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

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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 ± 129 cm³, 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.

Introduction

Recently, postoperative hepatic failure was remarkably reduced by the adequate evaluation of hepatic function before surgery and estimated resected liver volume. Liver volume is usually measured by computed tomography (CT). Volumetric measurement of the liver using CT (CT-vol) is used in the field of hepatic resection or living related liver transplantation. 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) 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 (± 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 and liver activity at 15 minutes (LHL15) of 99mTc-GSA scintigraphy. The estimated resected liver volume, excluding tumor volume (cm³), is measured by CT volumetry. Basically, when the permitted resected volume of the liver calculated by Takasaki's formula 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 (cm²) 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 (cm³) 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:

\[ \text{SLV (mL)} = 706.2 \times \text{BSA (m2)} + 2.4 \]

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 ± 173 cm³ (ranging, 260-1014 cm³), 459 ± 119 cm³ (ranging, 252-675 cm³), 667 ± 129 cm³ (ranging, 483-992 cm³) and 1128 ± 129 cm³ (ranging, 875-1387 cm³), 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**

<table>
<thead>
<tr>
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<th>RGV (r)</th>
<th>Significance</th>
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<tbody>
<tr>
<td>Age</td>
<td>0.001</td>
<td>0.995</td>
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<td>BSA</td>
<td>0.254</td>
<td>0.155</td>
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<td>Blood loss (ml)</td>
<td>0.201</td>
<td>0.261</td>
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<td>Blood transfusion (ml)</td>
<td>0.114</td>
<td>0.526</td>
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<td>LHL15 by 99mTc-GSA</td>
<td>0.154</td>
<td>0.401</td>
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<td>Alanine aminotransferase (IU/L)</td>
<td>0.019</td>
<td>0.916</td>
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<tr>
<td>Platelet count (mm³)</td>
<td>0.137</td>
<td>0.448</td>
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<tr>
<td>Prothrombin activity (per cent)</td>
<td>0.232</td>
<td>0.195</td>
</tr>
<tr>
<td>Total cholesterol (mg/dl)</td>
<td>0.200</td>
<td>0.267</td>
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</table>
Figure 1. Correlation between resected liver volume/stan-
dard 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 ob-
structive jaundice and the closed circle shows chronic hepati-
tis or cirrhosis.

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

<table>
<thead>
<tr>
<th>Parameter</th>
<th>RSV/SLV P value</th>
<th>RMV/SLV P value</th>
<th>RGV/RMV P value</th>
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<tr>
<td>Prolonged ascites</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>No</td>
<td>0.49±0.14</td>
<td>0.43±0.12</td>
<td>1.62±0.58</td>
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<td>Yes</td>
<td>0.55±0.14</td>
<td>0.181</td>
<td>0.40±0.12</td>
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<tr>
<td>Hepatic failure</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>0.52±0.13</td>
<td>0.41±0.11</td>
<td>1.55±0.46</td>
</tr>
<tr>
<td>Yes</td>
<td>0.55±0.08</td>
<td>0.714</td>
<td>0.43±0.18</td>
</tr>
</tbody>
</table>

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. Morbidity and mortality after
hepatectomy have been reduced by the appropriate di-
agnosis of tumor growth, precise estimation of preop-
erative hepatic function by ICGR 15 or 99mTc-GSA
scintigraphy, and improvement of operative procedure
or perioperative treatments. However, in 140 pa-
tients 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 pa-
tients 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 he-
patic function for regeneration of the liver. Using
our protocol, the ratio of remnant liver has been de-
cided by the permitted volume of Takasaki's criteria
using ICGR15 since 1994. The morbidity and mortal-
ity rate in our series has remarkably improved com-
pared to that before 1994. In this study, we note the
relationship between RMV and SLV calculated by
BSA. 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 vol-
ume 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 he-
patic 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 trans-
plantation, the donated hepatic volume compared to
SLV is a reliable parameter of successful the trans-
plantation. Fan et al. reported that the residual liver
volume exceeds 30% of the total liver volume was safe
for adult-to-adult liver transplantation. RMV/SLV is
a useful parameter of expected liver regeneration after
major hepatectomy as well and hepatic fibrosis or si-
nusoidal damage is closely correlated with hepatic re-
generation. In the rat liver, the 90% hepatectomy is
available and, however, this extent of hepatic resec-
tion is critical for human. 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. 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 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

9. Mann DV, Lam WW, Hjelm NM, So NM, Young DK, Metreweli C, Lau WY: Human liver regeneration: hepatic energy economy is less efficient when the organ is diseased. Hepatology 34:557, 2001