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Predictive value of intra-hepatectomy ICGR15 of the remnant liver for post-hepatectomy liver failure in hemi-hepatectomy: a prospective study

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Abstract

Background and objective Post-hepatectomy liver failure (PHLF) is one of the major complications following hepatectomy for hepatocellular carcinoma (HCC). Early identification and precise prediction of PHLF are essential for effective management. This study aimed to evaluate the predictive value of intra-hepatectomy indocyanine green retention rate at 15 min (ICGR15) for the remnant liver for grade B/C PHLF in HCC patients undergoing hemi-hepatectomy.

Methods This prospective study recruited 31 HCC patients who underwent hemi-hepatectomy. ICGR15 was measured at three time points: pre-hepatectomy, intra-hepatectomy (for the remnant liver), and post-hepatectomy. The primary endpoint was the occurrence of grade B/C PHLF according to ISGLS criteria. Logistic regression analysis was employed to evaluate the predictive performance of each parameter and to conduct risk assessment. The XGBoost algorithm was utilized to compare the predictive values of various parameters by calculating the mean Shap values.

Results Among the study participants, 25.8% (8 patients) developed grade B/C PHLF. The intra-hepatectomy ICGR15 for remnant liver exhibited the highest predictive accuracy for grade B/C PHLF, with a ROC-AUC of 0.864 and a PR-AUC of 0.791. The optimal threshold for ICGR15-intra was established at 19.8%. Patients with ICGR15-intra value of 19.8% or higher were found at significantly increased risk of grade B/C PHLF (OR[95% CI] = 3.602[1.437–6.750], *P* value = 0.004), and experienced a higher incidence of severe post-hepatectomy complications.

Conclusion Intra-hepatectomy ICGR15 for the remnant liver was an important predictor of grade B/C PHLF in patients undergoing hemi-hepatectomy for HCC. An intra-hepatectomy ICGR15 threshold of 19.8% might effectively identify patients at high risk of developing grade B/C PHLF and severe post-hepatectomy complications, helping surgeons' final decision-making on the table.

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Keywords Hepatocellular carcinoma, Hemi-hepatectomy, Indocyanine green retention test, Post-hepatectomy liver failure, Prediction

Introduction

Hepatectomy is a primary treatment modality for hepatocellular carcinoma (HCC), providing substantial survival benefits to HCC patients. With refinement of perioperative management and surgical techniques, the indications for hepatectomy have expanded, resulting in a higher proportion of major resections [1], and in consequence, an increase of postoperative complications [2, 3]. Post-hepatectomy liver failure (PHLF) is a prevalent complication and a leading cause of mortality following hepatectomy [4, 5]. Therefore, early identification and precise prediction of PHLF are essential for effective postoperative management.

The liver's reserve function represents the compensatory potential that the organ can mobilize in response to increased physiological demands. The indocyanine green (ICG) test quantitatively and dynamically assesses liver reserve function and is widely used in preoperative evaluations, particularly in Asian countries. The pre-hepatectomy ICG test serves as an important indicator for determining the extent of hepatectomy and significant predictor for PHLF [6, 7]. According to the standards set by the University of Zurich [8] and the University of Tokyo [9], the pre-hepatectomy indocyanine green retention rate at 15 min (ICGR15) should be less than 14% and 10%, respectively. The pre-hepatectomy ICGR15 has been recommended to evaluate overall liver reserve function by the guidelines of many societies [10–12]. However, it might not accurately reflect the reserve function of individual hepatic segments due to heterogeneity.. Especially, the pre-hepatectomy ICGR15 detection of the whole liver might not precisely measure the reserve function of the remnant liver. Thomas et al. [13] observed in 20 anatomic liver resections that intraoperative ICG clearance measurements enable real-time monitoring of liver function during surgery. However, the optimal cut-off value for intra-hepatectomy ICGR15 has not been well standardized. This lack of standardization may be attributed to the variations in the hepatectomy procedures and differences in the primary observed outcomes described in prior studies. The study conducted by Cheung et al. [14] investigated the safe upper limit of intra-hepatectomy ICGR15 during hemi-hepatectomy. The findings indicate that if the intra-hepatectomy ICGR15 surpasses 50%, the post-hepatectomy mortality rate may rise from 1.1% to 50%. In our preliminary research, an intra-hepatectomy ICGR15 value of $\leq$10% was identified as a safe upper limit in right hemi-hepatectomy [15]. However, this criterion may be too strict to exclude some HCC patients who might be benefit from therapeutic hepatectomy. Therefore, it is important to establish an optimal cut-off value for the intra-hepatectomy ICGR15 in hemi-hepatectomy.

Our study encompassed 31 patients diagnosed with HCC who underwent hemi-hepatectomy. During the procedure, we measured the intra-hepatectomy ICGR15 for the remnant liver. We assessed the predictive value of various parameters at three stages—pre-hepatectomy, intra-hepatectomy, and post-hepatectomy—for the occurrence of clinically significant PHLF, classified as ISGLS grades B and C. Furthermore, we determined and suggested a cut-off value for intra-hepatectomy ICGR15 detection in hemi-hepatectomy.

Methods

Patients

This study was a prospective investigation involving HCC patients who underwent hemi-hepatectomy and had intra-hepatectomy ICGR15 measurements at the First Affiliated Hospital of Guangxi Medical University between 2016 and 2023. Exclusion patients were those hepatectomy procedures were modified, those undergoing localized hepatectomy, and cases with incorrect intra-hepatectomy ICGR15 measurement techniques, such as delayed injection of the ICG solution. Ultimately, 31 patients met the inclusion criteria, as detailed in Flowchart 1 (Fig. 1).

Indocyanine green retention rate test and hepatectomy

Showed in Fig. 2, ICGR15 was assessed at three distinct time points: (1) pre-hepatectomy: within two weeks prior to hepatectomy (ICGR15-pre); (2) intra-hepatectomy: during the clamping of the Glisson's pedicle of the planed-resected left/right lobe (ICGR15-intra); (3) post-hepatectomy: at the time of abdominal closure following the hepatectomy (ICGR15-post). The time interval between the ICGR15-intra and ICGR15-post measurements was maintained at over 30 min to allow for adequate ICG clearance. The DDG-3300 device from Nihon Kohden Co. (Tokyo, Japan), set to BV/K detection mode, was employed to measure ICGR15. The dosage of ICG, at a concentration of 5 mg/ml, was tailored for each patient based on their body height and weight. Placement of the nasal probe was carefully verified on the patient's nasal ala. The surgical team comprised experienced hepatobiliary surgeons, and the hepatectomy procedure involved exposing and

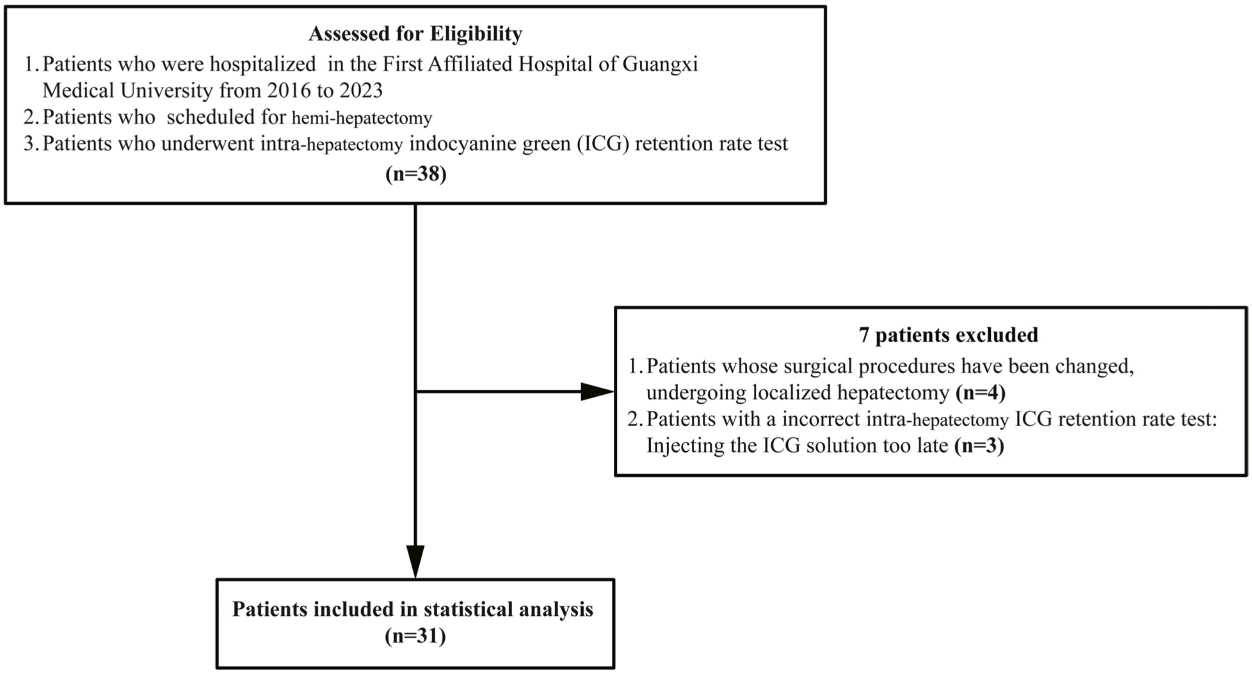

Fig. 1 Flow chart. The criteria for selecting the participants

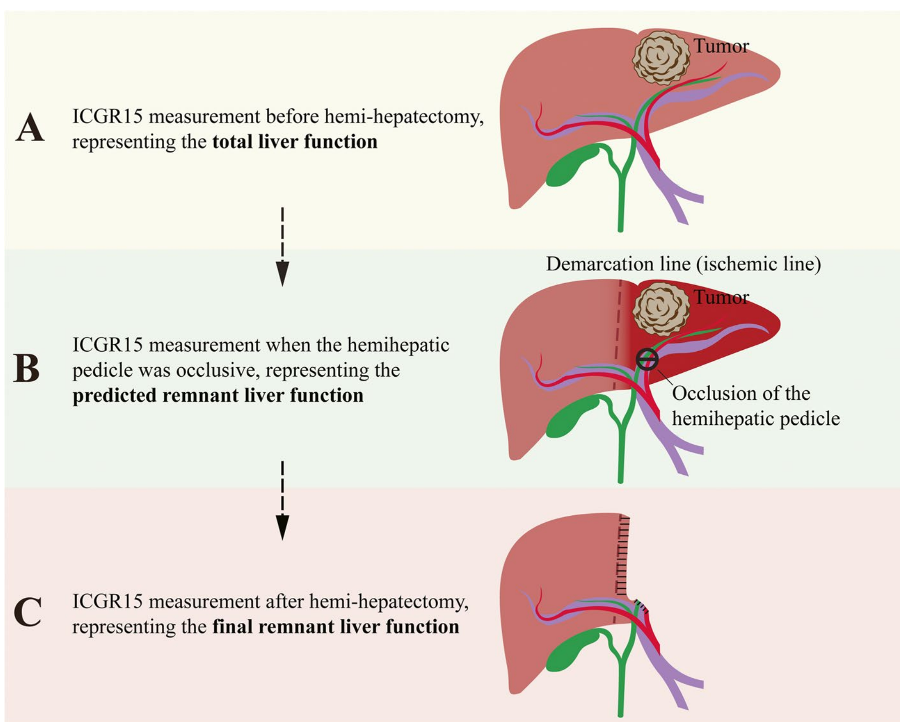

Fig. 2 ICGR15 measurements for liver function assessment during hemi-hepatectomy. Note: Figure illustrated the use of indocyanine green retention rate at 15 min (ICGR15) to evaluate liver function at different stages in hemi-hepatectomy procedure. **A** Pre-hepatectomy measurement of total liver function. **B** Intra-hepatectomy measurement with occlusion of the hemi-hepatic pedicle, representing predicting remnant liver function. Shows demarcation (ischemic) line and occlusion point. C: Post-hepatectomy measurement of final remnant liver function after hemi-hepatectomy

clamping the Glisson's pedicle at the hepatic hilum of left/right lobe. Following this maneuver, the demarcation line was confirmed, and the pedicle was ligated and severed. Subsequent steps included isolating the liver by severing surrounding ligaments and performing the hepatectomy using the Pringle maneuver. Each clamping episode was kept under 15 min with intervals exceeding 5 min.

Parameters and outcome

The metrics collected encompass demographic data (e.g., gender and age), liver function indicators (e.g., ALT and AST), liver function scoring systems (e.g., Model for End-stage Liver Disease (MELD) and Albumin-Bilirubin (ALBI)), liver fibrosis scoring systems (e.g., Fibrosis-4 (FIB-4) [16]), and hepatectomy metrics (e.g., remnant liver volume proportion, blood loss, and duration of hepatectomy). The standardized future liver remnant volume (sFLR) was calculated using the formula: FLR-volume/standard total liver volume (sTLV). And for Chinese individuals, the sTLV is determined by the equation: $11.508 \times \text{Body Weight} + 334.024$.

In this study, the primary endpoint was the occurrence of grade B/C PHLF, with the secondary endpoint being the incidence of severe post-hepatectomy complications. The definition of PHLF grading adheres to the ISGLS standards [5], and the classification of post-hepatectomy complications follows the Clavien-Dindo system [17].

Statistical analysis

For continuous variables such as age and BMI, we calculated the mean and standard deviation, and assessed significant differences using the T-test. For other continuous variables, we reported the median along with the 25 th and 75 th percentiles, and evaluated significant differences using the Mann–Whitney U test. For categorical variables, we recorded the frequency and percentage, employing Pearson's Chi-Squared Test or Fisher's Exact Test for significance testing. Logistic regression was used to determine the discrimination ability (ROC-AUC, PR-AUC), sensitivity, specificity, and accuracy of each parameter in predicting grade B/C PHLF. The optimal cut-off values were identified at the maximum J-index, and the risk analysis based on the cut-off value was Logistic regression. Regarding variable importance assessment, all parameters were incorporated into the XGBoost model, and their importance was quantified by calculating the mean Shap values for each parameter. This study encountered minor missing in baseline data, which were not subsequently imputed. A *P*-value of less than 0.05 was deemed statistically significant.

Results

Patient characteristics

Table 1 presented the baseline characteristics of the study population. All patients had Child–Pugh class A disease. The average age was 48 years, with a male-to-female ratio of 4:1. Additionally, 71% of the participants underwent a right hemi-hepatectomy.

Among the 31 patients, 8 (25.8%) developed Grade B/C PHLF. The Grade B/C PHLF group exhibited higher MELD scores, ALBI scores, and FIB-4 scores compared to the group without Grade B/C PHLF. Additionally, this group had elevated pre-hepatectomy, intra-hepatectomy, and post-hepatectomy ICGR15 levels, greater blood loss, and higher ishak inflammation scores. Notably, only the ALBI score (−2.85[−3.03;−2.61] *vs.* −2.49[−2.69;−2.28], $P = 0.045$) and intra-hepatectomy ICGR15 (9.20[6.95;13.7] *vs.* 19.9[15.7;26.4], $P = 0.002$) were statistically significant.

Post-hepatectomy complication

Table 2 illustrated that patients with grade B/C PHLF experienced longer hospital stays and incurred higher hospitalization costs following hepatectomy, along with a higher rate of severe complications. Nevertheless, the rates of pneumonia, pleural effusion, ascites, and bile leakage were similar between the two groups.

Feature importance

The predictive value of various parameters on grade B/C PHLF was presented in Table 3. Using logistic regression, we assessed the clinical characteristics that might influence the occurrence of Grade B/C PHLF. The results suggested that intra-hepatectomy parameters generally offer superior predictive performance. Notably, the intra-hepatectomy ICGR15 demonstrated the highest discriminative ability, with a ROC-AUC of 0.864 and a PR-AUC of 0.791, also exhibiting high specificity, sensitivity, and accuracy. The second most effective predictors were the pre-hepatectomy parameters, among which the ALBI score indicated a strong predictive capability (ROC-AUC = 0.740, PR-AUC = 0.606). In contrast, the pre-hepatectomy ICGR15 showed less satisfactory results (ROC-AUC = 0.560, PR-AUC = 0.660). Post-hepatectomy parameters generally exhibited weaker predictive performance, with the post-hepatectomy ICGR15 having a ROC-AUC of 0.592 and a PR-AUC of 0.686.

In Fig. 3, we conducted a model using the XGBoost algorithm to predict grade B/C PHLF, incorporating all parameters detailed in Table 3. We calculated the mean Shap values to evaluate the importance of each parameter. The results indicate that the ICGR15-intra was the most significant contributor to the model's prediction, both at the population level and in individual patient level.

Table 1 Characteristics of the study population

	None-PHLF group	B/C PHLF group	*P* value
No. of patients	23	8	
Demography related			
Male, (%)	17 (73.9)	8 (100.0)	0.298
Age, mean (SD)	47.39 (8.69)	52.38 (8.45)	0.17
BMI, mean (SD)	22.36 (2.99)	22.85 (2.01)	0.672
Liver function related			
INR, median [IQR]	0.99 [0.96, 1.02]	1.00 [0.93, 1.10]	0.803
TB, (median [IQR])	10.80 [8.55, 15.30]	15.00 [13.01, 23.75]	0.109
ICGR15-pre, median [IQR]	3.50 [3.27, 5.03]	4.50 [1.68, 8.93]	0.721
Liver cirrhosis, (%)	13 (56.5)	5 (62.5)	1
MELD, median [IQR]	2.70 [0.42, 5.03]	3.42 [1.34, 5.74]	0.685
ALBI, median [IQR]	−2.85 [−3.03, −2.61]	−2.49 [−2.69, −2.28]	0.045
FIB-4, median [IQR]	1.57 [0.96, 2.24]	2.70 [1.87, 3.05]	0.136
Tumor related			
AFP, median [IQR]	7.08 [3.13, 316.85]	33.20 [9.51, 77.97]	0.374
Conversion therapy, (%)	4 (17.4)	2 (25.0)	0.634
Single tumor, (%)	17 (73.9)	7 (87.5)	0.642
Tumor size, max, median [IQR]	6.80 [4.00, 10.60]	9.25 [6.75, 12.50]	0.354
Hepatectomy related			
Right hepatectomy, (%)	16 (69.6)	6 (75.0)	1
sFLR, median [IQR]	0.74 [0.67, 0.89]	0.73 [0.69, 0.76]	0.588
ICGR15-intra, median [IQR]	9.20 [6.95, 13.65]	19.90 [15.70, 26.40]	0.002
Duration of hepatectomy, min, median [IQR]	345.00 [272.50, 432.50]	384.50 [347.75, 496.00]	0.149
Blood loss, ml, median [IQR]	400.00 [300.00, 600.00]	800.00 [450.00, 850.00]	0.127
Duration of HPO, min, median [IQR]	38.00 [23.50, 47.25]	49.00 [19.00, 62.00]	0.438
ICGR15-post, median [IQR]	17.00 [9.73, 25.65]	30.10 [14.15, 33.05]	0.226
Pathology related			
Ishak inflammation, median [IQR]	3.00 [3.00, 4.00]	5.50 [3.00, 6.00]	0.214
Ishak fibrosis, median [IQR]	2.00 [2.00, 4.00]	2.50 [2.00, 4.50]	0.923

Values were described as n (%), mean (SD), or median [IQR]

Abbreviations: *PHLF* Post-hepatectomy liver failure, *ICGR15* Intraoperative indocyanine green retention rate at 15 min, *MELD* End-stage Liver Disease, *ALBI* Albumin-Bilirubin, *FIB-4* Fibrosis-4, *sFLR* Standardized future liver remnant, *BMI* Body mass index, calculated as weight in kilograms divided by height in meters squared, *NLR* Neutrophil to lymphocyte ratio, *TB* Total bilirubin, *AFP* Alpha-fetoprotein, *HPO* Hepatic portal occlusion, *SD* Standard deviation, *IQR* Interquartile range

Cut-off value and clinical use

From the comparison above, it was evident that ICGR15-intra was a critical predictor of grade B/C PHLF following hemi-hepatectomy. Utilizing the ROC curve, the optimal cut-off value for ICGR15-intra was established at 19.8%, with a corresponding J-index of 0.582 (see Fig. 4). By categorizing patients using a threshold of 19.8%, it was observed that those with ICGR15-intra values of 19.8% or higher had a significantly higher risk of grade B/C PHLF (OR[95% CI] = 3.602[1.437–6.750], *P* value = 0.004; Fig. 4) and experienced more grade B/C PHLF and severe complications (Table 2).

Discussion

Hepatectomy is the predominant treatment for HCC [18], with PHLF representing a major concern, particularly in major hepatectomy. PHLF not only impacts short-term recovery [19, 20] but is also linked to increased recurrence and mortality risk [21, 22], thereby influencing long-term survival outcomes [23–26]. The pre-operative MELD [27] and ALBI [28] scoring systems are effective in predicting PHLF; however, their reliance primarily on blood test indicators or subjective assessments may limit their prediction performance. Specifically, the ALBI score was developed predominantly from data involving HCC patients, only 28% of whom underwent hepatectomy,

Table 2 Comparisons of post-hepatectomy complications based on PHLF grade and ICGR15-intra level

	None-PHLF group	B/C PHLF group	*P* value	ICGR15-intra < 19.8%	ICGR15-intra ≥ 19.8%	*P* value
PHLF, (%)			< 0.001			0.002
Grade 0	22 (95.7)	0 (0.0)		21 (84.0)	1 (16.7)	
Grade A	1 (4.3)	0 (0.0)		1 (4.0)	0 (0.0)	
Grade B	0 (0.0)	3 (37.5)		2 (8.0)	1 (16.7)	
Grade C	0 (0.0)	5 (62.5)		1 (4.0)	4 (66.7)	
Days of post-hepatectomy, median [IQR]	7.00 [6.00, 8.00]	8.50 [8.00, 9.25]	0.096	8.00 [6.00, 9.00]	8.00 [6.50, 8.75]	0.826
Cost, RMB, median [IQR]	54311.49 [48244.29, 60491.13]	59518.58 [55595.87, 68751.01]	0.188	54311.49 [46809.56, 62474.10]	58280.40 [56128.26, 59689.36]	0.419
Pneumonia, (%)	10 (43.5)	4 (50.0)	1	10 (40.0)	4 (66.7)	0.37
Pleural effusion, (%)	7 (30.4)	3 (37.5)	1	7 (28.0)	3 (50.0)	0.358
Ascites, (%)	9 (39.1)	3 (37.5)	1	10 (40.0)	2 (33.3)	1
Bile leakage, (%)	0 (0.0)	1 (12.5)	0.258	1 (4.0)	0 (0.0)	1
Clavien-Dindo ≥ III grade, (%)	3 (13.0)	5 (62.5)	0.013	4 (16.0)	4 (66.7)	0.026

Values were described as n (%) and median [IQR]

Abbreviations: *PHLF* Post-hepatectomy liver failure, *ICGR15* Intraoperative indocyanine green retention rate at 15 min, *IQR* Interquartile range

Table 3 Predict values of important parameters related to PHLF

Parameters	ROC-AUC	PR-AUC	SEN	SPE	ACC
Before hemi-hepatectomy					
ICGR15-pre	0.560	0.660	0.500	0.783	0.710
sFLR	0.565	0.845	1.000	0.174	0.387
FIB-4	0.679	0.645	0.625	0.783	0.742
ALBI	0.742	0.606	0.625	0.913	0.839
MELD	0.549	0.676	0.250	0.957	0.774
Intra hemi-hepatectomy					
ICGR15-intra	0.864	0.792	0.625	0.957	0.871
Duration of HPO	0.590	0.650	0.375	0.957	0.806
Blood loss	0.682	0.676	0.625	0.826	0.774
Duration of hepatectomy	0.674	0.631	0.375	0.957	0.806
Post hemi-hepatectomy					
ICGR15-post	0.592	0.686	0.500	0.826	0.742
Ishak fibrosis	0.511	0.748	0.250	0.826	0.677
Ishak inflammation	0.639	0.684	0.625	0.826	0.774

The statistical values were calculated based on logistic regression, and the end point was grade B/C PHLF

Abbreviations: *PHLF* Post-hepatectomy liver failure, *ICGR15* Intraoperative indocyanine green retention rate at 15 min, *MELD* End-stage Liver Disease, *ALBI* Albumin-Bilirubin, *FIB-4* Fibrosis-4, *sFLR* standardized future liver remnant, *HPO* Hepatic portal occlusion, *ROC-AUC* Receiver operating characteristic area under the curve, *PR-AUC* Precision-recall area under the curve, *SEN* Sensitivity, *SPE* Specificity, *ACC* Accuracy

potentially rendering it less suitable for broader PHLF prediction [29]. Beyond traditional scoring systems, numerous studies have developed PHLF prediction models using pre-hepatectomy parameters [30–33], all achieving commendable predictive performance. Several studies have also developed convenient online tools. However, a prevalent limitation in these models was the omission of critical intra-hepatectomy parameters. To improve predictive efficiency, Xu et al. [34] incorporated intra-hepatectomy parameters, including the extent of hepatectomy and blood loss, into their model, resulting in a robust predictive effect (AUC =0.838). Unlike the aforementioned studies, our research assessed additional critical parameters by comparing parameters from pre-hepatectomy, intra-hepatectomy, and post-hepatectomy. Our findings suggested that intra-hepatectomy parameters were predominantly important in predicting Grade B/C PHLF.While prior studies investigated intra-hepatectomy ICGR15 in mixed liver resections (e.g., segmentectomies) or non-HCC populations, our study specifically focused on HCC patients undergoing hemi-hepatectomy. This homogeneity reduces confounding factors such as heterogeneous liver function or resection volumes, allowing us to establish a validated cutoff (19.8%) tailored to this high-risk cohort.

The standardized future liver remnant (sFLR) is a critical predictor for PHLF. Recent research has indicated that an sFLR below 0.56 significantly increases the risk of PHLF [35]. However, in our study, sFLR did not demonstrate a distinct advantage compared to other parameters. This may be attributed to the potential non-uniformity and segmental heterogeneity within the liver. A large volume does not necessarily equate to adequate liver function. In addition to measuring sFLR, liver function tests that focus on liver-specific metabolism have significantly advanced in recent years. The LiMAx test, predominantly utilized in Western medical centers, relies on the hepatocyte-specific metabolism of

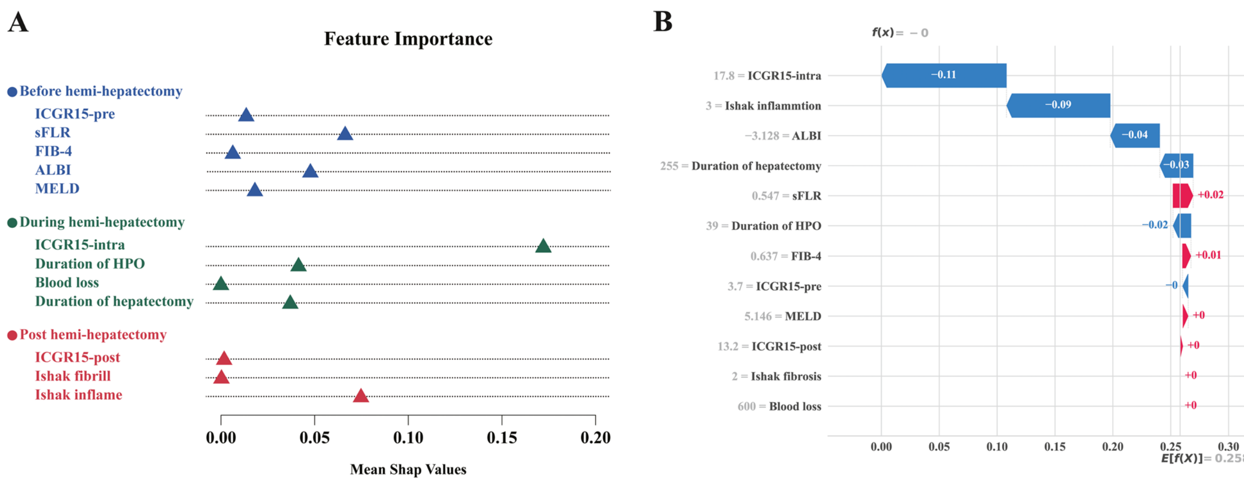

Fig. 3 Parameter Importance at the Population and Individual Levels. Note: the mean Shap values of parameters were calculated basing on XGBoost algorithm. **A** The dotchart presented parameters importance in the total participant level. The dot's position on the x axis showed the impact that parameter had on the model's prediction. **B** The waterfall chart demonstrated parameter importance in the individual level. Abbreviation: PHLF, post-hepatectomy liver failure; ICGR15, intraoperative indocyanine green retention rate at 15 min; MELD, End-stage Liver Disease; ALBI, Albumin-Bilirubin; FIB-4, Fibrosis-4; sFLR, standardized future liver remnant; HPO, hepatic portal occlusion

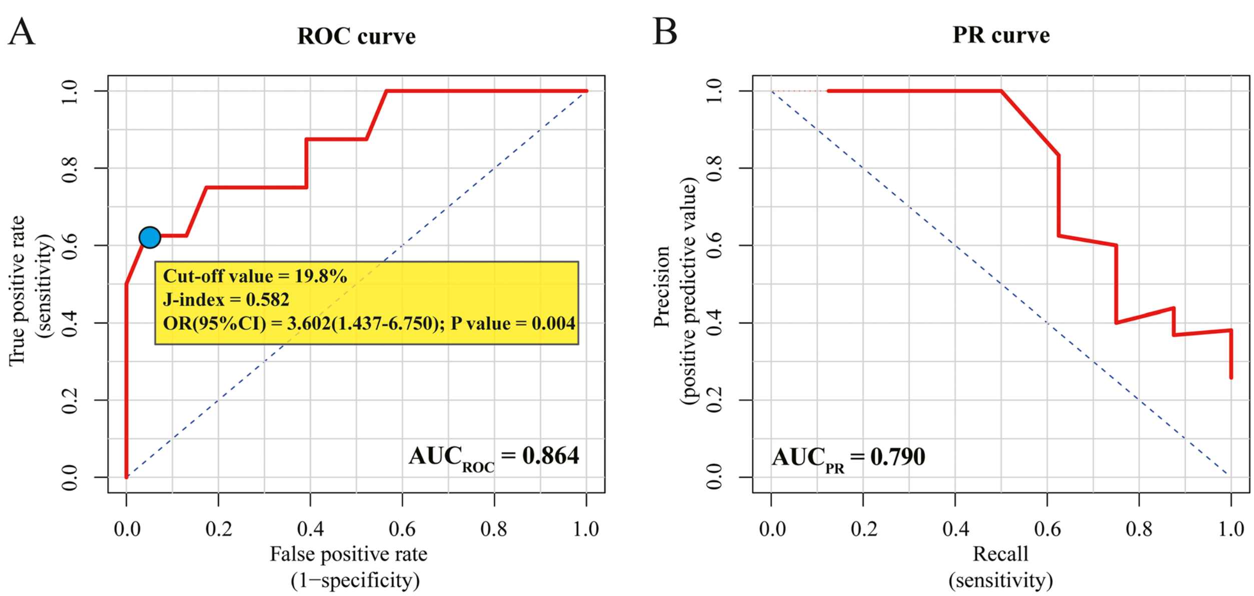

Fig. 4 Receiver operating characteristic curve and precision-recall curve for intra-hepatectomy ICGR15 in predicting grade B/C PHLF. Note: the cut-off value and OR (95%CI) were calculated based on Logistic regression, and the optimal cut-off value was identified at the maximum J-index

the 13 C-labeled substrate by the cytochrome P450 1 A2 enzyme, which exhibits ubiquitous activity throughout the liver [36]. Furthermore, the ICG clearance test is predominantly utilized in Asian medical centers. This test leverages the liver's unique ability to uptake ICG and excrete it via bile, facilitating real-time monitoring of liver function during hepatectomy [37, 38]. However, the ICG test is unsuitable for patients with biliary obstruction due to the competitive binding of bilirubin and ICG to the same transport polypeptides.Although ICGF-K (combining CT volumetry and ICG clearance) is widely used in preoperative planning, its reliance on preoperative imaging and complex calculations limits intraoperative utility. In contrast, intra-hepatectomy ICGR15 provides real-time, direct functional assessment of the remnant liver during surgery, enabling immediate decision-making without delays for volumetric analysis. This simplicity is particularly advantageous in resource-constrained settings or urgent surgical scenarios.

The prediction of PHLF often lacks high accuracy, primarily because many studies concentrate solely on the size of the remnant liver volume or the total liver function [39]. Several studies have suggested the quantitative assessment of liver function in the remnant liver as a critical tool for accurately predicting PHLF [40, 41]. It has been recommended to employ liver-specific contrast agents such as 99 mTc-galactosyl or 99 mTc-mebrofenin. This method quantifies liver function in a specific segment by measuring the intensity of the contrast agent within that segment [42–45]. Although these methods are non-invasive, they remain costly and technically complex, limiting their widespread adoption. After occluding blood flow to specific liver segments, an ICG test can be conducted on the targeted liver segment to evaluate its function. This method was straightforward and provides precise measurements. A small-sample study by Thomas et al. suggests that intra-hepatectomy ICG plasma disappearance rate (PDR) and ICGR15 can accurately predict post-hepatectomy liver function [13]. Sato et al. [46] found that intra-hepatectomy ICGR15 (C-index = 0.834) could effectively predict the occurrence of Grade B/C PHLF. Our study evaluated the predictive value of pre-hepatectomy, intra-hepatectomy, and post-hepatectomy ICGR15 for Grade B/C PHLF. The results indicated that intra-hepatectomy ICGR15 had the highest predictive performance, aligning with previous research. Conversely, post-hepatectomy ICGR15 demonstrated poor predictive performance. This may be attributed to the use of the Pringle maneuver during hepatectomy, which can lead to early lactate accumulation and subsequently affect PHLF assessment [47].

The superior predictive accuracy of intra-hepatectomy ICGR15 over post-hepatectomy values may stem from surgical stress and ischemia–reperfusion injury during parenchymal transection. Intra-hepatectomy ICGR15 reflects the remnant liver's functional reserve immediately after vascular occlusion but before parenchymal disruption, whereas post-hepatectomy measurements capture the impact of hemodynamic changes, residual inflammation, or transient ischemia from the Pringle maneuver. These perioperative confounders likely diminish the post-operative test's reliability.To minimize interference from residual ICG, we maintained a 30-min interval between measurements, consistent with prior evidence showing > 95% ICG clearance within 20 min. Unlike laparoscopic fluorescence imaging (which retains parenchymal staining), our spectrophotometric clearance measurements are unaffected by residual dye. This protocol ensures accuracy in dynamic liver function assessment.

In our previous study, we empirically established an intra-hepatectomy ICGR15 cutoff value of 10% for patients scheduled for right hemi-hepatectomy. Although this threshold is highly conservative, it may result in missed hepatectomy opportunities for patients who might have been eligible for the procedure. Consequently, it is essential to determine the upper limit of intra-hepatectomy ICGR15 to improve decision-making in hemi-hepatectomy. Horisberger et al. [48] observed in a study of 15 patients undergoing ALPPS that an intra-hepatectomy ICGR15 exceeding 11.4% was significantly associated with an increased risk of severe postoperative complications. Naoya et al.'s data indicated that an intra-hepatectomy ICGR15 exceeding 19.4% could effectively differentiate the occurrence of Grade B/C PHLF [46]. Notably, their study encompassed 12.9% of patients undergoing liver segment resection. Akita et al.'s research demonstrated that patients exhibiting intra-hepatectomy ICGR15 exceeding 20% were likely to endure prolonged postoperative recovery periods and elevated postoperative bilirubin levels [37]. Wang et al. [40] analyzed 35 patients undergoing anatomical hepatectomy and posited that an intraoperative ICG-R15 exceeding 22.7% constituted a risk factor for PHLF. Consequently, a consensus on the optimal cutoff value for intraoperative ICG-R15 has yet to be established. In our study of patients undergoing hemi-hepatectomy, we proposed an optimal cutoff value for intra-hepatectomy ICGR15 at 19.8%. Exceeding this threshold significantly increased the incidence of severe complications and Grade B/C PHLF, serving as a clinical warning. Our study was distinct from previous research in that it exclusively involved patients with HCC undergoing hemi-hepatectomy, thereby ensuring a greater homogeneity among participants. This specificity contributes to the credibility of the cutoff value derived from our study.If intra-hepatectomy ICGR15 exceeds 19.8%, we propose the following strategies: Abort planned hemi-hepatectomy if feasible (e.g., consider alternative resections or non-surgical therapies); Augment postoperative care with intensive monitoring, albumin infusion, and prophylactic antibiotics; Preoperative portal vein embolization (PVE) in borderline cases to enhance future remnant liver function. These measures aim to balance oncologic radicality with postoperative safety, particularly in high-risk patients.

This study offered multiple strengths. First, its prospective design ensures comprehensive data collection and enhances reliability. Second, it establishes an effective reference for intra-hepatectomy ICGR15, facilitating surgical decision-making for patients undergoing hemi-hepatectomy. Our study's single-center design and small sample size ($n = 31$) limit generalizability. However, a post-hoc power analysis ($\alpha = 0.05$, effect size OR $= 3.6$) indicated 78% power to detect significant differences, meeting acceptable thresholds for pilot studies. To address this, we are actively collaborating with multicenter institutions to validate these findings in a larger cohort. Future studies should also explore whether this threshold applies to non-HCC populations or minor resections.

Conclusion

During hemi-hepatectomy, the intra-hepatectomy ICGR15 was essential for predicting grade B/C PHLF. The optimal threshold for intra-ICGR15 is 19.8%. Values equal to or exceeding this threshold significantly increase the likelihood of grade B/C PHLF and severe postoperative complications in hemi-hepatectomy.

Abbreviations

HCC	Hepatocellular carcinoma
PHLF	Post-hepatectomy liver failure
ICGR15	Intraoperative indocyanine green retention rate at 15 min
OR	Odds ratio
CI	Confidence interval
ROC-AUC	Receiver operating characteristic area under the curve
PR-AUC	Precision-recall area under the curve
MELD	End-stage Liver Disease
ALBI	Albumin-Bilirubin
FIB-4	Fibrosis-4
sFLR	Standardized future liver remnant
sTLV	Standard total liver volume
BMI	Body mass index
NLR	Neutrophil to lymphocyte ratio
TB	Total bilirubin
AFP	Alpha-fetoprotein
HPO	Hepatic portal occlusion
SD	Standard deviation
IQR	Interquartile range
SEN	Sensitivity
SPE	Specificity
ACC	Accuracy

Authors' contributions

Tianyi Liang contributed to data acquisition and analysis, as well as manuscript drafting. Yongfei He was responsible for data acquisition and analysis. Shutian Mo, Yuan Liao, Ketuan Huang, Qiang Gao, Xiaoqiang Shen, Chengkun Yang, Xiwen Liao, Wei Qin, Guangzhi Zhu, Hao Su, and Xinping Ye contributed to data acquisition and interpretation. Chuangye Han was involved in data analysis and manuscript revision. Tao Peng contributed to study design and provided critical revisions to the manuscript.

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Data availability

Data is provided within the manuscript.

Declarations

Ethics approval and consent to participate

This study received approval from the Institutional Review Board of the First Affiliated Hospital of Guangxi Medical University with an ethical approval number of 2022-KY-E-(291). All clinical routine data used in the study were anonymized, encompassing data cleaning and statistical management.All participants in the study have signed informed consent forms, ensuring that the ethical guidelines of the Declaration of Helsinki are strictly followed.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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