Calculation of Child and Adult Standard Liver Volume for Liver Transplantation

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Despite refinements in surgical techniques for liver transplantation, liver size disparity remains one of the most common problems in pediatric patients. Optimal liver graft size remains unknown and the volume of diseased liver in the recipient is not indicative of the volume (standard liver volume [LV]) optimal for the recipient's metabolic demands. To establish a formula for calculating the standard LV in the pediatric and adult populations for liver transplantation, whole LVs were measured using computed tomography (CT) in 96 patients (65 pediatric and 31 adolescent or adult subjects) with normal liver whose disease conditions did not seem to affect body weight (BW) or LV. In the 96 subjects, the ratio of estimated LV to BW decreased gradually as age increased until approximately 16 years, when it started to level off. On the other hand, there seemed to be a directly proportional relationship between the estimated LV *in vivo* and body surface area (BSA) (r = .981; r^2 = .962; $P < .0001$) in the subjects as a whole, and the formula, LV (mL) = 706.2 × BSA (m^2) + 2.4, was established from the measured data by simple regression analysis. Another predicting equation, LV (mL) = 2.223 × BW $(kg)^{0.426}$ × body height (BH) $(cm)^{0.682}$, was produced by multiple regression analysis (r^2 = .969; $P < .0001$). Considering its simplicity of use, we adopted the first formula for predicting standard LV in an individual patient. (HEPATOLOGY 1995;21:1317-1321.)

Because of the shortage of grafts for pediatric recipients requiring liver transplantation, procedures using reduced-size grafts have been used with increasing frequency.[1-3] Based on clinical experience of such graft size modifications, new techniques using split-liver grafts[4] and partial liver grafts from living adult donors[5,6] have been introduced successfully for pediatric liver transplantation. Furthermore, the transplantation of small liver grafts from cadaveric child donors[7] or partial grafts from living donors (Hashikura Y, et al, Lancet 1994;343:1233-1234, Correspondence) into adult patients has been reported.

In these situations, some of the postoperative complications that occur are related to the disproportionate size of the liver graft in comparison with the recipient's native liver volume (LV). When a large-for-size graft is transplanted into a small recipient, hepatic artery or portal vein thrombosis may occur caused by graft compression and poor perfusion.[8-10] On the other hand, small-for-size grafts may cause primary nonfunction and graft dysfunction[11] and increase the risk of rejection.[12] To minimize these complications associated with graft size disparity, the LV (standard LV) optimal for the metabolic demands of an individual patient needs to be estimated preoperatively because accurate assessment of this parameter can provide useful information for selection of the graft reduction procedure in reduced-size liver transplantation or for selection of the type of donor hepatectomy in living-related liver transplantation (LRLT).[13,14]

The aim of the present study was to establish a standard relationship between recipient body size and LV.

PATIENTS AND METHODS

LV and Weight Determinations in LRLT Recipients. Nine male and 10 female pediatric patients ranging in age from 5 months to 15 years with an average age of 5.3 ± 5.0 years underwent LRLT for end-stage liver disease (14 cases of biliary atresia, 4 cases of postnecrotic cirrhosis, and 1 case of postnecrotic cirrhosis with hepatocellular carcinoma) at the First Department of Surgery, Shinshu University, between June 1990 and May 1994.

These 19 children were subjected to the whole LV measurement using computed tomography (CT) before surgery. Serial abdominal transverse CT taken at 0.8- or 1.0-cm intervals including the segment between the dome of the liver and the most inferior part of the organ were used to calculate the LV by the method of Heymsfield et al[15] with minor modifications. The perimeter of the whole liver was outlined on each slice using a track ball device, and the enclosed area was measured on an Apple Macintosh IIci computer (Apple Japan, Inc., Tokyo, Japan) using the National Institutes of Health Image 1.41 public domain program. We added these areas together and multiplied the total by the slice width to assess the total LV.

Abbreviations: LV, liver volume; LRLT, living-related liver transplantation; CT, computed tomography; BW, body weight; BH, body height; BSA, body surface area; DRWR, donor-to-recipient weight ratio.

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The recipient's liver was weighed after the attached ligaments and gallbladder had been dissected and removed. The weight determination was performed without knowledge of the previously estimated volume calculated from the CT images. The absolute value of liver weight was considered to be equivalent to the actual volume because the density of the liver is nearly the same as that of water.[16]

LV Determinations in Subjects With Normal Liver. A total of 61 male and 35 female patients, ranging in age from 1 month to 27 years with an average age of 11.1 ± 8.8 years, were investigated retrospectively for this study. During the period between April 1989 and February 1994, these patients had undergone serial abdominal CT scans at Shinshu University Hospital or affiliated hospitals for the following reasons: abdominal pain, fever, constipation, or macrohematuria of unknown cause; abdominal trauma; localization of tumors in patients showing increased levels of urinary vanillylmandelic acid; screening and staging of malignancies; determination of segmental LV for preoperative assessment as LRLT donors. None of the patients studied showed any liver abnormalities at CT examination or at follow-up (Table 1).[17,18] All of the children were between the 5th percentile and the 95th percentile on the standard physical growth chart.[19] Patients with malignant tumors that appeared to weigh more than 0.5% of total body weight (BW) were excluded. For patients with malignancies, we calculated the LV using CT films taken before surgical treatment or chemotherapy.

BW and body height (BH) recorded at the time of CT examination were used for calculating the body surface area (BSA). Because the DuBois formula tends to underestimate BSA in infants,[20] BSA was calculated using the equation of Haycock et al[21]: BSA (m^2) = BW (kg)$^{0.378}$ × BH (cm)$^{0.3964}$ × 0.024265 for children who weighed less than 15 kg, and that of DuBois and DuBois[22] for children and adults who weighed 15 kg or more: BSA (m^2) = BW (kg)$^{0.425}$ × BH (cm)$^{0.725}$ × 0.007184, as used by Whitington et al.[23]

LVs were measured from CT scan films using the technique described above. Moreover, the ratio of LV to BW (LV/BW ratio) and the ratio of LV to BSA (LV/BSA ratio) in the infant group (<2 years) were compared with those in the adolescent/adult (≥16 years) group. The LV/BSA ratio was also compared between males and females.

TABLE 1. Reasons for Abdominal CT Scanning in 96 Patients

Condition	No. of Patients
Abdominal trauma	33
Abdominal pain	20
Neuroblastoma (stage 1, 2A, 4S)*	16
Increased urinary VMA level	9
Abdominal mass	4
Constipation	3
LRLT donor	2
Macrohematuria	2
Fever	2
Non-Hodgkin's lymphoma (stage I)†	2
Teratoid tumor	2
Total	96

NOTE. In all of the cases, hepatic involvement was excluded.
Abbreviation: VMA, vanillylmandelic acid.
* Staging in accordance with Brodeur et al.[17]
† Staging in accordance with Murphy et al.[18]

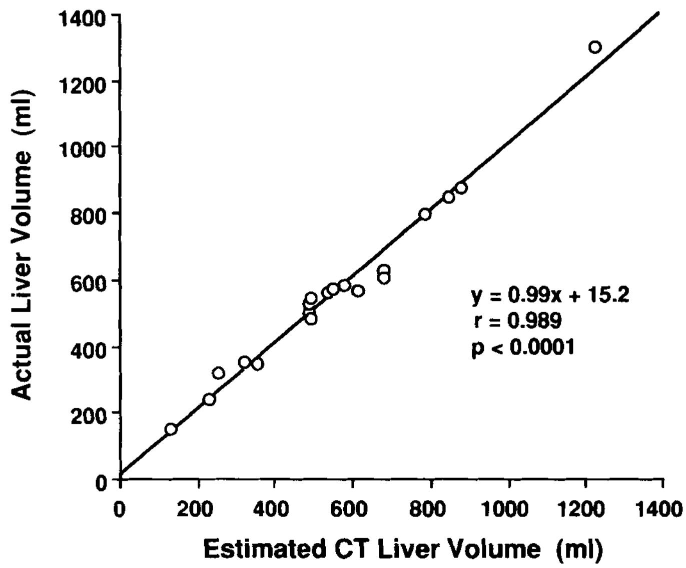

FIG. 1. Relationship between CT-estimated and actual LVs in LRLT recipients.

Statistical Analysis. The actual LVs were plotted against the estimated CT liver volumes in the 19 LRLT recipients. The calculated CT LVs were plotted against age, BH, BW, and BSA in the 96 subjects. The LV/BW ratios were also plotted against age. A microcomputer-based program of least-squares regression was used to establish possible linear relationships between the dependent and individual independent variables. Then, analysis of residuals was used to evaluate the fit of the regression equations, and multiple regression analysis was used in the prediction equation for independent variables as necessary. The significance of regressions was determined by F test. The significance of differences between means was determined by Student's *t*-test for unpaired populations. The null hypothesis was rejected at a *P* value of less than .05. Data are presented as means ± SD except where indicated.

RESULTS

Relationship Between Actual Volume and Estimated CT Volume of Pediatric Recipients' Livers. The weight of the 19 livers removed at surgery averaged 568 ± 260 g with a range of 151 to 1,300 g. The estimated CT volume of these 19 livers averaged 560 ± 261 mL, and ranged from 131 to 1,230 mL. The differences between radiographically determined and actual organ volumes, expressed as percentage of actual volume, ranged from −12.4% to 20.5%, with a mean of 2.4 ± 7.8%. The relationship between actual volume and CT-estimated volume for the 19 livers is shown in Fig. 1 (r = .989; P < .0001). As a whole, the CT-calculated LV was considered to have been estimated with acceptable accuracy on comparison with the actual LV in the pediatric population.

Standard LV in Children and Adults. The calculated CT volume of the 96 normal livers averaged 764 ± 380 mL (range, 138 to 1,544 mL), with an average BW of 33.8 ± 21.6 kg (4.0 to 78.0 kg), an average BH of 126.6 ± 40.9 cm (53.6 to 178.0 cm), and an average BSA of

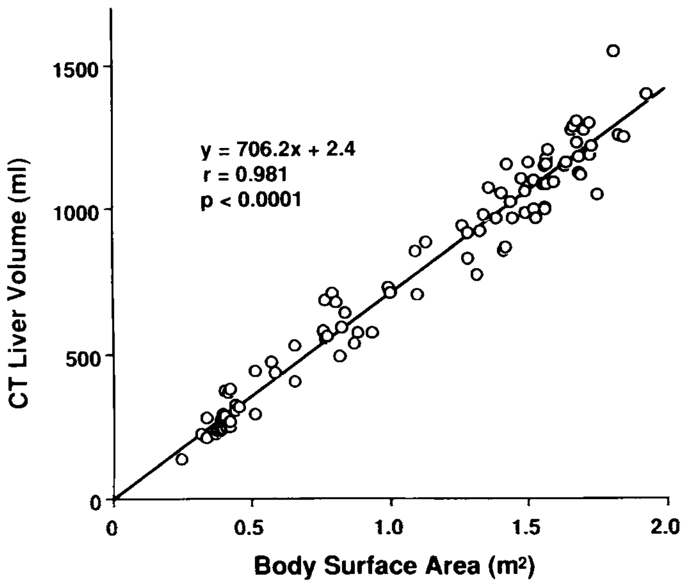

FIG. 2. Relationship between BSA and CT-estimated LV in 96 subjects with normal livers.

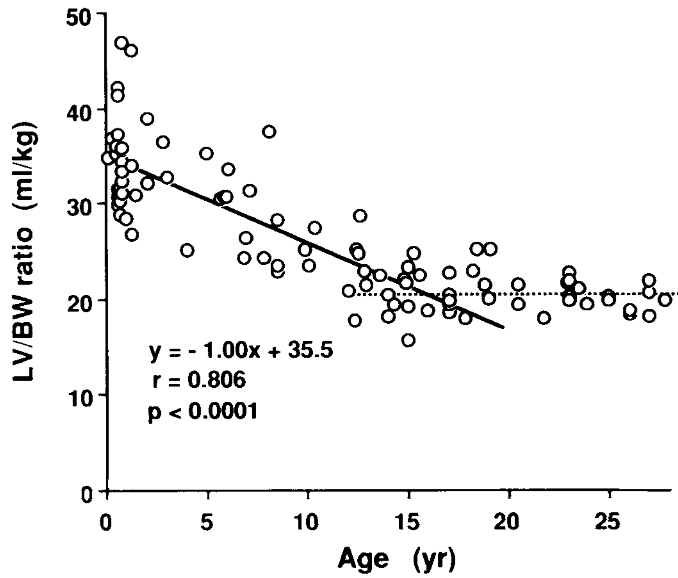

FIG. 3. Relationship between age and LV/BW ratio in 96 subjects with normal liver. A significant negative correlation was observed in subjects younger than 16 years of age.

1.078 ± 0.528 m^2 (0.248 to 1.935 m^2). The estimated CT LV *in vivo* was significantly related to age (r = .905; P < .0001), BW (r = .972, P < .0001), BH (r = .968; P < .0001), and BSA (r = .981; P < .0001). The analysis of residuals demonstrated that liver size *in vivo* was correlated most linearly with BSA among the four parameters. On the basis of these results, the following equation was derived from our data by linear regression analysis (Fig. 2) to predict the LV for normal children and adults:

$$\text{LV (mL)} = 706.2 \times \text{BSA (m}^2) + 2.4.$$

The value of the coefficient of determination, "r^2," was .962. The size of the coefficient of determination, "adjusted R squared," which one would expect to see in another group of application, was .962.

Another equation for predicting the liver size *in vivo* was established from our data by multiple regression analysis. BH and BW were taken as independent variables, and calculated CT LV as the dependent; the relationship was analyzed in the form:

$$\log \text{(liver volume)} = x \log \text{BW} + y \log \text{BH} + \log z \text{ (equivalent to: liver volume} = \text{BW}^x \times \text{BH}^y \times z).$$

The least squares best fit for this equation yielded the formula:

$$\text{liver volume (mL)} = \text{BW (kg)}^{0.426} \times \text{BH (cm)}^{0.682} \times 2.223 \ (r^2 = .969;\ \text{adjusted } R^2 = .968;\ P < .0001).$$

A plot of LV/BW ratio versus age is shown in Fig. 3. The LV/BW ratio decreased as age increased, until approximately 16 years, when it began to level off. There was a significantly negative correlation between LV/BW ratio and age in subjects younger than 16 years of age with normal liver (r = .806; P < .0001). The mean value of LV/BW ratio was 34.5 ± 5.1 mL/kg in infants (younger than 2 years of age), which was significantly larger than the value in adolescents and adults (≥16 years of age; 20.5 ± 1.9 mL/kg; P < .001) (Table 2).

On the other hand, the LV/BSA ratio averaged 707.6 ± 79.8 mL/m^2 in the subjects as a whole. It was 687.9 ± 98.6 mL/m^2 in infants (younger than 2 years of age), and 712.0 ± 51.2 mL/m^2 in adolescents and adults (≥16 years of age) (Table 2). The ratios in males and females were 709.2 ± 73.8 mL/m^2 and 705.0 ± 90.5 mL/m^2, respectively. No significant differences in the LV/BSA ratio were observed between the infant and adolescent/adult groups (P > .1) or between males and females (P > .1).

The mean LVs in adolescent/adult (≥16 years of age) males and females were 1,225 ± 124 mL and 1,057 ± 108 mL, respectively.

TABLE 2. Volumetric Data in the Infant and Adolescent/Adult Groups

	Infant (<2 yr)	Adolescent/ Adult (≥16 yr)
No.	26	31
Sex (male/female)	19/7	17/14
BW (kg)*†	8.0 ± 1.4	56.5 ± 8.5
BH (cm)*†	69.4 ± 5.9	164.8 ± 8.1
BSA (m^2)*†	0.398 ± 0.049	1.613 ± 0.513
CT liver volume (mL)*†	274 ± 53	1149 ± 142
LV/BW ratio (mL/kg)*†	34.5 ± 5.1	20.5 ± 1.9
LV/BSA ratio (mL/m^2)*	687.9 ± 98.6	712.0 ± 51.2

* Data expressed as mean ± SD.
† SD (P < .001) between the two groups.

DISCUSSION

For reduced-size liver transplantation, the donor-to-recipient weight ratio (DRWR) has been widely used as a criterion for roughly estimating the graft size to fit the recipient's abdominal cavity.[2,3,24-26] However, whole-liver weight based on autopsy data is reported to be approximately 5% of BW at birth but only 2% in adults.[27] As described in this article, the LV/BW ratio was found not to be constant during the growing period. The ratio decreased gradually as age increased until approximately 16 years, and then reached a plateau (Fig. 3). Patients who require liver transplantation are often outside standard physical growth range for the corresponding age because various degrees of nutritional deficit are usually associated with end-stage liver disease.[28,29] Under these circumstances, liver size cannot be predicted only on the basis of the recipient's BW and/or age.

BSA is another parameter used frequently in physiology and clinical medicine to normalize measures of biological function with respect to variations in body size and conformation. Its use is based on some metabolic principles that can also apply to children. Caloric needs, total body water, and extracellular water are more closely related to BSA than to BW.[30,31] Therefore, we considered that the liver mass required to meet the metabolic demands of the patient should correlate more closely with BSA than with other parameters such as BW, BH, or age. In spite of the significant disparity between the infant and adolescent/adult groups in BH, BW, BSA, LV, and LV/BW ratio, there was no difference in LV/BSA ratio between them (Table 2). Another finding was that males and females had essentially the same LV for a given value of BSA. This is in agreement with the results of autopsy measurements in adults reported by DeLand et al.[32]

To predict liver size in proportion to body size, we first computed a simple regression model for BSA:

$$\text{LV (mL)} = 706.2 \times \text{BSA (m}^2\text{)} + 2.4.$$

We then calculated another formula for predicting liver volume using multiple regression analysis with two independent variables, BW and BH, without considering age:

$$\text{LV (mL)} = 2.223 \times \text{BW (kg)}^{0.426} \times \text{BH (cm)}^{0.682}.$$

As described by Haycock et al[21] and DuBois and DuBois,[22] BSA can also be calculated from two independent control variables for body size, i.e., BW and BH, and thus our two models remain essentially the same. And yet the values of "r^2," the coefficient of determination, and adjusted R^2, the size of the coefficient of determination one would expect to see in another group of application, are almost the same in the two models. Considering its simplicity of use, we adopted the first formula for predicting the standard LV for liver transplantation.

Most previous reports based on autopsy measurements give the range of liver weight for males or females and the ratios of organ weight to BW according to age.[33-35] To our knowledge, there has been only one report describing the relationship between liver weight and BSA in adults,[32] and no data are available on the definitive relationship between liver size and BSA in a pediatric population.

One autopsy study showed that liver weight in Japanese adults was lower than in European and American adults, whereas the liver weight to BW ratio in Japanese adults was slightly higher.[33] The investigators suggested that these findings might be caused by differences in body proportion between the two groups.

The values of LV we obtained from CT scans *in vivo* are somewhat small in comparison with those of liver weight in previous autopsy studies. The values of organ weight at autopsy in normal Japanese adolescent/adult (16 to 25 years of age) males and females averaged 1,483 and 1,159 g, respectively,[33] whereas in our study (16 to 27 years of age), they were 1,225 and 1,057 mL, respectively. The ratio of liver weight to BW in Japanese adolescents and adults (17 to 25 years of age) is approximately 26 g/kg from autopsy measurements,[33] compared with 20.5 mL/kg from our present data (Table 2). The reason for this is not clear, but the following factors may be significant. Usually in a legal postmortem examination, data from autopsy studies include the weight of the gallbladder, the attached ligaments, and the hepatic vena cava, whereas in our study these were excluded; also previous autopsy studies dealt with subjects who had died of acute causes involving some cases of shock such as cardiac failure and traffic accidents, which might have altered the liver weight through mechanisms associated with shock-related hepatic congestion.[36,37] Blood accumulation in the liver, which represents one of these postmortem alterations, may affect the weight of the organ in autopsy measurements.

In summary, total LV was estimated from CT scan images with acceptable accuracy in comparison with the actual volume of the organ obtained in a pediatric population. The liver volume to BW ratio is not constant during the growth period. However, the relationship between total LV and BSA in the pediatric and adult population can be established, and should provide useful information for preoperative estimation of standard LV in recipients and help the planning of liver transplantation.

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