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# Cholesterol-modified prognostic nutritional index as an independent prognostic biomarker in primary biliary cholangitis patients

Huiling Zhu[1†], Mengyao Zheng[1†], Wenbin Li[2†], Yaqin Huang[1], Lili Zhang[1], Wenting Yang[1] and Jinhui Yang[1*]

## Abstract

**Background** Primary biliary cholangitis (PBC) is a chronic cholestatic liver disease characterized by inflammation of the interlobular bile ducts, often associated with malabsorption of fat-soluble vitamins and osteoporosis. Thus, evaluating the nutritional status of patients with PBC and implementing appropriate interventions are significant. But CPNI in determining the nutritional status and forecasting survival outcome among patients with PBC remains unclear.

**Methods** A total of 262 patients with PBC were retrospectively enrolled at the Second Affiliated Hospital of Kunming Medical University between January 2013 and November 2023. We used the receiver operating characteristic (ROC) curve, Kaplan–Meier survival curve, and logistic regression analysis to evaluate the predictive effects of several nutritional assessments. These assessments included the controlling nutritional status (CONUT), geriatric nutritional risk index (GNRI), prognostic nutritional index (PNI), and Cholesterol-modified Prognostic Nutritional Index (CPNI), which were evaluated for their predictive effect on the prognosis of PBC patients.

**Results** In our study, after adjusting for various confounding factors, multivariate cox regression analyses revealed that CPNI (HR: 1.114, 95% CI: 1.003–1.237, $P=0.044$), age (HR: 1.071, 95% CI: 1.018–1.127, $P<0.009$), total bilirubin (HR:1.019, 95% CI:1.009–1.09, $P<0.001$) were independent risk factors for death in patients with PBC. The Kaplan–Meier curves and ROC curves used to assess predictive accuracy showed that CPNI(0.788) had superior prognostic performance for OS compared to other nutritional indices, such as CONUT(0.724), GNRI(0.755), PNI(0.776), and UK-PBC(0.660)($P<0.05$).

**Conclusions** CPNI is superior to other nutritional scores in the prognostic assessment of PBC patients.

**Keywords** Primary biliary cholangitis, CPNI, Prognosis

## Introduction

Primary Biliary Cholangitis (PBC) is a chronic autoimmune liver disease characterized by progressive destruction of intrahepatic bile ducts, mainly affecting adult women aged 40–70 years [1, 2]. A progressive disorder in the processes of bile secretion and enterohepatic bile salt circulation in patients with PBC in its early stages. The incidence of PBC in advanced countries is stable, but the prevalence is increasing, which is probably associated with better diagnosis of the disease in the early stages [3].

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The majority of PBC patients are asymptomatic at the time of diagnosis, and the clinical course is typically slow and progressive [4]. And patients with PBC often have abnormal lipid metabolism [5]. At present, ursodeoxycholic acid (UDCA) is the first-line treatment for patients with PBC. There are several prognostic scoring systems that predict the prognosis of PBC patients treated with UDCA [6], but there have been no published data on the prognostic role of nutritional factors in predicting the prognosis of PBC patients. Thus, evaluating the nutritional status of patients with PBC and implementing appropriate interventions are of great significance for improving their quality of life. Currently, there are no clear assessment criteria or standardized methods to determine the nutritional status of patients with PBC.

The prognostic nutritional index (PNI) which is calculated based on serum albumin concentration and blood lymphocyte count has been widely used to evaluate the nutritional status of patients [7]. The Controlling Nutritional Status (CONUT) score has recently been introduced as a nutritional screening tool, including serum albumin concentration, total cholesterol, and lymphocyte count [8]. The geriatric nutritional risk index (GNRI) was first described by Bouillanne et al. [9] and is a simple tool for predicting the risk of morbidity and mortality in elderly patients by using albumin and body weight parameters. Recently, many studies have revealed the prognostic role of the GNRI in a variety of cancers, including gastric cancer, hepatocellular carcinoma, and breast cancer [10–12]. Cholesterol-modified Prognostic Nutritional Index (CPNI) is used as a nutritional and immunological index and has been reported as a prognostic marker for breast cancer. However, the performance of CPNI in determining the nutritional status and forecasting survival outcome among patients with PBC remains unclear. Our primary objective is to investigate the correlation between CPNI and Overall Survival (OS) in patients with PBC, and evaluated its predictive accuracy in comparison to other objective nutritional indicators.

## Patients and methods

### Study design and data selection

This retrospective cohort study was approved by the Ethics Committee of the Second Affiliated Hospital of Kunming Medical University and was conducted in accordance with the Declaration of Helsinki. Between January 2013 and November 2023, 262 PBC patients were consecutive enrolled in this study at the Second Affiliated Hospital of Kunming Medical University using clinical care database (Lianzhong). A diagnosis can be made if two of the following three criteria are met: (1) Biochemical evidence of cholestasis (mainly elevated ALP and GGT), with imaging studies excluding extrahepatic or intrahepatic large duct obstruction.

(2) Positive AMA/AMA-M2, or other PBC-specific autoantibodies (e.g., anti-gp210 antibodies, anti-sp100 antibodies). (3) Histological evidence of non-suppurative destructive cholangitis and small duct destruction [13]. we excluded 30 patients due to incomplete clinical or survival data, resulting in 232 for final data analysis (Fig. 1). Due to the retrospective nature of this analysis, consent forms were not required.

The inclusion criteria were as follows: (1) patients who fulfilled the PBC diagnostic criteria, according to the guidelines of the European Association for the Study of

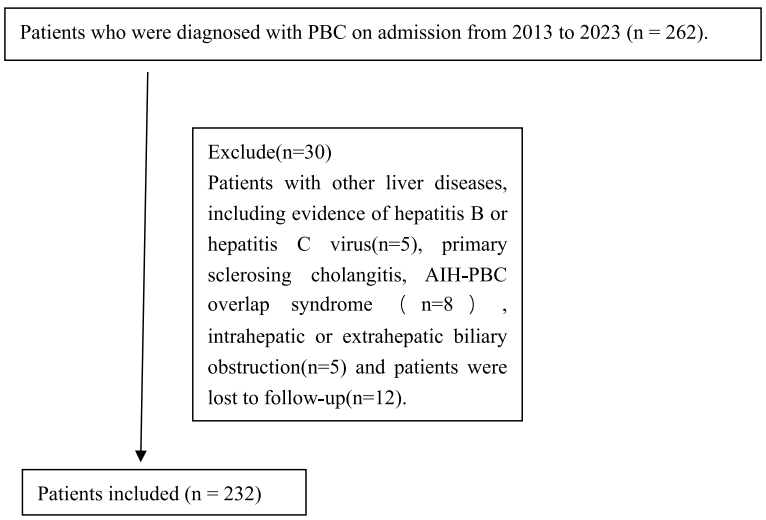


**Fig. 1** Flowchart of participant selection

Liver Disease; (2) patients with or without a history of oral UDCA administration, who began to take 13–15 mg/kg/day UDCA orally from the baseline date and received continuous and regular treatment; and (3) qualified patients with complete data at baseline.

Patients who fulfilled any one of the following criteria were excluded: evidence of viral hepatitis, primary sclerosing cholangitis or other liver diseases, intrahepatic or extrahepatic biliary obstruction, and individuals with incomplete baseline covariate data.

#### Demographic and clinical outcomes of patients with PBC

Demographic information, clinical parameters, laboratory tests, and physical measurements of all included patients at baseline were comprehensively collected. All these data were obtained from the electronic medical record system. The primary endpoint of this study was OS, which was defined as the duration from diagnosis to death from any cause. Patient survival information was sourced through regular telephone contact, outpatient visits, or hospitalizations. The follow-up process was continued until either the patient's death or the point at which we could no longer contact the patient.

#### Definition of malnutrition

For the included 232 patients, BMI was calculated as weight (kg)/height$^2$ (m). All patients were sorted in four categories based on their BMI: underweight (< 18.5 kg/m$^2$), normal weight (18.5 to 24.0 kg/m$^2$), overweight (24.0 to 28.0 kg/m$^2$), and obese (≥ 28.0 kg/m$^2$) [14]. The CONUT score is calculated using three parameters, including serum albumin concentration, total lymphocyte count, and total cholesterol concentration (Table S1). This scoring system ranges from 0 to 12, Malnutrition was defined as a CONUT score ≥2 [15]. The PNI =albumin (g/L) +5 ×Lymphocyte count (× 10$^9$), patients were classified by the presence (PNI <45) or absence (PNI ≥45) of malnutrition [16]. The GNRI was calculated using the following formula: [9, 17](1.489 ×10 ×serum albumin (g/dL)) +(41.7 ×weight (kg)/ideal body weight (kg)). The ideal body weight was calculated as follows: 0.75 ×height (cm)−62.5 for male patients, 0.60 ×height (cm)−40 for female patients. In addition, those with no risk of malnutrition (GNRI >98) and those at risk of malnutrition (GNRI ≤98). The Cholesterol-modified Prognostic Nutritional Index (CPNI) =4.8 ×cholesterol (mmol/L) −1.5× albumin (g/L)—7.7 ×lymphocyte (× 10$^9$) +126 [10]. There was a nonlinear relationship between nutritional indices (CPNI) and OS of PBC patients (median value used as cutoff point), according to RCS analysis using the Cox proportional hazards model, as depicted in Fig. 2, CPNI >82.06 points indicate malnutrition. Meanwhile, patients with alkaline phosphatase (ALP) levels >1.67 ×upper limit of normal after 1 year of UDCA treatment were considered nonresponders.

#### Statistics analysis

Data with a normal distribution were expressed as mean ±SD, whereas those not conforming to a normal distribution were expressed as the median (IQR). The

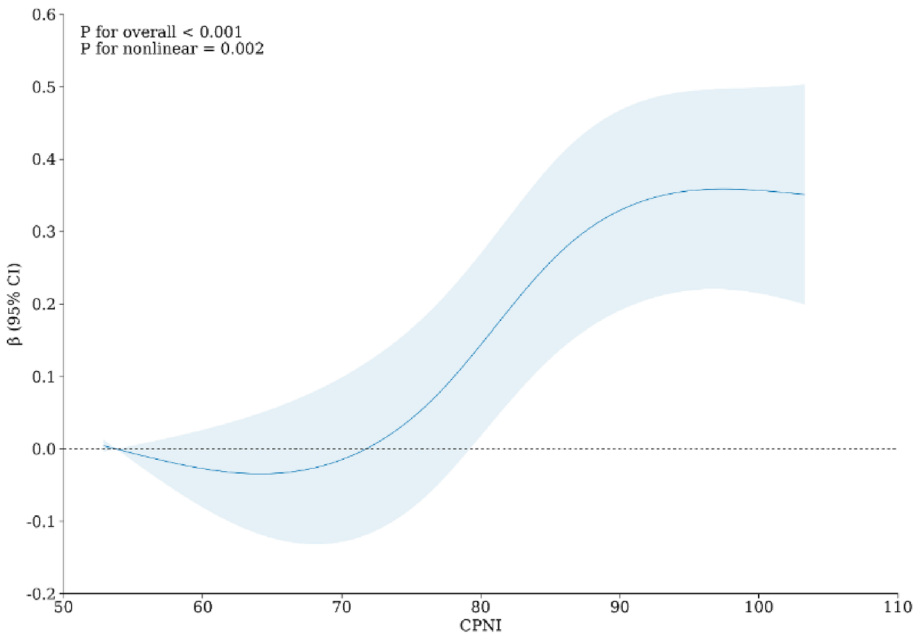


**Fig.2** RCS analysis using the Cox proportional hazards model to explore the nonlinear relationship between nutritional indices (CPNI) and OS

Student's t-test was used to evaluate distributed continuous variables, while the Mann–Whitney U test was used to assess non-normally distributed variables. Categorical data were reported as percentages and analyzed using $\chi 2$ or Fisher's exact tests. To determine the independent predictive significance of nutritional markers for OS in PBC, univariate and multivariate cox regression analysis were performed. Kaplan–Meier curves were used for survival comparisons between groups. All analyses adopted a significance level of 0.05 and were conducted in SPSS 26.0 software.

## Results

### Baseline characteristics of patients with PBC

Ultimately, 232 patients were included in the study. The cohort comprised 191 (82.3%) females and 41 (17.7%) males, average age of patients with PBC was 58.89 ± 10.90. A significant proportion of the patients were overweight or obese; 14(6.03%) were classified as overweight, and 51 (21.98%) as obese. Some patients had coexisting autoimmune disease, including Sjögren syndrome35(15.9%) and thyroid disease 25(10.78%). Cases were admitted to hospital with pruritus4(1.72%) and fatigue12(5.17%). Additionally, we compared the baseline data of male and female patients; the detailed baseline characteristics of the patients of PBC are shown in Table 1. We compared the characteristics of patients with and without liver cirrhosis of baseline in Supplementary Table S2. There is a difference in age, nonresponse to UDCA, Lymphocyte, PLT between patients with cirrhosis and those without($P < 0.05$).

### CPNI is an independent risk factor for prognosis in PBC patients: Cox Regression model results

Univariate Cox regression analysis showed that age, sex, albumin, platelets, total bilirubin, hemoglobin, FIB-4 and CPNI were risk factors for death ($P < 0.05$). Variables that were considered clinically relevant and statistically significant in cox regression analysis were entered into the multivariate model. In the multivariate cox regression analysis, we developed three models adjusted for different covariates to confirm the stability of the results. Model A, which was adjusted for age, sex, and BMI, indicated that CPNI (HR: 1.051, 95% CI: 1.030–1.072, $P < 0.001$) and age (HR: 1.062, 95% CI: 1.028–1.098, $P < 0.001$) were independent risk factors for death. Model B, which was adjusted for age, sex, BMI, pruritus, jaundice, and thyroid disease suggested that CPNI (HR: 1.051, 95% CI: 1.030–1.072, $P < 0.001$) and age (HR: 1.062, 95% CI: 1.027–1.097, $P < 0.001$) were independent risk factors for death. Model C, which was adjusted for age, sex, BMI, Sjogren's syndrome, thyroid disease, pruritus, fatigue, albumin, total bilirubin, ALP, GGT, AST, triglycerides, neutrophils, platelets, hemoglobin, L3SMI, FIB-4, UDCA response, and CPNI showed that CPNI (HR: 1.14, 95% CI: 1.003–1.237, $P = 0.044$), age (HR: 1.071, 95% CI: 1.018–1.127, $P < 0.009$), total bilirubin (HR:1.019, 95% CI:1.009–1.09, $P < 0.001$)were independent risk factors for death.(Table 2).

### Trend analysis was performed to analyze the association between the CPNI and prognosis of patients with PBC

The age, sex and BMI adjusted HR for overall Survival in subjects with the highest quartile versus the lowest quartile was (16.076 [95% CI 33.505–73.727]). After multivariate adjustment (model B), the highest quartile conferred a higher risk of overall survival than the lowest quartile (15.973 [95% CI 33.474–73.438]). In the full adjustment model (model C), the highest quartile of overall Survival was significantly associated with 10.998-fold increased risk ($P < 0.05$), compared with the lowest quartile, respectively. (Table 3).

### Evaluating the prognostic effectiveness of nutritional indices

The ROC analysis assessing the prognostic predictive power of CONUT, GNRI, PNI, UK-PBC, and CPNI in PBC patients, the areas under the ROC curve (AUC) are 0.724,0.755, 0.776, 0.66 and 0.788($P < 0.001$) show that CPNI was the most accurate in predicting OS compared to the other nutritional indices (Fig. 3).Kaplan–Meier curves were utilized to explore the association between malnutrition diagnosed using different nutritional indicators and OS.(Fig. 4) Patients diagnosed with malnutrition using the CPNI, CONUT, GNRI, and PNI indices had lower survival rates than those without malnutrition($P < 0.05$). We further compared UK-PBC scores and CPNI, however, the results were unsatisfactory, possibly due to the relatively small sample size. Kaplan–Meier survival curves suggest that CPNI acts as an independent prognostic factor for PBC patients. Furthermore, the ROC curve demonstrated that the predictive capability of CPNI exceeded that of the previously mentioned nutritional indicators.

## Discussion

To our knowledge, this is the first study to explore the association between CPNI and prognosis of PBC patients. In this study, we assessed the capability of the CPNI to evaluate.

nutritional status and predict survival in PBC patients. Univariate and multivariate binary logistic regression analyses revealed that CPNI is an independent predictor of OS in patients with PBC. The Kaplan–Meier curves and ROC curves used to assess predictive accuracy showed that CPNI had superior prognostic

**Table 1** Baseline characteristics of the patients with PBC

| Characteristic | Overall(n = 232) | Female(n = 191) | Male(n = 41) | *P*-value |
|---|---|---|---|---|
| Age, years, mean ± SD | 58.89 ± 10.90 | 58.75 ± 10.87 | 59.54 ± 11.18 | 0.676 |
| Height, cm, media(IQR) | 158.00(155.00–163.75) | 158.00(155.00–162.00) | 160.00(155.00–165.00) | < 0.001 |
| Weight, kg, media(IQR) | 57.00(52.00–62.00) | 56.00(51.00–62.00) | 61.00(55.00–68.00) | 0.002 |
| BMI, kg/m$^2$,media(IQR) | 22.51(20.81–24.22) | 22.37(20.80–24.03) | 23.03(20.96–25.18) | 0.178 |
| BMI group, n(%) | | | | |
| Normal weight | 149(64.22) | 126(65.97) | 23(56.10) | |
| Obesity | 51(21.98) | 42(21.99) | 9(21.96) | |
| Overweight | 14(6.03) | 8(4.19) | 6(14.63) | |
| Underweight | 18(7.76) | 15(7.85) | 3(7.32) | |
| Thyroid disease, n(%) | 25(10.78) | 18(9.42) | 7(17.07) | 0.152 |
| Sjogren syndrome, n(%) | 35(15.09) | 31(16.23) | 4(9.76) | 0.293 |
| Pruritus, n(%) | 4(1.72) | 3(1.57) | 1(2.44) | 0.419 |
| Fatigue, n(%) | 12(5.17) | 11(5.76) | 1(2.44) | 0.384 |
| Albumin, g/l, media(IQR) | 36.70(30.93–41.20) | 36.90(30.90–41.50) | 34.30(30.90–40.25) | 0.537 |
| Alkaline phosphatase, U/L, media(IQR) | 178.50(127.25–297.75) | 176.00(128.00–287.00) | 211.00(123.50–388.00) | 0.274 |
| Bilirubin,μmol/l, media(IQR) | 20.50(13.90–37.70) | 18.70(13.60–35.40) | 25.60(18.05–68.20) | < 0.001 |
| γ-Glutamyl transferase, U/L, media(IQR) | 151.00(60.00–316.25) | 131.00(56.00–285.00) | 249.00(113.50–551.00) | 0.662 |
| Triglycerides, mmol/l, media(IQR) | 1.30(0.95–1.89) | 1.24(0.95–1.83) | 1.41(0.99–2.24) | 0.116 |
| Hemoglobin, g/l, media(IQR) | 113.00(73.00–135.00) | 112.00(81.00–135.00) | 127.00(5.17–137.00) | 0.713 |
| Platelets,10$^9$/l, media(IQR) | 139.90(96.00–190.75) | 140.20(96.00–201.00) | 138.00(103.00–154.00) | 0.459 |
| Neutrophils,10$^9$/l, media(IQR) | 3.05(2.12–4.36) | 2.91(2.03–4.20) | 3.59(2.69–5.24) | 0.018 |
| Lymphocyte,10$^9$/l, media(IQR) | 1.58(1.06–2.22) | 1.5(0.98–2.16) | 1.82(1.30–2.54) | 0.060 |
| Creatinine, μmol/l, media(IQR) | 60.00(51.00–70.00) | 58.00(50.00–66.00) | 70.00(61.00–90.50) | < 0.001 |
| L3 SMI (IQR) | 37.75(32.74–43.03) | 35.84(32.19–40.74) | 47.85(41.06–54.53) | < 0.001 |
| Sp100, n(%) | 58(25) | 44(23) | 14(34) | 0.136 |
| Gp210, n(%) | 54(23) | 45(24) | 9(22) | 0.812 |
| CONUT, n(%) | | | | |
| Malnutrition | 88(38) | 117(61) | 27(66) | |
| No malnutrition | 144(62) | 74(39) | 14(34) | |
| GNRI, n(%) | | | | |
| Malnutrition | 94(41) | 80(42) | 14(34) | |
| No malnutrition | 137(59) | 110(58) | 27(66) | |
| PNI, n(%) | | | | |
| Malnutrition | 117(51) | 95(50) | 22(54) | |
| No malnutrition | 115(49) | 96(50) | 19(46) | |
| CPNI, n(%) | | | | |
| Malnutrition | 116(50) | 93(49) | 23(56) | |
| No malnutrition | 116(50) | 98(51) | 18(44) | |
| FIB −4 | 5.45 ± 5.83 | 5.27 ± 4.52 | 6.33 ± 9.92 | 0.292 |
| Cirrhosis, n(%) | 232 (45) | 88(46) | 18(44) | 0.800 |
| Follow-up duration(month) | 41.81 ± 33.83 | 44.49 ± 34.26 | 29.37 ± 26.90 | 0.801 |
| Prognosis(death), n(%) | 40(17.2) | 33(17.3) | 7(17.1) | 0.975 |

performance for OS compared to other nutritional indices. Despite significant advancements in both the assessment and management of patients with liver disease, the provision of appropriate nutritional support for these patients is frequently lacking, an omission that has a large impact on clinical outcomes and quality of life.

Currently, there is limited research available on the incidence of malnutrition in patients with PBC. Patients with PBC-AIH overlap syndrome or primary sclerosing

**Table 2** Cox regression analysis results of CPNI and prognosis in PBC patients

| Variable | Univariate analysis | | Multivariate analysis | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | Model A | | Model B | | Model C | |
| | HR (95% CI) | *P*-value | HR (95% CI) | *P*-value | HR (95% CI) | *P*-value | HR (95% CI) | *P*-value |
| Age (years) | 1.047(1.016–1.080) | 0.003 | 1.062(1.028–1.098) | < 0.001 | 1.061(1.026–1.097) | < 0.001 | 1.071(1.018–1.127) | 0.009 |
| Sex (male/female) | 1,493(0.657–3.393) | 0.338 | 1.703(0.733–3.956) | 0.216 | 1.667(0.704–3.951) | 0.246 | 3.622(0.783–16.749) | 0.099 |
| BMI | 0.995(0.907–1.093) | 0.918 | 1.016(0.934–1.105) | 0.711 | 1.016(0.934–1.105) | 0.716 | 0.878(0.774–0.995) | 0.042 |
| Thyroid disease | 0.480(0.065–3.555) | 0.472 | | | 1.509(0.179–2.706) | 0.705 | 0.083 (0.008–0.904) | 0.041 |
| Pruritus | 0.733(0.177–3.044) | 0.669 | | | 0.788(0.176–3.525) | 0.756 | 3.399 (0.376–3.721) | 0.276 |
| Fatigue | 0.998(0.135–7.403) | 0.998 | | | 0.744(0.087–6.343) | 0.787 | 1.574 (0.007–0, 904) | 0.902 |
| Jaundice | 0.706(0.701–1.573) | 0.606 | | | 0.787(0.080–1.307) | 0.905 | 1.003(0.447–1.336) | 0.900 |
| Albumin (g/l) | 0.865(0.822–0.911) | < 0.001 | | | | | 1.035(0.861–1.245) | 0.714 |
| Total bilirubin (umol/L) | 1.004(1.000–1.008) | 0.035 | | | | | 1.019(1.009–1.029) | < 0.001 |
| Alkaline phosphatase (u/l) | 1.000(0.998–1.001) | 0.736 | | | | | 0.995(0.991–0.999) | 0.026 |
| γ-Glutamyl transferase (u/l) | 1.000(0.999–1.001) | 0.662 | | | | | 1.000(0.998–1.002) | 0.930 |
| Triglycerides (mmol/L) | 0.918(0.613–1.374) | 0.678 | | | | | 0.341(0.101–1.154) | 0.084 |
| Neutrophils ($\times 10^9$/l) | 0.990(0.938–1.045) | 0.714 | | | | | 1.164(1.018–1.331) | 0.027 |
| Platelets,$10^9$/l | 0.993(0.989–0.998) | 0.009 | | | | | 0.991(0.981–1.001) | 0.092 |
| Hemoglobin, g/l | 0.992(0.986–0.999) | 0.021 | | | | | 0.985(0.969–1.001) | 0.065 |
| $L_3$ SMI | 1.005(0.971–1.040) | 0.779 | | | | | 1.002(0.939–1.069) | 0.961 |
| AST(U/L) | 1.001(0.998–1.003) | 0.632 | | | | | 1.001(0.995–1.007) | 0.764 |
| UDCA response | 0.568(0.302–1.067) | 0.007 | | | | | 0.218(0.069–0.690) | 0.010 |
| FIB-4 | 1.037(1.025–1.090) | < 0.001 | | | | | 0.936(0.829–1.056) | 0.282 |
| CPNI | 11.289(3.477–36.647) | < 0.001 | 1.051(1.030–1.072) | < 0.001 | 1.051(1.030–1.072) | < 0.001 | 1.114(1.003–1.237) | 0.044 |

Model A: adjusted for age, sex, and BMI

Model B: adjusted for age, sex, BMI, thyroid disease, pruritus, jaundice

Model C: adjusted for age, sex, BMI, thyroid disease, pruritus, jaundice, albumin, total bilirubin, ALP, GGT, triglycerides, neutrophils, platelets, hemoglobin, AST, $L_3$SMI, UDCA response, FIB-4 and CPNI

**Table 3** Trend analysis of prognosis in patients with PBC based on CPNI

| Variable | Univariate Analysis | | Model A | | Model B | | Model C | |
|---|---|---|---|---|---|---|---|---|
| | HR (95%CI) | *P* for trend | HR (95%CI) | *P* for trend | HR (95%CI) | *P* for trend | HR (95%CI) | *P* for trend |
| Quantile 1 | reference | < 0.001 | reference | < 0.001 | reference | < 0.001 | reference | 0.035 |
| Quantile 2 | 0.622(0.055–7.084) | 0.702 | 0.547(0.047–6.317) | 0.629 | 0.635(0.054–7.416) | 0.718 | 0.552(0.041–7.405) | 0.654 |
| Quantile 3 | 8.235(1.795–37.782) | 0.007 | 7.066(1.517–32.904) | 0.013 | 6,950(1.490–32.423) | 0.014 | 6.858(0.999–47.067) | 0.050 |
| Quantile 4 | 17.600(3.896–79.502) | < 0.001 | 16.076(3.505–73.727) | < 0.001 | 15.973(3.474–73.438) | < 0.001 | 10.998(1.220–99.149) | 0.033 |

Model A: adjusted for age, sex, and BMI

Model B: adjusted for age, sex, BMI, Sjögren syndrome, and thyroid disease; fatigue

Model C: adjusted for age, sex, BMI, Sjogren's syndrome, thyroid disease, pruritus, fatigue, albumin, total bilirubin, ALP, GGT, AST, triglycerides, neutrophils, platelets, hemoglobin, $L_3$SMI,FIB-4, UDCA response, and CPNI

cholangitis have a worse prognosis compared to those with PBC alone. [18] In our study, these patients were excluded. Patients with PBC is associated with damage to subcellular structures in the intrahepatic bile duct epithelial cells and with a change in the metabolism of bile acids due to the disrupted processes of bile secretion and their enterohepatic circulation. Progressive intrahepatic cholestasis results in an insufficient release of bile acids into the duodenum and increased accumulation in the hepatocytes and plasma [19, 20]. Gradually and imperceptibly

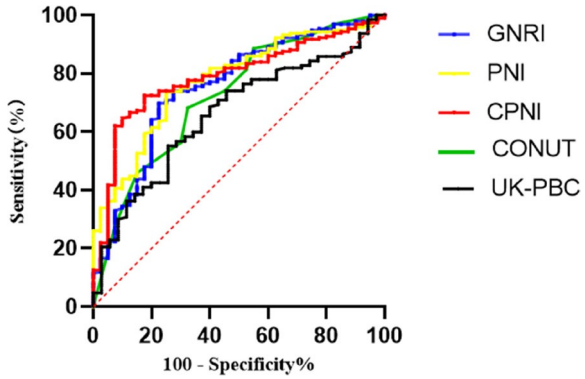


**Fig. 3** The ROC curve of nutrition-relative indicators for predicting overall survival in patients with PBC

progressing steatorrhea leads to malnutrition and slowly progressive weight loss in patients with PBC, which manifests only by general weakness or lower performance for quite a long time [21]. Even a slight nutrient deficiency is accompanied by gradually progressing glycogenolysis and a reduction in glycogenogenesis, which results in the activation of compensatory mechanisms. The latter is aimed at protecting vital organs that require high energy consumption [22]. As a result, reserves of adipose tissue are used as an energy material. The use of fatty acids as an energy material and activation of β-oxidation of fatty acids is accompanied by the development of slowly progressive weight loss and malnutrition in patients with PBC [23, 24]. It is currently believed that PBC is accompanied by dyslipidemia which is the compensatory response of the body to the appearance of bile acids in systemic circulation [25, 26]. A recent serum lipidomic study by LH Zheng et al. [5] suggesting patients with PBC having baseline TC levels above 5.2 mmol/L have unique lipidome characteristics and are at a higher risk of poor clinical outcomes [5]. This also reminds us the need to pay attention to the dyslipidemia of the patients with PBC. This may also be the reason why the CPNI had superior prognostic performance for OS compared to other nutritional indices. Meanwhile, we compared the UK-PBC score with the nutritional score. The results of the UK-PBC score were not as satisfactory as expected. We speculate that this may be due to the relatively small sample size.

BMI is the most widely used and readily available metric for assessing malnutrition in studies of human subjects. Nevertheless, Body Mass Index (BMI) is no longer as widely applicable because emerging nutritional assessment indicators are more effective in

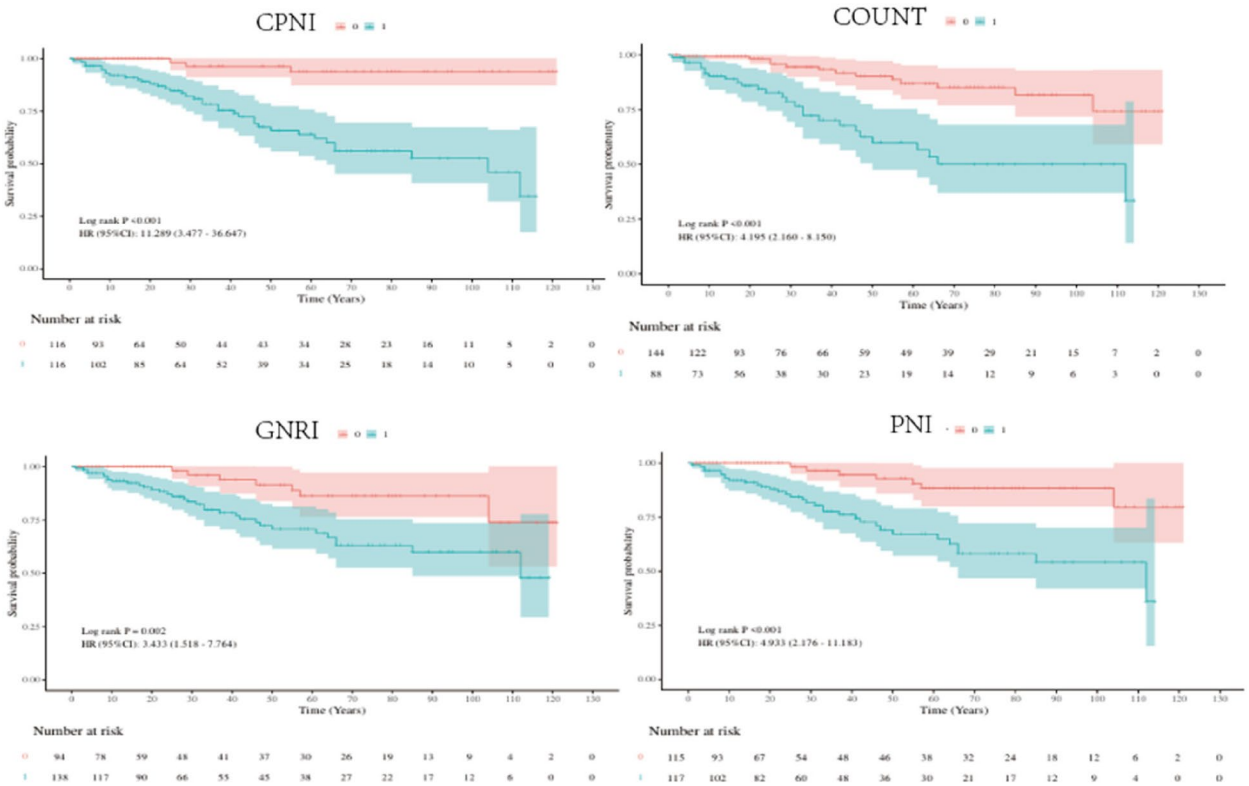


**Fig. 4** Kaplan–Meier curves of PBC patients with and without malnutrition(1,0) based on CPNI, COUNT, GNRI, and PNI indices

identifying malnutrition and offer a more thorough assessment of overall health [27]. CPNI, a recently introduced instrument for nutritional assessment, has demonstrated greater precision and consistency in evaluating the nutritional condition of patients compared to various established nutritional indices [10, 14]. On the other hand, Serum albumin is a broadly recognized indicator for nutrition status, and previous studies documented that the albumin can be used to assess disease progression and prognosis [28, 29]. Its objectivity, derived from routine blood test parameters, and its non-invasive nature, has positioned CPNI as a more promising tool for assessing the nutritional status of PBC patients and for forecasting their outcomes in this study.

Our study also has certain limitations. First, it is a single-center retrospective study. Second, Due to the small sample size, the area under the ROC curve of our UK-PBC score is not satisfied, more large-sample data are still needed in the future to further confirm the relationship between CPNI and the nutritional status and prognosis in patients with PBC. Last but not least, in cirrhosis, albumin and cholesterol are decreased, further research is needed for future validation in advanced liver disease.

In our study, we evaluated the prognostic value of CPNI in primary biliary cholangitis (PBC) patients. We found that CPNI serves as an independent prognostic biomarker. Additionally, we compared the prognostic performance of CONUT, GNRI, PNI, and CPNI in PBC patients. The areas under the ROC curve (AUC) for CONUT, GNRI, PNI, and CPNI were 0.724, 0.755, 0.776, and 0.788, respectively ($P < 0.001$). In conclusion, CPNI is superior to other nutritional scores in the prognostic assessment of PBC patients.

## Supplementary Information

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Supplementary Material 1.

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**Authors' contributions**
Huiling Zhu, Mengyao Zheng and Wenbin Li designed the study and drafted the manuscript. Huiling Zhu, Yaqin Huang, Lili zhang, and Wenting Yang collected the clinical data. Jinhui Yang reviewed the data and revised the manuscript. All authors approved the final version.

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**Data availability**
The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to ethical restrictions.

## Declarations

**Ethics approval and consent to participate**
The present study protocol was approved by the Ethics Committee of the Second Affiliated Hospital of Kunming Medical University. The requirement for informed consent was waived by Ethics Committee of the Second Affiliated Hospital of Kunming Medical University due to retrospective nature of study. The study was conducted in compliance with the Declaration of Helsinki.

**Consent for publication**
Not applicable.

**Competing interests**
The authors declare no competing interests.

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