Clinical Significance of Spleen–Remnant Liver Volume Ratio in Hepatocellular Carcinoma Surgery

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Abstract The objective of this study was to explore the value of spleen–remnant liver volume ratio for hepatocellular carcinoma surgery and liver reserve assessment. Spleen–remnant liver volume ratio postoperation was measured with imageological methods and water displacement, and the liver function postoperation and hospital stay of patients with different spleen–remnant liver volume ratios were compared. Spleen–remnant liver volume ratio was closely related to liver function assessment postoperation. The higher the ratio, the higher the assessment score of liver function postoperation would be. When spleen–remnant liver volume ratio was ≤ 0.9 , the patients had a fast recovery and short hospital stay. Spleen–remnant liver volume ratio can effectively predict the recovery and liver reserve of patients with hepatocellular carcinoma postoperation. When postoperative spleen–remnant liver volume ratio is predicted to be ≤ 0.9 , the operation can be performed; and when the ratio is predicted to be ≥ 1.2 , the operation is not suggested.

Keywords Primary hepatocellular carcinoma · Operation · Spleen–remnant liver volume ratio

Operation is one of the fundamental therapies for hepatocellular carcinoma, and the major risks come from intraoperative hemorrhage and liver failure postoperation. With the advance of surgical technology, intraoperative hemorrhage is less threatening as before, while liver failure still remains a major risk. Insufficient liver reserve is the primary reason for liver failure. The study aims to establish proper preoperative assessment criteria through a noninvasive method, have a

reasonable evaluation of liver reserve of patients with liver cirrhosis and hepatocellular carcinoma, and improve the therapy effect of hepatocellular carcinoma surgery.

Materials and Methods

Clinical Materials

Fifty-six patients with hepatocellular carcinoma underwent surgery during September of 2005 to September of 2008 in our hospital. They had routinely enhanced CT examination prior to the surgery, and liver tissue specimens were obtained after intraoperative liver resection. There were 47 males and 9 females, aged between 23 and 68 years, and the average years was 45.6 ± 12.3 years. All the liver tumors lay on the right lobe of the liver. The patients underwent hemihepatic vascular occlusion, liver hanging and binding through retrohepatic tunnel, and liver resection with anterior approach, and the bare area of the liver with a cutting edge of 1–2 cm from the mass had continuous suture using atraumatic suture.

CT Scanning

Picker SeleCT SP CT scanner was used in the study. Both the slice thickness and distance were 10 mm. From the diaphragmatic dome, 12–15 slices were spirally scanned downwards, including the whole spleen and liver surface; plain scan and enhanced examination were performed at 120 kV, 180 mAs, FOV 430 mm, and matrix 512×512 . Window level was about 100, and window width was about 200. Spleen–liver volume was obtained from CT picture with the Heymsfield method [1]. To improve the accuracy of measurement, big vessels (including inferior vena cava, intrahepatic portal, and extrahepatic portal), major fissures (interlobar fissure), and gallbladder were excluded (Fig. 1). The liver and the tumor were

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Fig. 1 Spleen–liver volume measurement by computed tomography. The red area stand for the propotion of liver and the blue area the propotion of spleen

delineated together, and remnant liver volume was obtained by subtracting the resected specimen volume from the total volume.

Assessment of Liver Function Postoperation and Patient Grouping

Liver function was assessed with the Child–Pugh scoring method (Table 1). As the patients would be infused with protein after the surgery, the item of albumin was deleted and the item of prealbumin was added in the Child–Pugh scoring system: less than 100 mg/l was scored 3, 100–200 mg/l was scored 2, and more than 200 mg/l was scored 1.

With regard to grouping, the patients were categorized according to their liver function 7 days after the surgery. Patients who had a score of less than 9 (including 9) were in group A and the patients who had a score of more than 9 were in group B.

Table 1 Modified Child–Pugh scoring

Measure	Score		
	1	2	3
Ascites	Absent	Mild/moderate	Severe/refractory
Bilirubin (μmol/l)	17.1~34.2	34.2~51.3	>51.3
Prealbumin (mg/l)	>180	100~180	100<
Encephalopathy	Absent	Mild (I~II)	Severe (III~IV)
Prothrombin activity (%)	>50	30~50	<30

Explanation of Indices

Specimen volume was measured with instant immersion method after the resection; remnant liver volume measurement formula was as follows: remnant liver volume postoperation (ml)=total liver volume measured with CT specimen volume; spleen–liver volume ratio=spleen volume/remnant liver volume postoperation. Standard remnant liver volume was measured as per the method of Urata et al. [2], i.e., first, calculate the body surface area (BSA) with the formula $BSA = \text{weight (kg)} \times 0.425 \times \text{height (cm)} \times 0.725 \times 0.007184 \text{ (m}^2\text{)}$; calculate the standard liver volume (SLV) with the formula $SLV = [706.2 \times BSA \text{ (m}^2\text{)} + 2.41 \text{ ml}]$; then, standard remnant liver volume (ml)=SLV specimen volume.

The hospital discharge criteria include absence of complications, normal appetite and urination and defecation, assessment score of liver function ≤ 6 , and incision suture removal.

Statistical Analysis

SPSS 13.0 was used for statistical analysis. Multivariate logistic regression analysis was used to explore the relation between liver function postoperation and spleen–liver volume ratio, operation time, intraoperative blood loss, and standard remnant liver volume, and regression equations were derived. Measurement data were subjected to *t* test, and Satterthwaite's approximate *t* test was used if variances were not equal. The relation between assessment score of liver function and hospital stay was examined with Kaplan–Meier analysis, and the significance was examined with log-rank test, with 95 % confidence interval.

Results

Spleen–Liver Volume Ratio Calculation

Figure 1 gives an illustration on how to calculate spleen–liver volume ratio with CT.

Patient Spleen–Liver Volume Ratio and Mortality

Two patients in group B died of liver failure and massive upper gastrointestinal hemorrhage during hospital stay. They died 6 and 8 days after the surgery, and their spleen–liver volume ratios were 1.42 and 1.50, respectively; no death was found in group A, and the overall mortality rate of the two groups combined was 3.6 %. Two patients in group B whose spleen–liver volume ratios were 1.51 and 1.47, respectively, witnessed recurrent chronic hepatic insufficiency after hospital discharge and died of upper gastrointestinal hemorrhage and liver failure 3 months and half year after the surgery, respectively.

Comparison of Hospital Stay of the Two Groups

The median hospital stay of group A was 14 days (8–29 days) and that of group B was 19 days (8–49 days) (Fig. 2). Log-rank test showed that $P=0.046$, which was less than 0.05. The difference of two groups was significant, indicating that assessment criteria of liver function designed in this study could predict the hospital stay of patients.

Factors Affecting Assessment of Liver Function

The scatterplot of spleen–liver volume ratio and liver function was drawn (Fig. 3), indicating that the two were of good relation.

Multivariate logistic regression analysis showed that $F=23.463$ and $P<0.001$, indicating that the multivariate regression model was of statistical significance, standard remnant liver volume and spleen–liver volume ratio was related to assessment score of liver function postoperation, and operation time was irrelevant to blood loss and assessment score of liver function postoperation ($P>0.05$). The regression equation was derived as $Y=1.367+8.022X-0.06Z$ (where Y is the assessment score of liver function, X is the spleen–remnant liver volume ratio, Z is the standard remnant liver volume), i.e., assessment score of liver function can be derived from spleen–liver volume ratio and standard remnant liver volume (see Table 2 for results).

The 95 % confidence intervals of spleen–liver volume ratios of group A and group B were 0.4233~0.9273 and 0.8926~1.1312, respectively.

Discussion

Patients with hepatocellular carcinoma in China are generally complicated with liver cirrhosis, with the presence of

Fig. 2 Comparison of hospital stay of the two groups

Fig. 3 Scatterplot of spleen–liver volume ratio and liver function

decreasing liver reserve and poor liver regeneration, and are easily subjected to liver failure postoperation [3], which may induce a higher mortality rate. To improve the effect of hepatocellular carcinoma surgery, scientific assessment of liver reserve, in particular remnant liver reserve, is important to prevent liver failure postoperation. It is generally believed that with the worsening of liver cirrhosis, liver reserve is also decreasing. A normal liver can stand more than 75 % resection, while a patient with liver cirrhosis may not even stand 50 % liver resection. While the Child–Pugh classification is used to evaluate the severity of liver cirrhosis, it cannot predict liver reserve necessary against invasion, so it is not able to make accurate assessment of liver function [4]. ICG clearance is an internationally recognized index for assessment of liver reserve and prediction of liver failure postoperation [5, 6], but it is designed for the total liver reserve and can be affected by many factors; therefore, it has little value for the assessment of remnant liver reserve postoperation and preoperative prediction of mortality.

With the popularity and development of imageology, the accuracy of organ volume measurement with imageological technology has been recognized, and assessment of liver reserve and surgery risk based on morphological features has made some progress. Ogasawara et al. [7] found that liver volume and liver weight could be considered as important indices as the Child–Pugh classification. Shirabe et al. [8] found that compared to total liver volume, remnant liver volume was of more value; when remnant live volume measured by CT was less than 250 ml/m², it is more possible that the patient would be subjected to liver failure postoperation. A similar report in China found [9] that the surgery was relatively safer if remnant liver volume was kept more than 250 ml. It was also reported that patients with liver cirrhosis generally had bigger spleen volumes and similar liver volumes as compared to those of normal people [10], indicating that it is improper to evaluate liver cirrhosis and liver reserve just based on spleen–liver volume change. Zhang et al. [11] thought that measurement of total liver volume was not of statistically

Table 2 Data (mean±SD) on the factors that affect liver function in groups A and B

	Group A (30 cases)	Group B (26 cases)	<i>t</i> value	<i>P</i> value
Spleen and liver volume ratio	0.675±0.244	1.012±0.296	7.831	0.00
Standard remnant liver volume (ml)	485±102	379±98	2.504	0.016
Intraoperative blood loss (ml)	1,080±820	680±133	0.086	0.931
Operation time (min)	157±59	168±56	0.546	0.588
Median hospital stay (day)	14 (8–29)	19 (8–49)	3.992	0.046

significant in differentiating early liver cirrhosis from the normal liver.

The liver and spleen are closely related in anatomy, as their blood is supplied by the celiac artery branches and the spleen vein regurgitates to the liver. The relation in anatomy reminds people that the two may have certain relation in function. Liver cirrhosis is generally complicated with spleen volume increase, so some researchers believed that the spleen might participate in the genesis and development of liver cirrhosis [12]. Some researchers also noticed that liver cirrhosis was complicated with spleen volume increase of different degrees, and the spleen volume increase of patients with chronic liver diseases was positively related to their hepatic fibrosis degree [13]. Hoefs [14] observed spleen volumes of 26 cases with chronic liver diseases and found that the degree of spleen volume increase was significantly related to severity of hepatic fibrosis. Tu [15] found that spleen–liver volume ratio was a good index for liver cirrhosis diagnosis; the ratio of patients with liver cirrhosis should be 0.2–1.6, not overlapping with that of normal group (0.04–0.19).

Based on the above studies and our clinical practice, we used spleen and remnant liver volume ratio to assess remnant liver reserve postoperation and indirectly evaluate liver reserve. We found in our observation that group A whose score was ≤ 9 had better and faster recovery, lower complication incidence rate, and shorter hospital stay; the differences between group A and group B (assessment score of liver function ≥ 10) were of statistical significance. The 95 % confidence intervals of spleen–remnant liver volume ratios of group A (assessment score of liver function ≤ 9) and group B were 0.4233–0.9273 and 0.8926–1.1312, and the two had little overlapping. It was suggested that when spleen–remnant liver volume ratio was less than 0.9, patients would have faster recovery, shorter hospital stay postoperation, and fewer complications. In our study, we found that when the ratio was more than 1.2, the recovery would be difficult; even though patients reached the hospital discharge criteria, they still would be hospitalized again because of chronic hepatic insufficiency and recurrent ascites and even die of massive upper gastrointestinal hemorrhage.

To have a comprehensive assessment of liver function postoperation, this study adopted indices like the Child–Pugh classification and hospital stay instead of liver function

failure rate and the Child–Pugh classification variation; as patients would be infused with plasma or albumin which affects serum albumin, while prealbumin concentration is not much affected by the treatment, and can reflect liver function impairment, the albumin item in the Child–Pugh classification was substituted by prealbumin. It demands further study to identify whether the modification in the Child–Pugh classification is consistent with the facts. In consideration that patients generally had metabolic disorders during the period of 5–7 days after liver resection, assessment of liver function was generally performed 7 days after the surgery.

We believe that the length of hospital stay indicates the situation of complications postoperation, so this study did not compare complications postoperation, but compared hospital stay instead. In consideration that group B had early mortality cases, which would have great influence on statistics, this study only calculated the correlation between spleen–liver volume ratio and assessment score of liver function and did not investigate the correlation between spleen–liver volume ratio and hospital stay.

The study also found that remnant liver volume was related to liver function postoperation, consistent to the report in literature [16], but the partial regression coefficient of the regression equation $Y=1.367+8.022X-0.06Z$ (where X is the spleen and liver volume, Y is the liver function assessment, and Z is the standard remnant liver volume) demonstrated that spleen–liver volume ratio had more influence on liver function assessment than standard remnant liver volume. Other investigators [17] believed that operation time and intraoperative blood loss determined the liver failure, different from the conclusion of our study; this might be because of the following: (1) different indices result in different conclusions, as previous studies analyzed risk factors of the surgery using the indices like liver failure ratio, jaundice, or ascites postoperation, while our study used modified the Child–Pugh classification system; (2) in our study, all patients underwent hemihepatic occlusion, and this might be one of the reasons that operation time was not a risk factor.

In summary, diagnosis of liver cirrhosis severity, assessment of liver server, and prediction of complications postoperation are inclined to take noninvasive method and integrated consideration of morphological and functional features in the future, and comparison of spleen–liver volume

ratio variation might become a valuable means for assessing compensation of liver function. Based on our results, if pre-operative imageological analysis indicates that spleen–remnant volume ratio is ≥ 1.2 , one-stage resection should be avoided and TACE and three-dimensional conformal radiotherapy should be considered, and if spleen–remnant volume ratio is ≤ 0.9 , then the operation is feasible.

Conflict of Interest No conflict of interest exists in the submission of this paper.

Ethical Standards All cases of cancer were pathologically confirmed. All patients provided written informed consent for the use of their tissues, and this study was approved by the hospital's Committee of Human Subject Protection.

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