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Integrating Psoas metrics and ascites into MELD-Na for survival prediction after TIPS: a temporal validation study

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Abstract

Background

Accurate risk prediction following transjugular intrahepatic portosystemic shunt (TIPS) remains challenging. We evaluated the incremental prognostic value of incorporating continuous height-normalized transverse psoas muscle thickness (TPMT/H) and clinically significant ascites into the Model for End-Stage Liver Disease–sodium (MELD-Na), assessing temporal generalizability in a distinct later cohort.

Methods

This retrospective study included 328 patients with cirrhosis undergoing TIPS at the First Affiliated Hospital of the University of Science and Technology of China (USTC) between April 2015 and May 2022. Cox proportional hazards models adding TPMT/H, ascites, or both (MELD-NSA) to MELD-Na were derived in an earlier cohort (*n* = 163) and evaluated without recalibration in a temporally distinct validation cohort (*n* = 165). Model discrimination, prediction error, and calibration were evaluated at 6, 12, and 24 months.

Results

In the temporal validation cohort, MELD-NSA markedly improved prognostic discrimination, elevating the 24-month concordance index from 0.627 to 0.723 (paired difference: 0.096; 95% confidence interval 0.012–0.167). The C-indices of MELD-NSA at 6 and 12 months were 0.738 and 0.734, respectively. Furthermore, MELD-NSA demonstrated superior overall performance, yielding a lower 24-month Brier score (0.159 vs 0.177) and robust risk-group stratification across cohorts. Concurrently integrating continuous TPMT/H and ascites provided superior incremental prognostic value compared with individual additions.

Conclusions

Integrating quantitative muscle metrics and ascites burden with MELD-Na significantly enhances post-TIPS survival discrimination across calendar periods. This readily accessible, multidimensional risk profile provides a robust foundation for refining individualized patient counseling and post-procedural management.

Background

Transjugular intrahepatic portosystemic shunt (TIPS) is a key intervention for managing complications of portal hypertension, with proven survival benefits in selected patient populations with cirrhosis [1, 2].

Consequently, Baveno VII consensus defines clear indications for TIPS in variceal bleeding and refractory ascites [3]. Given the marked heterogeneity in liver disease severity and baseline susceptibility across patients undergoing TIPS, accurate prognostic assessment remains critical.

Originally derived from a Cox model predicting post-TIPS survival [4], the Model for End-Stage Liver Disease (MELD) incorporates serum bilirubin, creatinine, and the international normalized ratio (INR) [5], with MELD-sodium (MELD-Na) further integrating serum sodium [6–8]. However, these laboratory-based scores do not directly account for nutritional status or ascites, leaving essential clinical dimensions of prognosis unmeasured.

Sarcopenia has been consistently linked to adverse outcomes following TIPS [9, 10], suggesting that muscle-related parameters could complement established risk scores [11]. Such risk stratification is particularly critical when evaluating patients undergoing TIPS for refractory ascites [12]. Collectively, these observations provide a strong rationale for integrating muscle-related parameters and ascites burden with MELD-Na to refine survival prediction.

We therefore hypothesized that combining height-normalized transverse psoas muscle thickness (TPMT/H) and clinically significant ascites with MELD-Na would provide incremental predictive value, and that this benefit would remain robust in a temporally distinct validation cohort. To test this, we compared MELD-Na alone against models incorporating either feature individually or both in combination (MELD-NSA). Model coefficients were derived in the earlier cohort and applied directly to the later cohort without recalibration. Discrimination, prediction error, and calibration were comprehensively evaluated to assess both risk ranking and the accuracy of absolute risk estimation.

Methods

Study design and participants

In this retrospective cohort study, 419 consecutive patients who underwent TIPS at the First Affiliated Hospital of USTC between April 2015 and May 2022 were initially screened. The inclusion criteria were age 18–75 years and a confirmed diagnosis of cirrhosis. The exclusion criteria were (1) concurrent hepatocellular carcinoma exceeding the Milan criteria or other extrahepatic malignancy; (2) missing critical clinical or imaging data; and (3) loss to follow-up within one year after the procedure. Ultimately, 328 eligible patients were enrolled. The cohort was split by date of TIPS: patients treated between April 2015 and December 2019 formed the training cohort (n = 163), and those treated between January 2020 and May 2022 formed the temporal validation cohort (n = 165) (Fig. 1).

Reporting was checked against the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) and Transparent Reporting of a multivariable prediction model for Individual Prognosis Or Diagnosis with artificial intelligence (TRIPOD + AI) recommendations [13, 14].

Transjugular intrahepatic portosystemic shunt procedure

All TIPS procedures were performed by a specialized team of interventional radiologists using a standardized approach. Briefly, under ultrasound guidance and local anesthesia, the right internal jugular vein was cannulated, and portal vein access was established with a transjugular liver access set (RUPS-100; Cook Medical, USA). After successful puncture, the pre-stent portal-systemic pressure gradient (PPG) was measured. The intrahepatic tract was predilated with a 6–7 mm balloon, and an 8-mm polytetrafluoroethylene (PTFE)-covered stent was deployed and post-dilated to its nominal diameter. The stent was the device available at the time of treatment, and stent types differed substantially between the two calendar periods (Table 1). Portal venography was performed to confirm stent position and assess collateral flow, and variceal embolization was added when clinically indicated. Technical success was defined as successful stent placement with a post-stent PPG of ≤ 12 mmHg or a reduction of > 50% from baseline.

Table 1
Baseline characteristics and survival in the training and temporal validation cohorts

Variable[a]	Training cohort (*n* = 163)	Temporal validation cohort (*n* = 165)	*P* value[b]
Age, years	53 (46–60)	54 (48–64)	0.084
Sex			0.034
Male	105 (64.4)	124 (75.2)	
Female	58 (35.6)	41 (24.8)	
Etiology			0.070
HBV	101 (62.0)	91 (55.2)	
Alcoholic	9 (5.5)	21 (12.7)	
Other	53 (32.5)	53 (32.1)	
Puncture site			0.256
Left portal	63 (38.7)	52 (31.5)	
Right portal	87 (53.4)	93 (56.4)	
Other	13 (8.0)	20 (12.1)	
TIPS indication[c]			0.160
Bleeding	129 (79.1)	119 (72.1)	
Ascites	29 (17.8)	34 (20.6)	
Other	5 (3.1)	12 (7.3)	
Stent type			< 0.001
VIATORR	38 (23.3)	131 (79.4)	
Fluency	14 (8.6)	16 (9.7)	
Other	111 (68.1)	18 (10.9)	
TPMT/H, mm/m	11.03 (8.63–13.75)	12.17 (9.76–14.89)	0.014
PNI	36.5 (32.97–40.73)	37.8 (34.1–41.45)	0.236
Diabetes			0.317
No	140 (85.9)	135 (81.8)	
Yes	23 (14.1)	30 (18.2)	
Ascites			0.001

Variable[a]	Training cohort (*n* = 163)	Temporal validation cohort (*n* = 165)	*P* value[b]
Mild or none	64 (39.3)	38 (23.0)	
Significant	99 (60.7)	127 (77.0)	
WBC, × 10^9/L	2.88 (2.15–4.62)	4.04 (2.72–6.13)	< 0.001
PLT, × 10^9/L	66 (43.85–96)	63 (45–100)	0.712
ALT, U/L	21 (15–30.9)	22 (15–32)	0.434
AST, U/L	28 (21.45–38)	30.9 (21.5–43)	0.162
TBIL, μmol/L	19.5 (13.19–25.8)	22.1 (13.8–33.9)	0.031
ALB, g/L	33 (30.6–37.7)	32.3 (28.3–35.1)	0.006
Cr, μmol/L	62 (52–73.5)	64 (53–81)	0.140
K, mmol/L	3.87 (3.59–4.14)	3.93 (3.57–4.29)	0.334
Na, mmol/L	140 (136–142)	138 (135–141)	0.001
INR	1.2 (1.08–1.38)	1.27 (1.13–1.49)	0.005
PT, s	14.4 (13.05–16.3)	15.3 (13.4–17.1)	0.033
APTT, s	38.3 (33.5–43.8)	35.8 (31–41.5)	0.003
TT, s	16.6 (15.55–18.45)	17.6 (16.5–18.9)	0.002
Child–Pugh class[d]			< 0.001
A	67 (41.1)	35 (21.2)	
B	82 (50.3)	110 (66.7)	
C	14 (8.6)	20 (12.1)	
Child–Pugh score	7 (6–8)	8 (7–9)	< 0.001
MELD score	9 (6.5–11.5)	10 (7–13)	0.060
MELD-Na score	9 (7–12.35)	11 (8–15)	0.017
FIPS score	−0.59 (− 1.17 to − 0.08)	−0.29 (− 0.97 to 0.16)	0.008
6-month survival, %[e]	93.9	87.3	0.042
12-month survival, %[e]	89.0	84.8	0.249
24-month survival, %[e]	84.7	77.3	0.086

Variables and definitions

The primary endpoint was overall survival, defined as the time interval from TIPS creation to death from any cause. Patients surviving through the end of the study period were censored at their last clinical follow-up; no patient underwent liver transplantation in the analyzed cohort. Transverse psoas muscle thickness was measured perpendicular to the axial diameter at the L3 vertebral level on computed tomography (CT) and normalized by height (TPMT/H, mm/m) to serve as a continuous metric of muscle quantity. Clinically significant ascites was defined as moderate-to-large-volume ascites (grade ≥ 2) versus mild or absent ascites (grade < 2); notably, this binary classification does not specifically denote refractory ascites.

Model specification and prediction

To evaluate incremental prognostic performance, MELD-Na alone was compared against nested Cox proportional hazards models incorporating continuous TPMT/H, clinically significant ascites, or both (termed MELD-NSA). In addition, separate Cox models were fitted using MELD, the Freiburg index of post-TIPS survival (FIPS), or the Child–Pugh score as the sole continuous predictor, yielding seven total specifications. All model coefficients and baseline cumulative hazards were estimated within the training cohort. Comparator absolute risks were generated directly from these fitted models rather than using previously published risk equations. Full model coefficients, reference specifications, baseline hazards, and an illustrative risk calculation are detailed in Additional file 1 (Table S1).

In the present analysis, the three-variable MELD-NSA model was fixed, with its coefficients, baseline hazards, and risk-group stratification cutoff derived from the training cohort and subsequently applied to the temporal validation cohort without recalibration or model updating. Internal validation was performed to quantify model optimism resulting from coefficient estimation within this predefined specification.

Statistical analysis

All statistical analyses were performed using R (version 4.6.1). Continuous variables were summarized as medians and interquartile ranges (IQRs) and compared using the Mann–Whitney U test. Categorical variables were compared using the chi-squared (χ^2) test or Fisher's exact test, as appropriate.

Predictive discrimination was evaluated at predefined time horizons of 6, 12, and 24 months using Harrell's concordance index (C-index) with follow-up truncated at each respective time point [15]. Incremental discrimination was quantified as the difference in C-index relative to MELD-Na alone, with 95% confidence intervals (CIs) estimated from 1000 paired bootstrap resamples of the fixed predictions. Model optimism during training was separately quantified by refitting the predefined models across 1000 bootstrap samples [16]. Predictive performance was further comprehensively assessed using cumulative/dynamic area under the receiver operating characteristic curve (AUROC) with Kaplan–Meier

censoring weights [17], inverse-probability-of-censoring weighted (IPCW) Brier scores, and time-dependent R^2 metrics [18]. Model calibration was assessed through observed-to-expected (O:E) mortality ratios, calibration plots across quintiles of predicted risk, and the Cox calibration slope—fitted using the fixed training linear predictor as the sole covariate over the entire follow-up period. Decision curve analysis (DCA) was conducted to quantify potential clinical net benefit at 24 months [19].

For risk-group analyses, hazard ratios (HRs) and log-rank test statistics were evaluated using follow-up truncated at 24 months. Multivariable Cox proportional hazards models combining both cohorts were implemented to evaluate the association between treatment period and mortality, before and after adjusting for MELD-Na, TPMT/H, and ascites. Nested model comparisons in the training cohort were performed using likelihood-ratio tests across full follow-up. All statistical tests were two-tailed, and $P < 0.05$ was considered statistically significant. Further details regarding statistical calculations and categorization schemes are available in Additional file 1.

Manuscript preparation

ChatGPT (OpenAI) was used to assist language editing, condensation and adaptation of the manuscript to the journal format. The authors retain responsibility for the accuracy and integrity of the work.

Results

Patient characteristics

The study analyzed 163 patients in the training cohort and 165 patients in the temporal validation cohort, with 32 and 38 deaths recorded over full follow-up, respectively (Table 1). Median follow-up was 51.7 months (interquartile range [IQR], 44.4–63.3) in the training cohort and 32.6 months (IQR 26.0–40.0) in the validation cohort. Baseline liver disease severity, serum albumin, serum sodium, muscle quantity, and stent type varied significantly between calendar periods, whereas TIPS indications were comparable ($P = 0.160$). In the pooled cohort ($n = 328$; 70 total deaths), treatment period was not significantly associated with overall mortality in either univariable analysis (HR 1.41; 95% CI 0.87–2.28; $P = 0.163$) or after multivariable adjustment for MELD-Na, TPMT/H, and ascites (HR 1.32; 95% CI 0.81–2.15; $P = 0.271$).

Model estimates

In the multivariable Cox model derived from the training cohort, individual HRs were 1.069 per MELD-Na point, 0.904 per mm/m increment in TPMT/H, and 1.966 for the presence of clinically significant ascites (Table 2). The global test for proportional hazards confirmed that the model satisfied proportional hazards assumptions ($P = 0.58$). A prognostic nomogram based on this derivation model is detailed in **Additional file 1 (Figure S1)**.

Table 2
Training cohort Cox regression analyses of factors associated with survival after TIPS

Variable[b]	Univariable Cox regression			Multivariable Cox regression[a]		
	HR	95% CI	*P*[c]	HR	95% CI	*P*[c]
Age, years	1.027	0.996–1.060	0.088	—	—	—
Sex, female	0.953	0.459–1.977	0.897	—	—	—
Etiology						
Alcoholic	1.119	0.260–4.809	0.880	—	—	—
Other	1.114	0.530–2.340	0.776	—	—	—
Puncture site						
Right portal	1.061	0.507–2.222	0.875	—	—	—
Other	1.172	0.331–4.154	0.806	—	—	—
Stent type						
Fluency	0.576	0.159–2.081	0.400	—	—	—
Other	0.424	0.196–0.915	0.029	—	—	—
TPMT/H, mm/m	0.912	0.822–1.011	0.080	0.904	0.816–1.001	0.053
PNI	0.998	0.940–1.060	0.954	—	—	—
Diabetes	1.492	0.614–3.626	0.378	—	—	—
Ascites	2.664	1.151–6.167	0.022	1.966	0.818–4.722	0.131
WBC, × 10^9/L	1.065	0.932–1.217	0.358	—	—	—
PLT, × 10^9/L	1.000	0.995–1.005	0.937	—	—	—
ALT, U/L	1.005	1.001–1.009	0.010	—	—	—
AST, U/L	1.009	1.001–1.016	0.022	—	—	—
TBIL, μmol/L	1.034	1.016–1.053	< 0.001	—	—	—
ALB, g/L	0.885	0.825–0.950	< 0.001	—	—	—
Cr, μmol/L	1.007	1.003–1.010	< 0.001	—	—	—
K, mmol/L	1.486	0.710–3.111	0.294	—	—	—
Na, mmol/L	0.916	0.870–0.964	< 0.001	—	—	—
INR	2.515	0.788–8.021	0.119	—	—	—

Variable[b]	Univariable Cox regression			Multivariable Cox regression[a]		
	HR	95% CI	*P*[c]	HR	95% CI	*P*[c]
PT, s	1.094	0.987–1.213	0.086	—	—	—
APTT, s	1.037	1.004–1.072	0.028	—	—	—
TT, s	0.971	0.863–1.093	0.625	—	—	—
Child–Pugh	1.316	1.070–1.619	0.009	—	—	—
MELD	1.126	1.047–1.211	0.001	—	—	—
MELD-Na	1.077	1.038–1.118	< 0.001	1.069	1.028–1.111	< 0.001
FIPS	2.196	1.362–3.541	0.001	—	—	—

Incremental prediction and performance in the temporal validation cohort

In the temporal validation cohort, the MELD-NSA model demonstrated C-indices of 0.738 (95% CI 0.625–0.829), 0.734 (95% CI 0.640–0.817), and 0.723 (95% CI 0.640–0.798) at 6, 12, and 24 months, respectively, consistently outperforming MELD-Na alone (0.676, 0.651, and 0.627, respectively; Fig. 2; Table 3). At 24 months, the validation Brier scores were 0.159 for MELD-NSA, 0.177 for MELD-Na, and 0.178 for MELD (**Additional file 1, Figure S2**). Among the four primary prognostic models evaluated, MELD-NSA achieved the highest point estimates for validation C-indices, although FIPS showed the highest 6-month training C-index (0.845). Decision curve analysis indicated potential clinical net benefit across broad threshold ranges at 24 months (Fig. 3).

Table 3
Predictive performance at 6, 12, and 24 months

Model	Training cohort		Temporal validation	Brier score[b]	R^{2b}
	Apparent C-index[a]	Optimism-corrected C-index[c]	C-index[a]	Training / validation	Training / validation
6 months					
MELD	0.666 (0.424–0.909)	0.661	0.633 (0.503–0.747)	0.056 / 0.113	0.029 / −0.017
MELD-Na	0.709 (0.464–0.911)	0.708	0.676 (0.554–0.784)	0.054 / 0.112	0.062 / −0.013
FIPS	0.845 (0.640–0.964)	0.842	0.649 (0.496–0.775)	0.051 / 0.109	0.110 / 0.022
MELD-NSA	0.805 (0.591–0.954)	0.795	0.738 (0.625–0.829)	0.051 / 0.105	0.123 / 0.054
12 months					
MELD	0.720 (0.573–0.874)	0.713	0.620 (0.504–0.723)	0.090 / 0.129	0.083 / −0.004
MELD-Na	0.765 (0.619–0.885)	0.763	0.651 (0.535–0.752)	0.090 / 0.130	0.085 / −0.010
FIPS	0.748 (0.607–0.876)	0.748	0.658 (0.522–0.774)	0.085 / 0.120	0.132 / 0.063
MELD-NSA	0.785 (0.636–0.914)	0.774	0.734 (0.640–0.817)	0.084 / 0.117	0.145 / 0.090
24 months					

Model	Training cohort		Temporal validation	Brier score[b]	R^{2b}
	Apparent C-index[a]	Optimism-corrected C-index[c]	C-index[a]	Training / validation	Training / validation
6 months					
MELD	0.699 (0.575–0.811)	0.694	0.595 (0.502–0.680)	0.118 / 0.178	0.089 / −0.016
MELD-Na	0.726 (0.603–0.830)	0.724	0.627 (0.535–0.714)	0.116 / 0.177	0.107 / −0.009
FIPS	0.723 (0.592–0.845)	0.720	0.591 (0.479–0.691)	0.112 / 0.168	0.139 / 0.044
MELD-NSA	0.754 (0.628–0.859)	0.741	0.723 (0.640–0.798)	0.107 / 0.159	0.177 / 0.093

Simultaneously incorporating continuous TPMT/H and ascites into MELD-Na yielded an absolute C-index increment of 0.096 (95% CI 0.012–0.167) at 24 months in the validation cohort (Table 4). In comparison, adding TPMT/H alone increased the C-index by 0.061 (95% CI − 0.006 to 0.126), and adding ascites alone increased it by 0.047 (95% CI − 0.006 to 0.093). Likelihood-ratio tests over full follow-up in the training cohort confirmed significant incremental fit when adding TPMT/H ($P = 0.046$) or both components combined ($P = 0.039$). Internal validation via 1000 training bootstrap resamples was performed for each of the four main models (Table 3). The optimism-corrected C-indices for MELD-NSA were 0.795, 0.774, and 0.741 at 6, 12, and 24 months, respectively. Across full follow-up, MELD-NSA showed an apparent C-index of 0.719, an estimated model optimism of 0.014, and an optimism-corrected C-index of 0.705.

Table 4
Validation discrimination and calibration with training cohort nested model tests

Model	Validation C-index[a]	Validation ΔC-index (95% CI)[a]	Training LRT *P* (full follow-up)[b]	Validation O:E at 24 months[a]
MELD-Na	0.627	Reference	—	1.288
MELD-Na + TPMT/H	0.688	0.061 (− 0.006 to 0.126)	0.046	1.370
MELD-Na + ascites	0.674	0.047 (− 0.006 to 0.093)	0.104	1.231
MELD-NSA	0.723	0.096 (0.012 to 0.167)	0.039	1.303
MELD	0.595	−0.032 (− 0.107 to 0.033)	—	1.353
FIPS	0.591	−0.036 (− 0.168 to 0.085)	—	1.177
Child–Pugh	0.592	−0.034 (− 0.138 to 0.068)	—	1.250

Abbreviations: C-index, concordance index; CI, confidence interval; ΔC-index, difference in C-index relative to MELD-Na; LRT, likelihood-ratio test; O:E, observed-to-expected mortality ratio. MELD, Model for End-Stage Liver Disease; MELD-Na, MELD incorporating serum sodium; FIPS, Freiburg index of post-TIPS survival; MELD-NSA, model combining MELD-Na, TPMT/H, and ascites; TPMT/H, transverse psoas muscle thickness normalized by height; TIPS, transjugular intrahepatic portosystemic shunt.

[a] C-index, ΔC-index, and O:E refer to temporal validation at 24 months. Reference denotes MELD-Na as the benchmark for ΔC-index. CIs were obtained from 1000 paired bootstrap resamples.

[b] LRT *P* values compare each nested extension with MELD-Na in the training cohort over full follow-up. — indicates that the LRT is not applicable: MELD-Na is the reference model, whereas MELD, FIPS, and Child–Pugh are non-nested comparators. These are not validation performance tests. Validation predictions used the fixed training coefficients and baseline hazards without recalibration.

Absolute-risk calibration in the temporal validation cohort

MELD-NSA exhibited observed-to-expected (O:E) mortality ratios of 1.83, 1.20, and 1.30 at 6, 12, and 24 months, respectively, and a full-follow-up calibration slope of 0.93 (95% CI 0.54–1.31) in the validation cohort (Additional file 1, Figure S4 and Table S2). At 24 months, O:E ratios exceeded 1.0 across all seven models (range 1.18–1.37), corresponding to an underprediction of absolute mortality in the temporal validation cohort.

Risk stratification and survival

Risk stratification was established using the median linear predictor from the training cohort (0.404) as the universal cutoff (**Additional file 1, Table S1**). Through 24 months, mortality was significantly higher in the high-risk group than in the low-risk group in both the training cohort (HR 6.02; 95% CI 2.06–17.54; log-rank $P = 0.0002$) and the temporal validation cohort (HR 5.72; 95% CI 2.39–13.73; log-rank $P < 0.0001$; Fig. 4).

Discussion

In this temporal validation study, concurrently integrating continuous TPMT/H and clinically significant ascites with MELD-Na markedly improved prognostic discrimination in a temporally distinct validation cohort, elevating the 24-month C-index from 0.627 to 0.723 (paired difference: 0.096; 95% CI 0.012–0.167). MELD-NSA consistently yielded higher C-index point estimates at 6 and 12 months, along with lower Brier scores and higher time-dependent R^2 values (**Additional file 1, Figure S3**). Crucially, because model coefficients derived from the earlier derivation cohort were applied to the later cohort without recalibration, these findings reflect true generalizability across calendar periods rather than optimistic apparent fit.

Our findings substantially build upon prior efforts to incorporate body composition metrics into post-TIPS prognostic models. While Xiong et al. previously evaluated CT-defined sarcopenia as an additive variable [11] and Saltini et al. reported improved risk discrimination when adding sarcopenia to standard models in elderly patients ($\geq$ 70 years) [20], we extended this concept by evaluating continuous TPMT/H alongside ascites burden, using MELD-Na as a consistent baseline reference. Our nested model comparisons explicitly quantify the incremental contribution of each component individually and in combination, with the temporal validation cohort providing compelling evidence for their joint incorporation. Furthermore, comparisons with the Freiburg index of post-TIPS survival (FIPS) highlight why prognostic performance must be interpreted within specific clinical populations and temporal contexts. Although FIPS was specifically developed for post-TIPS survival [21] and demonstrated superior performance in a Chinese cohort [22], Chapin et al. observed declining performance in a contemporary North American cohort [23], and other recent validation work similarly emphasizes the necessity of cross-setting evaluation [24]. In our study, while FIPS achieved the highest 6-month training C-index, MELD-NSA consistently demonstrated superior discrimination in the temporal validation cohort among all primary models evaluated. Because all models were compared within a unified Cox proportional hazards framework, the paired nested comparison relative to MELD-Na provides direct evidence supporting the added prognostic value of TPMT/H and ascites over existing tools. Collectively, these results demonstrate that combining laboratory-based disease severity with quantitative muscle metrics and ascites burden provides a more comprehensive and robust risk assessment after TIPS.

Muscle assessment using TPMT/H complements laboratory measures of liver disease severity by providing a measure of muscle mass. Protein–energy malnutrition, hypermetabolism, and systemic inflammation provide plausible mechanistic links between progressive muscle depletion and adverse outcomes in cirrhosis [25, 26]. Although muscle abnormalities have been repeatedly associated with

post-TIPS complications and mortality [10, 27–31], a recent meta-analysis noted a stronger association with overt hepatic encephalopathy than with survival [32]—underscoring the necessity of evaluating muscle metrics within specific clinical decision-making contexts.

Ascites provides a distinct, complementary clinical dimension by serving as a direct marker of severe portal hypertensive decompensation [3]. Recent studies have linked ascitic decompensation and pre-TIPS paracentesis burden to post-procedural disease trajectory and long-term survival [33–35]. Integrating clinically significant ascites and continuous TPMT/H with MELD-Na bridges standard biochemical parameters, portal hypertensive status, and cross-sectional body composition. This multidimensional synthesis enables nuanced risk discrimination among patients with comparable laboratory-defined MELD-Na scores who otherwise exhibit marked phenotypic heterogeneity.

The temporal analysis highlights critical considerations for future model refinement. The temporal validation cohort exhibited marked shifts in liver disease severity, serum albumin, muscle quantity, and stent selection, presenting a changing clinical landscape in which to rigorously evaluate the fixed prediction model. Across all seven models evaluated, a systematic underprediction of 24-month mortality was observed (O:E ratios: 1.18–1.37)—a shared pattern indicative of calibration drift secondary to temporal population shifts. Crucially, MELD-NSA preserved its discrimination capacity, and its full-follow-up calibration slope (0.93; 95% CI 0.54–1.31) suggests that updating the baseline hazard may be an effective strategy to restore absolute risk calibration. These observations align with established guidance on prediction modeling, which emphasizes the necessity of model reassessment and updating when applied across changing patient populations [36].

From a clinical perspective, incorporating TPMT/H and ascites into risk assessment is highly feasible and directly aligns with current practice guidelines. TPMT/H can be routinely measured on pre-TIPS abdominal CT scans without incurring additional imaging burden or radiation exposure, while ascites severity is universally evaluated during routine workup. This approach strongly echoes guidance from the American Association for the Study of Liver Diseases (AASLD) and the European Association for the Study of the Liver (EASL), which advocates integrating sarcopenia assessment via clinically indicated imaging alongside comprehensive nutritional evaluation into cirrhosis management and TIPS candidate selection [12, 37]. The distinct risk-group discrimination and potential net clinical benefit observed in our temporal validation cohort support further prospective studies to evaluate the clinical impact of MELD-NSA stratification on optimizing targeted nutritional interventions and informing personalized post-TIPS surveillance strategies.

This study has several limitations. First, the retrospective, single-center design and the exclusion of patients with missing covariates or early loss to follow-up may introduce selection bias and residual confounding. Second, TPMT/H assesses cross-sectional muscle quantity only; data on muscle strength, physical performance, and longitudinal trajectory were not available [9, 38]. Third, the calibration and net benefit of comparator models reflect Cox proportional hazards models refitted using linear predictors of established scores in the training cohort. Finally, prospective multicenter studies with standardized

muscle and ascites protocols are needed to validate model recalibration and quantify the real-world clinical impact of risk-guided management.

Conclusions

Concurrently integrating continuous TPMT/H and clinically significant ascites into MELD-Na markedly improved 24-month prognostic discrimination in a temporally distinct patient cohort. These findings support combining quantitative muscle metrics and portal hypertensive status with traditional biochemical parameters for post-TIPS risk assessment. Prospective multicenter studies evaluating pre-specified clinical pathways are needed to translate this predictive gain into improved patient outcomes.

Abbreviations

AASLD
American Association for the Study of Liver Diseases
ALB
albumin
ALT
alanine aminotransferase
APTT
activated partial thromboplastin time
AST
aspartate aminotransferase
AUROC
area under the receiver operating characteristic curve
CI
confidence interval
C-index
concordance index
Cr
creatinine
CT
computed tomography
DCA
decision curve analysis
EASL
European Association for the Study of the Liver.

Declarations

Ethics approval and consent to participate

This retrospective cohort study was conducted in accordance with the Declaration of Helsinki. The study protocol was approved by the Institutional Review Board of the First Affiliated Hospital of the University of Science and Technology of China (USTC) (approval No. 2026-RE-138; approval date 26 March 2026). The Board waived the requirement for written informed consent to participate because of the retrospective design and use of anonymized clinical data.

Consent for publication

Not applicable. This manuscript contains no identifiable individual participant information.

Availability of data and materials

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request (weifulv@ustc.edu.cn), subject to requirements for protecting participant privacy.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

WFL and MY conceived and designed the study. MY, SZZ, CZZ and DLC collected the data. MY, SZZ and DLC interpreted the data. MY drafted the manuscript, and WFL critically revised it. All authors read and approved the final manuscript.

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References

1. Bureau C, Thabut D, Oberti F, Dharancy S, Carbonell N, Bouvier A, et al. Transjugular Intrahepatic Portosystemic Shunts With Covered Stents Increase Transplant-Free Survival of Patients With Cirrhosis and Recurrent Ascites. Gastroenterology. 2017;152(1):157–63. 10.1053/j.gastro.2016.09.016.
2. Larrue H, D'Amico G, Olivas P, Lv Y, Bucsics T, Rudler M, et al. TIPS prevents further decompensation and improves survival in patients with cirrhosis and portal hypertension in an individual patient data meta-analysis. J Hepatol. 2023;79(3):692–703. 10.1016/j.jhep.2023.04.028.

3. de Franchis R, Bosch J, Garcia-Tsao G, Reiberger T, Ripoll C, Baveno VII. Faculty. Baveno VII - Renewing consensus in portal hypertension. J Hepatol. 2022;76(4):959–74. 10.1016/j.jhep.2021.12.022.
4. 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(4):864–71. 10.1053/he.2000.5852.
5. Wiesner R, Edwards E, Freeman R, Harper A, Kim R, Kamath P, et al. Model for end-stage liver disease (MELD) and allocation of donor livers. Gastroenterology. 2003;124(1):91–6. 10.1053/gast.2003.50016.
6. Kim WR, Biggins SW, Kremers WK, Wiesner RH, Kamath PS, Benson JT, et al. Hyponatremia and mortality among patients on the liver-transplant waiting list. N Engl J Med. 2008;359(10):1018–26. 10.1056/nejmoa0801209.
7. Biggins SW, Kim WR, Terrault NA, Saab S, Balan V, Schiano T, et al. Evidence-based incorporation of serum sodium concentration into MELD. Gastroenterology. 2006;130(6):1652–60. 10.1053/j.gastro.2006.02.010.
8. Krishnan A, Woreta TA, Vaidya D, Liu Y, Hamilton JP, Hong K, et al. MELD or MELD-Na as a Predictive Model for Mortality Following Transjugular Intrahepatic Portosystemic Shunt Placement. J Clin Transl Hepatol. 2023;11(1):38–44. 10.14218/jcth.2021.00513.
9. 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;303(3):711–9. 10.1148/radiol.211172.
10. Vanderschueren E, Meersseman P, Wilmer A, Vandecaveye V, Dubois E, Van Eldere A, et al. Sarcopenia in patients receiving TIPS is independently associated with increased risk of complications and mortality. Dig Liver Dis. 2025;57(2):549–57. 10.1016/j.dld.2024.10.013.
11. Xiong B, Yang C, Zhu X, Zhou C, Chen S, Zhang Z, et al. The Added Value of Sarcopenia on Existing Risk Scores to Predict Mortality after TIPS Placement: A Multicenter Study. Acad Radiol. 2023;30(Suppl 1):S246–56. 10.1016/j.acra.2023.03.011.
12. European Association for the Study of the Liver. EASL Clinical Practice Guidelines on TIPS. J Hepatol. 2025;83(1):177–210. 10.1016/j.jhep.2025.01.029.
13. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. PLoS Med. 2007;4(10):e296. 10.1371/journal.pmed.0040296.
14. Collins GS, Moons KGM, Dhiman P, Riley RD, Beam AL, Van Calster B, et al. TRIPOD + AI statement: updated guidance for reporting clinical prediction models that use regression or machine learning methods. BMJ. 2024;385:e078378. 10.1136/bmj-2023-078378.
15. Harrell FE Jr., Califf RM, Pryor DB, Lee KL, Rosati RA. Evaluating the yield of medical tests. JAMA. 1982;247(18):2543–6. 10.1001/jama.1982.03320430047030.

16. Harrell FE Jr., Lee KL, Mark DB. Multivariable prognostic models: issues in developing models, evaluating assumptions and adequacy, and measuring and reducing errors. Stat Med. 1996;15(4):361–87. 10.1002/(sici)1097-0258(19960229)15:4%3C361::aid-sim168%3E3.0.co;2-4.
17. Blanche P, Dartigues JF, Jacqmin-Gadda H. Estimating and comparing time-dependent areas under receiver operating characteristic curves for censored event times with competing risks. Stat Med. 2013;32(30):5381–97. 10.1002/sim.5958.
18. Graf E, Schmoor C, Sauerbrei W, Schumacher M. Assessment and comparison of prognostic classification schemes for survival data. Stat Med. 1999;18(17–18):2529–45. 10.1002/(sici)1097-0258(19990915/30)18:17/18%3C2529::aid-sim274%3E3.0.co;2-5.
19. Vickers AJ, Cronin AM, Elkin EB, Gonen M. Extensions to decision curve analysis, a novel method for evaluating diagnostic tests, prediction models and molecular markers. BMC Med Inf Decis Mak. 2008;8:53. 10.1186/1472-6947-8-53.
20. Saltini D, Nardelli S, Miraglia R, Roccarina D, Gioia S, Banchelli F, et al. Sarcopenia Predicts Mortality and Hepatic Encephalopathy After TIPS in Older Adults With Cirrhosis and Improves Prognostic Scores. Liver Int. 2026;46(7):e70733. 10.1111/liv.70733.
21. 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(6):1362–72. 10.1016/j.jhep.2021.01.023.
22. 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;219(2):255–67. 10.2214/ajr.21.27301.
23. Chapin SE, Goldberg DS, Kaplan DE, Mahmud N. External Validation of the FIPS Score for Post-TIPS Mortality in a National Veterans Affairs Cohort. Dig Dis Sci. 2022;67(9):4581–9. 10.1007/s10620-021-07307-5.
24. Walia N, Nilsen O, Cheung E, Abdelmalak J, Spurio J, Fernandez M, et al. Prognostic scores for early mortality following transjugular intrahepatic portosystemic shunt insertion: external validation in a contemporary Australian cohort. Intern Med J. 2026;56(4):552–62. 10.1111/imj.70373.
25. Dasarathy S, Merli M. Sarcopenia from mechanism to diagnosis and treatment in liver disease. J Hepatol. 2016;65(6):1232–44. 10.1016/j.jhep.2016.07.040.
26. Tandon P, Montano-Loza AJ, Lai JC, Dasarathy S, Merli M. Sarcopenia and frailty in decompensated cirrhosis. J Hepatol. 2021;75(Suppl 1):S147–62. 10.1016/j.jhep.2021.01.025.
27. Nardelli S, Lattanzi B, Torrisi S, Greco F, Farcomeni A, Gioia S, et al. Sarcopenia Is Risk Factor for Development of Hepatic Encephalopathy After Transjugular Intrahepatic Portosystemic Shunt Placement. Clin Gastroenterol Hepatol. 2017;15(6):934–6. 10.1016/j.cgh.2016.10.028.
28. Ahmed Z, Badal J, Gangwani MK, Nawaz A, Badal B, Arif SF, et al. Sarcopenia is a risk factor for post-transjugular intrahepatic portosystemic shunt hepatic encephalopathy and mortality: A systematic review and meta-analysis. Indian J Gastroenterol. 2024;43(4):748–59. 10.1007/s12664-023-01465-2.

29. Mukund A, Bhardwaj V, Jindal A, Patidar Y, Sarin SK. Transjugular Intrahepatic Portosystemic Shunt Related Hepatic Encephalopathy in Cirrhotics With Refractory Ascites: Incidence and Correlation With TIPS Stent Diameter and Pre-TIPS Sarcopenia. J Clin Exp Hepatol. 2026;16(1):103125. 10.1016/j.jceh.2025.103125.
30. Stoffel E, Hwang SY, Qian X, Geller B, Morelli G, Zhang W. Sarcopenia is an independent risk factor for short-term mortality in patients undergoing transjugular intrahepatic portosystemic shunt. Eur J Gastroenterol Hepatol. 2024;36(8):1010–5. 10.1097/meg.0000000000002790.
31. Delgado MG, Mertineit N, Bosch J, Baumgartner I, Berzigotti A. Combination of Model for End-Stage Liver Disease (MELD) and Sarcopenia predicts mortality after transjugular intrahepatic portosystemic shunt (TIPS). Dig Liver Dis. 2024;56(9):1544–50. 10.1016/j.dld.2024.03.003.
32. de Brito Nunes M, Delgado MG, Bosch J, Berzigotti A. Outcomes after TIPS in patients with cirrhosis and sarcopenia: A systematic review and meta-analysis. JHEP Rep. 2026;8(2):101699. 10.1016/j.jhepr.2025.101699.
33. Balcar L, Tonon M, Semmler G, Calvino V, Hartl L, Incicco S, et al. Risk of further decompensation/mortality in patients with cirrhosis and ascites as the first single decompensation event. JHEP Rep. 2022;4(8):100513. 10.1016/j.jhepr.2022.100513.
34. Piecha F, Radunski UK, Ozga AK, Steins D, Drolz A, Horvatits T, et al. Ascites control by TIPS is more successful in patients with a lower paracentesis frequency and is associated with improved survival. JHEP Rep. 2019;1(2):90–8. 10.1016/j.jhepr.2019.04.001.
35. Balcar L, Tonon M, Valls J, Calvino V, Simonis L, Embacher J, et al. Risk of portal hypertensive complications preventable by TIPS in patients with ascites. JHEP Rep. 2025;7(8):101469. 10.1016/j.jhepr.2025.101469.
36. Van Calster B, McLernon DJ, van Smeden M, Wynants L, Steyerberg EW. Calibration: the Achilles heel of predictive analytics. BMC Med. 2019;17(1):230. 10.1186/s12916-019-1466-7.
37. Lai JC, Tandon P, Bernal W, Tapper EB, Ekong U, Dasarathy S, et al. Malnutrition, Frailty, and Sarcopenia in Patients With Cirrhosis: 2021 Practice Guidance by the American Association for the Study of Liver Diseases. Hepatology. 2021;74(3):1611–44. 10.1002/hep.32049.
38. Cruz-Jentoft AJ, Bahat G, Bauer J, Boirie Y, Bruyère O, Cederholm T, et al. Sarcopenia: revised European consensus on definition and diagnosis. Age Ageing. 2019;48(1):16–31. 10.1093/ageing/afy169.

Figures

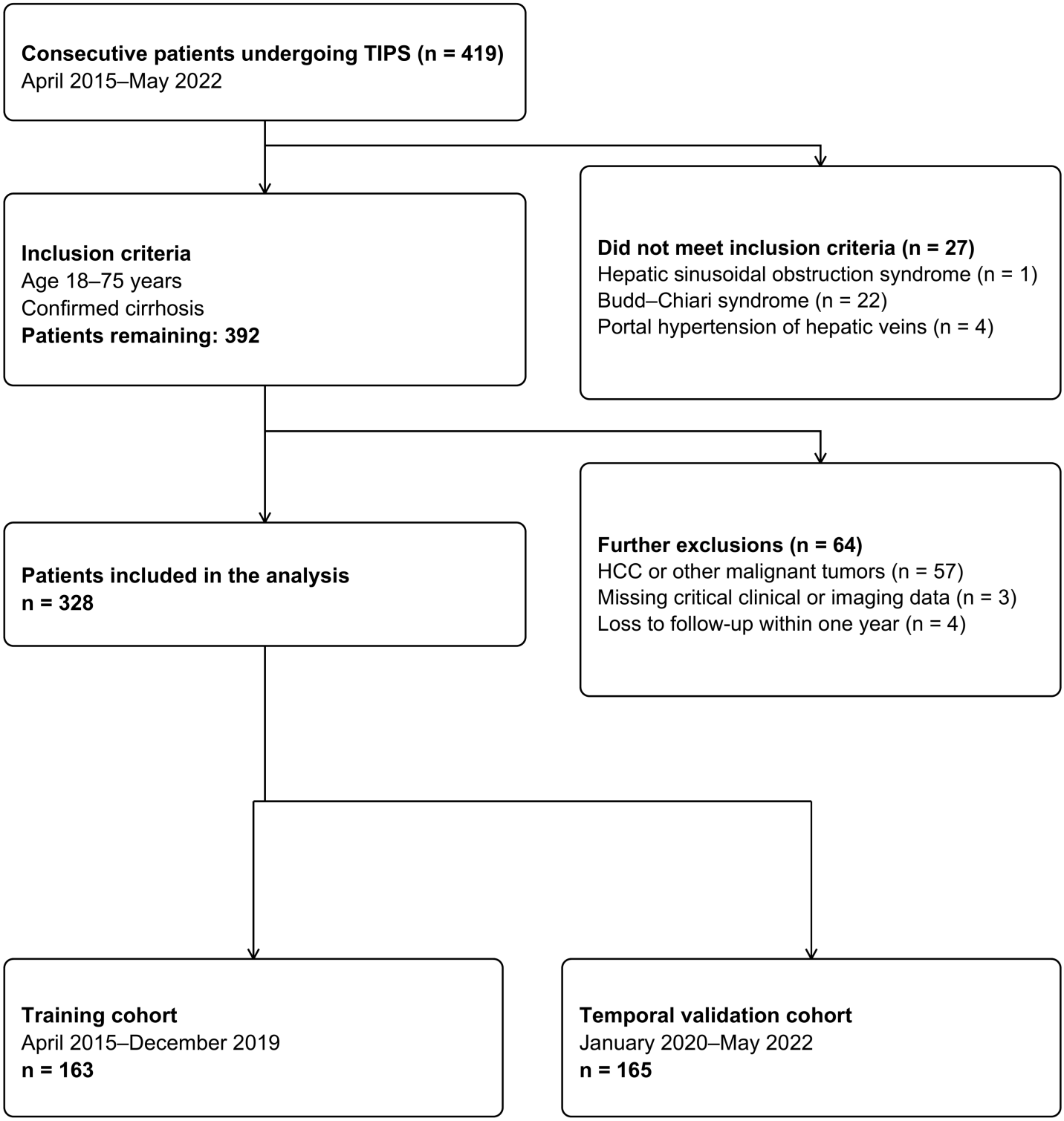


Figure 1

Patient selection and cohort allocation. TIPS, transjugular intrahepatic portosystemic shunt; HCC, hepatocellular carcinoma.

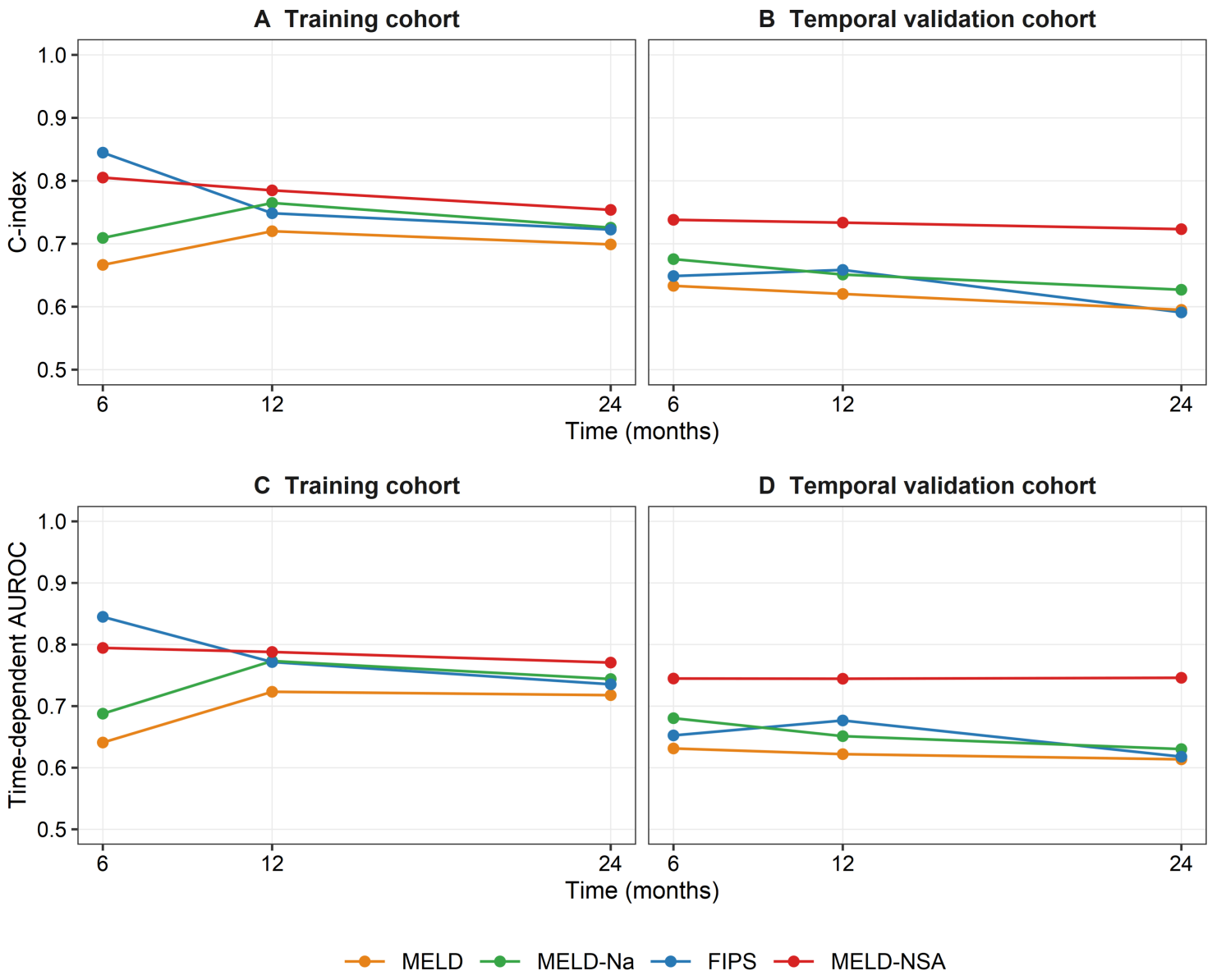


Figure 2

Discrimination at 6, 12, and 24 months. Panels A and B show Harrell's C-index in the training and temporal validation cohorts, respectively; panels C and D show time-dependent AUROC in the corresponding cohorts. C-index, concordance index; AUROC, area under the receiver operating characteristic curve; MELD, Model for End-Stage Liver Disease; MELD-Na, MELD incorporating serum sodium; FIPS, Freiburg index of post-TIPS survival; MELD-NSA, model combining MELD-Na, TPMT/H, and ascites; TPMT/H, transverse psoas muscle thickness normalized by height; TIPS, transjugular intrahepatic portosystemic shunt.

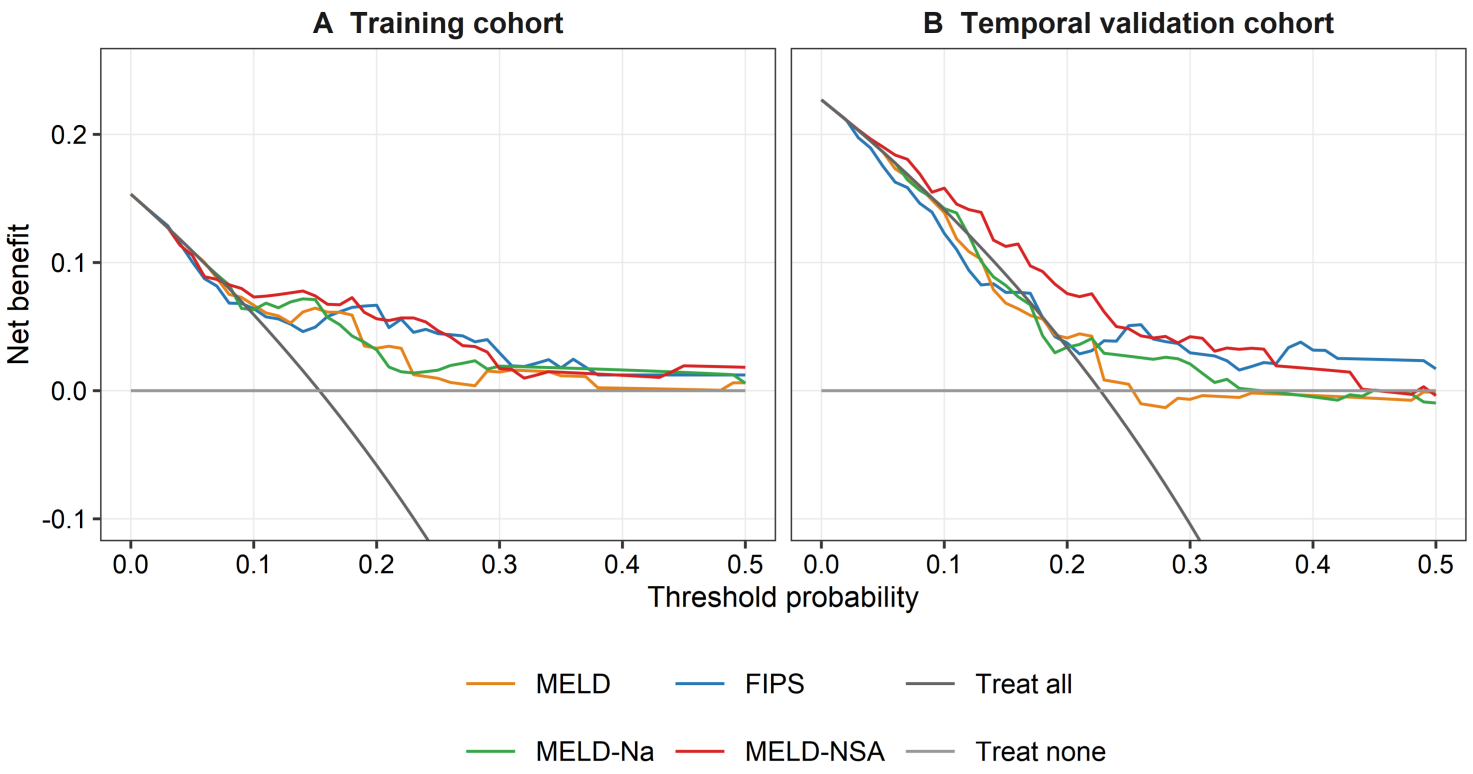


Figure 3

Decision curve analysis at 24 months. (A) Training cohort; (B) temporal validation cohort. Curves compare the potential net benefit of the fitted models with the treat-all and treat-none strategies. Absolute risks were derived from Cox models fitted in the training cohort. MELD, Model for End-Stage Liver Disease; MELD-Na, MELD incorporating serum sodium; FIPS, Freiburg index of post-TIPS survival; MELD-NSA, model combining MELD-Na, TPMT/H, and ascites; TPMT/H, transverse psoas muscle thickness normalized by height; TIPS, transjugular intrahepatic portosystemic shunt.

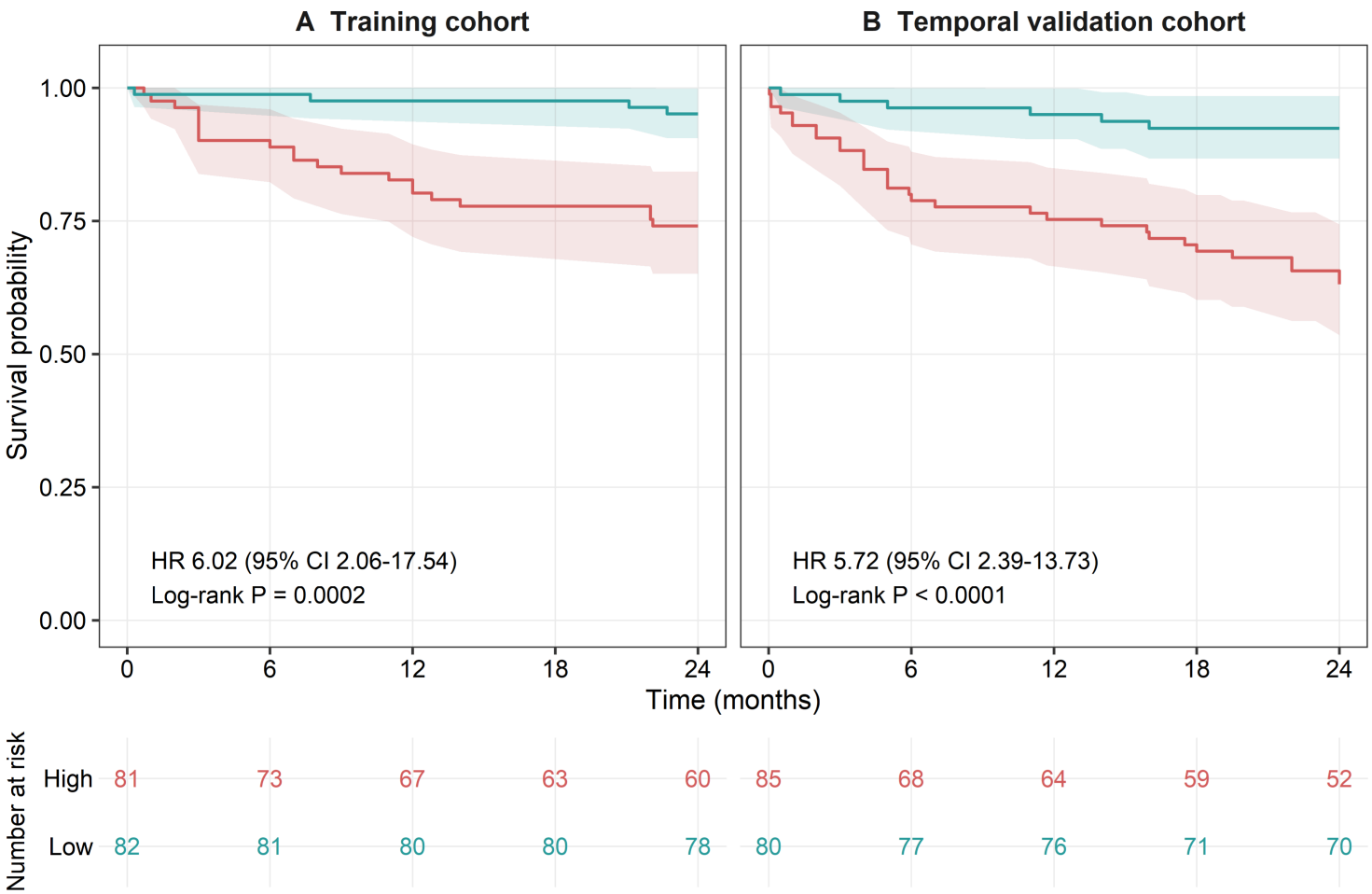


Figure 4

Risk stratification and survival through 24 months. Kaplan–Meier curves were stratified using the training median MELD-NSA linear predictor (0.404, rounded for display), with the same cutoff applied in both cohorts. High risk indicates a linear predictor above the training median; low risk indicates a value at or below the median. (A) Training cohort; (B) temporal validation cohort. Shaded areas indicate 95% CIs. Numbers at risk are shown below the curves. HRs and log-rank *P*values use follow-up truncated at 24 months. HR, hazard ratio; CI, confidence interval; MELD-NSA, model combining MELD-Na, TPMT/H, and ascites; MELD-Na, Model for End-Stage Liver Disease incorporating serum sodium; TPMT/H, transverse psoas muscle thickness normalized by height.

Supplementary Files

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