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DATABASE ANALYSIS

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Prediction of Patient Survival with Psoas Muscle Density Following Transjugular Intrahepatic Portosystemic Shunts: A Retrospective Cohort Study

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Data Interpretation D
Manuscript Preparation E
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Background: Psoas muscle density (PMD) as a nutritional indicator is a tool to evaluate sarcopenia, which is commonly diagnosed in patients with liver cirrhosis. However, there are limited data on its role in patients who have received a transjugular intrahepatic portosystemic shunt (TIPS). We aimed to determine the utility of PMD in predicting mortality of patients with TIPS implantation and to compare the clinical value of PMD, Child-Pugh score, model for end-stage liver disease (MELD) score, and MELD paired with serum sodium measurement (MELD-Na) score in predicting post-TIPS survival in 1 year.

Material/Methods: This retrospective study included 273 patients who met the criteria for study inclusion. All participants underwent computed tomography (CT) scans, Child-Pugh score evaluation, MELD-Na scoring, and MELD scoring. Post-TIPS survival time was estimated using the Kaplan-Meier survival curve. The prognostic values of scoring models such as the Child-Pugh score, MELD, MELD-Na, and PMD were evaluated using receiver operating characteristic curves.

Results: During the 1-year follow-up period, 31 of 273 (11.36%) post-TIPS patients died. Multivariate analysis identified PMD as an independent protective factor. PMD showed a good ability to predict the occurrence of an endpoint within 1 year after TIPS. The area under the receiver operating characteristic curves for PMD, Child-Pugh score, MELD score, and MELD-Na for predicting mortality were, respectively, 0.72 (95% confidence interval [CI]: 0.663-0.773), 0.59 (95% CI: 0.531-0.651), 0.60 (95% CI: 0.535-0.655), and 0.58 (95% CI: 0.487-0.608).

Conclusions: PMD has appreciable clinical value for predicting the mortality of patients with TIPS implantation. In addition, PMD is superior to established scoring systems for identifying high-risk patients with a poor prognosis.

Keywords: Liver Cirrhosis • Portasystemic Shunt, Transjugular Intrahepatic • Psoas Muscles • Sarcopenia

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Background

Sarcopenia is characterized as the generalized loss of skeletal muscle mass, strength, and physical function [1]. The major component of malnutrition in liver disease is the loss of skeletal muscle mass or sarcopenia [2]. The complication rate of sarcopenia in patients with liver cirrhosis (LC) was reported to be 30-70% [3,4], and in patients with end-stage liver disease, the proportion is 40-60% [5-7]. A variety of measurements have been applied to assess the nutritional status of patients with LC [1,8]. Although a number of studies have measured the psoas muscle cross-sectional area (PMA) at the L3 vertebra level by computed tomography (CT) to quantify nutritional status [9,10], it may not be comprehensive because the PMA measurements did not include muscle mass or fat infiltration. A recent review proposed that psoas muscle density (PMD) is a more accurate assessment of muscle mass and function [11]. In related studies, low skeletal muscle density, rather than PMA, was associated with poorer muscle function and higher mortality in patients after cardiovascular surgery [12]. PMD has been shown to have potential in the prediction of noncancer mortality in patients with prostate cancer [13], incidence of postoperative complications after operative fixation of acetabular fractures, and survival of gastrointestinal surgery [14-16]. Reduced PMD is associated with prolonged hospital stays in patients undergoing transcatheter aortic valve implantation [17].

Transjugular intrahepatic portosystemic shunt (TIPS), a side-to-side portacaval shunt, is a proven technique that can significantly reduce portal venous pressure and reduce the complications of decompensated LC patients [18]. In past decades, numerous studies identified a significant decrease in the incidence of recurrent variceal bleeding or other complications due to portal hypertension through the use of TIPS [19,20]. MELD and Child-Pugh scores are commonly used to evaluate the severity of chronic liver disease and predict the prognosis in various clinical situations [21]. The MELD score has also been used to predict the survival in patients who have undergone TIPS [22]. It has been found to be less influenced by subjective interpretation of variables than the Child-Pugh score [23] since it is based on 3 objective parameters, including serum creatinine, bilirubin, and international normalized ratio. Multiple studies have found that MELD-Na, a composite index including the MELD score and measurement of serum sodium, significantly improves the effectiveness in predicting mortality and postoperative complications rates after liver transplantation [24-28]. MELD-Na was officially applied in the United Network for Organ Sharing after 2016, and it was also shown to be an effective predictor of short-term mortality after TIPS [29-31]. However, MELD, MELD-Na, and Child-Pugh scores have a critical drawback because they do not include the assessment of the nutritional status of LC patients [32].

The MELD-Sarcopenia score performed better in predicting waiting list mortality in cirrhotic liver transplant candidates than the MELD score [33]. PMD may be a reliable, simple, quantitative, noninvasive, reproducible measurement method for predicting mortality in post-TIPS patients. Although PMD has shown its capability in predicting survival in LC patients, its applicability in patients with TIPS implantation has not yet been explored. Therefore, the aim of our study was to compare the clinical values of the MELD score, MELD-Na score, Child-Pugh score, and PMD for predicting the survival rates of patient with TIPS implantation.

Material and Methods

The diagnosis of LC is determined by imaging, liver biopsy, or unequivocal clinical and biochemical profile [34]. Portal hypertension is the primary vascular consequence of cirrhosis, and it is responsible for the majority of the potentially life-threatening complications of LC [35]. TIPS effectively decompresses the pressure in the portal venous system and has much lower morbidity and mortality than surgical shunting [36]. In our study population, a standard TIPS procedure was performed by an experienced gastroenterologist. TIPS was mainly used to prevent the variceal bleeding and refractory cirrhotic ascites as a way of secondary prevention, but additional indications have been proposed over the past years [37]. All patients treated with TIPS were evaluated preoperatively by experienced clinicians and met the treatment guidelines [38].

Study Population

The present retrospective cohort study was approved by the Ethics Committee of the First Affiliated Hospital of Wenzhou Medical University, and the requirement for informed consent was waived. The following patients were excluded: (a) under the age of 18 years; (b) those without nonenhanced CT image; (c) those with lack of follow-up record in our institution; (d) those with skeletal muscle-related disease such as myasthenia gravis, muscular pseudohypertrophy, myodystrophy, or polio; and (e) recipients of a liver transplant less than 1 year after TIPS. After the exclusion criteria were applied, 273 LC patients who underwent TIPS at the First Affiliated Hospital of Wenzhou Medical University between November 2013 and March 2019 were finally enrolled in this study.

Data Collection

Laboratory parameters and essential information such as sex, age, etiology of LC, diabetes mellitus, hypertension, splenectomy, indications of TIPS, and targeted puncture of TIPS were collected within 24 h of the patients' admission. Ascites was evaluated by referring to guidelines [39], and hepatic encephalopathy

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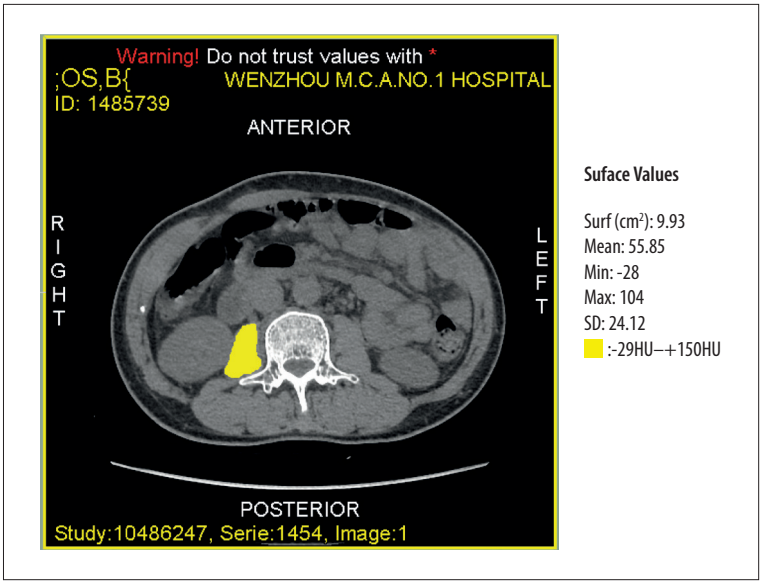

Figure 1. Computed tomography image at the midlevel of the third lumbar vertebra demonstrates a region of interest created by manually outlining the borders of both psoas muscles.

was assessed and graded referring to the West-Haven classification criteria [40]. All subjects were assessed by the Child-Pugh score and the MELD score [41] in the first 24 h after admission. Survival data were recorded from medical charts or clinical correspondence.

CT imaging of the patients during hospitalization was analyzed and calculated by 2 research fellows trained with sliceOmatic software (Tomovision, Montreal, QC Canada). They were blinded to clinical data. All CT scans were performed in the same scanner. Areas of interest were outlining in a single cross-sectional CT image at the level of mid L3 [42]. To reduce the interference of adipose tissue and ascitic fluid, a threshold defined by -29 Hounsfield units (HU) and +150 HU was used [43]. This provided the values of area in square millimeters and density in HU of each psoas muscle at this level (**Figure 1**).

All subjects were regularly followed up via telephone, regular clinic visits, and outpatient or hospital medical records. Patients were followed up after the first month and then every 3 months after TIPS. Follow-up ended on March 1, 2020. The endpoint was defined as the occurrence of death or 1 year after TIPS.

Statistical Analysis

Descriptive statistics are expressed as numbers and corresponding percentages or mean values (±SD), as appropriate. Continuous variables are expressed as means±SD or medians with interquartile ranges. The *t* test or the Mann-Whitney U test was used to compare different groups, and χ^2 test or Fisher exact test was used to compare categorical variables. Univariate and multivariate Cox proportional hazard models were used to determine the association between clinical parameters and the occurrence of post-TIPS death, and a hazard ratio with a 95% confidence interval (CI) was calculated. Area under the receiver operating characteristic (ROC) curve was calculated and compared between different scoring systems. The optimal cutoff for PMD was defined as the point with the most significant log-rank test split, and corresponding Kaplan-Meier survival curves were generated. Cox proportional hazards regression models were used to estimate the relative hazards and 95% CIs for MELD score, Child-Pugh score, and PMD. To compare the net benefit rate of each indicator, decision curve analysis was used. Positive cases based on the risk model were visually shown by the clinical impact curve, and the cumulative risk analysis was used to identify the cumulative incidence of death. Log-rank test was used to compare among the groups. Further nomogram construction was performed. Statistical significance was denoted by $P<0.05$. Statistical software Stata (version 14.0, StataCorp, College Station, Texas), SPSS 22, R package (version 3.6.1; R Foundation), and MedCalc (version 19.0.4; Ostend, Belgium) were used for statistical analysis.

Results

A total of 324 patients were screened, and 273 patients were ultimately included in this study. Fifty-one patients were excluded as follows: 2 patients underwent liver transplantation less than 1 year after TIPS; 39 patients had previously missed CT scans; and 10 patients were lost to follow-up. Thirty-one patients (11.36%) died during 1 year of follow-up. The major etiology of LC was virus infection (151/273). Among the remaining patients, 53 had alcoholism, 35 had a clinical history of both alcoholism and hepatitis, and 34 had a less common etiology. The participants included 194 men and 79 women aged 53.54±10.51 years. The vast majority of patients underwent TIPS because of esophageal gastric-fundus variceal

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Table 1. Characteristics of the study population, stratified by survival event.[a]

Variables	All patients n=273	Nonsurvivor n=31	Survivor n=242	*P* value[b]
Basic information				
Age, y	53.54±10.51	57.55±9.63	53.02±10.53	0.024
BMI	22.67 (20.51-25.01)	22.76 (20.49-25.17)	22.19 (20.69-23.82)	0.590
Sex				
Male	194	22	172	0.990
Female	79	9	70	
Diabetes	69	12	57	0.068
Hypertension	27	3	24	0.932
Smoking	105	11	94	0.717
Splenectomy	22	1	21	0.294
Etiology of cirrhosis				0.115
Alcoholic	53	6	47	
Viral (HBV or HCV)	151	14	137	
Both alcohol and viral	35	3	32	
Others[c]	34	8	26	
Reasons for TIPS				0.563
EGVB	246	26	220	
RF	13	3	10	
Portal vein thrombosis	7	1	6	
Others[d]	7	1	6	
TIPS targeted puncture				0.007
Left branch of the intrahepatic portal vein	199	20	179	
Right branch of the intrahepatic portal vein	61	6	55	
Others[e]	13	5	8	
Laboratory parameters				
RBC, $\times 10^{12}$	2.93 (2.47-3.44)	2.91 (2.53-3.46)	2.93 (2.47-3.44)	0.788
WBC, $\times 10^{9}$	3.79 (2.51-36.33)	3.60 (2.90-4.86)	3.85 (2.45-6.54)	0.695
Lymphocyte, $\times 10^{9}$	0.76 (0.51-1.19)	0.72 (0.50-0.97)	0.77 (0.52-1.25)	0.461
Neutrophil, $\times 10^{9}$	2.42 (1.51-4.30)	2.46 (1.54-3.60)	2.42 (1.49-4.33)	0.659
Platelet, $\times 10^{9}$	64.0 (45.5-92.5)	56.0 (42.0-85.0)	64.5 (46.5-93.3)	0.415
Hemoglobin, g/L	83.0 (69.0-97.0)	86.0 (75.0-101.0)	82.5 (69.0-96.0)	0.306
Albumin, g/L	30.18±5.39	28.34±4.10	30.41±5.49	0.015
Total bilirubin, μmol/L	20.0 (13.5-29.5)	20.0 (13.5-29.5)	19.0 (13.0-28.0)	0.003
ALT, U/L	24.0 (17.0-36.0)	39.0 (20.0-52.0)	23.0 (17.0-34.0)	0.007

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Table 1 continued. Characteristics of the study population, stratified by survival event.[a]

Variables	All patients n=273	Nonsurvivor n=31	Survivor n=242	*P* value[b]
AST, U/L	35.0 (26.5-52.0)	50.0 (33.0-86.0)	35.0 (25.0-48.0)	0.001
Serum creatinine, μmol/L	64.0 (52.0-75.0)	63.0 (50.0-79.0)	64.0 (53.0-75.0)	0.698
Serum sodium, mmol/L	138.0 (135.0-141.0)	138.0 (134.0-140.0)	138.0 (136.0-141.0)	0.383
Prothrombin time, s	16.9 (15.6-18.5)	17.2 (16.0-19.4)	16.9 (15.6-18.4)	0.146
PMD, HU	51.7 (46.4-55.1)	47.5 (43.4-50.4)	52.2 (47.1-55.4)	<0.001
INR	1.40 (1.26-1.58)	1.39 (1.24-1.60)	1.41 (1.27-1.58)	0.402
Clinical scores				
Child-Pugh score	7 (6-9)	8 (7-9)	7 (6-9)	0.090
MELD score	11.45 (9.72-13.63)	12.02 (10.67-14.39)	11.29 (9.57-13.58)	0.081
MELD-Na score	10.92 (7.47-14.50)	12.92 (9.13-15.33)	12.92 (9.13-15.33)	0.147

ALT – alanine aminotransferase; AST – aspartate aminotransferase; BMI – body mass index; EGVB – esophageal gastric-fundus variceal bleeding; HBV – hepatitis B virus; HCV – hepatitis C virus; HU – Hounsfield units; INR – international standardization ratio; MELD – model for end-stage liver disease; MELD-Na – composite index of model for end-stage liver disease and serum sodium; PMD – psoas muscle density; RBC – red blood cell count; RF – refractory ascites; TIPS – transjugular intrahepatic portosystemic shunt; WBC – white blood cell count.

[a] Data were tested for normality. Descriptive statistics are expressed as numbers or mean values (±SD), as appropriate. Continuous variables are expressed as means±SD or medians with interquartile ranges. [b] The *t* test or the Mann-Whitney U test was used to compare 2 groups, and χ^2 test or Fisher exact test was used to compare categorical variables. [c] Others included primary biliary cirrhosis, autoimmune diseases, Budd-Chiari syndrome, and cryptogenic cirrhosis. [d] Others included preventive therapy, portal system thrombosis, and alleviation of abdominal discomfort. [e] Others included portal vein trunk, right branches of the portal vein, and confluence of the left branches of the portal vein.

Table 2. The results of univariate and multivariate Cox analysis of the association between clinical parameters and 1-year mortality rate.[a]

Variables	Univariate analysis			Multivariate analysis		
	Hazard ratio	95% CI	*P* value	Hazard ratio	95% CI	*P* value
Age	1.03	1.00-1.07	0.160			
Sex: male	0.76	0.32-1.80	0.973			
Albumin	0.94	0.88-1.00	0.049			
Total bilirubin	1.01	1.01-1.03	0.001	1.02	1.00-1.04	<0.001
PMD	0.90	0.87-0.94	<0.001	0.90	0.86-0.94	<0.001
TIPS targeted puncture						
Left	Reference	Reference	Reference			
Right	0.218	0.082-0.583	0.002			
Others	0.210	0.064-0.688	0.010			

CI – confidence interval; PMD – psoas muscle density; TIPS – transjugular intrahepatic portosystemic shunt.

[a] Hazard ratios and *P* values were estimated using the Cox proportional hazard model.

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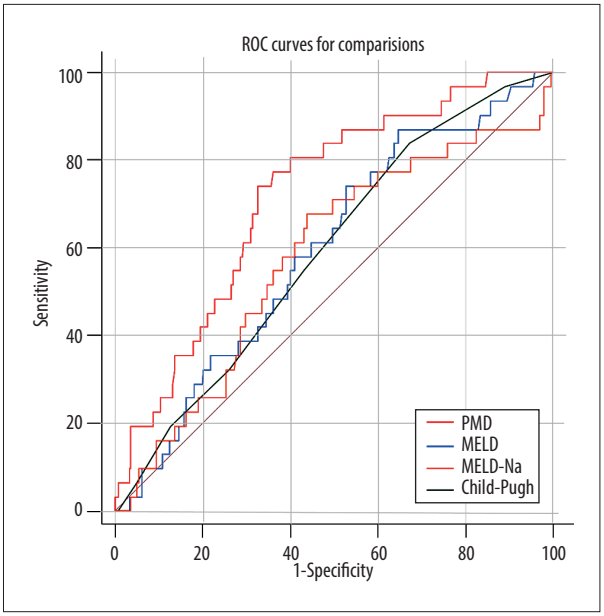

Figure 2. The receiver operating characteristic (ROC) curve of the predictive ability of psoas muscle density (PMD), Child-Pugh score, and model for end-stage liver disease (MELD) to predict post-transjugular intrahepatic portosystemic shunt death in 1 year.

bleeding (90.11%), and the remaining patients had refractory ascites (n=13) or thrombosis (n=7). **Table 1** lists the baseline characteristics of these subjects.

Results of the univariate and multivariate Cox analysis are shown in **Table 2**. There were 6 indicators selected via univariate and multivariate Cox analysis, including age, sex, TIPS targeted puncture, albumin, total bilirubin, and PMD. Multivariate Cox regression analysis was performed with the forward LR (forward stepwise regression based on maximum likelihood estimation) method. Finally, PMD and total bilirubin were screened out, which were statistically significant ($P<0.05$). PMD had negative regression coefficients, indicating that the mortality of post-TIPS within 1 year decreased as PMD increases. Meanwhile, total bilirubin had a positive regression coefficient (**Table 2**).

The optimal PMD threshold for predicting survival was 49.92 HU ($P=0.0449$) (**Figure 2**). All patients were stratified according to the cutoff value (low-PMD <49.92 HU, high-PMD ≥49.92 HU). PMD measurements below the threshold were associated with significantly increased mortality after TIPS creation ($P<0.001$). The mortality of patients was statistically different between 2 groups ($P<0.001$). There was a significant decrease

Table 3. Characteristics of the study population, stratified by PMD measurement.[a]

Variables	All patients n=273	Low PMD n=102	High PMD n=171	*P* value[b]
Basic information				
Survival	242	79	163	<0.001
Age, y	53.54±10.51	58.68±8.10	50.47±10.61	<0.001
Sex				
Male	194	61	133	0.002
Female	79	41	38	
BMI	22.87±3.15	24.08±3.49	22.29±2.83	0.016
Hypertension	27	17	10	0.004
Smoking	105	33	72	0.109
Splenectomy	22	9	13	0.720
Etiology of cirrhosis				0.217
Alcoholic	53	23	30	
Viral (HBV or HCV)	151	50	101	
Both alcohol and viral	35	12	23	
Others[c]	34	17	17	
Reasons for TIPS				0.099
EGVB	246	87	159	
RF	13	8	5	
Others[d]	14	7	7	

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Table 3 continued. Characteristics of the study population, stratified by PMD measurement.[a]

Variables	All patients n=273	Low PMD n=102	High PMD n=171	*P* value[b]
TIPS targeted puncture				0.007
Left branch of the intrahepatic portal vein	199	66	133	
Right branch of the intrahepatic portal vein	61	30	31	
Others[e]	13	6	7	
Stent-graft diameters, mm	8 (8-9)	8 (8-10)	8 (8-9)	0.002
Laboratory parameters				
RBC, $\times 10^{12}$	3.02±0.71	2.86±0.68	3.11±0.72	0.006
WBC, $\times 10^{9}$	5.06±3.59	5.22±4.00	4.96±3.33	0.566
Lymphocyte, $\times 10^{9}$	0.99±0.87	0.95±0.61	1.01±1.01	0.580
Neutrophil, $\times 10^{9}$	3.34±2.68	3.50±2.97	3.24±2.49	0.447
Platelet, $\times 10^{9}$	81.42±61.95	86.23±63.57	78.56±60.97	0.324
Hemoglobin, g/L	85.78±24.74	83.50±21.44	87.13±26.49	0.241
Albumin, g/L	30.18±5.39	28.97±5.98	30.89±4.88	0.004
Total bilirubin, μmol/L	24.30±17.60	25.93±17.90	23.33±17.40	0.239
ALT, U/L	43.02±106.98	40.66±75.20	44.43±122.25	0.778
AST, U/L	55.24±100.32	56.39±63.21	54.55±117.16	0.884
Serum creatinine, μmol/L	66.15±17.06	66.22±30.95	66.11±17.60	0.970
Serum sodium, mmol/L	137.44±4.37	137.22±4.66	137.56±4.21	0.526
Prothrombin time, s	17.34±2.67	17.72±3.52	17.11±1.98	0.067
INR	1.42±0.24	1.42±0.25	1.42±0.23	0.986
Clinical scores				
Child-Pugh score	7 (6-9)	7 (6-9)	9 (8-10)	<0.001
MELD score	11.45 (9.76-13.46)	11.69 (9.59-14.02)	11.18 (9.82-13.20)	0.224
MELD-Na score	10.91 (7.47-14.50)	12.22 (7.31-15.27)	10.62 (7.44-14.07)	0.207

ALT – alanine aminotransferase; AST – aspartate aminotransferase; BMI – body mass index; EGVB – esophageal gastric-fundus variceal bleeding; HBV – hepatitis B virus; HCV – hepatitis C virus; HU – Hounsfield units; INR – international standardization ratio; MELD – model for end-stage liver disease; MELD-Na – composite index of model for end-stage liver disease and serum sodium; PMD – psoas muscle density; RBC – red blood cell count; RF – refractory ascites; TIPS – transjugular intrahepatic portosystemic shunt; WBC – white blood cell count.

[a] Descriptive statistics are expressed as numbers or mean values (±SD), as appropriate. Continuous variables are expressed as means±SD or medians with interquartile ranges. [b] The *t* test or the Mann-Whitney U test was used to compare 2 groups, and χ^2 test or Fisher exact test was used to compare categorical variables. [c] Others included primary biliary cirrhosis, autoimmune diseases, Budd-Chiari syndrome, and cryptogenic cirrhosis. [d] Others included preventive therapy, portal system thrombosis, and alleviation of abdominal discomfort. [e] Others included portal vein trunk, right branches of the portal vein, and confluence of the left branches of the portal vein.

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Table 4. Diagnostic accuracy of different scoring systems in predicting post-transjugular intrahepatic portosystemic shunt mortality within 1-year at the optimal cutoff point.

Prognostic models	AUROC	*P* value	Cutoff point	Sensitivity	Specificity	Youden Index	PLR	NLR	PPV	NPV
PMD	0.720	<0.001	49.92	74.2	67.4	0.42	2.27	0.38	0.23	0.95
MELD	0.596	0.047	10.17	87.1	35.1	0.22	1.34	0.37	0.15	0.96
MELD-Na	0.580	0.155	11.46	67.7	56.0	0.24	1.06	0.58	0.13	0.96
Child-Pugh	0.592	0.034	6.00	83.9	32.6	0.17	1.25	0.49	0.14	0.94

AUROC – area under the receiver operating characteristic curve; MELD – model for end-stage liver disease; NLR – negative likelihood ratio; NPV – negative predictive value; PLR – positive likelihood ratio; PPV – positive predictive value.

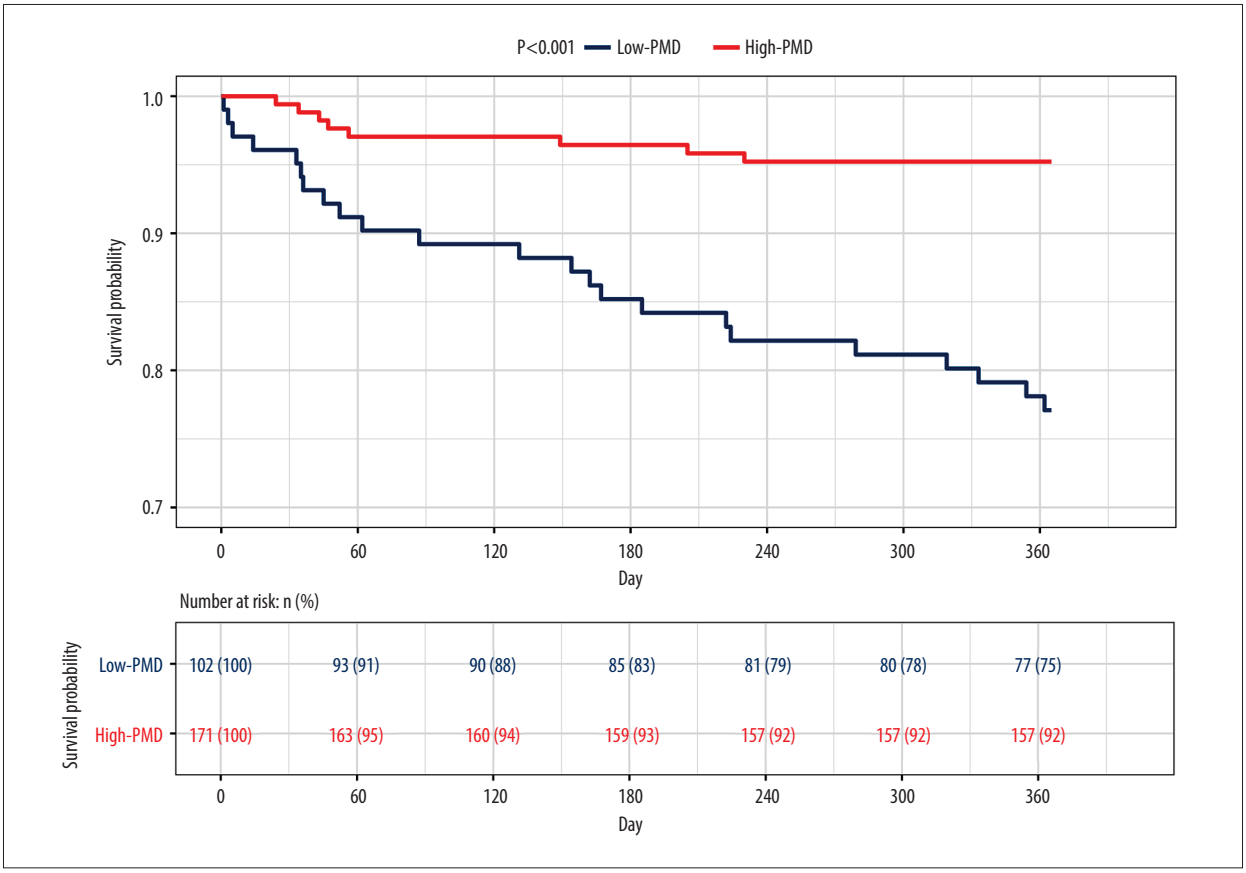

Figure 3. Kaplan-Meier survival curves stratified with psoas muscle density (PMD) level. Survival probability is greater when PMD is more than 49.92 Hounsfield units (HU).

in PMD with the process of aging (low-PMD 58.68±8.10, high-PMD 50.47±10.61, *P*<0.001) (**Table 3**). The 2 groups also had significant differences in red blood cell count (RBC), albumin, and Child-Pugh score (**Table 3**).

PMD was negatively correlated with mortality (r=0.90, *P*<0.05) by the Spearman test. Meanwhile, PMD had a better discriminative ability to predict the incidence of death within 1 year after TIPS, as shown in **Figure 2**, than the MELD score (AUC: 0.72 vs 0.60, 95% CI: 0.663-0.773 vs 0.535-0.655). As shown in **Table 4**, when the best PMD cutoff point (PMD=49.92 HU) was used, the sensitivity, specificity, negative and positive likelihood ratios, and negative and positive predictive values were 0.742, 0.674, 0.38, 2.27, 0.95, and 0.23, respectively. The Kaplan-Meier survival curves (**Figure 3**) stratified with the PMD level. Survival probability was greater when PMD was more than 49.92 HU. Because sex and age are closely related to sarcopenia [44], we made ROC curves in LC patients stratified by age

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Table 5. Subgroup ROC curves of the association between PMD and 1-year mortality rate.

Variables	AUROC	*P* value	Cutoff point	Sensitivity	Specificity	Youden Index	PLR	NLR	PPV	NPV
Sex										
Female	0.656	0.056	49.92	88.89	52.86	0.4175	1.89	0.21	0.20	0.97
Male	0.742	<0.001	51.01	77.27	67.44	0.4471	2.37	0.34	0.23	0.96
Age, y										
>60	0.693	0.009	51.93	100	39.13	0.3913	1.64	0.00	20.8	100
≤60	0.723	<0.001	50.44	75.00	69.36	0.4436	2.45	0.36	22.1	96

AUROC – area under the receiver operating characteristic curve; MELD – model for end-stage liver disease; NPV – negative predictive value; NLR – negative likelihood ratio; PPV – positive predictive value; PLR – positive likelihood ratio; ROC – receiver operating characteristic.

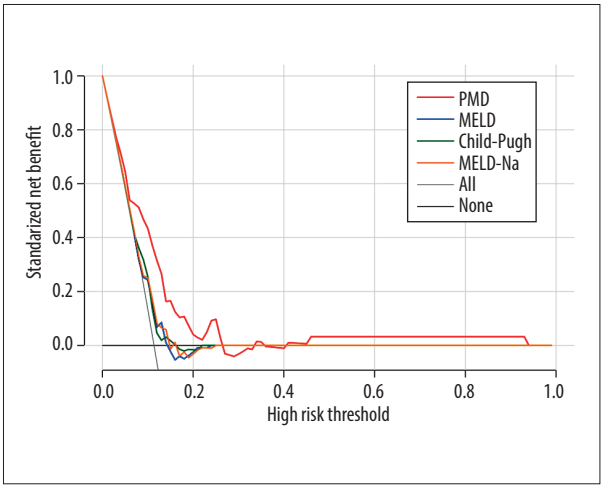

Figure 4. Decision curves for 3 ways to predict an event in the patients. MELD – model for end-stage liver disease; MELD-Na – composite of model for end-stage liver disease and serum sodium; PMD – psoas muscle density.

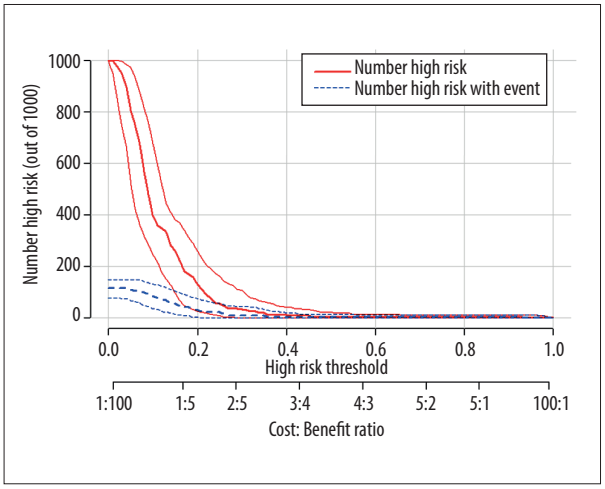

Figure 5. Clinical impact curve for the psoas muscle density (PMD) measurement.

(>60 years and ≤60 years) and sex. As presented in **Table 5**, PMD had a better ability to predict the 1-year mortality in men than in women. Decision curve analysis was conducted to assess the clinical utility of PMD [45]. It was obvious that PMD could be helpful in selecting patients who would benefit from TIPS implantation, as shown in **Figure 4**. To display the relationship between the events screened by the PMD level and the true positive events intuitively, we made a clinical impact curve [45]. In **Figure 5**, the solid red line shows patients with each risk threshold identified by PMD as high risk, and the blue dotted line shows the true number of positive patients. Based on the Cox regression model analysis, both bilirubin and PMD were excellent predictors of the post-TIPS mortality. The improved total bilirubin-PMD model is presented in **Figure 6** as a nomogram for individualized survival prediction.

Discussion

Over the past few years, sarcopenia, defined as a muscle mass that is 2 standard deviations or more below the healthy young adult mean value [46], has been the subject of extensive research in LC patients. Comprehensive systematic reviews and meta-analyses have shown that patients with LC and sarcopenia experience adverse clinical outcomes [47,48]. Cross-sectional imaging studies have also reported that the prevalence of sarcopenia is 30%-70% among patients with LC [49]. Ronald et al [50] and Shoreibah et al [51] have explored the role of combined muscle mass index in survival after TIPS and found that the combination of MELD and sarcopenia appeared to be superior in predicting survival as compared with the MELD score alone. It also has been demonstrated that the failure to reverse sarcopenia after TIPS implantation is associated with a decreased survival rate [52,53]. So, studies on sarcopenia and mortality in patients with TIPS are still insufficient. This

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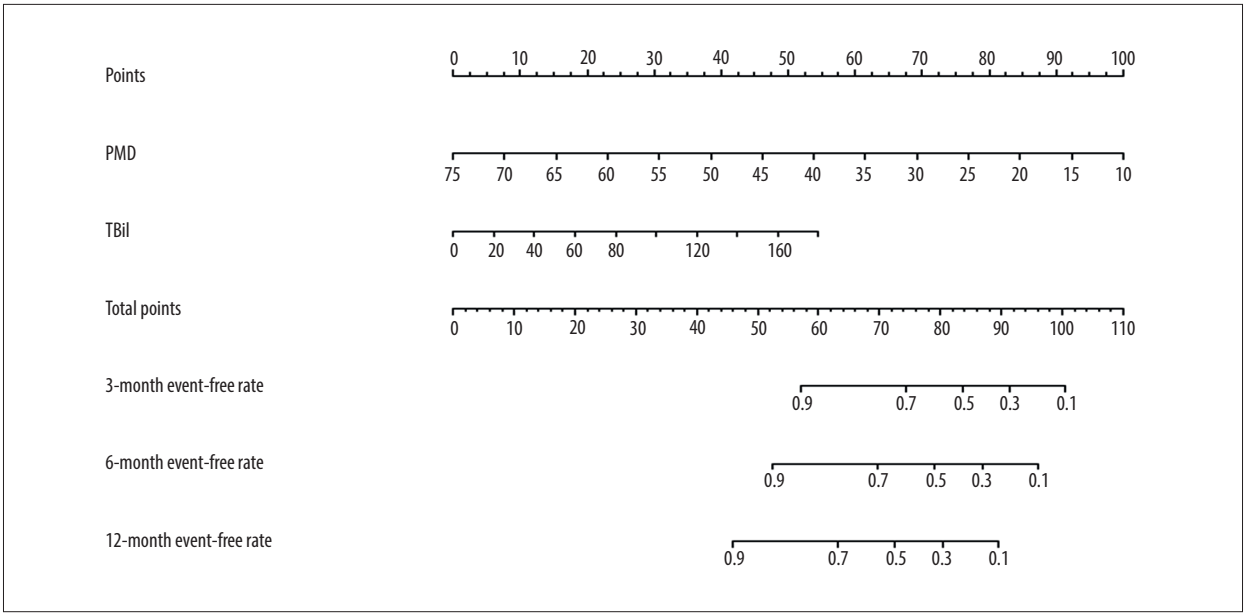

Figure 6. The nomogram of improved psoas muscle density (PMD) measurement. TBil – total bilirubin.

study explored whether PMD is a reliable, simple quantitative indicator for predicting the mortality of patients with TIPS.

There are various imaging criteria for sarcopenia, but there is no universally accepted definition. The skeletal muscle index (SMI), which normalizes muscle area to patient height, is a commonly used nutritional index. North American liver transplant centers proposed cutoffs of SMI <50 cm^2/m^2 in male patients and <39 cm^2/m^2 in female patients listed for liver transplant [8]. In addition to SMI, several ways have been used to predict outcomes in patients with LC, including psoas muscle thickness, psoas muscle index, and PMA [11]. In fact, due to fluid retention in patients with LC, the above assessments cannot accurately differentiate body composition, which affects results [54]. In recent years, PMD has been widely used to predict the mortality [33,51,55-58].

In our study, the overall cumulative 1-year mortality rate was 11.36% (31/273). Different institutions have shown all-cause mortality in patients with TIPS ranging from 7% to 70% [37,59,60]. The survival rate was relatively high compared with other studies, and several possible explanations should be considered. First, the vast majority of patients were in Child-Pugh A/B class (233/273). Secondly, the drainage of the left branch of the intrahepatic portal vein (PV) (199/273) may have made a difference. A meta-analysis by Zuo et al [61] showed that TIPS conducted via the left PV was associated with decreased rates of postoperative hemorrhage and TIPS dysfunction. The pattern of muscle decay varies with age and sex, as shown in previous research [44]. In our study, PMD decreased with aging, and it differed by sex (**Table 3**). Levels of serum zinc, serum vitamin D, blood ammonia, and testosterone may cause variation in the muscle between individuals of different ages and sex [1]. Our study of 273 patients who underwent TIPS showed that MELD outperformed MELD-Na in predicting 1-year mortality. A small study of 69 subjects from Ahmed et al [62] showed that MELD-Na was superior to MELD in predicting 30-day mortality, but Young et al [31] reported the opposite conclusion. However, a considerable number of studies have shown that MELD-Na is a good predictor of prognosis in liver transplantation patients, and it has entered clinical practice in the United States. Nevertheless, there is still a limited amount of research on the predictive capacity of MELD-Na for 1-year mortality in TIPS patients [29,31,62,63]. The MELD score seemed no different between the low-PMD group and the high-PMD group (P=0.224), which was similar to previous findings [32,51,64]. Hence, the MELD for patients with a low PMD (<49.92 HU) who undergo TIPS creation may poorly predict survival owing to the presence of an advanced degree of sarcopenia. Our study showed a good ability to predict patient survival (ROC=0.72, 95% CI: 0.663-0.773); however, the positive predictive value was 0.23, which is low. The reason is rooted in the limited number of cases and lower overall cumulative 1-year death (31/273) compared with other studies. In addition, PMD is an indicator of the state of the body, which is influenced by factors such as individual diet, exercise, drugs, and so on. Our study also demonstrated that the low-PMD group (PMD <49.92 HU) had higher post-TIPS mortality. The findings support an association between sarcopenia and worsening survival after TIPS, consistent with previous studies.

At present, multiple tools are used for evaluating the nutritional condition of LC patients, but a clinically available tool is still lacking. PMD is an objective, noninvasive quantitative indicator

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that uses clinically common software. As a routine inspection item, CT does not increase hospitalization costs. Clinically, early screening of LC patients with a poor prognosis and a high risk of death will improve survival time and quality of life. In summary, PMD will be useful to clinicians as a reliable tool to help in treatment decision-making for LC patients in clinical practice. Sarcopenia-based TIPS may provide even less benefit. It may be a better option to give TIPS after improving the patient's nutritional status. The review by Ebadi et al [11] has shown that early, planned multimodal interventions, including nutritional support, physical exercise, and pharmacological intervention, are necessary to prevent and/or treat sarcopenia. Whether exercise, medication, or other treatments decrease mortality in patients with TIPS remains uncertain. More related work is needed in the future.

Our current research has limitations. First, our study was a retrospective single-center study, and external validation is needed. Due to the technical difficulty of TIPS and the clinical characteristics of patients at different medical centers, prospective multicenter validation is needed to acquire further evidence to support the use of PMD in clinical practice.

Conclusions

In conclusion, PMD measurement is an easy, objective, economical approach with repeatable clinical value for predicting the 1-year mortality of patients with TIPS. Further multicenter studies with larger cohorts or prospective trials are needed to validate our findings.

Declaration of Figures' Authenticity

All figures submitted have been created by the authors who confirm that the images are original with no duplication and have not been previously published in whole or in part.

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