The C-reactive protein-albumin-lymphocyte (CALLY) index predicts survival in hepatitis B-related hepatocellular carcinoma after radical resection: a propensity score-matched analysis in a Chinese cohort

Keywords
Prognosis, Hepatocellular carcinoma, Hepatitis B virus, CALLY index, Radical resection

Abstract

Introduction

The C-reactive protein–albumin–lymphocyte (CALLY) index has emerged as a promising prognostic tool in various malignancies, yet its role in patients with hepatitis B virus (HBV)-related hepatocellular carcinoma (HCC) remains underexplored. This study aimed to evaluate the association between the preoperative CALLY index and survival outcomes following radical resection in Chinese patients with HBV-related HCC.

Material and methods

In this retrospective cohort study, we included 789 Chinese patients with HBV-related HCC who underwent radical resection. Recurrence free survival (RFS) and overall survival (OS) were assessed using Kaplan–Meier analysis. Multivariable Cox regression and propensity score matching (PSM) were employed to identify independent prognostic factors and minimize confounding bias.

Results

The CALLY index was identified as an independent prognostic factor for both RFS and OS. Compared with the low-CALLY group, the high-CALLY group demonstrated significantly superior 1-, 3-, and 5-year RFS (96.3%, 65.7%, and 43.8% vs. 95.3%, 57.6%, and 35.0%, respectively; P = 0.014) and OS (98.5%, 91.0%, and 66.6% vs. 97.9%, 89.4%, and 56.9%; P = 0.008). These survival benefits remained statistically significant following propensity score matching (PSM) adjustment.

Conclusions

A high preoperative CALLY index is strongly associated with improved survival after radical resection in patients with HBV-related HCC, supporting its utility as an easily accessible prognostic biomarker for clinical risk stratification.

The C-reactive protein-albumin-lymphocyte (CALLY) index predicts survival in hepatitis B-related hepatocellular carcinoma after radical resection: a propensity score-matched analysis in a Chinese cohort

Abstract

Introduction: The C-reactive protein – albumin – lymphocyte (CALLY) index has emerged as a promising prognostic tool in various malignancies, yet its role in patients with hepatitis B virus (HBV)-related hepatocellular carcinoma (HCC) remains underexplored. This study aimed to evaluate the association between the preoperative CALLY index and survival outcomes following radical resection in Chinese patients with HBV-related HCC.

Methods: In this retrospective cohort study, we included 789 Chinese patients with HBV-related HCC who underwent radical resection. Recurrence-free survival (RFS) and overall survival (OS) were assessed using Kaplan–Meier analysis. Multivariable Cox regression and propensity score matching (PSM) were employed to identify independent prognostic factors and minimize confounding bias.

Results: The CALLY index was identified as an independent prognostic factor for both RFS and OS. Compared with the low-CALLY group, the high-CALLY group demonstrated significantly superior 1-, 3-, and 5-year RFS (96.3%, 65.7%, and 43.8% vs. 95.3%, 57.6%, and 35.0%, respectively; $P = 0.014$) and OS (98.5%, 91.0%, and 66.6% vs. 97.9%, 89.4%, and 56.9%; $P = 0.008$). These survival benefits remained statistically significant following propensity score matching (PSM) adjustment.

Conclusions: A high preoperative CALLY index is strongly associated with improved survival after radical resection in patients with HBV-related HCC, supporting its utility as an easily accessible prognostic biomarker for clinical risk stratification.

Keywords: CALLY index; Hepatocellular carcinoma; Hepatitis B virus; Radical resection; Prognosis

Introduction

Hepatocellular carcinoma (HCC) stands as the predominant form of primary liver

cancer and represents the third most fatal malignancy globally[1, 2]. Chronic hepatitis B virus (HBV) infection represents one of the primary etiological factors contributing to the development of HCC, particularly in regions such as East Asia and sub-Saharan Africa[3, 4]. In China, more than 80% of HCC cases are attributable to HBV infection[5]. Current clinical management relies heavily on surgical intervention as the primary curative approach for early-stage cases, owing to limited liver donor availability[6, 7]. However, the high recurrence rate, which may reach up to 70% within five years after resection of HCC, along with approximately 50% of HCC patients experiencing recurrence within two years, significantly compromises the therapeutic outcome[8, 9]. Despite significant advances in therapeutic strategies, including transarterial chemoembolization, programmed death-1/programmed death-ligand 1 inhibitors, and molecular-targeted therapies, the five-year survival rate for patients with HCC remains unsatisfactory. Therefore, a reliable, convenient, and preoperative prognostic biomarker is urgently needed to improve risk stratification and guide individualized clinical decision-making..

In recent years, the prognostic relevance of systemic inflammation and nutritional status in cancer has gained increasing recognition. Inflammation exerts a significant influence throughout the entire spectrum of tumor progression, from initiation to metastasis, and compromises adaptive immune responses[10, 11]. Concurrently, malignancies impose elevated metabolic demands on the host, while cancer-related anorexia and compromised digestive function exacerbate malnutrition, potentially leading to an unfavorable prognosis[12]. Several biomarkers reflecting inflammatory and nutritional status have been linked to survival in various cancers[13-15]. However, most existing prognostic indices rely on one or two parameters and do not comprehensively integrate inflammation, immune competence, and nutritional condition.

Recently, the C-reactive protein–albumin–lymphocyte (CALLY) index has been proposed as a novel composite biomarker that concurrently reflects inflammatory (CRP), nutritional (albumin), and immune (lymphocyte) status. It has shown promising prognostic value in several malignancies[16, 17], as well as in other diseases such as chronic kidney disease[18]. Nevertheless, data specifically focusing on the prognostic role of the CALLY index in Chinese HBV-related HCC after radical resection remain limited. This study aimed to investigate the association between the

preoperative CALLY index and survival outcomes after radical resection in patients with HBV-related HCC.

Methods

Study design and patient selection This retrospective cohort study included consecutive Chinese patients with HBV-related HCC who underwent radical resection between January 2016 and December 2021. This study was approved by the Medical Ethics Committee of Mengchao Hepatobiliary Hospital of Fujian Medical University (No. 2021-035-01). Written informed consent was waived due to the retrospective nature of the study. The inclusion criteria were as follows: (1) histopathologically confirmed HCC with chronic HBV infection; (2) underwent curative (R0) resection; (3) Child-Pugh class A or B liver function; and (4) age between 18 and 70 years. Patients were excluded if they met any of the following criteria: (1) diagnosis of combined hepatocellular-cholangiocarcinoma; (2) history of other malignant tumors; (3) prior receipt of invasive treatments such as transarterial chemoembolization or radiofrequency ablation; (4) presence of multiple intrahepatic metastases, invasion of adjacent organs, or distant metastases; or (5) incomplete clinical data or perioperative mortality.

Data Collection and Definition

The clinical data were retrospectively collected from medical record, including baseline data [(age, sex, body mass index, type 2 diabetes mellitus, excessive alcohol consumption, HBsAg, HBV DNA, alpha-fetoprotein (AFP), albumin, total bilirubin, alanine transaminase, prothrombin time, leukocyte, neutrophil, lymphocyte, monocyte, platelet, CRP, cirrhosis, Child-Pugh grade, Barcelona Clinic Liver Cancer (BCLC) stage, etc.], antiviral treatment, surgical methods (open or laparoscopic), operation time, and tumor characteristics (diameter, number, differentiation, capsule, microvascular invasion, microsatellite lesions, etc.).

Radical resection, or R0 resection, was defined as complete tumor removal with no microscopic residual tumor at the margins, confirmed by histopathological analysis.

HCC recurrence was defined as the presence of new hepatic lesions identified through imaging examinations that fulfilled the diagnostic criteria for HCC. Moreover, the inflammatory-nutritional markers, including CALLY, prognostic nutritional index (PNI), systemic inflammatory response index (SIRI), aggregate systemic inflammation index (AISI), and neutrophil-to-lymphocyte ratio (NLR), were calculated based on clinical parameters. CALLY = albumin (g/l) × lymphocyte (10^9/L) / (CRP (mg/L) × 10), PNI = albumin (g/l) + 5 × lymphocyte (10^9/L), SIRI = (neutrophil × monocyte) / lymphocyte, AISI = (neutrophil × monocyte × platelet)/ lymphocyte, NLR = neutrophil/ lymphocyte.

Follow-up

Patients with HBV-related HCC who underwent radical resection received systematic follow-up evaluations every three months during the first two years, every six months from year two to five, and annually thereafter. The following examinations were performed in each case: biochemical tests, HBV DNA, AFP, and abdominal contrast-enhanced computed tomography or magnetic resonance imaging. The final follow-up was conducted in December 2024. The primary endpoints were recurrence-free survival (RFS), defined as the time from radical resection to radiologically confirmed recurrence, and overall survival (OS), defined as the time from radical resection to death by any or the final follow-up.

Statistical analysis

Continuous variables, presented as medians with interquartile ranges (IQR), were compared using the t-test or Mann-Whitney U test based on distribution normality. Categorical variables, reported as counts (percentages), were analyzed using the χ^2 test or Fisher's exact test according to expected frequencies. The receiver operating characteristic (ROC) curve was constructed, and the optimal cut-off value was determined by maximizing the Youden index. The preoperative CALLY index and other inflammation-related nutritional biomarkers were stratified into high and low groups according to their respective optimal cut-off values. RFS and OS curves were evaluated using Kaplan-Meier curves with log-rank testing for group comparisons.

Cox proportional hazards regression models identified independent prognostic factors for RFS and OS. Propensity score matching (PSM) using a 1:1 nearest-neighbor algorithm with a caliper width of 0.1 standard deviations was rigorously conducted to reduce baseline imbalances between propensity-matched cohorts stratified into low and high CALLY index groups. Variables significant ($P < 0.05$) in univariate analysis were included in multivariate models, with hazard ratios (HR) and 95% confidence intervals (CI) reported. Statistical analyses were performed using R software (version 4.1.1) and the MatchIt package (version 4.3.0). Statistical significance was defined as a two-tailed $P < 0.05$.

Results

Clinicopathological Characteristics

The study cohort comprised 789 patients with HBV-related HCC undergoing radical resection (Figure 1). All patients received preoperative nucleoside/nucleotide analog antiviral therapy. As summarized in Table 1, the majority of patients were male (81.2%), with a median age of 56.0 years (48.0–62.0) and a median body mass index of 23.0 (21.1–24.9). Most patients had an HBV DNA level ≥500 IU/mL (88.8%) and underlying liver cirrhosis (81.1%). Tumor characteristics included a median diameter of 4.0 cm (2.5–6.8), solitary lesions in 87.8% of cases, microvascular invasion in 54.8%, and microsatellite lesions in 22.6%. A complete tumor capsule was observed in only 22.9% of specimens, and 52.5% of tumors were poorly differentiated. According to clinical staging, 89.7% of patients were classified as BCLC stage A and 93.2% as Child–Pugh class A.

RFS and OS after radical resection in patients with HBV-HCC

The median RFS and OS for the cohort were 48.0 months and 66.0 months, respectively. The 1-year, 3-year, and 5-year RFS probabilities were 96.2%, 62.2%, and 39.6%; correspondingly, the 1-year, 3-year, and 5-year OS probabilities were 98.9%, 91.3%, and 62.4% (Figure 2A, B).

ROC curve analysis for comparing prognostic performance of indices

We performed ROC curve analysis to compare the predictive value of the CALLY index with that of other inflammatory nutritional biomarkers, including the PNI, SIRI, AISI, and NLR, for the 5-year overall survival rate of patients with HBV-related HCC after radical resection. The results demonstrated that the CALLY index yielded the largest area under the curve (AUC = 0.713), outperforming the PNI (AUC = 0.630), SIRI (AUC = 0.624), NLR (AUC = 0.618), and AISI (AUC = 0.592). Furthermore, the CALLY index exhibited the highest Youden index (0.377). At an optimal cutoff value of 2.5, the sensitivity and specificity were 75.40% and 62.38%, respectively (Table 2 and Figure 3).***Prognostic factors for RFS after radical resection in patients with HBV-HCC***

Univariate and multivariate Cox regression analyses demonstrated that tumor diameter ≥5 cm, tumor number ≥ 2, BCLC stage B, and low CALLY index were independent risk factors for RFS after radical resection in patients with HBV-related HCC (all $P < 0.05$) (Table 3).

Prognostic factors for OS after radical resection in patients with HBV-HCC

Univariate and multivariate Cox regression analyses demonstrated that tumor diameter ≥ 5 cm, tumor number ≥ 2, poor tumor differentiation, no tumor capsule, and low CALLY index were independent risk factors for OS after radical resection in patients with HBV-related HCC (all $P < 0.05$) (Table 4).

Comparison of Low and High CALLY Groups

Given the significant association between the CALLY index and survival outcomes revealed by Cox regression analysis, we conducted an analysis to further assess its prognostic significance for patients with HBV-related HCC following radical resection. The clinicopathological characteristics of the low CALLY group (n = 402) and the high CALLY group (n = 387) were presented in Table 5. Kaplan-Meier survival analyses demonstrated that the high CALLY group exhibited significantly higher 1-, 3-, and 5-year RFS rates (96.3%, 65.7%, and 43.8%, respectively) compared to the low CALLY group (95.3%, 57.6%, and 35.0%; $P = 0.014$; Figure 4A). Similarly, the high CALLY group showed superior 1-, 3-, and 5-year OS rates (98.5%, 91.0%, and

66.6% vs. 97.9%, 89.4%, and 56.9% in the low CALLY group; $P = 0.008$; Figure 4B).

PSM Analyses for CALLY Index

To address the observed clinicopathological characteristic differences between the low and high CALLY groups, we applied PSM to reduce the impact of potential confounding variables. Following PSM, 628 patients were successfully matched, with 314 patients in each group. No statistically significant differences were observed in baseline characteristics between the two groups (all $P > 0.05$; Table 5). The 1-, 3-, and 5-year RFS rates in the high CALLY group remained higher than those in the low CALLY group (97.4%, 67.4%, and 43.0% vs. 95.2%, 59.1%, and 35.7%; $P = 0.013$; Figure 4C). Similarly, the 1-, 3-, and 5-year OS rates in the high CALLY group were consistently higher than those in the low CALLY group (98.7%, 91.7%, and 66.3% vs. 98.1%, 89.0%, and 54.2%; $P = 0.003$; Figure 4D).

Discussion

This study represents the first large-scale investigation focusing on Chinese patients with HBV-related HCC to comprehensively evaluate the association between the preoperative CALLY index and survival outcomes after radical resection. Our results confirmed that a high preoperative CALLY index was an independent favorable prognostic factor for both RFS and OS, and these prognostic values remained stable after PSM adjustment. These findings highlight that the CALLY index, which comprehensively reflects systemic inflammation, nutritional status, and immune function, can serve as a convenient, low-cost, and robust biomarker for preoperative risk stratification in HBV-related HCC.

The prognostic value of the CALLY index has been gradually verified in a variety of solid tumors. Previous studies have confirmed the prognostic role of the CALLY index in gastric cancer, colorectal cancer, esophageal cancer, pancreatic cancer, and other digestive system malignancies[19-25]. In these tumors, a higher CALLY index consistently indicates lower systemic inflammation, better nutritional reserve, and preserved immune function, which are associated with more favorable survival. This

consistency across cancer types supports the reliability of the CALLY index as a universal immunonutritional prognostic biomarker.

In the field of HCC, several studies have explored the prognostic role of the CALLY index. Iida et al. first reported that the CALLY index was superior to traditional inflammatory markers such as NLR, PLR, and PNI in predicting prognosis after hepatectomy for HCC[26]. Müller et al. validated the prognostic value of the CALLY index in unresectable HCC patients treated with transarterial chemoembolization[27]. More recently, Zhao et al. further demonstrated that the CALLY index had better prognostic performance than the TNM staging system in liver cancer patients[28]. These studies consistently support the effectiveness of the CALLY index as a prognostic biomarker in HCC. However, most previous studies included HCC patients with heterogeneous etiologies and did not use PSM to reduce baseline confounding. In contrast, our study focused exclusively on Chinese HBV-related HCC, the dominant subtype in China and East Asia, and used 1:1 PSM to minimize selection bias and baseline imbalance. Moreover, all patients in our cohort received nucleoside/nucleotide analog antiviral therapy, eliminating confounding effects of antiviral treatment on recurrence and survival. These features enhance the specificity and clinical relevance of our findings for the high-risk HBV-related HCC population.The biological rationale for this association is well-supported. The CALLY index integrates three biologically complementary components: CRP (inflammation), albumin (nutrition), and lymphocyte (immune function). As an acute-phase inflammatory marker, CRP reflects the severity of systemic inflammation and promotes tumor progression and immune suppression[29-31]. Albumin indicates hepatic synthetic function and nutritional status, and hypoalbuminemia is closely associated with postoperative complications and poor survival[32, 33]. Lymphocytes are essential for cellular anti-tumor immunity, and lymphopenia indicates impaired immune surveillance[34, 35]. By combining these three indicators, the CALLY index provides a more holistic and balanced assessment of host physiological status than single or dual-parameter scores, which explains its stable and powerful prognostic performance[21,

[36].This study has several limitations. First, its single-center, retrospective design may introduce selection bias, though the large sample size mitigates this concern. Second, the CALLY index was evaluated only at baseline; postoperative dynamic monitoring could reveal additional prognostic insights. Third, our cohort was restricted to patients undergoing radical resection; the index's value in palliative or non-surgical settings remains to be determined. Fourth, as optimal cutoff values for CALLY may vary, external validation in multicenter prospective cohorts is essential before widespread clinical implementation[37]. Finally, due to the inherent limitations of retrospective data, we could not exclude patients with preoperative acute infections, systemic inflammatory diseases, or those receiving corticosteroids, all of which may independently influence CRP and lymphocyte levels and potentially bias the prognostic assessment of the CALLY index. Thus, further prospective studies are warranted to validate our findings.

In conclusion, the preoperative CALLY index is a robust, independent, and convenient prognostic biomarker for patients with HBV-related HCC after radical resection. Its integrative nature provides a superior reflection of the host's inflammatory, nutritional, and immune status. While promising for risk stratification, its translation into routine clinical practice requires further validation through prospective studies.

Acknowledgments None.

Conflict of interest None.

Data availability statement Data are available upon reasonable request from the first or corresponding author.

References

1. Bray F, Laversanne M, Sung H, et al. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2024;74(3):229-263.

2. Xia C, Dong X, Li H, et al. Cancer statistics in China and United States, 2022: profiles, trends, and determinants. Chinese Medical Journal. 2022;135(5):584-590.
3. Korean Liver Cancer Association (KLCA) and National Cancer Center (NCC) Korea. 2022 KLCA-NCC Korea Practice Guidelines for the Management of Hepatocellular Carcinoma. Korean Journal of Radiology. 2022;23(12):1126-1240.
4. Nwude VN, Lesi OA, Onyekwere C, et al. Clinical Characteristics of Hepatitis B Virus-Associated Hepatocellular Carcinoma Patients in Southwest Nigeria. Pathogens. 2025;14(2):169.
5. Lin J, Zhang H, Yu H, et al. Epidemiological Characteristics of Primary Liver Cancer in Mainland China From 2003 to 2020: A Representative Multicenter Study. Frontiers in Oncology. 2022; 12:906778.
6. Singal A G, Llovet J M, Yarchoan M, et al. AASLD Practice Guidance on prevention, diagnosis, and treatment of hepatocellular carcinoma. Hepatology. 2023,78(6):1922-1965.
7. Yang F, Ma L, Yang Y, et al. Contribution of Hepatitis B Virus Infection to the Aggressiveness of Primary Liver Cancer: A Clinical Epidemiological Study in Eastern China. Frontiers in Oncology. 2019; 9:370.
8. Tanemura A, Noguchi D, Shinkai T, et al. Prognostic significance of early and multiple recurrences after curative resection for hepatocellular carcinoma. BMC Surgery. 2024;24(1):339.
9. Famularo S, Donadon M, Cipriani F, et al. Hepatocellular carcinoma surgical and oncological trends in a national multicentric population: the HERCOLES experience. Updates in Surgery. 2020;72(2):399-411.
10. Bakrim S, Fessikh ME, Elhrech H, et al. Targeting inflammation in cancer therapy: from mechanistic insights to emerging therapeutic approaches. Journal of Translational Medicine. 2025;23(1):588.
11. Akkız H, Şimşek H, Balcı D, et al. Inflammation and cancer: molecular

mechanisms and clinical consequences. Frontiers in Oncology. 2025; 15:1564572.

12. Lu J-N, Zhou L-S, Zhang S, et al. Performance of nutritional and inflammatory markers in patients with pancreatic cancer. World Journal of Clinical Oncology. 2024;15(8):1021-1032.

13. Ding Pa, Yang J, Wu J, et al. Combined systemic inflammatory immune index and prognostic nutrition index as chemosensitivity and prognostic markers for locally advanced gastric cancer receiving neoadjuvant chemotherapy: a retrospective study. BMC Cancer. 2024;24(1):1014.

14. Liu Q-W, Liu L, Hu J-X, et al. Nomogram based on a novel nutritional immune-inflammatory status score to predict postoperative outcomes in esophageal squamous cell carcinoma. World Journal of Gastroenterology. 2025;31(4):101749.

15. Zhao H, Wu J, Wu Q, et al. Systemic immune-inflammation index values are associated with non-melanoma skin cancers: evidence from the National Health and Nutrition Examination Survey 2010-2018. Arch Med Sci. 2024;20(4):1128-1137.

16. Chen D, Ma Y, Li J, et al. Prognostic and clinicopathological significance of C-reactive protein–albumin–lymphocyte (CALLY) in patients with digestive system neoplasms: a systematic review and meta-analysis. World Journal of Surgical Oncology. 2025;23(1):114.

17. Wu B, Liu J, Shao C, et al. Integrating inflammation, nutrition, and immunity: the CALLY index as a prognostic tool in digestive system cancers - a systematic review and meta-analysis. BMC Cancer. 2025;25(1):672.

18. Sun Y, Sun Q, Zheng C, et al. C-reactive protein-albumin-lymphocyte (CALLY) index in chronic kidney disease and mortality: insights into inflammation, nutrition, and immune status. Arch Med Sci. 2026;22(3). doi:10.5114/aoms/216398.19. Liu G, Zhao S, Xia M, et al. The CALLY index as a comprehensive inflammation-nutrition-immunity marker for

prognosis in gastric cancer surgery. Surg Endosc. 2026 Feb 23. doi: 10.1007/s00464-026-12665-0. Epub ahead of print.

20. Ishizuka C, Imaizumi K, Ichikawa N, et al. The CALLY index as a predictive biomarker for the prognosis and treatment outcomes of colorectal cancer. Surg Today. 2026 Feb 11. doi: 10.1007/s00595-026-03254-8. Epub ahead of print.

21. Meng P, Gu T, Xu J, et al. Pretreatment CALLY index as promising novel biomarker in the prediction of surgical and oncological outcomes in esophageal cancer: a multi-center retrospective cohort study. Front Immunol. 2025; 16:1605067.

22. Zhu L, Kong Y, Xing Y, et al. The Prognostic and Early Efficacy Prediction Value of Baseline C-Reactive Protein-Albumin-Lymphocyte (CALLY) Index in Advanced Pancreatic Cancer. International Journal of General Medicine. 2025; 18:3363-3372.

23. Xi P, Huang G, Huang K, et al. The Prognostic Significance of the CALLY Index in Ampullary Carcinoma: An Inflammation-Nutrition Retrospective Analysis. Journal of Inflammation Research. 2025; 18:621-635.

24. Zhang H, Shi J, Xie H, et al. Superiority of CRP-albumin-lymphocyte index as a prognostic biomarker for patients with gastric cancer. Nutrition. 2023; 116:112191.

25. Jia P, Shen F, Zhao Q, et al. Association between C-reactive protein-albumin-lymphocyte index and overall survival in patients with esophageal cancer. Clin Nutr. 2025; 45:212-222.

26. Iida H, Tani M, Komeda K, et al. Superiority of CRP-albumin-lymphocyte index (CALLY index) as a non-invasive prognostic biomarker after hepatectomy for hepatocellular carcinoma. Hpb. 2022;24(1):101-115.

27. Müller L, Hahn F, M Hringer-Kunz A, et al. Immunonutritive Scoring for Patients with Hepatocellular Carcinoma Undergoing Transarterial Chemoembolization: Evaluation of the CALLY Index. Cancers. 2021;13(19):5018.

28. Zhao H, Yin B, Li X, et al. The CRP-albumin-lymphocyte index provides enhanced prognostic value in liver cancer compared to the TNM staging system. Scientific reports. 2025;15(1):20090.
29. Kim E-S, Kim SY, Moon A. C-Reactive Protein Signaling Pathways in Tumor Progression. Biomolecules & Therapeutics. 2023;31(5):473-483.
30. Okumura T, Kimura T, Iwadare T, et al. Prognostic Significance of C-Reactive Protein in Lenvatinib-Treated Unresectable Hepatocellular Carcinoma: A Multi-Institutional Study. Cancers. 2023;15(22):5343.
31. Lin K-Y, Chen Q-J, Tang S-C, et al. Prognostic implications of alpha-fetoprotein and C-reactive protein elevation in hepatocellular carcinoma following resection (PACE): a large cohort study of 2770 patients. BMC Cancer. 2023;23(1):1190.
32. Wang X, Xu J, Zhang H, Qu P. The effect of albumin and hemoglobin levels on the prognosis of early-stage cervical cancer: a prospective, single-center–based cohort study. BMC Women's Health. 2023;23(1):553.
33. Kuhlmann AD, Spies C, Schulte E, et al. Preoperative hypoalbuminaemia in liver surgery: an observational study at a university medical centre. BMJ Open. 2023;13(5): e068405.
34. Ning J, Wang Y, Tao Z. The complex role of immune cells in antigen presentation and regulation of T-cell responses in hepatocellular carcinoma: progress, challenges, and future directions. Frontiers in Immunology. 2024; 15:1483834.
35. Liu X, Qiu Z, Ndhlovu E, et al. Establishing and Externally Validating a Hemoglobin, Albumin, Lymphocyte, and Platelet (HALP) Score-Based Nomogram for Predicting Early Recurrence in BCLC Stage 0/A Hepatocellular Carcinoma Patients After Radical Liver Resection: A Multi-Center Study. Journal of Hepatocellular Carcinoma. 2024; 11:1127-1141.
36. Calder PC, Ortega EF, Meydani SN, et al. Nutrition, Immunosenescence, and Infectious Disease: An Overview of the Scientific Evidence on Micronutrients

and on Modulation of the Gut Microbiota. Advances in Nutrition. 2022;13(5): S1-S26.

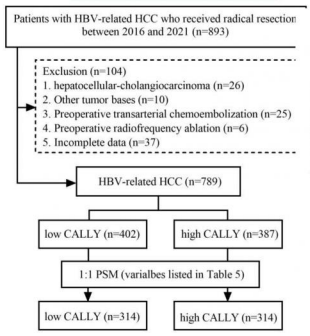
37. Zhu D, Lin Y-D, Yao Y-Z, et al. Negative association of C-reactive protein-albumin-lymphocyte index (CALLY index) with all-cause and cause-specific mortality in patients with cancer: results from NHANES 1999–2018. BMC Cancer. 2024;24(1):1499.

38. Wang S, Liu C, Zheng X, et al. Prognostic value of the C-reactive protein-albumin-lymphocyte index in cancer patients with sarcopenia: A study on overall survival. Nutrition. 2025; 140:112893.

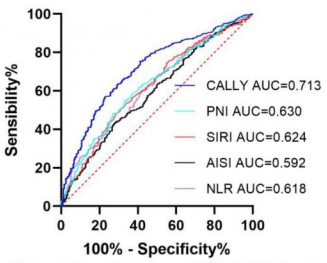
1. Table 1. Clinicopathological characteristics of patients with HBV-related HCC undergoing radical resection
2. Table 2. Comparison of prognostic performance of different indices using ROC curve analysis
3. Table 3. Cox regression analysis of RFS after radical resection in patients with HBV-HCC
4. Table 4. Cox regression analysis of OS after radical resection in patients with HBV-HCC
5. Table 5. Clinicopathological characteristics before and after PSM stratified by CALLY index
6. Figure 1. Flow chart for the selection of the study population
7. Figure 2. Kaplan-Meier curves for RFS (A) and OS (B)
8. Figure 3. Comparison of prognostic performance of different indices using ROC curve analysis
9. Figure 4. Kaplan-Meier curves for RFS and OS stratified by CALLY index before (A, B) and after (C, D) PSM
10. Graphical Abstract. CALLY index predicts prognosis in HBV-related HCC after resection

CALLY index predicts survival in HBV-related HCC after radical resection

Methods/Study design

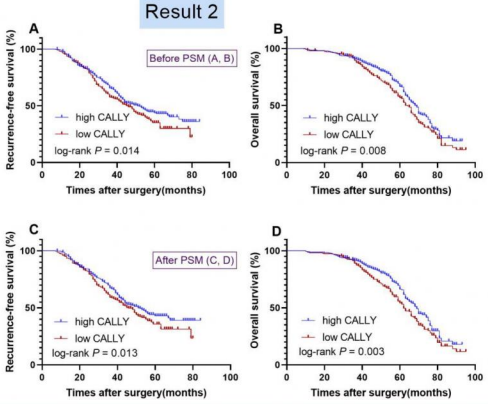


Result 1



Prognostic performance of different indices

Result 2



Abbreviations: AISI, aggregate systemic inflammation index; CALLY, Creactive protein albumin lymphocyte index; HBV, hepatitis B virus; HCC, hepatocellular carcinoma; NLR, neutrophil to lymphocyte ratio; PNI, prognostic nutritional index; PSM, propensity score matching; RFS, recurrence free survival; SIRI, systemic inflammatory response index.

Conclusion The preoperative CALLY index serves as a simple and reliable prognostic biomarker for risk stratification in patients with HBV-related HCC after radical resection.

Table 1. Clinicopathological characteristics of patients with HBV-related HCC undergoing radical resection

Variables	Total (n = 789)	Variables	Total (n = 789)
Age (years)	56.0 (48.0-62.0)	Complete	181 (22.9%)
Male	641 (81.2%)	Incomplete	494 (62.6%)
Body mass index	23.0 (21.1-24.9)	No tumor capsule	114 (14.4%)
Type 2 diabetes mellitus	101 (12.8%)	Microvascular invasion	360 (45.6%)
Excessive alcohol consumed	71 (9.0%)	Microsatellite lesions	184 (23.3%)
HBV DNA ≥ 500 (IU/mL)	701 (88.8%)	BCLC stage	
Antiviral treatment	789 (100%)	0	8 (1.0%)
Albumin (g/L)	39.0 (36.0-42.0)	A	708 (89.7%)
Total bilirubin (μmol/L)	16.3 (12.0-21.9)	B	73 (9.3%)
Alanine transaminase (IU/L)	33.0 (23.0-49.0)	Surgical method	
Prothrombin time (s)	13.3 (12.7-13.9)	Open	368 (46.6%)
AFP (μg/L)	48.0 (6.3-697.4)	Laparoscopic	421 (53.4%)
Cirrhosis	641 (81.2%)	Operation time (min)	120.0 (90.0-160.0)
Child-Pugh grade		Leukocyte count ($\times10^9$/L)	5.8 (4.7-7.1)
A	735 (93.2%)	Neutrophil count ($\times10^9$/L)	3.6 (2.6-4.9)
B	54 (6.8%)	Lymphocyte count ($\times10^9$/L)	1.5 (1.1-1.9)
Tumor diameter (cm)	4.0 (2.5-6.8)	Monocyte count ($\times10^9$/L)	0.4 (0.3-0.5)
Number of tumors		Platelet count ($\times10^9$/L)	163.0 (119.0-213.0)
1	680 (86.2%)	C-reactive protein (mg/L)	2.3 (1.0-7.9)
≥ 2	109 (13.8%)	CALLY	2.7 (0.56-7.0)
Tumor differentiation		PNI	46.6 (42.5-51.1)
Well	12 (1.5%)	SIRI	0.9 (0.6-1.7)
Moderate	363 (46.0%)	AISI	146.5 (81.4-270.6)
Poor	414 (52.5%)	NLR	2.2 (1.6-3.9)
Tumor capsule			

Abbreviations: CALLY, C-reactive protein-albumin-lymphocyte index; PNI, prognostic nutrition index; SIRI, systemic inflammation response index; AISI, aggregate systemic inflammation index; NLR, neutrophil to lymphocyte ratio.

Table 2. Comparison of prognostic performance of different indices using ROC curve analysis

Indices	AUC	95% CI	Youden index	Cut-off value	Sensitivity	Specificity	*P* value
CALLY	0.713	0.675-0.752	0.377	2.5	0.754	0.623	< 0.001
PNI	0.630	0.588-0.672	0.214	46.8	0.546	0.668	< 0.001
SIRI	0.624	0.581-0.666	0.200	0.8	0.672	0.528	< 0.001
AISI	0.592	0.549-0.635	0.154	116.1	0.720	0.435	< 0.001
NLR	0.618	0.576-0.661	0.179	2.4	0.578	0.601	< 0.001

Table 3. Cox regression analysis of RFS after radical resection in patients with HBV-HCC

Variables	Univariate		Multivariate	
	HR (95% CI)	*P* value	HR (95% CI)	*P* value
Age ≥ 60 (years)	1.129 (0.925-1.378)	0.234		
Male	1.046 (0.813-1.346)	0.727		
Excessive alcohol consumed	1.129 (0.832-1.531)	0.436		
HBV DNA ≥ 500 (IU/mL)	1.069 (0.779-1.468)	0.678		
AFP ≥ 400 (μg/L)	1.276 (1.043-1.561)	0.018	1.172 (0.949-1.447)	0.140
Cirrhosis	1.177 (0.910-1.524)	0.215		
Tumor diameter (≥ 5 cm)	1.409 (1.157-1.715)	0.001	1.295 (1.054-1.591)	0.014
Tumor number (≥ 2)	1.475 (1.142-1.904)	0.003	1.367 (1.052-1.775)	0.019
Tumor differentiation (poor vs. well/moderate)	1.105 (0.907-1.347)	0.320		
Tumor capsule (no vs. complete/incomplete)	1.129 (0.858-1.486)	0.387		
Microvascular invasion	1.323 (1.084-1.615)	0.006	1.156 (0.936-1.426)	0.178
Microsatellite lesions	1.393 (1.116-1.739)	0.003	1.187 (0.939-1.501)	0.152
BCLC stage B	1.542 (1.162-2.047)	0.003	1.522 (1.144-2.026)	0.004
Child-Pugh grade A	0.867 (0.578-1.301)	0.491		
Open surgery	0.993 (0.816-1.209)	0.947		
High CALLY (≥ 2.5)	0.777 (0.638-0.947)	0.012	0.811 (0.664-0.989)	0.038
High PNI (≥ 46.8)	0.731 (0.601-0.890)	0.002		
High SIRI (≥ 0.8)	1.263 (1.037-1.538)	0.020		
High AISI (≥ 116.1)	1.278 (1.008-1.497)	0.042		
High NLR (≥ 2.4)	1.211 (0.994-1.474)	0.057		

Abbreviations: RFS, recurrence-free survival; HR, hazard ratio; CI, confidence interval; Other abbreviations as in Table 1.

Table 4. Cox regression analysis of OS after radical resection in patients with HBV-HCC

Variables	Univariate		Multivariate	
	HR (95% CI)	*P* value	HR (95% CI)	*P* value
Age ≥ 60 (years)	1.131 (0.925-1.382)	0.225		
Male	0.943 (0.735-1.210)	0.645		
Excessive alcohol consumed	1.115 (0.652-2.284)	0.608		
HBV DNA ≥ 500 (IU/mL)	1.166 (0.844-1.611)	0.353		
AFP ≥ 400 (μg/L)	1.180 (0.713-1.810)	0.023	1.093 (0.813-1.741)	0.147
Cirrhosis	1.092 (0.847-1.408)	0.493		
Tumor diameter (≥ 5 cm)	1.294 (1.063-1.575)	0.010	1.350 (1.093-1.668)	0.005
Tumor number (≥ 2)	1.104 (1.130-1.869)	0.047	1.427 (1.074-2.342)	0.015
Tumor differentiation (poor vs. well/moderate)	1.404 (1.019-1.508)	0.041	1.092 (1.086-1.764)	0.039
Tumor capsule (no vs. complete/incomplete)	1.254 (1.024-1.528)	0.031	1.388 (1.059-2.286)	0.027
Microvascular invasion	1.128 (1.016-2.126)	0.030	1.303 (0.983-1.982)	0.176
Microsatellite lesions	1.194 (1.030-2.299)	0.012	1.482 (0.848-1.814)	0.227
BCLC stage B	1.232 (1.088-2.670)	0.018	1.256 (0.920-2.028)	0.151
Child-Pugh grade B	1.165 (0.807-1.514)	0.128		
Open surgery	0.952 (0.782-1.560)	0.627		
High CALLY (≥ 2.5)	0.774 (0.636-0.942)	0.009	0.779(0.651-0.972)	0.025
High PNI (≥ 46.8)	0.745 (0.612-0.907)	0.003		
High SIRI (≥ 0.8)	1.307 (1.073-1.592)	0.008		
High AISI (≥ 116.1)	1.136 (0.933-1.383)	0.204		
High NLR (≥ 2.4)	1.283 (1.054-1.561)	0.013		

Abbreviations: OS, overall survival; HR, hazard ratio; CI, confidence interval; Other abbreviations as in Table 1.

Table 5. Clinicopathological characteristics before and after PSM stratified by CALLY index

Variables	Before PSM Process			After PSM Process		
	Low CALLY（n=402）	High CALLY（n=387）	*P* value	Low CALLY（n=314）	High CALLY（n=314）	*P* value
Age (years)	56.0 (48.0-62.0)	57.0 (48.0-62.0)	0.544	56.0 (48.0-63.0)	57.0 (49.0-63.0)	0.274
Male	321 (79.9%)	320 (82.7%)	0.308	256 (81.5%)	262 (83.4%)	0.529
Body mass index	22.8 (20.8-24.8)	23.1 (21.3-25.0)	0.222	22.4 (20.8-24.6)	23.2 (21.3-25.0)	0.072
Type 2 diabetes mellitus	51 (12.7%)	50 (12.9%)	0.922	31 (9.9%)	39 (12.4%)	0.310
Excessive alcohol consumed	42 (10.4%)	29 (7.5%)	0.147	30 (9.6%)	23 (7.3%)	0.315
HBV DNA ≥ 500 (IU/mL)	364 (90.5%)	337 (87.1%)	0.122	284 (90.4%)	274 (87.3%)	0.205
Albumin (g/L)	39.0 (36.0-42.0)	39.0 (36.0-43.0)	0.301	39.0 (36.0-42.0)	39.0 (36.0-42.9)	0.542
Total bilirubin (μmol/L)	16.8 (12.0-21.9)	16.1 (11.8-21.7)	0.600	15.7 (11.7-22.2)	16.5 (12.0-21.9)	0.630
Alanine transaminase (IU/L)	33.0 (23.0-49.3)	33.0 (24.0-48.0)	0.645	33.0 (23.0-50.0)	34.0 (24.0-52.0)	0.880
Prothrombin time (s)	13.4 (12.7-13.8)	13.3 (12.7-13.9)	0.450	13.3 (12.6-13.8)	13.3 (12.8-13.9)	0.480
AFP (μg/L)	52.3 (5.9-530.7)	45.5 (7.1-946.1)	0.981	73.1 (7.2-720.0)	53.3 (7.8-1151.0)	0.925
Cirrhosis	331 (82.3%)	310 (80.1%)	0.421	256 (81.5%)	250 (79.6%)	0.545
Child-Pugh grade			0.035			0.247
A	367 (91.3%)	368 (95.1%)		291 (92.7%)	298 (94.9%)	
B	35 (8.7%)	19 (4.9%)		23 (7.3%)	16 (5.1%)	
Tumor diameter (cm)	4.0 (2.5-7.2)	3.9 (2.6-6.5)	0.350	4.3 (2.9-7.5)	4.0 (2.8-6.5)	0.534
Number of tumors			0.182			0.383
1	340 (84.6%)	340 (87.9%)		274 (87.3%)	281 (89.5%)	
≥ 2	62 (15.4%)	47 (12.1%)		49 (14.2%)	38 (11.0%)	
Tumor differentiation			0.716			0.434
Well	5 (1.2%)	7 (1.8%)		5 (1.3%)	6 (1.9%)	
Moderate	182 (45.3%)	181 (46.8%)		136 (43.3%)	149 (47.5%)	

Poor	215 (53.5%)	199 (51.4%)		174 (55.4%)	159 (50.6%)	
Tumor capsule			0.276			0.170
Complete	90 (22.4%)	91 (23.5%)		72 (22.9%)	73 (23.2%)	
Incomplete	246 (61.2%)	248 (64.1%)		183 (58.3%)	199 (63.4%)	
No tumor capsule	66 (16.4%)	48 (12.4%)		59 (18.8%)	42 (13.4%)	
Microvascular invasion	199 (49.6%)	161 (41.8%)	0.028	153 (48.7%)	133 (42.4%)	0.109
Microsatellite lesions	102 (25.4%)	82 (21.2%)	0.165	78 (24.8%)	70 (22.3%)	0.452
BCLC stage			0.493			0.123
0	3 (0.7%)	5 (1.3%)		1 (0.3%)	5 (1.6%)	
A	358 (89.1%)	350 (90.4%)		281 (89.5%)	286 (91.1%)	
B	41 (10.2%)	32 (8.3%)		32 (10.2%)	23 (7.3%)	
Surgical method			0.617			0.173
Open	191 (47.5%)	177 (45.7%)		151 (48.1%)	134 (42.7%)	
Laparoscopic	211 (52.5%)	210 (54.3%)		163 (51.9%)	180 (54.6%)	
Operation time (min)	125.0 (95.0-165.0)	117.0 (85.0-157.0)	0.206	125.0 (95.0-165.0)	119.0 (85.0-155.0)	0.398
Leukocyte count ($\times 10^9$/L)	5.8 (4.6-7.0)	5.7 (4.7-7.2)	0.430	5.8 (4.7-7.0)	5.8 (4.8-7.2)	0.584
Neutrophil count ($\times 10^9$/L)	3.6 (2.7-4.8)	3.5 (2.6-4.9)	0.102	3.5 (2.7-4.8)	3.6 (2.7-5.0)	0.254
Lymphocyte count ($\times 10^9$/L)	1.5 (1.0-1.9)	1.49 (1.1-2.0)	0.014	1.5 (1.1-2.0)	1.43 (1.0-1.9)	0.231
Monocyte count ($\times 10^9$/L)	0.4 (0.3-0.5)	0.4 (0.3-0.5)	0.111	0.4 (0.3-0.5)	0.4 (0.3-0.5)	0.924
Platelet count ($\times 10^9$/L)	163.0 (116-212.3)	162.0 (121.0-214.0)	0.417	169.0 (123.8-214.0)	160.5 (112.0-213.0)	0.701
C-reactive protein (mg/L)	2.4 (1.1-8.8)	2.2 (0.9-6.9)	0.315	2.2 (0.9-6.8)	2.7 (1.0-8.9)	0.623
PNI	46.3 (42.4-50.3)	47.1 (42.5-52.0)	0.039	46.6 (43.0-51.1)	46.4 (41.5-51.2)	0.287
SIRI	0.9 (0.6-1.6)	0.9 (0.5-1.7)	0.015	0.9 (0.5-1.5)	0.9 (0.6-1.9)	0.248
AISI	151.1 (80.8-280.4)	145.4 (82.1-262.0)	0.127	141.9 (78.7-260.1)	157.1 (94.9-270.7)	0.420
NLR	2.3 (1.7-3.8)	2.2 (1.5-4.1)	0.014	2.2 (1.6-3.5)	2.4 (1.6-4.5)	0.200

Abbreviations: PSM, Propensity score matching; Other abbreviations as in Table 1.

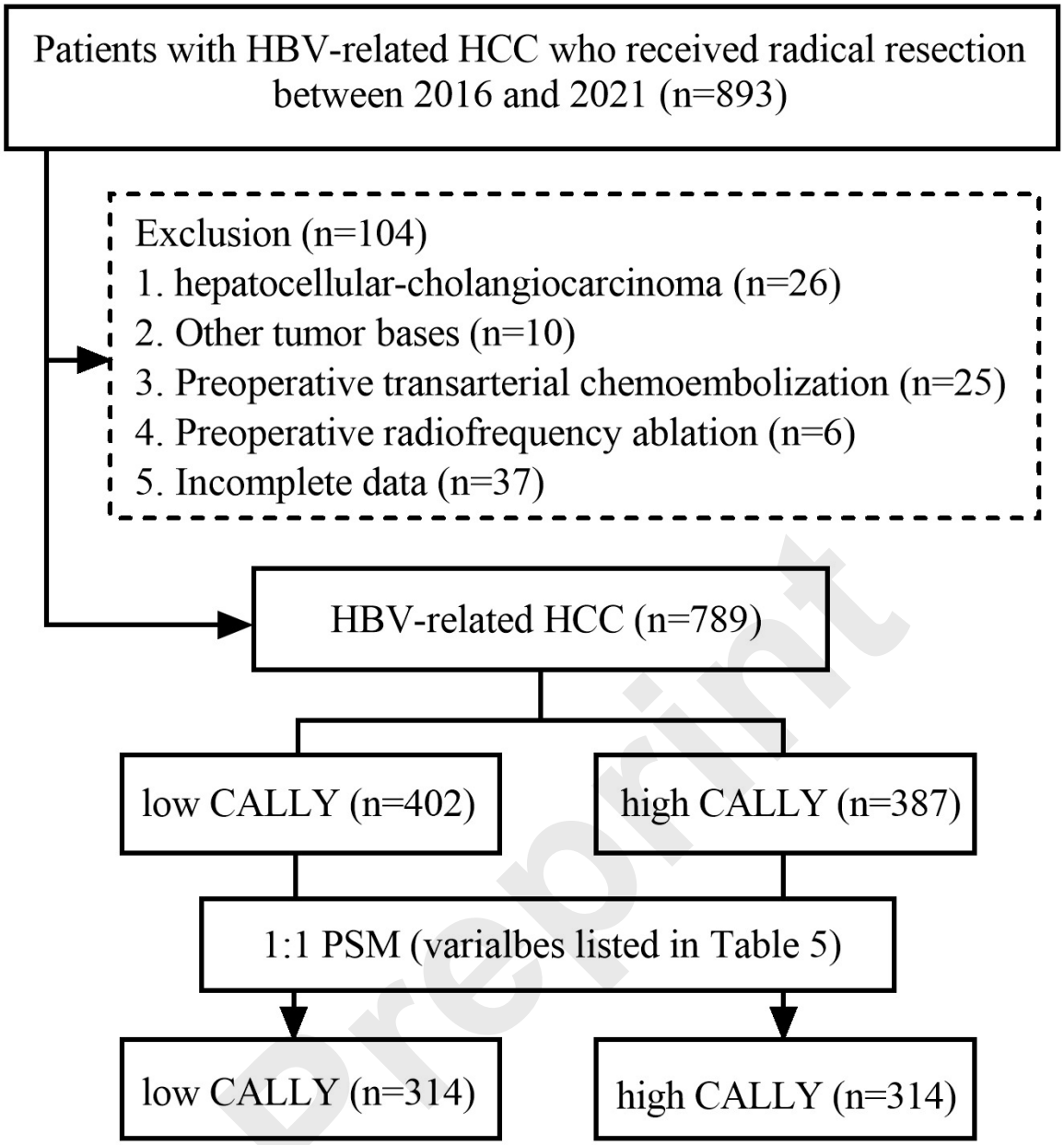


Figure 1. Flow chart for the selection of the study population

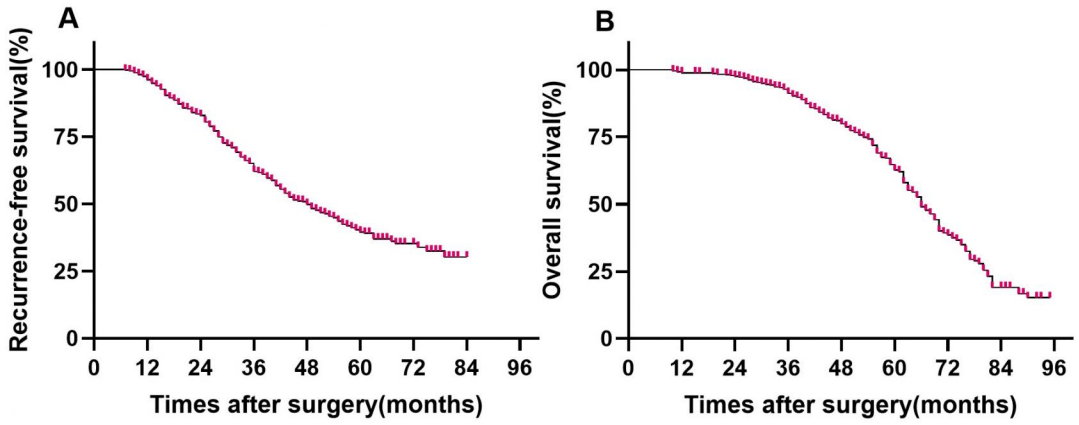


Figure 2. Kaplan-Meier curves for RFS (A) and OS (B)

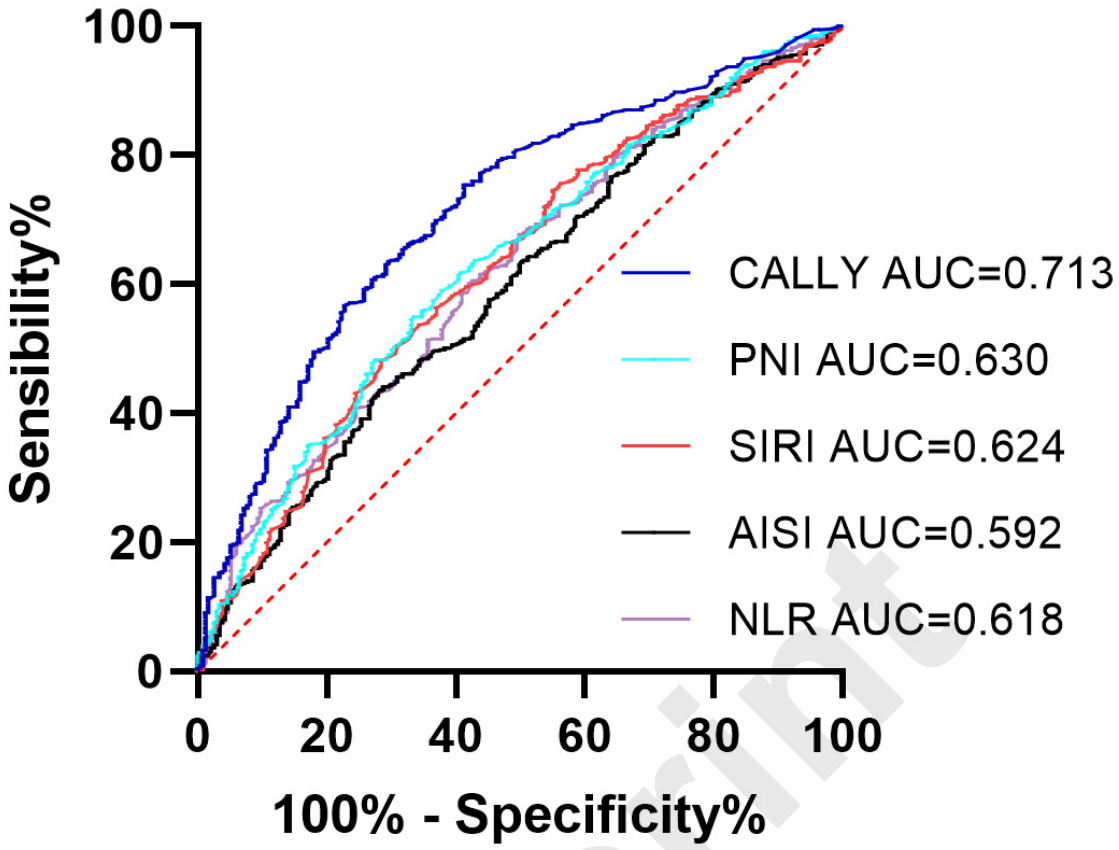


Figure 3. Comparison of prognostic performance of different indices using ROC curve analysis

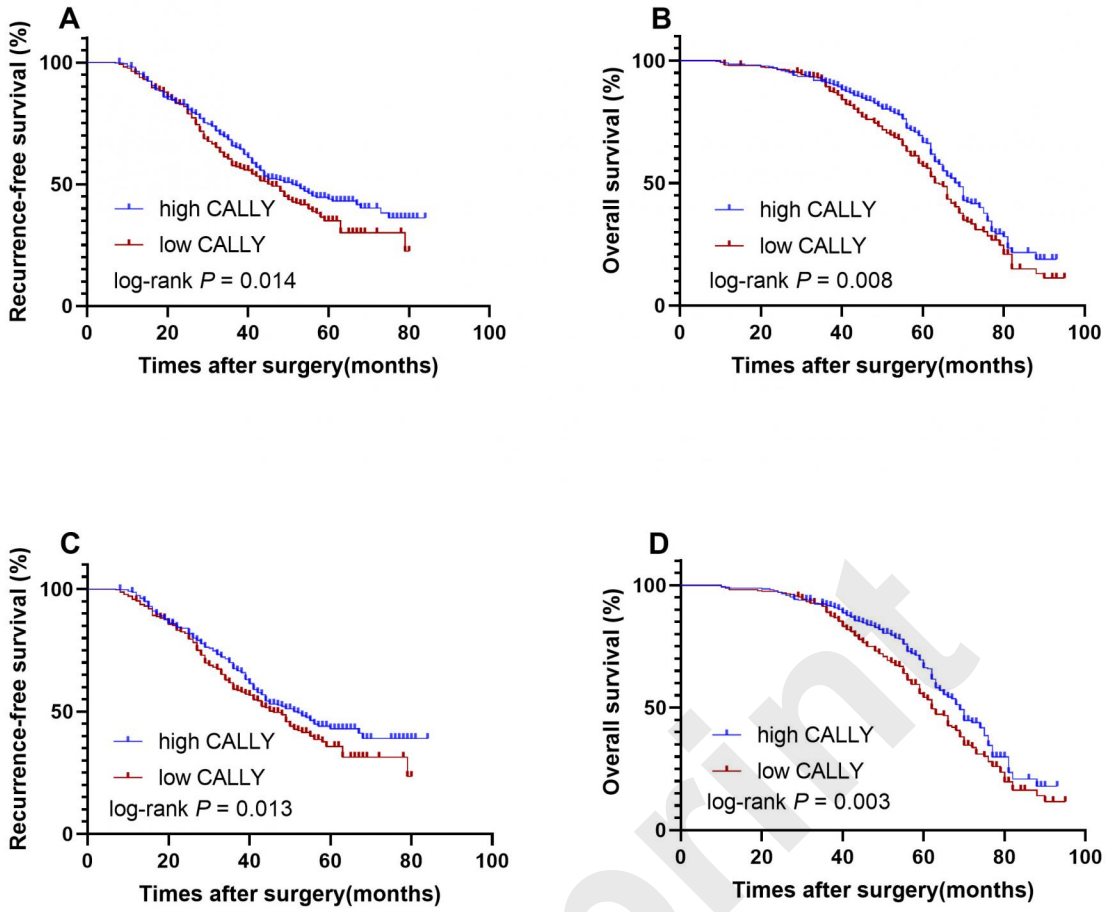


Figure 4. Kaplan-Meier curves for RFS and OS stratified by CALLY index before (A, B) and after (C, D) PSM