−0.350	0.020
Albumin	−0.111	0.412	−0.084	0.536	−0.063	0.644
Cholinesterase	−0.222	0.098	−0.130	0.337	0.167	0.216
Prothrombin time	−0.144	0.291	−0.143	0.295	0.177	0.193
Hepaplastin test	−0.067	0.616	−0.006	0.963	0.437	0.001

V = liver volume, FV = functional liver volume, k = k-value, ICG R15 = plasma retention rate of indocyanine green (ICG) at 15 min, r = correlation coefficient.

curve was taken as the saturation value. The ^{99m}Tc-GSA disappearance curve was determined by subtraction from the liver saturation value. From the new curve, we were able to determine the time for 50% of the radioactivity to disappear from the blood, that is, the disappearance half-time (T1/2). The disappearance rate constant (k = 0.693/T1/2) was determined for each curve (Fig. 1). The average k-value for each slice was obtained by taking the product of the k-value and functional slice volume and dividing it by the overall functional slice volume. The average k-value for the entire liver was obtained by taking the sum of the product of the k-value and functional liver volume for each slice and dividing it by the sum of the overall functional liver volume.

Calculation of the predictive residual index (PRI)

A region of interest (ROI) was marked over each slice of the liver, excluding the heart and gall bladder, and an incision line was then drawn while referring to the computed tomographic images. The k-value of the residual liver, the post-operative functional liver volume and the total functional liver volume were then obtained. Variations in radionuclide counts were seen at both the superior and inferior margins of the liver, presumably due to the effects of respiratory movement. However, these variations had no serious effect on the PRI because the liver volume was small in these areas. The formula used to calculate the PRI was:

$$\Sigma (k_i \times Fv_i)/k_n \times FV$$

where k_i is the k-value in the planned residual liver of the i-th voxel of interest; Fv_i is the planned residual functional liver volume of the i-th voxel of interest; k_n is the normal k-value; and FV is the pre-operative total functional liver volume. The average value of 0.21, obtained for the entire liver in 10 normal volunteers, was taken as the kn value.[20] Figure 2 demonstrates the process of obtaining the PRI in one patient. The PRI in each patient was calculated and its critical value was compared with the post-operative clinical course.

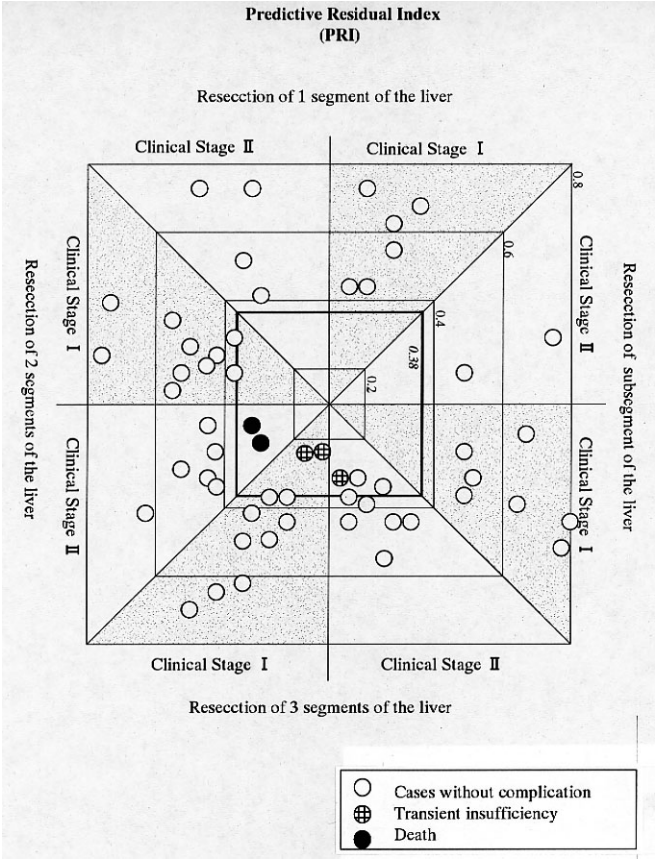


Fig. 3 Relationship between the predictive residual index (PRI) and post-operative clinical course in 57 patients with liver disease who underwent hepatectomy. Post-operative complications were observed in 5 patients. The values of PRI were 0.24, 0.26 and 0.37 each for 3 patients who developed transient hepatic insufficiency, and 0.36 and 0.37 each for 2 patients who died of hepatic insufficiency. When the value of PRI was above 0.38, no patient died or had symptoms of hepatic failure. Clinical Stage I and Clinical Stage II were determined based on the General Rules for the Clinical and Pathological Staging of Primary Liver Cancer.[19]

Correlation between ^{99m}Tc-GSA parameters and biochemical liver function tests

Laboratory data that are conventionally used as parameters of hepatic functional reserve, including ICG R15, serum bilirubin, serum albumin, cholinesterase, prothrombin time and hepaplastin test were determined, and their correlations with V, FV and k-value examined.

Statistical analysis

All results were represented as mean ± S.D. The significance of differences between ^{99m}Tc-GSA parameters including V, FV and k-value and biochemical liver function tests was evaluated by Student's paired t-test. A p value of less than 0.05 was considered significant.

RESULTS

Correlation between ^{99m}Tc-GSA parameters and biochemical liver function tests

The correlations between ^{99m}Tc-GSA parameters including V, FV and k-value and biochemical liver function tests are summarized in Table 1. There was no correlation between V and FV and biochemical liver function tests. However, k-value slightly correlated with ICG R15 ($r = -0.422$, $p = 0.002$), serum bilirubin ($r = -0.350$, $p = 0.02$) and hepaplastin test ($r = 0.437$, $p = 0.001$).

PRI and post-hepatectomy clinical course

Regarding the relationship between the PRI and post-hepatectomy clinical course, post-operative complications were observed in 5 patients (Fig. 3). In these patients, transient hepatic insufficiency was seen in 3 and the remaining 2 died of hepatic insufficiency more than 1 month following the operation. The peak level of serum bilirubin occurred 1–2 weeks post-hepatectomy, and gradually decreased to the normal range after another 1–2 weeks. In some patients with persistent hyperbilirubinemia, the level slowly improved to the normal range. We considered that these cases showed transient hepatic dysfunction. The PRI values were 0.24, 0.26 and 0.37 for 3 patients who developed transient hepatic insufficiency, and 0.36 and 0.37 for 2 patients who died of hepatic insufficiency. Of the remaining 52 patients, 50 patients had PRI values higher than 0.38, and these patients had no symptoms of hepatic failure or died. Two patients having PRI values lower than 0.38, on the other hand, survived without any liver failure. Using the cutoff value of 0.38 for PRI, the positive and negative predictive values for hepatectomy with or without complications were 71.4% and 100%, respectively.

DISCUSSION

With advances in hepatic surgery and hepatic radiotherapy, various treatments for patients with primary liver cancer have become available. It has accordingly become important to evaluate the operative risk corresponding to the reserve hepatic function, and to select the proper operative technique based on this risk.

To prevent post-operative hepatic insufficiency, it is necessary to assess the residual liver volume by taking into consideration its functional capacity (i.e. the functional liver volume). One important factor determining post-operative liver function is blood flow to the residual hepatic parenchyma. The disappearance rate of intravenously injected radiocolloids such as ^{198}Au-colloid or ^{99m}Tc-Sn colloid is thought to be a measure of the hepatic blood flow. Tanabe et al.[21] previously examined the properties of ^{99m}Tc-Sn colloid in a hepatic perfusion study and found that there were significant differences between the k-value using ^{99m}Tc-Sn colloid dynamic SPECT for normal volunteers and patients with liver cirrhosis. Hino et al.[22] showed that k-value using ^{99m}Tc-Sn colloid dynamic SPECT significantly correlated with ICG R15. Our previous study which included normal liver patients showed that k-value using ^{99m}Tc-GSA dynamic SPECT significantly correlated with ICG R15 ($r = -0.616$, $p < 0.001$).[23] Furthermore, that study demonstrated a significant correlation between liver volumes from computed tomography and ^{99m}Tc-GSA dynamic SPECT.[23] In the present study, we performed ^{99m}Tc-GSA dynamic SPECT in various liver diseases to obtain the k-value, with the results showing that k-value correlated well not only with ICG R15 but also with both serum bilirubin and hepaplastin test.

Several methods for detecting the hepatic functional volume with ^{99m}Tc-Sn colloid, ^{99m}Tc-phytate, ^{99m}Tc-PMT and ^{99m}Tc-HSA have been reported.[24] However, ^{99m}Tc-Sn colloid and ^{99m}Tc-phytate hepatic scintigraphy mainly reflect reticuloendothelial function and do not always indicate hepatic function. ^{99m}Tc-PMT is a hepatobiliary imaging agent, but with this agent it is difficult to obtain satisfactory SPECT images for volume measurement because it is excreted rapidly into the biliary system. ^{99m}Tc-HSA is a vascular image agent, and does not reflect hepatocyte function. On the other hand, ^{99m}Tc-GSA specifically binds to the ASGP-R on the hepatocyte membrane. Functional volume assessment by ^{99m}Tc-GSA SPECT has several advantages,[16] including the fact that the method counts the number of ASGP-R expressed on the hepatocyte plasma membrane and, therefore, the functional volume is related to parenchymal cell volume.

In the currently used method of functional liver volume measurement using ^{99m}Tc-GSA, the contours of the liver are generally identified by a cut-off method. Wu et al.[24] reported that the functional liver volume using ^{99m}Tc-GSA SPECT truly reflected the functional hepatocyte mass and showed a good correlation between functional liver volume and ICG R15. However, the functional volume measured by the cut-off method is not suitable because the calculation is performed based on the assumption that the ^{99m}Tc-GSA is uniformly distributed

within the liver. The functional liver volume should be weighted depending on the degree of ^{99m}Tc-GSA accumulation. In the present study, we obtained the maximum count for all SPECT slices and estimated the slice thickness of each voxel as 1.08 cm, for which the count was above 80% of the maximum count. Furthermore, the thickness of each voxel for which the count was between 54% and 80% of maximum was obtained by ^{99m}Tc-GSA counts multiplied by the number of voxels in the slice to obtain the functional liver volume. The values of 54% and 80% were determined from a previous phantom study.[20] However, in contrast with the study by Wu et al.,[24] none of the preoperative laboratory tests in the present study were correlated with functional liver volume obtained by ^{99m}Tc-GSA dynamic SPECT. In the present study, the k-value might be more sensitive to the grade of liver disease severity than functional liver volume.

The PRI in the present study was devised by combining the functional liver volume and the k-value. The limits of resection of the liver were assessed by comparing the PRI value with the patient's post-operative course. The PRI limit was found to be around 0.38, based on data from 2 patients who died and 3 patients who developed transient hepatic insufficiency after surgery. This finding suggests that the probability of hepatic failure after hepatic resection is low in cases in which the PRI is above 0.38.

Hino et al.[22] have shown previously that the PRI using ^{99m}Tc-Sn colloid would be clinically more useful in liver disease patients with clinical stage II than clinical stage I. In their study,[22] in 6 of 8 patients with values below the predictive index limit using ^{99m}Tc-Sn colloid, there were no major problems observed during the post-operative course, and all of these 6 patients were of clinical stage I. In the present study, there was no difference between clinical stage I and stage II patients. This difference suggests that ^{99m}Tc-Sn colloid may be related to the reticuloendothelial system, and, ^{99m}Tc-GSA to hepatocyte function. Thus, ^{99m}Tc-GSA liver dynamic SPECT is useful for preoperative assessment of liver surgery not only in clinical stage I but also in clinical stage II patients and may be superior to that using ^{99m}Tc-Sn colloid.

In the present study, the strongest predictive parameter was the PRI, which was below 0.37 in patients who died post-operatively or developed hepatic insufficiency. The higher the PRI, the greater the residual liver function after hepatectomy, and the greater likelihood of patient survival. The diagram shown as Figure 3 indicates that the two patients that died were in stage II and had resection of 2 segments. Both of them were hepatocellular carcinoma patients. The conventional criteria, such as Child-Pugh score, remaining liver volume or parenchymal resection rate estimated preoperatively using CT volumetry did not predict hepatic death accompanying major hepatic resection either. Of the 3 that developed hepatic insufficiency, two were in stage I, one in stage II and all had 3 segments removed. The staging does not reflect directly the extent of spread, since 11 patients were in stage I and had 3 segment partial hepatectomy. The cutoff point of PRI 0.38 gives a positive predictive value of 71.4% and 100% for the negative predictive value. However, the limitation of this study is that the total number of complicated patients was only 5 out of a total 57. Clinical trials among a larger population are required to determine the exact role of dynamic liver SPECT using ^{99m}Tc-GSA for the preoperative assessment of liver cancer.

CONCLUSION

We have described a new method for obtaining dynamic liver SPECT images using ^{99m}Tc-GSA to determine the limitations of hepatectomy in patients with liver disease and devised a predictive index to assess residual hepatic function. The findings suggest that patients with a PRI value above 0.38 should be able to tolerate hepatectomy well.

REFERENCES

1. Iwatsuki S, Esquivel CO, Gordon RD, Starzl TE. Liver resection of metastatic colorectal cancer. *Surgery* 1986; 100: 804–810.
2. Nagasue N, Kohno H, Chang YC, Taniura H, Yamanoi A, Uchida M, et al. Liver resection for hepatocellular carcinoma. Results of 229 consecutive patients during 11 years. *Ann Surg* 1993; 217: 375–384.
3. Scheele J, Stangl R, Altendolf-Hofmann A, Gall FP. Indicators of prognosis after hepatic resection for colorectal secondaries. *Surgery* 1991; 100: 13–29.
4. Noguchi T, Imai T, Mizumoto R. Preoperative estimation of surgical risk of hepatectomy in cirrhotic patients. *Hepatogastroenterology* 1990; 37: 165–171.
5. Bismuth H, Chiche L, Adam R, Castaing D, Diamond T, Dennison A. Liver resection versus transplantation for hepatocellular carcinoma in cirrhotic patients. *Ann Surg* 1993; 218: 145–151.
6. Franco D, Smadja C, Meakins JL, Wu A, Berthoux L, Grange D. Improved early results of elective hepatic resection for liver tumors. One hundred consecutive hepatectomies in cirrhotic and noncirrhotic patients. *Arch Surg* 1989; 124: 1033–1037.
7. Kawasaki S, Makuuchi M, Miyagawa S, Kakazu T, Hayashi K, Kasai H, et al. Result of hepatic resection for hepatocellular carcinoma. *World J Surg* 1995; 19: 31–34.
8. Kwon A-H, Ha-Kawa SK, Uetsuji S, Kamiyama Y, Tanaka Y. Use of technetium 99m diethylenetriamine-pentaacetic acid-galactosyl-human serum albumin liver scintigraphy in the valuation of preoperative and postoperative hepatic functional reserve for hepatectomy. *Surgery* 1995; 117: 429–434.
9. Uesaka K, Nimura Y, Nagino M. Changes in hepatic lobar function after right portal vein embolization: An appraisal by biliary indocyanine green excretion. *Ann Surg* 1996; 223: 77–83.
10. Takeuchi S, Nakano H, Kim YK, Kumada K, Nagasaki H,

Sasaki J, et al. Predicting survival and post-operative complications with Tc-GSA liver scintigraphy in hepatocellular carcinoma. *Hepatogastroenterology* 1999; 46: 1855–1861.
11. Ha-Kawa SK, Tanaka Y. A quantitative model of technetium-99m-DTPA-galactosyl-HSA for the assessment of hepatic blood flow and hepatic binding receptor. *J Nucl Med* 1991; 32: 2233–2240.
12. Torizuka K, Ha-Kawa SK, Kudo M, Kubota Y, Yamamoto K, Itoh K, et al. Phase III multi-center clinical study on ^{99m}Tc-GSA, a new agent for functional imaging of the liver. (in Japanese) *KAKU IGAKU (Jpn J Nucl Med)* 1992; 29: 159–181.
13. Kudo M, Todo A, Ikekubo K, Hino M. Receptor index via hepatic asialoglycoprotein receptor imaging: correlation with chronic hepatocellular damage. *Am J Gastroenterol* 1992; 87: 865–870.
14. Shiomi S, Kuroki T, Enomoto M, Ueda T, Masaki K, Ikeoka N, et al. Fuluminant hepatic failure monitored by technetium-99m-DTPA-galactosyl-human serum albumin scintigraphy. *J Nucl Med* 1996; 37: 641–643.
15. Yumoto Y, Umeda M, Ohshima K, Ogawa H, Kurokawa T, Kajitani M, et al. Estimation of remnant liver function before hepatectomy by means of technetium-99m-diethylenetriamine-pentaacetic acid galactosyl human albumin. *Cancer Chemother Pharmacol* 1994; 33: S1–S6.
16. Tanaka A, Shinohara H, Hatano E, Sato S, Kanazawa A, Yamaoka Y, et al. Preoperative changes in hepatic function as assessed by asialoglycoprotein receptor indices by technetium-99m galactosyl human serum albumin. *Hepatogastroenterology* 1999; 46: 369–375.
17. Fujisawa H, Shinozuka A, Takenaka H. Study on the evaluation of total and regional liver function using ^{99m}Tc-GSA dynamic SPECT. (in Japanese) *KAKU IGAKU (Jpn J Nucl Med)* 1997; 34: 885–899.
18. Hwang EH, Taki J, Shuke N, Nakajima K, Kinuya S, Konishi S, et al. Preoperative assessment of residual hepatic functional reserve using ^{99m}Tc-DTPA-galactosyl-human serum albumin dynamic SPECT. *J Nucl Med* 1999; 40: 1644–1651.
19. Liver Cancer Study Group of Japan. *The general rules for the clinical and pathological study of primary liver cancer*, July 1992, third edn.
20. Kiuchi T, Kawasaki Y, Hino I, Kojima K, Ohkawa M, Tamai T, et al. Evaluation of liver function in carbon tetrachloride-damaged rabbits by dynamic SPECT: comparison of ^{99m}Tc-GSA and ^{99m}Tc-Sn. (in Japanese) *Nippon Acta Radiol* 1994; 54: 1018–1029.
21. Tanabe M, Tamai T, Mimura H, Orita K, Tsumura M, Mizukawa K, et al. Clinical values for an index predicting postoperative residual liver function by pre-operative liver scintigraphy in patients with liver. *Ann Nucl Med* 1989; 3: 25–29.
22. Hino I, Tamai T, Satoh K, Takashima H, Ohkawa M, Tanabe M. Index for predicting post-operative residual liver function by pre-operative dynamic liver SPET. *Nucl Med Commun* 1997; 18: 1040–1048.
23. Wakabayashi H, Nishiyama Y, Ushiyama T, Maeba T, Maeta H. Evaluation of the effect of age on functioning hepatocyte mass and liver blood flow using liver scintigraphy in preoperative estimations for surgical patients: Comparison with CT volumetry. *J Surg Res* 2002; 106: 246–253.
24. Wu J, Ishikawa N, Takeda T, Tanaka Y, Pan X, Sato M, et al. The functional hepatic volume assessed by ^{99m}Tc-GSA hepatic scintigraphy. *Ann Nucl Med* 1995; 9: 229–235.