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RESEARCH ARTICLE

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Muscle fat content correlates with postoperative survival of viral-related cirrhosis patients after the TIPS: a retrospective study

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ABSTRACT

Purpose: Early prediction of the prognosis of viral-related cirrhosis patients after transjugular intrahepatic portosystemic shunt (TIPS) is beneficial for clinical decision-making. The aim of this study is to explore a comprehensive prognostic assessment model for evaluating the survival outcomes of patients post-TIPS.

Materials and methods: A total of 155 patients treated with TIPS were included in the study. The data were collected from electronic records. The nutritional status of the patient is evaluated using imaging examinations measuring by the axial CT images from the L3 vertebral level. The primary endpoint was set as death within 1 year after TIPS. Multivariate Cox regression was performed to determine the factors associated with mortality.

Results: The Cox regression analysis revealed that the lower PMFI was associated with a lower risk of all-cause mortality after TIPS (hazard ratio [HR] 1.159, 95% confidence interval [CI] 1.063–1.263, $p=0.001$). Furthermore, subgroup analyses according to gender revealed the PMFI was associated with postoperative death both in male (HR 2.125, 95% CI, 1.147–3.936, $p=0.017$) and female patients (HR 1.070, 95% CI, 1.001–1.144, $p=0.047$). The area under the curve (AUC) for predicting death within 1 year was 0.807. The clinical impact curve analysis showed that PMFI had higher levels of risk threshold probability and a smaller gap between actual and predicted curves.

Conclusions: In viral-related cirrhosis patients with portal hypertension, increased muscle fat content might be a potential prognostic marker and associated with postoperative death after TIPS.

KEY POINTS

Early prediction of post-TIPS patient survival is currently a clinical challenge.

- The absolute muscle fat content is correlated with post-TIPS survival time.
- The muscle fat infiltration can be used as a new evaluation method.

Abbreviations: AIH: autoimmune hepatitis; ALB: serum albumin; ALD: alcoholic liver disease; AUC: area under the curve; BMI: body mass index; CI: confidence interval; Cr: creatinine; CT: computed tomography; EGVB: esophagogastric variceal bleeding; FIB: fibrinogen; GLB: serum globulin; HB: haemoglobin; HBV: hepatitis B virus; HR: hazard ratio; Hu: Hounsfield unit; INR: international standard ratio; IQR: interquartile range; MELD scores: Model for End-Stage Liver Disease scores; NAFLD: non-alcoholic fatty liver disease; PLT: platelet; PMA: psoas muscle area; PMD: psoas muscle density; PMFI: psoas muscle fat index; PACS: Picture Archiving and Communication System; ROC: receiver operating characteristic curve; Tbil: total bilirubin; TC: total cholesterol; TG: triglyceride; TIPS: transjugular intrahepatic portosystemic shunt; WBC: white blood cell

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1. Introduction

Transjugular intrahepatic portosystemic shunt (TIPS) has been established as a pivotal therapeutic intervention for addressing bleeding oesophageal and gastric varices, as well as refractory ascites, which are prevalent complications of portal hypertension [1]. Despite the advancements in TIPS procedures, a subset of patients does not derive substantial benefit from this intervention, thereby highlighting the critical necessity for early prognostic assessment to inform clinical decision-making.

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Currently, the Model for End-Stage Liver Disease (MELD) score is widely used to assess post-TIPS prognosis [2,3]. Recently, several novel indices have been introduced and have demonstrated effective validation [4–6]. However, these indices are predominantly serum-based, rendering them susceptible to transient fluctuations in serum markers, which may potentially undermine the accuracy of clinical predictions. Notably, studies have indicated significant prognostic benefits of TIPS in patients with hepatorenal syndrome [7], yet the MELD score may overestimate their condition, potentially leading to missed treatment opportunities. Moreover, these indices often overlook the impact of overall nutritional status in cirrhotic patients, despite previous research indicating its critical role in overall survival [8]. Therefore, emphasizing patient nutritional status may be crucial in the prognostic evaluation post-TIPS.

Given the multifaceted aetiologies of cirrhosis, which frequently involve fluid and sodium retention, the development of standardized assessment systems for nutritional status remains a significant challenge [9]. Recent validation studies have underscored the value of assessing muscle and fat distribution as an objective measure of patient nutritional status [10]. Furthermore, hormonal imbalances in cirrhotic patients can lead to ectopic distribution of muscle and fat, further complicating the assessment process [11]. Thus, comprehensive evaluation of muscle and fat status provides a more objective reflection of nutritional health and aids in prognostic assessments.

Therefore, to mitigate the influence of fat, this study selected patients with virus-related cirrhosis as its subjects. The aim of this study is to explore a more comprehensive prognostic assessment model for evaluating the survival outcomes of patients post-TIPS, with the goal of enhancing clinical decision-making.

2. Methods

2.1. Patient selections

We enrolled consecutive patients who underwent TIPS for portal hypertension at Xiangya Hospital Central South University between June 2014 and June 2021. These patients were diagnosed with viral-related cirrhosis and had available abdominal CT scans within 1 month before TIPS. The exclusion criteria for eligibility were concurrent malignancy, skeletal muscle-related disorders (such as myasthenia gravis and muscle pseudohypertrophy), and non-viral-related chronic liver disease including alcoholic liver disease (ALD), non-alcoholic fatty liver disease (NAFLD) and autoimmune hepatitis (AIH). Patients who lost to follow-up within 1 year after the TIPS procedure were also excluded from this study.

The diagnosis of cirrhosis was determined by hepatologists through unequivocal clinical, radiological and biochemical findings. Referring to previous studies and guidelines [12–14], TIPS treatment was indicated for patients with Child-Pugh scores ≤13 who had gastro-oesophageal variceal bleeding refractory to endoscopic and drug therapy, refractory ascites or hydrothorax. The decision to treat with TIPS was made by a Multi-Disciplinary Team and the procedure was performed by interventional radiologists.

Clinical and demographic data were retrospectively collected from electronic records by two independent clinical investigators. The nutritional status of all patients was assessed by NRS-2002 upon admission [10]. The radiological data were obtained by two radiologists who were blinded to clinical data randomly.

2.2. Muscle and fat assessment

Based on previous research, we assessed muscle and fat distribution in patients using imaging techniques, measuring psoas muscle area (PMA) and psoas muscle density (PMD) to quantify muscle size and fat infiltration, respectively [15,16]. Additionally, we used psoas muscle fat index (PMFI) to represent the absolute fat content within muscles [17].

The axial CT images at the L3 vertebral level were reviewed by the Picture Archiving and Communication System (PACS) and analysed with SliceOmatic V4.3 software (Tomovision, Montreal, QB, Canada), which enabled the measurement of the density and area of specific tissues using Hounsfield unit (Hu) thresholds. Axial slices with a thickness of 0.63–3.00 mm were utilized. The bilateral psoas muscles were selected as regions of interest, defined by geometric areas without a specific radiodensity range limitation, and were delineated using the tool according to anatomical boundaries.

In cases where the spine's oblique orientation in an axial image prevented the identification of both transverse processes, the left and right psoas muscles were mapped on two separate slices where the corresponding transverse processes were most clearly defined. The left and right psoas muscle regions in each CT image were identified using Hu thresholds of −29 to +150. Subcutaneous and intermuscular adipose tissues were quantified with thresholds of −190 to −30. The fat concentration in the psoas muscle was measured by the mean psoas muscle density, calculated automatically and illustrated in Figure 1.

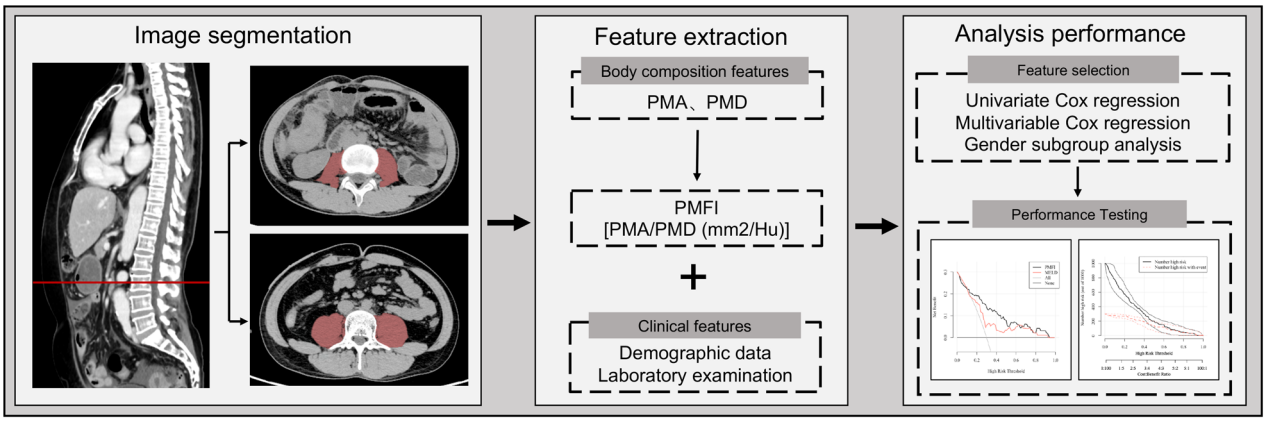

Figure 1. The workflow including abdominal CT image segmentation, feature extraction, and analysis performance testing for this study. The delineated region of interest in red corresponds to the PMA, and the mean density of this red region is indicative of the PMD. The PMFI is calculated as the ratio of PMA to PMD. PMA: psoas muscle area; PMD: psoas muscle density; PMFI: psoas muscle fat index.

The mean value of area (cm^2) and radiodensity (Hu) of bilateral psoas muscles were calculated to define the PMA and PMD, respectively. The PMFI was used to measure the absolute fat content of the psoas muscle. According to previous studies [17], the PMFI was calculated as follows: PMFI = psoas area (mm^2)/psoas density (Hu), indicating that a higher muscle fat content corresponds to a higher PMFI value.

2.3. Definitions

According to the pre-established treatment plan at our hospital, all patients who underwent TIPS were regularly revisited through outpatient clinics. The follow-up period lasted for at least one year after the operation, with follow-up concluding in June 2022. The primary endpoint was defined as death within 1 year after TIPS.

2.4. Statistical analysis

Continuous data were presented as mean values ± standard deviation (SD) for parametrically distributed data, and as median values with interquartile range (IQR) for non-parametric data. The Mann–Whitney U test was used for comparing continuous variables. Categorical data were presented as numbers and corresponding percentages and compared using Fisher's exact test or Chi-square tests. Potential prognostic factors for predicting post-TIPS death were included in the univariate regression analysis. Variables with a *p*-value less than 0.1 in univariate Cox regression were included in multivariate Cox regression to further calculate the hazard ratios. Considering that PMFI may be influenced by gender, age and BMI, hazard ratios were adjusted for these factors in subsequent analyses. Kaplan–Meier method was used to generate survival curves. The decision curve and clinical impact curve were employed to evaluate the clinical efficiency of variables. All reported *p*-values are two-tailed, with a *p*-value of <0.05 indicating statistical significance. All analyses were performed using SPSS software version 26 (SPSS Inc., Chicago, IL, USA), with GraphPad Prism version 7 (GraphPad Software, La Jolla, CA, USA) employed for figure creation.

2.5. Ethics declarations

This study adhered to the Declaration of Helsinki of 1964 and its later amendments. This study was approved by the Ethics Committee of Xiangya Hospital Central South University (ID: 202211239). The requirement for informed consent was waived by the same institute.

3. Results

3.1. Patient characteristics

A total of 193 patients with cirrhosis treated with TIPS were initially screened, and 155 patients were included in this study (Figure 2). Among them, 109 (70.3%) were male, and 136 (87.7%) had hepatitis B virus (HBV) infection. The median age was 52 years (range, 44 to 59 years). All patients underwent TIPS creation at the first attempt, achieving a success rate of 100%. Additionally, 116 (74.8%) patients underwent the TIPS procedure for gastrointestinal bleeding, while the remaining patients underwent the procedure for refractory ascites. According to the Child-Pugh classification, 38 patients were classified as Child A, 100 as Child B, and 17 as Child C before the operation, with

a median Model for End-Stage Liver Disease (MELD) score of 9.0 (range, 5.4 to 11.6). The baseline data of the study participants are summarized in Table 1.

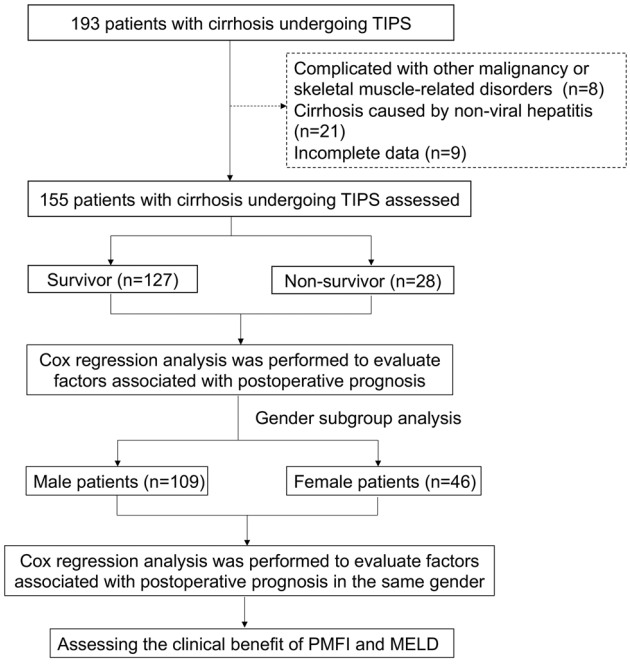

Figure 2. The flowchart of patient selection. TIPS: Transjugular intrahepatic portosystemic shunt; PMFI: psoas muscle fat index; MELD: Model for End-Stage Liver Disease scores.

3.2. Baseline comparison of cirrhotic patients with different clinical outcomes

After a median follow-up of 2.5 years (range, 1.6 to 3.8 years), 28 patients died within the first year after the TIPS procedure, resulting in a 1-year mortality rate of 18.1%. Comparisons of baseline characteristics between patients with different outcomes are shown in Table 1. Patients who died within 1 year postoperatively had higher MELD and cholesterol levels compared to survivors. Additionally, survivors exhibited better coagulation function, with significant differences in fibrinogen and D-dimer levels between the two groups. Notably, survivors had a significantly lower PMFI compared to patients who died within the first year after TIPS ($p=0.038$). In contrast, there were no significant differences in PMA and PMD between the two groups ($p>0.05$). Multivariate Cox regression analysis revealed that a lower PMFI (HR 1.159, 95% CI, 1.063–1.263, $p=0.001$) was associated with a lower risk of all-cause mortality after TIPS in cirrhotic patients, even after adjusting for age, gender and BMI (Table 2).

3.3. Comparison of cirrhotic patients with different clinical outcomes by gender subgroups

To eliminate the bias in body composition caused by gender, subgroup analyses were performed according

Table 1. Characteristics of the study population stratified by survival event.

Variable	Final Cohort ($n=155$)	Survivor ($n=127$)	Non-survivor ($n=28$)	p^*
Male, No. (%)	109 (70.3%)	91 (71.7%)	18 (64.3%)	0.586
Age, median (IQR), years	52.0 (44.0, 59.0)	51.0 (44.0, 58.0)	53.0 (50.0, 60.8)	0.139
Disease course, median (IQR), months	12.0 (5.0, 48.0)	12.0 (5.0, 48.0)	22.5 (3.0, 57.0)	0.885
BMI, median (IQR), kg/m^2	21.6 (20.3, 23.6)	21.6 (20.3, 23.8)	21.5 (20.2, 23.4)	0.233
Child-Pugh class				
A	38 (24.5%)	34 (26.7%)	4 (14.3%)	0.164
B	100 (64.5%)	79 (62.2%)	21 (75.0%)	0.288
C	17 (11.0%)	14 (11.0%)	3 (10.7%)	0.962
MELD, median (IQR)	9.0 (5.4, 11.6)	8.9 (6.0, 10.6)	10.0 (5.3, 12.4)	0.042
Blood transfusion treatment, No. (%)	77 (49.7%)	59 (46.5%)	18 (64.3%)	0.088
Splenomegaly, No. (%)	148 (95.5%)	121 (95.3%)	27 (96.4%)	0.790
Laboratory examination				
WBC, median (IQR), $\times10^9$/L	2.8 (1.9, 4.4)	2.7 (1.9, 4.4)	3.3 (2.4, 5.2)	0.250
HB, median (IQR), g/L	80.0 (69.0, 97.0)	80.0 (69.0, 92.0)	77.5 (67.3, 103.3)	0.748
PLT, median (IQR), $\times10^9$/L	51.0 (36.0, 88.0)	54.0 (37.0, 90.0)	44.5 (33.5, 85.0)	0.368
ALB, median (IQR), g/L	30.4 (26.8, 35.3)	30.8 (22.5, 29.7)	30.3 (27.2, 32.2)	0.251
GLB, median (IQR), g/L	26.2 (22.8, 29.9)	25.8 (22.5, 29.7)	27.9 (25.4, 34.9)	0.053
Tbil, median (IQR), μmol/L	19.7 (14.4, 29.4)	19.9 (14.7, 30.4)	19.1 (11.9, 27.5)	0.485
Cr, median (IQR), μmol/L	52.1 (41.4, 71.2)	52.0 (41.6, 72.7)	52.4 (41.6, 69.4)	0.884
TG, median (IQR), mmol/L	0.9 (0.7, 1.3)	1.0 (0.7, 1.3)	0.9 (0.8, 1.3)	0.839
TC, median (IQR), mmol/L	2.8(2.3, 3.4)	2.8 (2.3, 3.4)	3.1 (2.8, 3.9)	0.048
INR, median (IQR)	1.3 (1.2, 1.5)	1.3 (1.2, 1.5)	1.3 (1.1, 1.5)	0.058
FIB, median (IQR), g/L	1.7 (1.1, 2.2)	1.6 (1.1, 2.1)	2.0 (1.3, 2.7)	0.041
D-dimer, median (IQR), mg/L	0.7 (0.4, 1.5)	0.6 (0.3, 1.4)	1.0 (0.6, 1.8)	0.030
Radiological examination				
PMA, median (IQR), cm^2	16.6 (11.3, 20.1)	16.3 (11.2, 19.9)	14.6 (11.5, 18.7)	0.376
PMD, median (IQR), Hu	47.4 (37.3, 52.9)	47.9 (39.2, 52.7)	44.4 (29.8, 53.0)	0.246
PMFI, median (IQR), mm^2/Hu	38.0 (30.1, 45.9)	37.0 (30.2, 44.1)	43.7 (26.7, 54.4)	0.038

Abbreviations: BMI: Body mass index; MELD scores: Model for End-Stage Liver Disease scores; TIPS: Transjugular intrahepatic portosystemic shunt; EGVB: esophagogastric variceal bleeding; WBC: white blood cell; HB: haemoglobin; PLT: platelet; ALB: serum albumin; GLB: serum globulin; Tbil: total bilirubin; Cr: creatinine; TG: triglyceride; TC: total cholesterol; INR: international standard ratio; FIB: fibrinogen; PMA: psoas muscle area; PMD: psoas muscle density; PMFI: psoas muscle fat index; IQR: interquartile range.

*Mann–Whitney U test for continuous variables and chi-square or Fisher's exact probability test for proportions.

Table 2. Cox proportional hazards regression models evaluating predictors of overall patient mortality after TIPS.

	Univariate analysis		Multivariate analysis*	
Variable	HR (95%CI)	*p*	HR (95%CI)	*p*
Male	1.371 (0.633, 2.971)	0.423	1.160 (1.056, 1.273)	0.002
Age, years	1.023 (0.988, 1.060)	0.197	0.729 (0.264, 2.013)	0.542
Disease course, months	0.999 (0.994, 1.004)	0.718		
BMI, kg/m^2	0.881 (0.719, 1.079)	0.221	1.107 (0.784, 1.565)	0.563
Child-Pugh score	1.258 (0.375, 4.219)	0.710		
MELD	1.085 (1.018, 1.157)	0.012	1.061 (0.891, 1.263)	0.507
Blood transfusion treatment	1.819 (0.833, 3.974)	0.133		
Splenomegaly	1.392 (0.189, 9.246)	0.745		
Laboratory examination				
WBC, $\times10^9$/L	0.995 (0.880, 1.124)	0.932		
HB, g/L	1.001 (0.985, 1.017)	0.925		
PLT, $\times10^9$/L	0.997 (0.989, 1.006)	0.564		
ALB, g/L	0.952 (0.892, 1.015)	0.134		
GLB, g/L	1.045 (0.992, 1.102)	0.097	1.088 (0.976, 1.214)	0.129
Tbil, μmol/L	0.990 (0.967, 1.013)	0.397		
Cr, μmol/L	1.005 (0.997, 1.014)	0.215		
TG, mmol/L	1.002 (0.358, 2.806)	0.997		
TC, mmol/L	1.377 (1.096, 1.730)	0.006	2.527 (1.412, 4.521)	0.002
INR	0.455 (0.092, 2.235)	0.332		
FIB, g/L	1.452 (1.013, 2.063)	0.043	0.688 (0.249, 1.901)	0.471
D-dimer, mg/L	1.194 (0.929, 1.535)	0.166		
Radiological examination				
PMA, cm^2	1.021 (0.963, 1.083)	0.486		
PMD, Hu	0.987 (0.955, 1.020)	0.435		
PMFI, mm^2/Hu	1.044 (1.012, 1.077)	0.007	1.159 (1.063, 1.263)	0.001

Abbreviations: BMI: Body mass index; MELD: Model for End-Stage Liver Disease scores; WBC: white blood cell; HB: haemoglobin; PLT: platelet; ALB: serum albumin; GLB: serum globulin; Tbil: total bilirubin; Cr: creatinine; TG: triglyceride; TC: total cholesterol; INR: international standard ratio; FIB: fibrinogen; PMA: psoas muscle area; PMD: psoas muscle density; PMFI: psoas muscle fat index; HR: hazard ratio; CI: confidence interval.

*The multivariate analysis included the following variables: age, gender, BMI, MELD, GLB, TC, FIB and PMFI.

to gender. In male patients, multivariate Cox regression showed that a lower PMFI was an independent risk factor for mortality, adjusted for variables including age, BMI, MELD, globulin levels, cholesterol levels, fibrinogen and D-dimer, as indicated by univariate analyses (HR 2.125, 95% CI, 1.147–3.936, $p=0.017$) (Table 3). For female patients, univariate analysis revealed that cholesterol levels, MELD and PMFI were potential variables associated with postoperative mortality. However, only PMFI remained significantly related to death within the first year after adjustment for other variables using multivariate Cox regression analysis (HR 1.070, 95% CI, 1.001–1.144, $p=0.047$) (Table 4).

3.4. Subgroup analyses of cirrhotic patients with different clinical outcomes by indication for TIPS

Subgroup analyses were conducted based on the indication for TIPS. In the subgroup with variceal bleeding as the primary indication, univariate analysis identified MELD score and PMFI as potential predictors of postoperative mortality. After adjustment for confounding variables using multivariate Cox regression analysis, PMFI remained significantly associated with mortality within the first postoperative year (HR 4.843, $p=0.05$) (Supplementary Table 1). Conversely, in the subgroup with ascites as the primary indication, multivariate Cox regression analysis revealed that fibrinogen level was significantly associated with postoperative mortality (HR 1.266, $p=0.011$), whereas PMFI was not (Supplementary Table 2).

3.5. Differences in performance between the PMFI and the MELD

The receiver operating characteristic curve (ROC) analyses were applied with 1-year survival as the endpoint to evaluate the differences in performance between the PMFI and the MELD. Firstly, we revealed a modest correlation between the PMFI and the MELD ($R=0.250$, $p=0.002$) (Figure 3(a)). Then, we found that PMFI had relatively high specificity and sensitivity in predicting poor survival. The area under the curve (AUC) for predicting death within 1 year was 0.698 for MELD and 0.807 for PMFI, respectively (Figure 3(b, c)).

ROC curve analysis was applied to determine the sex-specific cutoff values. The optimal cut-off value of PMFI was 37.7mm^2/Hu for male patients and 45.5 mm^2/Hu for female patients (Figure 3(d, e)). Then, patients were divided into the high-PMFI group or the low-PMFI group based on the sex-specific cutoff values. Compared with patients in the low-PMFI group, those in the high-PMFI group had significantly higher

Table 3. Cox proportional hazards regression models evaluating predictors of overall patient mortality after TIPS in the male subgroup.

	Univariate analysis		Multivariate analysis*	
Variable	HR (95%CI)	*p*	HR (95%CI)	*p*
Age, years	1.028 (0.987, 1.071)	0.180	1.298 (0.864, 1.950)	0.210
Disease course, months	0.999 (0.994, 1.005)	0.809		
BMI, kg/m^2	0.858 (0.679, 1.085)	0.201	1.062 90.727, 1.552)	0.757
Child-Pugh score	1.028 (0.107, 9.883)	0.981		
MELD	1.078 (1.001, 1.160)	0.047	0.987 (0.763, 1.278)	0.923
Blood transfusion treatment	0.570 (0.221, 1.471)	0.245		
Splenomegaly	0.934 (0.124, 7.022)	0.947		
Laboratory examination				
WBC,10^9/L	0.996 (0.861, 1.151)	0.952		
HB, g/L	1.000 (0.981, 1.019)	0.987		
PLT, 10^9/L	0.998 (0.987, 1.008)	0.654		
ALB, g/L	0.954 (0.880, 1.035)	0.256		
GLB, g/L	1.074 (1.004, 1.149)	0.039	1.061 (0.934, 1.206)	0.360
Tbil, μmol/L	0.977 (0.939, 1.016)	0.238		
Cr, μmol/L	1.003 (0.990, 1.016)	0.620		
TG, mmol/L	0.876 (0.142, 5.406)	0.887		
TC, mmol/L	1.309 (1.010, 1.697)	0.042	1.098 (0.988, 1.219)	0.083
INR	0.128 (0.012, 1.362)	0.188		
FIB, g/L	1.756 (1.167, 2.642)	0.007	0.631 (0.214, 1.860)	0.404
D-dimer, mg/L	1.037 (0.714, 1.506)	0.849		
Radiological examination				
PMA, cm^2	0.945 (0.872, 1.024)	0.170		
PMD, Hu	0.980 (0.943, 1.019)	0.307		
PMFI, mm^2/Hu	1.041 (1.001, 1.083)	0.047	2.125 (1.147, 3.936)	0.017

Abbreviations: BMI: Body mass index; MELD scores: Model for End-Stage Liver Disease scores; WBC: white blood cell; HB: haemoglobin; PLT: platelet; ALB: serum albumin; GLB: serum globulin; Tbil: total bilirubin; Cr: creatinine; TG: triglyceride; TC: total cholesterol; INR: international standard ratio; FIB: fibrinogen; PMA: psoas muscle area; PMD: psoas muscle density; PMFI: skeletal muscle fat index; IQR: interquartile range; HR: hazard ratio; CI: confidence interval.
*The multivariate analysis included the following variables: age, BMI, MELD, GLB, TC, FIB and PMFI.

Table 4. Cox proportional hazard regression models evaluating predictors of overall patient mortality after TIPS in the female subgroup.

	Univariate analysis		Multivariate analysis*	
Variable	HR (95%CI)	*p*	HR (95%CI)	*p*
Age, year	1.012 (0.949, 1.080)	0.708	0.984 (0.878, 1.102)	0.774
Disease course, month	0.999 (0.988, 1.010)	0.846		
BMI, kg/m^2	0.882 (0.504, 1.543)	0.660	0.963 (0.361, 2.570)	0.941
Child-Pugh score	1.605 (0.197, 3.047)	0.196		
MELD scores	1.108 (1.969, 1.266)	0.093	1.139 (0.955, 1.358)	0.147
Blood transfusion treatment	1.910 (0.478, 7.638)	0.360		
Splenomegaly	4.374 (0.738, 8.374)	0.756		
Laboratory examination				
WBC, ×10^9/L	1.024 (0.807, 1.298)	0.847		
HB, g/L	1.002 (0.973, 1.033)	0.871		
PLT, ×10^9/L	0.984 (0.959, 1.008)	0.191		
ALB, g/L	0.960 (0.856, 1.076)	0.479		
GLB, g/L	0.995 (0.905, 1.095)	0.926		
Tbil, μmol/L	0.978 (0.934, 1.024)	0.340		
Cr, μmol/L	1.011 (0.993, 1.029)	0.231		
TG, mmol/L	0.781 (0.170, 3.579)	0.750		
TC, mmol/L	2.298 (1.040, 5.079)	0.040	1.890 (0.776, 4.604)	0.161
INR	1.786 (0.358, 8.898)	0.479		
FIB, g/L	0.876 (0.404, 1.897)	0.737		
D-dimer, mg/L	1.404 (0.798, 2.468)	0.239		
Radiological examination				
PMA, cm^2	1.106 (0.937, 1.306)	0.233		
PMD, Hu	0.961 (0.909, 1.016)	0.162		
PMFI, mm^2/Hu	1.060 (1.002, 1.122)	0.041	1.070 (1.001, 1.144)	0.047

Abbreviations: BMI: Body mass index; MELD scores: Model for End-Stage Liver Disease scores; WBC: white blood cell; HB: haemoglobin; PLT: platelet; ALB: serum albumin; GLB: serum globulin; Tbil: total bilirubin; Cr: creatinine; TG: triglyceride; TC: total cholesterol; INR: international standard ratio; FIB: fibrinogen; PMA: psoas muscle area; PMD: psoas muscle density; PMFI: psoas muscle fat index; IQR: interquartile range; HR: hazard ratio; CI: confidence interval.
*The multivariate analysis included the following variables: age, BMI, MELD, TC and PMFI.

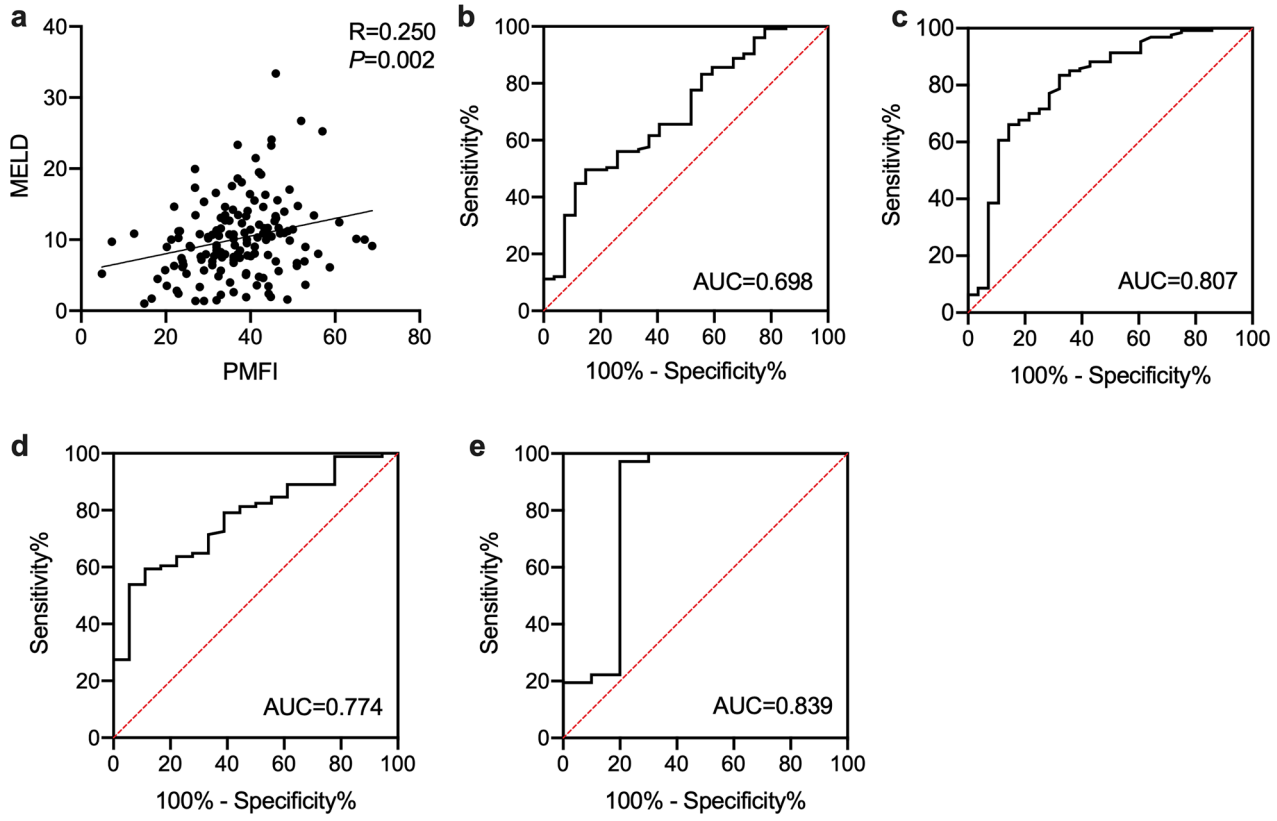

Figure 3. Differences in performance between the PMFI and the MELD. (a). Correlation analysis between the PMFI and the MELD. (b). Receiver-operating curve analysis for MELD to predict the mortality within 1 year. (c). Receiver-operating curve analysis for PMFI to predict the mortality within 1 year. (d). Receiver-operating curve analysis for PMFI to predict the mortality within 1 year in the male patients. (e). Receiver-operating curve analysis for PMFI to predict the mortality within 1 year in the female patients. PMFI: Psoas muscle fat index; MELD: Model for End-Stage Liver Disease scores.

cumulative survival rates at 1 year ($p < 0.001$). The results are illustrated in Figure 4.

3.6. Clinical efficiency of PMFI and MELD in evaluating mortality events in patients with cirrhosis after TIPS

The decision curve was used to evaluate the clinical efficiency of PMFI and MELD. Within a reasonable risk threshold range, the net benefit of PMFI was higher than that of MELD in assessing survival time after TIPS (Figure 5(a)). Further, the clinical impact curve was performed to evaluate the benefit of the PMFI or MELD in predicting death within 1 year after TIPS operation. The PMFI showed higher levels of risk threshold probability and a smaller gap between actual and predicted curves, representing a superior estimation of decision outcomes (Figure 5(b, c)).

3.7. Indicator validation

To further evaluate the accuracy of the PMFI, internal validations were performed in our study. For internal validation, 30% of the cohort was randomly selected for training, and this process was repeated 50 times. The results showed that the accuracy of PMFI in predicting postoperative death events was 0.85.

4. Discussion

Malnutrition has been shown to be associated with poor prognosis in various diseases [18]. Recently, increasing evidence has suggested that muscle quality, rather than muscle size, more accurately reflects nutritional conditions [19]. In this study, we found that increased muscle fat content was associated with the death within one year after TIPS, potentially providing evidence for clinical decision-making regarding the creation of TIPS.

The 1-year mortality rate was 18.1% among the 155 cirrhosis patients treated with TIPS in this study. Patients who died within 1 year had higher MELD and PMFI values. Moreover, there was a modest correlation between MELD and PMFI, suggesting that muscle fat content may be associated with chronic liver dysfunction to some extent [20]. However, PMFI, rather than

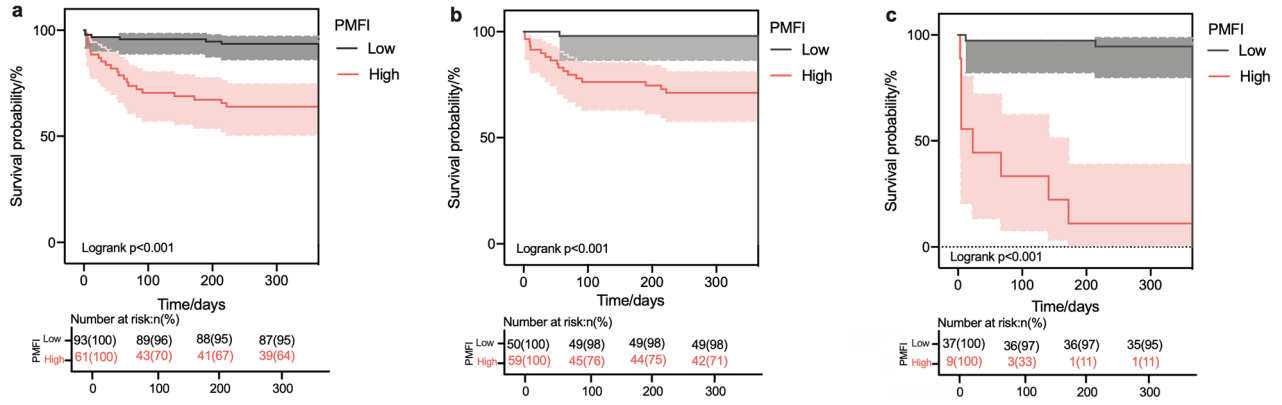

Figure 4. Kaplan–Meier curves for cumulative survival of patients with high PMFI (red) and or low PMFI (black). Statistical significance was calculated by the log-rank test for (a) all patients, (b) male and (c) female. PMFI: Psoas muscle fat index.

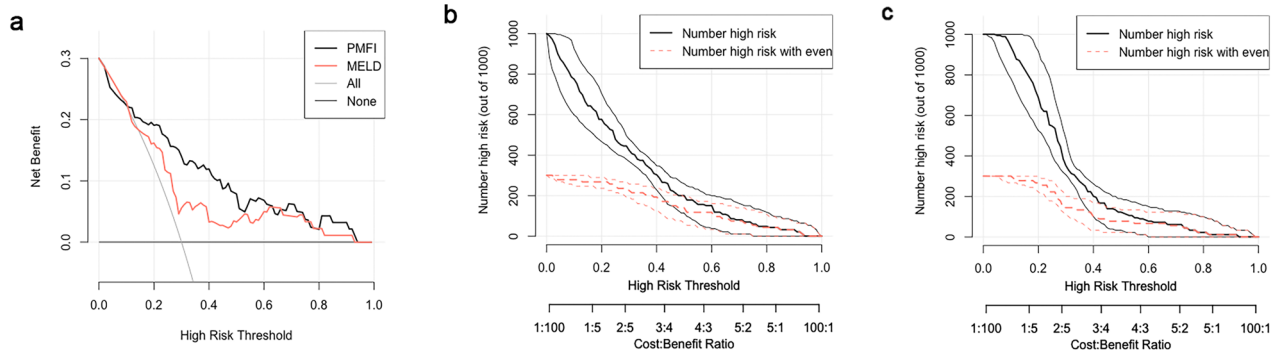

Figure 5. Clinical efficiency of PMFI value and MELD scores in evaluating mortality events in patients with cirrhosis after TIPS. (a). The decision curve evaluates the clinical efficiency of PMFI (black) and MELD (red). (b). The clinical impact curve evaluates the benefit of the PMFI in predicting the occurrence of death events within 1 year after TIPS operation. (c). The clinical impact curve for MELD. The black curve refers to the number of patients with high risk of death within 1 year assessed by different indicators under different risk thresholds, while the red curve refers to the number of patients who actually have death events. PMFI: Psoas muscle fat index; MELD: Model for End-Stage Liver Disease scores; TIPS: transjugular intrahepatic portosystemic shunt.

MELD, showed a significant correlation with postoperative death in multivariate Cox regression after adjusting for other confounding factors. Previous studies have indicated that MELD alone fails to reflect the overall condition of patients with chronic liver disease [21]. In contrast, a score combining MELD and PMA has shown better performance in predicting post-TIPS mortality [22]. Taken together, PMFI, as a new index of the absolute fat content in muscles, not only indirectly reflects poor nutritional status but may also be related to the deterioration of liver function. Therefore, PMFI may be a more powerful biomarker in predicting postoperative mortality in patients treated with TIPS compared to MELD.

PMA and PMD, commonly used indicators of muscle quantity and quality, have been reported as prognostic biomarkers in several diseases [23,24]. However, in this cohort, neither PMA nor PMD was associated with death within 1 year after TIPS. This discrepancy may be attributed to differences in patient selection between our study and previous studies. To eliminate the impact of metabolic liver disease on fat deposition, we excluded patients with non-viral-related chronic liver disease. Additionally, in patients with cirrhosis, the total fibres and cross-sectional area of myocytes are generally reduced [25], leading to an increased relative ratio of adipocyte area to myocyte area in the case of muscle atrophy. Consequently, lower or unchanged muscle density may amplify the presence of pathological fatty infiltration in severe muscle atrophy, where lipids are concentrated in a narrow muscle compartment, leading to an inaccurate evaluation of muscle conditions [17]. Hence, PMFI might more accurately reflect the absolute amount of fat than PMA and PMD, especially in patients with viral-related cirrhosis.

The mechanisms of pathological lipid infiltration in cirrhotic patients remain controversial. Fat infiltration in muscle can promote lipotoxicity, leading to

mitochondrial dysfunction and the release of pro-inflammatory cytokines [26,27]. These cytokines drive macrophages and other immune cells to infiltrate body tissues [28]. Therefore, intramuscular fat deposition may indirectly represent the degree of inflammation in patients with cirrhosis. Recent studies have shown that inflammatory status is a critical factor affecting the prognosis of patients after TIPS [29,30]. This may also explain why patients with high PMFI have a poor prognosis.

Metabolic disturbances are common in patients with cirrhosis, as the liver is crucial for the synthesis and decomposition of various nutrients [10,31]. Previous clinical studies have reported that abnormal cholesterol levels in peripheral blood are associated with the severity of liver dysfunction [32,33]. Interestingly, transferring cholesterol from the bone to the liver has been shown to improve liver function and reduce liver fibrosis in mice with hepatic osteodystrophy [34]. In this study, we found significantly lower levels of serum cholesterol in patients who died within 1 year after TIPS. However, it remains unclear whether abnormal cholesterol metabolism is associated with increased muscle fat content.

In addition, further stratified analyses were performed according to the distinct indications for TIPS. Within the subgroup characterized by variceal bleeding as the predominant indication, PMFI exhibited a significant association with postoperative mortality events. However, in the subgroup with ascites as the primary indication, PMFI did not. This discrepancy may be attributable to the fact that, compared with patients with variceal bleeding, those with ascites are more prone to coagulopathy, have a lower hepatic functional reserve and exhibit poorer nutritional status [35,36], all of which may have masked the significance of PMFI. Alternatively, the smaller sample size in the ascites subgroup may have influenced the overall analytical results, necessitating further investigation with an expanded sample size in future studies.

This study has several limitations. First, it is a retrospective study conducted at a single centre with a small sample size, leading to potential selection bias; thus, the findings should be verified through external validation. Second, although we have conducted strict screening, it may not be possible to rule out the possibility of some patients having non-alcoholic fatty liver disease, which may affect the analysis of body composition. Moreover, the relatively small sample size was insufficient to estimate an optimized cut-off value of PMFI to guide clinical practice.

5. Conclusion

In conclusion, this study demonstrated that increased muscle fat content is associated with postoperative mortality in viral-related cirrhosis patients treated with TIPS for portal hypertension. These findings suggest that PMFI might be a valuable prognostic marker and warrant further evaluation in a larger sample.

Acknowledgement

Figure 1 in our manuscript is an original image created by Photoshop and is not sourced from a third party.

Authors contributions

SL, YL, CYC and LRS contributed to study concept and design.SL, CLP, JXX and LRS contributed to acquisition of data. SL, CHZ, YZZ, CYC and TMW contributed to analysis and interpretation of data. YL, CHZ, XPY, TMW and CLP contributed to statistical analysis.SL, YL and YZZ drafted the manuscript. SL, HPL, FL and LRS contributed to critical revision of the manuscript for important intellectual content. All authors approved the final version of the manuscript, including the authorship list.

Disclosure statement

No potential conflict of interest was reported by the author(s).

Availability of data and material

The datasets generated or analysed during the study are available from the corresponding authors upon reasonable request.

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