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ORIGINAL ARTICLE

Volumetric and Functional Regeneration of Remnant Liver after Hepatectomy

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Abstract

Background Post-hepatectomy liver regeneration is of great interest to liver surgeons, and understanding the process of regeneration could contribute to increasing the safety of hepatectomies and improving prognoses.

Methods Five hundred thirty-eight patients who underwent hepatectomy were retrospectively analyzed. Postoperative outcomes were evaluated, with a focus on the effects of portal vein resection and resected liver volume on remnant liver regeneration in patients with liver tumors. Remnant liver volumes (RLVs) and laboratory data were measured postoperatively using multidetector computed tomography on day 7 and months 1, 2, 5, 12, and 24 after the operation.

Results Liver regeneration speed peaked at 1 week postoperatively and gradually decreased. Regeneration with large resections was longer than that with small resections, with the remnant liver regeneration rate being significantly lower in the former at all time points. Remnant liver regeneration plateaued around 5 months postoperatively, when regeneration is almost complete. Up to 1 month postoperatively, laboratory data were significantly worse when more portal veins was resected. After 2 months postoperatively, these data recovered to near normal levels.

Conclusion The speed and rate of remnant liver regeneration primarily showed a strong correlation with the number of resected portal veins and the amount of removed liver parenchyma. The larger the resection ratio, the longer it took the liver to regenerate. We confirmed that recovery of the liver's functional aspects accompanies recovery of the RLV.

Keywords Volumetric regeneration · Functional regeneration · Liver regeneration speed · Liver regeneration rate · Remnant liver · Hepatectomy

Introduction

Organisms have the ability to self-regenerate to functionally repair tissues and organs that have been impaired or injured. The ability of the liver to regenerate is particularly strong and, thus, has often been used in research as an organ-regeneration model; however, its regenerative ability is limited.[1,2] That is, if an impairment or injury exceeds the liver's ability to regenerate, regeneration may be suppressed. In clinical practice, this means that if hepatectomy goes beyond a certain limit, such as that for radical cure, remnant liver regeneration would not progress, which could in turn result in fatal complications, such as postoperative liver failure or massive ascites. While much research on the factors that contribute to remnant liver regeneration has been performed, a consensus has yet to be reached.

Recent advances in image-processing technology, particularly the appearance of multidetector computed tomography (MDCT), have enhanced conventional flat image information into a more easily understandable three-dimensional (3D)

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space.[3,4] In the field of hepatectomy, this has led to the development of simulation software for liver images that allows for more advanced functional diagnostics than previous visual diagnostics. Several institutions have already introduced these tools. The software uses hemodynamics to calculate the regions supplied by the portal and hepatic veins. Virtual hepatectomies performed with the software enable preoperative quantitative assessments of the postoperative remnant liver volume based on the number of portal vein and hepatic vein resections.

In this study, we evaluated the outcomes of hepatectomies that were performed according to conventional criteria for the permissible extent of liver resection, which is based on hepatic reserve and remnant liver volume. We also assessed the regions supplied by the portal veins and remnant liver volume using 3D image-processing technology. In addition, we examined liver volumetric regeneration and functional recovery post-hepatectomy with or without portal vein resection, taking the differences in resected liver volume into consideration.

Materials and Methods

Patient Population and Selection

We retrospectively analyzed 686 consecutive patients who underwent hepatic resection for liver tumors at Osaka Medical College Hospital, Takatsuki City, Japan, between January 2010 and July 2017. Hepatic resection is performed when a liver tumor can be curatively resected. There is no limitation on the number or size of liver tumors with regard to hepatic functional reserve after resection. All patients were fully informed of the study design and provided their written, informed consent to participate. This study was approved by the Ethics Committee on Clinical Investigation of Osaka Medical College Hospital (nos. 2001 and 2059).

The preoperative workup consisted of a specified protocol, including blood tests, abdominal ultrasound, MDCT scanning, magnetic resonance imaging, and fluorodeoxyglucose-positron emission tomography. Hepatic function was evaluated using the Child–Pugh classification[5] of liver dysfunction. Liver volumetry was estimated using Synapse Vincent (Fujifilm Medical, Tokyo, Japan) and MDCT.

Patients who underwent additional therapy, such as repeat hepatic resection or radiofrequency ablation during the six postoperative months, were excluded. Patients who received preoperative portal vein embolization were also excluded. Hence, a total of 538 patients who underwent hepatic resection and whose liver volumetric data were obtained at four time points were included in the analysis.

Moreover, data on demographic and clinical variables on admission, including age, sex, body mass index (BMI), hepatitis viral infection, diabetes mellitus, pathology, serum albumin, serum total bilirubin, prothrombin time (PT), platelet count, and indocyanine green retention rate at 15 min (ICGR 15), were obtained; clinical variables were measured at the central laboratory of our hospital.

Liver Volume Measurements

Three hepatobiliary surgeons with expertise in performing abdominal computed tomography (CT) (YI, KF, and KU) traced the contours of the total liver. The Volume Analyzer SYNAPSE VINCENT image analysis system automatically calculated the approximate total liver volume (TLV) from preoperative CT scans.

On preoperative CT, we measured TLV, the volume of the right and left lobes of the liver, the volumes of each segment (according to the Couinaud classification[6]), the future liver remnant volume, and the remnant sectional volumes, which included the caudate lobe, lateral section (segments II and III), median section (segment IV), anterior section (segments V and VIII), and posterior section (segment VI and VII). Remnant liver volumes (RLVs) were measured using MDCT at day 7 and months 1, 2, 5, 12, and 24 after the operation.

We calculated the following values: RLV at day 0 after the operation ((TLV + tumor volume) − resected liver volume), regeneration speed ((RLV at day 7 and at 1, 2, 5, 12, and 24 months/RLV at days 0, 7 and at 1, 2, 5, and 12 months) × 100), and regeneration rate ((RLV at day 7 and at 1, 2, 5, 12, and 24 months/TLV) × 100).

Surgical Procedure

The indications for surgical resection used in this study were in accordance with the criteria of Makuuchi et al.[7] An additional criterion for operability was a ratio of remnant liver weight to body weight of at least 0.8, as estimated with preoperative imaging.[8]

Details of the surgical technique routinely used in our department have been described previously.[9–11] Briefly, a standard diagnostic and staging laparotomy was conducted. The liver was mobilized, and intraoperative ultrasonography was routinely performed. Parenchymal transection was achieved using the Sonop 5000 ultrasonic dissector (Hitachi Aloka Medical, Ltd., Tokyo, Japan). Small vessels were ligated or coagulated using a soft-coagulation system or bipolar electrocautery. Intraparenchymal control of major vessels was accomplished using non-absorbable sutures, and biliary and vascular vessels were ligated with stapling devices or non-absorbable sutures. The hepatic pedicle was always isolated to enable Pringle maneuver when required. Intermittent clamping was applied (i.e., 15-min clamping and 5-min release periods). Surgical margin was confirmed using

intraoperative ultrasonography; a surgical margin of 2–10 mm was obtained when possible.

Definitions

Operative procedures were classified according to the eight segments of the liver based on the Couinaud classification.[6] Anatomical resection was defined as the resection of the neoplasm, which involves the portal vein and the surrounding hepatic territory. Non-anatomical resection was defined as the resection of a lesion without regard to segmental, sectional, or lobar anatomy. Major hepatectomy was defined as resection of three or more liver segments, according to the Brisbane 2000 system.[12]

Complications were stratified according to the Clavien–Dindo classification of surgical complications.[13,14] Postoperative bile leakage and post-hepatectomy liver failure (PHLF) were defined based on the criteria of the International Study Group of Liver Surgery.[15,16] Moreover, we defined massive ascites as that which could not be mobilized or could not be satisfactorily prevented with medical therapy.[17] Hepatic fibrosis was scored as follows: stage 0, no fibrosis; stage 1, portal fibrosis without septa; stage 2, portal fibrosis with rare septa; stage 3, numerous septa without cirrhosis; and stage 4, cirrhosis.[18]

Patient Follow-Up

Patients were closely followed until July 1, 2018. They were examined using ultrasonography and contrast-enhanced CT on day 7 and months 1, 2, 5, and 12 postoperatively and every 6–12 months thereafter. Blood tests were performed at 1–2 months after discharge and every 2–3 months thereafter.

Statistical Analysis

Continuous variables were expressed as median ± standard deviation. Univariate analysis results were compared using Student's t test, χ^2 test, Mann–Whitney U test, Wilcoxon signed-rank test, or Fisher's exact test, as appropriate. P values < 0.05 were considered statistically significant. All statistical analyses were performed using JMP version 12 (SAS Institute, Inc., Cary, NC, USA).

Results

Background of Patients with Hepatic Resection

Data from 538 patients (366 men, 172 women; median age, 69 years (range, 22–93 years)) were analyzed. Patient demographics, the type of hepatic resection performed, intraoperative factors, and short-term outcomes following hepatic resection are summarized in Table 1. The platelet count was lower and the ICG-R15 higher than in major hepatectomy ($P = 0.001$ and 0.005), and the tumor size was smaller than in major hepatectomy ($P < 0.001$). PHLF occurred in 22 (4.1%) of 538 patients. The overall in-hospital mortality was 4.3% (23 of 538 patients); the overall morbidity, 25.1% (135 of 538 patients). Re-operations were needed for ten patients (1.9%) because of postoperative hemorrhage in six, bile leakage in one, non-obstructive mesenteric ischemia in one, and perforation of the small intestine in one and the descending colon in another one.

Resected Liver Volume and Remnant Liver Regeneration after Hepatectomy

Table 2 shows the correlations between resected liver volume and remnant liver regeneration. Liver regeneration speed peaked at 1 week postoperatively, which gradually decreased. Remnant liver volume plateaued around 5 months postoperatively, when regeneration is almost complete. For the regeneration rate, however, regeneration was longer with large resections than with smaller resections, with the remnant liver regeneration rate being significantly lower in the former at all time points. Moreover, the incidence rate of PHLF increased as the resected liver volume increased ($P < 0.001$).

Resected Portal Vein Number and Remnant Liver Regeneration after Hepatectomy

Treatment of portal veins was performed: one portal vein for each of Couinaud's segment,[11] one portal vein for the medial segment, and two portal veins for the lateral, anterior, and posterior segments; three for the medial and lateral or anterior segments commonly described in bisegmentectomy; four for the anterior and posterior segment or left lobe described in right hepatectomy or left trisegmentectomy; and five for the medial segment and right lobe described in right trisegmentectomy. Table 3 shows the correlations between portal vein resection and resected liver volume. The greater the resected liver volume, the more portal veins were resected.

As shown in Table 4, the remnant liver regeneration speed increased as the number of portal veins resected increased. Regeneration speed approached its peak at 1 week postoperatively, showed no difference 1 month postoperatively, and plateaued around 5 months postoperatively. Moreover, similar to the resected liver volume, the regeneration rate was significantly low as the number of portal veins resected increased. The incidence rate of PHLF increased as the number of resected portal veins increased ($P = 0.005$).

Postoperative Changes in Laboratory Data

Up to 1 month postoperatively, serum albumin, serum total bilirubin, PT, and platelet count were significantly worse

Table 1 Preoperative clinical and laboratory patient data

Factor	Median (range)			*P* value
	All patients	Major hepatectomy	Minor hepatectomy	
Number	538	101	437	
Age, years	69 (22–93)	68 (22–88)	69 (28–93)	0.135
Sex (male/female)	366:172	74:27	292:145	0.457
BMI, kg/m^2	22.8 (13.9–34.9)	22.6 (13.9–31.0)	22.8 (14.8–34.9)	0.500
Hepatitis B viral infection, %	154/384 (28.6%)	22 (21.8%)	132 (30.3%)	0.160
Hepatitis C viral infection, %	106/431 (19.8%)	13 (12.9%)	93 (21.4%)	0.154
Diabetes mellitus, %	145 (27.0%)	28 (27.7%)	117 (26.8%)	0.992
HCC/metastasis, others	254/284	45/56	209/228	0.839
Serum albumin, g/dL	4.0 (2.0–5.2)	4.0 (2.5–4.8)	4.0 (2.0–5.2)	0.209
Serum total bilirubin, mg/dL	0.6 (0.2–4.6)	0.6 (0.2–4.6)	0.6 (0.2–2.7)	0.111
Prothrombin time, %	101 (13–150)	100 (49–150)	101 (13–150)	0.968
Platelet count, × 10^4/μL	19.3 (2.6–62.2)	22.5 (4.2–62.2)	18.8 (2.6–49.1)	0.001*
ICG-R15, %	11.9 (0.4–72.2)	9.3 (1.5–33.8)	12.2 (0.4–72.2)	0.005*
Number of tumors	1 (1–24)	1 (1–18)	1 (1–24)	0.141
Size of largest tumor, cm	3.0 (0.5–28.0)	4.6 (1.5–18.2)	2.7 (0.5–28.0)	< 0.001*
Total liver volume, cm^3	1130 (613–2675)	1237 (663–2053)	1114 (613–2675)	0.002*
Each segment/total liver volume, %				
Caudal segment	2.8 (0.2–8.5)	3.1 (1.4–8.5)	2.4 (0.2–6.6)	0.086
Lateral section	22.5 (5.0–36.6)	23.4 (15.7–31.9)	19.3 (5.0–36.6)	0.186
Median section	15.9 (4.0–41.2)	17.1 (6.8–41.2)	13.9 (4.0–30.5)	0.176
Anterior section	34.5 (15.5–55.4)	32.9 (15.5–39.9)	33.2 (21.7–55.4)	0.607
Posterior section	31.6 (6.3–51.3)	27.8 (12.4–45.1)	31.3 (6.3–51.3)	0.628
Type of hepatic resection (anatomical/non-anatomical)	236/302	101/0	135/302	< 0.001*
Lobectomy	109 (20.3%)	89 (88.1%)	0	< 0.001*
Segmentectomy	105 (19.5%)	12 (11.9%)	113 (25.9%)	
Sectionectomy	21 (3.9%)	0	21 (4.8%)	
Partial resection	303 (56.3%)	0	303 (69.3%)	
Laparoscopic hepatic resection, %	209 (38.8%)	5 (5.0%)	204 (46.8%)	< 0.001*
Repeat operation, %	95 (17.7%)	14 (13.9%)	81 (18.5%)	0.540
Number of hepatic resections	1 (1–16)	1 (1–5)	1 (1–12)	0.973
Additional gastrointestinal procedures, %	53 (9.9%)	21 (20.8%)	38 (8.7%)	0.053
Thoracotomy, %	22 (4.1%)	8 (8.0%)	14 (3.2%)	0.096
Operative time, min	221 (30–810)	300 (120–798)	209 (30–810)	< 0.001*
Blood loss, mL	250 (0–10,970)	550 (0–8280)	200 (0–10,970)	< 0.001*
Portal vein resection, %	214 (39.8%)	101 (100%)	134 (25.9%)	< 0.001*
Hepatic vein resection, %	188 (34.9%)	101 (100%)	87 (19.9%)	< 0.001*
Resected liver volume, %	13.3 (0.3–70.0)	45.1 (19.4–70.0)	10.6 (0.3–68.3)	< 0.001*
Hepatic fibrosis (F0–2/F3, 4)	400/138	83/18	280/157	0.002*
Surgical margin, mm	5 (0–48)	5 (0–48)	5 (0–37)	0.802

BMI body mass index, *HCC* hepatocellular carcinoma, *ICGR-15* indocyanine green retention rate at 15 min

when more portal veins were resected. After 2 months postoperatively, however, none of the laboratory data exhibited significant differences, although the data showed recovery toward near normal levels (Fig. 1).

Discussion

Survival rates of hepatocellular carcinoma, metastatic liver cancer, and other forms of liver cancer have increased along

Table 2 Resected liver volume and remnant liver regeneration

	Resected liver volume/total liver volume (%)				*P* value
	< 10%	10–30%	30–50%	> 50%	
Number	228	183	84	43	
TLV before operation, cm^3	1121 (630–2675)	1105 (613–1918)	1190 (750–2053)	1218 (678–1894)	0.019*
At day 0 after operation, %	97.2 (90.0–99.9)	82.8 (70.7–89.7)	64.7 (50.2–69.6)	45.5 (27.3–49.6)	< 0.001*
Regeneration speed (remnant liver volume/previous remnant liver volume)					
At day 7, %	108.2 (78.7–174.0)	119.0 (58.0–171.4)	122.6 (70.6–202.6)	126.9 (78.9–208.9)	< 0.001*
At month 1, %	94.2 (80.4–116.8)	92.9 (68.2–138.9)	106.4 (54.3–144.7)	110.7 (77.6–132.7)	0.002*
At month 2, %	102.3 (81.7–111.9)	98.6 (74.9–132.5)	105.5 (86.8–111.1)	105.3 (95.5–118.6)	0.487
At month 5, %	101.9 (82.0–122.8)	106.1 (85.8–130.6)	102.4 (89.7–118.1)	103.7 (71.1–148.8)	0.133
At month 12, %	101.3 (76.4–136.4)	101.1 (63.2–150.6)	99.3 (66.5–115.2)	102.5 (78.9–123.7)	0.486
At month 24, %	97.7 (63.8–133.0)	100.0 (85.1–131.9)	101.0 (87.1–114.9)	101.3 (85.6–129.4)	0.338
Regeneration rate (remnant liver volume/total liver volume)					
At day 0 after operation, %	97.2 (90.0–99.9)	82.8 (70.7–89.7)	64.7 (50.2–69.6)	45.5 (27.3–49.6)	< 0.001*
At day 7, %	102.7 (77.2–168.0)	100.6 (45.5–148.8)	79.0 (46.1–122.8)	62.1 (43.7–110.9)	< 0.001*
At month 1, %	99.3 (84.7–132.8)	91.4 (59.6–133.8)	85.7 (38.2–139.9)	73.0 (34.9–109.3)	< 0.001*
At month 2, %	100.9 (78.5–133.7)	94.6 (65.6–133.4)	94.0 (38.9–143.5)	79.8 (57.3–129.6)	< 0.001*
At month 5, %	99.9 (66.0–131.9)	96.0 (51.4–136.8)	89.0 (70.0–131.9)	84.4 (59.9–132.7)	< 0.001*
At month 12, %	99.4 (64.7–145.5)	95.8 (53.7–131.1)	90.6 (61.3–166.6)	85.9 (53.6–127.0)	< 0.001*
At month 24, %	98.7 (74.2–136.0)	94.0 (68.4–139.5)	92.8 (68.4–109.7)	86.7 (60.3–108.3)	0.006*
PHLF	1 (0.4%)	9 (4.9%)	7 (8.3%)	5 (11.6%)	< 0.001*

*$P < 0.05$

TLV total liver volume, *PHLF* post-hepatectomy liver failure

with the development of various treatment strategies.[19,20] Among the available treatments, hepatectomy provides the best chance of a radical cure. While several institutions could perform hepatectomies for liver cancer, PHLF remains an extremely important problem. Even small liver resections could result in postoperative liver failure.

Several institutions have reported their own methods for assessing the liver's ability to tolerate surgery.[21,22] These methods have reduced the incidence of PHLF. However, in-hospital deaths from liver failure due to poor liver regeneration continue to occur. To prevent this complication, we must not only investigate methods of preoperatively assessing the patient's overall ability to tolerate surgery but also carefully examine preoperative liver functions and hepatectomy techniques that include assessments of the liver's regenerative capacity. Moreover, post-hepatectomy liver regeneration is of great interest to liver surgeons, and understanding the process of regeneration could contribute to increasing the safety of hepatectomies and improving prognoses.

Table 3 Portal vein resection and resected liver volume

Number of portal vein resections	Number	Resected liver volume, cm^3	Resected liver volume, %
0	303	60 (3–1400)	5.4 (0.3–55.5)
1	30	180 (90–1780)	15.7 (8.5–62.1)
2	104	300 (100–760)	26.4 (5.6–67.0)
3	43	360 (97–940)	28.6 (10.2–58.2)
4	57	700 (300–2600)	51.8 (24.1–72.7)
5	1	960 (960–960)	64.4 (64.4–64.4)

Table 4 Portal vein resection and remnant liver regeneration

	Resected liver volume/total liver volume (%)			*P* value
Number of portal vein resections	0	1, 2	3, 4, 5	
Number	303	134	101	
TLV before operation, cm^3	1107 (626–2675)	1124 (613–1918)	1237 (663–2053)	< 0.001*
At day 0 after operation, %	95.4 (69.3–99.7)	78.6 (31.7–90.1)	59.2 (32.9–80.6)	< 0.001*
Regeneration speed (remnant liver volume/previous remnant liver volume)				
At day 7, %	112.6 (70.6–174.0)	121.9 (58.1–208.9)	120.6 (74.6–203.9)	0.012*
At month 1, %	94.2 (68.2–138.9)	100.6 (54.3–132.6)	109.5 (74.2–144.7)	< 0.001*
At month 2, %	98.6 (74.9–131.0)	101.5 (88.3–132.5)	105.6 (92.1–145.0)	0.152
At month 5, %	102.7 (82.0–122.8)	102.7 (86.8–130.6)	99.6 (71.1–148.8)	0.521
At month 12, %	101.3 (76.4–136.4)	98.8 (63.2–129.3)	101.7 (78.9–150.6)	0.061
At month 24, %	98.3 (63.8–133.0)	100.3 (81.2–123.7)	101.3 (81.9–131.9)	0.096
Regeneration rate (remnant liver volume/total liver volume)				
At day 0 after operation, %	95.4 (69.3–99.7)	78.6 (31.7–90.1)	59.2 (32.9–80.6)	< 0.001*
At day 7, %	102.7 (65.8–168.0)	90.4 (45.5–140.6)	73.9 (43.7–127.3)	< 0.001*
At month 1, %	98.5 (63.7–133.8)	91.3 (38.2–139.9)	82.4 (34.9–119.7)	< 0.001*
At month 2, %	99.0 (65.6–133.7)	94.6 (38.9–129.6)	85.4 (59.3–155.5)	< 0.001*
At month 5, %	100.9 (65.6–131.9)	92.4 (51.4–136.8)	88.4 (59.9–140.2)	< 0.001*
At month 12, %	99.8 (64.7–145.5)	90.3 (53.7–128.6)	91.7 (53.6–127.0)	< 0.001*
At month 24, %	98.7 (74.2–136.0)	93.1 (68.4–109.7)	91.6 (60.3–139.5)	0.011*
PHLF	8 (2.6%)	4 (3.0%)	10 (9.9%)	0.005*

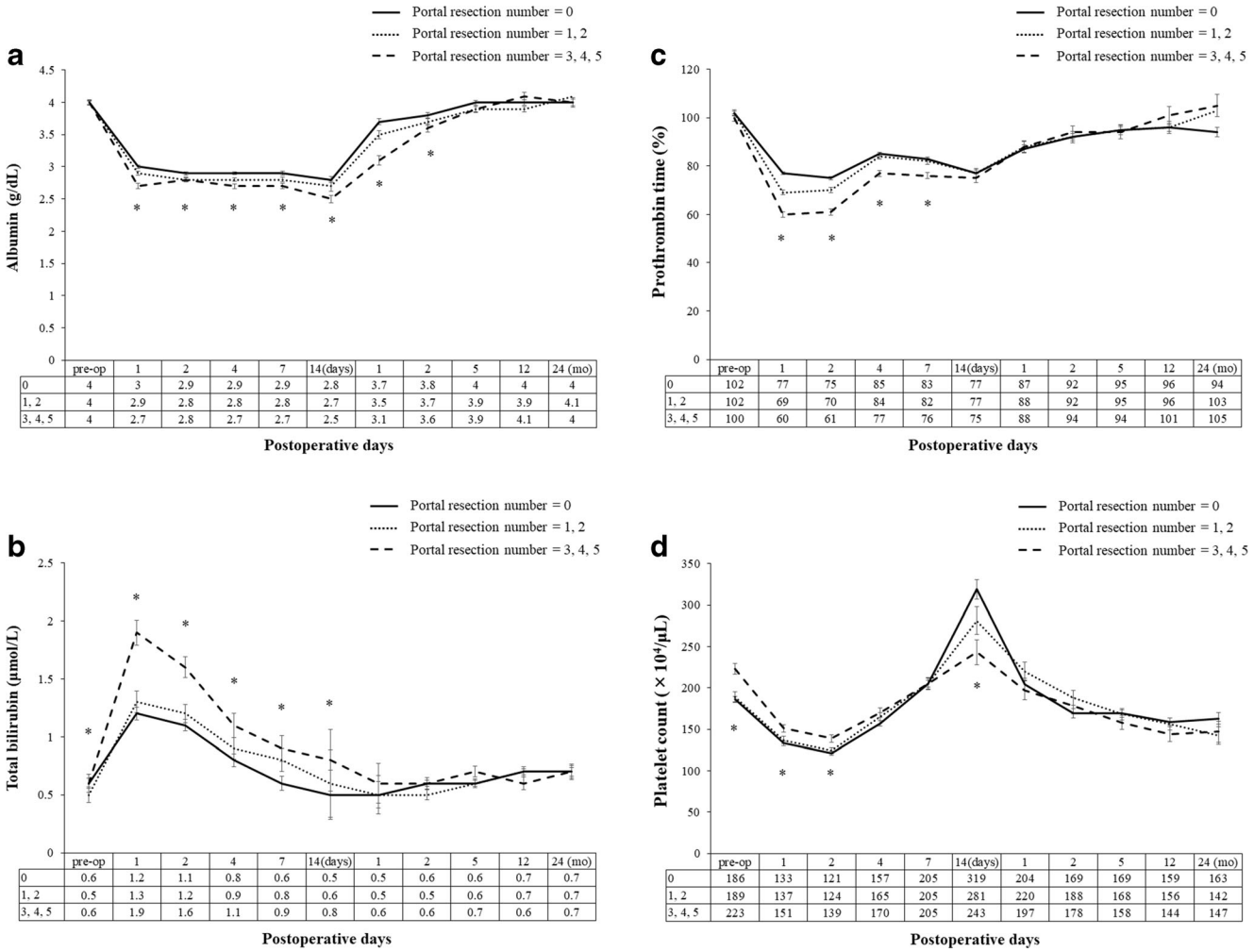
*$P < 0.05$

TLV total liver volume, *PHLF* post-hepatectomy liver failure

In liver cancer, and hepatocellular carcinoma in particular, it is possible to resect microlesions, including transportal intrahepatic metastasis and venous thrombus, that are in the same section of the tumor, thereby making anatomical resection a superior choice to obtain a radical cure.[23,24] Thus, we examined how liver regeneration correlated with RLV when accompanied by portal vein resection. The results showed that the resected liver volume increased as more portal veins were resected, and at all time points, the rate of recovery toward preoperative liver volume was low. Further, liver regeneration speed correlated positively with the number of resected portal veins and the resected liver volume, which means that as more portal veins were resected and the resected liver volume increased, the regeneration speed also increased. In addition, as the blood inflow of the portal vein to the postoperative remnant liver was similar to preoperative levels, remnant liver hypertrophy occurred. As the resected liver volume increased, the amount of remnant liver parenchyma decreased, which in turn increased the ratio of blood flow to the remnant liver, thereby apparently promoting early regeneration of the remnant liver. However, when numerous portal veins were resected or when a large amount of the parenchyma was resected, liver regeneration took a long time to complete, even with increased regeneration speed. In terms of total remnant liver regeneration, Yamamoto et al.[21] and Morioka et al.[25] also reported similar results. However, there are few detailed reports on the effect of resected liver volume and number of portal veins on post-hepatectomy liver regeneration, and the population in their study was only evaluated according to liver volume change.

Furthermore, in addition to measuring changes in RLV, evaluating the recovery of liver functions is also vital to assess liver regeneration. Examinations that evaluate the functional aspects of liver regeneration, such as those that measure serum albumin, serum total bilirubin, PT, and platelet count, showed that it takes approximately 1–2 months for the levels to return to the normal range, depending on the resected liver volume or the number of portal veins resected. In this study, RLV increased markedly in the first month postoperatively, with the remnant liver growing particularly rapidly up to day 7 postoperatively. As the remnant liver regenerated, its functions also improved.

Generally, surgeons aim to completely remove all cancer cells and eliminate the possibility of recurrence during the postoperative course. However, if liver failure or other complications occur, the patients' lives could be at risk, which is something that should be avoided. The speed of postoperative liver regeneration primarily showed a strong correlation with the number of portal veins resected and the amount of liver parenchyma removed. For the liver regeneration rate, the



a	pre-op	1	2	4	7	14(days)	1	2	5	12	24 (mo)
0	4	3	2.9	2.9	2.9	2.8	3.7	3.8	4	4	4
1, 2	4	2.9	2.8	2.8	2.8	2.7	3.5	3.7	3.9	3.9	4.1
3, 4, 5	4	2.7	2.8	2.7	2.7	2.5	3.1	3.6	3.9	4.1	4

b	pre-op	1	2	4	7	14(days)	1	2	5	12	24 (mo)
0	0.6	1.2	1.1	0.8	0.6	0.5	0.5	0.6	0.6	0.7	0.7
1, 2	0.5	1.3	1.2	0.9	0.8	0.6	0.5	0.5	0.6	0.7	0.7
3, 4, 5	0.6	1.9	1.6	1.1	0.9	0.8	0.6	0.6	0.7	0.6	0.7

c	pre-op	1	2	4	7	14(days)	1	2	5	12	24 (mo)
0	102	77	75	85	83	77	87	92	95	96	94
1, 2	102	69	70	84	82	77	88	92	95	96	103
3, 4, 5	100	60	61	77	76	75	88	94	94	101	105

d	pre-op	1	2	4	7	14(days)	1	2	5	12	24 (mo)
0	186	133	121	157	205	319	204	169	169	159	163
1, 2	189	137	124	165	205	281	220	188	168	156	142
3, 4, 5	223	151	139	170	205	243	197	178	158	144	147

Fig. 1 Postoperative changes in laboratory data in relation to portal resection number (0; 1, 2; and 3, 4, 5). Postoperative total bilirubin (**a**), serum albumin (**b**), platelet count (**c**), and prothrombin time (**d**) of patients after hepatectomy

larger the resection ratio, the longer it would take the liver to regenerate. In addition, we confirmed that recovery of the liver's functional aspects accompanies recovery of the RLV. Thus, investigating post-hepatectomy regeneration of the remnant liver is extremely important.

This study has some limitations, such as variation in the patients' characteristics and an insufficient number of cases; thus, the level of evidence in this study could not be considered high. Future studies should include and examine more cases.

Author Contributions YI conceived the study and design, was involved in patient care, and drafted the manuscript. KF, MI, SK, AT, HH, WO, YT, SM, MY, AA, KK, TS, MA, SF, FH, YN, KH, and KU were involved in the creation of the study concept and design, patient care, and drafting of the manuscript. All authors have read and approved the final version of the manuscript.

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Abbreviations RLV, remnant liver volume; MDCT, multidetector computed tomography; 3D, three-dimensional; CT, computed tomography; BMI, body mass index; PT, prothrombin time; ICG-R15, indocyanine green retention rate at 15 min; TLV, total liver volume; PHLF, post-hepatectomy liver failure; OR, odds ratio; CI, confidence interval

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