Estimation of standard liver volume for liver transplantation in the Korean population.

Hee Chul Yu,1,5 Heecheon You,2 Ho Lee,3 Zhe-Wu Jin,1 Jang Il Moon,4 and Baik Hwan Cho1,5

1Department of Surgery, Chonbuk National University Medical School, Jeonju, Jeonbuk 561-180, Korea (R.O.K.)
2Department of Industrial Engineering, Pohang University of Science and Technology, Pohang, Kyungbuk 790-784, Korea (R.O.K.)
3Department of Forensic Medicine, National Institute of Scientific Investigation, Daejeon 305-348, Korea (R.O.K.)
4Division of Liver/GI Transplant, Department of Surgery, University of Miami School of Medicine, Miami, FL 33136, USA
5Research Institute of Clinical Medicine, Chonbuk National University Hospital, Jeonju, Jeonbuk 561-712, Korea (R.O.K.)

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Correspondence author:

Name                 Prof. Baik Hwan Cho
Address              Department of Surgery, Chonbuk National University Hospital
                     634-18, Keumam-dong, Dukjin-gu, Jeonju, Jeonbuk 561-712, Korea (R.O.K.)
Tel.                 +82-63-250-1579
Fax.                 +82-63-271-6197
E-mail:             chobh@chonbuk.ac.kr

Abbreviations:

LV, liver volume; BSA, body surface area; LW, liver weight; LD, liver density; BH, body height; BW, body weight; CT, computed tomography
Abstract

The standard liver volume (LV) of a recipient is estimated in liver transplantation to determine the minimum LV necessary for the recipient. Simple linear formulas of LV estimation were developed for the Japanese and Caucasian populations. The present study examined the applicability of the reported formulas to the Korean population. Liver density (LD) was determined by analyzing 24 healthy livers. Data of liver weight (LW), body weight (BW), body height (BH), body surface area (BSA), and age were obtained from 652 postmortem examination reports (age, 42.4 ± 16.5 years) showing normal livers. The LV of each subject was estimated by LW/LD and the relationships between LV, BW, BSA, and age were analyzed. LD was 1.04 ± 0.07 kg/L. The ratio of LV/BW decreased as age increased in the children but became leveled off in the adults; the rate of increase in LV along BSA in BSA < 1.2 m² appeared less than the corresponding rate in BSA ≥ 1.2 m². The Japanese formula produced underestimates (226.9 ± 289.4 mL) for the Korean population, while the Caucasian formula produced random errors (-30.64 ± 281.5 mL). A better LV estimation formula was established: LV (mL) = 21.585 × BW (kg)⁰.⁷³² × BH (cm)⁰.²²⁵ (adjusted $R^²$ = 0.59; SE = 275.8 mL). In conclusion, this study indicates a nonlinear or piecewise linear model is more desirable than a simple linear model for LV estimation in children and adults because the ratios of LV/BW and LV/BSA are not constant along age and BSA.
Liver transplantation is a gold standard of therapy for a patient with the end-stage liver disease (a state showing a severe deterioration of liver function). Living donor liver transplantation and split liver transplantation were originally developed to overcome the shortage of pediatric donors. Since living donor liver transplantation was successfully applied to an adult patient, the practice of adult-to-adult living donor liver transplantation has steadily increased in countries where living donors are practically the only source of organs due to the scarcity of cadaver donors.

A major concern in liver transplantation is to determine the minimum graft volume required for a recipient to meet his/her metabolic demand. The transplantation of a large-for-size graft to a small recipient can pose an increased risk of immunological impairments and graft and vascular compromises due to compression. On the other hand, that of a small-for-size graft to a large recipient may cause impaired metabolic functions of the liver such as hyperbilirubinemia and coagulopathy and reduce the probability of graft survival after implantation. It is generally accepted that a ratio of graft volume to standard liver volume (LV) needs to be at least 30 to 40% to fit the hepatic metabolic demand of the recipient. Accurate estimation of standard LV is vital at the preoperative stage to determine the minimum LV necessary for the recipient and to evaluate qualification of the donor.

Urata et al. and Heinemann et al. established simple linear equations which estimate standard LV from body surface area (BSA) in the Japanese and Caucasian populations, respectively. However, these formulas produced LV estimates quite different from each other. The present study was to examine the applicability of the reported formulas to the Korean population and develop a better model of LV estimation as necessary.
Materials and Methods

Liver Density Determination. The data of liver weight (LW) and LV were collected by measuring 24 healthy livers. The livers were weighed and their volumes were measured by the principle of Archimedes. Liver density (LD) was calculated by LW/LV.

LV and BSA Estimation in Subjects with Normal Livers. Reviewing 962 postmortem examination reports prepared between June 2000 and May 2002 by the Department of Forensic Medicine, National Institute of Scientific Investigation in Korea, we selected 652 cases with normal livers to enroll in the present study. Excluded were cases having irrelevant morphology (such as injury and putrefaction) and/or pathologic findings (such as severe steatosis, cirrhosis, or tumor). Excluded also were child cases (< 18 years old) whose body height (BH) or body weight (BW) was beyond the range of the 5th and 95th percentiles on the 1998 standard physical growth charts of Korean children,\textsuperscript{14} as applied by Urata et al.,\textsuperscript{12} and adult cases whose BW was beyond \( \pm 25\% \) of normal weight (= BH [centimeters] – 100), as applied by Heinemann et al.\textsuperscript{13} Since the postmortem examinations in LW measurement included gallbladder and ligaments attached, LW was adjusted by subtracting 2.3\% of the routine LW, as described by Heinemann et al.\textsuperscript{13} BH, BW, LW, and age were obtained from the reports and LV was estimated by LW/LD. Then, BSA was estimated for cases with BW < 15 kg by the equation of Haycock et al.,\textsuperscript{15} \( BSA (m^2) = BW (kg)^{0.378} \times BH (cm)^{0.3964} \times 0.024265 \), and for cases with BW \( \geq 15 \) kg by the equation of Dubois et al.,\textsuperscript{16} \( BSA (m^2) = BW (kg)^{0.425} \times BH (cm)^{0.725} \times 0.007184 \), as described by Urata et al.\textsuperscript{12}

Statistical Analysis. The ratio of LV/BW and LV were plotted against age and BSA, respectively. Then, the relationships between LV, BSA, BH, and BW were formulated by
regression. Analysis of residuals was conducted to assess the adequacy of fit of a regression model, the significance of regression was tested at $\alpha = 0.01$, and the confidence intervals of regression coefficients were established. JMP IN v. 4.0.2 (SAS Institute Inc.) was used for statistical analysis.
Results

_Estimation of Liver Density._ The averages ± SDs of LW and LV were 1726.9 ± 369.1 g and 1663.8 ± 366.1 mL, resulting in an average ± SD of LD = 1.04 ± 0.07 kg/L.

_Anhropometric Data of Postmortem Examinations._ The anthropometric data of the selected female and male subjects in Table 1 shows the female group had significantly lower means of BW, BH, BSA, and LW except age at \( \alpha = 0.01 \). The 652 subjects were 4 months to 90 years old (42.4 ± 16.5 years).

[Insert Table 1 about here]

_Relationship between LV/BW Ratio and Age._ A plot of LV/BW ratio against age in the 652 subjects (see Figure 1) displays different patterns of change in LV/BW ratio along age. The LV/BW ratio decreased as age increased in the child group (< 18 years of age) but became leveled off in the adult group with an average ± SD = 23.1 ± 4.6.

[Insert Figure 1 about here]

_Regression Models for Liver Volume._ A plot of LV versus BSA in the 652 subjects in Figure 2 shows a nonlinear relationship between BSA and LV. The rate of increase in LV along BSA in the range of BSA < 1.2 m² appeared less than the corresponding rate in BSA ≥ 1.2 m², which indicates piecewise linear models for the two separate BSA ranges or a nonlinear model are preferred to better fit the LV data.
Simple linear, piecewise linear, and nonlinear models were constructed for LV estimation as shown in Table 2 by regression analysis and then compared with the models developed by Urata et al.\textsuperscript{12} and Heinemann et al.\textsuperscript{13} Urata et al.’s model produced underestimates (mean of errors = 226.9 mL) in LV estimation for the Korean subjects, while the rest of the models resulted in random errors (mean of errors = -30.6 to 0.0 mL). Of the models, the nonlinear model, \( \text{LV (mL)} = 21.585 \times \text{BW (kg)}^{0.732} \times \text{BH (cm)}^{0.225} \), had the largest adjusted \( R^2 \) (= 0.590, percentage of the variability in LV explained by the model) and smallest SE (= 275.8 mL, unbiased SD of estimation errors).
Discussion

The average ages ± SDs of the present study, Heinemann et al.,\textsuperscript{13} and Urata et al.\textsuperscript{12} were 42.4 ± 16.5, 50.6 ± 18.9, and 11.1 ± 8.8, indicating the study of Urata et al. mainly consisted of children (age < 18 years) whereas our study and Heinemann et al.’s consisted of adults. This difference in age distribution could explain the difference in LV estimation among the studies. While the application of Heinemann et al.’s model to the Korean subjects produced almost random errors with a mean of -30.64 mL in estimating LV, that of Urata et al.’s model resulted in fairly systematic errors with a mean of 226.90 mL. This underestimation tendency of Urata et al.’s model indicates that a LV estimation model based on child data would have low applicability for LV estimation in adults.

The LV linear model of Urata et al. (LV = 2.4 + 706.2 × BSA) and that of Heinemann et al. (LV = -345.7 + 1072.8 × BSA) corresponded statistically to the LV linear model of the present study in the child subjects (LV = 24.6 + 812.7 × BSA) and one in the adult subjects (LV = -506.1 + 1145.4 × BSA), respectively. In the child LV model of the present study, the 95% confidence intervals of the intercept and slope, [-161.4, 210.7] and [649.6, 975.9], included the intercept and slope of Urata et al.’s model; likewise, in the adult LV model of the present study, the corresponding confidence intervals, [-714.2, -298.0] and [1022.7, 1268.1], contained those of Heinemann et al.’s model.

The present study and Heinemann et al. developed regression models having lower values of adjusted $R^2$ (0.59 and 0.30) than that of Urata et al.’s model (0.96) due to larger variations of LV/BW ratio and LV versus BSA in adult subjects. Urata et al. reported 1.9 mL/kg of SD in LV/BW ratio in adolescent and adult subjects (≥ 16 years of age), which is less than half of the corresponding value (4.6 mL/kg) in the present study. In addition, Urata et al. presented a plot of LV versus BSA in which LV was scattered with a small variation
along the linear line in the range of BSA > 1.5 m², while both the present study and Heinemann et al. displayed much larger variations of LV in the BSA range.

The significant difference between the models of Urata et al. and Heinemann et al. and the plots of LV/BW ratio versus age and LV versus BSA indicate that a nonlinear or piecewise linear model is more desirable than a simple linear model to better fit LV data for children and adults. As observed in the present study and Urata et al., the ratio of LV/BW decreased along age in the child group but became stable in the adult group. Also, the rate of LV increase over BSA < 1.2 m² appeared less than the corresponding rate over BSA ≥ 1.2 m².

Therefore, to better fit LV data by BW or BSA for children and adults, a nonlinear or piecewise model on age or BSA would be preferred.

The present study developed nonlinear, piecewise linear, and simple linear models and compared these with the models of Urata et al. and Heinemann et al. in terms of adequacy of fit (adjusted $R^2$) and accuracy (SE), identifying the nonlinear model, $LV (mL) = 21.585 \times BW (kg)^{0.732} \times BH (cm)^{0.225}$, as the most preferred. Of the regression models under consideration, the nonlinear model showed the largest adjusted $R^2$ (= 0.590) and smallest SE (= 275.8 mL).

Records of postmortem examination and computed tomography (CT) are used to obtain LV data. Heinemann et al. observed no systemic change in LV by the time between death and postmortem examination; however, the postmortem LV can be under- or over-estimated depending on the cause of death (such as hypovolemia and cardiac failure) or intrahepatic blood accumulation after death. On the other hand, the CT-based LV can be affected by respiration, heartbeat, partial volume effect, and interobserver reliability; Urata et al. reported the CT-based LV differed from the actual LV by -12.4 to 20.5% (average ± SD = 2.4 ± 7.8%).

In summary, the present study shows a nonlinear or piecewise linear model is
desirable as the form of a LV estimation model for children and adults because the ratio of LV/BW and that of LV/BSA are not constant along age and BSA, respectively. This study and Heinemann et al.\textsuperscript{13} identified that application of a simple linear model derived from child data to the estimation of LV in adults produced significant underestimation errors. Examining various model candidates, we propose the nonlinear model, \( \text{LV (mL)} = 21.585 \times \text{BW (kg)}^{0.732} \times \text{BH (cm)}^{0.225} \), as a better model in terms of adequacy of fit and accuracy. Further research is needed to validate the suggested model for various ethnic populations and explore an improved model by incorporating relevant allometric and morphometric variables.
References


10. Lo CM, Fan ST, Liu CL, Yong BH, Chan JK, Wong J. Increased risk for living liver


Table 1. Anthropometric data of 652 subjects

<table>
<thead>
<tr>
<th></th>
<th>Females</th>
<th>Males</th>
<th>All</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of cases</td>
<td>222</td>
<td>430</td>
<td>652</td>
</tr>
<tr>
<td>Age (years)*</td>
<td>43.0 (18.0)</td>
<td>42.1 (15.6)</td>
<td>42.4 (16.5)</td>
</tr>
<tr>
<td>Body height (cm)*†</td>
<td>157.5 (9.1)</td>
<td>167.2 (15.7)</td>
<td>163.9 (14.6)</td>
</tr>
<tr>
<td>Body weight (kg)*†</td>
<td>54.5 (9.9)</td>
<td>63.7 (13.7)</td>
<td>60.6 (13.3)</td>
</tr>
<tr>
<td>Body surface area (m²)*†</td>
<td>1.54 (0.17)</td>
<td>1.71 (0.27)</td>
<td>1.65 (0.26)</td>
</tr>
<tr>
<td>Liver weight (g)*†</td>
<td>1244.8 (294.3)</td>
<td>1474.0 (392.6)</td>
<td>1396.0 (377.9)</td>
</tr>
</tbody>
</table>

* Data summarized as mean ± SD.

† Significant difference in means between the female and male groups at α = 0.01.
Table 2. Comparison of regression models for liver volume (LV in mL).

<table>
<thead>
<tr>
<th>Models</th>
<th>Adjusted $R^2$</th>
<th>Mean</th>
<th>Median</th>
<th>SD</th>
<th>SE</th>
</tr>
</thead>
<tbody>
<tr>
<td>(BW in kg, BH in cm, and BSA in m²)</td>
<td></td>
<td>Mean</td>
<td>Median</td>
<td>SD</td>
<td>SE</td>
</tr>
<tr>
<td><strong>The present study</strong></td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>$LV = 21.585 \times BW^{0.732} \times BH^{0.225}$</td>
<td>0.590</td>
<td>-27.96</td>
<td>-27.78</td>
<td>275.4</td>
<td>275.8</td>
</tr>
<tr>
<td>$LV = -492.3 + 1132.2 \times BSA + 267.6 (BSA - 1.652)^2$</td>
<td>0.462</td>
<td>0.00</td>
<td>-1.88</td>
<td>276.8</td>
<td>277.2</td>
</tr>
<tr>
<td>$LV = 186.3 + 509.2 \times BSA, BSA &lt; 1.2$</td>
<td>0.727</td>
<td>0.00</td>
<td>-0.89</td>
<td>277.1</td>
<td>277.3</td>
</tr>
<tr>
<td>$= -499.2 + 1142.1 \times BSA, BSA \geq 1.2$</td>
<td>0.346</td>
<td>0.00</td>
<td>0.00</td>
<td>277.1</td>
<td>277.3</td>
</tr>
<tr>
<td>$LV = 24.6 + 812.7 \times BSA, age &lt; 18$ years</td>
<td>0.762</td>
<td>0.10</td>
<td>-0.24</td>
<td>277.8</td>
<td>278.0</td>
</tr>
<tr>
<td>$= -506.1 + 1145.4 \times BSA, age \geq 18$ years</td>
<td>0.351</td>
<td>0.00</td>
<td>0.00</td>
<td>277.8</td>
<td>278.0</td>
</tr>
<tr>
<td>$LV = -226.5 + 982.1 \times BSA$</td>
<td>0.448</td>
<td>0.00</td>
<td>1.07</td>
<td>280.5</td>
<td>280.8</td>
</tr>
<tr>
<td><strong>Heinemann et al.’s formula</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$LV = -345.7 + 1072.8 \times BSA$</td>
<td>0.300†</td>
<td>-30.64</td>
<td>-29.88</td>
<td>281.5</td>
<td>281.7</td>
</tr>
<tr>
<td><strong>Urata et al.’s formula</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$LV = 2.4 + 706.2 \times BSA$</td>
<td>0.962†</td>
<td>226.90</td>
<td>213.31</td>
<td>289.4</td>
<td>289.6</td>
</tr>
</tbody>
</table>

* Differences between actual LV data and corresponding regression estimates.
† Values reported by Heinemann et al.¹³ and Urata et al.¹²

Figure Legends

Figure 1. Relationship between age and LV/BW ratio in 652 subjects with normal livers (LV: liver volume; BW: body weight).

Figure 2. Relationship between body surface area and liver volume in 652 subjects with normal livers.
Figure 1. Relationship between age and LV/BW ratio in 652 subjects with normal livers (LV: liver volume; BW: body weight).

Child group (age < 18)

\[ y = 33.60 - 0.65x \]

Adjusted \( R^2 = 0.24 \)

\( P = 0.003 \)
Figure 2. Relationship between body surface area and liver volume in 652 subjects with normal livers.