Body Surface Area and Body Weight Predict Total Liver Volume in Western Adults

Jean-Nicolas Vauthey,[*] Eddie K. Abdalla,[*] Dorota A. Doherty,[†] Philippe Gertsch,[‡] Marc J. Fenstermacher,[§] Evelyne M. Loyer,[§] Jan Lerut,[‖] Roland Materne,[¶] Xuemei Wang,[†] Arthur Encarnacion,[*] Delise Herron,[§] Christian Mathey,[#] Giovanni Ferrari,[‡] Chuslip Charnsangavej,[§] Kim-Anh Do,[†] and Alban Denys[#]

Computed tomography (CT) is used increasingly to measure liver volume in patients undergoing evaluation for transplantation or resection. This study is designed to determine a formula predicting total liver volume (TLV) based on body surface area (BSA) or body weight in Western adults. TLV was measured in 292 patients from four Western centers. Liver volumes were calculated from helical computed tomographic scans obtained for conditions unrelated to the hepatobiliary system. BSA was calculated based on height and weight. Each center used a different established method of three-dimensional volume reconstruction. Using regression analysis, measurements were compared, and formulas correlating BSA or body weight to TLV were established. A linear regression formula to estimate TLV based on BSA was obtained: TLV = −794.41 + 1,267.28 × BSA (square meters; $r^2 = 0.46$; $P < .0001$). A formula based on patient weight also was derived: TLV = 191.80 + 18.51 × weight (kilograms; $r^2 = 0.49$; $P < .0001$). The newly derived TLV formula based on BSA was compared with previously reported formulas. The application of a formula obtained from healthy Japanese individuals underestimated TLV. Two formulas derived from autopsy data for Western populations were similar to the newly derived BSA formula, with a slight overestimation of TLV. In conclusion, hepatic three-dimensional volume reconstruction based on helical CT predicts TLV based on BSA or body weight. The new formulas derived from this correlation should contribute to the estimation of TLV before liver transplantation or major hepatic resection. (*Liver Transpl 2002;8:233-240.*)

In the past decade, the role of computed tomography (CT) has extended beyond its use for liver imaging to include three-dimensional volumetric measurement before liver transplantation or major hepatic resection.[1-4] This has been possible because of a close correlation between the volume obtained by three-dimensional reconstruction of computed tomographic images and actual liver volume.[5]

In a recent Japanese study, a formula that enables calculation of total liver volume (TLV) from body surface area (BSA) was generated after study of CT-based three-dimensional volumetric measurement of livers of children and adults. This formula has been applied to calculate the graft to TLV ratio for living related donor liver transplantation[4,6] and the future liver remnant (FLR) to TLV ratio before liver resection.[2] However, the formula has not gained general acceptance at Western centers, and its accuracy has been questioned because of Western autopsy measurements that indicate on average a TLV of 323 cm^3 greater than expected based on the Japanese formula.[7] In addition, body weight, rather than BSA, has been used to estimate graft volume before liver transplantation, particularly donor-recipient weight ratio.[8-10] However, to our knowledge, the correlation between body weight and TLV has not been evaluated.

In addition to the issue of liver size match, the goal of preoperative liver volume estimation is to estimate hepatic metabolic demands of an individual patient.[11] Thus, a method that estimates appropriate volume based on patient characteristics (e.g., patient weight or BSA) in combination with a measure of liver volume (by CT) is desirable. Although caloric needs, total body water, and extracellular water correlate more closely to BSA than body weight in children, differences are minor.[12,13] Therefore, either weight or BSA could provide a standard means to estimate liver function, as well as size, before resection or transplantation.

We designed a multicenter study to evaluate the correlation between TLV and BSA or body weight in Western patients with normal livers who underwent CT for conditions unrelated to the hepatobiliary system. The newly derived formula based on BSA then was

*From the Departments of *Surgical Oncology, †Biostatistics, and §Radiology, The University of Texas M.D. Anderson Cancer Center, Houston, TX; #Department of Radiology, Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland; ‡Department of Surgery, Ospedale San Giovanni, Bellinzona, Switzerland; and the Departments of ‖Digestive Surgery and ¶Radiology, Université Catholique de Louvain, Cliniques Universitaires Saint-Luc, Louvain, Belgium.*

Address reprint requests to Jean-Nicolas Vauthey, MD, FACS, Department of Surgical Oncology, Box 444, The University of Texas M.D. Anderson Cancer Center, 1515 Holcombe Blvd, Houston, TX 77030. Telephone: 713-792-2022; FAX: 713-792-0722; E-mail: jvauthey@mdanderson.org

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compared with existing formulas from Japan and Western autopsy studies.

Materials and Methods

At four institutions in North America and Europe, TLV was measured in 292 individuals who underwent helical CT for conditions unrelated to the hepatobiliary system and who had no known hepatic abnormality (cirrhosis, fibrosis, or steatosis). Patient age, height, and weight were recorded, and BSA was calculated.[14] Patients with conditions potentially affecting the biliary tree (e.g., pancreas cancer) or associated with diffuse liver disease (e.g., lymphoma) were excluded. Patients who indicated that they were of African or Asian descent were excluded. Each center used a different established method of computed tomographic reconstruction, which depended on available scanners and software (described next).

CT Method at Center 1

Liver volume was measured on an ISG Allegro workstation (ISG Technologies Inc, Toronto, Canada) using a threshold function. Source images were contiguous 7- or 10-mm helical sections obtained during abdominal computed tomographic scanning (General Electric HiSpeed; General Electric, Milwaukee, WI). To create a three-dimensional object using this method, the liver was selected by the computer based on specified density (pixel intensity) of the tissue (liver). Unwanted contiguous areas (gallbladder and intrahepatic inferior vena cava) were manually excluded using a computer mouse-driven "cut" function for each computed tomographic image. Three-dimensional volumes were created by summation of two-dimensional section areas multiplied by the slice thickness.

CT Method at Center 2

At center 2, patients underwent abdominal helical computed tomographic scans capturing transverse images at 5- or 10-mm intervals (Philips – CT – Spyro Tomoscan AV Expander E 1, model 1997-98; Best, The Netherlands). In this method, the computer mouse was used to outline the perimeter of the liver (excluding the inferior vena cava and gallbladder) on each slice, and the enclosed area was measured. Combining these measurements with the distance between slices enabled three-dimensional reconstruction for TLV calculation (Helax TMS, version 5; Uppsala, Sweden).

CT Method at Center 3

At center 3, computed tomographic images were acquired using multicenter spiral CT (Lightspeed; General Electric, Milwaukee, WI). Images were obtained using a 5-mm thickness 60 seconds after injection of 100 mL of contrast medium (Imagopaque 300; Nicomed, Princeton, NJ). Liver volumes were calculated using an Advantage Windows workstation (Advantage Windows, software version 3.1; General, Redmond, WA). Contours of the liver were delineated consecutively on the screen, and volume was calculated by adding each slice's volume determined by the surface area, slice thickness, and space between slices.

CT Method at Center 4

At center 4, volumes were calculated using the summation-of-areas technique[1] on an EasyVision workstation (n = 26; Philips Medical Systems, Best, The Netherlands) or an MxView workstation (n = 27; Marconi Medical Systems, Cleveland, OH). The cross-sectional area of individual images was calculated automatically after manually tracing the perimeter of the liver with a computer mouse-driven stylus. Volume was determined by multiplying the sum of all areas by the image reconstruction interval.

Statistical Analysis

One-way analysis of variance models were used to test for intercenter differences for all variables considered in analysis. Linear regression analysis was used to predict TLV using body indices (age and functions of weight and height) as candidate predictors. BSA was calculated using Mosteller's formula[14]:

$$\text{BSA} = \sqrt{(\text{height [cm]} \times \text{weight [kg]}/3{,}600}$$

Body mass index (BMI) was obtained by using the formula: BMI = weight (kilograms)/square height (meters).[15]

Subset analyses, with patients grouped by either sex or center, also were performed to explore possible sex and center effects. Simple regression models were fit to age, BMI, and BSA. All multiple regressions excluded weight and height measurements to avoid colinearity. Normality assumptions about variables used in the model were checked by graphical methods (Q-Q plots). Comparisons of TLV estimation formulas used absolute deviation between TLVs predicted by the model and actual TLV measured. Data analysis was performed using SAS[16] (SAS Institute Inc, Cary, NC) and S-Plus[17] (Data Analysis Products Division, Seattle, WA) statistical software.

Results

Descriptive statistics of age, weight, height, BSA, and TLV for all subjects included in the estimation of TLV are listed in Table 1. Patients' mean ages and heights differed significantly among all centers ($P < .0001$), and mean patient weight in center 1 was significantly different from those in centers 2, 3, and 4 ($P < .0001$). This was associated with a significant increase in mean BSA of 1.94 m^2 in center 1 compared with BSAs of 1.79, 1.83, and 1.76 m^2 at centers 2, 3, and 4, respectively ($P < .0001$). Differences between TLV measurements were found ($P < .0001$), with mean TLVs of 1,762 cm^3 at center 1, 1,407 cm^3 at center 2, 1,518 cm^3 at center 3, and 1,380 cm^3 at center 4.

Two linear regression models for TLV are listed in

Table 1. Data Summary

Center	Variable	Mean	Median	Range
All				
(n = 292)	Age (yr)	54	56	14-90
	Weight (kg)	72	71	43-165
	Height (cm)	169	169	118-192
	BSA (m^2)	1.84	1.82	1.32-2.90
	BMI (kg/m^2)	24.84	24.84	15.89-84.03
	TLV (cm^3)	1531	1487	649-3,558
Center 1				
(n = 74)	Age (yr)	59	62	17-83
	Weight (kg)	80	78	50-165
	Height (cm)	171	172	118-192
	BSA (m^2)	1.94	1.92	1.48-2.90
	BMI (kg/m^2)	27.74	26.22	19.14-84.03
	TLV (cm^3)	1762	1669	944-3,558
Center 2				
(n = 63)	Age (yr)	62	64	29-90
	Weight (kg)	70	70	44-105
	Height (cm)	165	163	150-185
	BSA (m^2)	1.79	1.81	1.38-2.22
	BMI (kg/m^2)	25.55	25.40	17.19-41.02
	TLV (cm^3)	1407	1369	649-2,030
Center 3				
(n = 102)	Age (yr)	54	57	14-87
	Weight (kg)	71	72	43-112
	Height (cm)	170	170	146-187
	BSA (m^2)	1.83	1.85	1.32-2.31
	BMI (kg/m^2)	24.59	24.82	15.89-38.57
	TLV (cm^3)	1518	1481	911-2,729
Center 4				
(n = 53)	Age (yr)	34	33	19-59
	Weight (kg)	66	65	47-94
	Height (cm)	169	170	154-192
	BSA (m^2)	1.76	1.74	1.43-2.21
	BMI (kg/m^2)	22.90	23.23	18.36-28.72
	TLV (cm^3)	1380	1378	865-1,900

Table 2. The relationship between BSA and TLV was consistent at all centers. The pooled-sample regression for all centers combined was TLV = −794.41 + 1,267.28 × BSA (r^2 = 0.46; P< .0001); this result is shown graphically in Figure 1. When centers were considered separately, estimated r^2 for centers 1, 2, 3, and 4 were 0.47, 0.41, 0.39, and 0.38, respectively (all P < .0001).

Combining all four centers, the multiple regression equation fitting TLV to age and BSA simultaneously was TLV = −695.81 + 1,279.38 × BSA − 2.26 × age (r^2 = 0.47; P < .0001). However, when centers were considered separately, particularly centers 2 and 3, age was not significantly associated with TLV after adjusting for BSA (P = .202 and P = .593, respectively). Even when centers were combined, the partial correlation coefficient of TLV after adjusting for BSA was r^2 = 0.01, indicating a negligible independent effect of age on TLV. Age therefore was excluded from the final formula. Exclusion of BMI from the TLV regression model also was based on partial r^2 analysis. That BMI had no independent effect on TLV was concluded when the partial correlation of TLV and BMI after adjusting for BSA was estimated as r^2 = 0.02.

An identical analysis using body weight rather than BSA is listed in Table 3. The resulting formula derived from data from all centers excluding patient age, TLV = 191.80 + 18.51 × weight (r^2 = 0.48; P < .0001), is shown graphically in Figure 2. Existing formulas for the estimation of TLV based on BSA were compared with our formula. Figure 3 shows our regression line and the line for the Japanese population.[1] The two regression lines diverge as BSA increases, showing the greatest difference in patients with a high BSA. On average, the formula obtained using data from the Japanese population underestimates TLV in our sample by 232.70 ± 128.90 (SD) cm^3. Our regression line was compared (Figure 4) with the two previously reported formulas obtained from autopsy data of Western populations.[7,18] The formula from Heinemann et al[7] from Germany, reporting on 1,332 "Caucasians," overestimates TLV in our sample by 91.88 ± 44.69 (SD) cm^3, whereas the formula from DeLand and North[18] from the Johns Hopkins Hospital (which does not indicate patient race) slightly overestimates TLV by 1.71 ± 74.20 (SD) cm^3.

Discussion

In 1995, Urata et al[1] proposed a formula to estimate TLV based on BSA using computed tomographic imaging for three-dimensional reconstruction of the liver in 96 Japanese children and young adults. The present study also uses computed tomographic volumetric measurements, but it indicates a different correlation between BSA and TLV in this Western population. Although the Japanese formula is derived from measurements in a group of patients that is younger with a smaller average BSA (in the majority, BSA < 1.5 m^2), the current study includes a larger cohort (292 patients), all of Western origin. Median age (56 years; range, 14 to 90 years), weight (71 kg; range, 43 to 165 kg), and BSA (1.82 m^2; range, 1.32 to 2.90 m^2) reflect the adult population likely to undergo hepatic surgery in the West. The current formula is based on computed tomographic measurements, and its validity is corroborated by the close correlation with two formulas derived from Western autopsy studies.[7,18]

This study was undertaken based on data showing that computed tomographic volumetric analysis correlates with actual liver volume.[5,19,20] Previous studies

Table 2. Linear Regression Models for TLV With BSA

	No. of Patients	*P*	r^2
All centers			
TLV = −794.41 + 1,267.28 × BSA	292	<.0001	0.46
TLV = −695.81 + 1,279.38 × BSA − 2.26 × age		<.0001	0.47
Center 1			
TLV = −975.61 + 1,411.49 × BSA	74	<.0001	0.47
TLV = −152.61 + 1,366.63 × BSA − 12.43 × age		<.0001	0.55
Center 2			
TLV = −505.09 + 1,069.75 × BSA	63	<.0001	0.41
TLV = −227.47 + 1,015.97 × BSA − 2.93 × age*		<.0001	0.44
Center 3			
TLV = −570.79 + 1,143.30 × BSA	102	<.0001	0.39
TLV = −530.90 + 1,151.81 × BSA − 1.02 × age*		<.0001	0.40
Center 4			
TLV = −87.61 + 833.84 × BSA	53	<.0001	0.38
TLV = −83.13 + 985.06 × BSA − 12.99 × age		<.0001	0.48

*Models in which age is not a significant predictor of TLV.

showed errors in computed tomographic volume calculation that included the partial-volume effect and respiratory-phase and interobserver variation.[5,21] However, refinements in imaging techniques, the development of helical CT, and the availability of sophisticated software for three-dimensional reconstruction has improved estimation accuracy to within 5%.[1,22] In this study, the high degree of correlation between TLV and BSA obtained at four centers using four different CT scanners and three-dimensional reconstruction techniques reiterates the accuracy of computed tomographic volume measurement and shows that reliable results can be obtained using different equipment and software.

This study confirms the known negative correlation between age and TLV.[23,24] However, this effect of age on the correlation between BSA and TLV is negligible. This finding facilitates comparison of the current formula with other formulas and simplifies the calculation of TLV in a clinical setting.

Liver grafts that are too small for the recipient can compromise the results of transplantation.[25,26] Size of the liver graft has been estimated based on volume or

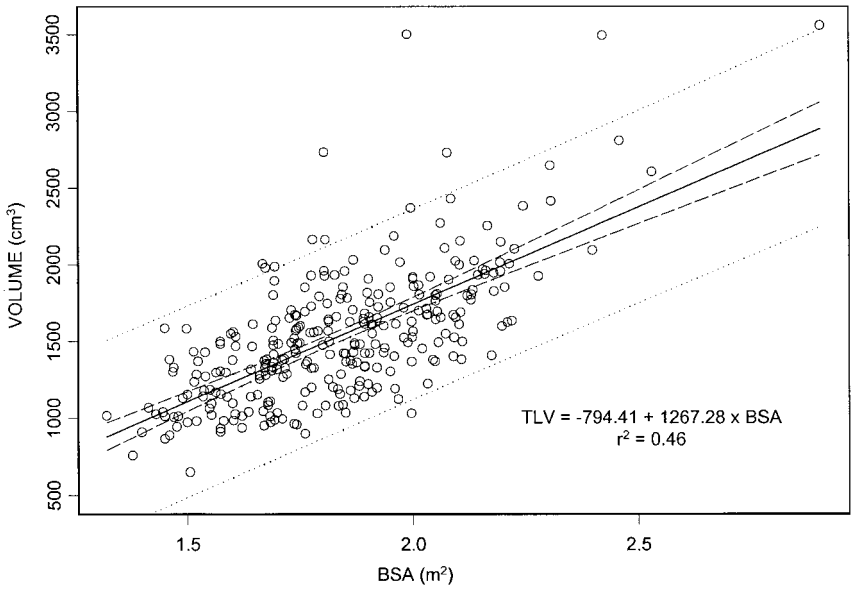

Figure 1. Correlation between BSA and TLV (—; n = 292) showing the 95% confidence interval (---) and 95% predictive interval (···).

Table 3. Linear Regression Models for TLV With Body Weight

	No. of Patients	*P*	r^2
All centers			
TLV = 191.80 + 18.51 × weight	292	<.0001	0.49
TLV = 322.57 + 18.83 × weight − 2.88 × age		<.0001	0.50
Center 1			
TLV = 202.05 + 19.42 × weight	74	<.0001	0.52
TLV = 983.48 + 18.87 × weight − 12.45 × age		<.0001	0.61
Center 2			
TLV = 318.09 + 15.53 × weight	63	<.0001	0.38
TLV = 578.74 + 14.68 × weight − 3.25 × age*		<.0001	0.40
Center 3			
TLV = 330.92 + 16.68 × weight	102	<.0001	0.39
TLV = 396.05 + 16.95 × weight − 1.55 × age*		<.0001	0.40
Center 4			
TLV = 432.26 + 14.33 × weight	53	<.0001	0.39
TLV = 702.31 + 16.87 × weight − 13.04 × age		<.0001	0.49

*Models in which age is not a significant predictor of TLV.

weight in the patient evaluation before living donor or split-liver transplantation.[4,21,26] Graft volume to standard liver volume values of 30% or less and graft weight to body weight ratios less than 0.8 are associated with increased morbidity and impaired patient and graft survival after transplantation. In these cases, ischemic damage and rejection further compromise a small preexisting functional liver volume. The current study indicates differences in TLV between Japanese and Western adults, with TLV greater in Western patients for the same BSA. Because weight also is used to calculate BSA, the current study suggests that the graft weight to body weight ratio method used in transplantation studies may not allow for a direct comparison of weight-based ratios between the East and West.

Estimation of TLV is necessary before major hepatic resection that will leave a small FLR.[2] In patients who are candidates for resection of a hepatic lobe or more, FLR size varies, and the safe minimal size for FLR is not well defined.[22,27] The standard technique for volumetric measurement is based on radiographic measurement of the whole liver, from which FLR can be deducted. That formula includes resected volume, tumor volume, and TLV: ([resected volume − tumor volume] ÷

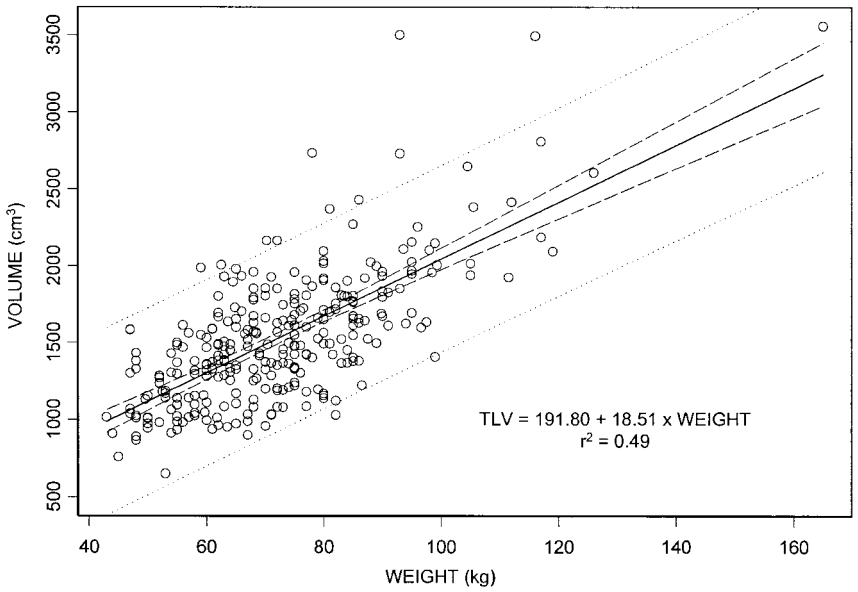

Figure 2. Correlation between weight and TLV (—; n = 292) showing the 95% confidence interval (----) and 95% predictive interval (···).

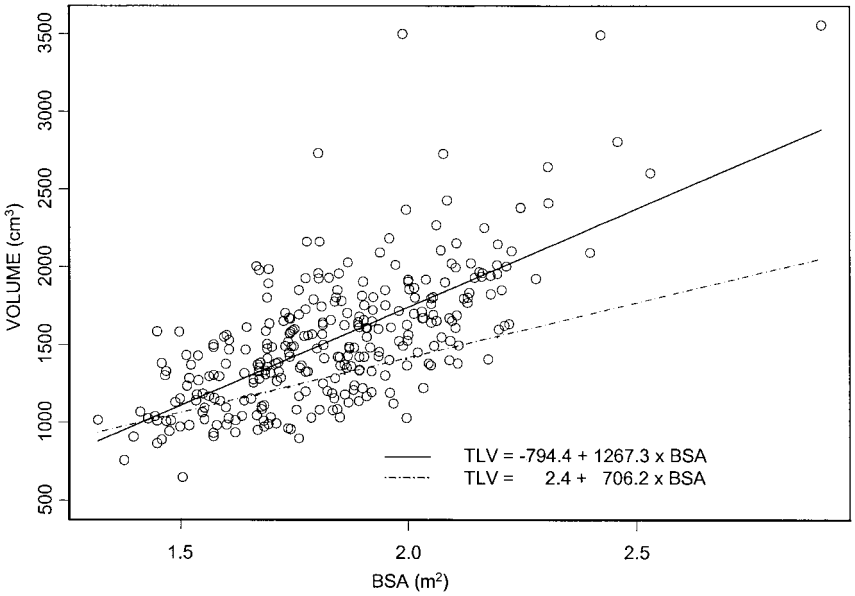

Figure 3. Regression line obtained using data for 292 Western adults (—) and the reference line for best-fit BSA using the formula of Urata et al[1] (–·–).

[TLV − tumor volume]). Multiple tumors and lesions beyond the resolution of imaging may cause errors in the estimation of resected functional liver volume. In patients with bile duct tumors, measurement of the compromised liver (because of bile duct dilatation, cholangitis, or vascular obstruction) may not be relevant using this formula.[2,19,27,28]

An alternate method of assessing the remnant liver similar to the method used before transplantation, which does not include tumor volume or resected volume, recently has been proposed. It is based on the FLR-TLV ratio. FLR volume (which is not compromised by tumor) is directly measured by computed tomographic three-dimensional reconstruction. TLV is calculated based on BSA. This alternate method allows for a uniform comparison of FLR volume before extended resection with or without preoperative portal vein embolization. Based on this method of calculation, a correlation between FLR volume and surgical outcome has been established,[2] supporting the use of a formula for the determination of TLV that incorporates patient characteristics (BSA or body weight) to generate

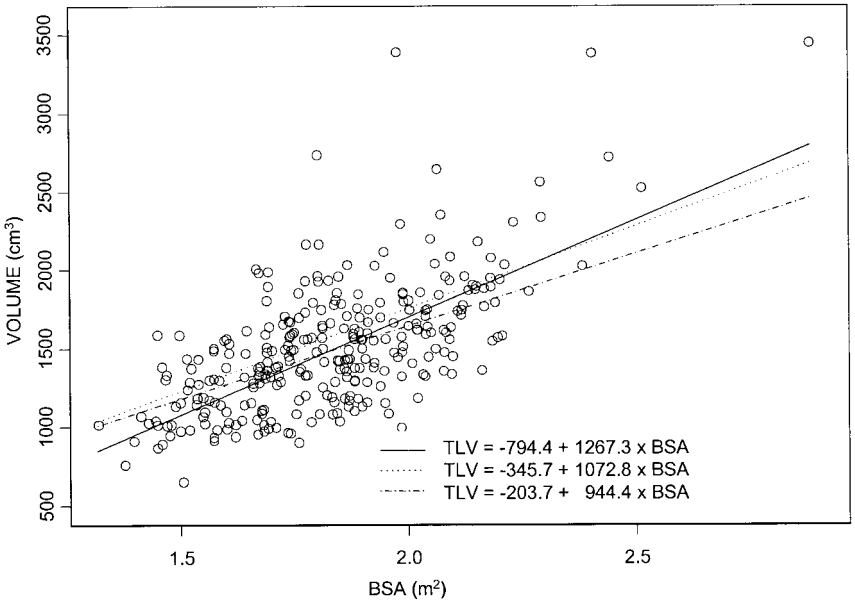

Figure 4. Regression line obtained using data for 292 Western adults (—) and reference line for best-fit BSA using the autopsy data–derived formulas of DeLand and North[18] (–·–) and Heinemann et al[7] (···).

an estimate of liver function that allows for comparison between patients.

It is important to recognize potential problems associated with the application of the Japanese-derived formula of Urata et al[1] in Western patients. Because the formula of Urata et al[1] underestimates TLV in Western patients, calculated TLV is 15% smaller on average for the same BSA. This difference is clinically relevant because a smaller TLV used as the denominator when calculating the ratios of transplanted liver volume to TLV or FLR volume to TLV will cause liver size to be overestimated. Complications are more likely if either a transplanted liver graft or an FLR after resection is too small.[2,3,25,26,29]

Currently, FLR size and factors potentially compromising liver function (cirrhosis or hepatitis and previous chemotherapy) are criteria by which patients are selected for portal vein embolization.[27,28,30] Small remnant liver volumes after hepatectomy may negatively influence outcome for different reasons. First, hepatic reserve may be reduced because of preexisting liver disease, and the liver remaining after hepatectomy may not provide sufficient function despite apparent adequate volume. Second, the remaining volume of a normally functioning liver may be insufficient, resulting in irreversible liver failure. The risk associated with hepatectomy in patients with chronic liver disease has been assessed by various liver function tests.[31] Major hepatectomy not only leads to parenchymal loss, but also amputates the hepatic vascular bed, resulting in increased portal pressure.[32,33] Also, an increase in hepatic portal resistance has been observed experimentally during liver regeneration, which may further aggravate functional recovery.[34] Hepatic portal overflow has been considered a possible initiator of progressive and irreversible liver insufficiency after hepatectomy.[35] Preoperative portal vein embolization has been performed in selected patients to induce ipsilateral liver atrophy and contralateral hypertrophy and thereby reduce the risk for postoperative liver insufficiency. Preoperative portal vein embolization also may reduce the risk for postoperative portal overflow.

Like other formulas for preresection or pretransplantation liver volume calculation, the new formulas should be considered estimates because of variability in TLV correlation with body weight and BSA. Although patients on our study had no known cirrhosis, fibrosis, steatosis, biliary disease, or other liver disease to confound the analysis, a range of TLVs for a given BSA or body weight was found. Steatosis as a reason for the observed variability is unlikely given similar variations in TLV at low and high weights or BSAs. The correlation coefficient determined in the Western autopsy study of Heinemann et al[7] of more than 1,000 patients ($r^2 = 0.30$) similarly reflects this variability. Consequently, some degree of overlap will exist; a proportion of patients with small liver volumes will not experience liver failure, whereas others with apparently adequate volumes will experience complications associated with a small liver remnant.

However, importantly, given the recognized value of body weight and BSA in liver transplantation and resection,[2,3,6,11,29] the newly described formulas may provide a useful estimation of metabolic demands after major liver surgery or transplantation in Western adults. In cases of extended liver resection, TLV estimations may contribute to better patient selection for preoperative portal vein embolization.[2] With the increasing use of split-liver transplantation in adults,[29] the two formulas also could facilitate graft-recipient matching. Standardized measurement techniques before resection and transplantation will allow for comparisons between centers so that the minimum required liver volume necessary to avoid complications can be determined.

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