

Inclusion of sarcopenia improves the prognostic value of MELD score in patients after transjugular intrahepatic portosystemic shunt

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Objective To explore the predictive value of model for end-stage liver disease (MELD)-Sarcopenia score for survival of cirrhotic patients after transjugular intrahepatic portosystemic shunt (TIPS) placement.

Methods 289 patients who underwent TIPS between February 2016 and December 2020 were included, they were divided into the sarcopenia group ($n = 138$) and non-sarcopenia group ($n = 151$) according to whether they were complicated with sarcopenia. Kaplan–Meier curve was used to analyze and compare the prognosis of the above two groups and multivariate Cox regression analysis was used to identify the independent prognostic factors. The performance of different predictive models was compared using C-index.

Results During the follow-up, Kaplan–Meier analyses indicated that cumulative survival was significantly lower in sarcopenia group than that in non-sarcopenia group [74.6% vs. 92.7%, HR, 0.24 (95% confidence interval (CI), 0.12–0.46), Log-rank $P < 0.001$]. After multivariate Cox analysis, age [HR, 1.040 (95% CI, 1.015–1.065), $P = 0.002$], sarcopenia [HR, 3.948 (95% CI, 1.989–7.838), $P < 0.001$], albumin [HR, 0.945 (95% CI, 0.897–0.997), $P = 0.037$], and MELD score [HR, 1.156 (95% CI, 1.097–1.217), $P < 0.001$] were identified as the independent risk factors for mortality after TIPS. The C-indexes of MELD-Sarcopenia, Child-Pugh, MELD, MELD-Na, and the Freiburg index of post-TIPS survival (FIPS) scores were 0.782, 0.688, 0.719, 0.734, and 0.770, respectively.

Conclusion Sarcopenia is independently correlated with post-TIPS mortality, and MELD-Sarcopenia score showed the best performance in predicting post-TIPS mortality than the traditional predictive models. *Eur J Gastroenterol Hepatol* 34: 948–955 Copyright © 2022 The Author(s). Published by Wolters Kluwer Health, Inc.

Introduction

In 2000, Malinchoc *et al.* first applied model for end-stage liver disease (MELD) score to predict the mortality of patients with end-stage liver disease after transjugular intrahepatic portal shunt (TIPS) placement [1], and confirmed that MELD score plays an important role in predicting the mortality of patients with end-stage liver disease [2]. Currently, MELD score became the most common clinical evaluation model for end-stage liver disease

[2] which is calculated based on serum bilirubin, international normalized ratio (INR), and serum creatinine. However, there are still some limitations in application of MELD score [3]. The fluctuation of various indicators caused by complications other than liver disease will directly affect the judgment of the real condition of liver disease. For example, kidney disease could cause a significant increase in serum creatinine and abnormal INR could occur in patients with coagulopathy [4]. Besides that, the complications related to portal hypertension, such as variceal hemorrhage and ascites, have direct impacts on the prognosis of patients, which are not reflected in MELD score [2]. Recently, a frequently reported shortcoming of MELD score is the lack of objective parameters reflecting the patient's nutritional status, but patients with malnutrition or sarcopenia should be given priority in waiting for transplantation [5].

Studies have shown that sarcopenia is independently correlated with the prognosis 6 months after TIPS [6], and the prognosis of patients with sarcopenia is worse than that without sarcopenia. In addition, sarcopenia is associated with mortality in compensatory and early decompensated cirrhosis, and the existing traditional prognostic factors have limited value for severe sarcopenia [7]. Therefore, including sarcopenia as a routine prognostic factor has added value, especially in compensatory and early decompensated cirrhosis. The classification of prognostic factors based on sarcopenia is helpful to evaluate the prognosis

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Keywords: model for end-stage liver disease score; model for end-stage liver disease-Sarcopenia score; mortality; sarcopenia; transjugular intrahepatic portosystemic shunt

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of cirrhosis. Montano-loza *et al.* included sarcopenia into MELD score (MELD-Sarcopenia score) [8] and found that modification of MELD to include sarcopenia is associated with improved prediction of mortality in patients with cirrhosis. However, there is little external validation of this modified score, and the validation of the MELD-Sarcopenia score with the mortality of patients after TIPS has not been reported. We observed and analyzed the survival of patients with cirrhosis after TIPS, and evaluated the predictive performance of MELD-Sarcopenia score for the survival of patients after TIPS.

Patients and methods

Patients and data acquisition

This study retrospectively collected 391 patients in our center from February 2016 to December 2020. After the exclusion criteria, 289 patients were finally included in the study (Fig. 1). Inclusion criteria were as follows: cirrhosis, refractory ascites or variceal bleeding and adequate liver and renal functions. Exclusion criteria were as follows: liver cancer or other malignant tumors; missing computer tomography (CT) data before TIPS; incomplete medical records. This retrospective cohort study was conducted according to the Declaration of Helsinki [9]. The protocol was approved by the institutional review board, and the requirement for informed consent was waived.

Skeletal muscle mass measurements

CT is considered to be an instrument for accurately measuring tissue content and the gold standard for the quantitation of muscle mass [10]. A GE Optima CT 660 64-slice spiral CT instrument was used for abdominal scanning. The tube voltage was 80–120 kVp and the tube current was automatically modulated. The slice thickness was 5 mm and the slice spacing was 5 mm. After the scan, the axial image with a thickness of 1.25 mm was reconstructed and imported into the GE post-processing workstation. A physician with 5 years of experience in abdominal imaging diagnosis and above drew the region of interest along the skeletal muscle at the third lumbar vertebra (L3) level (Fig. 2). CT value threshold was set as -29 to $+150$ HU to obtain the total cross-sectional area

of skeletal muscle, which included quadratus lumborum, psoas major, internal oblique, external oblique, transverse abdominis, and erector spinae. The corresponding skeletal muscle index (SMI) was calculated, through the following formula: $SMI = SMA (cm^2) / height^2 (m^2)$. Our study adopted the diagnostic criteria recommended by Lisa Martin [11]. According to the definition proposed by Martin *et al.*, patients were considered as sarcopenia as follows: $SMI < 53 cm^2/m^2$ in men with a $BMI > 25 kg/m^2$, $< 43 cm^2/m^2$ in men with a $BMI < 25 kg/m^2$, and $< 41 cm^2/m^2$ in women regardless of the BMI.

The definition of MELD-Sarcopenia score

According to the results of previous studies by Montano-Loza [8], the MELD-Sarcopenia score is calculated as follows: MELD +10.35 (sarcopenia), which corresponds to an increase of 10.35 points in the MELD score of patients with sarcopenia.

Transjugular intrahepatic portosystemic shunt procedure

As described previously [12], TIPS procedure was performed by the same team of experienced radiologists. Briefly, the right internal jugular vein was punctured with RUPS-100 (Cook Inc., Bloomington, USA) puncture device, intubated to the hepatic vein through the vena cava, and the portal vein was punctured under fluoroscopy to establish the direct channel between the hepatic vein and the portal vein. Then, portosystemic shunt was established by balloon expansion (6–8 mm) and stents were placed. A bare Stent (Bard E-LUMINEXX Vascular Stent, Karlsruhe, Germany) followed by a covered Stent (Fluency; Bard Inc., New Jersey, USA or Viabahn; GORE, Newark, USA) were used. During the procedure, portal vein pressure gradient was measured before and after the shunt was established.

Statistical analysis

SPSS (version 26.0) and R (version 4.0.3) statistical software were used for statistical analysis. The measurement data were expressed by the mean \pm SD ($X \pm S$). If they conformed to the normal distribution, the difference between groups would be tested by *t* test; if they did not conform to the normal distribution, the difference between groups would be tested by Mann–Whitney *U* test. Count data were expressed in terms of the number of cases and percentage [n (%)], and comparisons between groups were performed using χ^2 or Fisher's exact test. Cox survival analysis was performed on the two groups of patients. The survival function of the two groups was calculated by the cumulative method. The Kaplan–Meier curve was drawn, and the survival rate of the two groups was compared by log-rank test. The Cox proportional hazard regression model was used to analyze the factors affecting the prognosis. The variables with $P < 0.1$ were incorporated into the multivariate Cox analysis, and the nomogram was drawn based on the results of the multivariate analysis. By calculating the degree of discrimination (C-index) and calibration degree of various scores, the prediction performance of various scoring models were compared. Discrimination refers to the degree to which a model differentiates the survival prognosis after TIPS. The degree of discrimination is calculated by C-index and ranges from

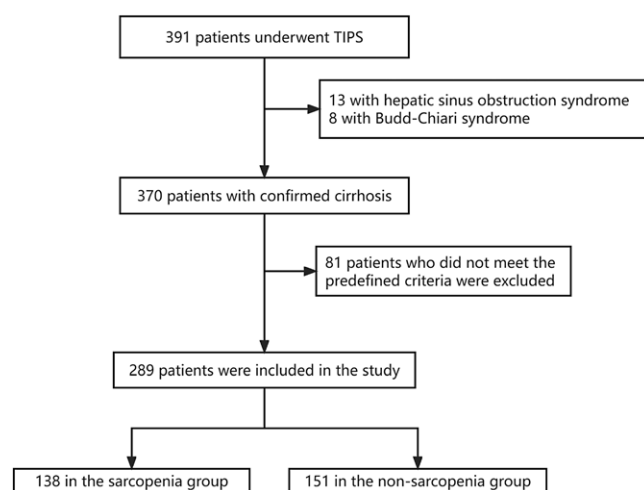


Fig. 1. Flowchart of the patient selection protocol.

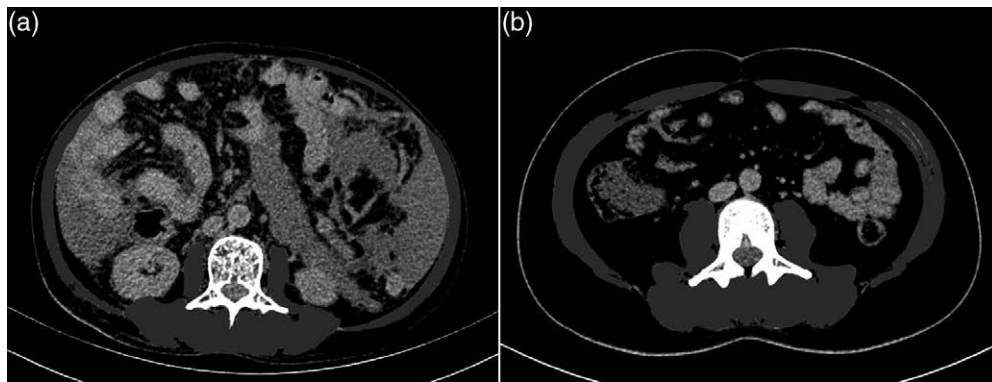


Fig. 2. Skeletal muscle area (cm²) at the level of the third lumbar vertebra (L3). (a) A female patient of sarcopenia group whose SMI is 33.33 cm²/m². (b) A female patient of non-sarcopenia group whose SMI is 41.41 cm²/m².

Table 1. Baseline characteristics of patients

Variables	All patients (N=289)	Sarcopenia (N= 138)	Non-sarcopenia (N= 151)	P values
Demographic characteristics				
Age, years	54.5 ± 11.5	55.1 ± 12.6	54.0 ± 10.4	0.398
Gender, male	191 (66.1)	98 (71.0)	93 (61.6)	0.106
Body weight, kg	61.1 ± 10.3	58.3 ± 10.8	63.4 ± 9.1	<0.001
Height	1.66 ± 0.07	1.66 ± 0.07	1.65 ± 0.07	0.245
BMI, kg/m ²	22.0 ± 3.0	20.8 ± 2.9	22.9 ± 2.7	<0.001
Indications for TIPS				
Variceal bleeding	256 (88.6)	115 (83.3)	141 (93.4)	0.009
Refractory ascites	33 (11.4)	23 (16.7)	10 (6.6)	
Etiology				
HBV	187 (64.7)	90 (65.2)	97 (64.2)	0.499
HCV	31 (10.7)	12 (8.7)	19 (12.6)	
Alcohol	17 (5.9)	11 (8.0)	6 (4.0)	
<i>Schistosoma</i>	24 (8.3)	10 (7.2)	14 (9.3)	
Others	30 (10.4)	15 (10.9)	15 (10.0)	
Laboratory parameters				
TBIL, mg/mL	1.60 ± 1.34	1.80 ± 1.62	1.41 ± 1.98	0.017
Albumin, g/L	30.7 ± 5.7	30.1 ± 5.6	31.3 ± 5.7	0.084
ALT, U/L	33.5 ± 29.0	32.0 ± 27.7	34.9 ± 30.2	0.397
AST, U/L	46.8 ± 46.2	47.1 ± 46.9	46.6 ± 45.6	0.925
Creatinine, mg/mL	0.84 ± 0.81	0.88 ± 0.81	0.80 ± 0.81	0.408
PT, s	16.8 ± 2.6	17.0 ± 2.7	16.6 ± 2.6	0.299
INR	1.39 ± 0.28	1.41 ± 0.30	1.37 ± 0.27	0.349
Platelet count, 10 ⁹ /L	98.7 ± 77.2	98.1 ± 77.2	99.4 ± 77.4	0.888
Sodium, mmol/L	138.4 ± 4.9	138.0 ± 4.7	138.9 ± 5.1	0.12
Child-Pugh score	7.6 ± 1.8	7.9 ± 1.8	7.3 ± 1.8	0.004
MELD score	11.9 ± 4.0	12.6 ± 4.4	11.3 ± 3.4	0.006
MELD-Na score	12.8 ± 5.1	13.7 ± 5.5	12.1 ± 4.5	0.007
FIPS score	-0.92 ± 0.99	-0.78 ± 1.05	-1.05 ± 0.91	0.022
Radiographic analysis				
Ascites	230 (79.6)	117 (84.8)	113 (74.8)	0.041
PVT	131 (45.3)	75 (54.3)	56 (37.1)	0.004
SPSS	50 (17.3)	19 (13.8)	31 (20.5)	0.162
L3 SMA, cm ²	119.8 ± 25.5	104.8 ± 19.0	133.5 ± 22.8	< 0.001
L3 SMI, cm ² /m ²	43.3 ± 7.8	37.6 ± 5.2	48.5 ± 5.9	< 0.001
Pre-TIPS PPG, mmHg	26.6 ± 5.7	27.1 ± 5.2	26.3 ± 5.8	0.293

Data presented as mean ± SD or number of patients (%) where appropriate.

ALT, alanine aminotransferase; AST, aspartate aminotransferase; FIPS, the Freiburg index of post-TIPS survival; HBV, hepatitis B virus; HCV, hepatitis C virus; INR, international normalized ratio; MELD, model for end-stage liver disease; PT, prothrombin time; PVT, portal vein thrombosis; PPG, portal pressure gradient; SMA, skeletal muscle area; SMI, skeletal muscle index; TBIL, total bilirubin; TIPS, transjugular intrahepatic portosystemic shunt.

0.5 to 1.0. The degree of calibration refers to the use of a calibration diagram to evaluate the consistency between the predicted calibration and the observed calibration. $P < 0.05$ is considered to be statistically significant.

Results

Patient characteristics

Baseline information of patients is shown in Table 1. In this study, a total of 289 patients were included, 138 (47.8%) and 151 (52.2%) cases were divided into the sarcopenia

and non-sarcopenia groups, respectively. Among all patients, 256 (88.6%) patients were treated with TIPS due to variceal bleeding, and 33 (11.4%) patients were refractory ascites. The average body weight of the sarcopenia group was lower than that of the non-sarcopenia group (58.3 ± 10.8 kg vs. 63.4 ± 9.1 kg, $P < 0.001$), and the BMI of the sarcopenia group was lower than that of the non-sarcopenia group (20.8 ± 2.9 vs. 22.9 ± 2.7, $P < 0.001$). The mean Child-Pugh score, MELD score, and MELD-Na scores in sarcopenia group were higher than those in non-sarcopenia group (P values < 0.05).

The association between sarcopenia and mortality

The median follow-up time of the sarcopenia and non-sarcopenia groups were 23.0 months [interquartile range (IQR) 15.0–36.3] and 25.0 months (IQR 18.0–38.0), respectively. In the entire study cohort, a total of 46 patients (15.9%) died, including 35 patients (25.4%) in the sarcopenia group and 11 patients (7.3%) in the non-sarcopenia group. Causes of death mainly included liver failure (20 cases), multiorgan failure (16 cases), and severe rebleeding (6 cases). Cox analysis showed that the cumulative survival rate of the sarcopenia group was significantly lower than that of the non-sarcopenia group [HR, 0.24 (95% CI, 0.12–0.46), Log-rank $P < 0.001$] (Fig. 3). The 1-year cumulative survival rates of the sarcopenia group and the non-sarcopenia group were 80.3% and 96.6%, respectively (Log-rank $P < 0.001$). The 2-year cumulative survival rates were 74.5% and 93.4%, respectively (Log-rank $P < 0.001$). The 3-year cumulative survival rates were 66% and 91.6%, respectively (Log-rank $P < 0.001$).

Factors associated with mortality after transjugular intrahepatic portosystemic shunt and the development of a nomogram

In the univariate Cox analysis (Table 2), age, recurrent ascites, L3 SMI, sarcopenia, TBIL, albumin, creatinine, PT, INR, Child-Pugh score, MELD score, MELD-Na score, MELD-Sarcopenia score, MELD-Na-Sarcopenia score, and FIPS score were confirmed as risk factors for patients with liver cirrhosis after TIPS. After adjusting for confounding factors, age, refractory ascites, sarcopenia, albumin, and MELD score were incorporated into the multivariate Cox regression model. Finally, Age [HR,

1.040 (95% CI, 1.015–1.065), $P = 0.002$], Sarcopenia [HR, 3.948 (95% CI, 1.989–7.838), $P < 0.001$], albumin [HR, 0.945 (95% CI, 0.897–0.997), $P = 0.037$], MELD score [HR, 1.156 (95% CI, 1.097–1.217), $P < 0.001$] were identified as independent risk factors for death after TIPS (Table 3). We incorporated the four variables of age, sarcopenia, albumin, and MELD score into the nomogram to predict the survival of patients at 1 and 2 years after TIPS (Fig. 4). The calibration diagram of the nomogram showed that MELD-Sarcopenia score had a strong predictive value for mortality at 3 months, 12 months, and 24 months after TIPS (Fig. 5).

Performance of the various predictive models

There were various predictive models for the prediction of mortality in patients with cirrhosis after TIPS placement, and we compared the performance of five different models (Table 4). The results showed that Child-Pugh score had the worst prediction of post-TIPS mortality, with a C-index of 0.688. MELD score alone did slightly better in predicting mortality, with a C-index of 0.719. The C-index of FIPS score was 0.770, which had better predictive performance than MELD score. MELD-Sarcopenia and MELD-Na-Sarcopenia, both of which take sarcopenia into account in scoring, had a C-index of 0.782. Among all the scores, Child-Pugh score had the lowest goodness of fit (0.094). MELD-Sarcopenia had the highest goodness of fit, which is 0.188.

Discussion

In this study, we confirmed that MELD-Sarcopenia score had a better predictive value for post-TIPS mortality in

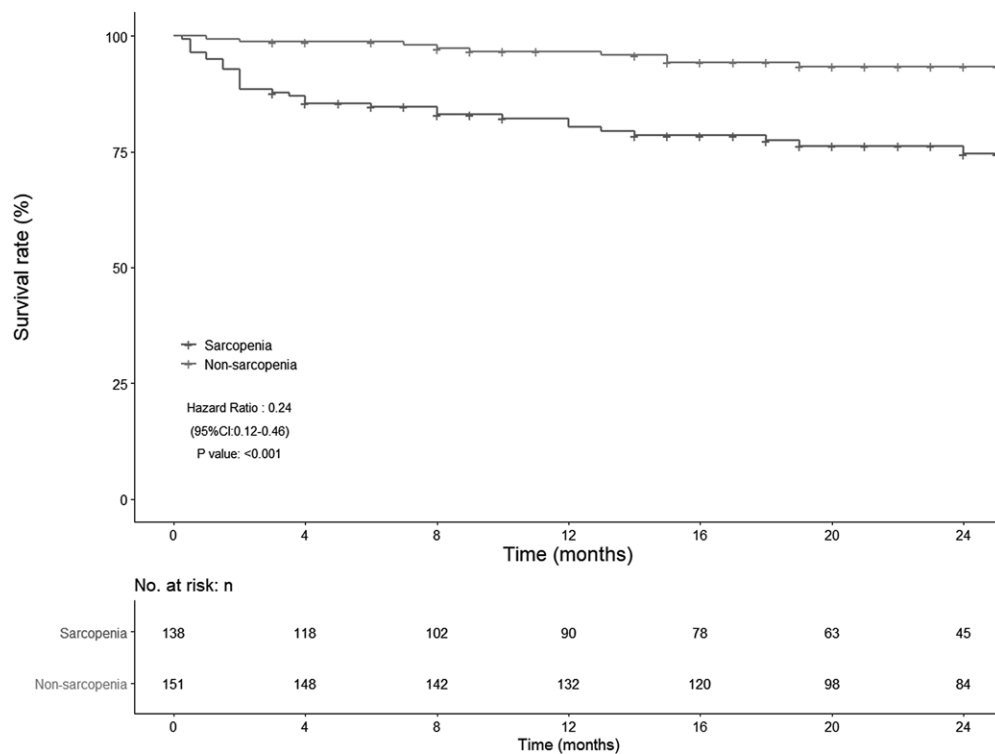


Fig. 3. Survival curves of two groups of patients. The postoperative survival of the sarcopenia group was significantly worse than that of the non-sarcopenia group.

Table 2. Univariate cox analysis of factors associated with mortality in cirrhotic patients after transjugular intrahepatic portosystemic shunt placement

Variables	Death (N=46)	Alive (N=243)	HR	95% CI	P value
Age, years	59.3 ± 12.3	53.6 ± 11.1	1.046	1.020–1.073	<0.001
Gender, male	35 (76.1)	156 (64.2)	1.598	0.810–3.151	0.176
BMI, kg/m ²	22.2 ± 3.1	21.9 ± 3.0	1.027	0.918–1.149	0.643
Ascites	42 (91.3)	188 (77.4)	2.624	0.940–7.323	0.065
Refractory ascites	12 (26.1)	21 (8.6)	0.288	0.149–0.558	<0.001
L3 SMA, cm ²	114.5 ± 20.7	120.8 ± 26.2	0.989	0.977–1.001	0.07
L3 SMI, cm ² /m ²	40.8 ± 6.1	43.8 ± 8.0	0.949	0.913–0.986	0.007
Sarcopenia	35 (76.1)	103 (42.4)	4.232	2.146–8.346	<0.001
TBIL, mg/mL	2.39 ± 1.92	1.44 ± 1.14	1.39	1.211–1.595	<0.001
Albumin, g/L	28.4 ± 5.3	31.1 ± 5.6	0.923	0.878–0.971	0.002
Creatinine, mg/mL	1.20 ± 1.48	0.77 ± 0.58	1.27	1.093–1.476	0.002
PT, s	17.8 ± 3.2	16.6 ± 2.5	1.114	1.028–1.207	0.009
INR	1.49 ± 0.35	1.37 ± 0.27	2.624	1.261–5.458	0.01
Sodium, mmol/L	137.8 ± 5.0	138.6 ± 4.9	0.974	0.926–1.024	0.3
Child-Pugh score	8.8 ± 2.0	7.4 ± 1.7	1.466	1.259–1.708	<0.001
MELD score	15.3 ± 5.6	11.2 ± 3.2	1.178	1.122–1.237	<0.001
MELD-Na score	16.7 ± 5.9	12.1 ± 4.6	1.131	1.084–1.179	<0.001
MELD-Sarcopenia score	22.9 ± 7.5	15.5 ± 6.1	1.149	1.106–1.194	<0.001
MELD-Na-Sarcopenia score	24.3 ± 7.8	16.4 ± 7.0	1.126	1.088–1.165	<0.001
FIPS score	-0.15 ± 1.10	-1.07 ± 0.90	2.670	1.982–3.595	<0.001

Data presented as mean ± SD or number of patients (%) where appropriate.

CI, confidence interval; FIPS, Freiburg index of post-TIPS survival; HR, hazard ratio; INR, international normalized ratio; MELD, model for end-stage liver disease; PT, prothrombin time; SMA, skeletal muscle area; SMI, skeletal muscle index; TBIL, total bilirubin.

Table 3. Multivariate cox analysis of factors associated with mortality in cirrhotic patients after transjugular intrahepatic portosystemic shunt placement

Variables	Death (N = 46)	Alive (N = 243)	HR	95% CI	P value
Age, years	59.3 ± 12.3	53.6 ± 11.1	1.04	1.015–1.065	0.002
Refractory ascites	40.8 ± 6.1	43.8 ± 8.0	–	–	–
Sarcopenia	35 (76.1)	103 (42.4)	3.948	1.989–7.838	< 0.001
Albumin, g/L	28.4 ± 5.3	31.1 ± 5.6	0.945	0.897–0.997	0.037
MELD score	15.3 ± 5.6	11.2 ± 3.2	1.156	1.097–1.217	< 0.001

Data presented as mean ± SD or number of patients (%) where appropriate. Variables included in the multivariate analysis were age, refractory ascites, sarcopenia, albumin, and MELD score. Child-Pugh score, international normalized ratio, prothrombin time, total bilirubin, creatinine, lumbar third skeletal muscle area, and lumbar third skeletal muscle index were not included to avoid collinearity.

HR, hazard ratio; CI, confidence interval; MELD, model for end-stage liver disease.

patients with cirrhosis than the traditional predictive models. We observed that sarcopenia was an independent risk factor for mortality in univariate and multivariate Cox regression analyses. Meanwhile, including sarcopenia improved the predictive value of the traditional predictive models. The C-index of MELD score was 0.719 and the C-index rose to 0.782 when sarcopenia was incorporated. The C-index of MELD-Na score was 0.734 and the C-index rose to 0.782 when sarcopenia was incorporated.

In MELD score, the effect of liver and kidney function on survival was taken into account only. However, sarcopenia, which is significantly associated with prognosis in patients with cirrhosis [13], has not been considered. After MELD score was proposed, many experts improved it and proposed prediction models such as MELD-Na, MELD-ICG, MELD-HVPG, and MELD-Sarcopenia successively [14–17]. In addition to MELD-Sarcopenia, most of the improved scores were based on a specific biochemical indicator and paid less attention to the overall nutritional status of the patient. Studies have shown that the poor survival of patients with sarcopenia is closely related to their nutritional status, but not to liver and kidney function [7], which also indicates that it is reasonable to combine sarcopenia with MELD score as a new prognostic scoring system for patients with cirrhosis. Our study also confirmed that MELD-Sarcopenia had higher predictive performance than MELD score alone. In addition, the FIPS score had

been raised to predict the prognosis of TIPS recently [18], which was composed of age, bilirubin, albumin, and creatinine. FIPS score was superior to Child-Pugh, MELD, and MELD-Na scores in predicting survival after TIPS placement, and have been externally validated [19]. However, our results suggested that MELD-Sarcopenia score was a better predictor of post-TIPS mortality than FIPS, perhaps because the FIPS score only took into account aspects such as liver and kidney function and did not include the powerful predictor of body state (sarcopenia). For patients with good liver and kidney function but poor body state (sarcopenia), we believe that MELD-Sarcopenia score predicts the prognosis of patients better.

Sarcopenia is a common complication of patients with end-stage liver disease [20]. In patients with cirrhosis, a large number of people are complicated with sarcopenia, and the proportion was 47.8% in our study. It is of great practical significance to include sarcopenia in the prognostic scoring system. After Montano-Loza [8] first proposed the inclusion of sarcopenia in MELD score, many studies have confirmed that compared with the initial MELD score, the improved score had a stronger value to predict the survival of patients with end-stage liver disease. TIPS is an effective method to reduce portal hypertension in cirrhotic patients, and it has been reported to reverse sarcopenia and improve muscle condition in patients [6,13,21,22]. However, no

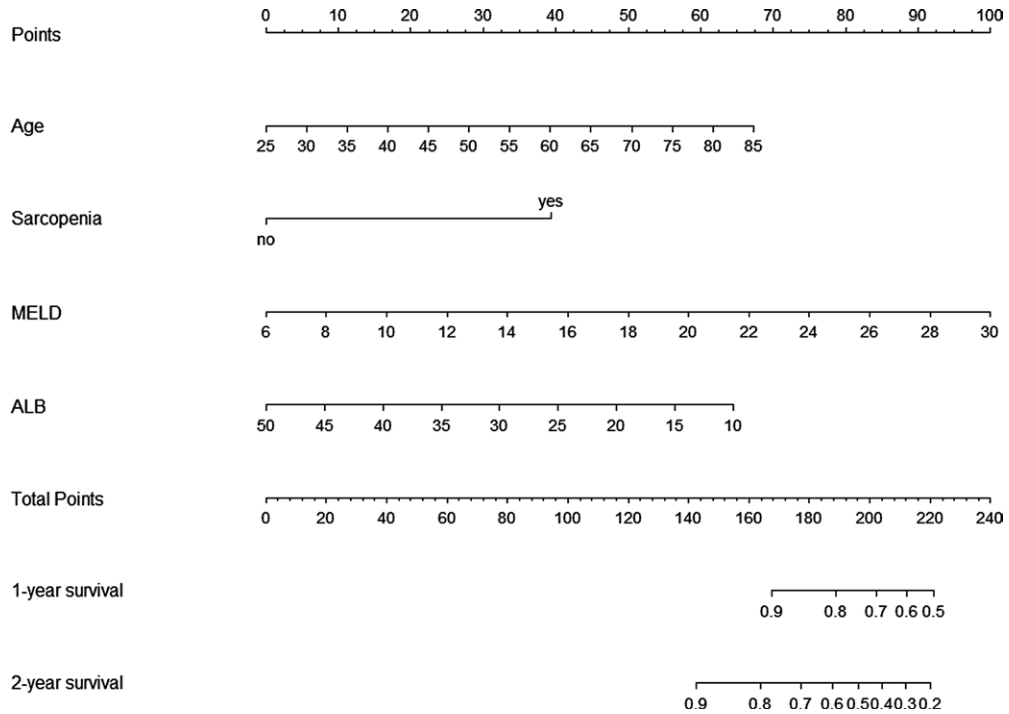


Fig. 4. The development of a nomogram. The Akaike information criterion based inverse stepwise selection method was used to select the factors of the final model. Age, sarcopenia, MELD, serum albumin levels, were all included in the complete model prior to selection. Each independent parameter associated with impaired survival was assigned a specific weighted score using regression coefficients from multivariate analysis. The sum of the specific weighted scores was plotted to correspond to the decline in survival. MELD, model for end-stage liver disease.

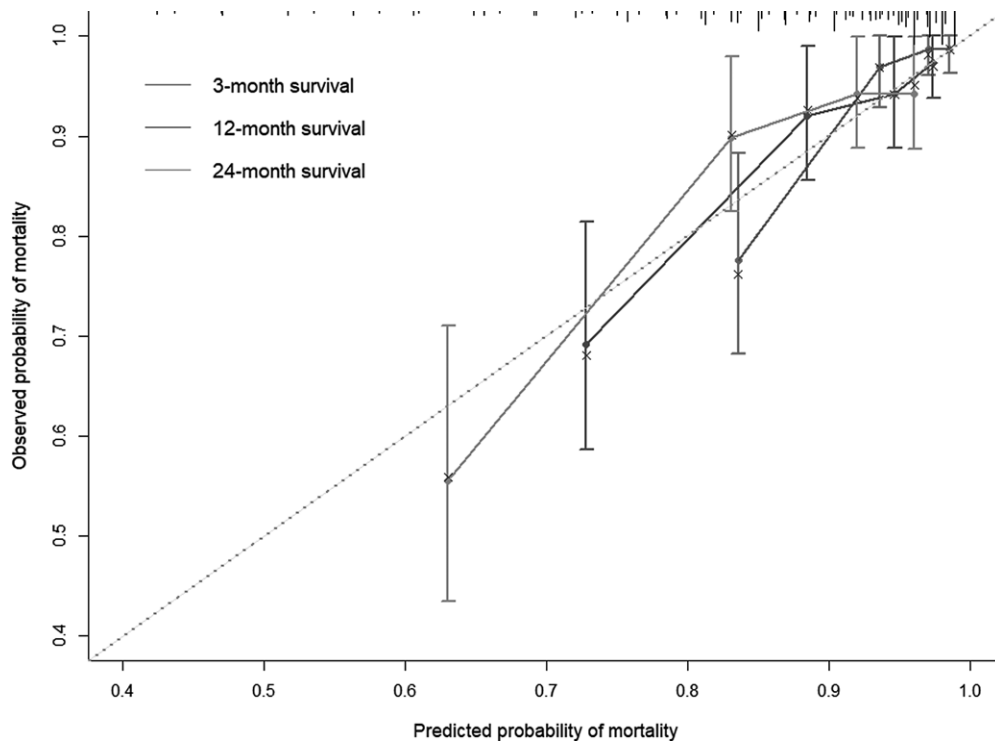


Fig. 5. Calibration diagram for the nomogram. The calibration diagram shows a high agreement between the predicted calibration and the observed calibration. The calibration diagram shows that MELD-Sarcopenia has a strong value to predict the mortality at 3, 12, and 24 months after TIPS. MELD, model for end-stage liver disease; TIPS, transjugular intrahepatic portosystemic shunt.

study had verified MELD-sarcopenia score by using the survival of patients with cirrhosis after TIPS. In addition, almost all studies were directed at the European and American population, and it is not clear how the

improved score can predict the Asian population with end-stage liver disease.

In a study that included 585 patients with end-stage liver disease, the MELD-Sarcopenia score proved to

Table 4. Performance of the various predictive models

Scores	HR	95% CI	P value	R ²	C-index
Child-Pugh	1.47	1.26–1.71	<0.001	0.094	0.688
MELD	1.18	1.12–1.24	<0.001	0.134	0.719
MELDNa	1.13	1.09–1.18	<0.001	0.111	0.734
FIPS	2.69	2.00–3.63	<0.001	0.162	0.770
MELD-Sarcopenia	1.15	1.11–1.20	<0.001	0.188	0.782
MELDNa-Sarcopenia	1.13	1.09–1.17	<0.001	0.173	0.782

CI, confidence interval; FIPS, Freiburg index of post-TIPS survival; HR, hazard ratio; MELD, model for end-stage liver disease; R², Goodness of Fit.

be a better predictor of 3-month mortality in patients awaiting liver transplantation [23], but it only analyzed short-term postoperative outcomes. Our study analyzed the short-term and long-term prognosis of patients after TIPS placement, confirming the good predictive value of MELD-Sarcopenia score for survival of patients with end-stage liver disease. We found that the survival outcomes of patients with sarcopenia were worse than those without sarcopenia. In accordance with our clinical experience, univariate and multivariate Cox analysis found that sarcopenia was an independent factor affecting survival and prognosis. Taking sarcopenia into account the MELD score, the new score predicted patients' survival better, and C-index of MELD-Sarcopenia score and MELD-Na-Sarcopenia score were higher than MELD score. But the goodness of fit of MELD-Na-Sarcopenia score was lower than MELD-Sarcopenia score. Meanwhile, the nomogram and its calibration diagram showed the prognostic factors and the excellent predictive value of MELD-Sarcopenia score more intuitively. MELD-sarcopenia score had demonstrated its excellent performance in predicting survival after TIPS, both in the short-term prognosis at 3 months and in the long-term prognosis at 1 and 2 years.

There are several limitations to this study, including those inherent to a retrospective observational study design. Besides, there is no recognized diagnostic criteria for sarcopenia, and we selected a better one. Recent consensus has suggested using both muscle mass and muscle function to define sarcopenia [24,25], and we did not measure related muscle function. In addition, we did not measure patients' SMI regularly and continuously. Our study cannot confirm whether improvement in sarcopenia will improve patient's survival. Undoubtedly, the application of MELD-Sarcopenia score requires manual measurement and calculation of CT images, which is time-consuming and laborious compared with the traditional MELD score. This may be one of its limitations in clinical practice before a simple method for evaluating sarcopenia is developed.

Conclusion

The survival prognosis of post-TIPS patients with sarcopenia is worse, and MELD-Sarcopenia score could better predict survival outcome of post-TIPS patients than the traditional MELD score.

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The study protocol was approved by the institutional review board of the Union Hospital, Tongji Medical college, Huazhong University of Science and Technology.

Informed consent was waived due to the retrospective nature of the current study, and data of the participants have been anonymized.

The dataset used and analyzed in the present study are available from the corresponding author on reasonable request.

Conflicts of interest

There are no conflicts of interests.

References

- Malinchoc M, Kamath PS, Gordon FD, Peine CJ, Rank J, ter Borg PC. A model to predict poor survival in patients undergoing transjugular intrahepatic portosystemic shunts. *Hepatology* 2000; 31:864–871.
- Kamath PS, Kim WR; Advanced Liver Disease Study Group. The model for end-stage liver disease (MELD). *Hepatology* 2007; 45:797–805.
- D'Amico G, Maruzzelli L, Airolidi A, Petridis I, Tosetti G, Rampoldi A, et al. Performance of the model for end-stage liver disease score for mortality prediction and the potential role of etiology. *J Hepatol* 2021; 75:1355–1366.
- Lladó L, Figueras J, Momba R, Xiol X, Baliellas C, Vázquez S, et al. Is MELD really the definitive score for liver allocation? *Liver Transpl* 2002; 8:795–798.
- Singal AK, Kamath PS. Model for end-stage liver disease. *J Clin Exp Hepatol* 2013; 3:50–60.
- Artru F, Miquet X, Azahaf M, Labreuche J, Ntandja Wandji LC, Sergent G, et al. Consequences of TIPSS placement on the body composition of patients with cirrhosis and severe portal hypertension: a large retrospective CT-based surveillance. *Aliment Pharmacol Ther* 2020; 52:1516–1526.
- Kang SH, Jeong WK, Baik SK, Cha SH, Kim MY. Impact of sarcopenia on prognostic value of cirrhosis: going beyond the hepatic venous pressure gradient and MELD score. *J Cachexia Sarcopenia Muscle* 2018; 9:860–870.
- Montano-Loza AJ, Duarte-Rojo A, Meza-Junco J, Baracos VE, Sawyer MB, Pang JX, et al. Inclusion of Sarcopenia within MELD (MELD-Sarcopenia) and the prediction of mortality in patients with cirrhosis. *Clin Transl Gastroenterol* 2015; 6:e102.
- World Medical Association. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. *JAMA* 2013; 310:2191–2194.
- Caan BJ, Cespedes Feliciano EM, Prado CM, Alexeeff S, Kroenke CH, Bradshaw P, et al. Association of muscle and adiposity measured by computed tomography with survival in patients with nonmetastatic breast cancer. *JAMA Oncol* 2018; 4:798–804.
- Martin L, Birdsell L, Macdonald N, Reiman T, Clandinin MT, McCargar LJ, et al. Cancer cachexia in the age of obesity: skeletal muscle depletion is a powerful prognostic factor, independent of body mass index. *J Clin Oncol* 2013; 31:1539–1547.

- 12 Yang C, Liu J, Shi Q, Huang S, Zhou C, Wang Y, *et al.* Effect of splenectomy on the outcomes in patients with cirrhosis receiving transjugular intrahepatic portosystemic shunt. *J Gastroenterol Hepatol* 2021; 36:2893–2902.
- 13 Liu J, Ma J, Yang C, Chen M, Shi Q, Zhou C, *et al.* Sarcopenia in patients with cirrhosis after transjugular intrahepatic portosystemic shunt placement. *Radiology* 2022; 211172.
- 14 Zipprich A, Kuss O, Rogowski S, Kleber G, Lotterer E, Seufferlein T, *et al.* Incorporating indocyanin green clearance into the Model for End Stage Liver Disease (MELD-ICG) improves prognostic accuracy in intermediate to advanced cirrhosis. *Gut* 2010; 59:963–968.
- 15 Ripoll C, Bañares R, Rincón D, Catalina MV, Lo Iacono O, Salcedo M, *et al.* Influence of hepatic venous pressure gradient on the prediction of survival of patients with cirrhosis in the MELD Era. *Hepatology* 2005; 42:793–801.
- 16 Walter A, Rudler M, Olivares P, Moga L, Trépo E, Robic MA, *et al.*; Salvage TIPS Group. Combination of model for end-stage liver disease and lactate predicts death in patients treated with salvage transjugular intrahepatic portosystemic shunt for refractory variceal bleeding. *Hepatology* 2021; 74:2085–2101.
- 17 Shoreibah MG, Mahmoud K, Aboueldahab NA, Vande Lune P, Massoud M, Bae S, *et al.* Psoas muscle density in combination with model for end-stage liver disease score can improve survival predictability in transjugular intrahepatic portosystemic shunts. *J Vasc Interv Radiol* 2019; 30:154–161.
- 18 Bettinger D, Sturm L, Pfaff L, Hahn F, Kloeckner R, Volkwein L, *et al.* Refining prediction of survival after TIPS with the novel Freiburg index of post-TIPS survival. *J Hepatol* 2021; 74:1362–1372.
- 19 Yang C, Chen Q, Zhou C, Liu J, Huang S, Wang Y, *et al.* FIPS score for prediction of survival after TIPS placement: external validation and comparison with traditional risk scores in a cohort of Chinese patients with cirrhosis. *AJR Am J Roentgenol* 2022. [Epub ahead of print].
- 20 Benmassaoud A, Roccarina D, Arico F, Leandro G, Yu B, Cheng F, *et al.* Sarcopenia does not worsen survival in patients with cirrhosis undergoing transjugular intrahepatic portosystemic shunt for refractory ascites. *Am J Gastroenterol* 2020; 115:1911–1914.
- 21 Tsien C, Shah SN, McCullough AJ, Dasarathy S. Reversal of sarcopenia predicts survival after a transjugular intrahepatic portosystemic shunt. *Eur J Gastroenterol Hepatol* 2013; 25:85–93.
- 22 Jahangiri Y, Pathak P, Tomozawa Y, Li L, Schlansky BL, Farsad K. Muscle gain after transjugular intrahepatic portosystemic shunt creation: time course and prognostic implications for survival in cirrhosis. *J Vasc Interv Radiol* 2019; 30:866–872.e4.
- 23 Praktiknjo M, Clees C, Pigliacelli A, Fischer S, Jansen C, Lehmann J, *et al.* Sarcopenia is associated with development of acute-on-chronic liver failure in decompensated liver cirrhosis receiving transjugular intrahepatic portosystemic shunt. *Clin Transl Gastroenterol* 2019; 10:e00025.
- 24 Cruz-Jentoft AJ, Sayer AA. Sarcopenia. *Lancet* 2019; 393:2636–2646.
- 25 Taguchi S, Nakagawa T, Fukuhara H. Inconsistencies in currently used definitions of sarcopenia in oncology. *Ann Oncol* 2020; 31:318–319.