

Preprocedural estimated glomerular filtration rate and all-cause mortality after TIPS in cirrhosis: a single-center retrospective cohort study

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Abstract

Background:

Renal dysfunction is increasingly recognized as an important determinant of prognosis in patients with cirrhosis undergoing transjugular intrahepatic portosystemic shunt (TIPS). However, the prognostic value of preprocedural estimated glomerular filtration rate (eGFR) in this setting remains insufficiently defined. This study evaluated the association between preprocedural eGFR and all-cause mortality after covered-stent TIPS.

Methods:

This single-center retrospective cohort study included patients with cirrhosis who underwent first-time covered-stent TIPS between January 2015 and January 2024. Preprocedural eGFR was calculated using the CKD-EPI 2021 creatinine-based equation and categorized as ≥ 90 , 60–89, or < 60 mL/min/1.73 m². Survival was assessed using Kaplan–Meier analysis and Cox proportional hazards models. Restricted cubic spline analysis was used to examine the dose–response relationship between eGFR and mortality. Sensitivity analyses were performed by additionally adjusting for the MELD score and by modeling eGFR as a continuous variable.

Results:

Among 618 patients, 146 died during a median follow-up of 36.5 months. Compared with eGFR ≥ 90 mL/min/1.73 m², eGFR < 60 mL/min/1.73 m² was associated with higher all-cause mortality after adjustment for age, serum sodium, and Child–Pugh score (HR = 2.21, 95% CI 1.39–3.53, $P < 0.001$), whereas eGFR 60–89 mL/min/1.73 m² was not significantly associated with mortality after adjustment. After additional adjustment for MELD score, the association for eGFR < 60 mL/min/1.73 m² was attenuated (HR = 1.63, 95% CI 0.95–2.80, $P = 0.078$). When modeled continuously, each 1 mL/min/1.73 m² increase in eGFR was associated with lower mortality risk (HR = 0.989, 95% CI 0.981–0.996, $P = 0.004$). Lower eGFR was also associated with higher proportions of hepatic encephalopathy and worsening ascites.

Conclusions:

Preprocedural eGFR < 60 mL/min/1.73 m² was associated with increased all-cause mortality after covered-stent TIPS in the primary model, although this association was attenuated after MELD adjustment. Preprocedural eGFR may serve as a practical reference marker for comprehensive pre-TIPS risk assessment, but should not be interpreted as a standalone prognostic criterion. Multicenter prospective validation is warranted.

Introduction

Transjugular intrahepatic portosystemic shunt (TIPS) effectively reduces portal venous pressure by creating a low-resistance channel between the hepatic vein and the portal vein, and has become an important therapeutic approach for portal hypertension-related complications, including refractory ascites, ruptured esophagogastric variceal bleeding, hepatic hydrothorax, and hepatorenal syndrome[1–3]. Although TIPS has demonstrated clear efficacy in alleviating symptoms related to portal hypertension, postoperative outcomes vary substantially, indicating the need to further optimize preprocedural risk stratification strategies[4, 5].

Traditional preprocedural risk assessment for TIPS has mainly relied on liver function scoring systems, such as the Child–Pugh score and the Model for End-Stage Liver Disease (MELD) score[6–8]. In recent years, the role of renal function in prognostic assessment among patients with cirrhosis has received increasing attention, particularly because acute kidney injury (AKI) is common in this population and is closely associated with adverse outcomes[9, 10]. Bettinger et al. proposed the Freiburg Index of Post-TIPS Survival (FIPS score), which incorporates four variables—age, serum creatinine, total bilirubin, and albumin—and demonstrated superior predictive performance compared with the traditional MELD and Child–Pugh scores in a German cohort[11]. External validation in a Chinese cohort also suggested that prognostic models incorporating renal function information may have potential advantages in post-TIPS outcome prediction[12].

Previous studies have commonly used serum creatinine as an indicator of renal function; however, serum creatinine is susceptible to factors such as muscle mass, nutritional status, and abnormal fluid distribution, which may lead to underestimation of the degree of renal dysfunction[13, 14]. In contrast, estimated glomerular filtration rate (eGFR) provides a more comprehensive reflection of glomerular filtration function[15, 16], but its value in preprocedural risk stratification for TIPS has not been fully validated. In addition, ascites, as an important manifestation of hepatic decompensation, is closely associated with renal dysfunction[17]. However, evidence remains insufficient as to whether the relationship between preprocedural renal function and postoperative prognosis is independent of ascites status.

Therefore, based on a TIPS cohort, the present study calculated preprocedural eGFR using the CKD-EPI 2021 equation[15], analyzed its association with the risk of all-cause mortality after TIPS, compared the proportions of major postoperative decompensation events across different eGFR groups, and explored whether this association was modified by different clinical and laboratory subgroups, including age, sex, Child–Pugh class, MELD score, albumin, serum sodium, and ascites status. This study aimed to provide evidence to inform clinical risk assessment.

Methods

Study design and reporting

This was a single-center retrospective cohort study. The study is reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement. All eligible patients with cirrhosis who underwent first-time covered-stent TIPS during the study period were screened according to predefined inclusion and exclusion criteria.

Patients

This was a single-center retrospective cohort study including patients with cirrhosis who underwent TIPS for the first time at the First Affiliated Hospital of the University of Science and Technology of China between January 1, 2015, and January 1, 2024. Cirrhosis was diagnosed according to clinical, imaging, laboratory, or histological criteria. Renal function was assessed using the serum creatinine value measured within 1 week before TIPS and closest to the date of the procedure. eGFR was calculated using the serum creatinine-based CKD-EPI 2021 equation[15].

To minimize the influence of acute factors on renal function assessment, preference was given to patients who had two consecutive preprocedural serum creatinine measurements at least 48 hours apart, with a change of $< 20\%$. For patients with only one preprocedural creatinine measurement, events within 7 days before TIPS that could clearly cause acute creatinine fluctuations and fail to reflect stable renal function were excluded, including large-volume paracentesis, use of nephrotoxic drugs, severe infection, or hemodynamic instability. Patients undergoing TIPS for recent gastrointestinal bleeding were not excluded if their serum creatinine levels met the above stability criteria.

Among the final 618 included patients, 502 patients (81.2%) met the stability criterion of $< 20\%$ change between two consecutive preprocedural creatinine measurements, while the remaining 116 patients had only a single measurement but showed no definite acute kidney injury events after review. According to commonly used clinical eGFR thresholds and the clinical significance of staging in the 2024 KDIGO guidelines[18], patients were classified into three combined groups: normal renal function group (eGFR ≥ 90 mL/min/1.73 m², n = 491), mildly impaired renal function group (eGFR 60–89 mL/min/1.73 m², n = 79), and significantly impaired renal function group (eGFR < 60 mL/min/1.73 m², n = 48). The study protocol was approved by the Ethics Committee of the First Affiliated Hospital of the University of Science and Technology of China (Ethics No. 2026-RE-155), and the study was conducted in accordance with the ethical principles of the Declaration of Helsinki.

The inclusion criteria were as follows: (1) age ≥ 18 years; (2) diagnosis of cirrhosis confirmed by clinical, imaging, or histological criteria; (3) first-time TIPS implantation with a covered stent; (4) serum creatinine measured within 1 week prior to TIPS and meeting the aforementioned stability criteria; (5) availability of complete baseline clinical data; and (6) at least one valid follow-up record after TIPS.

The exclusion criteria were as follows: (1) receipt of renal replacement therapy (hemodialysis or peritoneal dialysis) prior to TIPS; (2) history of liver or kidney transplantation; (3) uncontrolled cardiac or pulmonary failure; (4) technical failure during TIPS, defined as failure to successfully establish the shunt

tract; and (5) substantial missing clinical or follow-up data (missing key variables such as survival status or time of death > 20%).

Data Collection and Follow-up

Clinical, laboratory, and TIPS-related variables were extracted from the electronic medical record system:

(1) Demographic and clinical characteristics: age, sex, etiology of cirrhosis (viral, alcoholic, autoimmune/cholestatic, or other), comorbidities (diabetes mellitus and hypertension), and severity of ascites (none, mild, or moderate-to-severe, based on ultrasonographic findings and physical examination).

(2) Laboratory parameters:

☒ Hematological indices: white blood cell count (WBC), neutrophil percentage (NEUT%), neutrophil-to-lymphocyte ratio (NLR), hemoglobin (HGB), and platelet count (PLT);

☒ Liver function tests: alanine aminotransferase (ALT), aspartate aminotransferase (AST), total bilirubin (TBIL), albumin (ALB), prothrombin time (PT), and international normalized ratio (INR);

☒ Renal function parameter: preprocedural eGFR;

☒ Liver disease severity scores: Child–Pugh score and the Model for End-Stage Liver Disease (MELD) score. The MELD score was calculated using serum total bilirubin, INR, and serum creatinine according to the following formula:

$$\text{MELD} = 3.78 \times \ln[\text{total bilirubin (mg/dL)}] + 11.20 \times \ln[\text{INR}] + 9.57 \times \ln[\text{serum creatinine (mg/dL)}] + 6.43.$$

Laboratory values were converted to the required units before calculation, and values less than 1.0 were set to 1.0 before logarithmic transformation[8].

When available, TIPS-related procedural variables were extracted from the electronic medical record system and interventional radiology records, including the indication for TIPS, emergency or elective procedure status, stent diameter, concomitant variceal or collateral embolization, and pre- and post-TIPS portosystemic pressure gradient. However, because TIPS indication and several procedural variables were incompletely and inconsistently documented during the retrospective study period, these variables were not included in the primary multivariable model. The primary analysis therefore focused on baseline clinical and laboratory variables with adequate completeness and clinical relevance. The potential influence of unmeasured or incompletely measured TIPS-related factors was considered in the interpretation of the findings.

Patients entered follow-up from the date of the TIPS procedure. Follow-up was conducted regularly through telephone interviews, outpatient visit records, or the hospital information system. Patients were

followed up at 1 and 3 months after the procedure, and every 6–12 months thereafter. Follow-up assessments included liver and renal function, as well as major decompensation events, including hepatic encephalopathy, worsening ascites, and gastrointestinal rebleeding.

The primary outcome was all-cause mortality. Secondary outcomes included postprocedural hepatic encephalopathy, worsening ascites, and gastrointestinal rebleeding. Hepatic encephalopathy was diagnosed according to the West Haven criteria. Worsening ascites was defined as an increase in ascites volume after TIPS compared with the preprocedural status, the need for an increased dose of diuretics, or the need for therapeutic paracentesis. Gastrointestinal rebleeding was defined as recurrent hematemesis or melena after TIPS, or portal hypertension-related bleeding confirmed by endoscopy or imaging.

Surviving patients were censored at the date of their last follow-up. Because the proportion of patients undergoing liver transplantation after TIPS at our center was very low (< 3%), and no patients were lost to follow-up due to liver transplantation, liver transplantation was not treated as a competing event in a competing-risk model analysis.

Statistical Analysis

Data analyses were performed using R software version 4.4.3. Continuous variables were expressed as mean $\pm$ standard deviation or median with interquartile range, according to their distribution, and were compared using one-way analysis of variance or the Kruskal–Wallis rank-sum test, as appropriate. Categorical variables were presented as counts and percentages and were compared using the χ^2 test or Fisher's exact test.

Survival curves were generated using the Kaplan–Meier method, and survival differences among eGFR groups were compared using the log-rank test. Univariable Cox proportional hazards models were used to assess associations between baseline variables and all-cause mortality after TIPS. Variables with $P < 0.10$ in univariable analysis and clinically relevant covariates were considered as candidates for multivariable analysis.

Because the MELD score includes serum creatinine and eGFR is also derived from serum creatinine, these two variables contain structurally overlapping information. Therefore, the primary multivariable model was prespecified to include eGFR group, age, serum sodium, and Child–Pugh score, while excluding MELD score to reduce overadjustment related to creatinine-based information overlap. Two sensitivity analyses were subsequently performed. First, MELD score was additionally included in the primary model. Second, eGFR was modeled as a continuous variable to evaluate whether the association depended on the selected categorization thresholds.

The proportional hazards assumption was assessed using Schoenfeld residuals. Multicollinearity was evaluated using variance inflation factors. Restricted cubic spline analysis was used to examine the

dose–response relationship between preprocedural eGFR and all-cause mortality. Restricted cubic splines were fitted with four knots placed at the 5th, 35th, 65th, and 95th percentiles of eGFR.

For subgroup analyses, eGFR was dichotomized as < 60 versus ≥ 60 mL/min/1.73 m² to align with clinically relevant renal function thresholds. Stratified analyses were performed according to age, sex, Child–Pugh class, MELD score, ascites status, serum sodium, and albumin level. Interaction terms were tested to assess whether the association between eGFR category and mortality differed across subgroups. Because of the limited sample size in the eGFR < 60 mL/min/1.73 m² group and the limited number of events in some strata, subgroup analyses were considered exploratory.

Postprocedural hepatic encephalopathy, worsening ascites, and gastrointestinal rebleeding were analyzed as secondary outcomes and descriptively compared among eGFR groups. Because these secondary outcomes were not analyzed using time-to-event models, results were reported as proportions rather than risks. Variables with $< 5\%$ missing data were analyzed using complete-case analysis. All tests were two-sided, and $P < 0.05$ was considered statistically significant.

Results

Population characteristics

A total of 618 patients with cirrhosis were included in this study, of whom 491 (79.4%) had preprocedural eGFR ≥ 90 mL/min/1.73 m², 79 (12.8%) had eGFR 60–89 mL/min/1.73 m², and 48 (7.8%) had eGFR < 60 mL/min/1.73 m². Patients with lower preprocedural eGFR were older and had higher proportions of diabetes mellitus, hypertension, and moderate-to-severe ascites. They also had higher MELD scores and lower albumin and serum sodium levels. No statistically significant differences were observed among the three groups in sex distribution, cirrhosis etiology, or Child–Pugh class (Table 1).

Table 1
Baseline Characteristics of the Study Population According to Preprocedural eGFR Groups

Variable	Overall (N = 618)	eGFR ≥ 90 (n = 491)	eGFR 60–89 (n = 79)	eGFR < 60 (n = 48)	P value
Age (years)	55.0 (48.0–63.0)	53.0 (47.5–60.5)	60.0 (54.0–69.5)	60.0 (50.0–68.3)	< 0.001
Sex					0.568
Male, n (%)	427 (69.1)	343 (69.9)	54 (68.4)	30 (62.5)	
Female, n (%)	191 (30.9)	148 (30.1)	25 (31.6)	18 (37.5)	
Etiology of cirrhosis, n (%)					0.088
Viral	369 (59.7)	305 (62.1)	40 (50.6)	24 (50.0)	
Alcoholic	45 (7.3)	36 (7.3)	7 (8.9)	2 (4.2)	
Autoimmune/cholestatic	30 (4.9)	19 (3.9)	7 (8.9)	4 (8.3)	
Other/cryptogenic	174 (28.2)	131 (26.7)	25 (31.6)	18 (37.5)	
Comorbidities, n (%)					
Diabetes mellitus	95 (15.4)	66 (13.4)	10 (12.7)	19 (39.6)	< 0.001
Hypertension	63 (10.2)	35 (7.1)	21 (26.6)	7 (14.6)	< 0.001
Clinical features					
None/mild ascites	429 (69.4)	354 (72.1)	51 (64.6)	24 (50.0)	
Moderate/severe ascites	189 (30.6)	137 (27.9)	28 (35.4)	24 (50.0)	0.004
Child–Pugh class, n (%)					0.101
A	4 (0.6)	3 (0.6)	1 (1.3)	0 (0.0)	
B	353 (57.1)	291 (59.3)	42 (53.2)	17 (41.7)	
C	261 (42.2)	197 (40.1)	36 (45.6)	31 (58.3)	
Laboratory parameters					
MELD score	9.9 (7.8–12.6)	9.7 (7.7–11.9)	10.3 (7.6–13.1)	16.0 (13.4–20.4)	< 0.001
Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; INR, international normalized ratio; MELD, model for end-stage liver disease. Continuous variables are presented as median (interquartile range), i.e., M (Q1, Q3), and categorical variables are expressed as number (%). Group comparisons were performed using the Kruskal–Wallis rank-sum test or the χ^2 test, as appropriate.					

Variable	Overall (N = 618)	eGFR ≥ 90 (n = 491)	eGFR 60–89 (n = 79)	eGFR < 60 (n = 48)	P value
White blood cell (×10 ⁹ /L)	3.6 (2.4–5.6)	3.5 (2.3–5.3)	4.3 (2.9–6.6)	4.3 (2.5–9.0)	0.004
Hemoglobin (g/L)	80.5 (65.0–100.8)	80.0 (65.0–100.0)	82.0 (65.0–102.5)	80.5 (65.6–108.0)	0.758
Platelet count (×10 ⁹ /L)	69.0 (47.0–114.8)	67.0 (46.0–111.0)	75.6 (59.5–107.5)	73.5 (46.8–130.2)	0.437
ALT (U/L)	22.0 (15.0–34.0)	21.0 (15.0–33.0)	21.0 (14.5–32.5)	28.5 (18.5–51.2)	0.075
AST (U/L)	30.1 (21.5–44.0)	29.0 (21.0–42.0)	32.0 (24.0–45.0)	41.0 (30.0–77.0)	0.002
Total bilirubin (μmol/L)	21.0 (13.7–31.5)	20.7 (13.8–31.2)	21.1 (13.7–31.5)	21.4 (13.0–37.1)	0.986
Albumin (g/L)	32.6 (29.0–36.1)	32.9 (29.2–36.2)	31.9 (27.7–35.6)	31.3 (28.1–34.3)	0.040
Serum sodium (mmol/L)	139.0 (136.0–141.5)	139.0 (136.0–141.6)	138.5 (136.3–142.5)	136.1 (131.0–139.0)	< 0.001
INR	1.2 (1.1–1.4)	1.2 (1.1–1.4)	1.3 (1.1–1.4)	1.3 (1.2–1.6)	0.129
Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; INR, international normalized ratio; MELD, model for end-stage liver disease. Continuous variables are presented as median (interquartile range), i.e., M (Q1, Q3), and categorical variables are expressed as number (%). Group comparisons were performed using the Kruskal–Wallis rank-sum test or the χ^2 test, as appropriate.					

Kaplan–Meier Survival Analysis

As of the last follow-up, with a median follow-up duration of 36.5 months, 146 patients (23.6%) had died. According to preprocedural eGFR groups, the median survival time was not reached in the eGFR ≥ 90 mL/min/1.73 m² group, 52.1 months (95% CI 43.5–60.7) in the eGFR 60–89 mL/min/1.73 m² group, and 38.6 months (95% CI 28.4–48.8) in the eGFR < 60 mL/min/1.73 m² group. The survival difference among the three groups was statistically significant (log-rank $P < 0.001$). Kaplan–Meier survival analysis showed significant differences in postoperative survival rates among patients stratified by preprocedural eGFR (log-rank $P < 0.001$), with the lowest survival rate observed in the eGFR < 60 mL/min/1.73 m² group (Fig. 1).

Univariable and Multivariable Cox Regression Analyses

Univariable Cox regression analysis showed that, compared with the eGFR ≥ 90 mL/min/1.73 m² group, the eGFR 60–89 mL/min/1.73 m² group had an increased risk of mortality (HR = 1.78, 95% CI 1.14–2.79, P = 0.011), while the eGFR < 60 mL/min/1.73 m² group had a further elevated mortality risk (HR = 3.11, 95% CI 1.97–4.91, P < 0.001). In addition, age, MELD score, albumin, serum sodium, Child–Pugh score, and ascites status were also significantly associated with the risk of postoperative mortality (Table 2). After adjustment for age, serum sodium, and Child–Pugh score in the multivariable Cox regression analysis, preprocedural eGFR < 60 mL/min/1.73 m² remained associated with an increased risk of all-cause mortality after TIPS (HR = 2.21, 95% CI 1.39–3.53, P < 0.001), whereas the eGFR 60–89 mL/min/1.73 m² group did not show statistical significance after adjustment (P = 0.258). In addition, older age (HR = 1.03, 95% CI 1.01–1.05, P < 0.001) and higher Child–Pugh score (HR = 1.40, 95% CI 1.25–1.57, P < 0.001) were independently associated with higher all-cause mortality, while serum sodium was not statistically significant after multivariable adjustment (Table 3). The Schoenfeld residual test showed no clear evidence of violation of the proportional hazards assumption (global P = 0.064), and variance inflation factor analysis did not indicate substantial multicollinearity, with all values < 5.

Table 2
Univariate Cox Regression Analysis of All-Cause Mortality After TIPS

Variable	HR	95% CI	P value
Age (per 1-year increase)	1.04	1.025–1.057	< 0.001
Sex (male vs. female)	1.13	0.787–1.611	0.518
MELD score	1.06	1.043–1.079	< 0.001
White blood cell ($\times 10^9$ /L)	1.03	0.998–1.072	0.064
AST (U/L)	1.00	0.999–1.001	0.941
Albumin (g/L)	0.90	0.873–0.933	< 0.001
Serum sodium (mmol/L)	0.99	0.976–0.998	0.020
Child–Pugh score	1.32	1.185–1.468	< 0.001
Diabetes mellitus (yes vs. no)	1.26	0.817–1.937	0.297
Hypertension (yes vs. no)	0.92	0.530–1.596	0.767
Ascites (moderate/severe vs. none/mild)	1.59	1.145–2.220	0.006
eGFR group (reference: ≥ 90 mL/min/1.73 m ²)			
60–89 mL/min/1.73 m ²	1.78	1.141–2.791	0.011
<60 mL/min/1.73 m ²	3.11	1.970–4.909	< 0.001
Notes: HR, hazard ratio; CI, confidence interval; eGFR, estimated glomerular filtration rate; AST, aspartate aminotransferase.			

Table 3
Multivariable Cox Regression Analysis of All-Cause Mortality After TIPS

Variable	HR	95% CI	P value
eGFR group (reference: ≥ 90 mL/min/1.73 m ²)			
eGFR 60–89	1.31	0.82–2.09	0.258
eGFR < 60	2.21	1.39–3.53	< 0.001
Age (per 1-year increase)	1.03	1.01–1.05	< 0.001
Serum sodium (mmol/L)	0.99	0.98–1.01	0.293
Child–Pugh score	1.40	1.25–1.57	< 0.001

Sensitivity Analyses

To assess the robustness of the primary model results, two sensitivity analysis models were further constructed. Model 1 additionally included the MELD score on the basis of the primary model, whereas Model 2 incorporated eGFR as a continuous variable. The results showed that, after additional adjustment for MELD score, age, serum sodium, and Child–Pugh score, the association between eGFR < 60 mL/min/1.73 m² and increased mortality risk remained directionally consistent, although its statistical significance was attenuated (HR = 1.63, 95% CI 0.95–2.80, P = 0.078). The eGFR 60–89 mL/min/1.73 m² group still showed no statistically significant association with mortality risk (HR = 1.30, 95% CI 0.81–2.07, P = 0.273). Further sensitivity analysis using eGFR as a continuous variable showed that each 1 mL/min/1.73 m² increase in eGFR was associated with an approximately 1.1% reduction in mortality risk (HR = 0.989, 95% CI 0.981–0.996, P = 0.004). Spearman correlation analysis showed a weak negative correlation between MELD score and eGFR ($\rho = -0.18$, P < 0.001). In the candidate model including both MELD score and eGFR, all VIF/GVIF values were < 5, indicating no substantial multicollinearity (Table 4).

Table 4
Sensitivity Cox Regression Analysis After Inclusion of the MELD Score

Variable	Model 1 HR (95% CI)	P value	Model 2 HR (95% CI)	P value
eGFR group (reference: ≥ 90 mL/min/1.73 m ²)				
60–89	1.30 (0.81–2.07)	0.273	-	-
< 60	1.63 (0.95–2.80)	0.078	-	-
Continuous eGFR, per 1 mL/min/1.73 m ² increase	-	-	0.989 (0.981–0.996)	0.004
MELD score, per 1-point increase	1.03 (1.01–1.06)	0.011	1.03 (1.00–1.05)	0.044
Age (per 1-year increase)	1.03 (1.02–1.05)	< 0.001	1.03 (1.01–1.04)	0.003
Serum sodium (mmol/L)	0.99 (0.98–1.01)	0.326	0.99 (0.98–1.01)	0.343
Child–Pugh score	1.34 (1.19–1.51)	< 0.001	1.35 (1.20–1.52)	< 0.001
Note: Model 1 used eGFR as a categorical variable and was adjusted for MELD score, age, serum sodium, and Child–Pugh score. Model 2 used eGFR as a continuous variable and was adjusted for MELD score, age, serum sodium, and Child–Pugh score. HR, hazard ratio; CI, confidence interval; MELD, Model for End-Stage Liver Disease; eGFR, estimated glomerular filtration rate.				

Dose–Response Relationship Between eGFR and Mortality

Restricted cubic spline analysis showed an overall negative association between preprocedural eGFR and mortality risk (overall $P < 0.001$). As eGFR decreased, the risk of mortality gradually increased, with a more pronounced elevation in risk observed in the lower eGFR range. The test for nonlinearity did not reach statistical significance ($P = 0.055$), suggesting that this study did not confirm a definite nonlinear relationship between eGFR and mortality risk (Fig. 2).

Subgroup Analysis and Interaction Tests

Multivariable Cox modeling showed that the overall risk of mortality was higher in the eGFR < 60 mL/min/1.73 m² group than in the eGFR ≥ 60 mL/min/1.73 m² group (HR = 2.75, 95% CI 1.74–4.34, $P < 0.001$). Across strata defined by age, sex, Child–Pugh class, MELD score, albumin, serum sodium, and ascites status, the direction of this association was generally consistent, and none of the interaction tests reached statistical significance. Further stratified analysis by ascites status showed that eGFR < 60 mL/min/1.73 m² was associated with a higher risk of mortality both among patients with no or mild ascites and among those with moderate or severe ascites, suggesting that the association between

preprocedural renal dysfunction and adverse prognosis was not entirely dependent on the severity of ascites. However, because of the limited sample size in the eGFR < 60 mL/min/1.73 m² group and the limited number of events in some subgroups, the interaction tests may have been underpowered. Therefore, these findings should be interpreted as exploratory and require further validation in larger cohorts (Figs. 3 and 4).

Comparison of Major Post-TIPS Complications

During follow-up, the proportions of hepatic encephalopathy and worsening ascites increased with decreasing preprocedural eGFR. In the eGFR < 60 mL/min/1.73 m² group, hepatic encephalopathy occurred in 19 patients (39.6%) and worsening ascites occurred in 13 patients (27.1%), both of which were higher than the corresponding proportions in the eGFR ≥ 90 and 60–89 mL/min/1.73 m² groups. The between-group differences were statistically significant for hepatic encephalopathy and worsening ascites (P = 0.040 and P = 0.006, respectively). No statistically significant difference was observed in gastrointestinal rebleeding among the three groups (P = 0.623) (Table 5).

Table 5
Comparison of Major Post-TIPS Complications Among the Three Groups

Complication	Normal Renal Function (n = 491)	Mild Impairment (n = 79)	Significant Impairment (n = 48)	P value
Hepatic encephalopathy, n (%)	110 (22.4)	26 (32.9)	19 (39.6)	0.040
Worsening ascites, n (%)	54 (11.0)	11 (13.9)	13 (27.1)	0.006
Gastrointestinal rebleeding, n (%)	43 (8.8)	6 (7.6)	6 (12.5)	0.623
Notes: Data are presented as number (%). Group comparisons were performed using the chi-square test or Fisher's exact test, as appropriate. Complications refer to the first occurrence of events during follow-up.				

Discussion

This single-center retrospective cohort study evaluated the association between preprocedural eGFR and outcomes after TIPS in 618 patients with cirrhosis. The main finding was that preprocedural eGFR < 60 mL/min/1.73 m² was associated with a higher risk of all-cause mortality in the primary multivariable model, whereas mildly reduced eGFR, defined as 60–89 mL/min/1.73 m², was not significantly associated with mortality after adjustment. In sensitivity analysis including the MELD score, the association between eGFR < 60 mL/min/1.73 m² and mortality remained consistent in direction but was attenuated, suggesting that the prognostic information captured by eGFR may partially overlap with overall disease severity and creatinine-related components of liver disease scoring systems. Lower eGFR was also associated with higher proportions of postprocedural hepatic encephalopathy and worsening

ascites, although these secondary outcomes were analyzed descriptively and should be interpreted with caution.

These findings further support the important role of renal function in preprocedural risk assessment for TIPS in patients with cirrhosis. Previous prognostic studies of TIPS have commonly used serum creatinine as an indicator of renal function, although its limitations in patients with cirrhosis have been widely reported[13, 14]. In contrast, eGFR provides a more comprehensive reflection of glomerular filtration function and may therefore have greater value for risk identification in this population[15, 16]. In the present study, preprocedural renal function was assessed in detail using the CKD-EPI 2021 equation, which removes the race coefficient and is therefore more broadly applicable[15]. This approach may, to some extent, improve the clinical interpretability of renal function assessment.

The effect of mild renal impairment, defined as eGFR 60–89 mL/min/1.73 m², on prognosis may be partly influenced by confounding factors such as age, degree of liver dysfunction, and circulatory status. By contrast, when eGFR declines below 60 mL/min/1.73 m², it is more likely to indicate true and persistent renal dysfunction as well as reduced systemic organ reserve, resulting in a more stable association with adverse prognosis. This finding is consistent with the KDIGO guideline[18], which recognizes eGFR < 60 mL/min/1.73 m² as having clear clinical significance for risk stratification, and suggests that this threshold may have potential value for preprocedural risk identification before TIPS.

From a pathophysiological perspective, renal dysfunction in patients with cirrhosis is not merely a consequence of localized renal pathology, but rather the result of the combined effects of portal hypertension, splanchnic vasodilation, reduced effective circulating blood volume, and activation of neurohumoral systems. As cirrhosis progresses, persistent activation of the renin–angiotensin–aldosterone system, sympathetic nervous system, and antidiuretic hormone can lead to renal vasoconstriction, reduced renal perfusion, and water and sodium retention[9, 10]. Although TIPS can reduce portal venous pressure and improve renal hemodynamics in some patients[17], it may also increase cardiac volume load and induce or exacerbate hepatic encephalopathy[19]. Therefore, decreased preprocedural eGFR not only reflects impaired glomerular filtration function, but may also indicate reduced systemic circulatory reserve, impaired hepatorenal axis function, and diminished organ compensatory capacity.

In this study, two types of sensitivity analysis models were further constructed. First, after additional inclusion of the MELD score in the primary model, the association between eGFR < 60 mL/min/1.73 m² and increased mortality risk remained directionally consistent, although its statistical significance was attenuated. Although VIF/GVIF analysis did not reveal substantial statistical multicollinearity, both MELD score and eGFR contain creatinine-related information, indicating structural overlap between the two measures. Therefore, these findings suggest that the association between eGFR and post-TIPS prognosis may partly reflect overall liver disease severity and hepatorenal functional interactions, rather than being completely independent of the MELD score. Second, when eGFR was entered into the model as a continuous variable, higher eGFR remained associated with a lower risk of mortality, suggesting that

preprocedural eGFR, as a simple and reproducible indicator of renal function, retains potential value for risk stratification.

In subgroup analyses, the association between eGFR < 60 mL/min/1.73 m² and higher mortality after TIPS was generally consistent across strata defined by age, sex, Child–Pugh class, MELD score, ascites status, serum sodium, and albumin level. However, none of the interaction tests reached statistical significance. Therefore, there was no statistical evidence that these clinical factors modified the association between reduced eGFR and mortality. This finding is broadly consistent with previous studies on the relationship between renal function changes after TIPS and survival[20]. In particular, stratified analysis by ascites status showed a similar direction of association in patients with no/mild ascites and those with moderate/severe ascites, suggesting that the observed association was not explained solely by ascites severity. Nevertheless, because the number of patients with eGFR < 60 mL/min/1.73 m² was limited and some subgroups had few events, these findings should be regarded as exploratory rather than definitive.

TIPS can improve renal hemodynamics to some extent by reducing portal venous pressure, but its effects on renal function vary substantially among individuals[17]. Some studies have observed improvements in renal function after TIPS, whereas other patients may develop acute kidney injury (AKI). Post-TIPS AKI has been shown to be significantly associated with an increased risk of short-term mortality[21–23]. Therefore, decreased preprocedural eGFR reflects not only renal functional status itself, but also the overall deterioration of systemic circulatory function and organ reserve.

From a clinical practice perspective, patients with preprocedural eGFR < 60 mL/min/1.73 m² may be considered a potentially high-risk population after TIPS. For these patients, perioperative management should place greater emphasis on volume management, protection of renal perfusion, monitoring of serum sodium, and assessment of the risk of neurological complications. Postoperative follow-up should also be strengthened for hepatic encephalopathy and progression of ascites, while remaining alert to the occurrence of postprocedural AKI[22, 23]. As a simple, readily available, and reproducible laboratory indicator, eGFR has practical feasibility for incorporation into comprehensive preprocedural risk assessment before TIPS. However, eGFR should be interpreted together with established liver disease severity scores and the overall clinical context rather than as a standalone decision-making criterion.

Compared with previous studies that mainly used serum creatinine as a renal function marker, this study evaluated preprocedural renal function using eGFR calculated by the CKD-EPI 2021 equation. The study further examined the dose–response relationship between eGFR and long-term mortality after TIPS and assessed the clinical relevance of the eGFR < 60 mL/min/1.73 m² threshold. These findings may provide additional evidence for incorporating renal function assessment into preprocedural risk stratification before TIPS.

This study has several limitations. First, the single-center retrospective design may have introduced selection bias and residual confounding. Second, the number of patients with eGFR < 60 mL/min/1.73

m² was limited, resulting in relatively wide confidence intervals and limited statistical power for subgroup analyses. Third, renal function was primarily assessed using preprocedural creatinine-based eGFR, which may not fully capture dynamic renal function changes or subclinical acute kidney injury. Fourth, some TIPS-related information, including TIPS indication, emergency or elective procedure status, portosystemic pressure gradient reduction, stent diameter, concomitant embolization, and perioperative management, was incompletely documented during the retrospective study period. These variables were therefore not included in the primary multivariable model. Although the primary analysis adjusted for major baseline clinical and laboratory factors, residual confounding related to indication-specific and procedure-related characteristics cannot be excluded. Future prospective studies with standardized procedural data collection are warranted. Fifth, secondary outcomes were compared using proportions rather than time-to-event analyses; therefore, these results should be considered exploratory. Sixth, because liver transplantation after TIPS was rare in this cohort, competing-risk analysis was not performed. Finally, the study population was predominantly composed of patients with viral hepatitis-related cirrhosis, and caution is needed when generalizing the findings to other etiologies.

In conclusion, preprocedural eGFR < 60 mL/min/1.73 m² was associated with increased all-cause mortality after covered-stent TIPS in patients with cirrhosis in the primary multivariable model. This association was attenuated after additional adjustment for the MELD score, suggesting partial overlap between renal dysfunction and overall liver disease severity. Lower eGFR was also associated with higher proportions of postprocedural hepatic encephalopathy and worsening ascites, although these findings require confirmation using time-to-event analyses. Preprocedural eGFR may serve as a practical reference marker for comprehensive pre-TIPS risk stratification. However, it should not be interpreted as a standalone prognostic or decision-making criterion. Its clinical utility requires further validation in multicenter prospective studies.

Abbreviations

AKI

acute kidney injury

CI

confidence interval

eGFR

estimated glomerular filtration rate

HR

hazard ratio

INR

international normalized ratio

MELD

Model for End-Stage Liver Disease

TIPS

transjugular intrahepatic portosystemic shunt

Declarations

Ethics approval and consent to participate

This study was approved by the Ethics Committee of the First Affiliated Hospital of the University of Science and Technology of China, Hefei, China. The approval number was [2026-RE-155]. The requirement for informed consent was waived by the Ethics Committee because of the retrospective design and the use of anonymized clinical data. The study was conducted in accordance with the Declaration of Helsinki.

Consent for publication

Not applicable.

Availability of data and materials

The datasets generated and/or analyzed during the current study are not publicly available because of patient privacy and institutional restrictions. De-identified data may be available from the corresponding author on reasonable request and with permission from the First Affiliated Hospital of the University of Science and Technology of China and the relevant ethics committee.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

Han Cao and Jie Wu conceived and designed the study. Jun Shang, Yueyue Liu, and Ziyi Wang collected the clinical data. Han Cao and Jie Wu performed the statistical analyses. Han Cao drafted the manuscript. Jun Shang, Yueyue Liu, Ziyi Wang, Chun-Ze Zhou, and Rui-Feng Wang critically revised the manuscript for important intellectual content. Chun-Ze Zhou and Rui-Feng Wang supervised the study. All authors read and approved the final manuscript.

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Figures

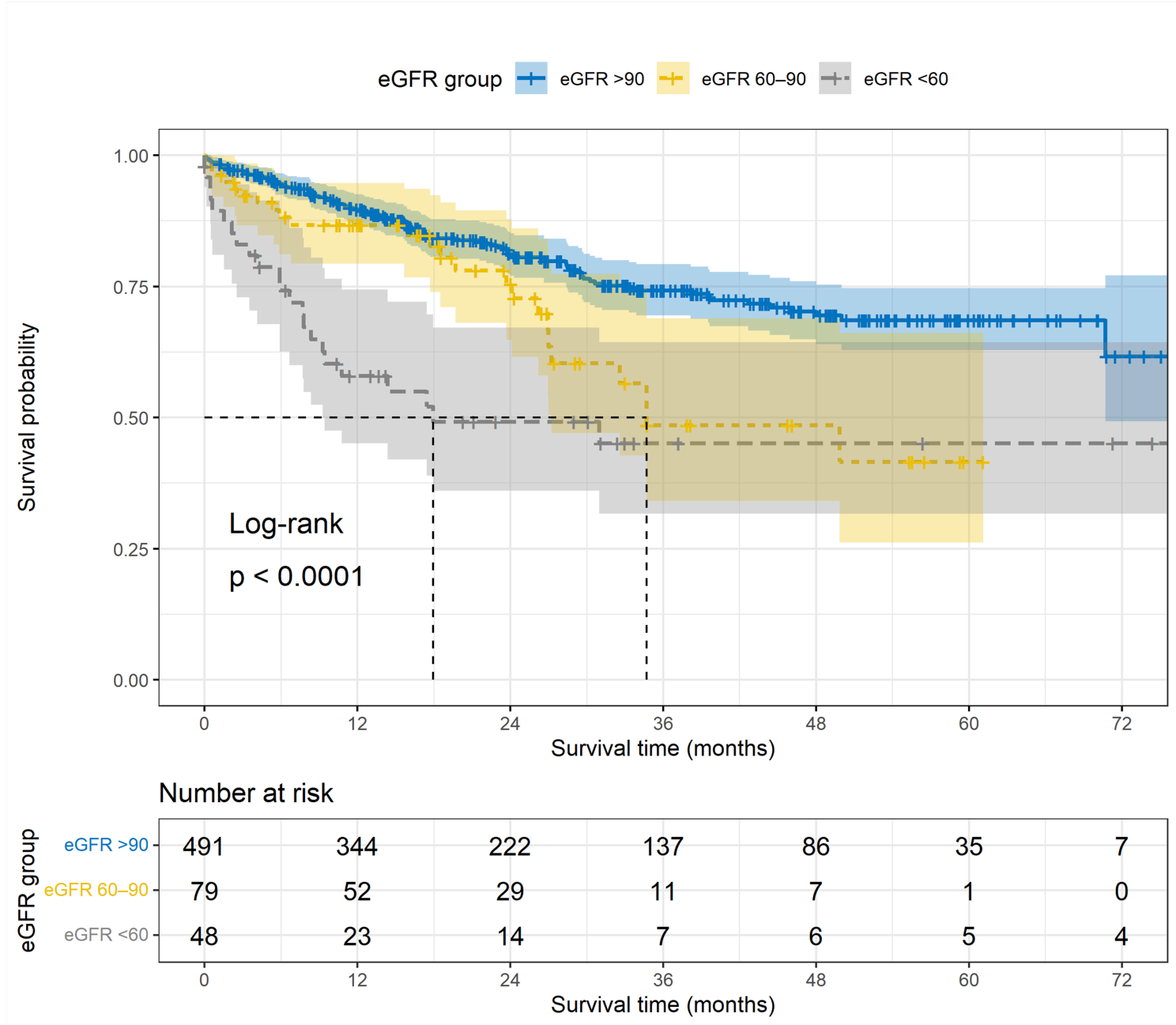


Figure 1

Kaplan–Meier survival curves after TIPS stratified by preprocedural eGFR groups.

Patients were categorized into three groups according to preprocedural eGFR: ≥ 90 , 60–89, and < 60 mL/min/1.73 m². Survival differences were compared using the log-rank test.

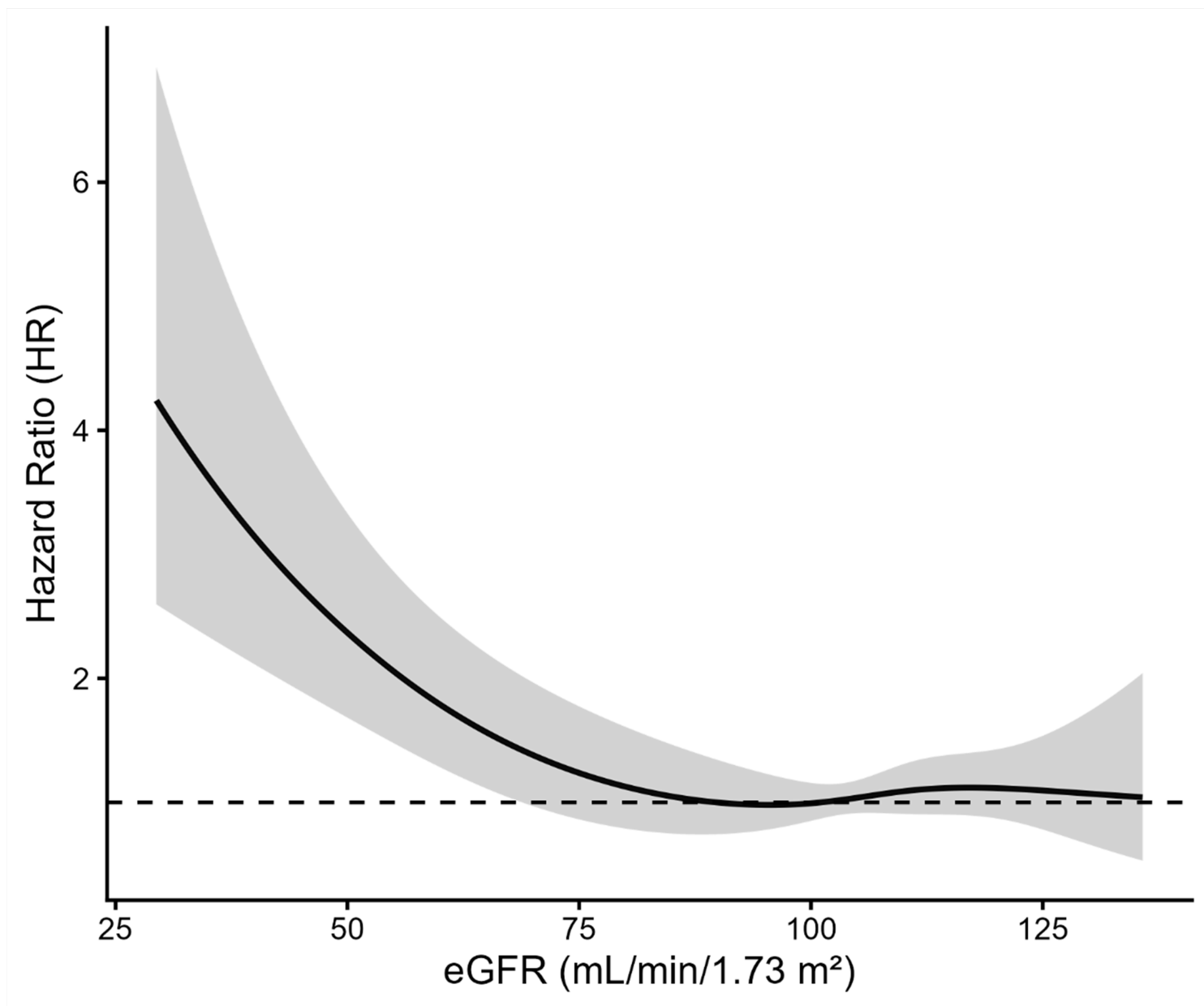


Figure 2

Restricted cubic spline analysis of the association between preprocedural eGFR and all-cause mortality after TIPS.

The solid line represents the estimated hazard ratio, and the shaded area represents the 95% confidence interval. The horizontal dashed line indicates a hazard ratio of 1.0.

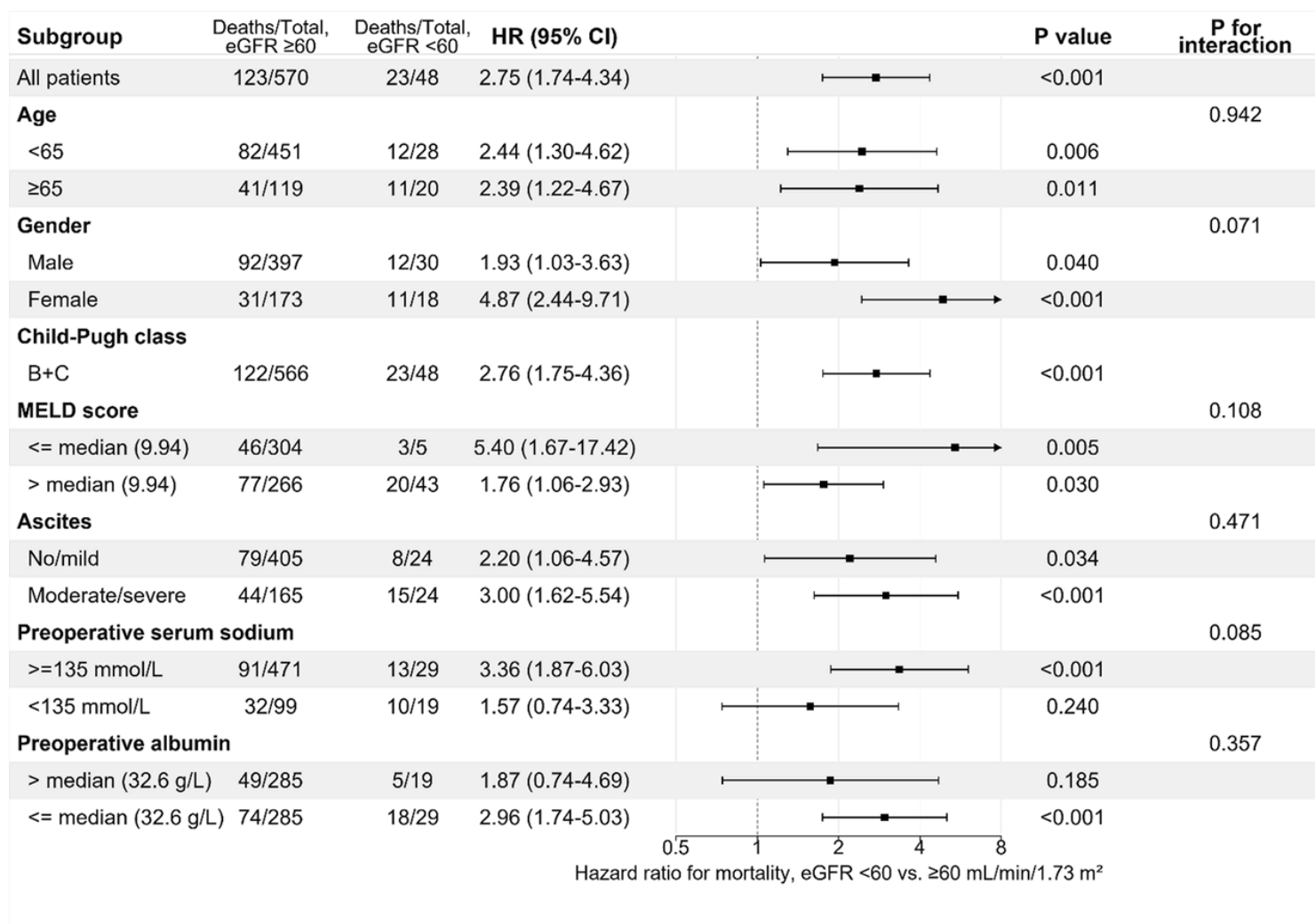


Figure 3

Subgroup analyses for all-cause mortality comparing preprocedural eGFR <60 versus ≥60 mL/min/1.73 m² after TIPS. Hazard ratios were estimated using Cox proportional hazards models. eGFR was dichotomized as <60 versus ≥60 mL/min/1.73 m². Interaction tests were performed to evaluate whether the association between eGFR category and mortality differed across subgroups. Estimates from strata with small numbers of patients or events should be interpreted cautiously. Child–Pugh class A was not analyzed separately because of the very small sample size.

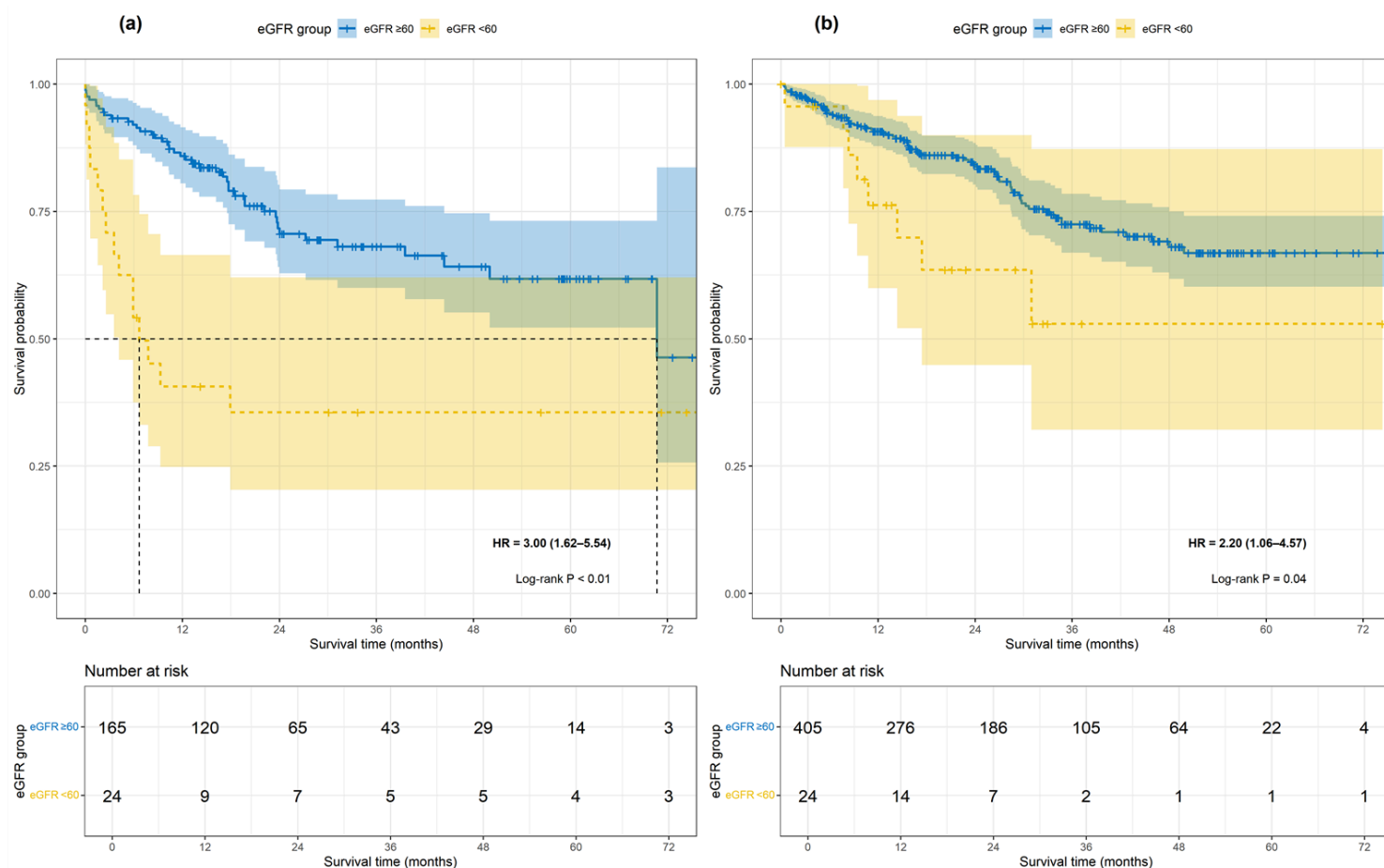


Figure 4

Kaplan–Meier survival curves stratified by ascites status and preprocedural eGFR category.

(a) Patients with moderate-to-severe ascites. (b) Patients with no or mild ascites. Survival differences were compared using the log-rank test.