Preoperative Assessment of Residual Hepatic Functional Reserve Using ^{99m}Tc-DTPA-Galactosyl-Human Serum Albumin Dynamic SPECT

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Preoperative assessment of residual hepatic functional reserve offers important strategic information for hepatic resection. To predict the postoperative residual liver function, we assessed the value of hepatic ^{99m}Tc-diethylenetriamine pentaacetic acid-galactosyl-human serum albumin (^{99m}Tc-GSA) clearance estimated by dynamic SPECT analysis. **Methods:** We investigated 114 consecutive patients with liver disease, including 55 hepatectomy cases. One minute after injection of 185 MBq ^{99m}Tc-GSA, 15 serial dynamic SPECT images were obtained every minute. The initial five sets of SPECT images were analyzed by Patlak plot to estimate the sequential initial hepatic ^{99m}Tc-GSA clearance (mL/min) as an index of hepatic function. The sum of hepatic ^{99m}Tc-GSA clearance of the segments immune from resection was categorized as predicted residual ^{99m}Tc-GSA clearance. In the hepatectomy cases, scintigraphy was performed before and 37 ± 10 d after the operation. **Results:** Good correlation was observed between the total hepatic ^{99m}Tc-GSA clearance and conventional hepatic function tests: plasma retention rate of iodocyanine green (ICG) at 15 min (ICG R15), $r = -0.600$, $P < 0.0001$, n = 94; plasma disappearance rate of ICG (K ICG), $r = 0.670$, $P < 0.0001$, n = 83; cholinesterase, $r = 0.539$, $P < 0.0001$, n = 121; serum albumin, $r = 0.421$, $P = 0.0001$, n = 123; and hepaplastin test, $r = 0.456$, $P < 0.0001$, n = 120. There was good correlation between the predicted residual ^{99m}Tc-GSA clearance and the postoperative total hepatic ^{99m}Tc-GSA clearance in patients who underwent segmentectomy or lobectomy ($r = 0.84$, $P < 0.0001$, n = 28) and between the pre- and postoperative total hepatic ^{99m}Tc-GSA clearance in patients who underwent subsegmentectomy ($r = 0.91$, $P < 0.0001$, n = 25). Five patients who had postoperative complications due to hepatic insufficiency (2 patients died of postoperative hepatic failure within 2 mo after operation) showed significantly lower predicted residual ^{99m}Tc-GSA clearance compared with the patients without complications (90.3 ± 37.2 versus 320.9 ± 158.8 mL/min; $P < 0.005$). **Conclusion:** The total hepatic ^{99m}Tc-GSA clearance reflected hepatic function. In addition, preoperative predicted residual hepatic ^{99m}Tc-GSA clearance was a good indicator of postoperative hepatic function and early prognosis. ^{99m}Tc-GSA dynamic SPECT is assumed to be a useful method for determining the surgical strategy in patients with hepatic tumor and especially in patients with hepatic dysfunction.

Key Words: ^{99m}Tc-DTPA-galactosyl-human serum albumin; dynamic SPECT; hepatic resection; functional reserve

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Assessment of hepatic functional reserve is one of the most important issues in hepatic resection. This is especially true with hepatocellular carcinoma, with which a majority of patients have concomitant liver damage such as liver cirrhosis, which limits hepatic resectability. For the estimation of hepatic functional reserve, many conventional tests including serum albumin, prothrombine time, hepaplastin test, serum choline estelase activity and indocyanine green (ICG) have been used in the assessment and evaluation of hepatic clinical efficacy. ^{99m}Tc-diethylenetriamine pentaacetic acid-galactosyl-human serum albumin (^{99m}Tc-GSA), a radiopharmaceutical that binds specifically to hepatic asialoglycoprotein receptor (AGR), has been developed and used clinically for hepatic functional reserve estimation. There are many reports of such analysis using ^{99m}Tc-GSA scintigraphy (*1–9*). Most of these have focused on the estimation of the global hepatic function. However, a few have dealt with regional hepatic functional estimation (*2,5*).

In this study, we estimated the regional hepatic ^{99m}Tc-GSA clearance as an index of hepatic functional reserve using dynamic SPECT, and we assessed the prognostic value of the estimated parameters.

MATERIALS AND METHODS

Patients

We recruited 114 consecutive patients with hepatic disease to this study. Sixty-three patients had chronic liver disease, 1 had acute liver disease (fulminant hepatitis), 54 had hepatocellular carcinoma (HCC), 22 had metastatic tumor, 13 had cholangiocellu-

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lar carcinoma, 12 had gallbladder carcinoma and 6 had benign lesions. Hepatic resection was performed in 55 patients: extended right lobectomy in 8, extended left lobectomy in 2, right lobectomy in 6, left lobectomy in 7, segmentectomy in 7 and subsegmentectomy in 25. Twenty patients were treated with nonoperative interventions: transarterial embolization in 14, percutaneous ethanol injection in 8, microwave coagulation therapy in 4 (6 patients underwent both transarterial embolization and percutaneous ethanol injection). Two patients who underwent extended right lobectomy died within 2 mo after the operation, and a patient with fulminant hepatitis died 47 d after scintigraphy due to hepatic failure. Three patients (after extended right lobectomy, left lobectomy and lateral segmentectomy, respectively) had postoperative complications due to hepatic insufficiency. In the hepatectomy cases, scintigraphy was performed before and 37 $\pm$10 d (range 13–56 d) after operation. In 2 patients who died of postoperative hepatic failure, follow-up scintigraphy could not be performed.

Data Acquisition

^{99m}Tc-GSA scintigraphy was performed after overnight fasting in all patients. Dynamic SPECT images were obtained using a three-head gamma camera system (Toshiba GCA9300A, Toshiba, Nasu, Japan) equipped with low-energy high-resolution collimators. One minute after the bolus injection of 3 mg (185 MBq) ^{99m}Tc-GSA into an antecubital vein, 15 sequential SPECT datasets were acquired for 15 min. Projection data were acquired using a 64×64 matrix from 90 views, using continuous rotation, and energy discrimination was centered on 140 keV and a 20% window. Fifteen sets of transaxial slices were reconstructed using a ramp filter with a Butterworth filter (order 8; cutoff frequency 0.24 cycle/pixel). The slice thickness was two pixels (12.8 mm). Scatter and attenuation corrections were not performed.

Image Analysis

A region of interest (ROI) was set over the cardiac ventricular cavity (65% cutoff of maximal count) on a selected slice that had a maximal blood pool count in the first SPECT frame to generate the blood count [B(t)] time-activity curve (TAC). B(t) was expressed in units of counts per milliliter that was standardized by voxel volume. ROIs were also generated over the entire liver on the last (15th) tomographic images using isocount methods (35% cutoff of maximal count) to estimate the functional liver volume. The threshold value of ROIs of the cardiac ventricular cavity and liver was selected on the basis of phantom studies. Simulated cardiac and liver phantom (volume of 150 mL and 1000 mL, respectively) were filled with ^{99m}Tc solution (37 MBq/L) and SPECT was performed as described previously.

We generated the regional TAC of the liver by plotting the liver counts in each of the voxels. We estimated the regional hepatic ^{99m}Tc-GSA clearance (Ku) for each voxel by using the Patlak plot method from the first 5 min data (*3*) and we generated functional images of Ku.

We proposed the Patlak plot for the linear approximation of the blood-to-organ tracer uptake constant using graphical analysis. Ku was calculated according to the following equation:

$$L(t)/B(t) = Ku \times \int_0^t B(\tau)\, d\tau/B(t) + Vh,$$

where L(t) is the hepatic radioactivity concentration, and Vh is the hepatic blood volume in a voxel of the liver.

Because this is a first-order equation, using measured data for L(t) and B(t), L(t)/B(t) can be plotted against $\int_0^t B(\tau)d\tau/B(t)$, and the linear regression analysis gives Ku and Vh from the slope and the intercept, respectively.

The sum of Ku of each voxel was estimated as the total hepatic ^{99m}Tc-GSA clearance that was expressed in mL/min.

The functional image of Ku was divided into four segments (left lateral, left medial, right anterior and right posterior) according to liver anatomy, and the segmental functional liver volume and clearance were also estimated. Predicted postoperative residual volume and predicted residual ^{99m}Tc-GSA clearance were calculated prospectively by the analysis of the segments that would be immune from resection.

As an index of hepatic function normalized by hepatic volume, mean ^{99m}Tc-GSA clearance was calculated by dividing total hepatic ^{99m}Tc-GSA clearance by functional liver volume (mL/min/mL liver).

Statistical Analysis

Spearman rank correlation analysis was applied to analyze the correlation between ^{99m}Tc-GSA parameters (functional liver volume, hepatic ^{99m}Tc-GSA clearance and mean ^{99m}Tc-GSA clearance) and each laboratory datum (plasma retention rate of ICG at 15 min [ICG R15], plasma disappearance rate of ICG [K ICG], cholinesterase, serum albumin, hepaplastin test and total bilirubin). Correlation between the pre- and postoperative ^{99m}Tc-GSA parameters was analyzed using Pearson correlation analysis, and the significance of differences between the pre- and postoperative ^{99m}Tc-GSA parameters was determined using Student paired *t* test. The significance of differences of ^{99m}Tc-GSA clearance between two patients groups (with or without complications) was determined using Mann-Whitney test. The significance of differences of mean ^{99m}Tc-GSA clearance among three patients groups (subsegmentectomy, moderate resection and large resection) was determined using one-way factorial analysis of variance (ANOVA) and multiple comparison tests. $P < 0.05$ was considered to be statistically significant.

RESULTS

Figure 1 shows CT (Figs. 1A and 1B), MR images (Figs. 1C and 1D) and ^{99m}Tc-GSA clearance map (Fig. 1E) in a patient with cholangiocellular carcinoma. Common hepatic duct and left hepatic duct were affected and diffuse intrahepatic bile duct dilatation was observed especially in the left lobe (arrow 1). Left lobe portal vein occlusion was proven by portography. T2-weighted MR images revealed abnormal hyperintensity in the left lobe (Figs. 1C and 1D; arrow 2). ^{99m}Tc-GSA clearance map (Fig. 1E) showed a remarkable reduction in the left lobe ^{99m}Tc-GSA uptake (arrow 3). The distribution of hepatic ^{99m}Tc-GSA clearance showed a marked difference between both lobes. The reduction of ^{99m}Tc-GSA clearance in the left lobe may reflect hepatic parenchymal injury, probably due to biliary obstruction or blood flow abnormality.

Correlation of ^{99m}Tc-Galactosyl-Human Serum Albumin Parameters with Conventional Hepatic Function Tests

The correlation between ^{99m}Tc-GSA parameters and laboratory data that are conventionally used as parameters of hepatic functional reserve are summarized in Table 1. Significant correlation was observed between total hepatic

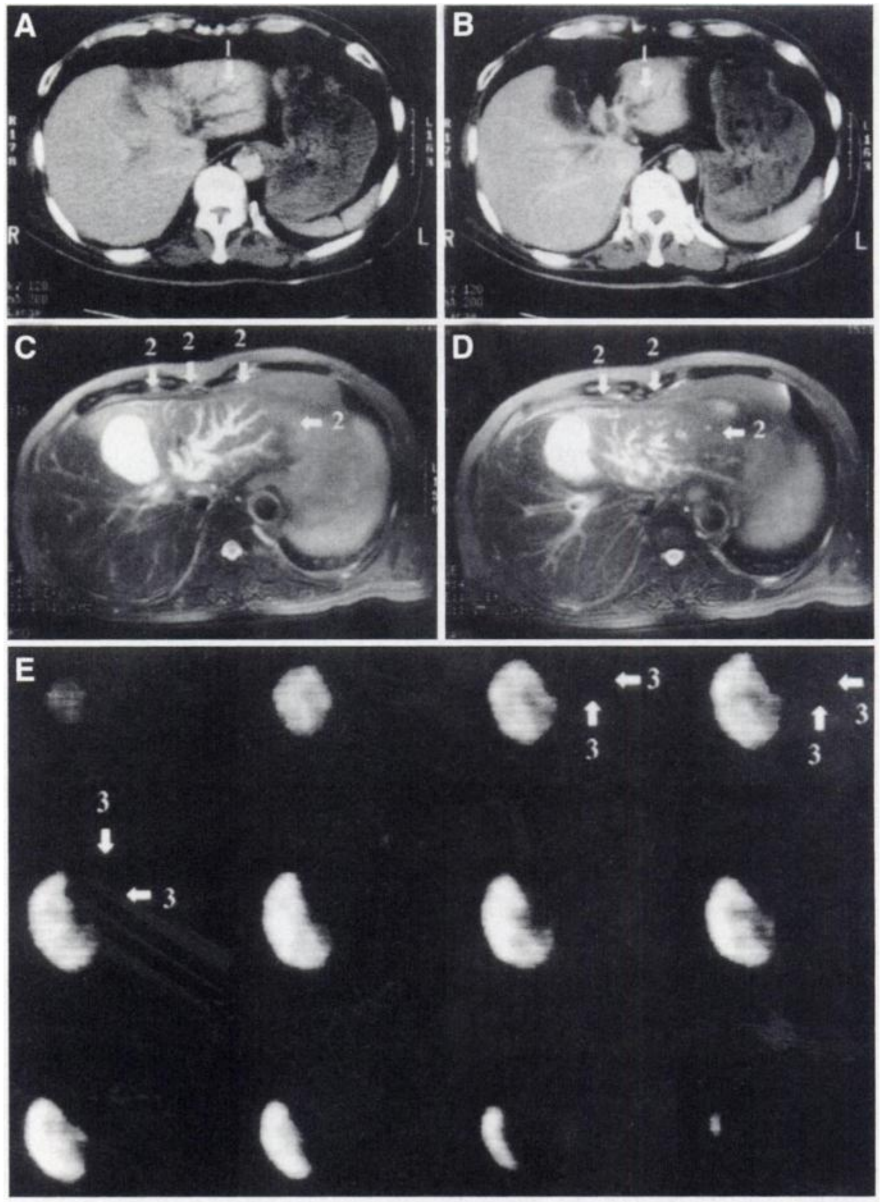

FIGURE 1. Patient with cholangiocellular carcinoma. Contrast-enhanced CT scans reveal intrahepatic bile duct dilatation due to biliary obstruction especially in left lobe (A and B; arrow 1), and T2-weighted MR images show abnormal hyperintensity in left lobe (C and D; arrow 2). (E) Clearance map reveals remarkable deterioration of ^{99m}Tc-GSA clearance in left lobe (arrow 3).

GSA clearance and laboratory data: ICG R15, $r = -0.600$, $P < 0.0001$, n = 94; plasma disappearance rate of ICG (K ICG), $r = 0.670$, $P < 0.0001$, n = 83; choline esterase, $r = 0.539$, $P < 0.0001$, n = 121; serum albumin, $r = 0.421$, $P = 0.0001$, n = 123; and hepaplastin, $r = 0.456$, $P < 0.0001$, n = 120. Significant correlation was also observed between mean ^{99m}Tc-GSA clearance and laboratory data: ICG R15, $r = -0.642$, $P < 0.0001$, n = 94; K ICG, $r = 0.689$, $P < 0.0001$, n = 83; choline esterase, $r = 0.584$, $P < 0.0001$, n = 121; serum albumin, $r = 0.412$, $P < 0.0001$, n = 123; and hepaplastin, $r = 0.506$, $P < 0.0001$, n = 120. The correlation between ^{99m}Tc-GSA clearance and total bilirubin was not significant. Correlation between total hepatic ^{99m}Tc-GSA clearance and ICG R15 and between mean ^{99m}Tc-GSA clearance and ICG R15 was plotted on the graph in Figure 2. These parameters correlated well in the exponential formula.

On the other hand, correlation between functional liver volume and laboratory data was not so significant.

According to the data of 15 patients with benign hepatic tumor or gallbladder tumor and normal liver, the normal value of ^{99m}Tc-GSA clearance was estimated as 697.1 ± 262.2 mL/min, and mean ^{99m}Tc-GSA clearance was estimated as 0.600 ± 0.176 mL/min/mL liver.

^{99m}Tc-Galactosyl-Human Serum Albumin Parameters in Patients with Hepatic Insufficiency

A patient with fulminant hepatitis who died of hepatic failure 47 d after scintigraphy had poor total hepatic ^{99m}Tc-GSA clearance (50.4 mL/min).

Two patients died of hepatic failure within 2 mo after extended right lobectomy. Three patients had postoperative complications due to hepatic insufficiency. Two patients had severe liver dysfunction with intractable ascites, and 1

TABLE 1
Correlations Between GSA Parameters and Other Hepatic Function Tests

	ICG R15			K ICG			Ch E			Alb			Hpt			T Bil		
	r	*P*	n	*r*	*P*	n	*r*	*P*	n	*r*	*P*	n	*r*	*P*	n	*r*	*P*	n
Volume	−0.170	0.1011	94	0.176	0.1124	83	0.179	0.0496	121	0.192	0.0336	123	0.161	0.0793	120	0.036	0.6889	124
Total clearance	−0.600	<0.0001	94	0.670	<0.0001	83	0.539	<0.0001	121	0.421	0.0001	123	0.456	<0.0001	120	−0.086	0.3415	124
Mean clearance	−0.642	<0.0001	94	0.689	<0.0001	83	0.584	<0.0001	121	0.412	<0.0001	123	0.506	<0.0001	120	−0.166	0.0668	124
ICG R15	—	—	—	−0.807	<0.0001	83	−0.500	<0.0001	91	−0.406	<0.0001	91	−0.468	<0.0001	91	0.049	0.6404	91
K ICG	−0.807	<0.0001	83	—	—	—	0.454	<0.0001	81	0.377	0.0004	83	0.342	0.0015	82	−0.109	0.3240	83

GSA = ^{99m}Tc-galactosyl-human serum albumin; ICG R15 = plasma retention rate of iodocyanine green (ICG) at 15 min; K ICG = plasma disappearance rate of ICG; Ch E = choline estelase; Alb = albumin; Hpt = hepaplastin test; T Bil = total bilirubin.

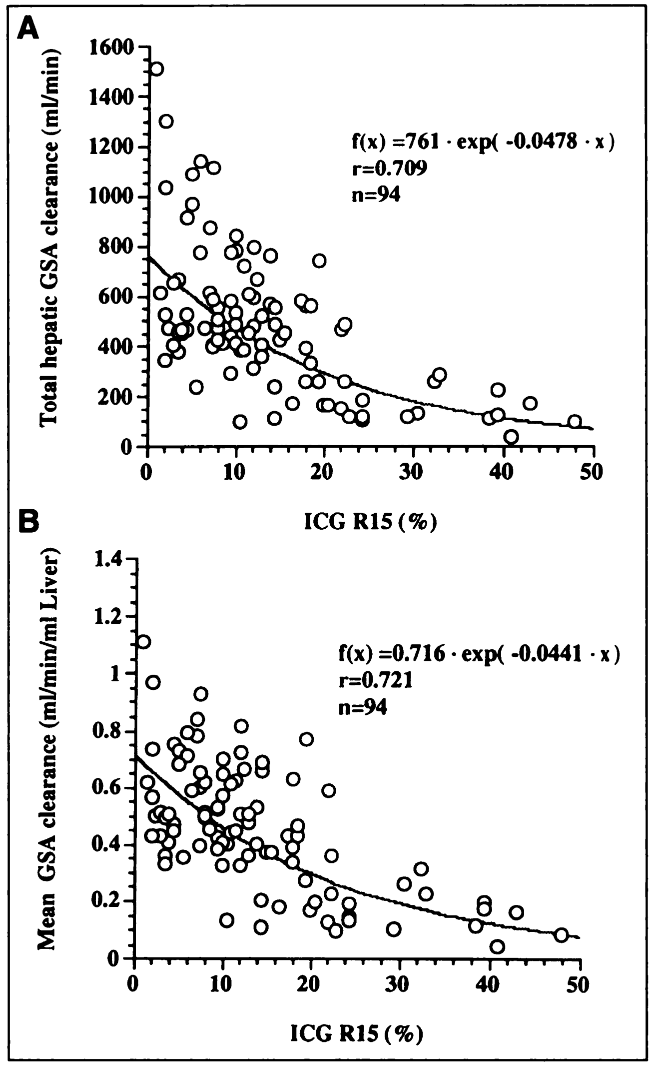

FIGURE 2. Correlation between total hepatic ^{99m}Tc-galactosyl-human serum albumin (GSA) clearance and plasma retention rate of iodocyanine green at 15 min (ICG R15) (A) and between mean GSA clearance and ICG R15 (B). There is good correlation in exponential formula.

patient had elevation of transaminase (aspartate transaminase > 200 U/L), elevation of bilirubin (>2.0 mg/dL) and bleeding tendency about 1 mo after operation.

These 5 patients showed significantly lower predicted residual ^{99m}Tc-GSA clearance (90.3 ± 37.2, range 41.6–129 mL/min) compared to the patients who underwent segmentectomy or lobectomy without postoperative complications (321 ± 159, range 120–701 mL/min; $P < 0.005$), whereas the total ^{99m}Tc-GSA clearance did not show significant difference (315 ± 298, range 97.4–770 mL/min versus 567 ± 282, range 219–1288 mL/min) (Fig. 3).

Changes of ^{99m}Tc-Galactosyl-Human Serum Albumin Parameters After Hepatic Resection

In the 25 patients who underwent subsegmentectomy, good correlation was observed between the pre- and postoperative total hepatic ^{99m}Tc-GSA clearance ($r = 0.91$, $P <$

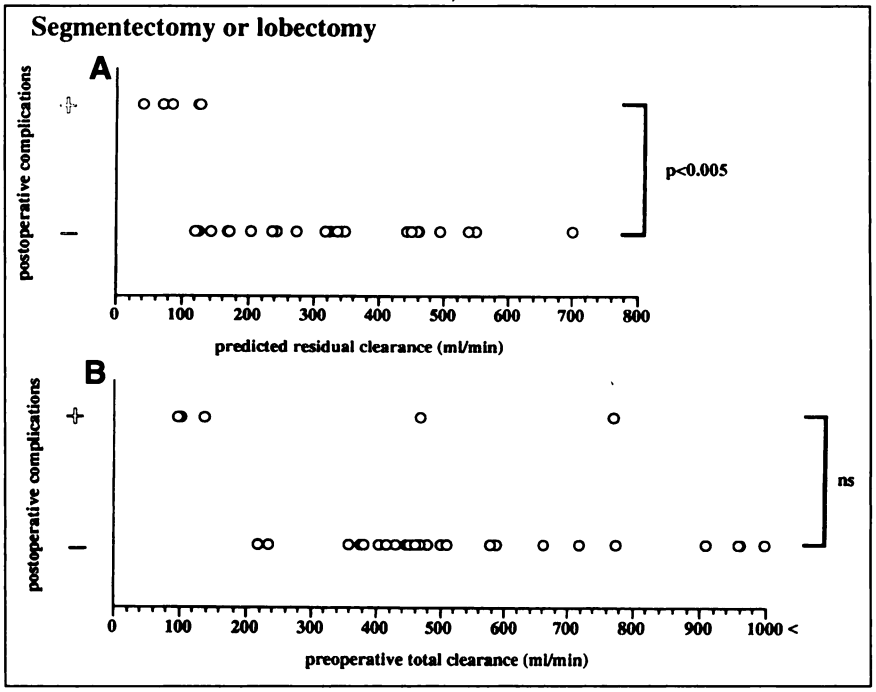

FIGURE 3. Distribution of predicted residual ^{99m}Tc-GSA clearance (A) and preoperative total ^{99m}Tc-GSA clearance (B) of patients who underwent segmentectomy or lobectomy. Predicted residual ^{99m}Tc-GSA clearance was significantly lower in patients with complications compared with patients without complications, whereas preoperative total ^{99m}Tc-GSA clearance was not different significantly (ns).

0.0001) (Fig. 4) and between the pre- and postoperative total functional liver volume ($r = 0.72$, $P < 0.0001$) (Fig. 5).

In the 28 patients who underwent major hepatic resection (segmentectomy or lobectomy), strong correlation was observed between the predicted residual hepatic ^{99m}Tc-GSA clearance and the postoperative total hepatic ^{99m}Tc-GSA clearance ($r = 0.84$, $P < 0.0001$) (Fig. 6). On the other hand, lesser correlation was observed between the predicted residual functional liver volume and the postoperative total functional liver volume ($r = 0.53$, $P < 0.005$) (Fig. 7). The postoperative total hepatic ^{99m}Tc-GSA clearance (371 $\pm$189 mL/min) was larger than the predicted residual ^{99m}Tc-GSA clearance (286 $\pm$158 mL/min; $P < 0.0005$) and the postoperative total functional liver volume (816 $\pm$183 mL) was also significantly larger than the predicted residual functional liver volume (602 $\pm$ 236 mL; $P < 0.0001$). The difference between the pre- and postoperative mean clearance was not significant (0.486 $\pm$ 0.190 versus 0.452 $\pm$

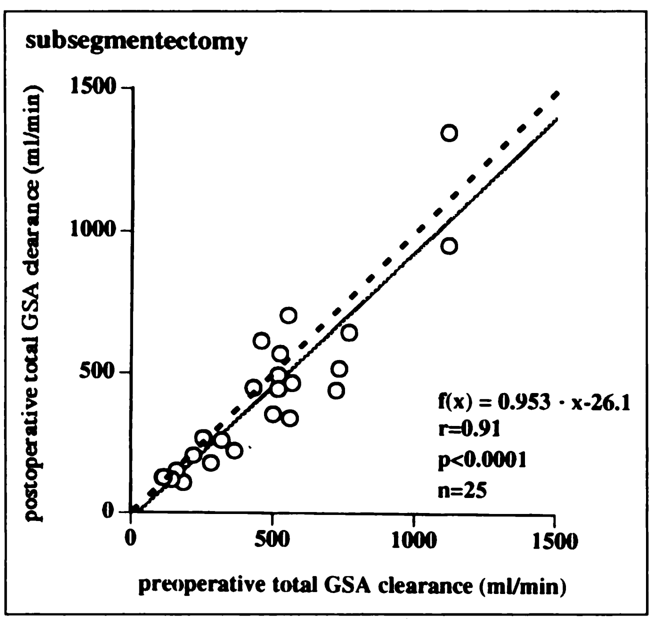

FIGURE 4. Correlation between preoperative total liver clearance and postoperative total liver clearance in patients who underwent subsegmentectomy. Dotted line is line of identity. GSA = ^{99m}Tc-galactosyl-human serum albumin.

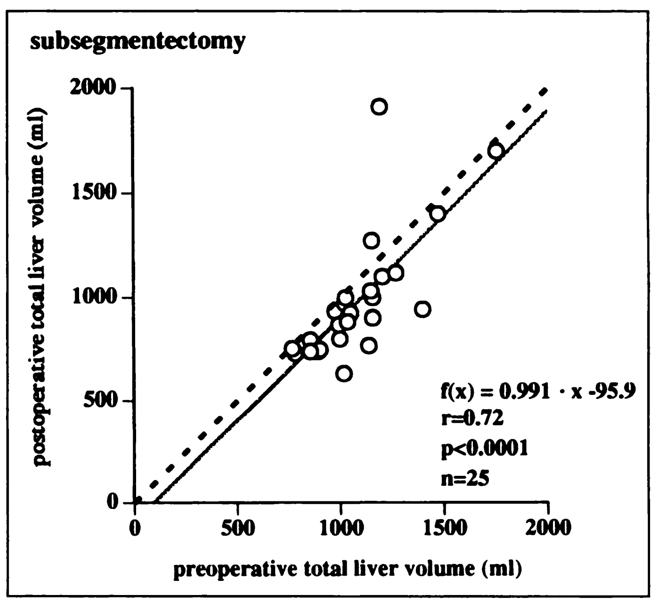

FIGURE 5. Correlation between preoperative total liver volume and postoperative total liver volume in patients who underwent subsegmentectomy. Dotted line is line of identity. GSA = ^{99m}Tc-galactosyl-human serum albumin.

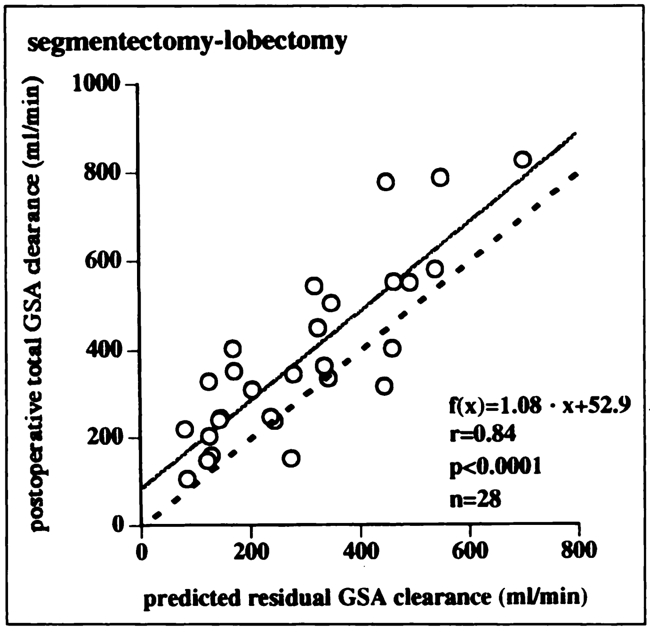

FIGURE 6. Correlation between preparative predicted residual clearance and postoperative total clearance in patients who underwent segmentectomy or lobectomy. Dotted line is line of identity. GSA = ^{99m}Tc-galactosyl-human serum albumin.

0.184 mL/min/mL liver). However, in some patients, there seemed to be discrepancies between the degree of postoperative liver volume expansion and the increase in residual hepatic ^{99m}Tc-GSA clearance. Especially in patients with large hepatic resection, the degree of volume expansion seemed to be larger than the increase in ^{99m}Tc-GSA clearance. Thus, we compared the changes of mean ^{99m}Tc-GSA clearance, which could reflect the discrepancies between

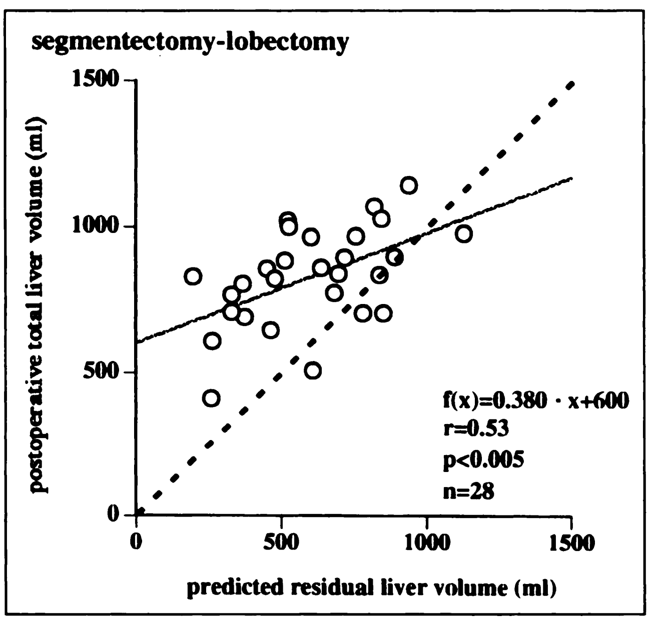

FIGURE 7. Correlation between preparative predicted residual volume and postoperative total volume in patients who underwent major hepatic resection. Dotted line is line of identity.

volume and ^{99m}Tc-GSA clearance changes, among the three subsets of patients: patients with subsegmentectomy; patients with moderate resection (the patients who underwent segmentectomy or lobectomy with residual volume ratio [RVR = predicted residual functional liver volume/ preoperative total functional liver volume] > 0.5; n = 17); and patients with large resection (the patients who underwent segmentectomy or lobectomy with RVR < 0.5; n = 11). Among these three groups, no significant differences were observed in the preoperative mean ^{99m}Tc-GSA clearance (0.418 ± 0.216, 0.434 ± 0.171, 0.571 ± 0.258 mL/min/mL liver, respectively). After hepatic resection, mean ^{99m}Tc-GSA clearance was decreased significantly in patients with large resection ($P < 0.01$). Whereas the other two groups showed no significant change (subsegmentectomy group, 0.419 ± 0.250 mL/min/mL liver; moderate resection group, 0.479 ± 0.199 mL/min/mL liver; large resection group, 0.405 ± 0.183 mL/min/mL liver) (Fig. 8).

DISCUSSION

^{99m}Tc-GSA is a radiopharmaceutical that specifically binds the AGR on the surface of hepatocyte. The hepatic ^{99m}Tc-GSA uptake is assumed to reflect the hepatic functional reserve, because the hepatic binding capacity of ^{99m}Tc-GSA might be defined by the total number of functioning hepatocytes. Many analytical methods to quantitate the hepatic ^{99m}Tc-GSA uptake have been reported and evaluated for clinical efficacy in hepatic function and reserve estimation (*1–9*). Most of these analytical methods were designed

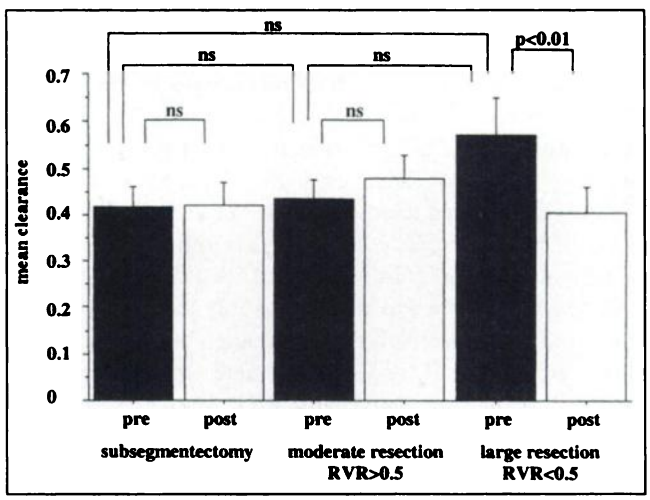

FIGURE 8. Comparison of mean GSA clearance among three divided groups—subsegmentectomy group, moderate resection group (residual volume ratio [RVR] > 0.5) and large resection group (RVR < 0.5)—and between pre- and postsurgery. There was significant difference between pre- and postsurgical mean ^{99m}Tc-GSA clearance in large resection group ($P < 0.01$), whereas no significant differences were observed in subsegmentectomy and moderate resection groups and in preoperative mean ^{99m}Tc-GSA clearance among three groups. Mean ^{99m}Tc-GSA clearance was apparently decreased after hepatectomy in large resection group. ns = not significant.

for planar scintigraphy to estimate total liver function. However, for segmental or spatial assessment of ^{99m}Tc-GSA distribution, tomographic imaging rather than planar imaging seems to be a more appropriate and accurate method as hepatic function often deteriorates inhomogeneously (*10–12*). Moreover, the residual (regional) hepatic functional reserve is more important than the global hepatic function in patients who are under consideration of hepatectomy. Therefore, estimation of the regional hepatic function by quantitative SPECT analysis is preferable.

Many studies about quantification of hepatic ^{99m}Tc-GSA uptake have been reported (*1–9*). Several pharmacokinetic models have been applied and the clinical value evaluated (*1–5*). However, most of these analytical methods were rather complicated and impractical in routine clinical work. In this study, we used Patlak plot because it is relatively simple and is suitable for matrix-by-matrix analysis, permitting functional imaging of hepatic ^{99m}Tc-GSA uptake. A similar analyzing protocol has been reported. However, the clinical impact of the estimated parameters is still under investigation (*5*). To our knowledge, this is the first clinical report of ^{99m}Tc-GSA dynamic SPECT analyzed with the Patlak plot for functional mapping.

Clinical Value of Estimated Parameters

Concerning the clinical efficacy of the measured ^{99m}Tc-GSA parameters in this study, fairly good correlation was observed between total hepatic ^{99m}Tc-GSA clearance and conventional hepatic function tests, especially in comparison with ICG R15, which is a relatively reliable parameter of hepatic function in routine clinical works. Total hepatic ^{99m}Tc-GSA clearance is assumed to be a good indicator of hepatic function as well as ICG R15. Moreover, ^{99m}Tc-GSA clearance seemed to have some advantages in prognostic value compared with ICG, because 4 of 5 patients who had postoperative hepatic insufficiency showed poor predicted residual ^{99m}Tc-GSA clearance (41.6, 70.1, 85.4 and 85.4 mL/min) but showed relatively preserved ICG R15 (14.5%, 6.0%, 10.5% and 6.5%, respectively). Furthermore, in 2 of the patients (ICG R15 14.5% and 10.5%), the total hepatic ^{99m}Tc-GSA clearance was also remarkably reduced (103 and 97.4 mL/min, respectively). Some authors also noticed the advantages of the ^{99m}Tc-GSA parameter in hepatic functional estimation compared with ICG. They reported that patients who died of hepatic failure after hepatectomy showed remarkably reduced ^{99m}Tc-GSA uptake parameter but showed relatively preserved ICG value. They also reported that the ^{99m}Tc-GSA parameter reflected the histological hepatic damage score more precisely than the ICG test (*4*). These observations suggest that the ICG test often underestimates the severity of liver damage and that ^{99m}Tc-GSA scintigraphy might provide more accurate information about hepatic functional reserve.

Mean ^{99m}Tc-GSA clearance correlated as well with conventional hepatic function tests as total hepatic ^{99m}Tc-GSA clearance, therefore, mean ^{99m}Tc-GSA clearance was also assumed to be a good indicator for hepatic functional reserve estimation.

On the other hand, no significant correlation was observed between functional liver volume and hepatic function tests. Some authors reported the clinical value of liver volume measurement in hepatic functional estimation (*13*). These reports suggested that liver atrophy reflects functional deterioration of the liver in chronic liver disease. However, in this study, functional liver volume did not show any clinical value in the estimation of hepatic functional reserve.

Perioperative Changes and Prognostic Values of ^{99m}Tc-Galactosyl-Human Serum Albumin Parameters in Hepatic Resection

There was good correlation between the predicted residual ^{99m}Tc-GSA clearance and the postoperative total hepatic ^{99m}Tc-GSA clearance. Five patients with poor predicted residual ^{99m}Tc-GSA clearance had poor early outcomes after surgery. A patient who died of fulminant hepatitis showed remarkably reduced total hepatic ^{99m}Tc-GSA clearance. The residual ^{99m}Tc-GSA clearance, which is assumed to reflect a residual functioning hepatocyte mass, appears to be a strong indicator of early prognosis. A report (*9*) that studied the early prognostic value of hepatic ^{99m}Tc-GSA uptake parameters in patients with fulminant hepatitis demonstrated that the patients with poor hepatic ^{99m}Tc-GSA uptake had poor prognoses, and these observations are compatible with the results in this study. Residual functioning hepatocyte mass after abrupt massive hepatocyte loss such as major hepatectomy or acute hepatitis is the most important prognostic predictor and could be quantitated by ^{99m}Tc-GSA scintigraphy.

After major hepatic resection, functional liver volume and hepatic ^{99m}Tc-GSA clearance seemed to increase vigorously. However, some discrepancies were observed between postoperative hepatic volume expansion and hepatic functional restoration. The restoration of the hepatic ^{99m}Tc-GSA clearance seemed to be relatively small in some patients, especially in patients who underwent large resection. Hepatic volume expansion may not be accompanied always by functional restoration, and there seemed to be functional pseudohypertrophy. This phenomenon was observed in perioperative mean clearance changes in largely resected liver that showed significant deterioration of mean clearance after operation. Some authors (*14*) also pointed out the discrepancies between volume expansion and functional restoration of liver in the early period after hepatectomy. One possible cause of these discrepancies is the modulation of the transport of asialoglycoprotein, because experimental data demonstrated the deterioration of the hepatocyte asialoorosomucoid uptake in regenerating liver after hepatectomy (*15*). However, the exact mechanisms of discordant volume expansion, more than the increase in ^{99m}Tc-GSA clearance after surgery, were unclear. Further investigations, such as histochemical study or more complex pharmacokinetic analysis, were necessary in which hepatic blood flow and receptor function could be quantitated individually, because ^{99m}Tc-GSA clearance might be defined by these two factors.

According to these observations, the postoperative volume expansion of the remnant liver does not always bring the restoration of the hepatic ^{99m}Tc-GSA clearance, and the preoperative predicted residual hepatic ^{99m}Tc-GSA clearance could define the postoperative ^{99m}Tc-GSA clearance at an early period after surgery. The predicted residual ^{99m}Tc-GSA clearance was assumed to be a good prognostic indicator early after hepatectomy.

Limitations

Several issues are considered in the quantification of dynamic SPECT analysis, because several factors produce quantitative errors such as photon attenuations, scatters and changes of radioactivity during SPECT acquisition. Attenuations and scatters would be eliminated by applying newly developed compensation methods (*5*). Changes of radioactivity of ^{99m}Tc-GSA in every minute were relatively small, and quantitative errors might be insignificant (*5,16*). Because this rather simple quantitative method for hepatic function using ^{99m}Tc-GSA correlated well with other laboratory data and prognosis, it might be sufficient for daily clinical use.

In this study, we demonstrated the early prognostic value of the hepatic ^{99m}Tc-GSA clearance estimated by dynamic SPECT. Future studies will clarify the prognostic value of these parameters.

CONCLUSION

Regional hepatic ^{99m}Tc-GSA clearance analyzed by dynamic SPECT with Patlak plot can predict postoperative hepatic ^{99m}Tc-GSA clearance quantitatively and is a useful indicator of postoperative hepatic function early after hepatectomy.

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REFERENCES

1. Ha-Kawa SK, Tanaka Y. A quantative 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.
2. Yumoto Y, Umeda M, Ohshima K, 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.
3. Shuke N, Aburano T, Nakajima K, et al. The utility of quantitative ^{99m}Tc-GSA liver scintigraphy in the evaluation of hepatic functional reserve: comparison with ^{99m}Tc-PMT and ^{99m}Tc-Sn colloid. *Jpn J Nucl Med.* 1992;29:573–584.
4. Kwon AH, Ha-Kawa SK, Uetsuji S, Inoue T, Matsui Y, Kamiyama Y. Preoperative determination of the surgical procedure for hepatectomy using technetium-99m-galactosyl human serum albumin (^{99m}Tc-GSA) liver scintigraphy. *Hepatology.* 1997; 25:426–429.
5. Ichihara T, Maeda H, Yamakado K, et al. Quantitative analysis of scatter- and attenuation-compensated dynamic single-photon emission tomography for functional hepatic imaging with a receptor-binding radiopharmaceutical. *Eur J Nucl Med.* 1997; 24:59–67.
6. Kim YK, Nakano H, Yamaguchi M, et al. Prediction of postoperative decompensated liver function by technetium-99m galactosyl-human serum albumin liver scintigraphy in patients with hepatocellular carcinoma complicating chronic liver disease. *Br J Surg.* 1997;84:793–796.
7. Kubota Y, Kitagawa S, Inoue K, et al. Hepatic functional scintigraphy imaging with ^{99m}technetium galactosyl serum albumin. *Hepato-Gastroenterol.* 1993;40: 32–36.
8. Kudo M, Todo A, Ikekubo K, et al. Quantitative assessment of hepatocellular function through in vivo radioreceptor imaging with technetium 99m galactosyl human serum albumin. *Hepatology.* 1993;17:814–819.
9. Shiomi S, Kuroki T, Kuriyama M, et al. Evaluation of fulminant hepatic failure by scintigraphy with technetium-99m-GSA. *J Nucl Med.* 1997;38:79–82.
10. Inoue Y, Machida K, Honda N, et al. Impaired hepatic function in segmental biliary obstruction demonstrated with a receptor-binding radiotracer. *Ann Nucl Med.* 1994;8:209–212.
11. Imaeda T, Kanematsu M, Asada S, Seki M, Doi H, Saji S. Utility of Tc-99m GSA SPECT imaging in estimation of functional volume of liver segments in health and liver disease. *Clin Nucl Med.* 1995;20:322–328.
12. Akaki S, Matsumori A, Kanazawa S, et al. Reduced radioactivity in the periphery of the liver in a patient with idiopathic portal hypertension. *Clin Nucl Med.* 1996; 22:369–371.
13. Yanaga K, Honda H, Ikeda Y, Nishizaki AT, Yamamoto K, Sugimachi K. Significance of liver size in hepatic surgery. *HPB Surg.* 1997;10:195–200.
14. Jansen PL, Chamleau RA, van Leeuwen DJ, Schipper HG, Busemann-Sokole E, van der Heyde MN. Liver regeneration and restoration of liver function after partial hepatectomy in patients with liver tumors. *Scand J Gastroenterol.* 1990;25:112–118.
15. Gartner U, Stockert RJ, Morell AG, Wolkoff AW. Modulation of the transport of bilirubin and asialoorosomucoid during liver regeneration. *Hepatology.* 1981;2:99–106.
16. Nakajima K, Shuke N, Taki J, et al. A simulation of dynamic SPECT using radiopharmaceuticals with rapid clearance. *J Nucl Med.* 1992;33:1200–1206.