# The psoas muscle depletion index is related to the degree of cirrhosis and skeletal muscle loss in patients with end-stage liver disease

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## Abstract

***Objective:*** **To establish a new psoas muscle depletion index (PDI) from healthy young donors and to explore the correlation between the PDI and the severity of cirrhosis in patients with end-stage liver disease (ESLD).**

***Methods:*** **Clinical data of 461 healthy donors were collected during the period 2014-2019, and clinical data of 331 patients with ESLD were collected during the period 2014-2018. The patients were divided into four groups by PDI severity: PDI ≥ 0.90, PDI = 0.75-0.90, PDI = 0.50-0.75 and PDI ≤ 0.50 (Gsev). Differences in international normalised ratio (INR), total bilirubin and serum creatinine levels, and Child-Pugh (CP) and model for end-stage liver disease (MELD) scores were compared. The sarcopenia incidence according to the PDI and the psoas muscle index (PMI) in different weight groups were also compared.**

***Results:*** **Gsev had the highest CP (10.2 ± 2.1) and MELD (20.1 ± 7.4) scores and total bilirubin (166.3 ± 192.0 umol/L) and blood creatinine (92.9 ± 90.2 umol/L) levels and the lowest haemoglobin (93.8 ± 21.7 g/L) and blood albumin (30.9 ± 5.8 g/L) levels. Gsev showed significant changes in INR (1.74 ± 0.65) and blood sodium (135.3 ± 5.65 mmol/L). If PDI <0.75 was used as the diagnostic criterion for sarcopenia, the incidence was 53.3% in patients weighing >90 kg and 53.6% in those weighing <60 kg. This differed from the PMI, with an incidence of 3.3% in patients weighing >90 kg.**

***Conclusions:*** **The PDI had no significant correlation with body height, body weight or body mass index (BMI) in healthy individuals and patients with ESLD. The PDI was significantly correlated with the severity of cirrhosis and loss of skeletal muscle.**
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**Keywords**: liver cirrhosis, sarcopenia, donor, psoas muscle index, psoas muscle depletion index.

## Introduction

Liver disease-associated sarcopenia, a type of secondary sarcopenia, is a common muscle abnormality in patients with end-stage liver disease (ESLD). Since Englesbe (1) first reported that sarcopenia was strongly correlated with mortality after liver transplantation in 2010, many studies have confirmed that sarcopenia is an independent risk factor for adverse outcomes for disease-related liver resection (2,3), liver transplantation (4,5) and the waitlist. (6) Due to reduced appetite, insufficient protein intake, indigestion caused by portal hypertension, abnormal protein consumption and high metabolic status in patients with ESLD, skeletal muscle depletion is accelerated, and patients with cirrhosis become highly prone to sarcopenia. According to different diagnostic criteria, the incidence of sarcopenia is 22%-70% in patients with ESLD, (7) which is higher than that for patients who do not have cirrhosis at 5.5%-25.7% (8).

Computed tomography (CT) cross-section imaging is the most used method to evaluate the anatomy of the blood vessels and biliary tract in patients undergoing hepatectomy and liver transplantation. It is useful to create a surgical plan or as a screen for hepatocellular carcinoma. Preoperative CT examination provides an opportunity to evaluate the skeletal muscle mass of patients with liver cirrhosis and is the best method for the diagnosis of skeletal muscle mass conditions. The total psoas muscle area (PMA) or skeletal muscle area, measured with the CT image normalised by body height (BH) and the psoas muscle index (PMI) or the skeletal muscle index (SMI), was the most commonly used method to obtain a cut-off value for the diagnosis of sarcopenia (9-11). To date, it is challenging to standardise the definition of sarcopenia in patients with ESLD with precise cut-off values for skeletal muscle mass. The field is currently hindered by heterogenous definitions, measurements and study designs. The most important reason for the diversity of diagnostic criteria arises from the individuals themselves, since skeletal muscle mass is related to many characteristics, including age, BH, body weight (BW), gender, body mass index (BMI), body surface area (BSA) and ethnicity (12-15). Although the SMI or the PMI partially eliminates the influence of BH on the sarcopenia diagnostic criteria, other factors remain. Considering that healthy or sick individuals gradually develop sarcopenia from the skeletal muscle mass peak, it should be possible to eliminate the influence of the above factors through individual self-comparison.

The aim of our study was to establish a psoas muscle depletion index (PDI) based on data from young, healthy donors and to test the correlation between PDI and age, BH, BW, gender, BMI, BSA and the severity of liver cirrhosis.

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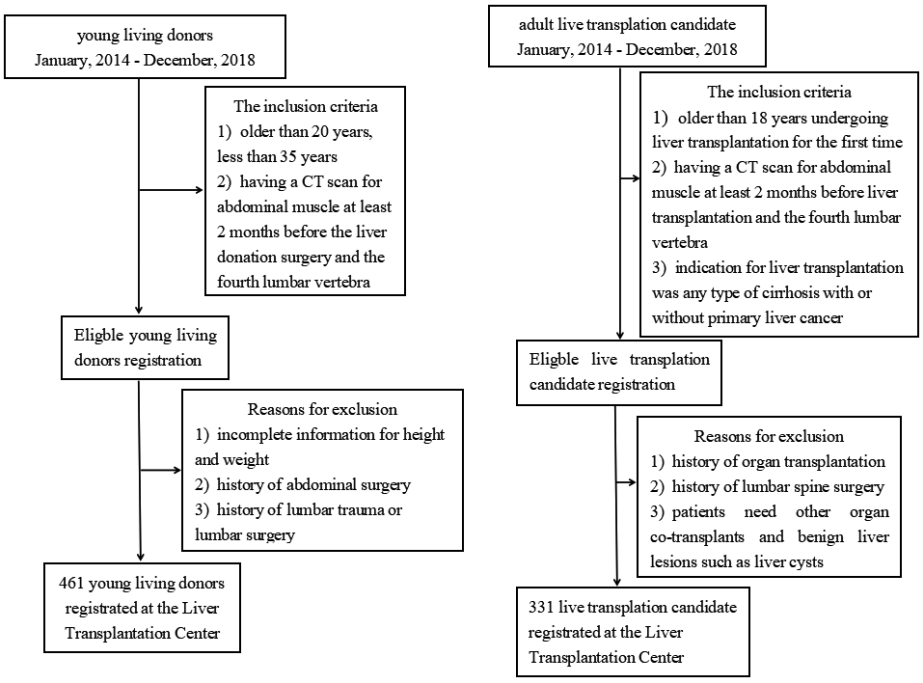


Figure 1. — Flow chart

## Patients and methods

*Inclusion and exclusion criteria for donors and recipients*

The retrospective analysis included the data of healthy young living liver donors and adult liver transplantation candidates collected between January 2014 and December 2018 at the Liver Transplantation Centre of Tianjin First Central Hospital, Tianjin, China. A flowchart of the study identification process is provided in Fig. 1.

For healthy liver donors, the inclusion criteria were: (1) older than 20 years and less than 35 years; (2) prior approval by the ethics committee of organ transplantation; (3) an abdominal CT scan including the fourth lumbar vertebra had been performed at least 2 months before the liver donation surgery.

Donor exclusion criteria were: (1) incomplete information for BH and BW; (2) a history of abdominal surgery; (3) a history of lumbar trauma or lumbar surgery. Based on the above criteria, 461 donors were included in the study.

For liver transplantation candidates, the inclusion criteria were: (1) patients older than 18 years undergoing liver transplantation for the first time; (2) an abdominal CT scan including the fourth lumbar vertebra had been performed at least 60 days before liver transplantation; (3) the indication for liver transplantation was any type of cirrhosis with or without primary liver cancer.

Recipient exclusion criteria were: (1) a history of organ transplantation; (2) a history of lumbar spine surgery; (3) patients needing other organ co-transplants, such as combined liver and kidney transplantation; (4) metastatic liver cancer, such as colon cancer liver metastasis, fulminant liver failure, benign liver lesions and cysts. According to these criteria, a total of 331 recipients were included in the study.

This study protocol conformed to the ethical guidelines of the 1975 Declaration of Helsinki and was approved by the hospital's institutional ethics review board. No donor organs were obtained from executed prisoners or other institutionalised individuals.

*Analysis of the PMA in the CT image*

Cross-sectional areas of the left and right psoas muscles at the level of the fourth lumbar vertebra were determined in the donors and patients with ESLD in our study population. To precisely locate the measured CT slide, the CT image with the longest transverse process on both sides of the fourth lumbar vertebra was used. The psoas muscle at this level had the clearest border lines. The PMA was measured with the area measurement tool provided by the CT imaging workstation (INFINITT, 3.0.11.3 [BN5], Shanghai, China). After an operator trained in musculoskeletal anatomy manually drew the boundaries of the psoas muscle, the area of the resulting enclosed region was computed to generate the cross-sectional area of the psoas muscle automatically (Fig. 2 and Fig. 3). The total PMA was equal to the sum of the bilateral PMAs.

*Establishment of the PDI and the cut-off value for the classic PMI*

Morphological indicators of healthy young donors, such as BH, BW and age, recorded in the donor medical charts were used for calculating BSA and BMI. Our goal was to develop a PMA prediction formula for men and

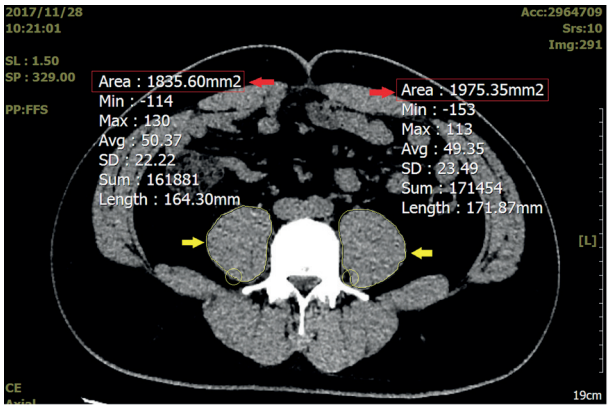


Figure 2. — Measurement of the PMA at the CT slide of the longest transverse section of the fourth lumbar vertebra. The red arrows show the automatically calculated bilateral PMA. The yellow arrows show the clear outline of bilateral psoas muscle. Example of a 26-year-old male liver donor: PMA is 1835.60 $mm^2$ (right) + 1975.35 $mm^2$ (left) = 3810.95 $mm^2$. PMI is 1125.6$mm^2/m^2$, PDI>1. *Abbreviation:* PDI, psoas muscle depletion index; PMA, psoas muscle area; PMI, psoas muscle index.

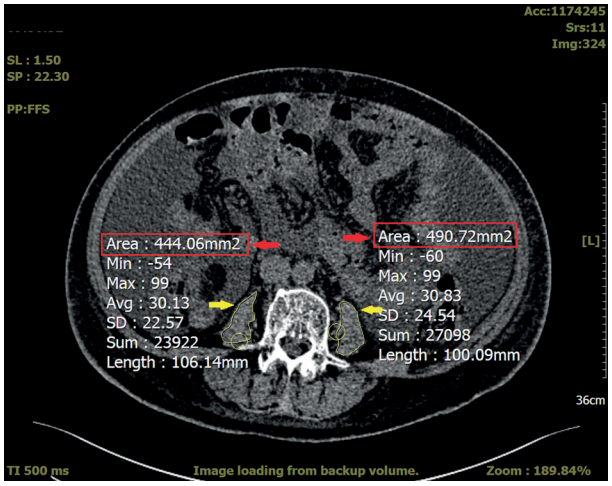


Figure 3. — A 58-year-old male hepatitis B related liver cirrhosis patient, Child-Pugh class C, height 184 cm, weight 95 kg, BMI 24.9 $kg/m^2$. The PMA at the fourth lumbar vertebra is 444.06 $mm^2$ (right) + 490.79 $mm^2$ (left) = 934.78 $mm^2$, PMI = 277.0$mm^2/m^2$, PDI = 0.36, with severe skeletal muscle depletion. The red arrows show the automatically calculated bilateral PMA. The yellow arrows show the outline of bilateral psoas muscle. *Abbreviation:* PDI, psoas muscle depletion index; PMA, psoas muscle area; PMI, psoas muscle index.

women using multiple linear regression. The formula was verified by random sampling. The PMA estimated by the formula from each sampled donor and recipient with ESLD was called the estimated PMA (PMAe), which sought to represent the peak value of the PMA in healthy individuals. The PMA computed from the CT image was called the actual PMA or disease-related PMA (PMAa). Therefore, the formula for PDI was:

$$PDI = PMAa / PMAe$$

We obtained the cut-off value for the diagnosis of sarcopenia through traditional methods based on the PMA data of healthy donors. Gender-specific cut-off points were set at −2 standard deviations compared to the mean reference value.

Other formulas, such as BSA and BMI, were:

$$BSA\ (m^2) = 0.007184 \times BW\ (kg)^{0.425} \times BH\ (cm)^{0.725} \quad (16)$$
$$BMI\ (kg/m^2) = BW\ (kg) / BH\ (m^2)$$
$$PMI\ (mm^2/m^2) = PMA\ (mm^2) / BH\ (m^2).$$

*Statistical analysis*

All the statistical analyses were carried out using SPSS™ Statistics version 22.0 for Windows (IBM Corporation, NY, USA). Normally distributed data were expressed as mean and standard deviation, and non-normally distributed data were presented as median and interquartile amplitude. We evaluated differences between groups using the independent samples t-test or the Mann−Whitney U test. The Student-Newman-Keuls method was used to compare the differences between subgroups and/or the Chi-squared test was used for categorical variables. The paired samples t-test was used to compare differences between PMAa and PMAe. The multiple linear regression method was used to establish the formula for PMAe. A p value of $<0.05$ was considered statistically significant.

## Results

*General characteristics of young donors and correlation with the classic PMI*

A total of 461 young donors were included in the study, comprising 190 males and 271 females. The PMI was 697.3 ± 183.1 $mm^2/m^2$, and the PMA was 1927.3 ± 533.2 $mm^2$. The average BH, BW and BMI were 165.0 ± 8.2 cm, 60.9 ± 11.0 kg and 22.3 ± 3.2 $kg/m^2$, respectively. Except for BMI and age, body size parameters were significantly greater in males than in females ($p < 0.001$). The morphological indicators of donors by gender are shown in Table 1.

The PMI was significantly related to the BW, BMI, BSA and PMA ($p < 0.01$) (Table 1). The PMI had no relationship with age since the age range was limited to 20−35 years. For male donors, the PMI had no relationship with BH because the data were normalised by BH squared, whereas the PMI still had a positive correlation with BH in female donors.

*Establishment and verification of the PDI and the PMA prediction formula*

The measured PMAa was significantly correlated with the BW ($p < 0.001$), BH ($p < 0.001$), BMI ($p < 0.001$) and BSA ($p < 0.001$). Since the BMI and BSA were derived from BH and BW, the equations below were derived from

Table 1. — **Morphological indicators of donors and correlation with PMI by sex**

| Parameter | Male (n=190) | | | Female (n=271) | | |
|---|---|---|---|---|---|---|
| | result | r value | P | result | r value | P |
| PMI ($mm^2/m^2$) | 852.9±157.1Δ | - | - | 588.3±104.3 | - | - |
| PMA ($mm^2$) | 2532.3±497.9Δ | 0.938 | 0.000** | 1503.1±267.2 | 0.924 | 0.000** |
| PMA ($mm^2$) | 29.2±3.3 | 0.019 | 0.793 | 28.3±3.6 | 0.117 | 0.056** |
| Height (cm) | 172.2±5.7Δ | 0.013 | 0.863 | 160.0±5.4 | -0.194 | 0.001** |
| Weight (Kg) | 67.2±10.5Δ | 0.449 | 0.000** | 56.5±9.1 | 0.274 | 0.000** |
| BMI ($Kg/m^2$) | 22.6±3.1 | 0.500 | 0.000** | 22.1±3.2 | 0.389 | 0.000** |
| BSA($m^2$) | 1.79±0.14Δ | 0.380 | 0.000** | 1.58±0.13 | 0.170 | 0.005** |

**: P<0.001; male versus female: Δ, P<0.01; -, null. *Abbreviations:* PMI, psoas muscle index; PMA, psoas muscle area; BMI, body mass index; BSA, body surface area.

Table 2. — **Correlation between PDI, PMI and body size parameters of another 78 donors**

| | PDI | | PMI | |
|---|---|---|---|---|
| | r value | P | r value | P |
| PMI | 0.593 | 0.000** | - | - |
| sex | 0.065 | 0.504 | -0.696 | 0.000** |
| Age (years) | -0.077 | 0.427 | 0.046 | 0.637 |
| Height (cm) | -0.029 | 0.767 | 0.485 | 0.000** |
| Weight (Kg) | 0.064 | 0.512 | 0.626 | 0.000** |
| BMI ($Kg/m^2$) | 0.094 | 0.336 | 0.484 | 0.000** |
| BSA ($mm^2$) | 0.039 | 0.690 | 0.631 | 0.000** |

**: P<0.001; -, null. *Abbreviations:* BMI, body mass index; BSA, body surface area; PDI, psoas muscle depletion index.

our data by multiple linear regression analysis to predict the PMA for young donor adults.

For males:

$$PMAe\ (mm^2) = 24.860 \times BW\ (kg) + 10.302 \times BH\ (cm) - 913.056$$
$$(r = 0.758,\ R^2 = 0.574,\ Durbin\text{-}Watson\ (U) = 1.221).$$

For females:

$$PMAe\ (mm^2) = 12.512 \times BW\ (kg) + 0.878 \times BH\ (cm) + 655.557$$
$$(r = 0.789,\ R^2 = 0.622,\ Durbin\text{-}Watson\ (U) = 1.143).$$

For validation, another sample of 78 donors, comprising 49 males and 29 females, was used to calculate PMAe using the above gender-specific formulas. The PMAe was significantly correlated with PMAa in males ($p = 0.000$, $r = 0.847$) and females ($p = 0.000$, $r = 0.885$). The mean difference between PMAe and PMAa was 10.8 ± 36.3 $mm^2$ ($p = 0.869$) for males and 24.3 ± 33.9 $mm^2$ ($p = 0.408$) for females.

The PDI was calculated by the formula:

$$PDI = PMAa / PMAe$$

The PDI was 0.99 ± 0.18 for males and 1.01 ± 0.14 for females ($p = 0.504$). The PDI had no relationship with age, BW, BH, BSA or BMA, and it was not related to gender; however, the PDI was related to the PMI (Table 2).

*General characteristics of patients with ESLD*

A total of 331 liver transplant candidates diagnosed with ESLD were included in the study, comprising 259 males and 72 females. The PMI and PDI were 626.2 ± 206.3 $mm^2/m^2$ and 0.745 ± 0.190, respectively, and were lower than those in healthy donors. The average model for end-stage liver disease (MELD) and Child-Pugh (CP) scores were 14.2 ± 6.9 and 8.1 ± 2.3, respectively. A total of 165 ESLD patients were diagnosed with hepatocellular carcinoma, 87 with viral hepatitis-related cirrhosis and 37 with autoimmune cirrhosis (Table 3).

*Comparison of clinical indicators between the different PDI groups*

The 331 patients with ESLD were grouped according to the PDI. Of these, PDI ≥ 0.90 was the normal group (Gnor) with <10% skeletal muscle loss; PDI = 0.75-0.90 was the mild depletion group (Gmin), or pre-sarcopenia group, with >10% skeletal muscle loss; PDI = 0.50-0.75 was the moderate depletion group (Gmod), or sarcopenia group, with >25% skeletal muscle loss; and PDI ≤ 0.50 was the severe depletion group (Gsev), or severe sarcopenia group, with <50% of skeletal muscle mass remaining.

There were 61 patients (18.4%) with ESLD in the Gnor group, 101 (30.5%) in the Gmin group, 124 (37.5%) in the Gmod group and 45 (13.6%) in the Gsev group. There were 270 patients with PDI ≤ 0.90 (81.6%) and 169 patients with PDI ≤ 0.75 (51.1%). There were significant

Table 3 — **Characteristics of ESLD patients of liver transplant candidates before the operation**

| Parameter | Gender (n=331) | | P value |
|---|---|---|---|
| | Male (n=259) | Female (n=72) | |
| Age (years) | 50.7±8.1 | 55.8±9.4 | 0.000** |
| BW (Kg) | 73.9±12.5 | 58.3±12.2 | 0.000** |
| BH (cm) | 172.7±5.7 | 162.0±5.1 | 0.000** |
| BMI (Kg/mm2) | 24.7±4.0 | 22.1±3.9 | 0.000** |
| PMI (mm2/m2) | 688.5±179.3 | 402.1±125.7 | 0.000** |
| PDI | 0.760±0.181 | 0.692±0.212 | 0.007** |
| Child–Pugh score | 8.0±2.4 | 8.6±2.1 | 0.076 |
| MELD score | 13.8±6.7 | 15.4±7.3 | 0.075 |
| TB (umol/L) | 75.6±124.0 | 99.3±164.6 | 0.109 |
| INR | 1.41±0.48 | 1.62±0.94 | 0.073 |
| Cr (mmol/L) | 77.9±45.1 | 71.6±29.7 | 0.099 |
| ALB (g/L) | 33.6±6.3 | 32.7±5.6 | 0.278 |
| Blood type (A/B/O/AB) n (%) | 71/100/60/28 (27.4/38.6/23.2/10.8) | 15/32/16/9 (20.8/44.4/22.2/12.6) | 0.663 |
| HCC (yes/no) n (%) | 147/112 (56.8/43.2) | 18/54 (25.0/75.0) | 0.000** |
| Liver cirrhosis | 72/6/20/14 (64.2/5.4/17.9/12.5) | 15/31/0/8 (27.8/57.4/0/14.8) | 0.000** |
| (viral/AI/alcohol/other), n (%) | | | |
| Child–Pugh class (A/B/C), n (%) | 82/106/71 (31.7/40.9/27.4) | 17/28/27 (23.6/38.9/37.5) | 0.200 |
| Diabetes Mellitus (yen/no) n (%) | 47/212 (18.1/81.9) | 13/59 (18.1/81.9) | 0.986 |

**: *P*<0.001. *Abbreviations:* AI, autoimmune; ALB, albumin; BH, body height; BW, body weight; BMI, body mass index; Cr, creatinine; HCC, hepatocellular carcinoma; INR, international normalized ratio; MELD, Model For End Stage Liver Disease; PDI, psoas muscle depletion index; PMI, psoas muscle index.

differences in the PMI, CP score, CP class, haemoglobin, total bilirubin, albumin, international normalised ratio (INR), blood creatinine, MELD score and blood sodium between the groups (Table 4).

The Gmin group had a PMI of 699.8 ± 127.8 $mm^2/m^2$, which was significantly lower than that of the Gnor group. The mean age of 51.9 ± 8.6 years in the Gmin group was significantly older that of the Gnor group; however, there were no significant differences in the other indicators between the Gmin and Gnor groups. The CP score, total bilirubin level and MELD score were significantly higher in the Gmod group than in the Gmin group, while blood haemoglobin and albumin levels were significantly lower. The Gsev group had skeletal muscle loss that exceeded 50% (Fig. 4). Compared with the other three groups, the Gsev group had the highest CP and MELD scores and total bilirubin and blood creatinine levels, and the differences were statistically significant, while the haemoglobin and blood albumin levels were the lowest. There were significant changes in INR and blood sodium levels in the Gsev group (Table 4).

*Comparison of the PDI and the classic PMI methods for the incidence of sarcopenia in patients with different body weights*

According to Table 2, using traditional methods, the gender-specific cut-off points were set at -2 standard deviations compared to the mean PMI value; thus, the cut-off value of sarcopenia was 538.7 $mm^2/m^2$ for males and 379.9 $mm^2/m^2$ for females. If the above were taken as the diagnostic criteria, the incidence of sarcopenia was only 3.3% when the BW was >90 kg and 10.4% when it was >80 kg, whereas the incidence of sarcopenia was as high as 60% when the BW was <50 kg (Fig. 4).

If skeletal muscle loss of >25% was used as the diagnostic criterion for sarcopenia, that is, the PDI was <0.75, the incidence of sarcopenia was 53.3% in patients weighing >90 kg and 53.6% in patients weighing <60 kg, with no statistical difference between the two BW groups.

Similarly, if the PDI was <0.5, that is, skeletal muscle loss of >50% was used as the diagnostic criterion for

Table 4. — **Comparison of clinical indicators related to liver cirrhosis by PDI grouping**

| Parameter | Groups(n=331) | | | | |
|---|---|---|---|---|---|
| | Gsev(n=45) | Gmod(n=124) | Gmin(n=101) | Gnor(n=61) | P value |
| PMI ($mm^2/m^2$) | 337.7±100.6$^{aabbcc}$ | 553.4±122.8$^{ddee}$ | 699.8±127.8$^{ff}$ | 866.6±162.2 | 0.000** |
| BW (Kg) | 65.2±19.1$^{abc}$ | 71.9±13.3 | 70.2±12.4 | 72.0±12.7 | 0.040* |
| BH (cm) | 168.9±8.6 | 170.6±6.7 | 170.2±7.1 | 171.4±6.6 | 0.348 |
| Gender (M/F) | 27/18$^{abc}$ | 99/25 | 82/19 | Oct-51 | 0.015* |
| BMI ($Kg/mm^2$) | 22.7±5.8$^{aabc}$ | 24.6±3.8 | 24.1±3.56 | 24.5±3.9 | 0.054 |
| Age (years) | 54.6±8.6$^{cc}$ | 52.8±8.7$^{ee}$ | 51.9±8.6$^{ff}$ | 47.8±9.0 | 0.000** |
| CP score | 10.2±2.1$^{aabbcc}$ | 8.4±2.2$^{ddee}$ | 7.4±2.1 | 7.3±2.0 | 0.000** |
| CP class (A/B/C) | 2/14/29$^{aabbcc}$ | 31/54/39$^{de}$ | 41/42/18 | 25/24/12 | 0.000** |
| WBC (109/L) | 5.7±3.3 | 4.2±3.2 | 4.5±2.5 | 4.6±2.1 | 0.208 |
| HGB (g/L) | 93.8±21.7$^{aabbcc}$ | 108.6±27.3$^{ddee}$ | 117.7±28.5 | 122.9±27.7 | 0.000** |
| PLT (109/L) | 100.8±108.7 | 91.5±78.9 | 113.9±95.7$^{f}$ | 99.7±60.0 | 0.136 |
| TB (umol/L) | 166.3±192.0$^{aabbcc}$ | 98.2±154.0$^{ddee}$ | 49.6±78.7 | 45.7±65.7 | 0.000** |
| INR | 1.74±0.65$^{aabbc}$ | 1.47±0.52 | 1.31±0.43 | 1.46±0.92 | 0.002** |
| Cr (umol/L) | 92.9±90.2$^{abbcc}$ | 73.8±35.8 | 71.8±19.7 | 69.6±21.01 | 0.002** |
| BUN (mmol/L) | 10.30±9.53$^{aabbcc}$ | 6.64±5.27$^{de}$ | 5.38±1.96 | 4.68±1.68 | 0.000* |
| MELD score | 20.1±7.4$^{aabbcc}$ | 14.8±6.9$^{ddee}$ | 11.9±5.7 | 12.2±5.5 | 0.000** |
| MELD>20 | 20/25$^{aabbcc}$ | 26/98$^{de}$ | 10/91 | 5/56 | 0.000** |
| ALB (g/L) | 30.9±5.8$^{abbcc}$ | 32.6±5.8$^{de}$ | 34.8±6.7 | 34.7±6.5 | 0.001** |
| Sodium | 135.3±5.65$^{aabbcc}$ | 141.0±5.0 | 143.81±3.2 | 142.0±3.5 | 0.000** |

Note: Gsev vs. Gmod: a, P <0.05; Gsev vs. Gmin: b, P <0.05 ; Gsev vs. Gnor: c, P <0.05; Gmod vs. Gmin: d, P <0.05 ; Gmod vs. Gnor: e, P<0.05 ; Gmin vs. Gnor: f, P <0.05; Gsev vs. Gmod: aa, P <0.01; Gsev vs. Gmin: bb, P <0.01; Gsev vs.Gnor: cc, P <0.01 ; Gmod vs. Gmin: dd, P <0.01; Gmod vs. Gnor: ee, P <0.01; Gmin vs. Gnor: ff, P <0.01.**: P<0.01; *: P<0.05. *Abbreviations:* ALB, albumin; BH, body height; BUN, blood urea nitrogen; BW, body weight; BMI, body mass index; CP, Child-Pugh; Cr, Creatinine; HGB, hemoglobin; INR, international normalized ratio; MELD, Model for End-Stage Liver Disease; PDI, psoas muscle depletion index; PLT, Platelets; PMI, psoas muscle index; TB, total bilirubin ; WBC, white blood cell.

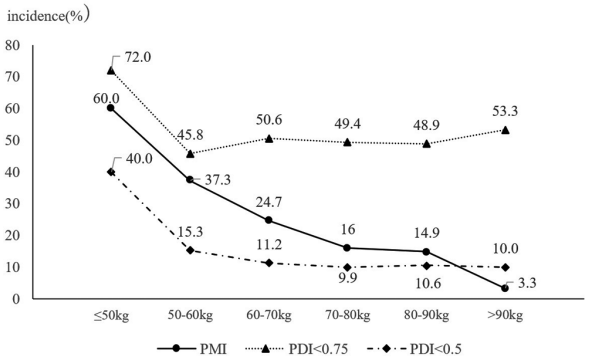


Figure 4. — Difference of the occurrence of sarcopenia according to PDI and PMI in different weight group patients. *Abbreviation:* PDI, psoas muscle depletion index; PMI, psoas muscle index.

severe sarcopenia, the incidence of sarcopenia in patients weighing >90 kg was 10.0%, and the incidence in patients weighing <60 kg was 22.6% (Table 5, Fig. 4).

## Discussion

This study demonstrates that the PDI, the ratio of the measured PMA to the estimated peak PMA of patients with ESLD, is closely related to the degree of liver cirrhosis. This new diagnostic method can remove the influence of age, BW, BH, BMI and gender on the diagnosis of sarcopenia by self-comparison. The PDI has a significant correlation with the PMI, and therefore it might be an important reference index for the diagnosis of sarcopenia.

Sarcopenia has been studied as part of aging and adverse outcomes in older patients. However, during the last decade, skeletal muscle mass loss has been found to be a strong independent predictor of adverse outcomes on both the waitlist and post-transplantation in patients with ESLD (4-6,17-19). Because of the heterogeneous definitions, study designs and measurements of skeletal muscle mass, it has been challenging to standardise the definition of sarcopenia in patients with ESLD with

Table 5. — **Incidence of sarcopenia with different body weight patients according to PDI and PMI**

| Weight (Kg) | | | | | | | |
|---|---|---|---|---|---|---|---|
| Criteria (Kg) | ≤50 Kg | 50-60 | 60-70 Kg | 70-80 Kg | 80-90 Kg | >90 Kg | total |
| PMI | 60.0% | 37.3% | 24.7% | 16.0% | 14.9% | 3.3% | 24.2% |
| (%) (n, yes/no)* | (15/10) | (22/37) | (22/67) | (13/68) | (7/40) | (1/29) | (80/251) |
| PDI<0.75 | 72.0% | 45.8% | 50.6% | 49.4% | 48.9% | 53.3% | 51.1% |
| (%) (n, yes/no) | (18/7) | (27/32) | (45/44) | (40/41) | (23/24) | (16/14) | (169/162) |
| PDI<0.5 | 40.0% | 15.3% | 11.2% | 9.9% | 10.6% | 10.0% | 13.6% |
| (%) (n, yes/no) | (10/15) | (9/50) | (10/79) | (8/73) | (5/42) | (3/27) | (45/286) |

Note: *, cut off values for sarcopenia were 538.7mm$^2$/m$^2$ for males and 379.9mm2/m2 for females. PDI, psoas muscle depletion index; PMI, psoas muscle index.

uncontroversial cut-off values for muscle mass. The most important reason for using different cut-offs to define sarcopenia is that skeletal muscle mass is related to indicators such as gender, BH, BW and BMI (9-11). Although the SMI or PMI eliminates some effects of BH by normalising by BH squared, other influencing factors exist. Skeletal muscle mass decreases with increasing age after reaching the middle-age peak, especially after the age of 50 years, with about 1% loss every year until the age of 70, after which the annual loss increases to 1.5% (20). However, the rate of muscle loss in patients with cirrhosis is twice as fast as that in healthy individuals and is related to the severity of the liver disease (21). It is envisaged that patients with cirrhosis should reach the peak of skeletal muscle mass in middle age, if not affected by the disease, and the elderly will gradually lose skeletal muscle after reaching the muscle mass peak. Therefore, we can predict with formulas the maximum value of muscle mass in middle age, which can apply to diseased or healthy individuals. By studying the PMA of healthy young donors, we have obtained a formula for predicting PMAe. By comparing the PMA measured in the diseased or aged status with PMAe, we determined the PDI, which is an indicator that reflects the current percentage of skeletal muscle loss (or the current percentage of skeletal muscle remaining), rather than an indicator of current skeletal muscle mass. In fact, patients with cirrhosis are affected by the disease and have a different muscle mass peak. This difference should be independent of age, but it can reflect the degree of muscle depletion. The PDI self-comparison method could eliminate the influence of age and morphological indicators such as BH, BW and BMI, both in donors and in patients with ESLD (Tables 2 and 4). Therefore, the PDI may be easier to standardise, and further research is warranted for cirrhosis and others.

Defining the cut-off point of the PMI or SMI from the third vertebra on the CT image is the method most recent studies have used, as this specific lumbar vertebral landmark significantly correlates with the whole-body muscle mass (22). In our study, the psoas muscle CT slide of the longest transverse process on both sides of the fourth lumbar vertebra was used for the following reasons: (1) The range of Hounsfield units used to identify skeletal muscles is still controversial and can increase the system measurement error; (2) The psoas muscle originates from the twelfth thoracic vertebra. Since muscle fibres generate from the anterior side of each lumbar vertebra and the intervertebral discs into the psoas muscle, the PMA becomes gradually stronger from the head side to the foot side (23). At the third lumbar vertebra, the boundary of the psoas muscle is difficult to distinguish in partial CT images of individuals since the lumbar quadrate and psoas muscles are close together; however, at the fourth lumbar vertebra, the psoas margin is clear and easy to measure (24); (3) The psoas muscle is located within the posterior abdominal cavity and is not influenced by external factors (25); (4) When muscle loss occurs, all the skeletal muscles, including the psoas muscle, are depleted. Therefore, the degree of depletion of the psoas muscle can reflect the skeletal muscle loss of the whole body.

Valero et al. (26) used gender-specific PMI cut-off values to define sarcopenia in 328 patients who underwent hepatic resection or liver transplantation. Sarcopenia was less frequently observed among obese patients with BMI ≥ 30 kg/m$^2$, where the incidence of sarcopenia was 21.7%, whereas, among patients with BMI ≤ 24.9 kg/m$^2$, the incidence was 64.7%. Ha et al. (27) defined sarcopenia as the SMI at the third lumbar vertebra of ≤45.8 cm/m$^2$ for males and ≤43.0 cm/m$^2$ for females and found that patients with sarcopenia were older, more likely to be female and had lower BMI. According to the mathematical formula, the PMI and SMI or BMI are normalised by BH in metres squared. Therefore, the correlation between the PMI and the BMI is actually the correlation between the PMA and BW. If BW had a significant influence on the PMI, sarcopenia would be undiagnosed in patients with sarcopenic obesity and hidden beneath a higher BMI. Our findings suggest that the results of traditional PMI methods in the diagnosis of sarcopenia are quite different from those of the method that we present in this study. If the traditional PMI

method was used to diagnose sarcopenia, cut-off values for sarcopenia were 538.7 $mm^2/m^2$ for males and 379.9 $mm^2/m^2$ for females, and the incidence of sarcopenia was only 3.3% in patients weighing >90 kg and 60.0% in patients weighing <50 kg, which is similar to most of the literature reports. If we set the PDI > 0.75, or a loss of skeletal muscle mass that exceeds 25% of the peak value, as the diagnostic criteria for sarcopenia, the incidence of sarcopenia in patients weighing >50 kg would be stable at about 50% and would not be influenced by weight gain. If we set the PDI > 0.5, or a loss of skeletal muscle mass that exceeds 50%, as the diagnostic criteria for severe sarcopenia, the incidence of severe sarcopenia in patients weighing >50 kg would be stable at about 10%. When the loss of skeletal muscle mass is >50% (Table 3), patients with severe sarcopenia have significant changes in BW because of a large depletion of muscle tissue; therefore, the incidences of sarcopenia and severe sarcopenia in patients weighing <50 kg were higher, at 72.0% and 40.0%, respectively. Another reason for the higher incidence rate of sarcopenia in patients with BW < 50 kg is that this group included 17 (68%) patients with autoimmune cirrhosis, and this cirrhosis type influenced muscle loss (28). To create standardised cut-off points for sarcopenia in cirrhosis, Carey et al. (29) recently defined sarcopenia as SMI < 50 $cm^2/m^2$ in male patients and SMI < 39 $cm^2/m^2$ in female patients with cirrhosis waitlisted for liver transplantation based on the data from North American centres. Studies using cut-offs without adjusting for age, gender, BW, BMI or ethnicity to identify sarcopenia should be interpreted with caution since there is a risk of misclassification of the studied population (30). For example, if a patient has high BW and the PMI is closely related to BW, this may cause a false negative diagnostic bias, whereas, for a patient with low BW, false positive bias is more likely to occur. Our findings suggest the PDI has no significant correlation with BH, BW, BMI or BSA in healthy individuals and patients with ESLD. Therefore, it is easy to standardise; however, the diagnostic efficiency needs to be confirmed in future research.

In the study, we also found that when the PDI was >0.75, there was no significant difference in the CP score, MELD score, haemoglobin, serum albumin, total bilirubin, total creatinine and other indicators between the pre-sarcopenia and normal groups. When the muscle residue was 50-75% of the maximum muscle content, there were obvious changes in the above indicators (Table 4). When the muscle loss continued, the skeletal muscle was depleted by >50%. The severe sarcopenia group had the highest CP score, MELD score, total bilirubin, total creatinine and the lowest haemoglobin and albumin levels compared to the other groups. There were also changes in blood sodium and INR values in the severe sarcopenia group, indicating that INR and blood sodium may be the last affected indicators in patients with ESLD. In addition, INR and blood sodium values were considered to be clinical indicators that were significantly related to the worse prognosis of patients with ESLD (31,32). The classic PMI method can only distinguish between sarcopenia or no sarcopenia, whereas this PDI method can detect the degree of muscle depletion. It is suggested that a PDI of 0.75 should be defined as the diagnostic standard of sarcopenia, and PDI ≤ 0.50 should be defined as severe sarcopenia. When the PDI is <0.75, clinicians should pay attention to the need for nutritional intervention to avoid further loss of muscle mass in patients with cirrhosis. According to the above criteria, the incidence of sarcopenia and severe sarcopenia in patients with ESLD was 51.1% and 13.6%, respectively, and the incidence of pre-sarcopenia was 30.5%.

This study has some limitations, however. First, because of the retrospective design of our study, muscle strength, such as grip strength and walking speed, which is usually regarded as one of the diagnostic criteria for sarcopenia, was not assessed. Second, according to the inclusion criteria, only patients with ESLD were included in this study, while patients with early or compensatory cirrhosis were not included, since they were not suitable for liver transplantation. The diagnostic method needs to be confirmed in further research. Third, it is very difficult to measure skeletal muscle mass conveniently and accurately at present, and therefore the PMA, rather than the total skeletal muscle mass, was used to determine the PDI in this study. Fourth, the formula for predicting PMAe by studying PMA in healthy young donors does not apply to all ethnicities and should change according to the ethnicity or origin of the patient.

In conclusion, this study demonstrated that the PDI was related not only to the degree of cirrhosis but also to the skeletal muscle mass. Moreover, this index has no significant correlation with many morphological parameters. Our findings suggest the PDI can be used as a diagnostic standard for muscle loss. Furthermore, this method was easy to standardise, which warrants further study.

**Ethics approval and consent to participate**

The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by ethics committee of Organ Transplantation center,Tianjin First Central Hospital (NO.2019N176KY). After explaining the operation steps, all patients gave their informed consent.

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## Competing Interest

All authors have completed the ICMJE uniform disclosure form. The authors have no conflicts of interest to declare.

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(IV) Collection and assembly of data: Hou JC and Shen ZY
(V) Data analysis and interpretation: Qiang Z,Shen ZYand Zhu LY
(VI) Manuscript writing: All authors
(VII) Final approval of manuscript: All authors

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## Availability of data and materials

All data generated or analyzed during this study are included in this published article

## Consent for publication

The manuscript is not submitted for publication or consideration elsewhere.

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