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12-Month Albumin and Platelets Predict Recompensation in Hepatitis B Cirrhosis with Ascites as the First Decompensation

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Abstract: Background and objective: Recompensation is a key point in the course of decompensated cirrhosis. Previous studies have focused on the prognostic factors at decompensation onset, but the determinants of the relatively stable stage after virus inhibition are not clear. The purpose of this study was to identify the prognostic factors for recompensation in hepatitis B virus (HBV) cirrhosis patients with ascites as the first decompensating event under regular antiviral therapy. Methods: This double-center retrospective cohort study included all HBV-related cirrhosis patients with ascites for the first time, regardless of previous antiviral treatment history, all patients received nucleos(t)ide analogues (NAs) treatment. Cox regression analysis was performed 12 months after decompensation (at this time, 93.6% of patients achieved virological inhibition), and independent predictive factors were identified. A prognosis model was constructed. The performance of the model was evaluated by bootstrap verification, time-dependent receiver operating characteristic (ROC) curve, and decision curve analysis Results: During the median follow-up of 23.7 months, 48 patients (34.3%) achieved recompensation. Albumin (ALB) and platelet count (PLT) at 12 months after decompensation were the only independent predictors. The model showed excellent discrimination ability (C index=0.798), and the decision curve analysis showed that its clinical net benefit was significantly better than the traditional model for end-stage liver disease (MELD) score and Child-Turcotte-Pugh (CTP) score. Conclusions: This study confirmed that 12-month ALB and PLT can predict the compensatory recovery of HBV-related cirrhosis with ascites after the first decompensation. The validation in different populations will establish its wider clinical application value.

Keywords: HBV-related cirrhosis; prognostic model; recompensation; albumin; platelets

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1. Introduction

The World Health Organization estimated in 2022 that 254 million people worldwide were living with HBV infection, among whom 1.1 million died from HBV-related diseases [1,2]. The natural history of cirrhosis is characterized by progression from compensated to decompensated stage, with decompensation marked by ascites, esophageal and gastric variceal bleeding (EGVB), and hepatic encephalopathy (HE) [3]. The advent of NAs has enabled some decompensated patients to achieve recompensation, a state of stable clinical improvement with resolution of decompensating events. Long-term antiviral therapy can significantly suppress HBV replication, reduce necro-inflammatory activity, and lead to fibrosis regression, ultimately reducing decompensation and development of hepatocellular carcinoma (HCC) [4]. According to the Baveno VII consensus, recompensation is closely associated with improved survival and reduced need for liver

transplantation (LT) [5]. However, previous prognostic studies have predominantly assessed prognostic factors at the time decompensation occurred, when viral loads are high and liver function is severely impaired, essentially evaluating a mixed state intertwined with viral activity, inflammation, fibrosis, and portal hypertension (PHT) [6-9]. Which factors truly influence recompensation in a relatively stable condition when most patients have achieved virological suppression remains to be further explored. This study employs a 12-month landmark analysis design to identify hepatic functional reserve indicators that determine recompensation, providing evidence for clinical risk stratification and individualized management.

2. Materials and Methods

2.1. Study Design

This study employed a landmark analysis design. Time zero was defined as the date of the patient's first presentation with abdominal distension and confirmed diagnosis of ascites, serving as a uniform starting point for disease progression. We chose 12 months as the landmark time point, based on the following clinical evidence: (1) the Baveno VII consensus requires that ≥ 12 months have no decompensation [4]; (2) Virological suppression usually occurred within 1 year in most patients [10,11]; (3) The 12-month interval was in line with standard clinical practice, covering 2-4 routine follow-up visits [12]; (4) This time point has been verified in previous studies of HBV re decompensation [5,13-15]; (5) This cycle can realize the evaluation of disease stability.

2.2. Study Population

This dual-center retrospective cohort study consecutively enrolled patients attending the First Affiliated Hospital of Zhejiang University School of Medicine and Shulan (Hangzhou) Hospital between January 1, 2016, and July 30, 2024. Both institutions are tertiary care hospitals with standardized protocols for cirrhosis management and follow-up.

Inclusion criteria: (1) age 18-70 years; (2) meeting diagnostic criteria for cirrhosis; (3) positive hepatitis B surface antigen; (4) first detection of ascites by imaging or physical examination; (5) regular follow-up for at least 1 year; (6) receiving NAs antiviral therapy after enrollment.

Exclusion criteria: (1) other chronic liver diseases; (2) history of other decompensating events prior to ascites, such as EGVB, HE, hepatorenal syndrome, or hepatopulmonary syndrome. (3) CTP score >12 points; (4) creatinine (Cr) >1.5 times the upper limit of normal; (5) active malignancy; (6) severe organ dysfunction; (7) severely incomplete electronic medical records; (8) follow-up <1 year; (9) self-discontinuation of medication or failure to attend follow-up at 12 months.

2.3. Data Collection and Follow-up

Baseline data collection included demographic characteristics and laboratory assessments. Laboratory parameters include hematological indexes (WBC, Hb, PLT), liver function markers (ALB, total bilirubin [TBil], alanine aminotransferase [ALT], aspartate aminotransferase [AST]), virological status, renal function (Cr, urea, glomerular filtration rate [GFR]), sodium, and coagulation parameters (PT, INR). We also recorded the clinical characteristics, prognosis score (CTP score, MELD score), and details of antiviral treatment. Relevant laboratory and clinical parameters were collected at the landmark time point. Subsequently, patients were followed every 3-6 months until recompensation, competing risk events, loss to follow-up, or study end (July 30, 2025). The collection of prognostic variables at the 12-month landmark was performed blinded to the subsequent recompensation outcomes.

2.4. Definition of Recompensation

Recompensation was defined according to Baveno VII consensus, requiring simultaneous fulfillment of three criteria sustained for ≥12 months: (1) sustained virological suppression (HBV DNA <100 IU/mL); (2) absence of decompensating events (no ascites, variceal hemorrhage, HE or hepatorenal syndrome); (3) improved liver function including ALB >35 g/L, INR <1.5, and TBil <34.2 μmol/L.

The recompensation determination process involved identifying the first time point when all three criteria were simultaneously met (taking the latest achievement date as the potential qualification point), then observing all follow-up records over the subsequent 12 months. If all follow-ups maintained the three criteria without decompensating events, recompensation was confirmed; otherwise, that qualification point was invalidated, and the next potential qualification point was sought.

2.5. Clinical outcome assessment

For survival analysis, the time origin was the landmark time point (12 months post-initial decompensation), with event time defined as the interval from landmark to confirmed recompensation. Censoring events included: failure to achieve criteria at last follow-up, loss to follow-up, and competing risk events (HCC, LT, death).

2.6. Development and Internal Validation of the Prognostic Model

2.6.1. Variable Selection and Model Construction

Candidate variables at 12 months were screened using univariate Cox regression ($P<0.10$). In multivariate analysis, composite scores were excluded while retaining components. Among collinear variables, the more established measure was selected. Multicollinearity was assessed by the variance inflation factor (VIF) (<5 acceptable). The final model retained variables with $P<0.05$.

We constructed a prognostic model based on the regression coefficient of multivariate Cox regression. The linear predictor (LP) was calculated as: $LP=\beta_1X_1+\beta_2X_2+ ...+\beta_n X_n$, where β is the regression coefficient and X is the value of each predictive variable. To obtain the individual recompensation probability at any time t after the 12-month reference point, the formula is applied: $P(t)=1- S_0(t)$ ^exp (LP), where $S_0(t)$ is the baseline survival function derived by the Breslow method.

2.6.2. Model Performance Evaluation

Discrimination was assessed by C index and time-dependent ROC curves. Calibration was evaluated using the Brier score (<0.20 acceptable). Proportional hazards assumption was verified by Schoenfeld residuals. Internal validation used 1000 bootstrap iterations. Decision curve analysis compared net benefits versus traditional scores. For risk stratification and clinical interpretation, patients were classified into three groups based on the LP value using an exploratory, data-driven approach, and their survival outcomes were compared via Kaplan-Meier curves with the log-rank test.

2.6.3. Sensitivity analysis

Fine gray competitive risk regression was used to deal with potential competitive events (HCC, LT, and death). This sensitivity analysis can directly compare SHR with the standard Cox regression model. At the same time, the CIF estimate was compared with the traditional Kaplan-Meier curve. The discrimination ability of the two modeling strategies was evaluated by comparing the C index of multiple follow-up periods.

2.6.4. Clinical Application Tools

In order to facilitate clinical implementation, we generated a nomogram visual model and developed a calculation tool based on Excel. The tool can provide individualized probability estimates for 12, 24, and 36 months after the landmark time point.

2.7. Statistical Analysis

Statistical analysis was performed using R software (version 4.4.1). Descriptive statistics use mean ±SD or median (IQR) to represent continuous variables, while classified variables use frequency and percentage. Between-center comparisons employed t-test, Mann-Whitney U test, χ^2 test, or Fisher's exact test as appropriate. We defined statistical significance as two-tailed $P<0.05$. To address missing data, we applied Little's MCAR test at the 12-month landmark. If confirmed as MCAR, missing values were imputed using center-stratified medians. Survival curves were generated using the Kaplan-Meier method, with differences between groups assessed using the log-rank test. Cox proportional hazards regression was used to identify independent prognostic factors and construct the prediction model, with the proportional hazard assumption tested using Schoenfeld residuals.

3. Results

3.1. Missing Data Pattern

At the 12-month landmark, 8 patients (5.7%) had missing laboratory parameters (overall missing rate: 1.07%). Missing data primarily involved hematological parameters (white blood cell count [WBC], hemoglobin [Hb], and PLT, each n=5, 3.6%) and coagulation indices (prothrombin time [PT], international normalised ratio [INR]; each n=3, 2.1%). Little's MCAR test confirmed a missing completely at random mechanism (χ^2=20.47, df=23, P=0.613), supporting the validity of median imputation.

3.2. Baseline and 12-Month Clinical Characteristics

A total of 312 HBV-related decompensated cirrhosis patients were screened for eligibility at the 2 participating hospitals, and 140 patients were enrolled for analysis (Figure 1). The initial cohort enrolled 166 patients, with a mean age of 51.7±10.9 years and 69.9% male. Prior to enrollment, 54.2% of patients had received antiviral therapy. Partial differences existed between centers at baseline, while PLT, TBil, and MELD score showed no significant differences between centers (Supplementary Table 1).

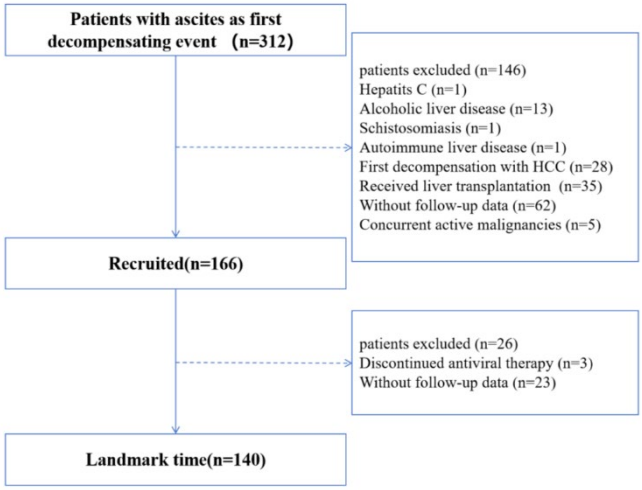

Figure 1. Flow chart of the patient selection process. HCC, hepatocellular carcinoma.

After 12-month landmark screening, 140 patients entered the final analysis. Compared with baseline, liver function at 12 months showed marked improvement: ALB increased from 32.1 g/L to 37.9 g/L, TBil decreased from 29.6 μmol/L to 17.2 μmol/L, CTP score decreased from 8 to 6, and MELD score decreased from 13 to 9. Virological response rate reached 93.6% (131/140, HBV DNA <100 IU/mL). At this time point, core prognostic variables, including ALB and PLT, showed no significant differences between centers (Table 1).

Table 1. 12-Month Clinical Characteristics between Two Centers.

Variable	Overall(N=140)	Center 1(N=69)	Center 2(N=71)	*P* value
Age (years)	53.09 ± 10.65	51.62 ± 11.74	54.52 ± 9.33	0.109
Male sex, n (%)	103 (73.6%)	54 (78.3%)	49 (69.0%)	0.294
Laboratory parameters				
HBV DNA (log_{10} IU/mL)	1.71 (1.71-1.71)	1.71 (1.71-1.71)	1.71 (1.71-1.71)	0.746
WBC (×10⁹/L)	3.50 (2.77-4.60)	3.65 (2.90-4.70)	3.40 (2.70-4.40)	0.363
Hb (g/L)	121.57 ± 28.13	124.65 ± 24.12	118.58 ± 31.43	0.201
PLT (×10⁹/L)	66.00 (47.00-93.00)	70.00 (49.00-93.00)	63.00 (46.00-88.00)	0.205
ALB (g/L)	37.91 ± 7.11	38.85 ± 6.15	37.00 ± 7.87	0.124
TBil (μmol/L)	17.15 (13.00-27.25)	17.00 (13.00-27.00)	18.00 (13.15-28.80)	0.623
ALT (U/L)	26.26 ± 11.02	26.88 ± 11.15	25.66 ± 10.93	0.514
AST (U/L)	34.99 ± 14.37	34.86 ± 14.82	35.11 ± 14.02	0.916
Cr(μmol/L)	70.00 (61.75-79.00)	70.00 (59.00-77.00)	71.00 (63.50-83.00)	0.162
Urea (mmol/L)	5.03 (4.36-6.14)	5.00 (4.30-6.36)	5.06 (4.39-6.05)	0.912
GFR (mL/min/1.73m²)	100.20 (92.22-107.05)	101.70 (94.00-113.88)	97.90 (87.20-104.35)	0.004**
Sodium (mmol/L)	142.00 (140.00-143.00)	141.00 (140.00-143.00)	142.00 (140.00-143.00)	0.463
PT (seconds)	13.85 (12.78-15.60)	13.20 (12.30-14.20)	14.90 (13.60-16.30)	<0.001***
INR	1.25 ± 0.17	1.18 ± 0.15	1.31 ± 0.18	<0.001***
Child-Pugh score	6.00 (5.00-7.00)	6.00 (5.00-7.00)	6.00 (5.00-7.50)	0.117
MELD score	9.00 (8.00-11.25)	8.00 (8.00-11.00)	10.00 (9.00-13.00)	0.001***
complications				
Ascites (Yes), n (%)	74 (52.9%)	35 (50.7%)	39 (54.9%)	0.742
HE (Yes), n (%)	3 (2.1%)	2 (2.9%)	1 (1.4%)	0.617

ALB, serum albumin level; ALT, alanine aminotransferase; AST, aspartate aminotransferase; Center 1, Shulan (Hangzhou) Hospital; Center 2, the First Affiliated Hospital of Zhejiang University School of Medicine; Cr, serum creatinine; CTP, Child-Turcotte-Pugh; GFR, glomerular filtration rate; HBV, hepatitis B virus;; Hb, hemoglobin; HE, hepatic encephalopathy; INR, international normalised ratio; MELD, model for end-stage liver disease; PLT, platelet count; PT, prothrombin time; TBil, total bilirubin; WBC, white blood cell count ; *P < 0.05; **P < 0.01; ***P < 0.001.

Among 26 patients who exited the study, 3 (1.8%) self-discontinued medication and 23 (13.9%) failed to attend follow-up. Patients lost to follow-up showed no significant differences from the analysis cohort in core prognostic variables (Supplementary Table 2), suggesting low risk of selection bias.

3.3. Prognostic Factor Analysis

We conducted univariate and multivariate Cox regression analysis, including factors readily available in routine clinical practice. The Univariate Cox regression analysis revealed that Hb, PLT, and ALB at 12 months were protective factors; TBil, AST, PT, and INR were adverse prognostic factors. Besides, prior antiviral therapy history showed no significant association with recompensation (Table 2). Following the selection criteria described in Methods, PLT, ALB, TBil, PT, and the center were included in multivariate analysis. VIF ranged from 1.08 to 1.85 (all <2), confirming acceptable collinearity (Supplementary Table 3). Results showed PLT and ALB were independently associated with recompensation (Supplementary Table 4). The final model retained only two independent prognostic factors: ALB and PLT (Table 2).

Table 2. Univariate and multivariate Cox Regression Analysis for Recompensation at 12-Month after the First Decompensation Event.

Variable	Univariate		multivariate	
	HR (95% CI)	*P* value	HR (95% CI)	*P* value
Age (years)	0.98 (0.95-1.00)	0.090		
Gender (Female vs Male)	0.74 (0.37-1.50)	0.408		
HBV DNA (log10 IU/mL)	0.71 (0.26-1.93)	0.500		
WBC (×10⁹/L)	1.07 (0.96-1.20)	0.209		
Hb (g/L)	1.02 (1.01-1.04)	<0.001***		
PLT (×10⁹/L)	1.01 (1.01-1.02)	<0.001***	1.01 (1.00-1.02)	0.027*
ALB (g/L)	1.22 (1.14-1.30)	<0.001***	1.20 (1.12-1.28)	<0.001***
TBil (μmol/L)	0.93 (0.89-0.96)	<0.001***		
ALT (U/L)	1.02 (0.99-1.04)	0.254		
AST (U/L)	0.97 (0.94-0.99)	0.002**		
Cr (μmol/L)	1.00 (0.99-1.01)	0.928		
Urea (mmol/L)	0.96 (0.82-1.12)	0.623		
GFR (mL/min/1.73m²)	1.00 (0.99-1.01)	0.706		
Sodium (mmol/L)	1.07 (0.95-1.20)	0.282		
PT (s)	0.67 (0.56-0.81)	<0.001***		
INR	0.01 (0.00-0.10)	<0.001***		
Prior antiviral therapy (Yes vs No)	0.946(0.53-1.68)	0.85		
Child-Pugh Score †	0.27 (0.17-0.45)	<0.001***		
MELD Score †	0.63 (0.52-0.76)	<0.001***		

ALB, serum albumin level; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CI, confidence interval; Cr, serum creatinine; GFR, glomerular filtration rate; HBV, hepatitis B virus; Hb, hemoglobin; HR, hazard ratio; INR, international normalised ratio; MELD, model for end-stage liver disease; PLT, platelet count; PT, prothrombin time; TBil, total bilirubin; WBC, white blood cell count;.

† Child-Pugh Score and MELD Score were excluded. *P < 0.05; **P < 0.01; ***P < 0.001.

3.4. Prognostic Model Construction

Following multivariate Cox regression analysis (Table 2), ALB and PLT at the 12-month landmark time point were identified as independent predictors of recompensation. Using these regression coefficients, we developed the recompensation assessment using platelet count and serum albumin level in decompensation (RAPID) score for HBV cirrhosis patients with ascites as the first decompensating event. The RAPID score is

calculated as: RAPID score = 0.008339 × PLT (×10⁹/L) + 0.180960 × ALB (g/L). This score serves as the LP in the Cox model, which is used to calculate individual cumulative recompensation probabilities via the survival function: P(t) = 1 - S_0(t)^exp (RAPID score), where S_0(t) is the baseline survival function at time t.

3.5. Model Performance and Validation

The RAPID score demonstrated excellent discrimination and calibration performance. Harrell's C-index was 0.798 (95%CI 0.742-0.853), and time-dependent ROC analysis showed the model maintained stable predictive performance at multiple post-landmark time points, with AUC values consistently exceeding 0.8 (Figure 2). The model showed a good calibration effect after 12 months. The calibration curve closely fits the 45 ° ideal line, and the Brier score is 0.1414, which is far below the acceptable threshold of 0.20 (Supplementary Figure 1). Schoenfeld residual test confirmed that the model met the proportional hazards assumption for ALB (p=0.898) and PLT (p=0.433). (Supplementary Figure 2).

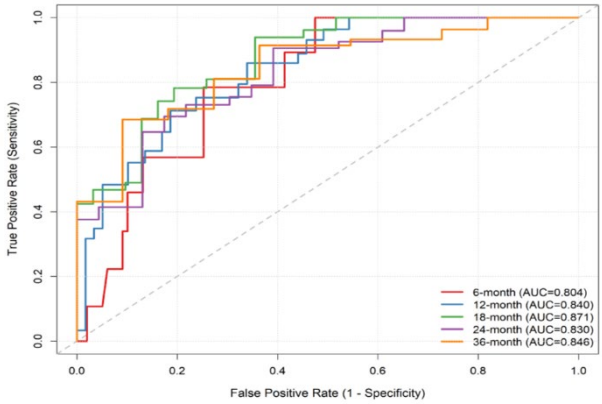

Figure 2. Time-dependent ROC curves for model predictive performance at multiple post-landmark time points. AUC, area under the curve; ROC, receiver operating characteristic.

Internal validation confirmed model robustness and clinical utility. Bootstrap validation with 1000 iterations yielded minimal optimism (0.004) with a corrected C index of 0.794, indicating the absence of overfitting (Supplementary Figure 3). HR for both prognostic variables proved stable across bootstrap iterations, with ALB ranging from 1.198 to 1.208 and PLT from 1.008 to 1.009 (Supplementary Figure 4). Decision curve analysis demonstrated that, to some extent, the RAPID score's net benefit was comparable to or exceeded those of MELD and CTP scores, with superior performance at lower (0.10-0.15) and higher (0.35-0.40) decision thresholds (Figure 3A).

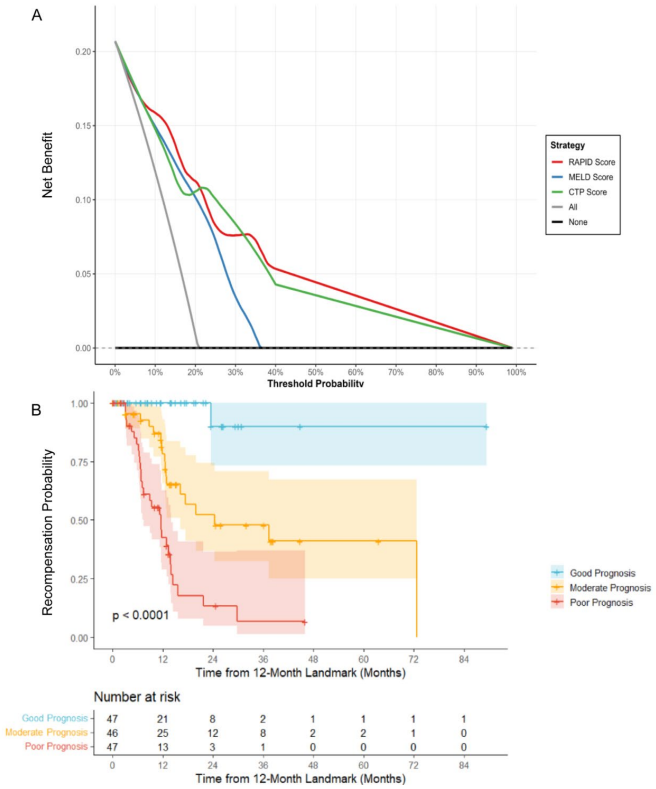

Figure 3. A Decision curve analysis comparing the net benefit of using RAPID, MELD, and CTP scores.Decision curve analysis comparing the net benefit of using RAPID, MELD, and CTP scores assessed at 12-month landmark to inform clinical decision-making for 12-month recompensation risk stratification. CTP, Child-Turcotte-Pugh; MELD, Model for End-stage Liver Disease; RAPID, recompensation assessment using platelet count and serum albumin level in decompensation.

Figure 3B Kaplan-Meier curves for cumulative recompensation probability stratified by RAPID score risk groups. LP, linear predictor; RAPID, recompensation assessment using platelet count and serum albumin level in decompensation.

3.6. Clinical Utility and Risk Stratification

3.6.1. Risk Stratification

Risk stratification based on LP tertiles divided patients into three groups with markedly different outcomes (log-rank P<0.0001). In the low-risk group (LP>8.15), 66.0% of patients achieved metabolic reconstruction, and the cumulative probability was close to 90% at 84 months. The moderate risk group (LP 6.91-8.15) performed moderately, 34.8% achieved recompensation, and the cumulative probability reached 40% at 72 months. In contrast, only 2.1% of high-risk patients (LP<6.91) achieved recompensation. These differences are reflected in the Kaplan-Meier curve, showing significant intergroup segregation (Figure 3B).

3.6.2. Clinical Application Tools

To promote clinical application, we developed a nomogram. (Figure 4), which can predict cumulative recompensation probabilities at 12 months, 24 months, and 36 months post-landmark.

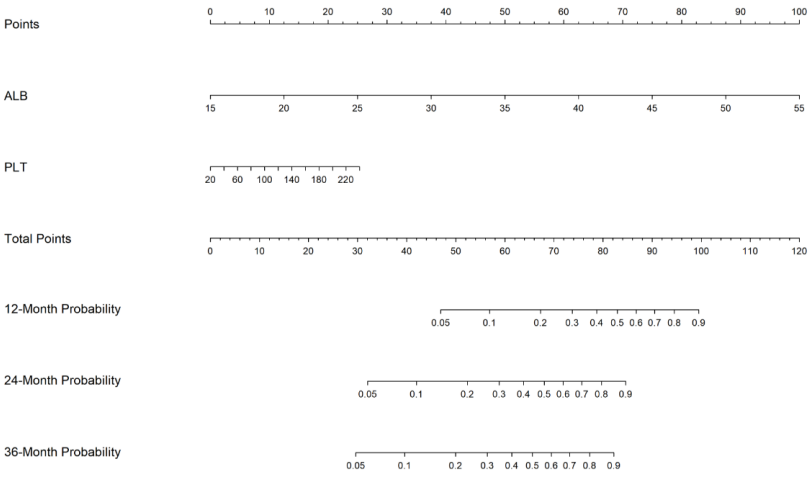

Figure 4. Nomogram for predicting recompensation probability in HBV-related cirrhosis patients with ascites. To use the nomogram: (1) Locate the patient's serum albumin level (ALB, g/L) on the ALB axis and draw a vertical line upward to the Points axis to determine the corresponding points. (2) Repeat this process for platelet count (PLT, ×10⁹/L). (3) Sum the points from both variables and locate the total on the Total Points axis. (4) Draw a vertical line downward from the Total Points to the probability axes to obtain the predicted cumulative recompensation probability at 12, 24, and 36 months post-landmark (12 months after initial decompensation). ALB, serum albumin level; PLT, platelet count.

3.7. Sensitivity Analysis

Among the 140 patients entering the analysis, 9 competing risk events (6.4%) were observed, including HCC in 6 cases, LT in 2 cases, and death in 1 case. Fine-Gray competing risk regression model results were highly consistent with the Cox model. (Supplementary Table 5). Discrimination capacity was comparable between the two models: Fine-Gray overall C-index of 0.825 versus the Cox model 0.798, with a difference of only 0.027.

Comparative analysis of CIF versus 1-Kaplan-Meier curves demonstrated high concordance in estimated cumulative recompensation incidence between the two methods in both overall population and risk-stratified analysis, with nearly overlapping curves (Supplementary Figure 5A). After stratification by prognostic model LP tertiles, CIF curves for the three risk groups showed significant separation (Gray's test $P<0.001$), further confirming that the prognostic model's risk stratification capability remains robust after accounting for competing risks (Supplementary Figure 5B). Notably, only 1 patient (2.1%, 1/47) in the high-risk group achieved recompensation, while recompensation rates in the intermediate- and low-risk groups were 34.8% (16/46) and 66.0% (31/47), respectively. The extremely low recompensation rate in the high-risk group not only validates the prognostic model's accurate identification of high-risk patients but also explains the shorter trajectory of the Kaplan-Meier curve for this group.

4. Discussion

A key distinction of this study is the timing of prognostic assessment. We employed a 12-month landmark design at which time point the vast majority of patients had achieved virological suppression. This design enables us to purely evaluate the impact of hepatic functional reserve and PHT severity on functional recovery against a background of virological homogeneity.

Recent studies by Wang et al. and Deng et al. similarly identified PLT and ALB as predictors of recompensation, with reported AUC=0.749 [10,16]. Our model demonstrated comparable discrimination (C index=0.798), reinforcing the prognostic value of these markers in patients with virological suppression.

The pairing of ALB and PLT is biologically sound. These two markers complement each other, providing a pathophysiological basis for recompensation prediction. ALB is a core indicator of hepatic synthetic function. Its recovery directly reflects improvement in hepatocyte reserve function and regenerative capacity [17]. Importantly, ALB does more than indicate nutritional status; it has antioxidant, anti-inflammatory, immunomodulatory, and endothelial protective effects [18]. Low ALB also contributes to ascites by decreasing plasma colloid osmotic pressure, while a rise in it helps restore circulating volume and alleviate PHT complications [19]. Conversely, PLT serves as a non-invasive marker of PHT severity. Thrombocytopenia results from PHT-induced hypersplenism, with massive PLT destruction and sequestration in the enlarged spleen [20,21]. PLT is closely associated with hepatic fibrosis and exhibits dynamic reversibility; It was demonstrated that post-antiviral PLT increases occur synchronously with fibrosis improvement and collagen reduction, indicating hepatic microcirculation improvement and fibrosis regression. Additionally, thrombocytopenia reflects impaired hepatocyte thrombopoietin (TPO) production; some studies confirm that TPO production and PLT recovery promptly with hepatic function restoration [22,23]. The unique advantage of PLT lies in its universal accessibility and objectivity as a basic complete blood count parameter, conferring favorable clinical dissemination value to platelet-based models.

Two aspects need to be improved simultaneously to achieve the recovery of liver function: the recovery of liver cell function and the improvement of portal vein hemodynamics. Both are indispensable. Baveno VII standard emphasizes that compensatory recovery not only means the disappearance of clinical symptoms, but also requires substantial improvement of liver function and portal hemodynamics [4]. This model follows this pathophysiological framework and accurately captures the key determinants of functional recovery.

Compared with the existing prognostic tools, this model has multiple advantages: first, its simplicity is better than the Brec-PAS score, which only needs two variables. Based on the sample size, the bivariate model achieves the best balance between prediction efficiency and over-fitting risk. Bootstrap verification confirmed its optimization, and the optimistic deviation was only 0.004. Variable simplification also improves the clinical operability and applicability. Although the model is simple, its discrimination ability (C index=0.798) is equivalent to that reported by Deng et al. (AUC=0.749), and is superior to the traditional MELD and CTP scores in the analysis of the decision curve. The landmark design avoids the time-dependent deviation, and the comprehensive verification, including time-dependent ROC curve, decision curve analysis, and fine gray competitive risk analysis, ensures the reliability of the model. We also found that previous antiviral therapy did not affect the recovery of liver function. This indicates that once virological suppression is achieved, the current liver function reserve determines the prognosis. This finding supports the universality of the model in people with different treatment backgrounds and emphasizes the importance of continuous antiviral therapy for HBV-related cirrhosis [24,25].

In clinical application, a RAPID score can provide clear risk stratification. Based on the 12-month liver function score (LP), we divided the patients into three groups: the 36-month recompensation rate in the high-risk group (LP <6.91) was only 2.1%, the moderate risk group (LP 6.91-8.15) was about 40%, and the low-risk group (LP>8.15) was 90%. The risk stratification can guide clinical management: high-risk patients with a very low probability of recompensation can benefit from strengthening nutritional support, optimizing PHT treatment, and timely evaluating LT; moderate-risk patients need to maintain regular follow-up and treatment compliance; low-risk patients can extend the follow-up interval. The calculator can quickly generate an individualized recompensation probability by inputting 12-month ALB and PLT values.

The recompensation rate (34.3%) in this study was lower than that in recent similar studies. Baveno VII standard requires that the three indicators last for ≥ 12 months, which is more stringent than most studies. However, this strict standard is helpful to identify the

real recompensation phenomenon and provide a more reliable basis for clinical decision-making.

Our study has several limitations. First, external validation is lacking, which limits confidence in the model's generalizability across different populations, geographic regions, and clinical settings. Multicenter prospective validation is urgently needed. Second, the sample size of 140, while statistically acceptable (EPV=24), constrained the number of variables that could be included in the multivariate model, potentially missing other important prognostic factors such as liver stiffness measurement (LSM), hepatic venous pressure gradient (HVPG), and intestinal microbiome alterations. These indicators have been proven to be associated with decompensation risk [4,26-28]. But due to limitations of retrospective research, these examinations were not routinely performed. Future prospective studies should integrate these objective indicators to further optimize the model. Third, 15.7% of patients were lost to follow-up, though core prognostic variables showed no significant differences from the analysis cohort.

Additionally, population specificity limits the results' generalizability. This study enrolled only HBV-related cirrhosis patients with ascites as the first decompensating event; results do not apply to other etiologies, nor to patients with their first EGVB or HE. Regarding competing risk events (6.4%), sensitivity analysis confirmed minimal impact on results.

Future research should address several areas. Multicenter prospective studies with larger, more diverse populations are needed to validate our findings externally. Dynamic prediction models incorporating ALB and PLT change rates from baseline to 12 months may improve prediction accuracy. Intervention trials in high-risk patients (LP<6.91) could determine whether intensified nutritional support, antifibrotic therapy, and other measures improve outcomes. The model should also be tested in other cirrhosis etiologies and different types of first decompensating events.

5. Conclusions

In summary, the RAPID score provides a practical tool for risk stratification and individualized management in HBV-related cirrhosis patients with ascites following virological suppression. This simple two-parameter model (ALB and PLT) helps identify patients who need intensive intervention. A calculator further simplifies clinical application. Validation in diverse populations will establish its broader clinical utility.

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Ethical Statement: This study was approved by the Ethics Committee of the First Affiliated Hospital of Zhejiang University School of Medicine (Approval No.: [2025B] IIT Ethics Approval No.0933) and the Ethics Committee of Shulan (Hangzhou) Hospital (Approval No.: KY2025104), in accordance with the ethical principles of the Declaration of Helsinki.

Data Sharing Statement: The data used to support the findings of this study are available from the corresponding author

Appendix

Supplementary Figure 1 Calibration plot for the RAPID score at 12 months post-landmark.

MAE, mean absolute error; RAPID, recompensation assessment using platelet count and serum albumin level in decompensation.

Supplementary Figure 2 Schoenfeld residuals plots testing the proportional hazards assumption.

Supplementary Figure 3 Bootstrap validation of model discrimination.

Supplementary Figure 4 Bootstrap validation of hazard ratio stability for prognostic factors.

Supplementary Figure 5 Competing risk analysis comparing Cox and Fine-Gray methods for recompensation prediction.

Supplementary Tables

Supplementary Table 1. Baseline Clinical Characteristics between Two Centers.

Variable	Overall(N=166)	Center 1 (N=82)	Center 2 (N=84)	*P* value
Age (years)	51.73 ± 10.93	49.74 ± 11.73	53.68 ± 9.78	0.020*
Male sex, n (%)	116 (69.9)	62 (75.6)	54 (64.3)	0.155
Laboratory parameters				
WBC (×10⁹/L)	3.60 (2.50-4.74)	3.70 (2.60-4.88)	3.10 (2.37-4.54)	0.170
Hb (g/L)	118.00 (101.00-128.00)	117.39 ± 20.35	111.64 ± 20.79	0.074
PLT (×10⁹/L)	68.00 (45.00-91.00)	73.00 (47.75-99.25)	62.00 (45.00-85.50)	0.090
ALB (g/L)	32.09 ± 6.22	34.42 ± 6.05	29.82 ± 5.55	<0.001***
GLB (g/L)	31.52 ± 6.96	30.43 ± 7.26	32.58 ± 6.53	0.046*
TBil (μmol/L)	29.55 (19.77-59.18)	28.00 (17.00-66.00)	29.60 (20.88-54.45)	0.777
ALT (U/L)	36.50 (25.00-76.75)	36.50 (28.00-72.50)	36.50 (23.25-86.50)	0.509
AST (U/L)	49.00 (35.25-91.50)	49.00 (36.00-87.25)	50.00 (34.25-95.75)	0.999
Cr (μmol/L)	63.00 (56.00-72.00)	64.88 ± 13.58	62.50 (56.75-72.25)	0.691
Urea (mmol/L)	4.44 (3.71-5.83)	5.05 (4.12-6.14)	4.06 (3.50-4.99)	0.001***
GFR (mL/min/1.73m²)	102.94 (94.12-110.97)	105.96 ± 17.06	100.50 (91.58-108.40)	0.003**
Sodium (mmol/L)	141.00 (139.00-142.00)	140.00 (139.00-142.00)	141.00 (139.00-143.00)	0.032*
PT (s)	15.45 (14.00-18.38)	14.75 (13.53-19.38)	16.10 (14.38-18.12)	0.166
INR	1.35 (1.22-1.62)	1.29 (1.19-1.67)	1.40 (1.24-1.60)	0.246
HBsAg (IU/mL)	1117.32 (361.94-2316.36)	1395.04 (545.00-2483.79)	988.38 (192.21-2027.18)	0.107
HBV DNA (log_{10} IU/mL)	3.79 (1.70-5.78)	3.16 (1.70-5.00)	4.60 (1.70-6.43)	0.006**
AFP (ng/mL)	7.25 (2.82-64.56)	7.00 (2.96-38.53)	8.05 (2.50-79.25)	0.795
Child-Pugh score	8.00 (7.00-10.00)	8.00 (7.00-9.00)	9.00 (8.00-10.00)	0.004**
MELD score	13.00 (10.00-16.00)	11.50 (9.00-17.75)	13.00 (10.00-15.25)	0.342

Others				
Prior antiviral therapy, No(%)	76 (45.8)	25 (30.5%)	51 (60.7%)	<0.001***
Duration of antiviral therapy (months) †	7.7 (1.0-47.0)	5.2 (1.3-42.3)	12.3 (0.9-73.0)	0.436
Follow-up time (months)	23.7 (17.4-31.8)	21.3 (16.0-28.1)	24.6 (18.9-32.4)	0.125

AFP, Alpha-Fetal Protein; ALB, serum albumin level; ALT, alanine aminotransferase; AST, aspartate aminotransferase; Center 1, Shulan (Hangzhou) Hospital; Center 2, the First Affiliated Hospital of Zhejiang University School of Medicine; Cr, serum creatinine; GFR, glomerular filtration rate; Hb, hemoglobin; HBsAg, Hepatitis B Surface Antigen; HBV, hepatitis B virus; HE, hepatic encephalopathy; INR, international normalised ratio; MELD, model for end-stage liver disease; PLT, platelet count; PT, prothrombin time; TBil, total bilirubin; WBC, white blood cell count;.
†Analyze only the patients who received antiviral therapy before admission; *P < 0.05; **P < 0.01; ***P < 0.001.

Supplementary Table 2. Baseline Clinical Characteristics between Included and Excluded Patients

Variable	Included (n=140)	Excluded (n=26)	*P* value
Age (years)	51.92 ± 10.60	50.73 ± 12.75	0.657
Male sex, n (%)	103 (73.6%)	13 (50.0%)	0.030*
Laboratory parameters			
WBC (×10⁹/L)	3.60 (2.60-4.80)	3.00 (1.98-4.15)	0.062
Hb(g/L)	118.00 (101.50-128.00)	111.00 (100.75-131.00)	0.601
PLT (×10⁹/L)	70.00 (49.50-92.50)	55.00 (36.75-78.00)	0.097
ALB (g/L)	32.20 ± 6.21	31.50 ± 6.40	0.608
GLB (g/L)	31.69 ± 7.06	30.58 ± 6.47	0.432
TBil (μmol/L)	30.50 (21.00-67.17)	22.20 (16.25-40.25)	0.043*
ALT (U/L)	40.50 (26.75-80.50)	28.00 (22.00-52.50)	0.033
AST (U/L)	51.00 (36.00-98.75)	40.00 (32.75-53.75)	0.059
Cr (μmol/L)	64.50 (56.00-74.00)	60.50 (55.25-66.25)	0.192
Urea (mmol/L)	4.44 (3.64-5.79)	4.55 (3.85-5.90)	0.553
GFR (mL/min/1.73m²)	102.55 (94.40-110.93)	107.15 (87.80-111.58)	0.734
Sodium (mmol/L)	141.00 (139.00-142.00)	141.00 (140.00-142.00)	0.316
PT (seconds)	15.50 (14.07-18.52)	15.00 (14.00-17.65)	0.598
INR	1.36 (1.22-1.62)	1.33 (1.23-1.57)	0.807
HBsAg (IU/mL)	1122.78 (416.41-2413.40)	640.39 (70.71-1666.85)	0.102
HBV DNA (log_{10} IU/mL)	3.89 (1.70-5.81)	3.07 (1.70-5.17)	0.160
AFP (ng/mL)	7.80 (2.80-68.97)	5.53 (3.09-20.42)	0.498
Child-Pugh Score	8.00 (7.00-10.00)	8.00 (7.00-9.00)	0.311
MELD Score	13.00 (10.00-17.00)	11.00 (9.00-14.75)	0.107
Others			
Duration of antiviral therapy (months) †	0.23 (0.00-7.65)	4.93 (0.00-43.23)	0.059
Prior antiviral therapy, No(%)	67 (47.9%) / 73 (52.1%)	9 (34.6%) / 17 (65.4%)	0.303

AFP, Alpha-Fetal Protein; ALB, serum albumin level; ALT, alanine aminotransferase; AST, aspartate aminotransferase; Cr, serum creatinine; GFR, glomerular filtration rate; Hb, hemoglobin; HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; HE, hepatic encephalopathy; INR, international

normalised ratio; MELD, model for end-stage liver disease; TBil, total bilirubin; PLT, platelet count; PT, prothrombin time; WBC, white blood cell count.

†Analyze only the patients who received antiviral therapy before admission; *P < 0.05; **P < 0.01; ***P < 0.001.

Supplementary Table 3. Variance Inflation Factors of Laboratory Parameters at 12-Month.

Variable	VIF	Multicollinearity
Hb(g/L)	1.70	Low
PLT (×10⁹/L)	1.25	Low
ALB (g/L)	1.72	Low
TBil (μmol/L)	1.78	Low
AST (U/L)	1.30	Low
Sodium (mmol/L)	1.39	Low
PT (seconds)	1.58	Low

ALB, serum albumin level; AST, aspartate aminotransferase; Hb, hemoglobin; PLT, platelet count; PT, prothrombin time; TBil, total bilirubin; VIF,variance inflation factors.

VIF < 5 indicates low multicollinearity; VIF 5-10 indicates moderate multicollinearity; VIF > 10 indicates high multicollinearity.

Supplementary Table 4. Multivariate Cox Regression Analysis for Recompensation at 12-Month after First Decompensation Event.

Variable	HR (95% CI)	*P* value
PLT (×10⁹/L)	1.008 (1-1.016)	0.039*
ALB(g/L)	1.164 (1.087-1.247)	<0.001***
TBil (μmol/L)	0.977 (0.936-1.019)	0.279
PT (s)	0.891 (0.731-1.084)	0.249
Center (2 vs 1)	0.903 (0.482-1.693)	0.750

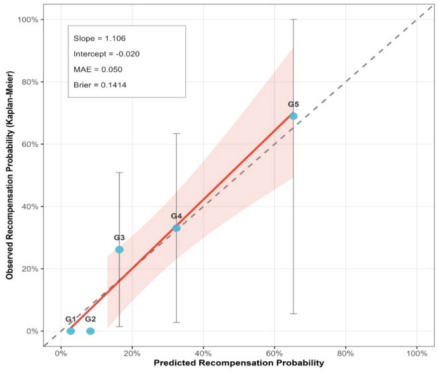
ALB, serum albumin level; CI, confidence interval; Center 1, Shulan (Hangzhou) Hospital; Center 2, the First Affiliated Hospital of Zhejiang University School of Medicine; HR, hazard ratio; PLT, platelet count; PT, prothrombin time; TBil, total bilirubin; *P < 0.05; **P < 0.01; ***P < 0.001.

Supplementary Table 5. Comparison of C-index between Cox and Fine-Gray Models.

Time Point	Cox Model C-index (95% CI)	Fine-Gray Model C-index
12 months	0.7141 (0.6263-0.8019)	0.8221
24 months	0.7708 (0.7043-0.8372)	0.8050
36 months	0.7882 (0.728-0.8484)	0.8063
Overall	0.7976 (0.7418-0.8533)	0.8247

CI, confidence interval.

Supplementary Figures



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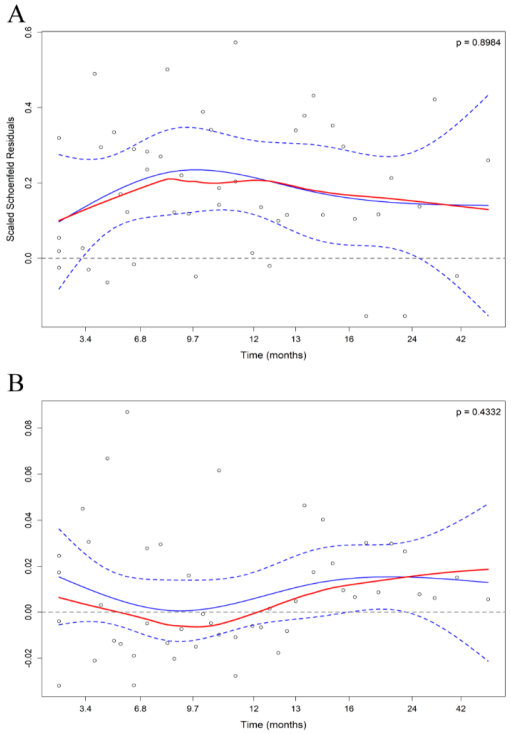

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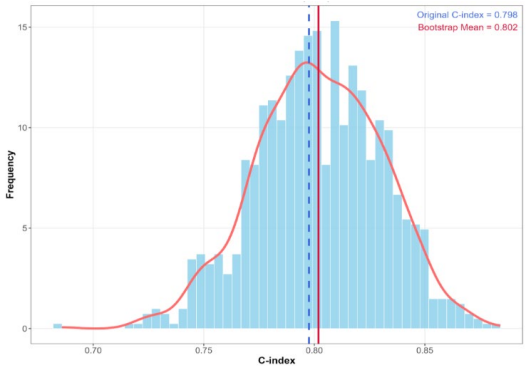

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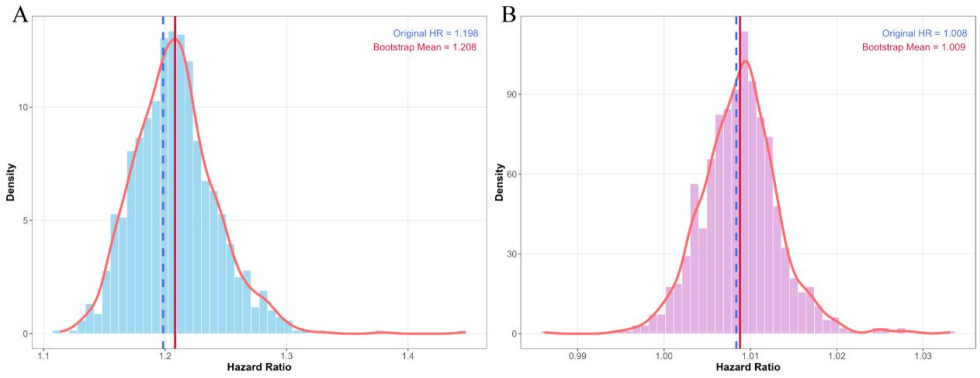

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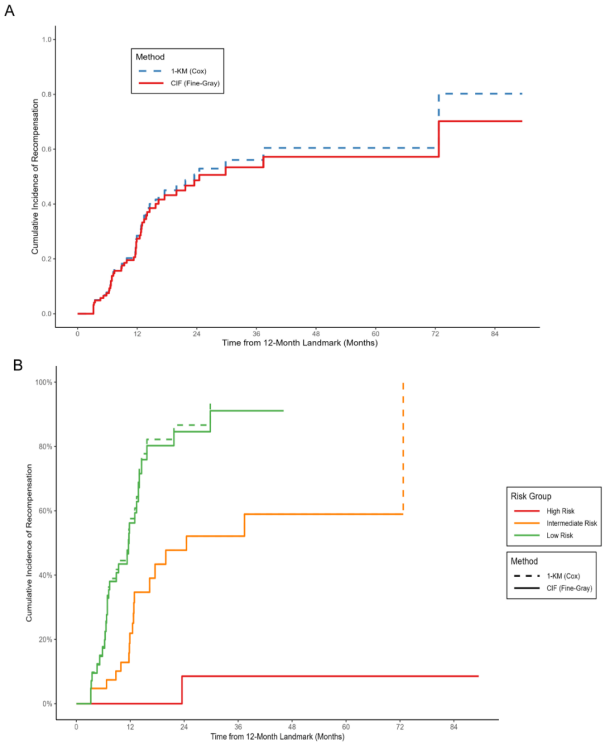

Supplementary Figure 5

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