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Impact of Clinically Relevant Posthepatectomy Liver Failure Predicted by Preoperative Evaluation of Functional Remnant Hepatic Reserve

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Background: Few studies have investigated the remnant hepatic functional reserve before hepatectomy by calculating the functional remnant liver rate (RLR) using three-dimensional computed tomography (3D-CT)/technetium-99m-diethylenetriamine-pentaacetic acid galactosyl human serum albumin (99mTc-GSA) single-photon emission CT (SPECT) fusion imaging. We aimed to preoperatively evaluate the predictive value of functional remnant liver rate (RLR) and indocyanine green (ICG) disappearance rate (KICG) in determining the occurrence of posthepatectomy liver failure (PHLF).

Summary of Background Data: The conventional method of volumetric rem-KICG calculated from remnant liver volume and the KICG is difficult to accurately reflect heterogenous remnant liver function.

Methods: In total, 106 patients who underwent major hepatectomy were retrospectively analysed. Of these, 24 (22.6%) developed clinically relevant PHLF grades B/C. We examined the ICG retention rate at 15 min (ICGR15) and KICG and constructed a 3D-CT/99mTc-GSA SPECT fusion image to calculate the volumetric RLR, functional RLR, volumetric rem-KICG, and functional rem-KICG.

Results: The multivariate analysis showed functional rem-KICG as the strongest independent risk factor for PHLF grade B/C. The functional-to-volumetric RLR ratios in the patients with portal vein obstruction and/or tumor volume of ≥500 mL was significantly

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higher. The volumetric rem-KICG determined that hepatectomy was unsafe in 7 patients, whereas the functional rem-KICG determined that it was unsafe in 3 patients.

Conclusions: Functional rem-KICG was more reliable than volumetric rem-KICG in predicting clinically relevant PHLF grade B/C, as the resected side's hepatic status highly influenced the function of the remnant liver. This finding could lead to a wider application of this technique.

Key words: Hepatic functional reserve – Posthepatectomy liver failure – Indocyanine green – Technetium-99m galactosyl human serum albumin – Remnant liver rate

After hepatectomy, posthepatectomy liver failure (PHLF) is one of the main reasons for serious complications and deaths in the hospital. This is usually associated with insufficient remnant liver function. The accurate assessment of remnant liver function is essential to predict and prevent PHLF.[1]

To assess hepatic functional reserve, several liver function tests including the indocyanine green retention rate at 15 minutes (ICGR15) tests are commonly used.[2] Indocyanine green (ICG) is a water-soluble dye that binds to plasma proteins and is almost completely cleared from the blood by the liver. In the ICGR15 test, ICG is administered intravenously, and the presence of ICG in the blood is analyzed 15 minutes later to calculate the ICG retention rate, a parameter of liver function. Makuuchi *et al* first reported using ICGR15 values to preoperatively determine the possible extent of hepatectomy, *i.e.,* whether a trisectionectomy, bisectionectomy, sectionectomy, or segmentectomy could be performed.[3] The Makuuchi criteria have been widely adopted in Japan and other Asian countries. However, these criteria cannot predict future remnant liver function because ICGR15 depends on hepatic blood flow, hepatocellular function, and biliary excretion.[4] The ICG disappearance rate (KICG) is also affected by hepatocellular volume; thus, the estimated volumetric remnant KICG value (rem-KICG) can be calculated by multiplying the preoperative KICG value by the remnant liver volume ratio as calculated by computed tomography (CT) volumetry. Previous studies have shown that rem-KICG values are significantly correlated with actual postoperative remnant liver function.[5,6] Several clinical studies performed in Japan[7,8] have suggested a volumetric rem-KICG cut-off value of 0.05 to allow safe hepatectomy.

Technetium-99m galactosyl human serum albumin (^{99m}Tc-GSA) is a specific liver scintigraphy agent that binds to asialoglycoprotein receptors on the hepatocellular membrane. In chronic liver diseases, asialoglycoprotein receptors in the liver are markedly decreased.[9,10] Therefore, ^{99m}Tc-GSA can be used to determine liver function.

As function is not homogeneous throughout the liver, the volumetric remnant liver rate (RLR), calculated using volume only, is usually different from the functional RLR,[11,12] calculated using ^{99m}Tc-GSA to measure functional volume. This is especially true for patients with large tumors, unilateral biliary obstruction, and/or unilateral portal vein (PV) occlusion.[13,14] Additionally, recent studies have revealed functional differences between the right and left lobes in a healthy liver owing to differences in blood flow and innervation.[15,16] Therefore, the conventional rem-KICG value calculated using CT volumetry does not always correctly estimate remnant liver function. It has recently been reported that CT/^{99m}Tc-GSA SPECT fusion imaging, in particular 3-dimensional-CT/^{99m}Tc-GSA SPECT fusion imaging, can be used to evaluate hepatic functional distribution accurately.[11,12,17–19]

Few studies have investigated the significance of the remnant hepatic functional reserve prior to hepatectomy as calculated by functional RLR using 3D-CT/^{99m}Tc-GSA SPECT fusion imaging. To prevent clinically relevant PHLF grade B/C, a precise assessment of future remnant liver function is essential to confirm that a hepatectomy is safe to perform. Determining specific indicators could be useful in predicting PHLF grade B/C. Therefore, this study aimed to evaluate the benefit of functional rem-KICG (functional RLR × KICG) for estimating remnant liver function.

Materials and Methods

Patients

We retrospectively collected data from 121 consecutive patients who underwent a major hepatectomy (bisectionectomy or trisectionectomy) at our hospital from July 2015 to December 2021. Of these 121 patients, 3 patients who underwent combined

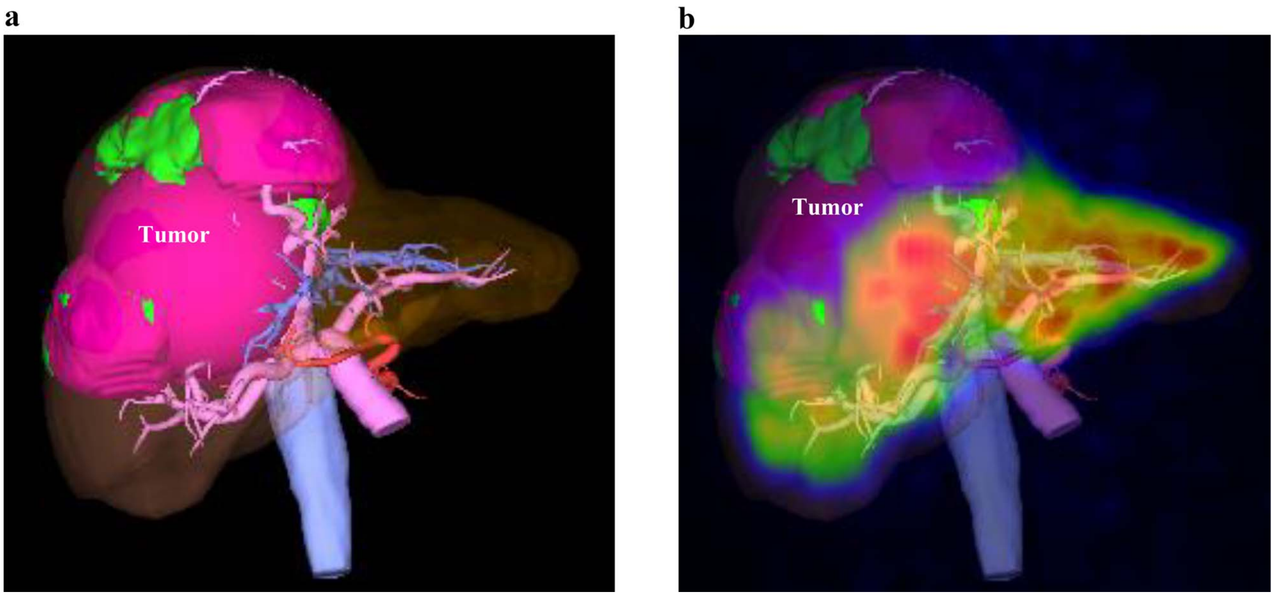

Fig. 1 Creation of a 3D-CT/^{99m}Tc-GSA SPECT fusion image using the volume analyzer Synapse Vincent. (a) Evaluation using the 3D image. (b) Evaluation using the SPECT/CT fusion image. CT, computed tomography; SPECT, single-photon emission computed tomography; ^{99m}Tc-GSA, technetium-99m-diethylenetriamine-pentaacetic acid galactosyl human serum albumin.

pancreaticoduodenectomy (n = 2) and combined distal pancreatectomy (n = 1) were excluded. Moreover, 12 patients who had postoperative PV thrombosis (n = 10) and postoperative hepatic artery aneurysm (n = 2) were also excluded, to evaluate PHLF accurately. The remaining 106 patients were included in the study.

Construction of the 3D-CT and ^{99m}Tc-GSA SPECT fusion image

Among these 106 patients, we examined the ICGR15, KICG, and the ratio of liver to heart-plus-liver radioactivity of ^{99m}Tc-GSA 15 minutes after injection (LHL15), which is an indicator of hepatic function, and constructed a 3D-CT/^{99m}Tc-GSA SPECT fusion image using a volume analyzer to calculate the volumetric and functional RLR[18]. Four-phase dynamic CT (64-row multidetector row CT) images were reconstructed from Digital Imaging and Communications in Medicine data using a 3D image analysis system (Synapse Vincent volume analyzer, Fujifilm Medical, Tokyo, Japan).

Calculation of volumetric rem-KICG and functional rem-KICG

The volumetric and functional RLR were calculated based on the Synapse Vincent data using the following formulas:

$$\text{Volumetric RLR}\,(\%) = \text{remnant liver volume}/(\text{total liver volume} - \text{tumor volume}) \times 100 \text{ based on 3D-CT}$$

and

$$\text{Functional RLR}\,(\%) = \text{scintillation counts of remnant liver}/\text{total scintillation counts in the whole liver} \times 100, \text{ based on the fusion images.}$$

The volumetric rem-KICG and functional rem-KICG were calculated using volumetric and functional RLRs as follows:

$$\text{Volumetric rem-KICG: volumetric RLR} \times \text{KICG value}$$

$$\text{Functional rem-KICG: functional RLR} \times \text{KICG value}$$

A 3D-CT/^{99m}Tc-GSA SPECT fusion image created using the SYNAPSE VINCENT volume analyzer is shown in Fig. 1. The 3D image reconstructed from the DICOM data of the multidetector CT was used to set the resection line (Fig. 1a), and this 3D-CT image was fused with the SPECT image (Fig. 1b). The patient shown in Fig. 1 was an 84-year-old woman who underwent extended right hepatectomy for hepatocellular carcinoma. The volumetric RLR was 49.5%, and the functional RLR was 71.2%. Based on these estimated remnant liver volumes and KICG, the functional rem-KICG (0.070) was significantly higher than the volumetric rem-KICG (0.049).

Indication of hepatectomy

The type of hepatectomy was determined based on ICGR15, LHL15, and future remnant liver volume using CT volumetry.[20] More than 40% of the estimated remnant liver volume in a normal liver should be preserved to ensure safe hepatectomy. We used the functional rem-KICG to select hepatectomy as the final parameter, which means that the functional rem-KICG was greater than 0.05. Additionally, PV embolization (PVE) was indicated to enhance the safety of hepatectomy, if (1) the estimated volume of the future remnant liver was 40% or less, (2) the functional rem-KICG was 0.05 or less, and (3) right hepatopancreaticoduodenectomy was necessary.[21]

Assessment of postoperative complications and liver dysfunction

Based on the International Study Group of Liver Surgery report, we assessed the degree of postoperative complications based on the Clavien–Dindo (C-D) classification and PHLF.[22] PHLF was diagnosed when there was an increased prothrombin time (PT-INR) and concomitant hyperbilirubinemia on or after postoperative day 5. The severity of PHLF was graded as follows: Grade non, no PHLF; Grade A, PHLF that required no change in the patient's clinical management; Grade B, PHLF that required a deviation from the regular course but did not require invasive therapy; and Grade C, PHLF that required invasive treatment.

Ethics approval and consent to participate

The study protocol was reviewed and approved by the Medical Ethics Committee of Mie University Hospital (No. H2019-032). Due to the observational nature of the study, the requirement for written consent was waived. All participants were informed of the study and were allowed to opt out via our institution's website.

Statistical analyses

Continuous variables are expressed as the median (range) and were assessed using a Student's *t*-test or the Mann–Whitney U-test. Categorical variables were assessed using the χ^2-test or Fisher's exact test. Correlations were evaluated using Pearson's correlation coefficient. Multivariate analysis was performed using a forward stepwise logistic regression analysis. All continuous variables used in the multivariate analysis were normalized using z-score transformation, resulting in values with a mean of 0 and a standard deviation of 1. Variables with a significance of $P < 0.20$ in the univariate analysis were entered into the multivariate analysis to ensure that certain variables that could be potential risk factors were not lost.[23] Comparisons were performed using the χ^2-test with Yates's correction in the univariate analysis. The Wilcoxon signed-rank test was used to compare volumetric rem-KICG and functional rem-KICG. All statistical analyses were performed using SPSS version 28 (IBM Corp., Armonk, NY, USA). Statistical significance was set at $P < 0.05$.

Results

Patient characteristics

Patient demographics and clinical characteristics are shown in Table 1. PHLF developed in 29 patients (27.3%): grade A, 5 patients; grade B, 20 patients; and grade C, 4 patients.

Comparison of patients with posthepatectomy liver failure non/A and B/C

We compared the backgrounds and postoperative courses of patients with grade non/A PHLF to those with B/C PHLF (Table 2). Univariate analysis showed significant differences in Child-Pugh score ($P = 0.020$), volumetric RLR ($P < 0.001$), functional RLR ($P < 0.001$), volumetric rem-KICG ($P < 0.001$), functional rem-KICG ($P < 0.001$), rate of bi/trisectionectomy ($P = 0.023$), operation time ($P = 0.029$), C-D classification $\geq$III ($P = 0.001$), and postoperative hospital stay ($P < 0.001$). Multivariate regression analysis was performed using variables with a significance of $P < 0.20$ in the univariate analysis were entered into the multivariate analysis. All continuous variables used in the multivariate analysis were normalized using z-score transformation, resulting in values with a mean of 0 and a standard deviation of 1. Functional rem-KICG [odds ratio (OR), 0.236; 95% confidence interval (CI), 0.103–0.540; $P < 0.001$), bi/trisectionectomy (OR, 7.280; CI, 1.096–48.352; $P = 0.040$), and operation time (OR, 1.763; CI, 1.046–2.972; $P = 0.033$) were independent risk factors for PHLF grade B/C.

Comparison of volumetric rem-KICG and functional rem-KICG

Fig. 2 shows the relationship between volumetric rem-KICG and functional rem-KICG in 106 patients. Functional rem-KICG values were significantly greater

Table 1 Demographics and clinical characteristics of 106 patients

Characteristic	Value
Age (y)	70 (20–85)
Sex (male/female)	68/38
Biliary drainage	27 (25.5%)
Portal vein obstruction*	20 (18.9%)
Diseases	
Hepatocellular carcinoma	39 (34.0%)
Perihilar cholangiocarcinoma	32 (30.2%)
Intrahepatic cholangiocarcinoma	9 (8.5%)
Liver metastasis	9 (8.5%)
Intrahepatic stone	7 (6.6%)
Others	13 (12.3%)
Preoperative liver function	
Child–Pugh score (5/6/7)	85/20/1
ALBI grade (1/2/3)	59/47/0
ICGR15	10.7 (0.7–34.8)
ICG K value (KICG)	0.141 (0.079–0.282)
LHL15	0.957 (0.831–0.984)
Type of hepatectomy	
Right hepatectomy	42 (39.6%)
Right trisectionectomy	3 (2.8%)
Left hepatectomy	52 (49.1%)
Left trisectionectomy	3 (2.8%)
Central bisectionectomy	5 (4.7%)
Lateral and posterior sectionectomy	1 (0.9%)
Hepaticojejunostomy	46 (43.4%)
Intraoperative outcomes	
Operation time (min)	446 (230–1038)
Blood loss (mL)	1,054 (2–10,148)
Postoperative outcomes	
Posthepatectomy liver failure (non/A/B/C)	77/5/20/4
Clavien–Dindo classification (≥III)	39 (36.8%)
Mortality	4 (3.8%)
Postoperative hospital stay (d)	20 (6–136)

*Portal vein obstruction caused by portal vein embolization or tumor thrombus. ICGR15, indocyanine green retention rate at 15 min; KICG, indocyanine green elimination rate constant; LHL15, hepatic uptake ratio of 99mTc-GSA scintigraphy at 15 min. Data are expressed as number (percentage) or median (range).

than volumetric rem-KICG values ($P < 0.001$). Based on volumetric rem-KICG values, 7 patients (6.6%) had values less than 0.05, which were considered unsafe for hepatectomy. Conversely, only 3 patients (2.8%) had a value less than 0.05 based on functional rem-KICG.

Functional-to-volumetric RLR ratio based on the status of the tumor side of the liver

Functional RLR is highly influenced by the status of the tumor side of the liver; thus, we examined the functional-to-volumetric RLR ratio (Fig. 3). When the patients had PV obstruction due to tumor invasion, tumor thrombus, preoperative PVE, and/or a tumor volume ≥500 mL on the tumor side, the ratio was significantly higher than that in those without PV obstruction and/or a tumor volume <500 mL. The values for those without PV obstruction versus that for those with PV obstruction were 1.094 versus 1.183 ($P < 0.001$). Moreover, the values for those with a tumor size ≥500 mL versus those with a tumor size <500 mL were 1.093 versus 1.188 ($P = 0.028$). No significant differences in the ratio were observed when PHLF versus non-PHLF and biliary drainage versus no biliary drainage were analyzed.

Background and postoperative course in patients with volumetric or functional rem-KICG <0.05

Eight patients had a volumetric or functional rem-KICG of <0.05. Among the 7 patients with a volumetric rem-KICG of <0.05, which was considered a contraindication for hepatectomy, only 2 patients had a functional rem-KICG of <0.05. An additional patient had a volumetric rem-KICG of >0.05 but a functional rem-KICG of <0.05. Although 7 had PHLF and 4 had postoperative complications with C-D IIIa or more, none of these patients died (Table 3).

Discussion

One of the most serious postoperative complications after major hepatectomy is PHLF. Precise evaluation of preoperative liver function is essential to prevent PHLF. Identifying predictors of PHLF would be very useful. Several studies have described methods to preoperatively predict PHLF, such as ICGR15 and KICG, the Child-Pugh score, liver damage classification, and the Makuuchi criteria.

In 2002, Okochi *et al* examined the relationship between KICG measured with pulse-dye densitometry before and after hepatectomy and volumetric RLR estimated by CT volumetry before hepatectomy in 22 patients and found that the estimated volumetric rem-KICG, which was calculated using the preoperative KICG value and the volumetric RLR, showed a significant correlation with the actual postoperative remnant liver function. They reported that the estimated volumetric rem-KICG value in 5 patients with prolonged jaundice was significantly lower than that in patients without jaundice.[5] Additionally, Ohwada *et al* performed a similar study in 2005 on 75 patients who underwent hepatectomy for HCC, revealing a significant correlation between the estimated and measured posthepatectomy KICG values. They found that the cut-off value of <0.090 for the estimated volumetric rem-

Table 2 Comparison of patients with posthepatectomy liver failure non/A and B/C

Characteristic	Univariate analysis			Multivariate analysis		
	PHLF non/A (n = 82)	PHLF grade B/C (n = 24)	*P* value	Odds ratio	95% CI	*P* value
Age (y)	69 (20–85)	72 (39–84)	0.136	-	-	-
Sex (male/female)	51/31	17/7	0.479			
Biliary drainage	17 (20.7%)	10 (41.7%)	0.060	-	-	-
Portal vein obstruction*	15 (18.3%)	5 (20.8%)	0.772			
Preoperative liver function						
Child–Pugh score (6 or more)	12 (14.6%)	9 (37.5%)	**0.020**	-	-	-
ALBI grade 2	32 (39.0%)	15 (62.5%)	0.061	-	-	-
ICGR15	10.2 (0.7–34.8)	12.8 (5.5–32.2)	0.075	-	-	-
ICG K value (KICG)	0.145 (0.080–0.282)	0.124 (0.079–0.175)	0.088	-	-	-
LHL15	0.957 (0.831–0.984)	0.954 (0.898–0.980)	0.610			
Future remnant liver function						
Volumetric remnant liver volume	70.3% (33.3–89.3)	48.9% (40.3–82.9)	**<0.001**	-	-	-
Functional remnant liver volume	76.7% (37.1–92.6)	54.1% (37.9–89.4)	**<0.001**	-	-	-
Volumetric rem-KICG	0.096 (0.041–0.196)	0.066 (0.036–0.109)	**<0.001**	-	-	-
Functional rem-KICG	0.106 (0.053–0.211)	0.074 (0.042–0.120)	**<0.001**	0.236	0.103–0.540	**<0.001**
Type of hepatectomy						
Bi-/tri-sectionectomy	80/2	20/4	**0.023**	7.280	1.096–48.352	**0.040**
Hepaticojejunostomy	32 (39.0%)	14 (58.3%)	0.106	-	-	-
Intraoperative outcomes						
Operation time (min)	438 (230–845)	507 (316–1,038)	**0.029**	1.763	1.046–2.972	**0.033**
Blood loss (mL)	804 (2–10,150)	1,499 (210–7,400)	0.117	-	-	-
Postoperative outcomes						
CD classification (≥III)	23 (28.0%)	16 (66.7%)	**0.001**			
Mortality	2 (2.4%)	2 (8.3%)	0.220			
Postoperative hospital stay (d)	16 (6–80)	34 (15–136)	**<0.001**			

*Portal vein obstruction caused by portal vein embolization or tumor thrombus. ICGR15, indocyanine green retention rate at 15 min; KICG, indocyanine green elimination rate constant; LHL15, hepatic uptake ratio of 99mTc-GSA scintigraphy at 15 min; CD, Clavien–Dindo; PHLF, posthepatectomy liver failure; CI, confidence interval. Data are expressed as number (percentage) or median (range). All continuous variables used in the multivariate analysis were normalized using z-score transformation, resulting in values with a mean of 0 and a standard deviation of 1.

KICG showed 88% sensitivity and 82% specificity for predicting liver failure.[6] These important studies indicate that the estimated volumetric rem-KICG value can be used as an objective index of remnant hepatic functional reserve. In 2006, Nagino *et al* studied outcomes in 240 biliary cancer patients who underwent PVE before an extended hepatectomy. They revealed that mortality was significantly higher in patients whose volumetric rem-KICG after PVE was <0.05, compared with those whose index was ≥0.05 (28.6% versus 5.5%, $P < 0.001$).[7] Based on these results, they proposed a volumetric rem-KICG cut-off value of 0.05 to determine whether liver resection can be safely performed. Thereafter, a volumetric rem-KICG of 0.05 became a standard index to indicate hepatectomy in Japan.

Liver function is not homogeneous in certain chronic liver diseases, including nonalcoholic fatty liver disease, non-alcoholic steatohepatitis,[24,25] and even in healthy livers.[15] Therefore, the volumetric rem-KICG value, which is calculated by multiplying the KICG value and the CT volumetric rate of the future remnant liver, does not always correctly estimate the remnant liver function. ^{99m}Tc-GSA scintigraphy evaluates the distribution of functioning hepatocytes and is an excellent method for assessing heterogeneous liver function. The introduction of 3D-CT/^{99m}Tc-GSA SPECT fusion imaging has precisely estimated focal regional liver function. Our study showed that the status of the liver's tumor side highly influences the function of the remnant liver. It is considered that the resected side's hepatic parenchyma is experiencing a decrease in hepatic function due to obstructive cholangitis, which is caused by biliary obstruction due to tumor infiltration. Additionally, the infiltration and compression of the tumor can lead to stenosis or occlusion of the main blood vessels, resulting in impaired blood flow. Similar observation study has been reported by Sumiyoshi and colleagues,

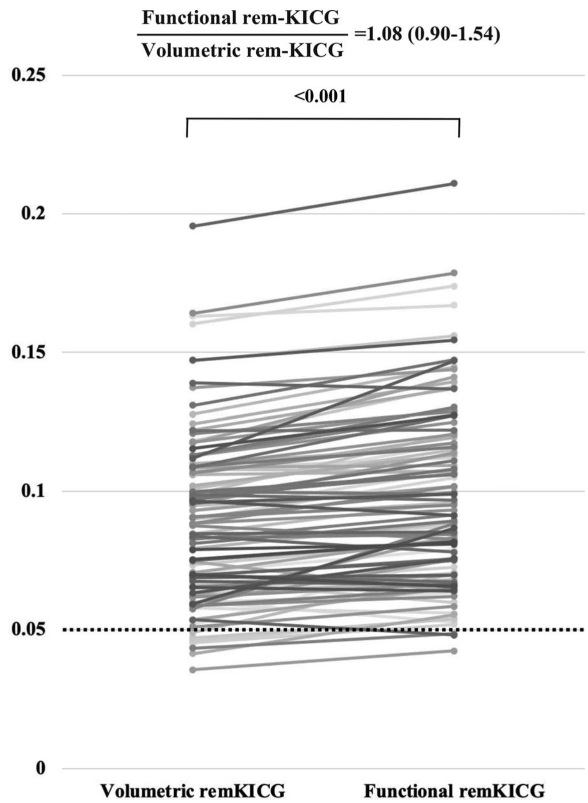

Fig. 2 Comparison of volumetric rem-KICG with functional rem-KICG. Functional rem-KICG values were significantly greater than volumetric rem-KICG values ($P < 0.001$). KICG, indocyanine green disappearance rate.

highlighting these aspects. They concluded that remnant liver function was better correlated with ^{99m}Tc-GSA SPECT findings than the CT findings for several reasons: (1) The extent of hepatic impairment in the region such as the segment or lobe occupied by a hepatic tumor was greater than that in a region without a tumor, (2) The hepatic parenchyma around the tumor was damaged by mechanical compression, and (3) Compression of blood vessels and bile ducts by the tumor causes secondary liver damage.[26]

Volumetric and functional RLRs among the 106 patients were evaluated to obtain the volumetric rem-KICG, functional rem-KICG, and functional-to-volumetric RLR ratio. When we compared the backgrounds and postoperative courses of patients with posthepatectomy liver failure non/A and B/C, the functional rem-KICG value was an independent risk factor for PHLF grade B/C in a multivariate analysis. Functional RLR was highly influenced by the tumor side of the liver. In particular, the functional-to-volumetric RLR ratios in patients with PV obstruction and/or a tumor volume of $\geq$500 mL on the tumor side were significantly higher than that in those without PV occlusion and/or a tumor volume of <500 mL. When we compared the 2 indicators of volumetric rem-KICG and functional rem-KICG using a cut-off value of 0.05, volumetric rem-KICG determined that hepatectomy was unsafe in 7 patients. In contrast, functional rem-KICG determined that it was unsafe in only 3 patients. Although all 8 patients were older than 68 years of age, none of them died after hepatectomy. Thus, functional rem-KICG is a more reliable indicator of remnant liver function than volumetric rem-KICG. This finding could lead to a wider application of this technique. Sumiyoshi *et al* previously reported calculating functional RLR using CT/^{99m}Tc-GSA SPECT fusion imaging. They estimated KICG by LHL15 (KGSA) to evaluate posthepatectomy remnant liver function in 30 patients with perihilar cholangiocarcinoma[12] and 10 hepatectomized patients with an ICGR15 >40%.[19] They then compared volumetric rem-KICG and functional rem-KGSA. Hepatectomy for perihilar cholangiocarcinoma was considered unsafe in 17% of patients using volumetric rem-KICG and 0% of patients using functional rem-KGSA. The patients in which hepatectomy was deemed unsafe based on the volumetric rem-KICG did not suffer from postoperative liver failure and mortality. Among the 10 hepatectomized patients with ICGR15 >40%, the KGSA values were significantly higher than the KICG values; similarly, the functional rem-KGSA values were higher than the volumetric rem-KICG values in all patients. Hepatectomy was deemed unsafe in 70% of patients as determined by volumetric rem-KICG and in 0% of patients as determined by functional rem-KGSA. No hepatic failure or postoperative mortality occurred. Although these were reports of a small number of cases, the results imply that KGSA is a more reliable tool than KICG and that functional RLR is a more accurate indicator of liver function assessment than volumetric RLR. In terms of methods for fusion image creation, we set the resection line using the 3D vascular image which was reconstructed based on DICOM data obtained from 4-phase dynamic CT, after which the acquired ^{99m}Tc-GSA SPECT image was fused with the 3D image. In contrast, Sumiyoshi *et al* set the resection line using plain CT images without vascular images.[12] Clinically, hepatic dissection is performed along the hepatic vein. Therefore, our method may be more useful and reliable.

In terms of other remnant liver function assessments, Morine *et al* reported the efficacy of dynamic magnetic resonance imaging with gadoxetate-

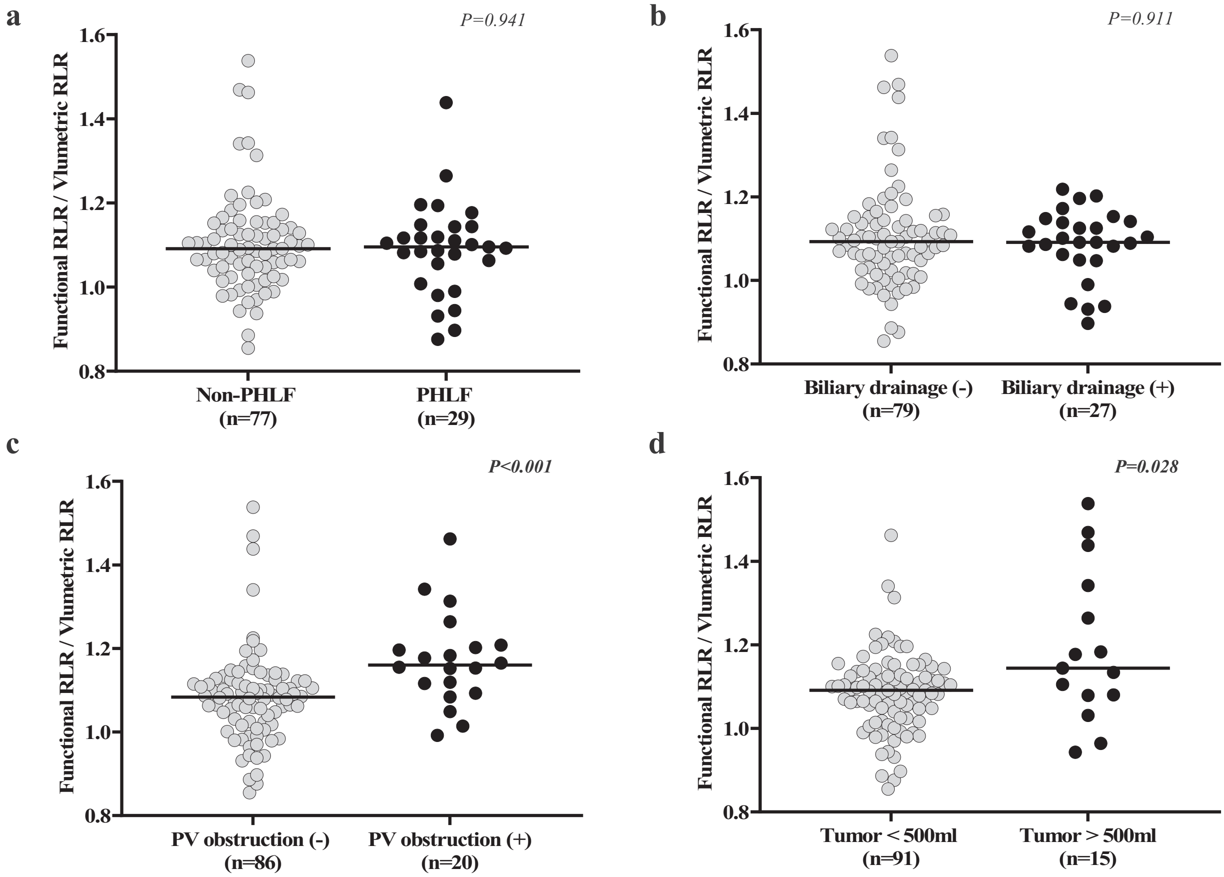

Fig. 3 Functional-to-volumetric RLR ratio based on the status of the tumor side of the liver. (a) Non-PHLF versus PHLF. (b) Preoperative biliary drainage (−) versus preoperative biliary drainage (+). (c) PV obstruction (−) versus PV obstruction (+). (d) Tumor volume <500 mL versus tumor volume ≥500 mL. PHLF, posthepatectomy liver failure; PV, portal vein; RLR, remnant liver rate.

ethoxybenzyl-diethylenetriamine penta-aceticpenta-acetic acid (EOB-MRI) to evaluate functional hepatic volume compared with ^{99m}Tc-GSA SPECT.[27] They suggested that the left lateral section of the liver may be underestimated using MDCT/^{99m}Tc-GSA SPECT fusion imaging; accordingly, EOB-MRI could be more reliable for estimating regional hepatic function. There are few prospective studies investigating the efficacy of preoperative evaluation of future remnant hepatic function in patients who undergo hepatectomy.[28,29] Based on our study, the 99mTc-GSA-based liver functional evaluation may be useful to determine surgical indications, although further studies are required.

Our study had some limitations. First, the number of patients who were retrospectively analyzed at a single center was relatively small; thus, our results should be confirmed in a multicenter study with a large number of patients. Second, ^{99m}Tc-GSA scintigraphy and 3D analysis (Synapse Vincent) are specialized tests that are not available in most community hospitals, although the technique has become popular in Japan.

In conclusion, to estimate remnant liver function preoperatively, functional rem-KICG was more reliable than volumetric rem-KICG because the status of the affected side of the liver highly influenced the function of the remnant liver. Functional rem-KICG was the best predictive factor for clinically relevant PHLF grades B/C.

Abbreviations

C-D: Clavien-Dindo
ICG: indocyanine green
ICGR15: indocyanine green retention rate at 15 min
KICG: indocyanine green disappearance rate
LHL15: ratio of liver to heart-plus-liver radioactivity of 99mTc-GSA 15 minutes after injection 99m
Tc-GSA: technetium-99m-diethylenetriamine-

Table 3 Background and postoperative course of patients with volumetric or functional rem-KICG <0.05

Case	Age (y)	Sex	Disease	Biliary drainage	PV obstruction	C-P score	ALBI grade	ICGR15	KICG	LHL15	Type of Hx	C-J	V-RLR (%)	F-RLR (%)	Volumetric rem-KICG	Functional rem-KICG	PHLF grade	CD	Mortality
(1)	78	M	IPNB	Yes	No	6	1	16.1	0.103	0.93	Left	No	43.9	50.4	**0.045**	0.052	B	IIIa	No
(2)	77	M	HCC	No	Yes	5	1	20.2	0.104	0.947	Right	No	44.3	52.4	**0.046**	0.054	non	-	No
(3)	73	F	PHC	Yes	No	6	2	17.2	0.099	0.956	Right	Yes	47.6	54.3	**0.047**	0.054	B	IIIa	No
(4)	84	F	HCC	No	No	6	2	16.8	0.099	0.95	Right	No	49.5	71.2	**0.049**	0.070	B	II	No
(5)	81	M	HCC	No	No	5	1	18.4	0.111	0.927	Right	No	37.3	50	**0.041**	0.056	B	-	No
(6)	76	M	HCC	No	No	6	2	24.5	0.084	0.957	Right	No	42.3	50.5	**0.036**	**0.042**	B	-	No
(7)	68	M	PHC	No	Yes	5	1	16.8	0.105	0.964	Right	Yes	41.3	46.2	**0.043**	**0.049**	C	IVb	No
(8)	82	M	PHC	Yes	No	6	2	9.9	0.127	0.95	Right	Yes	42.2	37.9	0.054	**0.048**	C	III	No

CD, Clavien–Dindo classification; C-J, choledochojejunostomy; C-P, Child–Pugh; F, female; F-RLR, functional remnant liver rate; HCC, hepatocellular carcinoma; Hx, hepatectomy; ICGR15, indocyanine green retention rate at 15 min; IPNB, intraductal papillary neoplasm of the bile duct; KICG, indocyanine green elimination rate constant; LHL15, hepatic uptake ratio of technetium-99m galactosyl human serum albumin (99mTc-GSA) scintigraphy at 15 min; M, male; PHC, perihilar cholangiocarcinoma; V-RLR, volumetric remnant liver rate; PHLF, posthepatectomy liver failure.

pentaacetic acid galactosyl human serum albumin
PHLF: posthepatectomy liver failure
PV: portal vein
PVE: portal vein embolization
RLR: remnant liver rate
SPECT: single-photon emission computed tomography
3D-CT: three-dimensional computed tomography

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