Resected or Remnant Liver Volume and Standard Liver Volume Ratio in Patients with Major Hepatectomy

Atsushi NANASHIMA, Hiroyuki YAMAGUCHI, Shinichi SHIBASAKI, Shigeyuki MORINO, Yorihisa SUMIDA, Noboru IDE, Tsunenori TAGUCHI, Tohru NAKAGOE, Takeshi NAGAYASU

Division of Surgical Oncology, Department of Translational Medical Sciences, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan

   To clarify the relationship between resected (RSV) or remnant hepatic volume (RMV) in major hepatectomy, and standard liver volume (SLV) and its clinical significance, the RSV/SLV, RMV/SLV and the volume of regeneration (RGV)/RMV were examined in 41 patients including 19 with chronic hepatitis and 5 with obstructive jaundice who underwent lobectomy or extended lobectomy. The hepatic function was maintained in all patients. SLV was calculated by the body-surface area using Urata's formula. RGV was calculated by subtracting the RMV from the remnant liver volume at day 28 after hemi-hepatectomy. Measurement of the hepatic volume was performed by computed tomography. The means of RSV, RMV, RGV and SLV were 591 ± 173, 459 ± 119, 667 ± 129 and $1128 \pm 129 cm^3$, respectively. The means of RSV/SLV, RMV/SLV and RGV/RMV were 0.52 ± 0.14, 0.41 ± 0.12 and 1.54 ± 0.47, respectively. RGV was inversely correlated with RMV/SLV ($p < 0.001$) but not with the other parameters. RSV/SLV and RMV/SLV were not associated with long-term ascites and hepatic failure. The tendency of these results was similar in each patient with a normal liver, obstructive jaundice and chronic viral hepatitis. If the hepatic functional reserve is maintained, a liver with lower hepatic volume has potentially sufficient regeneration even in patients with an injured liver.

ACTA MEDICA NAGASAKIENSIA 48 : 125—128, 2003

Address Correspondence: Atsushi Nanashima, M.D.
Division of Surgical Oncology, Department of Translational Medical Sciences, Nagasaki University Graduate School of Biomedical Sciences, 1-7-1 Sakamoto, Nagasaki 852-8501, JAPAN
TEL: +81-95-849-7304, FAX: +81-95-849-7306
E-mail: a-nanasm@alpha.med.nagasaki-u.ac.jp

Introduction

   Recently, postoperative hepatic failure was remarkably reduced by the adequate evaluation of hepatic function before surgery and estimated resected liver volume.[1] Liver volume is usually measured by computed tomography (CT).[2,3] Volumetric measurement of the liver using CT (CT-vol) is used in the field of hepatic resection[3,4] or living related liver transplantation.[5] The hepatic volume after hepatectomy is associated with postoperative liver function and patient outcome. In partial liver transplantation, Urata et al. proposed standard liver volume (SLV) calculated by body-surface area (BSA)[6] to decide the safety limit of the graft liver. SLV was closely correlated with the actual liver volume and was useful in both adults and children. This indicator may be useful to evaluate the safety volume in patients undergoing hepatic resection.

   In this study, the ratio between the resected or remnant hepatic volume in major hepatectomy and SLV was examined, and the relationship with liver regeneration and post-hepatectomy complications after hepatic resection was investigated.

Patients and Methods

Patients

   The subjects were 41 patients who underwent hepatectomy in the Division of Surgical Oncology, Department of Translational Medical Sciences, Nagasaki University Graduate School of Biomedical Sciences (NUGSBS) between January 1996 and June 2003. They included 28 males and 13 females with a mean age of 60.5 ± 11.2 years ($\pm$SD, range, 28-77 years). Liver diseases included 17 hepatocellular carcinomas, 5 intrahepatic cholangiocarcinomas, 12 metastatic liver carcinomas, 4 bile duct carcinomas, a gallbladder carcinoma and 2 benign liver diseases. The background liver diseases

included normal liver function in 17, chronic viral liver diseases in 19 (cirrhosis in 3, including those caused in 10 by hepatitis B virus and 9 by hepatitis C virus) and obstructive jaundice in five.

In our hospital, the volume of liver to be resected is assessed before surgery based on the results of the indocyanine green retention rate at 15 minutes (ICG R15) using Takasaki's formula[7] and liver activity at 15 minutes (LHL15) of ^{99m}Tc-GSA scintigraphy. The estimated resected liver volume, excluding tumor volume (cm^3), is measured by CT volumetry.[3, 4] Basically, when the permitted resected volume of the liver calculated by Takasaki's formula[7] was greater than the estimated resected volume of the liver, the planned hepatectomy was performed. LHL15 more than 0.875 was thought to be safety for major hepatectomy by our preliminary data (not published). Lobectomy was performed in 24 patients and extended lobectomy in 17 patients. Post-operative complications included long-term ascites in 22 (54%) (representing massive ascites even under treatment with diuretics for more than two weeks) and hepatic failure in 6 (15%) (represented by total bilirubin > 3 mg/dl at day 14 postoperatively or post-operative death with no other cause). The study design was approved by the Ethics Review Board of our institution and a signed consent was obtained from each subject. Data were retrieved from both the anaesthetic and patient charts plus the NUGSBS database for the duration of the initial hospitalization following hepatectomy.

Volumetric measurement by CT and SLV calculation

The hepatic area (cm^2) was measured using contrasted CT. Serial transverse scans at 0.7-1.0 cm intervals were recorded onto a personal computer. Using NIH Image (Scion Co., ML), the actual area without tumors and large vessels in each liver slice was traced and measured. The hepatic volume (cm^3) was calculated as the sum of the target area. The estimated resected volume (RSV) and remnant volume (RMV) of the liver were measured before hepatectomy. The remnant liver at day 28 after major hepatectomy was measured and the regenerating volume (RGV) was calculated by subtracting the RMV from the remnant liver volume after hepatectomy. The SLV was calculated based on BSA described by Urata et al. using the following formula[6]:
SLV (mL) = 706.2 x BSA (m2) + 2.4
The parameters of RSV/SLV and RMV/SLV were applied for this analysis.

Statistical analysis

All continuous data are expressed as the mean ± SD. Data of different groups were compared using one-way analysis of variance (ANOVA) and examined using Student's t-test. Correlations between two parameters were examined by calculating the Pearson's correlation coefficient. A two-tailed P value < 0.05 was considered significant. StatView Software for Windows, Version 5.0 (SAS Institute, Inc., Cary, NC) was used for all statistical analyses.

RESULTS

The mean values of RSV, RMV, the remnant liver volume after hepatectomy and SLV were 591±173cm^3 (ranging, 260-1014 cm^3), 459±119cm^3 (ranging, 252-675 cm^3), 667±129cm^3 (ranging, 483-992 cm^3) and 1128±129cm^3 (ranging, 875-1387 cm^3), respectively. The mean values of RSV/SLV, RMV/SLV and RGV/RMV were 0.52±0.14 (ranging, 0.26-0.95), 0.41±0.12 (ranging, 0.19-0.63) and 1.54±0.47 (ranging, 0.88-2.99), respectively.

RMV and RSV were not significantly correlated with RGV (r=0.312, p=0.077 and r=0.043, p=0.811). RGV was significantly correlated with RMV/SLV (Figure 1) but was not correlated with patient age, blood loss, blood transfusion, conventional liver functions, BSA and RSV/SLV (Table 1 and Figure 1). These correlation results were similar despite the background liver diseases (Figure 1).

Table 1. Correlation between RGV and clinicopathologic features

	RGV (r)	Significance
Age	0.001	0.995
BSA	0.254	0.155
Blood loss (ml)	0.201	0.261
Blood transfusion (ml)	0.114	0.526
LHL15 by ^{99m}Tc-GSA	0.154	0.401
Alanine aminotransferase (IU/L)	0.019	0.916
Platelet count (/mm^3)	0.137	0.448
Prothrombin activity (per cent)	0.232	0.195
Total cholesterol (mg/dl)	0.200	0.267

R=0.029(R^2 =0.001)
Y = 51.53 + .008 * X
P=0.871

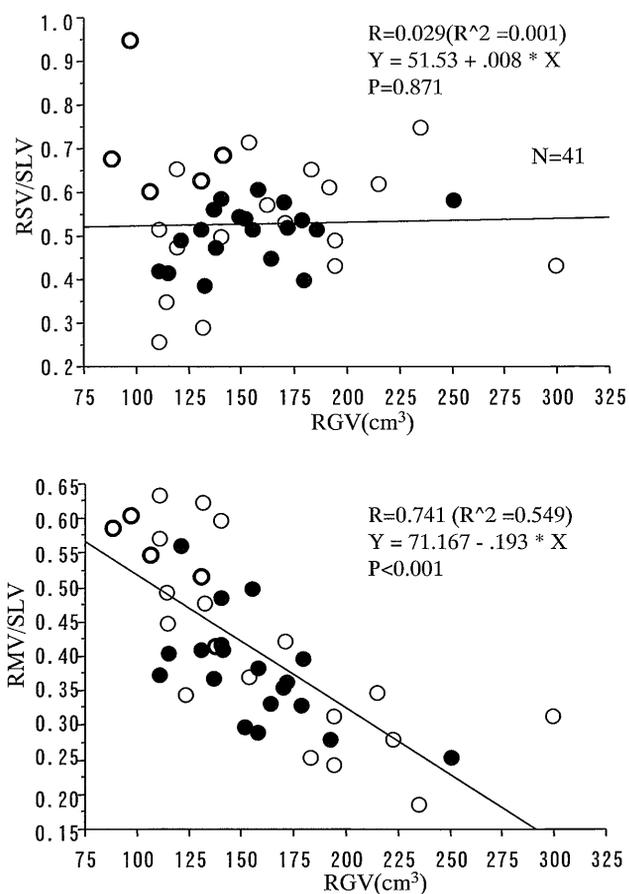N=41

R=0.741 (R^2 =0.549)
Y = 71.167 - .193 * X
P<0.001

Figure 1. Correlation between resected liver volume/standard liver volume (RSV/SLV) or remnant liver volume/SLV (RMV/SLV), and regenerated volume (RGV). The thin open circle shows a normal liver, the thick open circle shows obstructive jaundice and the closed circle shows chronic hepatitis or cirrhosis.

Table 2. Relationship between post-hepatectomy complications and each parameter of hepatic volume

	RSV/SLV	P value	RMV/SLV	P value	RGV/RMV	P value
Prolonged ascites						
No	0.49±0.14		0.43±0.12		1.62±0.58	
Yes	0.55±0.14	0.181	0.40±0.12	0.525	1.49±0.59	0.498
Hepatic failure						
No	0.52±0.13		0.41±0.11		1.55±0.46	
Yes	0.55±0.08	0.714	0.43±0.18	0.791	1.31±0.45	0.390

Table 2 shows the relationship between each value and the post-hepatectomy complications. RSV/SLV and RMV/SLV were not significantly associated with long-term ascites or hepatic failure. This tendency was similar despite the background liver diseases.

Discussion

The balance between hepatic functional reserve and the extent of hepatic resection is important in patients with an injured liver.[1] Morbidity and mortality after hepatectomy have been reduced by the appropriate diagnosis of tumor growth, precise estimation of preoperative hepatic function by ICGR15 or ^{99m}Tc-GSA scintigraphy, and improvement of operative procedure or perioperative treatments.[8] However, in 140 patients who have undergone hepatic resection in our series since 1996, long-term ascites was frequent (45 patients, 32%) despite careful management of dry-side hydration and the use of diuretics. Nine patients (6%) had hyperbilirubinemia or hepatic failure and two patients died during the initial hospital stay after hepatectomy. Therefore, the determination of cause of the above hepatic complications is still important for our liver surgeons.

Remnant liver volume is important to maintain hepatic function for regeneration of the liver.[9] Using our protocol, the ratio of remnant liver has been decided by the permitted volume of Takasaki's criteria using ICGR15[7] since 1994. The morbidity and mortality rate in our series has remarkably improved compared to that before 1994. In this study, we note the relationship between RMV and SLV calculated by BSA.[6] We usually evaluate the rate of remnant liver volume from the total liver excluding the tumor area and large vessels. Therefore, the total hepatic volume is not the initial hepatic volume before having a tumor. According to the increased tumor size, the volume of the intact liver does not necessarily increase. We hypothesized that the initial hepatic volume in each person in this study may determine the safety limit of RMV. On the other hand, the regeneration volume (RGV) of the remnant liver may also be an important factor to get over the deterioration of hepatic function after hepatectomy. In this study, RMV/SLV was the only associated parameter and the regenerating ability of the remnant liver should be different in each person. In living-related liver transplantation, the donated hepatic volume compared to SLV is a reliable parameter of successful the transplantation.[6] Fan et al. reported that the residual liver volume exceeds 30% of the total liver volume was safe for adult-to-adult liver transplantation.[10] RMV/SLV is a useful parameter of expected liver regeneration after major hepatectomy as well and hepatic fibrosis or sinusoidal damage is closely correlated with hepatic regeneration.[11, 12] In the rat liver, the 90% hepatectomy is available and, however, this extent of hepatic resection is critical for human.[13] Up to now, the precise

data of limit of hepatic resection in human has not been reported. We consider that the range between 70 and 80% hepatectomy may be the border of hepatic failure by our experiences although we have no supporting data. In the present series, a male-patient with normal liver underwent approximately 80% hepatectomy and, however, he had no severe complications. Otherwise patients underwent hepatectomy less than 75%. It should be very difficult to establish the limit of hepatectomy in patients with various background liver diseases although the donor liver usually has the normal liver function or the mild steatosis. Our results indicate that reduced remnant liver after major hepatectomy retains full potential for liver regeneration even in chronic hepatitis and obstructive jaundice, if the hepatic functional reserve is maintained. However, we could not show the limit of hepatic resection by the present data.

Excessive liver resection induces hepatic failure or other complications.[14, 15] In these results, RSV/SLV and RMV/SLV were not associated with post-hepatectomy complications. Basically, the permitted volume according to hepatic function was established in all patients in this study and, therefore, RMV/SLV may be of limited safety in our series using our protocol. Our previous report[16] and the recent analysis (unpublished data) in a large number of patients showed that the serum hyaluronic acid level was the most significant predictor of postoperative hepatic failure or long-term ascites by the multivariate analysis, which reflect the degree of hepatic fibrosis and sinusoidal endothelial cell damage.

In conclusion, the remnant volume after major hepatectomy and the standard liver volume ratio were negatively correlated with hepatic regeneration and any parameters were not associated with post-hepatectomy complications. If the hepatic functional reserve is maintained, a lower volume of remnant liver may have sufficient regeneration potential even in patients with an injured liver.

References

1. Miyagawa S, Makuuchi M, Kawasaki S, Kakazu T: Criteria for safe hepatic resection. Am J Surg 169:589,1995
2. Chen MF, Hwang TL, Hung CF: Human liver regeneration after major hepatectomy: A study of liver volume by computed tomography. Ann Surg 213:227, 1991
3. Ogasawara K, Une Y, Nakajima Y, Uchino J: The significance of measuring liver volume using computed tomographic images before and after hepatectomy. Jpn J Surg 25:43, 1995
4. Kubota K, Makuuchi M, Kusaka K, Kobayashi T, Miki K, Hasegawa K, Harihara Y, Takayama T: Measurement of liver volume and hepatic functional reserve as a guide to decision-making in resectional surgery for hepatic tumors. Hepatology 26:1176, 1997
5. Higashiyama H, Yamaguchi T, Mori K, Nakano Y, Yokoyama T, Takeuchi T, Yamamoto N, Yamaoka Y, Tanaka K, Kumada K: Graft size assessment by preoperative computed tomography in living related partial liver transplantation. Br J Surg 80:489, 1993
6. Urata K, Kawasaki S, Matsunami H, Hashikura Y, Ikegami T, Ishizone S, Momose Y, Komiyama A, Makuuchi M: Calculation of child and adult standard liver volume for liver transplantation. Hepatology 21:1317, 1995
7. Takasaki T, Kobayashi S, Suzuki S, Muto H, Marada M, Yamana Y, Nagaoka T: Predetermining postoperative hepatic function for hepatectomies. Int Surg 65:309, 1980
8. Jones SM, Roh MS: Results of surgical resection for hepatocellular carcinoma. Cancer Treat Res 109:59, 2001
9. Mann DV, Lam WW, Hjelm NM, So NM, Yeung DK, Metreweli C, Lau WY: Human liver regeneration: hepatic energy economy is less efficient when the organ is diseased. Hepatology 34:557, 2001
10. Fan ST, Lo CM, Liu CL, Yong BH, Chan JK, Ng IO: Safety of donors in live donor liver transplantation using right lobe grafts. Arch Surg 135:336, 2000
11. Miyazaki S, Takasaki K, Yamamoto M, Tsugita M, Otsubo T: Liver regeneration and restoration of liver function after partial hepatectomy: the relation of fibrosis of the liver parenchyma. Hepatogastroenterology 46:2919, 1999
12. Ogata T, Okuda K, Ueno T, Saito N, Aoyagi S: Serum hyaluronan as a predictor of hepatic regeneration after hepatectomy in humans. Eur J Clin Invest 29:780, 1999
13. Sakaguchi K, Takeuchi E, Suzuki M, Oda K, Nagino M, Nimura Y, Yoshida S: DNA polymerases and Ki-67 nuclear antigen are induced in correlation with the resected mass of rat liver up to 90%.Langenbecks Arch Surg 385:135, 2000
14. Moser M, Zhang M, Gong Y, Johnson J, Kneteman N, Minuk GY: Effect of preoperative interventions on outcome following liver resection in a rat model of cirrhosis. J Hepatol 32:287, 2000
15. Abdalla EK, Hicks ME, Vauthey JN: Portal vein embolization: rationale, technique and future prospects. Br J Surg 88:165, 2001
16. Nanashima A, Yamaguchi H, Shibasaki S, Sawai T, Yamaguchi E, Yasutake T, Tsuji T, Jibiki M, Nakagoe T, Ayabe H: Measurement of serum hyaluronic acid level during the perioperative period of liver resection for evaluation of functional liver reserve. J Gastroenterol Hepatol 16:1158, 2001