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Research article

Evaluation of liver regeneration after hemi-hepatectomy by combining computed tomography and post-operative liver function

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ABSTRACT

Background: Accurate evaluation of postoperative liver regeneration is essential to prevent post-operative liver failure.
Aims: To analyze the predictors that affect liver regeneration after hemi-hepatectomy.
Method: Patients who underwent hemi-hepatectomy in Hangzhou First People's Hospital and Hangzhou Shulan Hospital from January 2016 to December 2021 were enrolled in this study. The regeneration index (RI) was calculated by the following equation: RI = [(postoperative total liver volume {TLV_{post}} - future liver remnant volume {FLRV}/FLRV] × 100 %. Hepatic dysfunction was defined according to the "TBilpeak>7" standard, which was interpreted as (peak) total bilirubin (TBil) >7.0 mg/dL. Good liver regeneration was defined solely when the RI surpassed the median with hepatic dysfunction. Logistic regression analyses were performed to estimate prognostic factors affecting liver regeneration.
Result: A total of 153 patients were enrolled, with 33 in the benign group and 120 patients in the malignant group. In the entire study population, FLRV% [OR 4.087 (1.405–11.889), P = 0.010], international normalized ratio (INR) [OR 2.763 (95%CI, 1.008–7.577), P = 0.048] and TBil [OR 2.592 (95%CI, 1.177–5.710), P = 0.018] were independent prognostic factors associated with liver regeneration. In the benign group, only the computed tomography (CT) parameter FLRV% [OR, 11.700 (95%CI, 1.265–108.200), P = 0.030] predicted regeneration. In the malignant

Abbreviations: PHLF, post-hepatectomy liver failure; CT, computed tomography; TLV_{pre}, preoperative total liver volume; RLV, resected liver volume; FLRV, future liver remnant volume; TLV_{post}, postoperative total liver volume; RI, regeneration index; PHRR, parenchymal hepatic resection rate; WBC, white blood cells; AST, aspartate aminotransferase; ALT, alanine transaminase; TBil, total bilirubin; ROC, receiver operating characteristic; AUC, area under the curve; OR, odds ratio; INR, international normalized ratio; ALB, albumin; TACE, preoperative transcatheter arterial chemoembolization; PVE, preoperative portal vein embolization; ALPPS, associated liver partition and portal vein ligation for staged hepatectomy.

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group, parenchymal hepatic resection rate (PHRR%) [OR 0.141 (95%CI, 0.040–0.499), P = 0.002] and TBil [OR 3.384 (95%CI, 1.377–8.319), P = 0.008] were independent prognostic factors.
Conclusion: FLRV%, PHRR%, TBil and INR were predictive factors associated with liver regeneration.

1. Introduction

Post-hepatectomy liver failure (PHLF) is one of the most dreadful complications observed among patients undergoing partial liver excision. Furthermore, it is also the major cause of postoperative mortality, with an incidence of 10 % [1–4]. Liver regeneration after surgical resection, one of the distinctive characteristics of the liver, is very important in preventing PHLF. Understanding the predictive markers associated with post-hepatectomy liver regeneration could contribute to developing risk-adapted strategies, increasing the safety of hepatectomies, and avoiding postoperative liver insufficiency and even mortality [5,6]. However, most studies focused on liver examining regeneration are limited to malignant liver diseases [7–10], and few reports have examined liver regeneration after surgery for benign liver disease. It is uncertain whether the prognostic factors of liver regeneration after benign or malignant liver disease are identical.

Recently, significant enhancements in the safety and prognosis of partial hepatectomies have been achieved via preoperative assessment, advanced surgical techniques, and improved postoperative management [11–13]. Due to its potent reconstructive ability, computed tomography (CT) is the most used imaging modality for evaluating the liver volume [14]. Additionally, texture analysis based on CT also holds promise due to its heightened sensitivity in perceiving the heterogeneity of the lesion [9,15,16]. Therefore, accurate evaluation of remnant liver volume before operation is of vital importance to avoid postoperative liver insufficiency and even liver failure. Sex, age, obesity, intraoperative blood loss, laparoscopic surgery and postoperative complications are predictive factors influencing liver regeneration [1,8,17–19]. In this study, we aimed to analyze and compare the prognostic factors that affect liver regeneration after major hepatectomy for both benign and malignant liver diseases by assessment of imaging and liver function parameters.

2. Materials and methods

2.1. Study population

In this retrospective study, patients who conformed to the included criteria were enrolled at Hangzhou First People's Hospital and Hangzhou Shulan Hospital from January 2016 to December 2021. Patients were included if they underwent hemi-hepatectomy with resection along the middle hepatic vein (patients with or without caudate lobectomy were included). Patients were excluded if (1) Non-standard or expanded hemi-hepatectomy; (2) Lack of clinical data; (3) Lack of postoperative imagine data; (4) Postoperative imaging review less than 7 days; (5) Segmentation failure. The flowchart is detailed in Fig. 1.

2.2. Hepatectomy and patient management

All patients underwent standard left or right hemi-hepatectomy. The patient was placed in a supine position under general

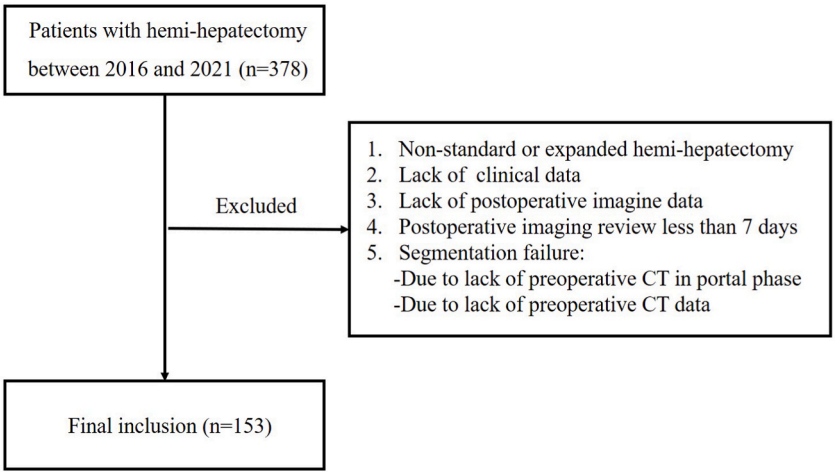

Fig. 1. Flowchart of patient enrollment and assessment.

anesthesia. Left/right arteries and portal veins were dissected, ligated, and divided, respectively. During the operation, the middle hepatic vein was completely isolated and exposed, and the liver tissue was resected along the middle hepatic vein and the base of the gallbladder. The small vessels and bile ducts on the cut surface were carefully coagulated to prevent postoperative bleeding and peritonitis. The type of hemi-hepatectomy, operation time, intraoperative blood loss, and blood transfusion were recorded.

2.3. Preoperative CT acquisition

Before hemi-hepatectomy, all patients underwent liver CT-enhanced examination using a CT scanner. CT examination was divided into three phases: venous phase, arterial phase, and portal venous phase. Since the portal venous phase can display the middle hepatic vein, it was selected for segmenting the liver image.

Hemi-hepatectomy data were depicted using uAl Research Portal (uRP) software that relies on multi-slice CT for 3D visualization and measurement of liver structures. The CT images were semi-automatically divided into left/right half liver using the plane of the middle hepatic vein directed toward the gallbladder fossa as boundaries (Fig. 2 a-b). This procedure was used to estimate the pre-operative total liver volume (TLV_{pre}), expected resected liver volume (RLV), and future liver remnant volume (FLRV) of the patient.

2.4. Postoperative CT image acquisition

CT images were collected between the duration of one month and one year after hemi-hepatectomy to estimate the postoperative total liver volume (TLV_{post}). If the patient underwent repeated CT scans during this period, CT images captured closest to the duration of 3–6 months after surgery were selected to calculate TLV_{post} (Fig. 2 c-d).

2.5. CT liver volumetry

The regeneration index (RI) was calculated based on the results of the previous software simulations. The following formula was used to calculate the RI after hemi-hepatectomy:

$RI = [(TLV_{post} - FLRV) / FLRV] \times 100\%$.

The concept of "actual FLRV" is represented by the parenchymal hepatic resection rate (PHRR). The PHRR was calculated using the formula [20]:

$PHRR = 1\text{-}FLRV/ [TLV_{pre}\text{-tumor volume (TV)}]$

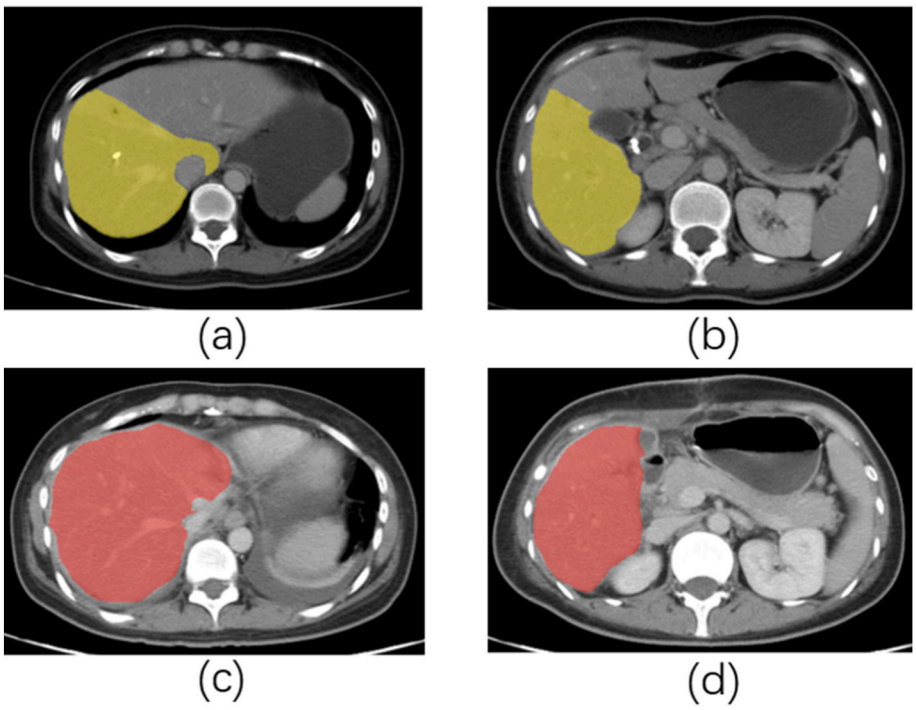

Fig. 2. Example of software-driven planning of right hemi-hepatectomy. (A–D) Images of the same computed tomography layer of one patient at postoperative.

The following formula was used to calculate the FLRV%:

FLRV% = FLRV/TLV.

2.6. Definition

Hepatic dysfunction was defined according to the "$TBil_{peak}$>7" standard [21]. Scenarios considering (Peak) TBil >7.0 mg/dL as a criterion are uncomplicated and can accurately predict liver-related death and disadvantageous outcomes after major hepatectomy [21]. Previous studies have typically defined liver regeneration solely based on CT imaging measurements of liver volume, overlooking the recovery of liver function [22]. In this study, to comprehensively consider the RI and functional recovery, we defined good liver regeneration when the RI was higher than the median [7] without the occurrence of hepatic dysfunction. Vice versa, poor liver regeneration was defined as RI below the median and/or event of hepatic insufficiency.

2.7. Statistical analysis

All statistical analyses were performed using SPSS version 26.0 (IBM Corporation). Clinical, intraoperative, and CT parameters were compared between good and poor liver regeneration groups using the Student's T-test, Mann-Whitney *U* test, or Fisher's exact test, depending on the variables being compared. SPSS version 26.0 was used to determine the cut-off value that predicted post-hepatectomy functional liver regeneration. Logistical regression analysis was performed examining these CT parameters and functional recovery to identify potential predictors of liver regeneration. Two-sided p values < 0.05 were considered statistically significant.

3. Result

3.1. Clinicopathological, laboratory, and CT characteristics

A total of 153 patients conformed to the inclusion criteria and were enrolled in this study. The median age was 57 (range 35–81) years. A total of 56 (36.6 %) patients were >60 years old and the male/female ratio was 1.86:1 (96/57). Most patients underwent left hemi-hepatectomy (103), and the median operation time was 5.5h. The median blood loss was 400 ml, and 32 patients received intraoperative blood transfusion. A total of 33 patients were included in the benign group (25 cases of biliary calculi, 1 case of liver atrophy, 5 case of hemangioma, and 2 case of liver abscess) and 120 patients in the malignant group (49 cases of hepatocellular carcinoma, 62 case of cholangiocarcinoma, 1 case of cholangiocarcinoma with hepatocellular carcinoma, 1 case of anaplastic carcinoma, 4 cases of borderline carcinoma, 1 case of sarcomatoid carcinoma, and 1 case of metastatic adenocarcinoma).

Patients in the malignant group had higher levels of white blood cells (WBC) and ferroprotein levels, as well as more blood loss and blood transfusion during the operation. Furthermore, the surgery was of a longer duration. The proportion of patients with liver cirrhosis and hepatitis B surface antigen was higher in the malignant group. The proportion of female patients in the benign group was

Table 1
Clinic characteristics of patients.

	Entire population (N = 153)	Benign diseases (N = 33)	Malignant diseases (N = 120)	P Value
Male n (%)	96 (62.75 %)	14 (42.42 %)	82 (68.33 %)	0.006
Age (years)	57 (50–65)	56 (50–66)	57 (51–65)	0.996
Hypertension n (%)	36 (23.53 %)	7 (21.21 %)	29 (24.17)	0.732
Diabetes mellitus	7 (4.58 %)	2 (6.06 %)	5 (4.17 %)	0.644
BMI	22.04(20.30–24.22)	21.77 (19.94–24.83)	22.24 (20.32–24.22)	0.639
WBC, $\times 10^9$/L	6.00 (4.80–7.85)	5.50 (4.45–6.80)	6.10 (5.00–8.00)	0.042
Platelets, $\times 10^9$/L	191.00 (145.50–252.00)	205.00 (155.50–290.50)	189.00 (145.00–250.00)	0.244
PT, s	12.00 (11.30–12.88)	11.80 (11.05–12.65)	12.10 (11.40–13.00)	0.097
INR	1.05 (0.99–1.13)	1.04 (0.98–1.13)	1.05 (1.00–1.13)	0.567
ALT, U/L	39.00 (20.00–67.00)	28.00 (16.00–67.00)	40.50 (23.00–66.75)	0.094
Albumin, g/L	37.20 (34.03–40.58)	37.90 (34.45–42.55)	37.10 (33.70–40.40)	0.345
TBil, umol/L	14.70(10.00–30.70)	13.10 (10.55–15.00)	17.00 (10.00–51.00)	0.084
AFP	3.20(2.19–7.12)	2.31 (1.73–2.80)	4.05 (2.40–37.03)	<0.0001
Liver cirrhosis	44 (28.76 %)	4 (12.12 %)	40 (50 %)	0.017
Fatty liver	17 (11.11 %)	3 (9.09 %)	14 (11.67 %)	0.677
HBsAg+	46 (30.07 %)	2 (6.06 %)	44 (36.67 %)	0.001
Left-Hemihepatectomy	103 (67.32 %)	28 (84.85 %)	75 (62.50 %)	0.015
Blood loss, ml, median (range)	400.00 (200.00–600.00)	300.00 (200.00–500.00)	400.00 (200.00–700.00)	0.034
Duration of operation, hours, median (range)	5.50(4.38–7.00)	4.50 (3.00–6.00)	5.50 (4.50–7.00)	0.043
PHLF	25 (16.34 %)	3 (9.09 %)	22 (18.33 %)	0.223

BMI, body mass index; WBC, white blood cell; PT, prothrombin time; INR, international normalized ratio; ALT, alanine aminotransferase; TBil, total bilirubin; AFP, a-fetoprotein; TACE, transcatheter arterial chemoembolization; PHLF, posthepatectomy liver failure.

higher than that in the malignant group. Additionally, no statistically significant difference was found between the malignant and benign groups with respect to age, hypertension, diabetes, aspartate aminotransferase (AST), alanine transaminase (ALT), total bilirubin (TBil), and other laboratory parameters. The above results are shown in Table 1.

In the entire study population, the TLV_{pre} was 1372.27 ml (1147.86–1633.69), the FLRV was 855.81 ml (699.44–1036.78), and the TLV_{post} was 1004.64 ml (832.95–1191.37) [7]. Liver regeneration volume was calculated as previously described, with a median regeneration volume of 139.25 ml (30.49–265.46). The median RI was 17.16 % (2.97%–33.97 %); however, it was highly variable, ranging from −38.21 to 254.13 %. In the benign group, the TLV_{pre} was 1287.63 ml (1081.55–1443.41), the FLRV was 870.60 ml (690.61–1079.11), and the TLV_{post} was 1050.04 ml (938.16–1298.19). In the malignant group, the TLV_{pre} was 1384.01 ml (1160.10–1671.37), the FLRV was 838.10 ml (696.91–1021.73), and the TLV_{post} was 970.28 ml (823.38–1183.12) (Table 2).

3.2. Outcomes of liver regeneration

According to our definition of liver regeneration, poor postoperative liver regeneration was observed in 82 patients. A total of 71 patients showed good liver regeneration after surgery. The integration of CT and liver function recovery allows for the identification of patients with poor liver function recovery, even among those initially classified as having good regeneration based on an RI greater than the median [7].

3.3. Prognostic factors for liver regeneration

Receiver operating characteristic (ROC) curves indicated that the area under the curve (AUC) was 0.756 for a cut-off FLRV% of 64 % (95%CI 0.568–0.743, P = 0.001) (Supplementary Fig. 1a). The results of univariate and multivariate analyses associated with liver regeneration in the entire study population are shown in Table 3. As shown by the univariate analysis, preoperative international normalized ratio (INR), FLRV%, albumin (ALB), TBil, left hepatectomy, and preoperative transcatheter arterial chemoembolization (TACE) history were associated with liver regeneration. When $P < 0.05$ was incorporated, FLRV% [odds ratio (OR) 4.087 (1.405–11.889), P = 0.010], INR [OR 2.763 (95%CI, 1.008–7.577), P = 0.048] and TBil [OR 2.592 (95%CI, 1.177–5.710), P = 0.018] were independent prognostic factors associated with liver regeneration (Table 3). The results of the likelihood ratio test for logistic regression and the evaluation of the model's goodness of fit in the entire study population are 0.0001 and 0.823 respectively (Supplementary Table 1).

In the benign group, the AUC of FLRV% obtained by ROC curve analysis was 0.744 (95 % CI 0.580–0.912, P = 0.017). The cut-off value of FLRV% was 78.5 % (Supplementary Fig. 1b). Regression analysis was performed to examine the factors affecting liver regeneration, which revealed that only CT parameters as FLRV% [OR, 11.700 (95%CI, 1.265–108.200), P = 0.030] was associated with liver regeneration (Table 4). The results of the likelihood ratio test for logistic regression in the benign group is 0.008 (Supplementary Table 1).

In the malignant group, the AUC of PHRR% obtained by ROC curve analysis was 0.673 (95 % CI 0.230–0.424, P = 0.001). The cut-off value of PHRR% was 33.9 % (Supplementary Fig. 1c). As demonstrated by univariate analysis, preoperative INR, PHRR%, TBil, left hepatectomy, and preoperative TACE history were associated with liver regeneration. When $P < 0.05$ was incorporated, PHRR% [OR 0.141 (95%CI, 0.040–0.499), P = 0.002] and TBil [OR 3.384 (95%CI, 1.377–8.319), P = 0.008] were independent prognostic factors associated with liver regeneration (Table 5). The results of the likelihood ratio test for logistic regression and the evaluation of the model's goodness of fit in the malignant group are 0.0001 and 0.775 respectively (Supplementary Table 1).

4. Discussion

Liver regeneration after hepatectomy, parenchymal injury, or drug-induced liver injury reflects compensatory hyperplasia and expansion of the residual liver to meet the demands of metabolic and physiological functions [23,24]. Hepatectomy, an anatomical resection performed as a definitive cure for patients with underlying liver disease, can significantly improve overall survival, but only if the remaining liver can adequately perform its function [11]. Therefore, accurate and timely assessment of liver regeneration after liver surgery is of great significance for the prediction of postoperative complications and mortality [12,14]. However, restoration of liver volume does not necessarily represent the recovery of liver function during liver regeneration [14,25]. Therefore, evaluation of

Table 2
Liver regeneration based on CT.

	Volume		
	Entire study population (N = 153)	Benign diseases (N = 33)	Malignant diseases (N = 120)
TLVpre (ml)	1372.27 (1147.86–1633.69)	1287.63 (1081.55–1443.41)	1384.01 (1160.10–1671.37)
FLRV (ml)	855.81 (699.44–1036.78)	870.60 (690.61–1079.11)	838.10 (696.91–1021.73)
FLRV% (%)	68 (52–75)	73.80 (64.20–81.65)	68 (51–74)
TLVpost (ml)	1004.64 (832.95–1191.37)	1050.04 (938.16–11298.19)	970.28 (823.38–1183.12)
Regeneration volume(ml)	139.25 (30.49–265.46)	154.05 (59.78–340.24)	132.55 (17.17–246.66)
RI (%)	17.16 (2.97–33.97)	16.17 (6.88–42.94)	17.36 (1.60–33.71)

TLVpre, total liver volume preoperative; FLRV, future liver remnant volume; RI, regeneration index; TLVpost, total liver volume postoperative.

Table 3
Uni- and multivariate logistic regression to identify predictors of liver regeneration after hemihepatectomy in the entire study population.

	Univariate analysis		Multivariate analysis	
	OR 95%CI	P-value	OR 95%CI	P-value
Male (vs Female)	1.871 (0.964–3.631)	0.064		
Age>60 years (vs ≤ 60 years)	1.253 (0.646–2.431)	0.501		
PT > 13.5s (vs ≤ 13.5s)	2.642 (0.900–6.738)	0.079		
INR>1.15 (vs ≤ 1.15)	3.123 (1.295–7.529)	**0.011**	2.763 (1.008–7.577)	**0.048**
FLRV%>64 % (vs ≤ 64 %)	3.778 (1.900–7.513)	**0.000**	4.087 (1.405–11.889)	**0.010**
Albumin<35 g/L (vs ≥ 35 g/L)	2.131 (1.043–4.355)	**0.038**		
TBil>21umol/L (vs ≤ 21umol/L)	3.781 (1.823–7.839)	**0.000**	2.592 (1.177–5.710)	**0.018**
ALT>40U/L (vs ≤ 40U/L)	0.841 (0.443–1.596)	0.596		
Left hemihepatectomy (vs Right)	2.268 (1.138–4.521)	**0.020**		
Malignancy diseases (vs Benign diseases)	0.814 (0.374–1.773)	0.605		
TACE (Yes vs No)	0.380 (0.163–0.885)	**0.025**		
hepatitis B virus (Yes vs No)	0.633 (0.316–1.269)	0.918		
liver cirrhosis (Yes vs No)	0.718 (0.356–1.450)	0.356		

PT, prothrombin time; INR, international normalized ratio; FLRV, future liver remnant volume; TBil, total bilirubin; ALT, Alanine aminotransferase; TACE, transcatheter arterial chemoembolization.

Table 4
Univariate logistic regression to identify predictors of liver regeneration after hemihepatectomy in benign grounp

	Univariate analysis	
	OR 95%CI	P
Male (vs Female)	2.778 (0.640–12.059)	0.173
Age>60 years (vs ≤ 60 years)	0.970 (0.240–3.918)	0.966
PT > 13.5s (vs ≤ 13.5s)	1.228 (0.671–2.249)	0.506
INR>1.15 (vs ≤ 1.15)	4.643 (0.477–45.205)	0.186
FLRV>857.3 cm^3 (vs ≤ 857.3 cm^3)	18.000 (1.860–174.211)	**0.013**
FLRV%>78.5 % (vs ≤ 78.5 %)	11.700 (1.265–108.200)	**0.030**
Albumin<35 g/L (vs ≥ 35 g/L)	5.400 (0.941–30.980)	0.058
TBil>21umol/L (vs ≤ 21umol/L)	1.125 (0.162–7.824)	0.905
ALT>40U/L (vs ≤ 40U/L)	1.018 (0.235–4.407)	0.981
Left hemihepatectomy (vs Right)	0.889 (0.128–6.182)	0.905
hepatitis B virus (Yes vs No)	0.722 (0.041–12.638)	0.824
liver cirrhosis (Yes vs No)	0.706 (0.087–5.734)	0.744

PT, prothrombin time; INR, international normalized ratio; FLRV, future liver remnant volume; TBil, total bilirubin; ALT, alanine aminotransferase.

Table 5
Uni- and multivariate logistic regression to identify predictors of liver regeneration after hemihepatectomy in malignant group.

	Univariate analysis		Multivariate analysis	
	OR 95%CI	P	OR 95%CI	P
Male (vs Female)	1.846 (0.848–4.022)	0.123		
Age>60 years (vs ≤ 60 years)	1.333 (0.626–2.838)	0.455		
PT > 13.5s (vs ≤ 13.5s)	2.255 (0.794–6.404)	0.127		
INR>1.15 (vs ≤ 1.15)	2.922 (1.116–7.650)	**0.029**		
FLRV>800.3 cm^3 (vs ≤ 800.3 cm^3)	7.862 (3.423–18.058)	**0.000**		
FLRV%>53.5 % (vs ≤ 53.5 %)	4.255 (1.850–9.784)	**0.001**		
Albumin<35 g/L(vs ≥ 35 g/L)	1.689 (0.762–3.746)	0.197		
TBil>21umol/L (vs ≤ 21umol/L)	3.730 (1.704–8.165)	**0.001**	3.384 (1.377–8.319)	**0.008**
ALT>40U/L (vs ≤ 40U/L)	0.818 (0.399–1.677)	0.584		
Left hemihepatectomy (vs Right)	2.613 (1.221–5592)	**0.013**		
TACE (Yes vs No)	0.377 (0.158–0.902)	**0.028**		
hepatitis B virus (Yes vs No)	0.640 (0.303–1.350)	0.241		
liver cirrhosis (Yes vs No)	0.740 (0.346–1.584)	0.439		
PHRR%>33.9 % (vs ≤ 33.9 %)	0.160 (0.062–0.411)	**0.000**	0.141 (0.040–0.499)	**0.002**

PT, prothrombin time; INR, international normalized ratio; FLRV, future liver remnant volume; TBil, total bilirubin; ALT, alanine aminotransferase; TACE, transcatheter arterial chemoembolization; PHRR, parenchymal hepatic resection rate.

the liver regeneration solely on the basis on CT-measured postoperative liver volume growth is inaccurate [26].

This is the study that attempted to establish a more accurate model for assessing liver regeneration by combining the assessment of the increase in hepatic mass quantified by CT with the recovery of hepatic function. Furthermore, it is the first study to investigate post-operation liver regeneration in the benign liver disease population and to observe whether the factors affecting liver regeneration in benign and malignant diseases are the same.

Good liver regeneration after hemi-hepatectomy is defined based on robust liver function and an RI higher than the median. According to the definition, 71 patients in the good liver regeneration group and 82 patients in the poor liver regeneration group were included. In the entire study population, logistic regression analysis showed that FLRV%, TBil and INR were independent risk factors for postoperative liver regeneration, which is consistent with some of the previous reports [15,27]. Next, we stratified the entire population in benign and malignant groups, to analyze whether the influencing factors affecting liver regeneration in the two populations were the same. In the benign group, logistic regression analysis revealed that only CT parameters as FLRV% was associated with liver regeneration. In the malignant group, PHRR% and TBil were independent prognostic factors associated with liver regeneration.

Accurate calculations of the FLRV prior to planned liver resections are gordian knots. Previous studies reported estimating FLRV by calculating the volume of each liver segment [28]. However, due to clinically significant interpatient variation in hepatic volumes and changes in the boundaries of liver segments caused by tumor compression, calculating FLRV using this method is associated with certain difficulties [29]. In addition, if the hemi-liver volume was used as FLRV, the volume can also be estimated through a fixed ratio or formula calculated based on certain characteristics [29,30]. For instance, accurate estimation of right hemi-liver can be made via portal vein diameter measurement [30]. However, the limitation of these methods is that they require the estimation of the liver volume indirectly based on certain characteristics rather than direct calculation. In this study, FLRV was obtained by calculating the volume of the remaining half of the liver. Therefore, this required strict adherence to the standard procedure of hemi-hepatectomy, dividing the liver into left/right hemi-hepates based on the middle hepatic vein and gallbladder fossa as the boundary [20,29].

Our findings were consistent those of previous studies, which also showed that the resected liver volume was associated with liver regeneration in patients after hepatectomy [7,31,32]. High-FLRV is a critical factor affecting the regeneration of the postoperative liver, and it is negatively correlated with liver regeneration [33,34]. This could be attributed to the fact that with more reserved liver mass after surgery, the residual liver can better fulfill functional requirements, potentially weakening the stimulus for liver regeneration. In addition, these findings may also be related to the increased content of hepatic trophic factors in portal blood per unit weight of residual liver tissue in patients undergoing liver resection [15,35]. However, this seems an ambivalent predictor of regeneration since if it is insufficient, the patient may experience liver failure rather than successful liver regeneration. Therefore, the surgeon needs to choose between the insufficiency of liver function caused by the extreme loss of liver mass and the ability to reduce FLRV% to promote liver regeneration. Preoperative portal vein embolization (PVE) and associated liver partition and portal vein ligation for staged hepatectomy (ALPPS) can help improve the liver reserve in patients with insufficient residual liver capacity [36,37]. Despite the increase in the pre-hepatectomy volume facilitated by PVE, postoperative liver regeneration is still related to the FLRV% before PVE [32]. Furthermore, the logistic regression analysis showed that TBil and INR were also associated with liver regeneration, which was not reported in previous studies. This is because the factors we included in the evaluation of functional liver regeneration are more comprehensive. Hence, the influencing factors obtained in our analysis are more accurate. The specific mechanisms by which TBil and INR affect liver regenerative capacity are not fully understood. We hypothesize that the increase of TBil and INR represents the destruction of liver function [38], and therefore, the ability of liver regeneration is impaired after surgery. In addition, the toxic effects of hyperbilirubinemia may impair some functions of the liver leading to a reduction in the ability of the liver to regenerate [39].

Our study found that liver regeneration was not affected by age, which is consistent with previously published results [7,8,40,41]. Although age is a very important consideration when selecting candidates for liver surgery, our study concluded that liver regeneration in older patients was similar to that in younger patients undergoing the same surgery. However, in contrast to previously reported results [7,15,42], cirrhosis appeared to not effect liver regeneration in our study. In this scenario, our hypothesis is grounded in reported studies suggesting that early liver regeneration in patients with liver cirrhosis may not attain the rate seen in normal liver regeneration. However, patients with cirrhosis can still achieve a sufficient hepatic mass if given ample time for recovery, eventually reaching a plateau in liver regeneration [42]. In our study, the extensive duration covered by the included CT scans allowed us to partially mitigate the gap between the two groups of patients, resulting in no significant difference in TLV_{post} across the total time points.

The results of our study should be interpreted with caution in terms of several limitations. Firstly, the small sample size implies that although we can validate our predictive model internally, we cannot use the data of patients from other institutions or from other time periods externally. Secondly, due to the nature of our retrospective study, the results are unavoidably susceptible to selection bias.

Despite these limitations, our results provide evidence that FLRV%, PHRR%, TBil and INR can strongly influence liver regeneration after hemi-hepatectomy. Furthermore, our study also found that the factors affecting postoperative liver regeneration in the benign group and the malignant group were not the same. This is of great significance for the accurate prediction of liver regeneration after liver resection. Our results, together with those of previous studies, suggest that FLRV% is the most important factor in predicting liver regeneration after hepatectomy. Simultaneously, PHRR% and TBil can accurately predict the degree of liver regeneration after hepatectomy for malignant tumors.

Ethics statement

This study was reviewed and approved by Ethics Committee of Hangzhou First People's Hospital with the approval number: 2021-

195-01. Informed consent was not required for this study because it was a retrospective study conducted with existing data without direct interaction with individuals.

Data availability statement

Because the information comes from the hospital case system, the data sets generated and analyzed during the current study period are not publicly available. The data that support the findings of this study are available from the corresponding author upon reasonable request.

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CRediT authorship contribution statement

Wenzhi Shu: Writing – original draft, Methodology, Data curation. **Yisu Song:** Writing – original draft, Methodology, Data curation. **Zuyuan Lin:** Writing – original draft, Methodology, Data curation. **Mengfan Yang:** Methodology, Data curation. **Binhua Pan:** Methodology, Data curation. **Renyi Su:** Methodology, Data curation. **Modan Yang:** Methodology, Data curation. **Zhengyang Lu:** Methodology, Data curation. **Shusen Zheng:** Supervision, Funding acquisition. **Xiao Xu:** Supervision, Funding acquisition. **Zhe Yang:** Supervision, Funding acquisition. **Xuyong Wei:** Supervision, Funding acquisition.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Not applicable.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2024.e30964.

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