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ORIGINAL ARTICLE

Prospective Study Standard liver weight model in adult deceased donors with fatty liver: A prospective cohort study

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Abstract

BACKGROUND

Standard liver weight (SLW) is frequently used in deceased donor liver transplantation to avoid size mismatches with the recipient. However, some deceased donors (DDs) have fatty liver (FL). A few studies have reported that FL could impact liver size. To the best of our knowledge, there are no relevant SLW models for predicting liver size.

AIM

To demonstrate the relationship between FL and total liver weight (TLW) in detail



involved with drafting of the manuscript; all authors have read and approve the final manuscript.

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statement: This study was reviewed and approved by the West China Hospital of Sichuan University Institutional Review Board.

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and present a related SLW formula.

METHODS

We prospectively enrolled 212 adult DDs from West China Hospital of Sichuan University from June 2019 to February 2021, recorded their basic information, such as sex, age, body height (BH) and body weight (BW), and performed abdominal ultrasound (US) and pathological biopsy (PB). The chi-square test and kappa consistency score were used to assess the consistency in terms of FL diagnosed by US relative to PB. Simple linear regression analysis was used to explore the variables related to TLW. Multiple linear regression analysis was used to formulate SLW models, and the root mean standard error and interclass correlation coefficient were used to test the fitting efficiency and accuracy of the model, respectively. Furthermore, the optimal formula was compared with previous formulas.

RESULTS

Approximately 28.8% of DDs had FL. US had a high diagnostic ability (sensitivity and specificity were 86.2% and 92.9%, respectively; kappa value was 0.70, P < 0.001) for livers with more than a 5% fatty change. Simple linear regression analysis showed that sex (R², 0.226; P < 0.001), BH (R², 0.241; P < 0.001), BW (R², 0.441; *P* < 0.001), BMI (R², 0.224; *P* < 0.001), BSA (R², 0.454; *P* < 0.001) and FL (R², 0.130; P < 0.001) significantly impacted TLW. In addition, multiple linear regression analysis showed that there was no significant difference in liver weight between the DDs with no steatosis and those with steatosis within 5%. Furthermore, in the context of hepatic steatosis, TLW increased positively (nonlinear); compared with the TLW of the non-FL group, the TLW of the groups with hepatic steatosis within 5%, between 5% and 20% and more than 20% increased by 0 g, 90 g, and 340 g, respectively. A novel formula, namely, -348.6 + (110.7 x Sex $[0 = \text{Female}, 1 = \text{Male}]) + 958.0 \times \text{BSA} + (179.8 \times \text{FL}_{US} [0 = \text{No}, 1 = \text{Yes}])$, where FL was diagnosed by US, was more convenient and accurate than any other formula for predicting SLW.

CONCLUSION

FL is positively correlated with TLW. The novel formula deduced using sex, BSA and FL_{US} is the optimal formula for predicting SLW in adult DDs.

Key Words: Standard liver weight; Body surface area; Fatty liver; Sex; Deceased donors

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Core Tip: This study was the first to explore the relationship between fatty liver (FL) and total liver weight (TLW) in detail using pathological biopsy based on adult deceased donors (DDs) and developed a new standard liver weight (SLW) formula. Moreover, to conveniently apply the SLW formula to the clinic, we introduced ultrasound (US). Notably, we found that FL was positively correlated with TLW and that US had a high diagnostic ability for mild to severe FL, which could increase liver weight significantly. The formula deduced using sex, BSA and FL_{us} is the optimal formula for predicting SLW in adult DDs.

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INTRODUCTION

Standard liver weight (SLW) is a key parameter in liver surgery. Its accurate evaluation is the basis for patient safety in both hepatectomy and liver transplantation



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(LT). In hepatectomy, the underestimation of SLW may lead to residual liver failure[1, 2], and in living donor liver transplantation (LDLT)/split liver transplantation (SLT), the underestimation of SLW can lead to small-for-size syndrome (SFSS)[3-5]. Since the establishment of Urata's standard liver volume (SLV) model[6], approximately 14 SLV models have been published worldwide, most of which are based on healthy people, living donors and autopsy donors from various medical centres. Deceased donor liver transplantation (DDLT) is a crucial donor liver source for alleviating the shortage of donor livers. Subsequently, SLT was established and further expanded the donor liver pool. Previous studies [7-10] have reported that SLT is not inferior to whole liver transplantation in terms of patient prognosis, which has encouraged the extensive use of SLT and necessitated an urgent demand for an SLW formula for DDLT to avoid severe mismatches, large-for-size syndrome[11,12] or SFSS. Moreover, deceased donors (DDs) and living donors (LDs) are from the general population and may have hepatic steatosis, which has a reported global incidence of 15%-30% [13,14]. To our knowledge, fatty liver (FL) may be associated with marginal grafts, as severe steatosis is a risk factor related to graft survival^[15] and may affect liver size^[16,17]. However, these associations have not been quantified conclusively. To the best of our knowledge, only one model[18] has been published for DDs, and it was based on a Western population and did not address FL. Therefore, this study prospectively collected adult DDs' clinical data combined with FL parameters to develop an SLW model

MATERIALS AND METHODS

The present study prospectively enrolled consecutive deceased liver donors from West China Hospital of Sichuan University from June 2019 to February 2021 and recorded basic patient information, such as sex, age, body height (BH) and body weight (BW). This study was reviewed and approved by the West China Hospital of Sichuan University Institutional Review Board and registered at http://www.chictr.org.cn. The registration identification number is ChiCTR2000041406. All the study participants, or their legal guardians, provided informed written consent prior to study enrollment, and the study protocol conformed to the ethical guidelines of the 1975 Declaration of Helsinki as reflected in a priori approval by the ethics committee. No executed prisoners were included in the study. A total of 212 DDs were enrolled, and brain death was confirmed in all of them before organ procurement. Advanced life support was maintained in an intensive care unit (ICU); moreover, abdominal ultrasound (US) examinations, liver function tests and kidney function tests were completed for each donor. Pathological biopsy (PB) was performed for all enrolled donor livers after they were obtained.

US examination

A US examination was carried out for all DDs before organ procurement. Scanning and diagnosis were conducted by 2 experienced (> 5 years) US doctors who were blinded to the final PB diagnosis. The examinations were performed by using a MultiWave ultrasound system (Aixplorer, France) equipped with an SC6-1 (1-6 MHz) transducer. FL was identified as a diffuse increase in fine echoes in the liver parenchyma. Representative images[19] are presented in Figure 1.

Donor liver weight measurement, tissue sampling and histological assessment

Donor livers were procured and trimmed in the operating room and were then weighed with a precision electronic balance (unit: kg, accurate to 0.001 kg, Figure 2) on a back table.

A single tissue wedge of approximately 1.0 cm × 1.0 cm × 1.0 cm was excised from the left lateral lobe surface of the donor liver, fixed in formalin and embedded in paraffin. Each donor liver was stained with haematoxylin and eosin (HE) and Masson's trichrome. The histological degree of liver pathology, including hepatic steatosis, ballooning of hepatocytes, lobular inflammation, necrosis, and fibrosis, was evaluated by two expert liver pathologists blinded to any other clinical information and laboratory data. The extent of hepatic steatosis was assessed by the percentage of hepatocytes containing large- and medium-sized intracytoplasmic lipid droplets (but not foamy microvesicles). The definition of ballooning of hepatocytes and lobular inflammation was as described by Kleiner *et al*^[20] and Bedossa *et al*^[21]. The definition of necrosis is described in Table 1. Fibrosis was scored according to the standard grading (inflammation) and staging (fibrosis) method based on the modified Scheuer



| Table 1 Characteristics of the deceased donors | | | |
|--|-----------------------|--|--|
| Characteristic | Total, <i>n</i> = 212 | | |
| Sex, male, <i>n</i> (%) | 167 (78.8) | | |
| Age, median (range), yr | 49 (18-68) | | |
| BH, median (range), cm | 168 (150-185) | | |
| BW, median (range), kg | 65 (45-90) | | |
| BMI, median (range), kg/m ² | 23.35 (15.57-30.48) | | |
| BSA, median (range), m ² | 1.73 (1.37–2.10) | | |
| TLW, median (range), g | 1400 (830–2100) | | |
| Cause of death, <i>n</i> (%) | | | |
| Trauma | 106 (50.0) | | |
| Cerebrovascular | 97 (45.8) | | |
| Other | 9 (4.2) | | |
| Degree of fatty change, median (range) | 0 (0-40%) | | |
| 0, n (%) | 151 (71.2) | | |
| > 0, < 5%, n (%) | 32 (15.1) | | |
| 5%-33%, n (%) | 22 (10.4) | | |
| > 33%, n (%) | 7 (3.3) | | |
| Ballooning of hepatocytes | | | |
| None | 24 (11.1) | | |
| Ballooned hepatocyte with normal size | 116 (54.9) | | |
| Enlarged ballooned hepatocyte | 72 (34.0) | | |
| Lobular inflammation | | | |
| None | 66 (30.9) | | |
| < 2 foci per lobule | 131 (61.7) | | |
| > 2 foci per lobule | 15 (7.4) | | |
| Necrosis | | | |
| None | 200 (94.4) | | |
| Focal or unicellular necrosis | 8 (3.7) | | |
| More extensive necrosis and above | 4 (1.9) | | |
| Stage of fibrosis ¹ | | | |
| 0 | 72 (33.8) | | |
| 1 | 88 (41.6) | | |
| 2 | 47 (22.1) | | |
| 3 | 4 (1.9) | | |
| 4 | 1 (0.6) | | |

¹According to the modified Scheuer system[22]. BH: Body height; BW: Body weight; BMI: Body mass index; BSA: Body surface area; TLW: Total liver weight.

system[22].

Estimating SLW using previous formulas

According to previous studies at our centre^[23] and other centres^[24-26], the density of the liver was determined to be 1 g/cm³; that is, the weight and volume of the donor liver were equal. For comparison, we calculated the estimated SLW according to

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Figure 1 Diagram of fatty liver diagnosed by ultrasound from the view of the liver and kidney. A: Diffuse increase in fine echoes in liver parenchyma with normal visualization of intrahepatic vessel borders; B: Diffuse increase in fine echoes in liver parenchyma. There was an increase in echogenicity of the liver compared with the echogenicity of the renal cortex.



Figure 2 Actual liver weight measurement by electronic balance. A: Zero correction of electronic balance; B: Donor liver weighing. The arrow indicates that a single tissue wedge of approximately 1.0 cm × 1.0 cm vas excised from the left lateral lobe surface of the donor liver.

previous formulas for adults[6-19]. Body mass index (BMI) = BW/BH^2 and body surface area (BSA) = $BW^{0.425} \times BH^{0.725} \times 0.007184$ using the Dubois formula[27] were also calculated.

Statistical analysis

In this study, simple linear regression analysis was used to explore the variables related to TLW. Multiple linear regression analysis was used to formulate the SLW. As BH, BW, BMI and BSA are collinear variables, each was applied in a different prediction model. The root mean standard error (RMSE) and interclass correlation coefficient (ICC) were used to test the fitting efficiency and accuracy of the model, respectively. The chi-square test and kappa consistency score were used to assess the consistency in terms of FL diagnosed by US relative to PB. Continuous variables were analysed by a paired-samples t test. Two-tailed statistical analysis was used, and P values less than 0.05 were considered to be statistically significant. SPSS, version 25.0 (IBM, Armonk, NY, United States) was used for all statistical analyses. GraphPad Prism 7.0 (GraphPad Software, Inc.) was used for drawing.

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RESULTS

Baseline data

This study included 167 males (78.8%). The median age was 49 years, ranging from 18 to 68 years. The median BH, BW, BMI, BSA and TLW were 1.68 m, 65 kg, 23.35 kg/m², 1.73 m² and 1400 g, respectively. The main causes of death of the DDs were trauma (50%), cerebrovasculature (45.8%), and other (4.2%), which included brain tumours and hypoxic-ischaemic encephalopathy. There were 151 DDs (71.2%) with no steatosis, 32 (15.1%) with steatosis within 5%, 22 (10.4%) with steatosis between 5% and 33%, and 7 (3.3%) with steatosis greater than 33%. Moreover, hepatocyte ballooning was observed in 88.9% of DDs. Lobular inflammation was observed in approximately 69.1% of DDs. Necrosis (focal or unicellular necrosis, in 3.7% of DDs samples, and more extensive necrosis, in 1.9% of DDs samples) was observed in only a few DDs liver tissue samples. Stage 0-2 Liver fibrosis was observed in approximately 97.5% of DDs (Table 1).

Impact factors related to the TLW of deceased donors

Simple linear regression analysis showed that sex, BH, BW, BMI, BSA and FL significantly impacted TLW (P < 0.001) (Table 2). BSA was the most influential factor related to liver size [R², 0.454; 95% confidence interval (CI): 1024.56–1383.79]. Multiple linear regression analysis showed that there was no significant difference in TLW between no steatosis and steatosis within 5% (P = 0.147, Figure 3A). Furthermore, in the context of hepatic steatosis, TLW increased positively (non-linear); compared with the TLW of the non-FL group, the TLW of the groups with hepatic steatosis within 5%, between 5% and 20% and more than 20% increased by 0 g, 90 g, and 340 g, respectively (Figure 3B).

Consistency test for FL diagnosis between US and PB

This study investigated 61 hepatic steatosis cases, which accounted for 28.8% of all cases, and moderate and severe steatosis cases, which accounted for 3.3%. The cases of hepatic steatosis and non-hepatic steatosis diagnosed by US were 38 and 174, respectively. The sensitivity and specificity of US were 55.7% and 97.4%, respectively, and the kappa value was 0.598 (P < 0.001). That is, its diagnostic consistency was good (Supplementary Table 1). Furthermore, when setting 5% as the cut-off value for diagnosing FL by PB, there were 174 cases within a 5% fatty change and 38 cases with more than a 5% fatty change diagnosed by US, with a sensitivity and specificity of 86.2% and 92.9%, respectively, and a kappa value of 0.70 (P < 0.001). Therefore, the diagnostic consistency between US and PB was high (Table 3).

Current formulas for estimating SLW

The SLW models were separately formulated based on four collinear variables, namely, BH, BW, BMI and BSA. Subsequently, three prediction model groups were established, two of which were used to assess the presence of FL based on US or PB; the third group did not include FL as an indicator. The present study showed that the SLW models based on BSA, FL and sex had the best fitness, and the adjusted R² and RMSE for PB and US were 0.546 and 169.985 and 0.546 and 169.913, respectively. The fitting efficiency of these two models was almost equal and better than that of the traditional method (adjusted R², 0.485; RMSE, 181.095) (Table 4).

Comparison between the current formula and previous formulas

Previously reported formulas were used to assess our DDs cohort, and the results showed that the fitting efficiency and accuracy of the SLW model introducing FL diagnosed by US were 168.3 (RMSE) and 0.71 (ICC), with a non-significant difference (P = 1.00) between the SLW and TLW of 1.5 g. The RMSE and ICC of Yu *et al*[25]'s and Lin et al[28]'s models were 187.5 and 0.61 and 188.0 and 0.63, respectively. There were no significant differences between the SLW and actual TLW for these two formulas, but those of the remaining formulas were significantly different (Table 5)[6,18,25-37].

DISCUSSION

The shortage of donor livers is a problem worldwide and has become a major obstacle hindering the development of LT. To date, experts in the LT field have explored expanding the donor liver pool, including via SLT, marginal donor LT, domino LT and



| Table 2 Factors related to the total liver weight of the deceased donors | | | | |
|--|----------------|---------|-----------------|--|
| Factor | R ² | P value | 95%CI | |
| Sex | 0.226 | < 0.001 | 220.89-369.68 | |
| ВН | 0.241 | < 0.001 | 13.92-22.78 | |
| BW | 0.441 | < 0.001 | 15.25-20.77 | |
| BSA | 0.454 | < 0.001 | 1024.56-1383.79 | |
| BMI | 0.224 | < 0.001 | 32.28-54.18 | |
| Degree of fatty change (< 5%, 5%-20%, > 20%) | 0.130 | < 0.001 | 116.89-244.17 | |
| Hepatic steatosis ¹ | 0.125 | < 0.001 | 149.67-318.33 | |

¹Diagnosed by ultrasound. BH: Body height; BW: Body weight; BSA: Body surface area; BMI: Body mass index.

Table 3 Results for livers with more than 5% fatty change diagnosed by ultrasound and pathological biopsy in the deceased donors

| Ultracound | Pathological biopsy | | Total | |
|-------------|---------------------|-----|--------|--|
| olitasoullu | + | • | I Uldi | |
| + | 25 | 13 | 38 | |
| - | 4 | 170 | 174 | |
| Total | 29 | 183 | 212 | |

According to the table above, livers with a fatty change of more than 5% were diagnosed by ultrasound, and the sensitivity and specificity were 86.2% and 92.9%, respectively. The chi-square test showed that the kappa value was 0.70, P < 0.001.

> so on. These schemes have successfully and significantly expanded the donor liver pool, and SLT has become one of the most valuable means of promotion. Graft weight (GW) plays a key role in recipients, especially in DDLT and LDLT. Therefore, it is necessary to evaluate the donor liver size in LT.

> DDs are patients with brain death caused by non-liver diseases. This study illustrated that 95.8% of DDs died from trauma or cardiovascular and cerebrovascular accidents. Biopsies showed that many donor livers had hepatocyte oedema and lobular inflammation, which can be explained by the cause of death. Trauma and cardiovascular and cerebrovascular accidents can cause instability of the circulatory system, leading to long-term ICU stays and the requirement for resuscitative therapy, which may cause unstable organ perfusion (hypoperfusion or hyperperfusion) and reperfusion injury. In addition, the use of a large number of vasoactive drugs may aggravate organ microcirculation disorder. Thus, the graft may have acute injury, such as lobular inflammation, hepatocyte oedema and even necrosis. The present study found that 28.8% of DDs had hepatic steatosis and that 2.5% had stage 3-4 Liver fibrosis. Unlike DDs, LDs screened from healthy populations rarely have FL or other acute liver injuries. In addition, it was unclear whether there was a difference in the SLW between DDs and LDs. To the best of our knowledge, there have been few relevant reports. Therefore, we explored the SLW model based on DDs data derived from West China Hospital.

> Simple linear regression analysis showed that liver size was correlated with sex. The liver size of males was larger than that of females, which was in line with previous studies[30,33]. We speculated that this might be related to the fact that the body size of men is generally larger than that of women and that men have a larger skeletal muscle system and higher daily consumption and metabolic requirements. Therefore, a larger liver mass is needed to meet physiological needs[38,39]. In addition, the present study found that BH, BW, BMI and BSA were closely related to liver size, which was similar to previous studies[6,25,31,40]. Indeed, multiple linear regression analysis revealed that the above four variables were collinear. From the perspective of morphology, liver size and physical indicators are supposed to be positively correlated. Moreover, in terms of energy requirements, to meet metabolic needs, a larger body size needs more organ support. Furthermore, the current study found that BSA was the most influential factor impacting TLW, which was consistent with previous studies[6,29,



Table 4 Results of multiple linear regression analysis performed to predict the total liver weight using each of the body anthropometric measures divided into groups of the traditional method and two new methods, which introduce the parameter of fatty liver diagnosed by ultrasound and pathological biopsy

| Groups | Formulas | Adjusted R ² | RMSE |
|--|--|-------------------------|-------|
| Traditional method | | | |
| ВН | - 809.4 + 167.3 x Sex + 12.6 x BH | 0.29 | 212.0 |
| BW | 322.1 + 147.0 x Sex + 15.2 x BW | 0.49 | 181.1 |
| BSA | - 466.9 + 99.0 x Sex + 1051.0 x BSA | 0.48 | 182.8 |
| BMI | 329.2 + 264.5 x Sex + 37.8 x BMI | 0.39 | 196.5 |
| Ultrasound method | | | |
| ВН | - 1011.9 + 149.7 x Sex + 13.6 x BH + 240.7 x ${\rm FL}_{\rm US}$ | 0.43 | 191.1 |
| BW | 392.7 + 158.3 x Sex + 13.5 x BW + 158.6 x $\rm FL_{\rm US}$ | 0.54 | 171.4 |
| BSA | - 348.6 + 110.7 x Sex + 958.0 x BSA + 179.8 x ${\rm FL}_{\rm US}$ | 0.55 | 169.9 |
| BMI | 453.7 + 264.5 x Sex + 31.2 x BMI + 162.9 x ${\rm FL}_{\rm US}$ | 0.45 | 187.5 |
| Pathological biopsy method (< 5%, 5%-20%, > 20%) | | | |
| ВН | - 803.7 + 178.5 x sex + 12.3 x BH + FL _{PB} (0 = 0, 1 = 163.5, 2 = 393.0) | 0.43 | 190.0 |
| BW | 414.5 + 172.6 x sex + 13.1 x BW + $\mathrm{FL}_{\mathrm{PB}}$ (0 = 0, 1 = 79.8, 2 = 280.7) | 0.54 | 170.8 |
| BSA | - 288.8 + 129.5 x sex + 919.6 x BSA + $\mathrm{FL}_{\mathrm{PB}}$ (0 = 0, 1 = 93.9, 2 = 304.5) | 0.55 | 170.0 |
| BMI | 478.1 + 276.5 x Sex + 30.0 x BMI + FL _{PB} (0 = 0, 1 = 105.3, 2 = 299.1) | 0.46 | 185.4 |

Sex and FL_{US} are binary variables; FL_{PB} is a dummy variable. Sex: 0 = Female, 1 = Male; FL_{US} : 0 = No, 1 = Yes; FL_{PB} : 0 < 5%, 1 = 5%–20%, 2 > 20%. BH: Body height; BW: Body weight; BSA: Body surface area; BMI: Body mass index; FL_{US}; Fatty liver diagnosed by ultrasound; FL_{PB}: Fatty liver diagnosed by pathological biopsy; RMSE: Root mean standard error.

> 31]. BSA is a widely used parameter in physiology and clinical medicine for normalizing biological function with respect to variations in body size and conformation. Thus, we believe that the liver size required to meet the metabolic demands of the individual may correlate more closely with BSA than with any other parameter. Additionally, previous studies [30,34] reported that age was associated with TLW; however, similar to Poovathumkadavil's study[35], we failed to identify an association between age and TLW. Several previous studies[31,40] reported that the partial regression coefficient of age was very small, and the authors considered the effect of this variable in adults to be negligible. Therefore, our negative result may be explained by the age distribution of patients in our study and the sample size, and further studies with larger sample sizes are needed to confirm the relation between age and TLW.

> Interestingly, this study found that more than a quarter of DDs from the general population had hepatic steatosis, which was similar to Zhou *et al*[41]'s report (29.2%). To our knowledge, an increasing number of individuals, especially those who are obese, suffer from FL worldwide[42,43]. Furthermore, the present study also found that 10.4% and 3.3% of livers had mild and moderate steatosis, respectively, while no liver was detected to have severe steatosis. Several studies have confirmed that mild steatosis grafts (< 33%) can be used safely in LT. However, the eligibility of livers with moderate steatosis is controversial, while livers with severe steatosis are generally discarded because of the increased probability of primary non-function[15,44,45]. Importantly, in the current study, simple linear regression analysis demonstrated that FL was correlated with TLW. Moreover, multivariate analysis showed that steatosis significantly affected TLW, and the degree of steatosis was positively correlated with liver size, which was consistent with previous studies[16,46,47]. Multiple linear regression analysis showed that compared with non-FLs, the presence of hepatic steatosis within 5%, 5%-20% and over 20% resulted in an increase in liver weight by 0 g, 93.9 g, and 304.5 g, respectively. In LT, we generally evaluate the feasibility of SLT



Table 5 Differences between the estimated and actual liver weights calculated using previous formulas in our deceased donor cohort.

| Ref. | Formula | Difference ¹ (g) | RMSE | ICC | <i>P</i> value² | |
|--|--|-----------------------------|-------|------|--------------------|--|
| Autopsy | | | | | | |
| DeLand <i>et al</i> [29] | 1020 × BSA - 220 | 135.5 (-366-632) | 221.2 | 0.52 | < 0.01 | |
| Heinemann et al[26] | 1072.8 × BSA - 345.7 | 95 (-421-556) | 202.5 | 0.56 | < 0.01 | |
| Yu et al[<mark>25</mark>] | $21.585 \times BW^{0.732} \times BH^{0.225}$ | 34.5 (-490-576) | 187.5 | 0.61 | 0.102 | |
| Choukèr <i>et al</i> [30] | [16–50 yr] 452 + 16.34 x BW + 11.85 × age - 166 × sex (1 = female, 0 = male) 51–70 yr] 1390 + 15.94 × BW - 12.86 × age | 435 (-301-1000) | 484.0 | 0.24 | < 0.01 | |
| General population/living donor | | | | | | |
| Urata[6] | $706.2 \times BSA + 2.4$ | -185 (-713-337) | 278.1 | 0.32 | < 0.01 | |
| Lin <i>et al</i> [<mark>28</mark>] | 13 × BH + 12 × BW - 1530 | 11.5 (-546-445) | 188.0 | 0.63 | 0.472 | |
| Vauthey <i>et al</i> [31] ³ | 1267.28 × BSA - 794.41 | -15 (-544-421) | 188.1 | 0.64 | < 0.01 | |
| Hashimoto et al[32] | 961.3 × BSA - 404.8 | -161 (-668–317) | 253.4 | 0.42 | < 0.01 | |
| Chan et al[33] | 218 + BW × 12.3 + sex × 51 (0 = female, 1 = male) | -356.5 (- 859–175) | 411.1 | 0.21 | < 0.01 | |
| Yuan et al[<mark>34</mark>] | 949.7 × BSA - 247.4–48.3 x age factor (1, < 40; 2, 41–60; 3, > 60) | -106 (-646-359) | 228.0 | 0.48 | < 0.01 | |
| Fu-Gui et al[23] | 11.508 × BW + 334.024 | -319 (-845-241) | 393.6 | 0.19 | < 0.01 | |
| Poovathumkadavil <i>et al</i> [<mark>35</mark>] | 12.26 × BW + 555.65 | -57 (-572-510) | 207.5 | 0.47 | < 0.01 | |
| Um et al[<mark>36</mark>] | 893.485 x BSA - 439.169 | -312.5 (- 816–173) | 372.8 | 0.24 | < 0.01 | |
| Cadaveric population | | | | | | |
| Yoshizumi et al[18] ³ | 772 × BSA | -79 (-602-416) | 214.6 | 0.45 | < 0.01 | |
| Current | - 348.6 + 110.7 x Sex (0 = Female, 1 = Male) + 958.0 x BSA + 179.8 x FL _{US} (0 = No, 1 = Yes) | 1.5 (- 477.0–450.0) | 168.3 | 0.71 | 1 | |

¹Difference between estimated and actual liver weight using previous formulas.

²Paired-samples *t* test.

³Mosteller's formula[37] was adopted for BSA, and the remaining formulas used the Dubois formula[27].

BH: Body height; BW: Body weight; BSA: Body surface area; BMI: Body mass index; FL_{US}: Fatty liver diagnosed by ultrasound; ICC: Interclass correlation coefficient: RMSE: Root mean standard error.

> based on the criteria of GW/SLW (30%-40%) or GW/BW (0.8%)[11]. Thus, for FL, the GW required for recipients would be underestimated if calculated according to the traditional SLV method, leading to an increased risk of SFSS. Therefore, the current study introduced the FL variable for the first time to develop an SLW model. To diagnose FL before organ procurement, US was performed for all DDs. Notably, for a diagnosis of mild steatosis and greater (\geq 5%), the sensitivity and specificity of US were 86.2% and 92.9%, respectively, and the ICC was 0.70 (P < 0.001). That is, US had a higher diagnostic consistency with PB. In addition, this study revealed that the size of livers with a fatty change less than 5% was not different from that of livers without fatty change but was different from that of livers with a fatty change of 5% or greater. The gap of liver size between these two hepatic steatosis categories was significant (180 g, P < 0.001), which laid a solid theoretical foundation to apply US in the diagnosis of FL and develop the SLW model, highlighting its clinical practical value.

> In this study, the deduced best fit formula based on US had equivalence with that based on PB and was better than the best fit traditional model. Furthermore, the present study showed that the formulas of Deland et al[29], Heinemann et al[26], and Chouker *et al*[30] overestimated liver size, while the formulas of Urata *et al*[6], Vauthey et al[31], Yoshizumi et al[18], Hashimoto et al[32], Chan et al[33], Yuan et al[34], Fu Gui et al[23], Poovathumkadavil et al[35], and Um et al[36] underestimated liver size. On the other hand, there was no significant difference between the actual liver weight and the predicted liver weight calculated by Yu *et al*[25]'s and Lin *et al*[28]'s formulas. This was speculated to be related to the characteristics of the study samples. Deland et al [29]'s, Heinemann *et al*[26]'s and Chouker *et al*[30]'s cohorts were autopsy samples. To





Figure 3 Total liver weight comparison of different groups according to the degree of fatty change of donor livers. A: Groups according to the degree of fatty change of 0, (0 <, < 5%), (5%-20%) and > 20%; B: Groups according to the degree of fatty change of < 5%, (5%-20%) and > 20%. Multiple linear regression analysis including parameters of sex, BSA, and FL_{PB}, which were dummy variables divided into groups according to the degree of fatty change in donor livers, was used. FL_{PB}, fatty liver diagnosed by pathological biopsy.

our knowledge, data from autopsy studies^[29] includes the weight of the gallbladder, the attached ligaments, and the hepatic vena cava. In addition, various causes of death, *i.e.*, cardiac failure and traffic accidents, might increase liver weight through mechanisms associated with shock-related hepatic congestion. On the other hand, due to long-term immersion in the fixed solution, the weight of the specimen may exceed the actual size in vivo. However, the autopsy study of Yu et al^[25] was not consistent with the other three autopsy studies but was similar to our study, which may be explained by racial differences. Additionally, the cohorts of Vauthey et al[31], Hashimoto *et al*[32], Chan *et al*[33], Yuan *et al*[34], Fu Gui *et al*[23], Poovathumkadavil et al[35], and Um et al[36] were based on healthy populations without liver disease. However, Lin et al[28]'s study cohort comprised 44 (57.1%) patients with chronic liver disease (alcoholic hepatitis, 9; hepatitis B, 24; and hepatitis C, 11), which may explain the difference from other studies based on the general population. Notably, the difference was significant between actual liver weight and estimated liver weight using the formula of Yoshizumi *et al*[18], which was the only previous study based on a cadaveric population. Their study included DDs of several races, most of which were Western, and subjects under 18 years were enrolled. These confounding factors may explain the difference. Therefore, for different study populations, the model for predicting liver size is supposed to be different, which highlights the need for this study for adult DDs. In addition, this study shows the practicability and rationality of the current SLW model in DDLT. Theoretically, it suggests that the current formula is the most suitable for recipients assigned with FL in SLT, and use of this formula is anticipated to reduce the risk of SFSS.

However, the sample size of this study was relatively small, especially in regard to cases of moderate to severe hepatic steatosis. Therefore, studies with larger sample sizes are warranted to optimize the SLW model. Additionally, the extrapolation and clinical practicability of the current SLW model need to be further verified.

CONCLUSION

In conclusion, this study was the first to demonstrate the positive correlation between the degree of hepatic steatosis and liver size based on pathological findings. Furthermore, this study creatively proposed and verified the equivalent value of FL diagnosed by US instead of that diagnosed by PB in terms of the FL variable in the SLW model as follows: SLW (g)= -348.6 + [110.7 x Sex (0 = Female, 1 = Male)] + 958.0 x BSA + [179.8 x FL_{US} (0 = No, 1 = Yes)]. This formula can be used to estimate the liver weight before liver procurement. Additionally, our formula lays a theoretical and practical basis for the further application of donor livers with fatty changes in SLT.

ARTICLE HIGHLIGHTS

Research background

Standard liver weight (SLW) is frequently used in liver transplantation, especially for living donor liver transplantation/split liver transplantation (SLT). However, some deceased donors (DDs) have fatty liver (FL). There have been a few studies to report that FL could impact liver size. This study was to develop a new formula including FL to predict liver size.

Research motivation

To explore SLW model in adult DDs with FL and help transplant doctors make allocation decisions, especially for recipients assigned with FL in SLT to reduce the risk of small-for-size syndrome.

Research objectives

To explore the liver pathology of DDs, such as hepatic steatosis, and diagnostic ability of ultrasound for FL, as well as the relationship between FL and total liver weight. Furthermore, to develop an SLW formula, combined with FL parameter, used to predict graft weight required for recipients in SLT.

Research methods

This study prospectively enrolled consecutive DDs from West China Hospital of Sichuan University from June 2019 to February 2021 and recorded basic patient information, and abdominal ultrasound (US) examination and pathological biopsy (PB) were performed for them. Furthermore, the chi-square test and kappa consistency score were used to assess the consistency in terms of FL diagnosed by US relative to PB. Simple linear regression analysis was used to explore the variables related to TLW. Multiple linear regression analysis was used to formulate SLW models.

Research results

More than a quarter of DDs had hepatic steatosis, and US had a high diagnostic ability for mild to severe FL. Furthermore, this study found that FL was positively correlated with liver size and deduced an optimal SLW formula in adult DDs with FL. However, the extrapolation and clinical practicability of the current SLW model need to be further verified in the future.

Research conclusions

FL is positively correlated with liver size. Our novel formula deduced using sex, BSA and FL_{US} is the optimal formula for predicting SLW in adult DDs with FL.

Research perspectives

To verify the extrapolation of the current SLW model using multicentre data and its clinical practicability in SLT.

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