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ORIGINAL RESEARCH

IINS Vs CALLY Index: A Battle of Prognostic Value in NSCLC Patients Following Surgery

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Objective: This research sought to assess the predictive potential of the inflammation-immunity-nutrition score (IINS) and the high-sensitivity C-reactive protein-albumin-lymphocyte (CALLY) index in individuals with NSCLC post-surgery.

Methods: The study enrolled 506 patients with NSCLC undergoing R0 resection at the First Affiliated Hospital of Xi'an Jiaotong University. The training cohort was analyzed utilizing X-tile software to identify the ideal threshold values for categorizing high-sensitivity C-reactive protein, albumin, lymphocyte count, and the CALLY index. The predictive significance of the IINS and CALLY index was evaluated through Kaplan–Meier survival curves and univariate and multivariate Cox regression analyses. Predictive capabilities of the IINS and CALLY index were compared utilizing receiver operating characteristic (ROC) curve analysis, time-dependent ROC curve analysis, and decision curve analysis (DCA). Internal validation was performed in the validation cohort and all data from both the training and validation cohorts using Kaplan–Meier curves and DCA.

Results: Patients with lower IINS exhibited prolonged overall survival (OS), whereas those with lower CALLY had shorter OS. Multivariate analysis identified N stage, NSE, and IINS as independent prognostic factors for individuals with NSCLC. ROC analysis revealed that IINS provided superior prognostic performance to CALLY and other traditional indicators (CAR, PLR, and NLR). Time-dependent ROC analyses and DCA further confirmed the superior prognostic value of IINS over the CALLY index at 1, 2, and 3 years.

Conclusion: This study reveals that both the IINS and CALLY index are effective in forecasting the prognosis of individuals with NSCLC following surgery, with the IINS demonstrating superior prognostic efficacy to the CALLY index.

Keywords: NSCLC, prognosis, IINS, CALLY index

Introduction

Lung cancer is the most frequently identified malignancy and the primary contributor to cancer-related mortality worldwide, with non-small cell lung cancer (NSCLC) occupies roughly 85% of instances.[1] Although the availability of various predictive biomarkers for NSCLC prognosis, few are effective, particularly after surgery. Consequently, there is a pressing need to investigate commonly used clinical indices to enhance the precision of prognostic evaluation for patients with NSCLC postoperatively.

Tumor markers such as CEA (Carcinoembryonic Antigen), NSE (Neuron Specific Enolase), and CYFRA21-1 (Cytokeratin 19 fragment) are linked to lung cancer prognosis but do not fully capture patient status.[2] The patient's overall state can be more thoroughly understood by examining the inflammatory response, immune status, and nutritional status, all of which are tied to tumor growth. Recently, various inflammation-nutrition-related immune indicators,

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encompassing the C-reactive protein/albumin ratio (CAR), neutrophil-to-lymphocyte ratio (NLR), and platelet-lymphocyte ratio (PLR), have shown prognostic significance in NSCLC.[3–6] However, these biomarkers, comprising distinct combinations of two serum indicators, fail to fully reflect the comprehensive status of inflammation, immunity, and nutrition within the body.

High-sensitivity C-reactive protein (hsCRP), albumin (ALB), and lymphocyte (LYM) levels are key markers of inflammation, immunity, and nutritional condition in patients. The inflammation-immunity-nutrition score (IINS), derived from these factors, along with the high-sensitivity C-reactive protein-albumin-lymphocyte (CALLY) index, has shown prognostic value (PV) in predicting postoperative outcomes in conditions such as colorectal cancer, hepatocellular carcinoma, and endometrial cancer.[7–12] Recent research has confirmed the PV of the CALLY index in NSCLC,[13] while the PV of the IINS in NSCLC remains undetermined. Additionally, the comparative PV of the IINS and CALLY indices has yet to be comprehensively assessed.

This research examined the PV of the IINS and CALLY index in individuals with NSCLC following surgery. Our findings indicate that both the IINS and CALLY index are valuable tools for predicting postoperative prognosis, with the IINS demonstrating superior prognostic efficacy compared to the CALLY index. Early identification of high-risk patient populations with unfavorable long-term prognoses allows clinicians to implement personalized immune, inflammatory, and nutritional interventions promptly.

Materials and Methodologies

Study Population

This research encompassed 506 individuals detected as having non-small cell lung cancer (NSCLC) at the First Affiliated Hospital of Xi'an Jiaotong University. The inclusion criteria were: (1) a pathology-confirmed diagnosis of NSCLC; (2) age between 18 and 75 years; (3) underwent R0 resection; and (4) no prior treatment before surgery. Exclusion criteria were: (1) incomplete medical and follow-up data; (2) unclear pathological TNM stage; (3) significant inflammatory conditions or immune system disorders; (4) presence of other malignant tumors; and (5) mortality occurring within 30 days after surgery or from non-tumor causes. Patients received care per the National Comprehensive Cancer Network (NCCN) protocols.

All individuals were divided into two cohorts. Initially, a retrospective investigation was performed on the training cohort, comprising 406 patients with NSCLC who underwent R0 resection between February 2008 and March 2013. On the basis of the specified selection criteria, 302 individuals with a minimum three-year follow-up period ending in March 2016 were incorporated. Subsequently, a prospective study, the validation cohort, was designed. In this cohort, 100 randomly selected individuals with NSCLC who underwent R0 resection between January 2018 and January 2021 were considered, and 82 individuals fulfilled the specified inclusion and exclusion parameters. These participants were monitored for a minimum of three years until January 2024. The study design and the patient inclusion flow chart are depicted in Figure 1.

The investigation adhered to the ethical principles set forth in the Helsinki Declaration and informed consent was obtained from all patients and subjects. The research protocol was sanctioned by the Ethics Committee of the First Affiliated Hospital of Xi'an Jiaotong University.

Data Collection

The subjects' clinicopathological features comprised tumor location, age, sex, histological type, differentiation, and pathological stage. Blood indicators encompassed neuron-specific enolase (NSE), carcinoembryonic antigen (CEA), cytokeratin 19 fragment (CYFRA21-1), hsCRP, LYM count, ALB, platelet count (PLT), and neutrophil count (NEUT). Additionally, demographic, clinical, and imaging data were obtained.

Follow-Up and Survival

For the first and second years following lung resection, patients were examined every three months, every six months for the third year, and yearly thereafter. These examinations included regular physical assessments and necessary auxiliary

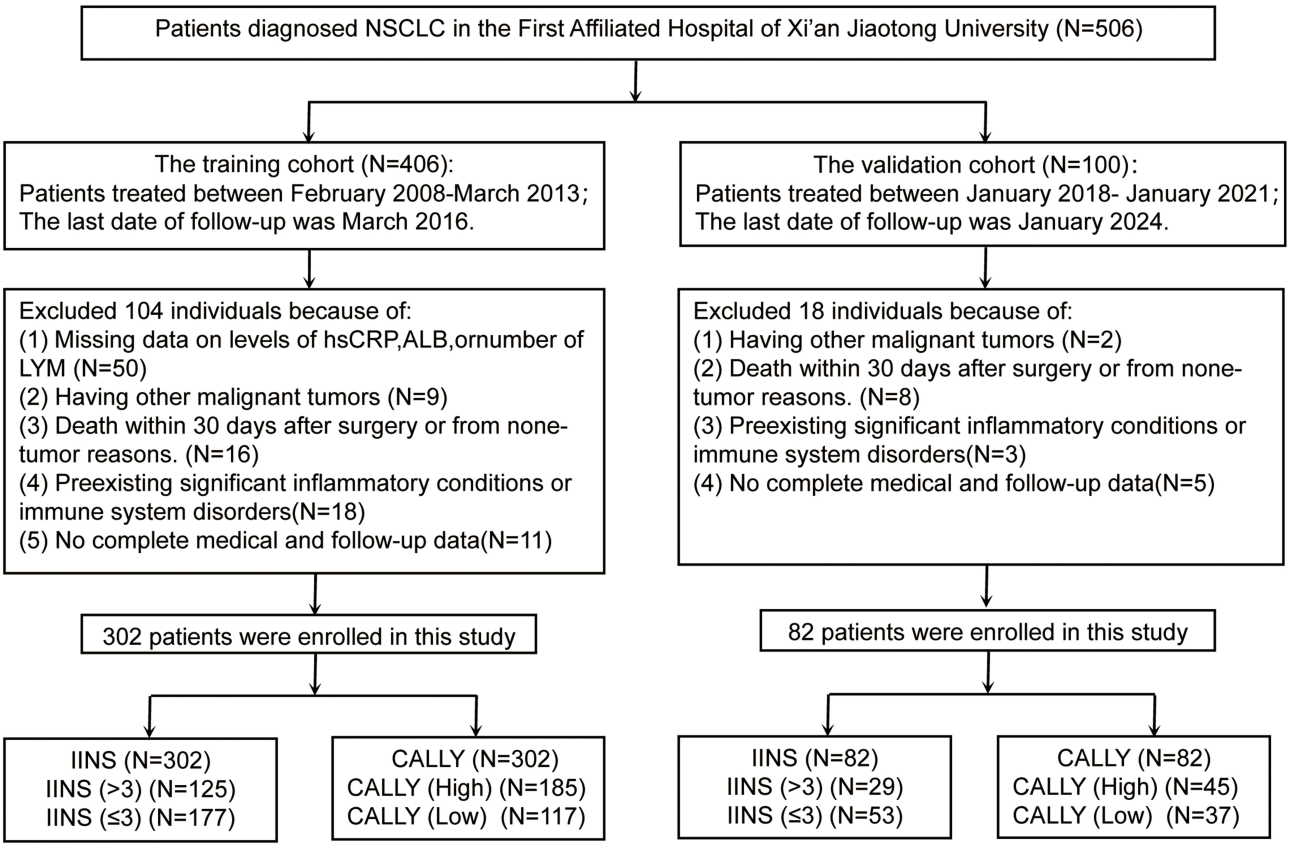

Figure 1 Flowchart of all NSCLC patients enrollment.
Abbreviations: NSCLC, non-small cell lung cancer; IINS, inflammation-immunity-nutrition score; CALLY, high-sensitivity C-reactive protein-albumin-lymphocyte index.

tests, like serum laboratory tests, enhanced computed tomography (CT), or magnetic resonance imaging (MRI). All individuals were monitored for a minimum of 3 years.

The criterion for determining the final result was overall survival (OS), characterized as the duration from the moment of tumor identification to the point of demise, loss of contact, or conclusion of monitoring (March 2016 for the training cohort and January 2024 for the validation cohort).

Calculations

IINS was computed by aggregating the values of hsCRP, LYM, and ALB. Optimal cutoff points for survival prediction were determined for hsCRP, LYM, and ALB based on their association with patient OS, utilizing X-tile software version 3.6.1 (https://medicine.yale.edu/lab/rimm/research/software/). On the basis of the determined cutoffs, hsCRP was classified into three cohorts: score 0 (≤ 2.20 mg/L), score 1 (2.20 mg/L < hsCRP ≤ 3.76 mg/L), and score 2 (> 3.76 mg/L). LYM and ALB classifications were as: LYM - score 0 (> 1.98 × 10^9/L), score 1 (1.00 × 10^9/L < score 1 ≤ 1.98 ×10^9/L), and score 2 (≤ 1.00 × 10^9/L); ALB - score 0 (> 44.20 g/L), score 1 (35.40 g/L < ALB ≤ 44.20 g/L), and score 2 (≤ 35.40 g/L). The IINS was subsequently calculated by aggregating the values of hsCRP, LYM, and ALB, resulting in a range from 1 to 6. In this study, with a median IINS of 3, participants were categorized into two cohorts: the low IINS cohort (IINS ≤ 3) and the high IINS cohort (IINS > 3).

The CALLY metric was computed utilizing the subsequent equation: CALLY = ALB × LYM / (hsCRP × 10). Optimal cutoff points for survival prediction were determined for CALLY utilizing X-tile software version 3.6.1 (https://medicine.yale.edu/lab/rimm/research/software/). On the basis of a single cutoff (Table 1), CALLY was divided into two cohorts: CALLY ≤ 1.38 defined as the Low cohort, and CALLY > 1.38 defined as the High cohort.

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Table 1 Optimal Cutoff Points of Inflammation, Immunity, and Nutrition Indicators Established Through X-Tile Software Version 3.6.1. in the Training Cohort

Variable	Range	N%	Range	N%	Range	N%
hsCRP	≤2.20	33(10.93%)	2.20< and ≤3.76	111(36.75%)	>3.76	158(52.52%)
LYM	≤1.00	38(12.58%)	1.00< and ≤1.98	181(59.93%)	>1.98	83(27.49%)
ALB	≤35.40	41(13.58%)	35.40< and ≤44.20	203(67.21%)	>44.20	58(19.21%)
CALLY	≤1.38	117(38.74%)	>1.38	185(61.26%)		

Abbreviation: CALLY, high-sensitivity C-reactive protein-albumin-lymphocyte index.

Other indices were calculated as follows: CAR = hsCRP / ALB, PLR = PLT / LYM, and NLR = NEUT / LYM. CAR represents the high-sensitivity C-reactive protein / albumin ratio, PLR the platelet / lymphocyte ratio, and NLR the neutrophil / lymphocyte ratio.

Statistical Analysis

The disparities among the two cohorts were evaluated employing the X^2 test, and the rank-sum test was applied for the ordinal data. *P*-values < 0.05 were deemed statistically significant.

Differences in Kaplan–Meier survival plots were evaluated utilizing the Log rank test. Univariate and multivariate Cox proportional hazard models were utilized to identify possible correlations among particular markers and OS of individuals with NSCLC, with associations denoted as hazard ratios (HRs) and 95% confidence intervals (CI). Furthermore, Receiver Operating Characteristic (ROC) curve analysis, time-dependent ROC curve analysis, and decision curve analysis (DCA) were utilized to compare the PVs of IINS and CALLY. All data analyses were assessed utilizing SPSS version 20.0 and R software version 4.2.1.

Results

General Clinicopathological Features of Individuals in the Training Cohort

The data of individuals treated between February 2008 and March 2013 were reviewed, ultimately including 302 subjects in the training cohort. This cohort comprised 207 males and 95 females, with 152 subjects aged ≥ 60 years and 150 subjects aged < 60 years. The cohort included 171 smokers and 131 nonsmokers. The distribution of T-stages was as: T1 (52 subjects), T2 (210 subjects), T3 (28 subjects), and T4 (12 subjects). The N-stages were distributed as follows: N0 (170 subjects), N1 (64 subjects), and N2 (68 subjects). Pathological stages were: I (123 subjects), II (100 subjects), and III (79 subjects). The degrees of differentiation were high (203 subjects), medium (75 subjects), and low or undifferentiated (24 subjects). The pathological types included adenocarcinoma (108 subjects), squamous cell carcinoma (160 subjects), and others, including adenosquamous cell carcinoma (34 subjects) (Table 2).

The Connection Between IINS or CALLY and OS in Individuals with NSCLC in the Training Cohort

Univariate and multivariate Cox regression analyses were conducted on data from 302 patients in the trial cohort, including clinicopathological characteristics and blood biomarkers (Table 3). Univariate analysis of OS identified significant associations with gender ($P = 0.029$), T stage ($P = 0.002$), N stage ($P < 0.001$), differentiation ($P = 0.042$), NSE ($P < 0.001$), PLR (P = 0.003), and IINS ($P = 0.003$). Multivariate analysis, informed by univariate results and clinical practice, further identified N stage (HR: 1.337, 95% CI: 1.049–1.704; $P = 0.019$), NSE (HR: 1.055, 95% CI: 1.044–1.066; $P < 0.001$), and IINS (HR: 1.385, 95% CI: 1.149–1.669; $P = 0.001$) as independent prognostic factors for individuals with NSCLC.

Kaplan–Meier survival analysis and Log rank tests suggested that, in the training cohort, individuals with elevated IINS scores exhibited notably poorer OS in comparison to those with lower IINS scores ($P = 0.001$) (Figure 2A). Conversely, patients with higher CALLY scores exhibited significantly better OS relative to those with diminished CALLY scores ($P = 0.010$) (Figure 2B).

Table 2 General Clinicopathological Feathers of Individuals in the Two Cohorts

Variable	Training Cohort N = 302	%	Validation Cohort N =82	%	*P*-value
Gender					0.965
Male	207	68.54	56	68.29	
Female	95	31.46	26	31.71	
Age					0.465
≥60	152	50.33	45	54.88	
<60	150	49.67	37	45.12	
Smoking					0.910
Yes	171	56.62	47	57.32	
No	131	43.38	35	42.68	
T stage					0.222
1	52	17.22	14	17.07	
2	210	69.54	50	60.98	
3	28	9.27	13	15.85	
4	12	3.97	5	6.10	
N stage					0.757
0	170	56.29	48	58.54	
1	64	21.20	16	19.51	
2	68	22.51	18	21.95	
Pathological stage					0.847
I	123	40.73	34	41.46	
II	100	33.11	24	29.27	
III	79	26.16	24	29.27	
Differentiation					0.093
High	203	67.22	64	78.05	
Medium	75	24.83	11	13.41	
Low or Unknown	24	7.95	7	8.54	
Histological type					0.077
Adenocarcinoma	108	35.76	37	45.12	
Squamous carcinoma	160	52.98	32	39.02	
Others (adenosquamous carcinoma, etc.)	34	11.26	13	15.86	

Abbreviations: IINS, inflammation-immunity-nutrition score; CALLY, high-sensitivity C-reactive protein-albumin-lymphocyte index.

Table 3 Univariate and Multivariate Analyses of the Prognostic Factors for OS in NSCLC Individuals in the Training Cohort

Variable	Univariate analysis		Multivariate analysis	
	HR(95% CI)	*P*-value	HR (95% CI)	*P*-value
Gender	0.590 (0.367,0.949)	0.029*	0.743 (0.456,1.211)	0.233
Age	1.041 (0.992,1.036)	0.228		
Smoking	1.341 (0.888,2.024)	0.163		
T stage	1.527 (1.171,1991)	0.002*	1.086(0.792,1.489)	0.608
N stage	1.624 (1.294,2.039)	0.000*	1.337(1.049,1.704)	0.019*
Differentiation	0.743 (0.557,0.989)	0.042*	0.758(0.559,1.027)	0.074
Histological type	1.162 (0.853,1.581)	0.342		
CEA	0.994 (0.980,1.008)	0.394		
CYFRA21-1	1.000 (0.992,1.008)	0.927		
NSE	1.057 (1.048,1.067)	0.000*	1.055(1.044,1.066)	0.000*

(*Continued*)

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Table 3 (Continued).

Variable	Univariate analysis		Multivariate analysis	
	HR(95% CI)	***P*-value**	**HR (95% CI)**	***P*-value**
CAR	5.470 (0.074,406.864)	0.440		
PLR	1.003 (1.001,1.006)	0.003*		
NLR	1.037 (0.989,1.087)	0.136		
IINS	1.315 (1.101,1.572)	0.003*	1.385(1.149,1.669)	0.001*
CALLY	0.919 (0.776,1.088)	0.327		

Note: *P<0.05.

Abbreviations: CEA, carcinoembryonic antigen; CYFRA21-1, cytokeratin 19 fragment antigen 21-1; NSE, Neuron Specific Enolase; CAR, high-sensitivity C-reactive protein/albumin ratio; PLR, platelet–lymphocyte ratio; NLR, neutrophil–lymphocyte ratio; IINS, inflammation–immunity–nutrition score; CALLY, high-sensitivity C-reactive protein-albumin-lymphocyte index; HR, hazard ratio; CI, confidence interval.

Evaluation of the PV of the IINS and CALLY in the Training Cohort

To evaluate the PVs of IINS, CALLY, and other traditional predictive indicators (CAR, PLR, and NLR) for NSCLC, ROC curves were plotted. The area under the curve (AUC) of the ROC curves demonstrated that IINS (AUC = 0.602, 95% CI: 0.533–0.672, P = 0.004) had superior prognostic performance compared to CAR, PLR, NLR, and CALLY (AUC = 0.460, 95% CI: 0.388–0.532, P = 0.261) (Supplemental Figure 1 and Supplemental Table 1). Furthermore, time-dependent ROC curves for OS indicated that the AUC for IINS (Figure 3A) was 0.621, 0.614, and 0.603 at 1, 2, and 3 years, respectively, while the AUC for CALLY (Figure 3B) was 0.418, 0.433, and 0.446 at the same time points. For a risk factor, an AUC > 0.5 indicates better prognostic accuracy, with values closer to 1 indicating better performance. Conversely, for a protective factor, an AUC < 0.5 indicates better prognostic accuracy, with values closer to 0 being optimal. Clearly, the AUC values for IINS were superior to those for CALLY at 1, 2, and 3 years.

DCA was employed to elevate the clinical value of the prognostic models or variables (ie, patient benefit). When comparing multiple models, the model that consistently provides a greater net benefit (difference in y-values) at a specific x–value is deemed superior. Notably, in the training cohort, the DCA curves for IINS were consistently higher than those for CALLY at 1, 2, and 3 years (Figure 4A-C), indicating that IINS provided a larger net benefit for survival prediction compared to CALLY with regard to OS.

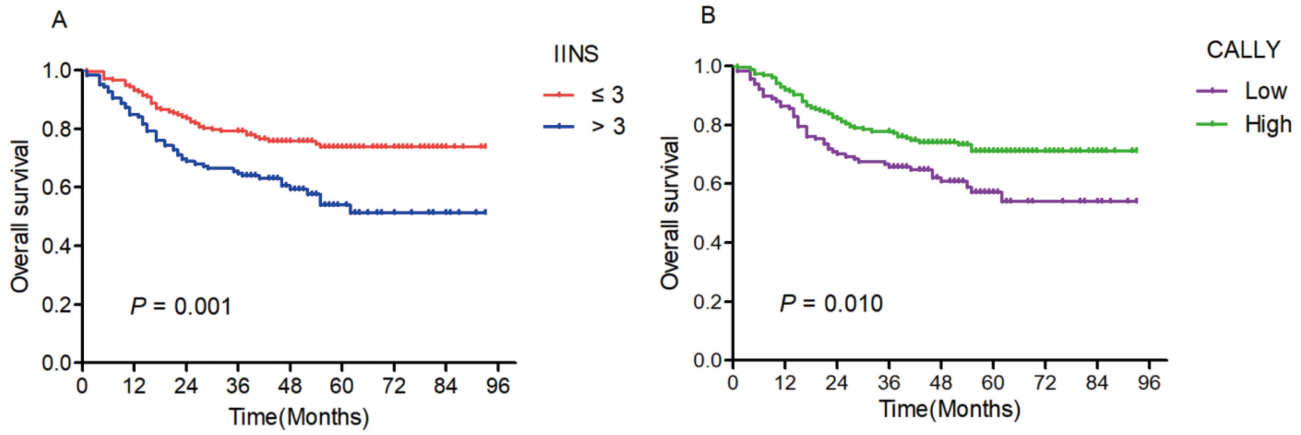

Figure 2 Kaplan–Meier overall survival (OS) curves for IINS and CALLY individuals in the training cohort. (**A**) Kaplan–Meier curve of IINS for OS; (**B**) Kaplan–Meier curve of CALLY for OS.

Abbreviations: IINS, inflammation-immunity-nutrition score; CALLY, high-sensitivity C-reactive protein-albumin-lymphocyte index.

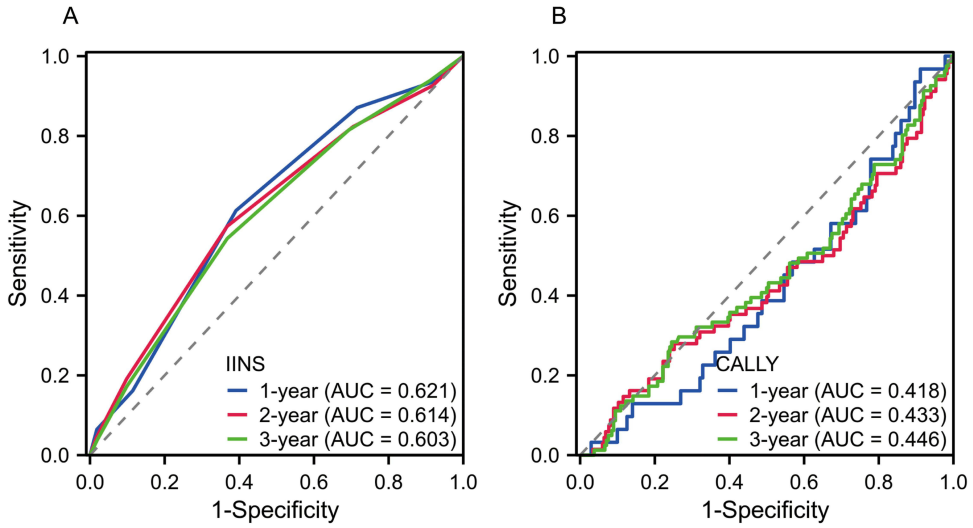

Figure 3 Time-dependent ROC curves of overall survival (OS) for IINS and CALLY patients in the training cohort. (**A**) Time-dependent ROC curve of OS for IINS patients. (**B**) Time-dependent ROC curve of OS for CALLY patients.
Abbreviations: IINS, inflammation-immunity-nutrition score; CALLY, high-sensitivity C-reactive protein-albumin-lymphocyte index.

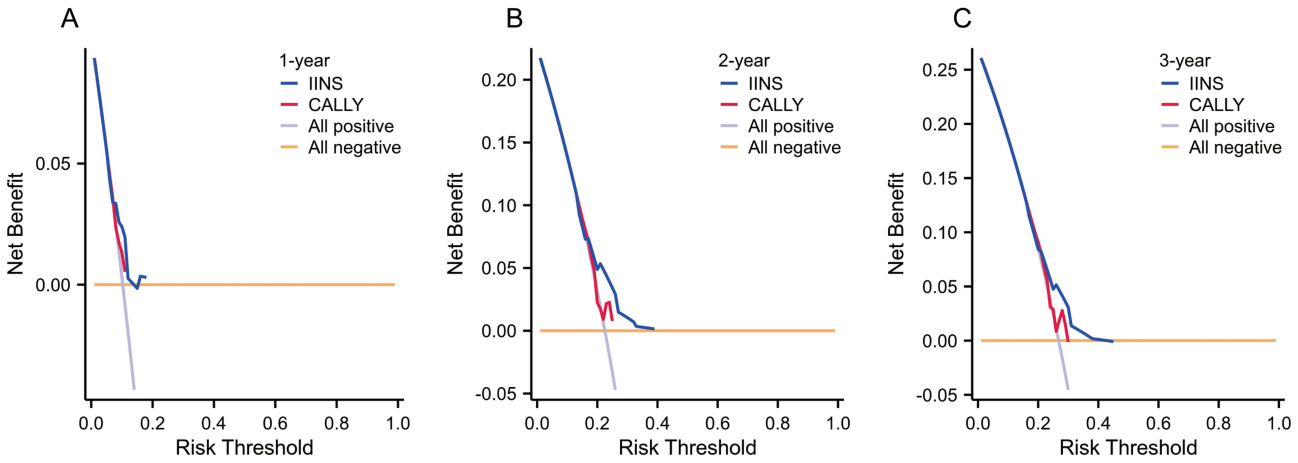

Figure 4 Decision curve analysis (DCA) of models in the training cohort for overall survival (OS). (**A**) Comparison of IINS and CALLY for predicting 1-year survival; (**B**) comparison of IINS and CALLY for predicting 2-year survival; (**C**) comparison of IINS and CALLY for predicting 3-year survival.
Abbreviations: IINS, inflammation-immunity-nutrition score; CALLY, high-sensitivity C-reactive protein-albumin-lymphocyte index.

Further Validation in the Validation Cohort

The validation cohort, a prospective study, utilized cutoff points derived from the retrospective analysis of the training cohort. Among patients treated from January 2018 to January 2021, 100 were randomly selected for the validation cohort. After applying inclusion and exclusion criteria, 82 patients were ultimately selected and monitored for a minimum of 3 years, with the final follow-up in January 2024.

In the prospective study, IINS was categorized into cohorts with scores ≤ 3 and > 3, based on the hsCRP, LYM, and ALB cutoff points established in the training cohort. Similarly, patients with CALLY ≤ 1.39 were defined as the low subgroup, and those with CALLY > 1.39 as the high subgroup. Table 2 demonstrates that the demographic and clinicopathological features of individuals in both cohorts were comparatively uniform, exhibiting no statistically meaningful disparities (*P*-values for all parameters > 0.05).

Survival analyses, encompassing Kaplan–Meier analysis and Log rank tests, displayed statistically meaningful disparities in survival among individuals with varying IINS and CALLY ratings ($P = 0.008$ and $P = 0.006$, respectively). Individuals possessing elevated IINS scores exhibited worse OS compared to those with lower IINS scores (Figure 5A), while Individuals

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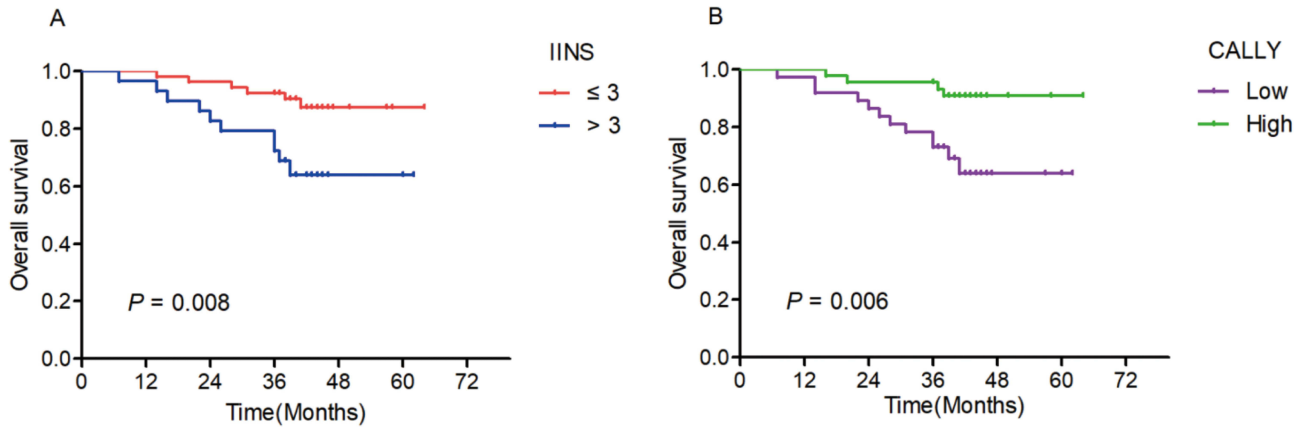

Figure 5 Kaplan–Meier survival curves for overall survival (OS) in individuals in the validation cohort with IINS and CALLY. (**A**) Kaplan–Meier curve of IINS for OS; (**B**) Kaplan–Meier curve of CALLY for OS.
Abbreviations: IINS, inflammation-immunity-nutrition score; CALLY, high-sensitivity C-reactive protein-albumin-lymphocyte index.

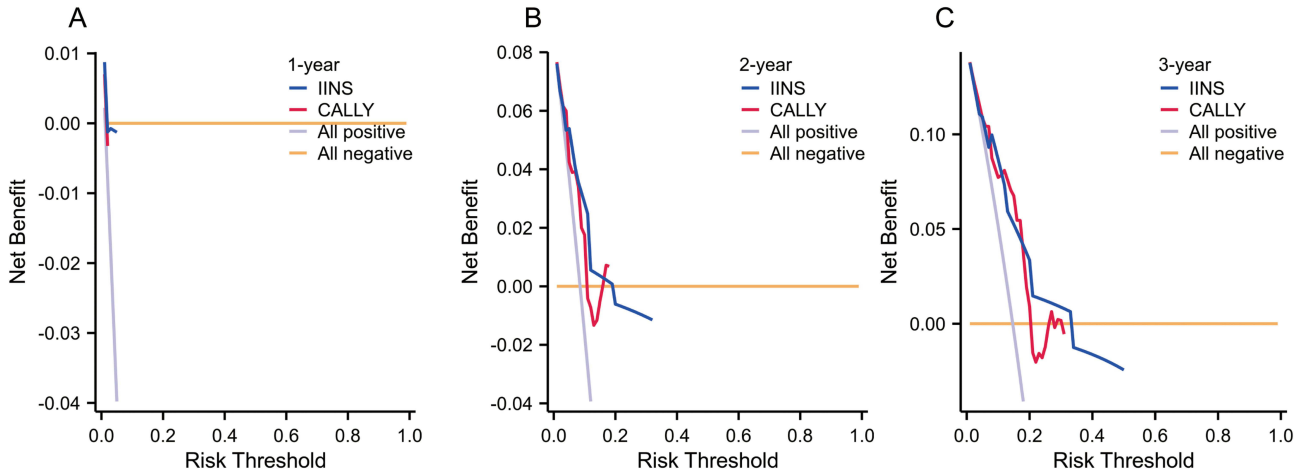

Figure 6 Decision curve analysis (DCA) of models in the validation cohort for overall survival (OS). (**A**) Comparison of IINS and CALLY for predicting 1-year survival; (**B**) Comparison of IINS and CALLY for predicting 2-year survival; (**C**) Comparison of IINS and CALLY for predicting 3-year survival.
Abbreviations: IINS, inflammation-immunity-nutrition score; CALLY, high-sensitivity C-reactive protein-albumin-lymphocyte index.

possessing elevated CALLY scores displayed better OS relative to those with lower CALLY scores (Figure 5B), consistent with the conclusions from the retrospective studies.

The DCA demonstrated that in the training cohort, the IINS model consistently outperformed the CALLY model in terms of net benefit at 1, 2, and 3 years (Figure 6A–C). These findings indicate that IINS may offer greater PV for individuals with NSCLC, aligning with conclusions from similar retrospective studies.

In the analysis, data from the training and validation cohorts were pooled. Survival analysis, encompassing Kaplan–Meier analysis and Log rank tests, displayed statistically significant differences in survival among individuals with different IINS and CALLY scores ($P < 0.001$ and $P = 0.001$, respectively). Individuals with elevated IINS scores had worse OS compared to those with lower IINS scores (Supplemental Figure 2A). Conversely, patients with higher CALLY scores exhibited better OS than those with lower CALLY scores (Supplemental Figure 2B), consistent with findings from similar retrospective studies.

The DCA confirmed that in the combined cohort, the IINS model curves consistently surpassed the CALLY model curves in net benefit at 1, 2, and 3 years (Supplemental Figure 3). These findings reinforce that IINS provides superior prognostic utility for patients with NSCLC, in line with conclusions from previous retrospective analyses.

Discussion

Nutritional status, inflammation, and immune status significantly impact cancer progression and prognosis.[3–6] Studies have shown that immune suppression, nutritional imbalances, or severe inflammatory conditions lead to poorer outcomes in patients with cancers. IINS and the CALLY index, calculated based on hsCRP, ALB, and LYM indices, serve as prognostic tools. Recent research has established the PV of the CALLY index in individuals with NSCLC,[13] yet the PV of IINS in predicting postoperative outcomes remains unexplored. This investigation evaluates the prognostic utility of IINS and CALLY in individuals with NSCLC undergoing surgery and compares their predictive capabilities.

HsCRP, a protein produced and released by hepatic cells, functions as an acute-phase reactant. Its expression is minimal in healthy individuals but significantly elevated during infections or acute trauma.[14] Elevated hsCRP levels have been linked to unfavorable outcomes in individuals with patients.[15,16] LYM, essential components of the immune system, include subtypes such as CD8+ T cells, helper T cells, and regulatory T cells, which maintain immune balance. Increased peripheral blood LYMs in malignant tumors correlate with improved prognosis,[17] and elevated tumor-infiltrating LYMs also suggest a better prognosis.[18] Similarly, serum ALB concentration reflects nutritional status.[19] Tumor-induced wasting and inflammation often decrease serum ALB levels in patients with cancers, impairing immune responses and promoting cancer growth.[19,20] A previous study has indicated a favorable association between serum ALB concentration and survival in individuals with NSCLC.[21] Kaplan–Meier survival analysis in this study showed that subjects with lower IINS scores had better OS compared to those with higher IINS scores. Low IINS scores are associated with low hsCRP levels, elevated LYM concentrations, and high serum ALB levels, consistent with established theories. The CALLY index showed an inverse relationship with hsCRP while demonstrating a direct association with ALB and LYM. Based on these correlations, patients with lower CALLY scores are expected to have a poorer prognosis, and our Kaplan–Meier survival analysis confirmed this conclusion.

To compare the PV of the IINS and CALLY, the AUC of the ROC curves was first analyzed, showing that the IINS had superior prognostic performance compared to CAR, PLR, NLR, and CALLY. Additionally, the time-dependent ROC curves for OS indicated that the AUC for IINS was better than that for CALLY at 1, 2, and 3 years. While ROC curves assess a model's accuracy based on sensitivity and specificity, DCA also considers clinical utility and patient benefit. This study demonstrated that the DCA model curves for IINS patients consistently surpassed those for CALLY patients at 1, 2, and 3 years, indicating that IINS provided a greater net benefit for survival prediction. Unlike simply categorizing recurrence risk as "high" or "low", such detailed prognostic results offer more compelling and useful insights, serving as important reference indicators for developing personalized treatment plans. A high IINS (>3 score) indicates that related therapy and vigilant monitoring ought to be taken into account.

IINS and CALLY can assist healthcare professionals in promptly identifying high-risk NSCLC patients with poor prognosis, facilitating the timely development of personalized immune-boosting, anti-inflammatory, and nutritional pre-treatment strategies. Currently, there are several clinical reports on interventions related to these actions. Research by Roszik J.[22] et al. Indicates that NSAIDs improve the overall survival of NSCLC patients. A systematic review and meta-analysis of 27 randomized controlled trials show that thymosin α1, and concomitant chemotherapy is beneficial to the patient, and provide evidence for optimal treatment regimens that may increase patient quality of life and survival.[23] Li M find that Perioperative nutritional intervention by Human Albumin can improve the albumin levels.[24] In addition, there are some reports related to traditional Chinese medicine treatments. Liu ZJ[25] et al found that carpus-ankle acupuncture combined with Erchen decoction significantly relieved symptoms, improved behavioral status, restored immune function, reduced inflammatory response, and improved quality of life in patients after radical lung cancer surgery, with a high degree of safety. Hu YF[26] et al conducted a retrospective analysis and showed Heat-sensitive moxibustion combined with Qi-Replenishing and Yin-Nourishing Decoction can improve the nutritional status and immune function of patients with lung cancer. Chen XI[27] et al conducted a randomized, double-blind study, which showed that modified Maimendong decoction can enhance immune function and strengthen the antitumor effect in lung cancer patients, thereby improving their quality of life. However, there are no studies focused on personalized comprehensive treatment addressing immunity, inflammation, and nutrition in patients with non-small cell lung cancer. In addition, existing studies have focused primarily on quality of life rather than survival. In future studies, we will explore the impact of personalized

integrated traditional Chinese and Western medicine treatment on the survival of non-small cell lung cancer patients, thus further validating our model.

The strengths of this study include the following: (1) It explored the prognostic effects of the IINS and CALLY, which are composite indices composed of hsCRP, ALB, and LYM, in patients with lung cancer and compared their efficacy. (2) The selected blood indices—hsCRP, ALB, and LYM—serve as ideal biomarkers due to their ease of acquisition, noninvasiveness, low cost, patient acceptance, and suitability for long-term follow-up. (3) This ambispective cohort study included both a training cohort and a validation cohort, significantly enhancing the reliability of the statistical analysis and facilitating model generalizability. Notwithstanding its merits, the investigation exhibits certain constraints. The mono-institutional approach restricts the caliber of the information and could potentially introduce prejudices. Additionally, the critical values of hsCRP, ALB, and LYM reported in this study may vary depending on sample selection, necessitating further studies to determine the most appropriate critical values.

Conclusion

The IINS outperformed the CALLY index in prognostic power for patients with NSCLC post-surgery. Both IINS and CALLY are easily accessible scoring tools that aid medical professionals in promptly recognizing individuals with high-risk NSCLC with poor prognoses, facilitating the timely development of personalized immune, inflammatory, and nutritional pretreatment strategies.

Data Sharing Statement

The data that support the findings of this study are not publicly available due to privacy and ethical restrictions but are available from the corresponding author upon reasonable request.

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Disclosure

The researchers affirm that they have no competing interests concerning the investigation, composition, or dissemination of this scholarly work.

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