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Liver remnant volume to body weight ratio of 0.65% as a lower limit in right hepatic trisectionectomy with bile duct resection

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ABSTRACT

Background: Previous studies have suggested the utility of an indocyanine green plasma clearance rate of the future liver remnant (FLR) (ICGK-F) ≥0.05 in hepatobiliary resection to reduce the surgical risk. The present study aimed to verify whether future liver remnant size rather than ICGK-F matters in extended hepatobiliary resection.
Methods: Between 2004 and 2021, patients who underwent right hepatic trisectionectomy with bile duct resection were included. The effect of the FLR volume-to-body weight ratio (FLR/BW) and ICGK-F on posthepatectomy liver failure was evaluated along with other parameters.
Results: Among 91 study patients, the median ICGK-F, FLR, and FLR/BW were 0.057 (range, 0.027–0.099), 392 mL (145–705), and 0.78% (0.40–1.37), respectively. Posthepatectomy liver failure occurred in 23 patients. The incidence was 10 (40%) in 25 patients with an ICGK-F <0.05 and 12 (18%) in 65 patients with an ICGK-F ≥0.05 ($P = .053$); 13 (52%) in 25 patients with a FLR/BW <0.65% and 10 (15%) in 66 patients with a FLR/BW ≥0.65% ($P = .001$). Multivariate analysis showed that a FLR/BW <0.65% (odds ratio, 11.7; $P = .005$), age ≥65 years (odds ratio, 31.7; $P < .001$), and blood loss ≥25 mL/kg (odds ratio, 22.1; $P = .004$) were independent predictors of posthepatectomy liver failure, but ICGK-F <0.05 was not ($P = .499$). According to the meeting number of 3 factors, posthepatectomy liver failure incidence was 0 of 22 (0%) in patients with 0 factors, 6 of 43 (14%) in patients with 1, and 17 of 26 (65%) in patients with 2 or 3 ($P < .001$).
Conclusion: A FLR/BW ≥0.65% may serve as a volumetric basis to reduce posthepatectomy liver failure after extended hepatobiliary resection.

Introduction

Major hepatectomy and extrahepatic bile duct resection, followed by bilioenteric anastomosis, is a standard surgical approach for hepatobiliary malignancy to achieve prolonged survival.[1] Among the various hepatobiliary resections, right trisectionectomy (H145678-B[2]) is characterized as the most extended hepatectomy, providing a long ductal margin length by proximal division of the left lateral segmental duct.[3-5] Therefore, this extended hepatectomy has been widely used in the West as a superior oncologic option for perihilar cholangiocarcinoma,[6-8] in conjunction with few technical demands.[9] This approach, however, has a major drawback of excessive liver loss; the future liver remnant (FLR), ie, left lateral segment, usually accounts for <20% of the whole liver in normal subjects.[10] In addition, postoperative incidences of liver failure and surgical death reached approximately 25% and 20%, respectively, under its proactive use in the West.[11,12] Thus, right trisectionectomy with bile duct resection should be strictly applied in selected patients to balance its oncologic advantages and high-risk nature.

In Japan, the indocyanine green (ICG) test and liver volumetry have been used to estimate the functional reserve of the FLR after hepatectomy. In particular, a plasma disappearance rate of ICG (ICGK) allocated for the FLR (ICGK-F) ≥0.05 serves as a safety requirement in perihilar cholangiocarcinoma.[13,14] This functional guide partly succeeded in reducing mortality rates after

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hepatobiliary resection in Japan; equally, a submarginal ICGK-F often hampers the implementation of right trisectionectomy.[15] The ICGK-F presupposes even excretory capacity of ICG in the entire liver even after unilateral biliary drainage and/or portal vein embolization. Theoretically, the value of the ICGK-F underestimates the real reservoir capacity of the FLR. Therefore, the lower limit of the functional reserve of the FLR needs to be reappraised to expand the applicability of this extended hepatectomy. This classic yet ongoing problem has been sparsely investigated in the context of hepatobiliary resections.[7,16-18]

The authors hypothesized that FLR size, rather than function (ICGK-F), would be associated with postoperative liver failure. The present study attempted to seek an optimal assessment of the FLR in homogeneous samples using patients who underwent right hepatic trisectionectomy with bile duct resection. The goal was to propose a new safety standard regarding FLR size in extended hepatobiliary resection.

Methods

Patients

Between January 2004 and December 2021, consecutive patients who underwent right hepatic trisectionectomy and bile duct resection (H145678-B[2]) followed by bilioenteric anastomosis for presumed malignancy at Nagoya University Hospital were retrospectively reviewed from prospectively maintained databases. This retrospective study was approved by the Human Research Review Committee of Nagoya University Hospital (approval number 2022-0297).

Preoperative management

Multidetector row computed tomography (MDCT) with contrast enhancement was routinely performed to survey tumor staging, biliovascular anatomy, and segmental liver volume calculation at initial presentation. Based on these findings, endoscopic biliary drainage was performed in the FLR alone as the first-line approach. CT volumetry was performed by a commercially available image analysis system (SYNAPSE VINCENT, Fujifilm, Tokyo, Japan), where the volume of each hepatic sector/segment was semiautomatically calculated as the volume of hepatic parenchyma minus that of tumor mass and major vessels. In the present study, the volumes of the left lateral segment and the whole liver were given as the FLR volume and total liver volume (TLV), respectively. The FLR (%) was defined as the FLR volume to TLV ratio, and the FLR/BW (%) was defined as the FLR volume to actually measured body weight ratio according to previous reports.[19,20] The ICG test was performed when the total bilirubin concentration decreased to <2 mg/dL. The functional reserve of the FLR was evaluated by the ICGK-F.[21-23] When the initial FLR (%) was less than 40%, portal vein embolization was usually performed 4 to 6 weeks before surgery after serum total bilirubin concentration declined to <5.0 mg/dL. The portal vein was accessed with a percutaneous transhepatic ipsilateral approach. A 4-Fr catheter or a microcatheter was used to select the portal vein branches. Gelatin sponge slurry was injected to the selected branch, and metallic coils were subsequently placed in the proximal portion. A few portal veins of segment 4 in addition to the right portal vein were usually embolized.[24] MDCT-based volumetry and ICG test were performed again 3 to 4 weeks after portal vein embolization. Kinetic growth rate (KGR), defined as increase of FLR/TLV (%) per week between the embolization and the initial CT assessment, was calculated.[25] An ICGK-F $\geq$0.05 served as a functional safety guideline during the study period.[13,14] Although not clearly predefined, selected patients with an ICGK-F <0.05 were scheduled for surgery provided that their general condition allowed. When the patients had cholangitis before surgery, the operation was rescheduled at least 2 weeks later. Antibiotics were given until normalization of the biochemical data as well as clinical symptoms, and the existing biliary drainage was changed as needed.

Surgery

The surgery was performed after the serum total bilirubin level was <2 mg/d and was rescheduled 2 weeks after cholangitis occurred. A key technique was mobilization of the umbilical portion of the left portal vein from the umbilical plate by division of tiny cranial portal veins as well as segment 4 portal veins, facilitating division of the proximal bile duct at the left side of the umbilical portion, as described previously.[3] Liver transection was performed using an ultrasonic dissector under an intermittent inflow clamp for 20 minutes with a 5-minute interval. Portal vein resection was performed only when the major vasculature was grossly involved during the surgery.[26] Regional lymph nodes in the hepatoduodenal ligament were removed in all patients; those around the pancreatic head and common hepatic artery were additionally resected in patients with presumed biliary malignancy. Intraoperative blood loss (mL) was adjusted by BW (kg).

Postoperative complications were graded according to the Clavien–Dindo classification.[27] The primary outcome in the present study was the incidence of posthepatectomy liver failure (PHLF), which was defined as grade B or C, according to the International Study Group of Liver Surgery (ISGLS).[28]

Statistics

The results are expressed as the median with ranges or as the number with percentages, unless otherwise specified. Statistical analysis was performed using the Mann–Whitney *U* test for continuous variables and Fisher exact test for categorical variables. The cutoff value dichotomizing the continuous variable was determined with reference to the receiver operating characteristic (ROC) curve and the area under the curve (AUC). Logistic regression analysis was performed to identify the predictors of PHLF, in which all significant variables ($P < .100$) from the univariate analysis were included in the multivariate analysis. All statistical tests were 2-sided, and statistical significance was set at $P < .05$. All statistical calculations were performed using IBM SPSS version 27 (IBM Japan, Inc, Tokyo, Japan) and EZR.[29]

Results

During the study interval, 91 patients were enrolled (Table I), excluding 9 patients who underwent additional pancreaticoduodenectomy. There were 49 men and 42 women, with a median age of 66 years (range, 22–81 years). The most common final pathology was cholangiocarcinoma in 79 patients (perihilar, $n = 75$ and intrahepatic, $n = 4$), followed by liver tumor involving the hepatic hilus in 7 patients, gallbladder carcinoma in 3, and IgG4-related sclerosing cholangitis in 2 patients. No patients with cholangiocarcinoma had underlying primary sclerosing cholangitis. The ICG test was not performed in 1 patient due to prolonged cholestasis.

Preoperative biliary drainage and portal vein embolization were performed in 80 (endoscopic, $n = 68$ and percutaneous, $n = 16$ with overlaps) and 82 patients (right portal vein alone, $n = 15$ and right portal vein plus segment 4 branch, $n = 67$), respectively. Preoperative chemotherapy was given for 9 patients. In the embolization group, the FLR increased by 122 mL, on average; subsequently, the

Table I
Clinical characteristics of the study patients

	$n = 91$	
Preoperative characteristics		
Age (years)	66	(22–81)
Sex ratio (M:F)	49:42	
Body weight (kg)	55	(25-76)
Body mass index (kg/m^2)	21.1	(13.1–28.6)
Body surface area (m^2)	1.56	(1.00-1.95)
Diabetes mellitus	11	(12.1)
Preoperative cholangitis	40	(44.0)
Preoperative biliary drainage	80	(87.9)
Portal vein embolization	82	(90.1)
Laboratory data before surgery		
Albumin (g/dL)	3.4	(2.6-4.6)
Platelet count ($\times 10^4$/μL)	23.7	(11.4–58.5)
Total bilirubin (mg/dL)	0.7	(0.3–2.4)
Prothrombin time (%)	98	(61-122)
Disease		
Cholangiocarcinoma	79	(86.8)
Gallbladder carcinoma	3	(3.3)
Colorectal liver metastasis	2	(2.2)
Neuroendocrine neoplasm	2	(2.2)
Benign cholangitis	2	(2.2)
Sarcoma	2	(2.2)
Hepatocellular carcinoma	1	(1.1)

Values in the table are shown as the number of patients (percentage) or median (range).

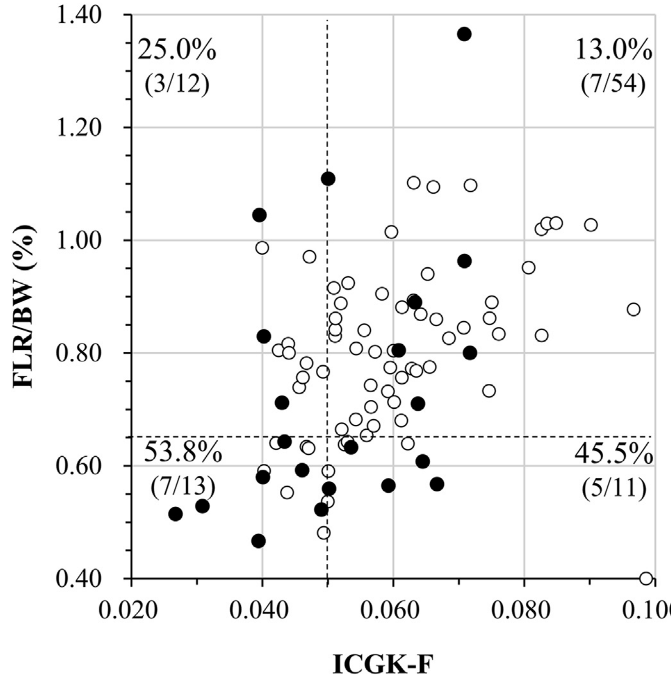

Figure 1. Scatter plot association between the ICGK-F and FLR/BW. Vertical and transverse dotted lines indicate the cutoff values for the ICGK-F (0.05) and FLR/BW (0.65%). One patient who did not receive ICG test was excluded. White and black circles indicate posthepatectomy liver failure of none/grade A and grades B/C, respectively, and the latter incidence was incorporated in each hazard-related quarter. *BW*, body weight; *FLR*, future liver remnant; *ICGK-F*, plasma clearance rate of indocyanine green of the FLR.

FLR (%) and FLR/BW increased by 9% and 0.27%, respectively, and the ICGK-F increased by 0.016 after portal vein embolization (Supplementary Table S1). Median KGR was 2.7% (-1.0 to 10.0) per week in 81 patients who received portal vein embolization (liver volume data before embolization lacked in 1 patient). Overall, the median FLR, FLR (%), and FLR/BW were 392 mL (range, 145–705), 35.1% (24.5–62.7), and 0.78% (0.40–1.37), respectively, just before surgery. Seventy, 45, and 9 patients had an FLR (%) <40%, <35%, and <30%, respectively; 25 and 3 patients had an FLR/BW <0.65% and <0.50%, respectively. The ICGK-F ranged from 0.027 to 0.099, with a median of 0.057; 25 and 3 patients had an ICGK-F<0.05 and <0.04, respectively. The scatter plot displaying the relationship between the FLR/BW and ICGK-F (Figure 1) showed a weak correlation (correlation coefficient, 0.427; $P < .001$).

Approximately half of the patients underwent portal vein resection. The median intraoperative blood loss was 991 (201–5,560) mL and 18.0 (3.7–185) mL/kg after adjustment by body weight. Major complications ≥grade III were found in 40 patients, 1 of whom died in the hospital on postoperative day 44 due to PHLF.

PHLF and perioperative factors

There were 26 patients with ISGLS grade A, 20 patients with grade B, and 3 patients with grade C, giving an incidence of PHLF of 25% in the present study. Three patients met the 50-50 criteria on postoperative day 5[30] (grade B in 2 and C in 1), and 10 patients had peak total bilirubin levels ≥7 mg/dL[31] (grade A in 2, B in 5, and C in 3).

Preoperative albumin, total bilirubin, prothrombin time, and platelet count, in addition to sex and body mass index, were not significantly different between the PHLF and non-PHLF groups. Patient age was more advanced and the FLR (%), ICGK-F, and FLR/BW were lower in the former group than in the latter group (Table II). Heavy blood loss with blood transfusion was more common in the PHLF group than in the non-PHLF group.

The FLR/BW, FLR (%), ICGK-F, blood loss, and age were associated with the incidence of PHLF (Figure 2). A PHLF incidence >50% was found in subsets with an FLR/BW <0.65% (52.0%, 13/25), an ICGK-F <0.04 (100%, 3/3), an FLR (%) <30% (56%, 5/9), and blood loss ≥30 mL/kg (56%, 9/16). The cutoff values were set as follows: age, 65 years; FLR (%), 35%; FLR/BW, 0.65%; and blood loss, 25 mL/kg (with reference to the ROC curves); that of the ICGK-F was set at 0.05 according to a Japanese guideline[14]; and that of KGR was set at 2.0% according to a previous report.[25]

Ten (40.0%) of the 25 patients with an ICGK-F <0.05 had PHLF, whereas 12 (18.4%) of the 65 patients with an ICGK-F ≥0.05 had PHLF ($P = .053$). The specificity, sensitivity, and accuracy of the ICGK-F of 0.05 were 0.779, 0.455, and 0.700, respectively. Thirteen (52.0%) of the 25 patients with an FLR/BW <0.65% had PHLF, whereas 10 (15.2%) of the 66 patients with an FLR/BW ≥0.65% had PHLF ($P = .001$). The specificity, sensitivity, and accuracy of an FLR/BW of 0.65% were 0.824, 0.565, and 0.758, respectively. As shown in Figure 1, among the 25 patients with an ICGK-F <0.05, 3 (25.0%) of the 12 patients with an FLR/BW ≥0.65% (upper left region) and 7 (53.8%) of the 13 patients with an FLR/BW <0.65% (lower left region) had PHLF ($P = .226$). PHLF was observed in 5 (29.4%) of 17 patients with KGR <2.0% and in 14 (21.5%) of 65 patients with KGR ≥2.0% ($P = .526$).

Risk factors for PHLF

The univariate analysis demonstrated that study period, age, FLR/BW, operation time, and blood loss were potential predictors of PHLF, whereas sex, preoperative cholangitis, and ICGK-F were not (Table III). The multivariate analysis revealed that age ≥65 years (odds ratio [OR], 31.7; 95% confidence interval [CI], 4.28–235; $P < .001$), FLR/BW <0.65% (OR, 11.7; 95% CI, 2.08–66.1; $P = .005$), and blood loss ≥25 mL/kg (OR, 22.1; 95% CI, 2.75–178; $P = .004$) were independent risk factors for PHLF.

Table II
Clinical characteristics of patients stratified by posthepatectomy liver failure (PHLF)

	PHLF (n = 23)		Non-PHLF (n = 68)		*P*
Study period, 2004–2012	14	(60.9)	26	(38.2)	.088
Age (years)	71	(49–78)	63	(22–81)	.001
Sex ratio (M:F)	14:9		35:33		.477
Preoperative cholangitis	10	(43.5)	30	(44.1)	1.000
ICGK*	0.154	(0.077–0.197)	0.166	(0.110–0.228)	.350
FLR (mL)	352	(145–669)	421	(264–705)	.003
TLV (mL)	1067	(575–1675)	1173	(431–1903)	.011
FLR (%)	33.8	(24.5–62.7)	36.6	(27–61.3)	.044
<35%	16	(69.6)	29	(42.6)	.031
<30%	5	(21.7)	4	(5.9)	.042
ICGK-F*	0.050	(0.027–0.072)	0.058	(0.040–0.099)	.039
<0.075	22	(100)	56	(82.4)	.034
<0.050	10	(45.5)	15	(22.1)	.053
FLR/BW (%)	0.63	(0.47–1.37)	0.80	(0.40–1.10)	.013
<0.65%	13	(56.5)	12	(17.6)	.001
Portal vein embolization	19	(82.6)	63	(92.6)	.223
Portal vein resection	10	(43.5)	36	(52.9)	.477
Operative time (min)	581	(387–695)	538	(302–795)	.482
Pringle time (min)	32	(20–81)	40	(10–138)	.258
Blood loss (mL/kg)	26	(4.8–185)	16	(3.7–51.6)	.002
Intraoperative blood transfusion	12	(52.2)	15	(22.1)	.009
Red blood cells	11	(47.8)	14	(20.6)	.016
Fresh frozen plasma	7	(30.4)	8	(11.8)	.052
Morbidity (≥Clavien–Dindo III)	14	(60.9)	26	(38.3)	.088
90-day mortality	1	(4.3)	0	(0)	.253

Values in the table are shown as the number of patients (percentage) or median (range).
BW, body weight; *PHLF*, posthepatectomy liver failure; *ICGK*, plasma clearance rate of indocyanine green; *FLR*, future liver remnant; *TLV*, total liver volume; *FLR* (%) indicates the FLR to TLV ratio; *ICGK-F*, ICGK of the FLR.
BW, body weight; *PHLF*, posthepatectomy liver failure; *ICGK*, plasma clearance rate of indocyanine green; *FLR*, future liver remnant; *TLV*, total liver volume; *FLR* (%) indicates the FLR to TLV ratio; *ICGK-F*, ICGK of the FLR.
* ICG test was not performed in 1 patient.

The cutoff values of the risk factors divided scatter plots into hazard-related quarters (Figure 3). A hot spot of PHLF was found in the overlapping risk area. The incidence rose with an increase in the matching number of the 3 risk factors (Figure 4). The PHLF incidence was 0% (0/22) in 0, 14% (6/43) in 1, and 65% (17/26) in 2 or 3 (AUC, 0.857; 95% CI, 0.769–0.945; *P* < .001).

Subset analysis for PHLF

The cutoff value of FLR/BW in 49 patients with age ≥65 years was 0.71% according to the ROC and AUC. In this subset, the incidence of PHLF was 55.6% (10/18) in the FLR/BW <0.71% group vs 29.0% (9/31) in the FLR/BW ≥0.71% group (*P* = .076), while 62.5% (10/16) in the FLR/BW <0.65% group vs 27.3% (9/33) in the FLR/BW ≥0.65% group (*P* = .028). Among patients with FLR/BW ≥0.65%, KGR was 2.8 (1.4–4.5)% per week in 10 patients with PHLF and 3.0 (0.6–10.0)% per week in 56 patients without (P = .736); PHLF occurred in 1 (8.3%) of 12 patients with KGR <2.0% and 7 (14.5%) of 48 patients with KGR ≥2.0% (*P* = 1.000).

Discussion

The main findings from this procedure-specific study are summarized as follows. First, 23 of the 91 patients who received right trisectionectomy with bile duct resection had PHLF, and 1 (4.3%) died. The case-fatality rate was not very high. Second, the FLR/BW with a cutoff value of 0.65% predicted PHLF more specifically than did the ICGK-F, FLR (%), and KGR, indicating that the size matters. Interestingly, "the larger, the better" phenomenon was not observed between FLR/BW and PHLF. Third, age and blood loss also showed a good predictive ability for PHLF. Multiple factors mutually triggered PHLF.

In this study, an ICGK-F with a cutoff value of 0.05 failed to demonstrate a predictive ability for PHLF, although the value was prospectively used as the safety guide during the study interval. This finding conflicted with the results of our previous studies[21-23]; however, it can be partly explained by differences in the study period, study sample, surgical technique, and perioperative patient care. Other than the theoretical problem of ICGK-F described in the Introduction section, most Western studies about PHLF have not analyzed ICGK-F as functional capacity since global availability of ICG test varies. The traditional value of "ICGK-F ≥0.05" was proposed to avoid surgical death more than 15 years ago by a retrospective study.[23] The 17 nonsurvivors in that study had age over 65 years (*n* = 13), much bleeding over 3 L (*n* = 10), but an ICGK-F ≥0.05 (*n* = 9), which suggests that these surgical deaths were attributed to age and blood loss rather than ICGK-F. In the present study, all 3 patients with an ICGK-F <0.04 fortunately survived PHLF, but they had other risk factors concomitantly. This observation may suggest the risky nature of an ICGK-F <0.04, as reported previously,[21-23] but the very limited number of cases impedes a conclusion.

The FLR volume should be considered in the context of increasing metabolic demand after massive hepatectomy. The normalization of the FLR remains controversial because many authors have employed various ratios/proportions, including the FLR to TLV proportion,[7,16,22] FLR to standard liver volume,[32,33] FLR to body surface area,[18] and FLR to body weight.[19,20] Similar to the ICGK-F, the former 2 ratios are fashioned on the premise of even quality in the entire liver; therefore, they are appropriate for use in hepatectomy for liver tumor but not for use in biliary tract cancer. However, the latter 2 indexes are suitable as body size-oriented assessments in patients with hepatic functional laterality. The authors used the FLR/BW in the present study, considering the easy-to-use nature in daily practice and analogy to graft-to-recipient weight ratio (GRWR) in living donor liver transplantation.[34] Traut et al[20] suggested that an FLR/BW of 0.5% was a lower limit to avoid PHLF after hepatectomy alone in the normal liver. The present cutoff was higher by 0.15% as an add-on safety margin associated

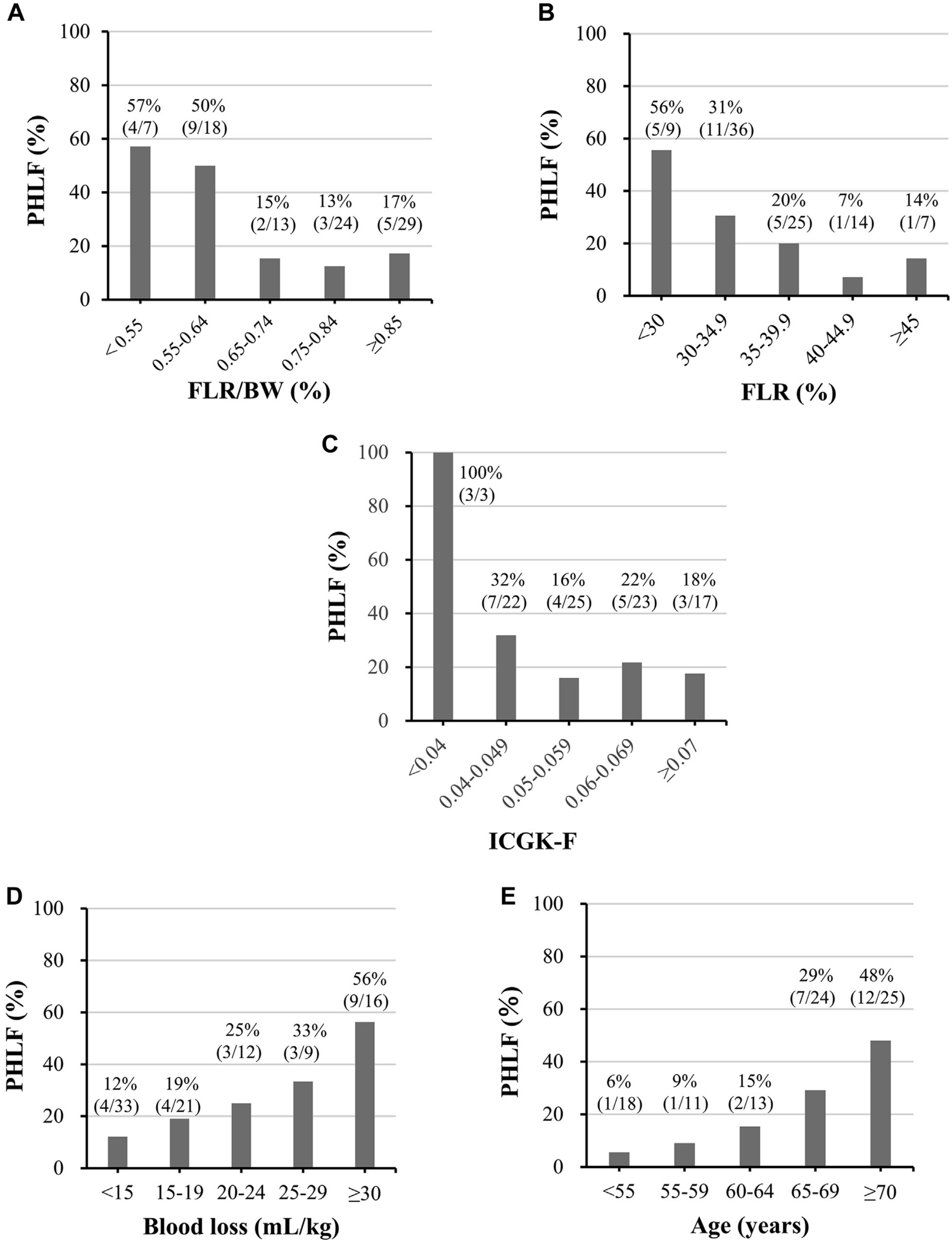

Figure 2. The incidence of posthepatectomy liver failure (PHLF) according to the FLR/BW (A), FLR (%) (B), ICGK-F (C), blood loss (D), and age (E). *BW*, body weight; *FLR*, future liver remnant; *ICGK-F*, plasma clearance rate of indocyanine green of the FLR; FLR (%) indicates the FLR to total liver volume ratio.

Table III
Univariable and multivariable analyses of posthepatectomy liver failure

Variables	No.	with PHLF No. (%)		Univariable	Multivariable	
				P	Odds ratio (95% CI)	P
Study period				.088		.561
2013–2021	51	9	(17.6)		1	
2004–2012	40	14	(35.0)		1.57 (0.35–7.10)	
Age (years)				.002		<.001
<65	42	4	(9.5)		1	
≥65	49	19	(38.8)		31.7 (4.28–235)	
Sex				.477		.581
Female	42	9	(21.4)		1	
Male	49	14	(28.6)		1.48 (0.37–5.98)	
Preoperative cholangitis				1.000		.119
Absent	51	13	(25.5)		1	
Present	40	10	(25.0)		3.47 (0.73–16.6)	
ICGK-F*				.053		.499
≥0.05	65	12	(18.5)		1	
<0.05	25	10	(40.0)		1.66 (0.38–7.17)	
FLR/BW (%)				.001		.005
≥0.65	66	10	(15.2)		1	
<0.65	25	13	(52.0)		11.7 (2.08–66.1)	
Operative time (min)				.060		.190
<600	66	13	(19.7)		1	
≥600	25	10	(40.0)		3.32 (0.55–19.9)	
Blood loss (mL/kg)				.006		.004
<25	66	11	(16.7)		1	
≥25	25	12	(48.0)		22.1 (2.75–178)	

BW, body weight; *PHLF*, posthepatectomy liver failure; *FLR*, future liver remnant; *ICGK-F*, plasma clearance rate of indocyanine green of the FLR.
* ICG test was not performed in 1 patient.

with bile duct resection and lymphadenectomy. Lee et al[17] first observed the risk-stratifying ability of the FLR/BW on PHLF in perihilar cholangiocarcinoma, where the hazard ratio of 0.5%–0.75% was 8.5 and that of less than 0.5% was 18.5, compared to 0.75% or more ($P < .001$). As this study did not focus on a specific lower limit of the FLR/BW, the optimal value may be located between 0.5% and 0.75%. The present study demonstrated FLR/BW of 0.71% as possible cutoff in patients aged ≥65 years, which might suggest a need of extra 0.05% for safety in elders. However, underpower due to the very limited number of patients failed to support the margin. Altogether, the safety window of FLR/BW may range around between 0.65% and 0.71%, depending on patients' age.

The FLR/BSA has been proposed as an analogous measure for liver volume assessments[35] and naturally shows a very strong linear correlation with the FLR/BW (correlation coefficient, 0.932; 95% CI, 0.899–0.955; $P < .001$; data not shown); therefore, both measures are interconvertible. Yamamoto et al[18] analyzed the FLR/BSA in perihilar cholangiocarcinoma and reported a minimal size of 300 mL/m^2 (corresponding to an FLR/BW of 0.8%) to avoid PHLF. A considerable proportion of patients undergoing left hepatectomy in their study evidently raised the cutoff value, compared to 0.65% (≈FLR/BSA of 230 mL/m^2), potentially narrowing the scope of surgical candidates for right trisectionectomy. Findings from the whole sample analysis should be carefully extrapolated into a specific subset because of the great risk differences among the various types of hepatectomy.[36-38]

Currently, there are 3 existing risk classification systems for PHLF after hepatobiliary resection,[7,17,18] in which some preoperative albumin level, cholangitis, total bilirubin level, FLR, and portal vein resection were used as determinants and intraoperative blood loss was not. In contrast, the above factors were not contributors to PHLF in this study, except for the FLR, and the proposed risk classification included 3 discrete variables: age, blood loss, and liver volume. This difference among systems can be explained by the nature of our cohort represented by complete biliary drainage of the FLR, delayed schedule against cholangitis, heavy use of portal vein embolization, and homogeneous hepatectomy type. The AUC of these systems ranged from 0.74 to 0.79,[7,17] while that of the present 3-tier system was 0.832, indicating superiority and reliability in predicting PHLF. This finding clearly suggests that blood loss as well as preoperative parameters are causative for PHLF and that surgeons should endeavor to minimize blood loss to avoid PHLF.

There were some limitations in this study. First, the retrospective nature of the study may have led to overfitting bias associated with a limited sample. Therefore, the reliability of the study results should be externally validated. Second, as patients with a very poor ICGK were initially excluded from surgical candidates, all the study patients satisfied a minimal quality of ICG excretion. This selection bias should be considered in the interpretation of the present results, possibly underestimating the ICGK-F. We never say that ICG test in itself is worthless in the present study; actually, we use 4 metrics including FLR volume, FLR (%), FLR/BW, and ICGK as initial hepatic assessment. In addition, the priority of size versus quality in the FLR should be continuously studied. Third, the present findings were found in patients who underwent right trisectionectomy and the generalization of results to patients who undergo whole hepatobiliary resection is unwarranted. Nonetheless, the present study clearly demonstrated a safety baseline of an FLR/BW ≥0.65% and suggested a simple prediction score for PHLF in right trisectionectomy with bile duct resection. Both may work as a simple evaluation in patient selection before surgery and in the prediction of PHLF after surgery. As a future prospect, the present results should be validated for generalization in patients who undergo any type of hepatobiliary resection, and the setup value of 0.65% should be reappraised with surgical advancements or optimized on the basis of patients' age in the future.

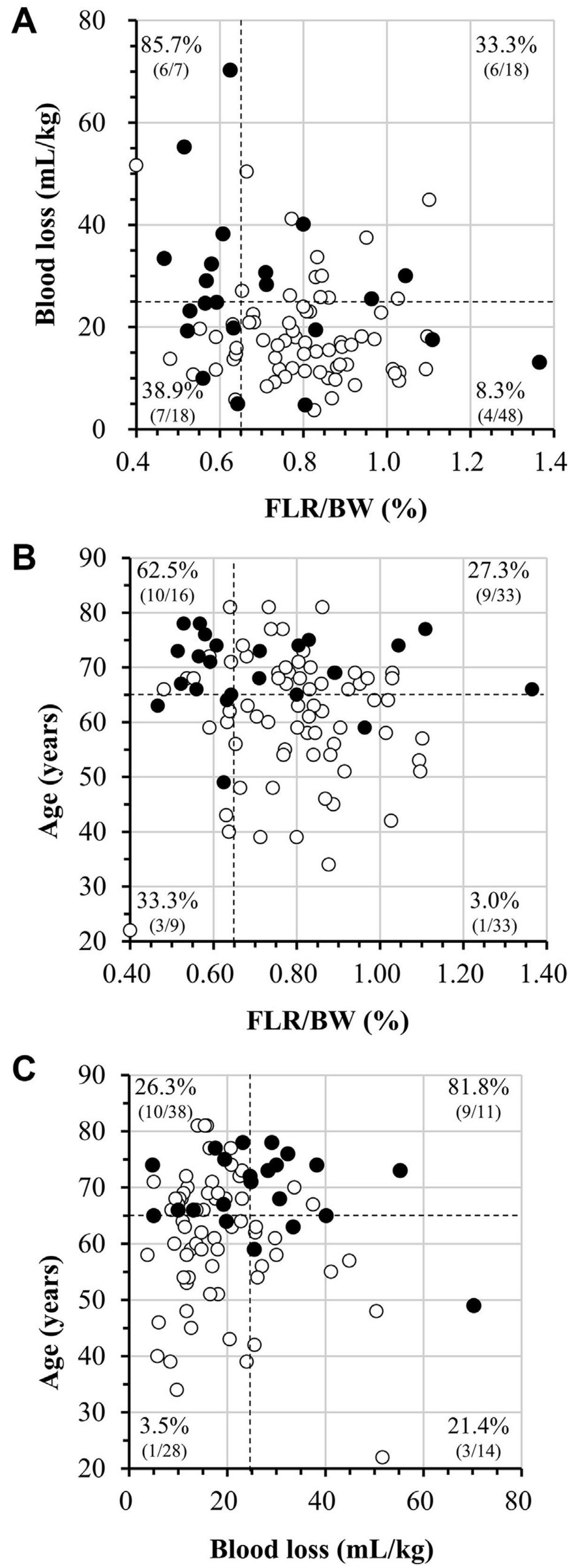

Figure 3. Scatter plot associations among blood loss, FLR/BW, and age. (A) Between the FLR/BW and blood loss. Vertical and transverse dotted lines indicate the cutoff values for FLR/BW (0.65%) and blood loss (25 mL/kg), respectively. (B) Between the FLR/BW and age. Vertical and transverse dotted lines indicate the cutoff values for FLR/BW (0.65%) and age (65 years), respectively. (C) between blood loss and age. Vertical and transverse dotted lines indicate the cutoff values for blood loss (25 mL/kg) and age (65 years), respectively. A 69-year-old patient whose blood loss of 185 mL/kg was not shown as outlier in A and C. White and black circles indicate posthepatectomy liver failure of none/grade A and grades B/C, respectively, and the latter incidence was incorporated in each hazard-related quarter.

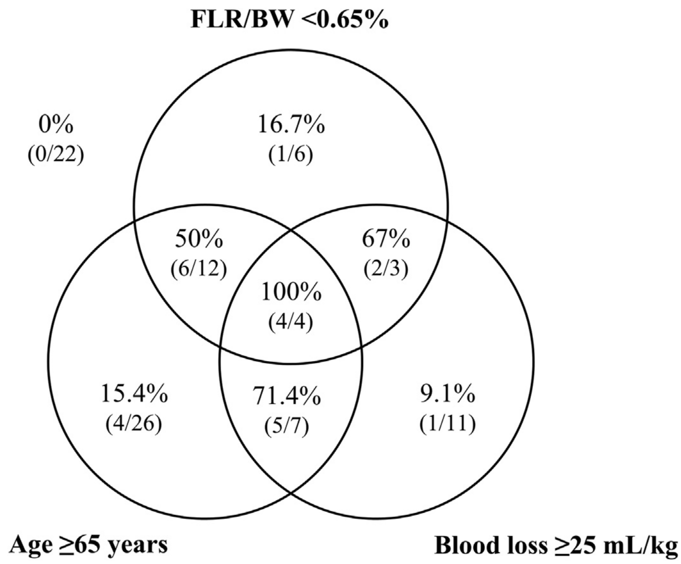

Figure 4. Incidence of posthepatectomy liver failure according to 3 risk factors. *FLR*, future liver remnant; *BW*, body weight.

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Conflict of interest/Disclosure

The authors declare no conflicts of interest.

Supplementary materials

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