New formula for predicting standard liver and spleen volumes in Chinese adults

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Abstract

BACKGROUND

The liver volume and spleen volum are useful index for cirrhosis patients with esphageal varices. But the calculation of the volume is time-consuming and boring. To solve the problem, we successfully established the liver and spleen volume formula using the body surface area. We compared the liver volume formula with other four formulas, which be proved with highest accuracy and lowest error. Until now, except for the new spleen volume formula in the research, there are few reports about it.

AIM

To obtain a reference range of morphological indices, and to establish a formula to accurately predict the standard liver and spleen volumes in Chinese adults.

METHODS

Computed tomography was used to calculate the estimated total liver volume and spleen volume of 305 Chinese adults without any diseases which could influence the volumes of these two organs. Gender, age, body height, body weight, body surface area and body mass index were determined. Correlation analysis and step-wise multiple linear regression analysis were performed to evaluate the impact of each parameter on the liver and spleen volumes, and then a formula to predict the liver and spleen volumes was established. Finally, the results obtained with the new liver volume formula with existing formulas in a validation group were compared.

RESULTS

The average liver and spleen volume values were 1043.18 ± 244.60 cm^3 and 175.07 ± 88.15 cm^3, respectively. Age, body height, body weight, body surface area and body mass index were significantly correlated with liver and spleen volume. Body surface area showed the strongest correlation with liver volume and spleen volume($p<0.005$ and $p<0.001$). Based on these results, new formulas to calculate the standard liver volume and standard spleen volume were established.

CONCLUSIONS

Compared the new liver volume formula with the existing formula, it is found that the new liver volume is more accurate. And the accuracy of the spleen volume formula is acceptable.

Core tip: To solve the problem of time-consuming and boring in calculating the liver and spleen volume, we successfully established the liver and spleen volume formula can be used in Chinese adult. Though there are some reports about the liver volume, but it is different in spleen volume. The liver volume and spleen volume radio is an useful index to predict the esophageal varices and bleeding risk for cirrhosis patients. Only liver volume formula is not enough, the finding of the spleen volume is very meaningful.

Introduction

The liver volume has been proven to correlate with liver function and it is a morphological index that is widely used in patients undergoing liver transplantation [1,2]. The accurate estimation of liver volume is very important during pre-transplantation assessment. In patients with cirrhosis, the volumes of the liver and spleen change due to the presence of portal hypertension [3,4]. The liver and spleen volumes have proven to be useful indices to evaluate the severity of esophageal varices and the bleeding risk[5–7].

Because the liver and spleen both are irregular organs, measuring their volumes is usually very difficult. The water overflow method was considered the gold standard to calculate the volume of irregular organs, but it is difficult to implement in human beings, and now it is only used intra-operatively and during autopsies[8,9]. However, with the development of medical imaging technology, many techniques are available to measure the volumes of the liver and spleen, such as computed tomography (CT), ultrasonography and magnetic resonance imaging (MRI). Among them, CT is the most widely used. The deviation in the estimation of the volume of irregular organs by three-dimensional CT reconstruction is reported to be within 5%, so CT is considered to be an effective means for the measurement of the volume of irregular organs. However, this involves calculating the surface area of each layer, which is very laborious and which may diminish its clinical utility[10,11]. Therefore, an accurate formula to calculate the volume of the liver and spleen is still a valuable tool, especially for patients with cirrhosis.

Liver and spleen sizes vary depending on the race, gender and body size [12]. Many researchers have reported formulas which can be used to calculate the liver volume in different ethnic groups. Among them, Urata's[13] formula is the most widely used, and Poovathumkadavil's[14] formula shows the lowest percentage error. Feng et al.[15] and Fu et al.[16] also reported formulas which can be used in the Chinese population and which have shown a higher degree of accuracy and less error.

Until now, there have been few reports on formulas to calculate the spleen volume[17,18] and this has been attributed to differences in methodology. Yet, an easy to use formula to calculate the splenic volume would be very useful for cirrhotic patients, since the liver volume formula alone is not enough to evaluate the severity of esophageal varices and the bleeding risk.

Due to increased blood flow in the portal and splenic veins, the PVD(portal venous diameter), PVCSA(portal venous cross-sectional area) and the SVD(spleen venous diameter) increase significantly in cirrhotic patients [19,20], so these indices can be used to determine if there is portal hypertension. However, these indices vary depending on the race, age and gender. Therefore, the aim of this study was to develop new formulas to calculate the volumes of the liver and spleen, using as input the morphological index values found in Chinese people, to apply them clinically in cirrhotic patients.

Materials And Methods

Patients

The data were obtained from patients who underwent upper abdominal CT scans between October 2016 and December 2018 at The Second Affiliated hospital of Xi'an Jiaotong University, (Xi'an, China) and who met the following eligibility criteria: (1) age > 18 years old, (2) normal liver function and no history of liver or hematologic diseases, (3) no history of cancer and 4) of either gender. The exclusion criteria were as follows: (1) history of viral hepatitis, alcoholic liver disease, non-alcoholic fatty liver disease, autoimmune liver disease or other forms of hepatitis; (2) history of liver cirrhosis or other liver diseases; (3) suspected of having liver cancer; (4) past liver or spleen resection; (5) history of diseases affecting the volume of the liver or spleen, such as cysts, hematologic diseases, or other benign lesions of the liver or spleen (more than one lesion, or if only one, having a diameter > 1 cm); (6) conditions having a hemodynamic effect on the PV or SV, such as thrombosis, embolism, or sponge-like appearance of the parenchyma.

A total of 207 subjects were included to establish the formula and another 98 subjects were included to validate the new liver formula. Basic information about each participant was recorded, including gender, age, body height(BH) and body weight(BW), and the Mosteller's formula was chosen to calculate the body surface area(BSA), as follows: [Due to technical limitations, this equation is only available as a download in the supplemental files section.] The body mass index(BMI) was calculated as follows: $BMI = BW/BH^2$.

The study protocol was reviewed and approved by the Institutional Ethics Committee of the second affiliated hospital of Xi'an Jiaotong University. As the study is a retrospective research, the Ethics Committee exempted the informed consent.

Assessment of TLV and TSV by CT

Upper abdominal CT scans were performed using a multi-slice spiral CT scanner (GE 128-slice spiral CT scanner; Inux Medical System, United States of America) with a collimated reconstruction thickness of 5 mm and an interval of 5 mm. The CT procedures were conducted by professional technicians in accordance with standard operating procedures. To improve the quality of examinations, patients were placed in the supine position and trained to hold their breath to prevent movement artifacts during scanning.

Multiple morphological indices were assessed at the same time, including CTLV, CTSV, SVD, PVD and PVCSA. These indices were measured on portal phase images using an image-analysis program (Inux imaging Workstation; Inux Medical Systems) by medical students blinded to the clinical characteristics of the patients and under the supervision of an experienced radiologist. The CTLV and CTSV were obtained by summation after manually tracing the boundaries on each transverse image, avoiding the large vessels, gallbladder, and fissures. The PVD and PVCSA were measured at the midpoint between the portal bifurcations and the venous confluences, while the SVD was measured 1 cm proximal to the confluence of the portal vein and the splenic vein.

Liver volume calculated using previous formulas

In the validation group, the liver volume formulas were applied from four other researchers and then these results were compared with their formula.

Statistical analysis

Statistical analyses were performed with SPSS (IBM SPSS, Chicago, IL, United States). Data are expressed as the mean ± SD. The correlations between CTLV, CTSV and age, BW, BH, BSA, and BMI were analyzed by using Pearson correlation analysis. Step-wise multiple linear regression analysis was performed to evaluate the impact of each parameter and to develop the new formula for liver and spleen volumes. The CTLV was compared with the SLV (calculated through formulas) by means of the t-test, with the absolute volume and percentage error, as follows: (SLV - CTLV)/CTLV × 100. ± 10% and ± 15% were used as acceptable ranges for differences between the estimated SLV and CTLV. The proportion of the estimates within these acceptable ranges was determined for each SLV formula to assess its level of accuracy. All statistical analyses were two-tailed, and p values less than 0.05 were considered statistically significant.

Results

Characteristics of Chinese adults

A total of 207 subjects (107 men and 100 women) were enrolled to develop the new formulas for the determination of liver and spleen volumes. There were significant differences between men and women with respect to other anthropometric variables, such as BH, BW, BSA and BMI (men vs women: BH 170.96 ± 5.26 cm vs 159.06 ± 4.74 cm; BW: 65.99 ± 9.74 kg vs 56.51 ± 9.18 kg; BSA: 1.77 ± 0.14 m^2 vs 1.58 ± 0.14 m^2; BMI: 22.54 ± 3.10 kg/m^2 vs 22.29 ± 3.53 kg/m^2; P<0.001). The CTLV and CTSV were significantly larger in men than in women. The average CTLV and CTSV values in men were 1136.84 ± 209.69 cm^3 and 192.37 ± 89.17 cm^3, respectively, whereas in women the values were 942.96 ± 240.40 cm^3 and 156.57 ± 83.57 cm^3,respectively (p<0.001). The mean PVD, SVD and PVCSA values were 8.84 ± 1.55 mm, 5.53 ± 1.28 mm and 98.33 ± 33.08 mm^3, with significant differences between men and women. The characteristics of the subjects are shown in Table 1.

Variables which correlate with CTLV and CTSV

Five variables were selected to conduct the Pearson correlation analysis for CTLV and CTSV, including age, BH, BW, BSA and BMI. Among these variables, age showed a negative correlation with CTLV and CTSV, whereas BH, BW, BSA and BMI showed a positive correlation. The correlation coefficients between CTLV and age, BH, BW, BSA and BMI were: −0.328, 0.438, 0.574, 0.592 and 0.390, respectively. The correlation coefficients between CTSV and age, BH, BW, BSA and BMI were: −0.182, 0.258, 0.353, 0.361 and 0.246, respectively (Table 2). Of these variables, BSA showed the strongest correlation. Next, a step-wise multiple linear regression analysis was conducted. The results showed that age and BSA were independent variables for CTLV. Because the partial regression coefficient for age was small (r = −

0.937/year), and the effect on CTLV was negligible, therefore it was removed. BSA was the only independent factor for CTSV. Next, this factor was used to calculate the new formulas, as follows: SLV = 858.186*BSA−393.349 (R^2 = 0.350), SSV = 188.813*BSA−140.981(R^2 = 0.126). The scatter plots are shown in Figure 1 and Figure 2.

Comparison of the new formula for liver volume with existing formulas

In the past, many researchers have proposed different formulas to calculate the liver volume. Among these, Urata's formula is the most frequently used. Thus, the level of agreement was assessed between this formula and their formula (Figure 3). The liver volume calculated by using our formula showed perfect agreement with the volume determined with Urata's formula (R^2 = 100%, $p<0.001$). On the other hand, Poovathumkadavil's formula has been shown to yield the lowest percentage error with respect to the actual liver volume. Chinese researchers have also proposed formulas to calculate the liver volume, such as the highly accurate Fu formula and Feng formula, which incorporates the body weight index and BSA index respectively. Therefore, these four formulas were chosen for comparison with their liver volume formula in another group of 98 participants, and the results are shown in Table 3. Of all the formulas analyzed, only Fu's formula and their formula yielded a mean percentage error below 5%. The mean percentage error using their formula was only 1.83%. 15% and 10% were chosen as the acceptable percentage errors to calculate the accuracy of their formula for liver and spleen volumes, and the results are shown in Table 4. The proportion of SLV and SSV estimated with their formula with percentage errors within ±10% and ±15 when compared with the CTLV and CTSV were 40.8% and 72.4%, and 21.4% and 25.6%, respectively. Hence, their liver formula showed the highest accuracy and lowest percentage error.

Discussion

In China, the number of patients newly diagnosed with liver cirrhosis is about 300,000 per year, and the number of deaths due to cirrhosis is as high as 110,000 per year[21−23]. Among the causes of death, bleeding due to esophageal varices is the most common[24,25].

Currently, the diagnosis of esophageal varices and evaluation of its severity is mainly performed by gastroscopy. However, gastroscopy is an invasive procedure, so it is important to explore alternative, non-invasive detection methods. In this regard, it has been shown that the ratio of liver volume to spleen volume is an effective non-invasive index. CT is the most commonly used method to calculate liver and spleen volumes, but it is a time-consuming and laborious procedure. Thus, many researchers have developed formulas to calculate the liver volume. In contrast, very little has been published regarding spleen volume formulas.

In this study, multiple morphological indexes were evaluated, including PVD, SVD, PVCSA, CTLV and CTSV, providing a reference range of these indexes for the Chinese population. Based on Pearson's correlation and step-wise multiple linear regression analysis, it was found that gender, BH, BW, BSA and BMI correlated with CTLV and CTSV, with BSA showing a very strong correlation. Hence, BSA was chosen

to establish an accurate formula for determining the liver volume and this new formula was compared with four other existing liver volume formulas. In addition, the proportion of values was calculated with percentage errors falling within an acceptable range when compared with CTLV and CTSV.

According to the literature, the liver in Asians is smaller than in Europeans[2]. The liver size in Chinese individuals reportedly ranges from 1099.1 to 1220.1 cm^3. Their results agree with these values, since the mean total liver volume of the 207 subjects in this study was 1043.18 ±244.60 cm^3. On the other hand, there are very few reports investigating the spleen volume. However, the mean total spleen volume was 175.07 ± 88.15 cm^3.

It has been reported that the liver volume correlates with many different factors, including gender, BH, BW, BSA and BMI. Of these, BSA is considered to be one of the strongest factors influencing the liver volume, so many researchers have developed liver volume formulas based on this parameter. Like the liver, the spleen is an irregular organ, but it is unknown how these indices correlate with its volume. Five indices mentioned above were chosen to establish their formulas. Many different formulas can be used to calculate the BSA. However, Mosteller's formula is more accurate in the Chinese population[26]. Therefore, this formula is chosen to calculate the BSA. In this study, it is proved that BSA showed a strong correlation with CTLV and CTSV.

Age is an important factor to consider when assessing the liver volume[27,28]. In this study, it is found that age influenced the liver volume, as shown by Pearson's correlation and step-wise multiple linear regression analysis. Therefore, BSA and age were initially incorporated to develop their new liver volume formula: SLV = 786.151*BSA–2.837*age–107.538(R^2 = 0.370). However, when the mean error was calculated between SLV and CTLV, its mean error was 3.19%, which was higher than when the formula included only the BSA value (mean error = 1.83). In addition, the proportion of SLV values with percentage errors falling within an acceptable range (10% and 15%) were 36.8% and 60.2%, respectively, which were also not better than when the formula included only the BSA value. Furthermore, the correlation coefficient for age was only –2.837 in the step-wise multiple linear regression analysis. Therefore, it is concluded that the effect on liver volume was small and it was eliminated. On the other hand, when the effect of age on the SLV was analyzed, it is found that age cannot be used as a factor to establish the spleen volume.

Although BH, BW and BMI were thought to affect the liver volume[29,30], and Pearson's correlation analysis showed that BH and BW correlated with CTLV, the correlation coefficients were 0.438,0.574 and 0.390, respectively. After the step-wise multiple linear regression analysis, both the factors were eliminated to establish the formula. A similar outcome was observed for the analysis of spleen volume.

Many formulas are currently available to calculate the liver volume. Urata's formula is the most widely used. Poovathumkadavil's formula has been shown to yield the lowest percentage error when compared with the actual liver volume. Fu's formula incorporates the BW and shows good agreement and low percentage error. Feng compared her formula with seven other proposed formulas and found it worked

better than the others. In this study, these four formulas were chosen to compare with new formula, and ±10% and ±15% are acceptable percentage errors. In addition, the SLV-CTLV mean error was calculated. It was found that the formula showed the highest percentage of agreement (within ±10% and ±15), and the lowest SLV-CTLV mean error (only 1.83%). Importantly, the formula showed perfect agreement with Urata's formula, and the mean error was significant lower (1.73% vs 17.3%). Thus, the formula may be a better choice to calculate the liver volume in the Chinese population.

Many researchers have tried to develop spleen volume formulas, with limited success. There are few reports on this topic, a situation that is attributed to the use of different methodologies. In this study, a spleen volume formula was determined: SSV = 188.813*BSA–140.981 (R^2 = 0.126). It is found that the proportion of estimated SSV values with percentage errors within ±10% and ±15 of the CTSV values were only 21.4% and 25.6%, and the mean error was 6.98%. Because the acceptable percent error values were not sufficiently high, the applicability of the spleen volume formula must be demonstrated through additional research.

In cirrhotic patients, due to the presence of portal hypertension and increased blood flow, the PVD, SVD and PVCSA values increase. A PVD > 13 mm is an important index to predict portal hypertension[31]. The mean PVD, SVD and PVCSA values in normal Chinese subjects in this study were 8.84 ± 1.55 mm, 5.53 ± 1.28 mm, 98.33 ± 33.08 mm^3, respectively.

In the past, even though there were some formulas about the liver and spleen volume, their clinical application is not clear. In our latter research, we combine the actual volume of liver and spleen with the volume calculated by our formulas, and we we have successfully established a model to predict the esophageal varices, as follow: ln[P(1-P)] = 12.925–0.014*CTLV+0.016*CTSV+0.009*(CTLV-SLV)–1.929*[(CTSV-SSV)/SSV]–0.216*PVD. The CTLV and CTSV is actual liver and spleen volume calculate by CT, and SLV and SSV is standard liver and spleen volume calculated by the formula. The area under the Roc curve is 87.3%, the specificity and sensitivity is 89.7% and 65.3%, respectively. The cutoff value is 0.85. If the P is higher than the cutoff value, we can think the presence of the esophageal varices. So the foundation of the formulas is very important for latter work. The foundation of the formulas is very meaningful.

Although the new accurate liver and spleen volume formulas were developed, there are still many limitations. The thickness of the CT slices was 5 mm, which may be a factor influencing the accuracy of the calculation of the actual liver and spleen volumes. In addition, normal study subjects were selected based on biochemical and imaging tests. Biopsies or bone marrow punctures was not performed. Therefore, certain occult liver or blood diseases may have gone undetected in their study. Also, their goal was to calculate the liver and spleen volumes of cirrhotic patients with these formulas, but the subjects in their study were all normal people. In cirrhotic patients, the BSA may be influenced by the ascites. Therefore, it is unclear whether the formulas would still be accurate and show low percentage error in cirrhotic patients. In the future, it is planned to use these formulas in patients with cirrhosis, and apply the

SLV and SSV ratio to establish a formula, which can be used to evaluate esophageal varices and the risk of bleeding after esophageal variceal ligation.

In conclusion, new liver and spleen volume formulas were established using the BSA which showed more accuracy and lower error than existing formulas. It is believed that these new formulas may be a better choice to predict the liver and spleen volumes in the Chinese population.

Abbreviations

BH: Body height; BW: Body weight; BSA: Body surface area; BMI: Body mass index; CTLV: Computed tomography estimated total liver volume; CTSV: Computed tomography estimated total spleen volume; PVD: Portal vein diameter; SVD: Spleen vein diameter; PVCSA: Portal vein cross-sectional area. SLV: Standard liver volume; SSV: Standard spleen volume.

Declarations

Ethics approval and consent to participate

The study protocol was reviewed and approved by the Institutional Ethics Committee of the second affiliated hospital of Xi'an Jiaotong University. As the study is a retrospective research, the Ethics Committee exempted the informed consent.

Consent for publication

Not applicable.

Availability of data and material

The datasets used and/or analyzed during the current study available from the corresponding author on reasonable request.

Competing interests

The authors declare no competing interests.

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No funding was obtained for this study.

Authors' contributions

All authors helped to perform the research; the project was complete by Lei Dong and Gang Zhao; data collection was completed by Cai-lan Xiao and Ying Zhang, data analysis was completed by Xin-xing Tantai and Cai-feng Yang; article writing was completed by Long-bao Yang and Hong Li.

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Tables

Table 1. Characteristics of study participants

	Total, n= 207	male, n=107	female, n=100	P, value
Age, yr	58.25±14.53	56.43±14.26	60.20±14.63	0.062
BH, cm	165.21±7.78	170.96±5.26	159.06±4.74	<0.001
BW, kg	61.41±10.57	65.99±9.74	56.51±9.18	<0.001
BSA, m^2	1.68±0.17	1.77±0.14	1.58±0.14	<0.001
BMI, kg/m^2	22.42±3.31	22.54±3.10	22.29±3.53	<0.001
CTLV,cm^3	1043.18±244.60	1136.84±209.69	942.96±240.40	<0.001
CTSV,cm^3	175.07±88.15	192.37±89.17	156.57±83.57	0.003
PVD, mm	8.84±1.55	9.14±1.59	8.51±1.44	0.003
SVD, mm	5.53±1.28	5.87±1.40	5.17±1.03	<0.001
PVCSA, mm^3	98.33±33.08	103.50±33.52	92.79±31.85	0.019

BSA: Body surface area; BMI: Body mass index; CTLV: Computed tomography estimated total liver volume; CTSV: Computed tomography estimated total spleen volume; PVD: Portal vein diameter; SVD: Spleen vein diameter; PVCSA: Portal vein cross-sectional area.

Table 2. Factors which correlate with CTLV and CTSV

	CTLV		CTSV	
Factor	r value	p value	r value	p value
Age	-0.328	<0.001	-0.182	0.009
BH	0.438	<0.001	0.258	<0.001
BW	0.574	<0.001	0.353	<0.001
BSA	0.592	<0.001	0.361	<0.001
BMI	0.390	<0.001	0.246	<0.001

BH: Body height; BW: Body weight; BSA: Body surface area; BMI: Body mass index

Table 3. Differences between CTLV and SLV calculated with various formulas

Researcher	Mean SLV-CTLV, cm^3	Mean error, %	P value
Urata	-129.86	17.30	<0.001
Poovathumkadavil	-249.38	29.30	<0.001
Fu	13.56	2.73	0.565
Feng	-80.50	12.3	0.002
Our	-14.03	1.73	0.556

Table 4 Proportions of SLV and SSV with percentage errors within acceptable agreement(10% and 15%) compare with CTLV and CTSV

	Proportions within acceptable agreement,%	
Researcher	±10	±15
Urata	22.4	42.9
Poovathumkadavil	16.3	20.4
Fu-Gui	40.8	62.6
Feng-lingmei	33.7	45.9
Ours	40.8	72.4
SSV	21.4	22.6

Figures

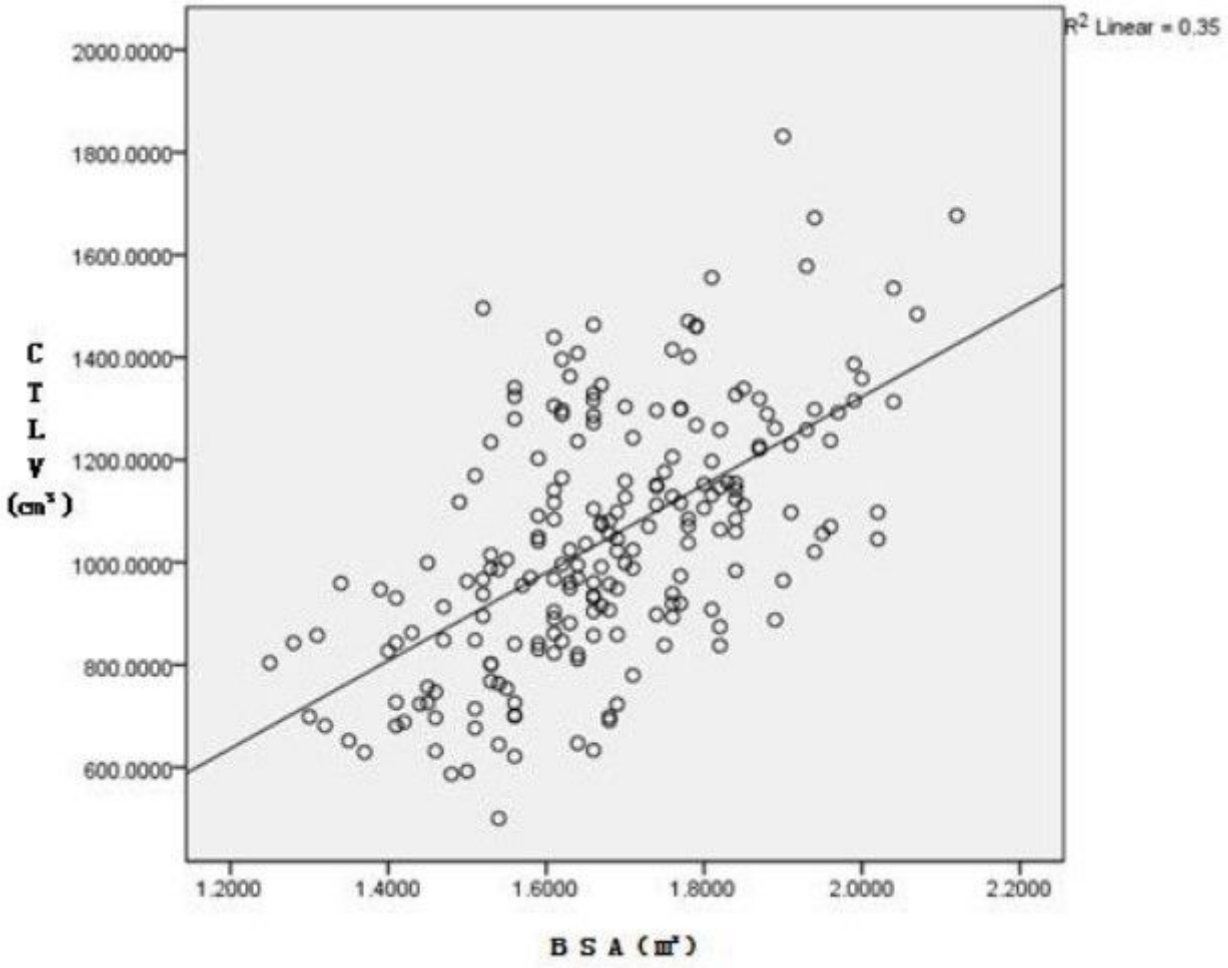

Figure 1

Correlation between CTLV and BSA. The 95% CI is shown (Dotted line). CTLV: the liver volume calculated by CT; BSA: body surface area.

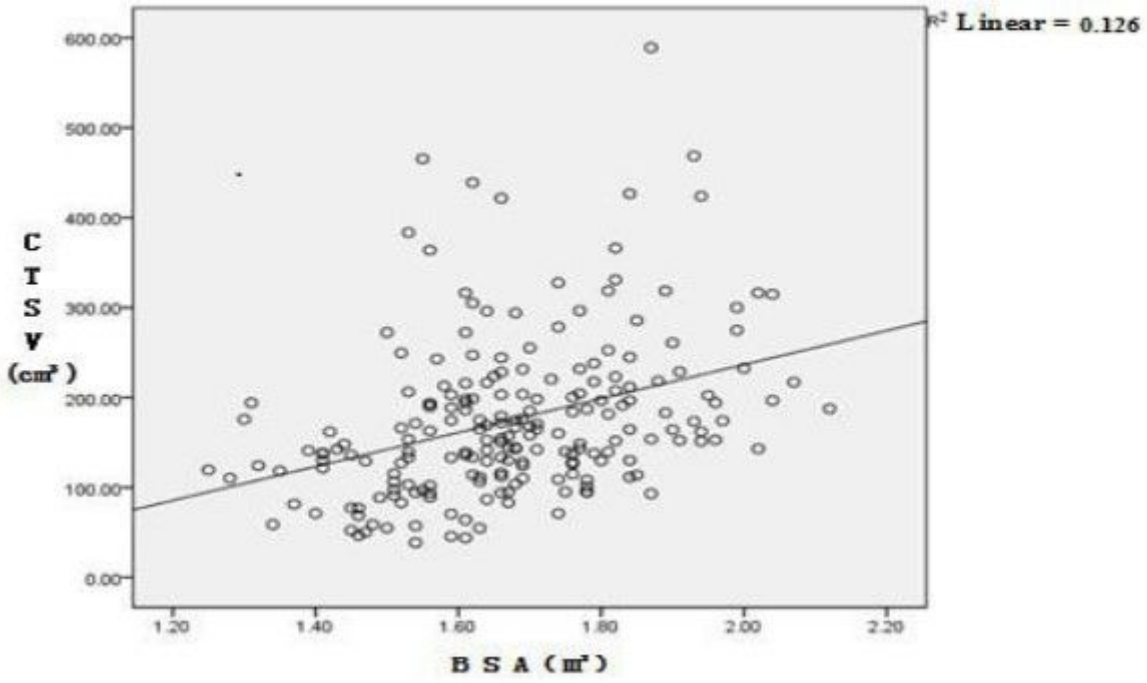

Figure 2

Correlation between CTSV and BSA. The 95% CI is shown (Dotted line). CTSV: the spleen volume calculated by CT; BSA: body surface area.

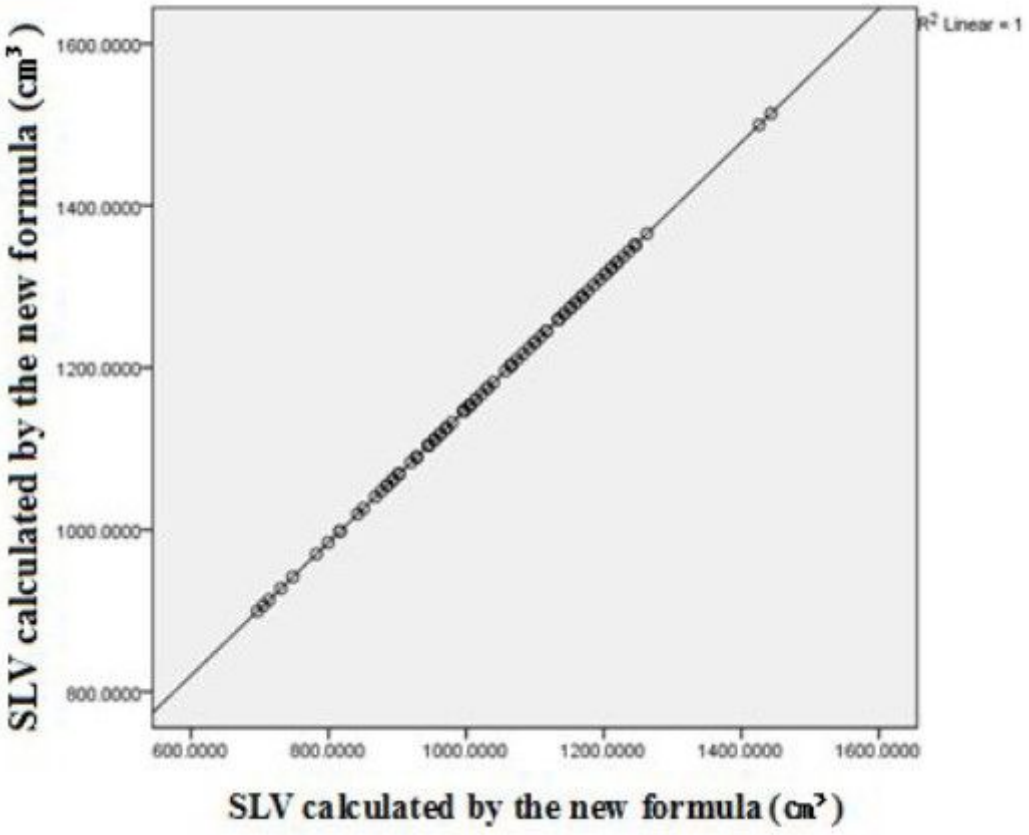

Figure 3

Correlation between liver volume calculated by our formula and Urata's formula.

Supplementary Files

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- eq1.jpg