

Prognostic Significance of Albumin-to-Neutrophil-to-Lymphocyte Ratio in Cancer Patients: Associations with Cachexia, Severe Malnutrition and Survival Outcomes

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Abstract

Background: This study aims to develop and validate a new inflammation-related indicator - the albumin/neutrophil-to-lymphocyte ratio (ANLR) through a multicenter cohort study. The study assesses the prognostic value of this indicator for the overall survival (OS) of cancer patients, as well as its association with severe malnutrition, cachexia, and Karnofsky Performance Status (KPS).

Methods: Kaplan–Meier and Cox proportional hazards regression analyses assessed the relationship between ANLR and OS. Restricted cubic spline (RCS) analysis was performed to evaluate nonlinear dose–response associations. Stratified forest plots were used to assess subgroup-specific effects and interaction terms. Logistic regression was applied to examine the associations of ANLR with cachexia and severe malnutrition. Sensitivity analyses were conducted after excluding patients who died within the early follow-up period.

Results: A total of 16,444 patients were randomly assigned to training ($n = 11,511$) and external validation ($n = 4,933$) cohorts. An ANLR cutoff of 10 was identified by ROC analysis ($AUC = 0.628$). High ANLR was associated with significantly better OS than low ANLR in both the training (60.7% vs. 38.7%) and validation cohorts (61.8% vs. 39.4%, $P < 0.001$). Higher ANLR independently predicted improved overall survival in the training ($HR = 0.644$, 95% CI: 0.603–0.688) and validation cohorts ($HR = 0.651$, 95% CI: 0.589–0.719, $P < 0.001$). RCS analysis demonstrated a nonlinear inverse association between ANLR and mortality risk ($P < 0.001$). High ANLR was associated with reduced risks of cachexia (discovery cohort: adjusted OR = 0.613, 95% CI: 0.556–0.675; validation cohort: adjusted OR = 0.646, 95% CI: 0.557–0.744), severe malnutrition (discovery cohort: adjusted OR = 0.429, 95% CI: 0.388–0.474; validation cohort: adjusted OR = 0.463, 95% CI: 0.398–0.538) and KPS score (discovery cohort: adjusted $\beta = 0.409$, 95% CI: 0.191–0.627; validation cohort: adjusted $\beta = 0.669$, 95% CI: 0.336–1.001), all $P < 0.001$.

Conclusion: ANLR is a simple composite biomarker that can independently predict the overall survival of cancer patients. It is correlated with cachexia, severe malnutrition, and a reduced risk of deteriorating physical condition, and shows stable predictive effects in different tumor types and stages.

Introduction

The global burden of malignant tumors continues to rise. In 2024, more than 20.9 million new cancer cases and over 10.6 million cancer-related deaths were reported worldwide¹. Malignant tumors have become one of the leading causes of death globally, imposing a substantial burden on healthcare systems worldwide^{2,3}. At present, the TNM staging system is widely used in clinical practice as the fundamental framework for guiding surgical management and radiotherapy or chemotherapy strategies. However, this system primarily reflects the local biological characteristics of tumors and does not adequately capture systemic pathological disturbances in the host. In patients with advanced cancer, chronic systemic inflammation, progressive skeletal muscle wasting, and malnutrition are common and

interrelated pathological features that collectively contribute to the development of cancer cachexia, impair treatment tolerance, reduce quality of life, and shorten survival^{4–6}. Therefore, a comprehensive and reliable tool is urgently needed to assess patients' inflammatory and nutritional status, enable early identification of high-risk individuals, facilitate prognostic risk stratification, and guide individualized clinical interventions.

Tumor-related chronic inflammation is a core hallmark of malignancy and plays a key driving role in cancer initiation, invasion, metastasis, and treatment resistance^{7,8}. The tumor microenvironment releases large amounts of proinflammatory cytokines, such as IL-6 and TNF- α , which promote peripheral neutrophil proliferation and lymphocyte apoptosis, leading to an increased neutrophil-to-lymphocyte ratio (NLR). Elevated NLR reflects suppressed antitumor immunity and excessive inflammatory activation and has been confirmed by multiple meta-analyses and multicenter cohorts to be associated with poor prognosis in various solid tumors, but this index reflects immune imbalance alone and does not capture the host's nutritional reserve^{9–13}. Serum albumin (ALB), synthesized by the liver, is the most widely used clinical marker of visceral nutritional status and has also been associated with poor outcomes in patients with cancer^{14–17}. Hypoalbuminemia indicates long-term inadequate protein intake and enhanced systemic muscle catabolism, directly reducing tolerance to antitumor therapy and increasing the risks of infectious complications and short-term mortality. Nevertheless, albumin levels are readily affected by non-tumor confounders, including chronic liver disease, kidney disease, and fluid retention, which limits their predictive performance when used alone.

Systemic inflammation and nutritional impairment are closely interrelated in patients with cancer ANLR and represent important determinants of treatment tolerance, quality of life, and long-term survival. Malnutrition not only exacerbates systemic inflammatory responses but also substantially increases the risks of postoperative complications, treatment interruption, and mortality^{18,19}. Systemic inflammation and nutritional imbalance should not be considered isolated processes; rather, they interact bidirectionally and jointly contribute to the progression of cancer²⁰. Compared with single biomarkers, composite indices that integrate inflammatory and nutritional dimensions may provide a more comprehensive assessment of the host response to malignancy and offer improved prognostic discrimination. Several inflammation- and nutrition-related biomarkers have been investigated in cancer prognosis, including the Glasgow Prognostic Score (GPS), C-reactive protein-to-albumin ratio (CAR), prognostic nutritional index (PNI), and neutrophil-to-lymphocyte ratio (NLR)²¹. By incorporating inflammatory and nutritional information to varying degrees, these indices may provide better prognostic discrimination than individual markers, such as NLR or albumin alone. Among these markers, NLR and albumin are two of the most widely used clinical indicators of systemic inflammation and nutritional status, respectively. Multiple studies have demonstrated that an elevated NLR is significantly associated with increased tumor aggressiveness, poor treatment response, and unfavorable prognosis in patients with cancer^{22,23}. Hypoalbuminemia has been identified as an independent predictor of postoperative complications, chemotherapy intolerance, and all-cause mortality in patients with cancer. The albumin-to-neutrophil-to-lymphocyte ratio (ANLR), calculated by integrating albumin and NLR, simultaneously

reflects host nutritional reserves and systemic inflammatory status. To date, no large-scale multicenter cohort study has systematically evaluated the prognostic value of ANLR in patients with cancer. Moreover, the development and validation of an individualized prognostic prediction tool based on ANLR have not yet been reported.

In summary, by integrating ALB and NLR, the present study developed a novel inflammation-related index, ANLR, and systematically evaluated its ability to predict overall survival (OS) in patients with cancer, while validating its independent prognostic value after adjustment for potential confounders. In addition, we examined the dose–response relationship between ANLR and mortality risk, assessed its stability across different cancer types and TNM stages, and explored its clinical relevance to cancer cachexia and severe malnutrition. This study aimed to address the lack of multicenter evidence regarding ANLR in cancer prognosis and to provide a novel, accessible biomarker and clinical tool for prognostic risk stratification, individualized treatment, and supportive interventions in patients with cancer.

Materials and Methods

Study Design and Study Population

This multicenter retrospective cohort study used de-identified clinical data from the Investigation on Nutrition Status and Clinical Outcome of Common Cancers (INSCOC) database, registered with the Chinese Clinical Trial Registry (ChiCTR1800020329). The INSCOC database systematically collects data on the nutritional status and long-term clinical outcomes of patients with common malignancies from multiple medical institutions in China, providing a robust pan-cancer data resource for prognostic and nutrition-related research. To ensure rigorous model development and validation, eligible patients were divided into a discovery cohort and a validation cohort. After screening according to predefined inclusion and exclusion criteria, a total of 16,444 eligible patients were included and randomly assigned at a 7:3 ratio using a random number table, with 11,511 patients allocated to the training cohort and 4,933 patients allocated to the independent validation cohort (Fig. 1). Eligible participants were required to meet the following criteria: (1) age ≥ 18 years at cancer diagnosis; (2) pathologically or cytologically confirmed malignant tumor of any type; (3) available peripheral blood inflammatory and nutritional marker data, including NLR and ALB, after the initial diagnosis; (4) complete clinical and follow-up data, including demographic characteristics, tumor characteristics, treatment regimens, and survival outcomes; and (5) written informed consent to participate in the INSCOC project and permit the use of clinical data for research purposes. The exclusion criteria were as follows: (1) missing serum biochemical data at enrollment; (2) acute or chronic inflammatory diseases affecting neutrophil or albumin levels; (3) a history of autoimmune disease; and (4) missing baseline medical data. The study protocol was approved by the institutional review boards of all participating medical centers, and all procedures were conducted in accordance with the ethical principles of the Declaration of Helsinki.

Definition of the ANLR Index

The ANLR was calculated as follows: serum albumin (g/L) ÷ NLR; the neutrophil-to-lymphocyte ratio (NLR) was calculated as peripheral blood neutrophil count ($\times 10^9/L$) ÷ lymphocyte count ($\times 10^9/L$).

Definition of Cachexia

Cachexia was diagnosed according to the 2023 criteria of the Asian Working Group for Cachexia (AWGC). Patients meeting any of the following conditions were diagnosed with cachexia: $\geq$ weight loss > 5% within 6 months, or weight loss > 2% when BMI < 20 kg/m²; $\geq$ at least one of the following: sarcopenia (assessed by bioelectrical impedance analysis, with skeletal muscle index < 7.0 kg/m² for men and < 5.7 kg/m² for women), anorexia, or elevated inflammatory markers (such as CRP > 5 mg/L)²⁴.

Definition of Malnutrition

Malnutrition was assessed using the Patient-Generated Subjective Global Assessment (PG-SGA). This scale is a validated tool specifically designed for patients with chronic diseases and integrates patient-reported data (such as weight change, food intake, and eating-related symptoms) with clinician assessment findings (such as muscle/fat status). According to standardized criteria and previous validation results, severe malnutrition was defined as a total PG-SGA score > 8, indicating significant nutritional deficiency that usually requires urgent intervention²⁵.

Definition of the Karnofsky Performance Status (KPS) Score

The Karnofsky Performance Status (KPS) score was used to assess patients' physical functional status and ability to perform daily activities. This scale is a standardized assessment tool widely used in oncology and chronic disease practice and can objectively reflect patients' self-care ability, physical activity level, and degree of disease-related functional impairment. It is an effective evaluation system for assessing performance status, guiding the selection of antitumor treatment strategies, and predicting prognosis²⁶.

Follow-up and Outcome

All enrolled patients underwent standardized follow-up to document survival status and clinical outcomes. Follow-up data were obtained through outpatient visits, telephone interviews, electronic medical records, and review of hospitalization and discharge documents. The follow-up schedule was standardized as follows: every 3 months during the first 2 years after cancer diagnosis, every 6 months from years 3 to 5, and annually thereafter until the study endpoint.

The primary outcome was OS, defined as the time from pathological or cytological confirmation of malignancy to death from any cause or the last available follow-up. For patients who were lost to follow-up or remained alive at the last follow-up, OS was censored at the date of the last valid follow-up. Secondary outcomes included: (1) cancer cachexia, diagnosed according to the 2023 AWGC consensus criteria; (2) severe malnutrition, defined as a PG-SGA score > 8, based on a validated tool for comprehensive nutritional assessment in patients with cancer. and (3) KPS score, used to assess patients' physical functional status and ability to perform daily activities. All outcome data were independently extracted and verified by two trained researchers. Any discrepancies were resolved by consensus with a senior clinical investigator to ensure data accuracy and reliability.

Statistical Analysis

Continuous variables with a normal distribution are presented as the mean $\pm$ standard deviation (SD), and between-group comparisons were performed using the independent-samples t test. Non-normally distributed variables are presented as the median and interquartile range (IQR), and between-group comparisons were performed using the Mann–Whitney U test. Categorical variables are presented as frequencies and percentages, and between-group differences were assessed using the χ^2 test. Using overall survival as the endpoint, the optimal cutoff value for ANLR was determined in the discovery cohort by receiver operating characteristic (ROC) curve analysis. Overall survival curves were generated using the Kaplan–Meier method, and survival differences between groups were compared using the log-rank test. The independent prognostic value of ANLR was evaluated using Cox proportional hazards regression models, with results reported as hazard ratios (HR) and 95% confidence intervals (CI). Restricted cubic spline (RCS) models were used to assess the potential nonlinear association between continuous ANLR and the risk of all-cause mortality. Stratified subgroup analyses were performed according to tumor type, TNM stage, and demographic characteristics, and stratified Cox models were used to evaluate the consistency of the prognostic effect of ANLR across subgroups. To assess the robustness of the findings, all regression analyses were repeated after excluding patients who died within the first 3 months of follow-up. Binary logistic regression models were used to examine the associations between ANLR and secondary clinical outcomes, including cancer cachexia and severe malnutrition, and odds ratios (OR) with 95% CIs were calculated. Multiple linear regression models were used to estimate regression coefficients (β) and 95% CIs for the association between ANLR and the KPS score. All statistical analyses were performed using R software (version 4.3.1). All tests were two-sided, and $P < 0.05$ was considered statistically significant.

Results

Baseline Characteristics

A total of 16,444 participants were included in the final analysis, comprising 11,511 patients in the discovery cohort and 4,933 in the validation cohort. No statistically significant differences were observed between the two cohorts in age, sex, tumor distribution, comorbidities, or laboratory parameters (all $P >$

0.05), indicating that baseline characteristics were well balanced and comparable (**Table S1**). In the training cohort, the median age was 58.0 years (IQR, 50–65), and 54.8% of patients were male. Lung cancer, colorectal cancer, and gastric cancer were the three most common tumor types. ROC curve analysis identified 10 as the optimal cutoff value for ANLR, with ANLR showing acceptable predictive performance in the discovery cohort (AUC = 0.628) (**Figure S1**). According to this cutoff value, patients were stratified into the low-ANLR group (< 10) and high-ANLR group (≥ 10), comprising 3,149 and 8,362 patients in the discovery cohort and 1,421 and 3,511 patients in the validation cohort. Significant differences in baseline characteristics were observed between the low- and high-ANLR groups. Compared with patients in the high-ANLR group, those in the low-ANLR group were older, were more frequently male, and had a significantly higher proportion of stage IV disease, as well as higher prevalences of hypertension, diabetes, smoking, and alcohol consumption. Regarding tumor distribution, lung cancer, colorectal cancer, and gastric cancer were more common in the low-ANLR group, whereas pancreatic cancer was relatively less common. Laboratory profiles in the low-ANLR group were characterized by lower albumin levels, higher neutrophil counts, lower lymphocyte counts, and higher NLR values. The low-ANLR group had higher PG-SGA and NRS2002 scores, an approximately twofold higher incidence of cachexia (2,196 vs. 1,368), a significantly higher incidence of severe malnutrition, and lower KPS scores (all $P < 0.001$) (**Table S2**).

Kaplan–Meier survival analysis of ANLR

Kaplan–Meier survival analysis consistently demonstrated a strong association between ANLR and OS in both the discovery cohort and the external validation cohort (log-rank $P < 0.001$). In the discovery cohort, patients with high ANLR had a significantly higher 5-year OS rate than those with low ANLR (60.7% vs. 38.7%) (Fig. 2A). This survival advantage was replicated in the validation cohort, where the 5-year OS rate was 61.8% in the high-ANLR group and 39.4% in the low-ANLR group (Fig. 2B). Subgroup survival analyses further confirmed the robust prognostic stratification ability of ANLR across cancer types. In the discovery cohort, tumor subtype-specific survival analyses were conducted for 11 common cancer types, including lung cancer, esophageal cancer, gastric cancer, hepatobiliary cancer, pancreatic cancer, colorectal cancer, breast cancer, gynecological tumors, urinary system tumors, nasopharyngeal carcinoma, and other malignancies. Patients in the low-ANLR group had significantly shorter OS than those in the high-ANLR group across all tumor types (all $P < 0.05$) (Fig. 3). A similar pattern was observed in the validation cohort. In analyses of the same 11 cancer types, patients with low ANLR had significantly shorter OS than those with high ANLR in most cancer types, except pancreatic cancer and breast cancer (all $P < 0.05$) (**Figure S2**). These findings highlight low ANLR as an adverse prognostic factor across multiple cancer types. ANLR also demonstrated stable prognostic performance across all TNM stages. In the discovery cohort, patients in the low-ANLR group had worse survival outcomes than those in the high-ANLR group, and OS rates progressively declined from stage I to stage IV. Low ANLR was consistently associated with poorer prognosis across all stages ($P < 0.05$) (**Figure S3**). A similar trend was observed in the validation cohort, where low ANLR was significantly associated with worse prognosis than high ANLR across all TNM stages ($P < 0.05$) (**Figure S4**).

Dose–Response Relationship Between ANLR and OS

RCS models integrated with Cox proportional hazards regression were used to examine the dose–response relationship between continuous ANLR levels and the risk of all-cause mortality. In the discovery cohort, RCS analyses consistently demonstrated a stable inverse association between ANLR and mortality risk across all three adjusted models. Both the nonlinearity test and the overall association test were statistically significant ($P < 0.001$) (Fig. 4). Similar findings were observed in the validation cohort, in which the log hazard ratio curve progressively declined with increasing ANLR levels, further confirming a significant inverse dose–response relationship between ANLR and all-cause mortality risk in patients with cancer ($P < 0.001$) (**Figure S5**).

Cox Regression Analysis of the Association Between ANLR and OS

In the discovery cohort, continuous-variable analysis showed that, after full adjustment for covariates in Model c, each one-standard-deviation increase in ANLR was associated with a 29.5% reduction in the risk of adverse prognosis among patients with cancer (HR = 0.705, 95% CI: 0.604–0.823, $P < 0.001$). Dichotomous analysis further showed that patients in the high-ANLR group had significantly better survival outcomes than those in the low-ANLR group. Although the HRs increased slightly with progressive covariate adjustment, the associations remained statistically significant across all models: Model a (unadjusted: HR = 0.477, 95% CI: 0.448–0.508, $P < 0.001$), Model b (HR = 0.638, 95% CI: 0.597–0.680, $P < 0.001$), and Model c (fully adjusted: HR = 0.644, 95% CI: 0.603–0.688, $P < 0.001$). Quartile analysis further demonstrated a significant graded association between ANLR and all-cause mortality. After full adjustment for covariates in Model c, the risk of all-cause mortality decreased progressively across increasing ANLR quartiles. Compared with patients in the lowest ANLR quartile (Q1), those in the highest quartile (Q4) had a 43.7% lower risk of death (HR = 0.563, 95% CI: 0.512–0.619, $P < 0.001$), indicating a clear risk gradient (Table 1). In the validation cohort, multivariable Cox regression analysis showed that dichotomized ANLR remained an independent prognostic factor for OS after adjustment for all confounding factors (HR = 0.651, 95% CI: 0.589–0.719, $P < 0.001$). Quartile analysis also showed a progressive reduction in the risk of adverse prognosis with increasing ANLR quartiles (HR = 0.595, 95% CI: 0.515–0.687, $P < 0.001$) (Table 2). Sensitivity analysis after excluding 693 patients who died within the first 3 months of follow-up further confirmed the robustness of these findings. Whether analyzed as a continuous, dichotomous, or quartile variable, ANLR remained an independent prognostic factor in patients with cancer, with statistically significant HRs across all adjusted models ($P < 0.001$) (**Table S3**).

Table 1
Association between ANLR and survival of patients with cancer at discovery cohort.

ANLR	Model a HR (95%CI)	p value	Model b HR (95%CI)	p value	Model c HR (95%CI)	p value
Continuous (per SD)	0.332 (0.275, 0.399)	< 0.001	0.672 (0.574, 0.786)	< 0.001	0.705 (0.604, 0.823)	< 0.001
Cutoff value						
C1 (< 10)	ref		ref		ref	
C2 ($\geq$ 10)	0.477 (0.448, 0.508)	< 0.001	0.638 (0.597, 0.680)	< 0.001	0.644 (0.603, 0.688)	< 0.001
Quartiles						
Q1 (< 9.323)	ref		ref		ref	
Q2 (9.323–16.289)	0.652 (0.602, 0.705)	< 0.001	0.723 (0.668, 0.783)	< 0.001	0.722 (0.666, 0.782)	< 0.001
Q3 (16.289–24.930)	0.440 (0.404, 0.480)	< 0.001	0.596 (0.546, 0.651)	< 0.001	0.599 (0.548, 0.655)	< 0.001
Q4 ($\geq$ 24.930)	0.369 (0.337, 0.405)	< 0.001	0.553 (0.503, 0.606)	< 0.001	0.563 (0.512, 0.619)	< 0.001
p for trend		< 0.001		< 0.001		< 0.001
Notes:						
Model a: No adjusted.						
Model b: Adjusted for age, sex, BMI, TNM stage, tumor type.						
Model c: Adjusted for age, sex, BMI, TNM stage, tumor type, chronic hepatitis, diabetes, hypertension, cardiovascular disease, chronic nephrosis, family history, smoking, drinking, education level, marital status, surgery, chemotherapy, radiotherapy.						

Table 2
Association between ANLR and survival of patients with cancer at validation cohort.

ANLR	Model a HR (95%CI)	p value	Model b HR (95%CI)	p value	Model c HR (95%CI)	p value
Continuous (per SD)	0.646 (0.546, 0.764)	< 0.001	0.920 (0.825, 1.026)	0.135	0.937 (0.843, 1.041)	0.227
Cutoff value						
C1 (< 10)	ref		ref		ref	
C2 ($\geq$ 10)	0.461 (0.419, 0.507)	< 0.001	0.647 (0.586, 0.714)	< 0.001	0.651 (0.589, 0.719)	< 0.001
Quartiles						
Q1 (< 8.945)	ref		ref		ref	
Q2 (8.945–15.771)	0.686 (0.609, 0.772)	< 0.001	0.827 (0.733, 0.932)	0.002	0.832 (0.737, 0.939)	0.003
Q3 (15.771–24.287)	0.449 (0.394, 0.512)	< 0.001	0.645 (0.564, 0.739)	< 0.001	0.648 (0.566, 0.742)	< 0.001
Q4 ($\geq$ 24.287)	0.372 (0.323, 0.427)	< 0.001	0.583 (0.506, 0.672)	< 0.001	0.595 (0.515, 0.687)	< 0.001
p for trend		< 0.001		< 0.001		< 0.001
Notes:						
Model a: No adjusted.						
Model b: Adjusted for age, sex, BMI, TNM stage, tumor type.						
Model c: Adjusted for age, sex, BMI, TNM stage, tumor type, chronic hepatitis, diabetes, hypertension, cardiovascular disease, chronic nephrosis, family history, smoking, drinking, education level, marital status, surgery, chemotherapy, radiotherapy.						

Subgroup Forest Plot Analysis

Forest plots derived from multivariable Cox regression analyses further demonstrated that ANLR remained an independent prognostic factor across most clinical subgroups in both the discovery and validation cohorts (Fig. 5), underscoring its broadly applicable prognostic value in diverse cancer populations. In subgroups stratified by age (< 65 vs. $\geq$ 65 years), sex, hypertension or diabetes status, smoking status, TNM stage (I–IV), and receipt of surgery, radiotherapy, or chemotherapy, high ANLR consistently acted as a protective factor for OS ($P < 0.001$).

Logistic Regression Analysis of the Association Between ANLR and Cachexia

To explore the association between ANLR and cachexia across different cancer types, box plots were generated to visualize the distribution of ANLR levels in patients with and without cachexia. Across multiple major cancer types, including lung cancer, bronchial cancer, esophageal cancer, liver cancer and intrahepatic cholangiocarcinoma, colorectal cancer, female breast cancer, gynecological cancers, and urinary system cancers, ANLR levels differed significantly between patients with and without cachexia (**Figure S6A**). Regardless of tumor type, patients without cachexia consistently exhibited higher ANLR levels (all $P < 0.001$). Univariable logistic regression analysis (Model a) showed a significant association between ANLR and cachexia in patients with cancer (OR = 0.478, 95% CI: 0.390–0.580, $P < 0.001$). After partial adjustment for confounding factors in Model b, ANLR remained independently associated with cachexia (OR = 0.775, 95% CI: 0.644–0.910, $P < 0.001$). After full adjustment for potential confounders in Model c, patients in the high-ANLR group had a 49.6% lower risk of cachexia than those in the low-ANLR group (OR = 0.504, 95% CI: 0.438–0.580, $P < 0.001$). Quartile-stratified analysis demonstrated a significant dose–response relationship, with the risk of cachexia decreasing progressively as ANLR levels increased. Compared with patients in Q1, those in Q4 had an 18.7% lower risk of cachexia (OR = 0.813, 95% CI: 0.781–0.847, $P < 0.001$), indicating a clear gradient of protective effect (Table 3). These findings were also confirmed in the validation cohort, where multivariable logistic regression analysis showed that, in Model c, ANLR remained an independent protective factor against cachexia in patients with cancer (OR = 0.869, 95% CI: 0.816–0.926, $P < 0.001$), with cachexia risk continuing to decrease as ANLR levels increased (**Table S4**).

Table 3
Logistic regression analysis of ANLR associated with cachexia at discovery cohort.

ANLR	Model a OR (95%CI)	p value	Model b OR (95%CI)	p value	Model c OR (95%CI)	p value
Continuous (per SD)	0.478 (0.390–0.580)	< 0.001	0.775 (0.644–0.910)	< 0.001	0.785 (0.653–0.918)	0.001
Cutoff value						
C1 (< 10)	ref		ref		ref	
C2 ($\geq$ 10)	0.464 (0.426–0.505)	< 0.001	0.621 (0.564–0.683)	< 0.001	0.613 (0.556–0.675)	< 0.001
Quartiles	ref		ref		ref	
Q1 (< 9.323)	0.572 (0.513–0.637)	< 0.001	0.709 (0.622–0.788)	< 0.001	0.693 (0.610–0.781)	< 0.001
Q2 (9.323–16.289)	0.433 (0.388–0.484)	< 0.001	0.615 (0.544–0.697)	< 0.001	0.615 (0.539–0.689)	< 0.001
Q3 (16.289–24.930)	0.396 (0.354–0.443)	< 0.001	0.542 (0.478–0.615)	< 0.001	0.542 (0.474–0.609)	< 0.001
Q4 ($\geq$ 24.930)	0.729 (0.703–0.756)	< 0.001	0.676 (0.638–0.731)	< 0.001	0.813 (0.781–0.847)	< 0.001
p for trend		< 0.001				< 0.001
Notes:						
Model a: No adjusted.						
Model b: Adjusted for age, sex, BMI, TNM stage, tumor type.						
Model c: Adjusted for age, sex, BMI, TNM stage, tumor type, chronic hepatitis, diabetes, hypertension, cardiovascular disease, chronic nephrosis, family history, smoking, drinking, education level, marital status, surgery, chemotherapy, radiotherapy.						

Logistic Regression Analysis of the Association Between ANLR and Severe Malnutrition

Box plots were used to compare the distribution of ANLR between patients with and without severe malnutrition across different cancer types, and statistical tests were performed to assess between-group differences. Significant differences in ANLR levels were observed across all cancer types, with patients without severe malnutrition consistently exhibiting higher ANLR values (**Figure S6B**). In the

discovery cohort, multivariable logistic regression analysis showed that, after adjustment for all potential confounders in Model c, each one-standard-deviation increase in ANLR was associated with a 32.6% reduction in the risk of severe malnutrition (OR = 0.674, 95% CI: 0.538–0.832, $P < 0.001$). Dichotomous analysis showed that patients in the high-ANLR group had a 59.1% lower risk of severe malnutrition than those in the low-ANLR group (OR = 0.409, 95% CI: 0.350–0.478, $P < 0.001$). Quartile-stratified analysis further confirmed a significant dose–response relationship, with the risk of severe malnutrition decreasing progressively across increasing ANLR quartiles. Compared with patients in Q1, those in Q4 had a 31.7% lower risk of severe malnutrition (OR = 0.683, 95% CI: 0.653–0.725, $P < 0.001$) (Table 4). These results were replicated in the validation cohort. In the fully adjusted Model c, each one-standard-deviation increase in ANLR was associated with a 54.0% reduction in the risk of severe malnutrition (OR = 0.460, 95% CI: 0.357–0.607, $P < 0.001$). Dichotomous analysis showed that the high-ANLR group had a 53.7% lower risk of severe malnutrition than the low-ANLR group (OR = 0.463, 95% CI: 0.398–0.538, $P < 0.001$). Quartile analysis further demonstrated a progressive decline in severe malnutrition risk with increasing ANLR levels, with patients in Q4 having a 26.7% lower risk than those in Q1 (OR = 0.733, 95% CI: 0.685–0.783, $P < 0.001$) (**Table S5**).

Table 4

Logistic regression analysis of ANLR associated with severe malnutrition at discovery cohort.

ANLR	Model a OR (95%CI)	p value	Model b OR (95%CI)	p value	Model c OR (95%CI)	p value
Continuous (per SD)	0.298 (0.233–0.380)	< 0.001	0.623 (0.496–0.773)	< 0.001	0.674 (0.538–0.832)	< 0.001
Cutoff value						
C1 (< 10)	ref		ref		ref	
C2 ($\geq$ 10)	0.319 (0.292–0.350)	< 0.001	0.419 (0.379–0.462)	< 0.001	0.429 (0.388–0.474)	< 0.001
Quartiles	ref		ref		ref	
Q1 (< 9.323)	0.453 (0.404–0.507)	< 0.001	0.530 (0.469–0.599)	< 0.001	0.538 (0.475–0.608)	< 0.001
Q2 (9.323–16.289)	0.261 (0.229–0.296)	< 0.001	0.351 (0.306–0.400)	< 0.001	0.359 (0.309–0.410)	< 0.001
Q3 (16.289–24.930)	0.243 (0.214–0.276)	< 0.001	0.338 (0.289–0.390)	< 0.001	0.348 (0.297–0.400)	< 0.001
Q4 ($\geq$ 24.930)	0.599 (0.575–0.624)	< 0.001	0.677 (0.637–0.733)	< 0.001	0.683 (0.653–0.725)	< 0.001
p for trend		< 0.001		< 0.001		< 0.001
Notes:						
Model a: No adjusted.						
Model b: Adjusted for age, sex, BMI, TNM stage, tumor type.						
Model c: Adjusted for age, sex, BMI, TNM stage, tumor type, chronic hepatitis, diabetes, hypertension, cardiovascular disease, chronic nephrosis, family history, smoking, drinking, education level, marital status, surgery, chemotherapy, radiotherapy.						

Linear Regression Analysis of the Association Between ANLR and KPS Score

The association between ANLR and KPS score in patients with cancer was analyzed in both the discovery and validation cohorts using hierarchical regression models: an unadjusted model (Model a), a model adjusted for demographic and tumor characteristics (Model b), and a fully adjusted model including all confounding factors (Model c). Continuous-variable analysis showed that each one-

standard-deviation increase in ANLR was significantly associated with a higher KPS score. This positive association remained stable after adjustment for confounders in both cohorts. In the fully adjusted model of the discovery cohort, the regression coefficient was $\beta = 0.409$ (95% CI: 0.191–0.627, $P < 0.001$) (**Table S6**). After stratifying ANLR into quartiles and using the lowest quartile as the reference, both cohorts showed a progressive increase in KPS score with increasing ANLR levels. The β coefficients for all quartile groups were statistically significant, and the trend tests were significant (P for trend < 0.001). In the fully adjusted Model c, patients in the highest ANLR quartile in the discovery cohort had an average 7.866-point higher KPS score than those in the lowest quartile (95% CI: 7.247–8.485, $P < 0.001$). A consistent pattern was observed in the validation cohort (**Table S7**). In the fully adjusted model, each one-standard-deviation increase in ANLR was significantly associated with a higher KPS score ($\beta = 0.669$, 95% CI: 0.336–1.001, $P < 0.001$). Patients in the highest quartile in the validation cohort had an average 6.686-point higher KPS score than those in the lowest quartile (95% CI: 5.730–7.642, $P < 0.001$). Overall, higher ANLR levels were independently associated with better functional status in patients with cancer.

Discussion

The prognostic significance of systemic inflammation and nutritional status in malignant tumors has become a major focus of research. The predictive value of biomarkers based on individual inflammatory or nutritional parameters has been well established in patients with cancer²⁷. However, these biomarkers typically capture only a single dimension—either inflammation or nutrition—and therefore cannot adequately reflect the synergistic and interactive effects of these two closely related processes on cancer progression. In this multicenter cohort study, we developed and validated a novel inflammation-related index, ANLR, by integrating ALB and NLR, and confirmed that ANLR is a robust and independent predictor of OS in patients with cancer. We further demonstrated its association with interrelated pathophysiological processes, including systemic inflammation and malnutrition. ANLR showed stable prognostic value across tumor types, TNM stages, and demographic subgroups, and was significantly associated with cancer cachexia, severe malnutrition, and physical performance status. These findings support ANLR as a clinically applicable assessment tool and address an important gap in current oncologic prognostic evaluation.

The biological rationale for ANLR as a prognostic biomarker lies in its integration of two core pathophysiological processes involved in tumor progression, namely systemic immune-inflammatory imbalance and depletion of nutritional reserves. From the inflammatory perspective, NLR is a core marker of tumor-related systemic inflammation. An elevated NLR represents excessive activation of neutrophils and depletion of antitumor lymphocytes. Neutrophils can promote tumor cell invasion, angiogenesis, and immune escape through the secretion of matrix metalloproteinases, vascular endothelial growth factor, and other mediators^{28–30}, whereas lymphocytes are the key effector cells of antitumor cellular immunity, and lymphopenia indicates impaired host antitumor immune surveillance^{31,32}. Therefore, an elevated NLR reflects an imbalanced state characterized by enhanced

protumor inflammation and weakened antitumor immunity, and is an important driving factor in the progression of cancer. From a nutritional perspective, albumin is a major visceral protein synthesized by the liver and reflects the body's protein reserve and overall muscle mass. Adequate albumin levels help maintain vascular endothelial integrity, suppress the release of proinflammatory mediators, and reduce the invasive and metastatic potential of tumors. In contrast, hypoalbuminemia indicates long-term inadequate nutritional intake and enhanced muscle catabolism, which may directly reduce tolerance to chemotherapy and surgery, increase the risks of infection and organ failure, and shorten survival³³. Thus, a higher albumin component in ANLR reflects more sufficient nutritional reserves and provides the biological basis for its protective prognostic effect. By calculating the ratio of albumin to NLR, ANLR integrates nutritional reserve and inflammatory status into a single index. A high ANLR indicates adequate nutritional reserve and a lower systemic inflammatory burden, reflecting better host tolerance to tumor burden and preserved antitumor immune potential. Conversely, a low ANLR indicates inflammation–nutrition imbalance. This condition may not only accelerate tumor progression but also reduce treatment tolerance and increase the risks of complications and death³⁴, which may explain the significantly worse prognosis observed in patients with low ANLR in the present study. By integrating these two components, ANLR simultaneously quantifies the adequacy of nutritional reserve and the degree of systemic immune-inflammatory imbalance, thereby overcoming the limitation that albumin or NLR alone captures only a single dimension. This may explain why ANLR provides superior prognostic discrimination compared with traditional single biomarkers³⁵.

This study showed that ANLR was significantly and independently associated with cancer cachexia, severe malnutrition, and KPS, and these associations remained robust after adjustment for potential confounders, including age, tumor stage, comorbidities, and antitumor treatment. Persistent inflammation promotes catabolism and contributes to nutritional depletion. Accordingly, the lower BMI and albumin levels observed in patients with cachexia may reflect limited anabolic reserve, impaired treatment tolerance, and an overt wasting phenotype, consistent with previous studies of inflammation-related indices in cachexia across multiple cancer types³⁶. The relationship between inflammation and malnutrition in cancer cachexia may not be fully explained by a simple linear model. From a pathophysiological perspective, macrophage-dominant immunometabolic programs within the tumor microenvironment can remodel cytokine signaling, substrate utilization, and redox homeostasis, thereby aggravating systemic metabolic imbalance and contributing to progressive wasting³⁷. The tumor microenvironment continuously releases large amounts of proinflammatory cytokines, such as IL-6 and TNF- α . These cytokines induce abnormal neutrophil proliferation and lymphocyte apoptosis, resulting in elevated NLR and impaired host antitumor immune surveillance. On the other hand, they inhibit hepatic albumin synthesis and activate the ubiquitin–proteasome pathway in muscle tissue, thereby accelerating persistent skeletal muscle protein degradation and gradually forming a vicious cycle of chronic inflammation activation leads to muscle depletion, resulting in protein malnutrition, and eventually the inflammation worsens further^{38,39}. Within this pathological loop, ANLR simultaneously integrates the muscle-nutritional reserve represented by albumin and the systemic immune-inflammatory burden reflected by NLR, with its value quantifying the severity of this circulating imbalance. The lower the ANLR,

the more likely it is to indicate insufficient albumin reserve and excessive systemic inflammatory burden, which are associated with a higher risk of muscle loss, severe malnutrition, and progression to overt cancer cachexia. Concurrently, physical activity capacity and tolerance to antitumor therapy decline, ultimately manifesting as lower KPS scores. A higher ANLR indicates sufficient visceral protein reserves, a controlled inflammatory response, and preserved skeletal muscle integrity, which may alleviate inflammation-mediated muscle degradation, delay the onset of cachexia, help maintain daily physical function, and support the completion of standardized antitumor treatments, including surgery, radiotherapy, and chemotherapy. As an integrated composite index, ANLR overcomes the limitations of single biomarkers and may provide a simple, noninvasive laboratory tool for the early clinical identification of patients at high risk of muscle wasting and malnutrition.

A key finding of this study is that ANLR maintained stable and independent prognostic value across different cancer types and TNM stages. Tumor type-specific subgroup analyses demonstrated the prognostic relevance of ANLR across a range of malignancies, highlighting its potential clinical utility in diverse oncologic settings. In the discovery cohort, ANLR retained significant prognostic value across 11 common cancer types. Its prognostic association was attenuated in patients with pancreatic or breast cancer in the validation cohort. This heterogeneity may reflect the distinct pathophysiological characteristics of these tumor types. Pancreatic cancer is characterized by intense systemic inflammation and persistent hypercatabolism, and severe muscle wasting and cachexia may develop even during the early stages of the disease. High circulating levels of proinflammatory cytokines may substantially amplify the adverse prognostic impact of pancreatic cancer and, to some extent, diminish the survival benefit associated with the sufficient nutritional reserve and lower inflammatory burden reflected by a high ANLR⁴⁰. In breast cancer, the predominantly female population and potential effects of estrogen on hepatic albumin synthesis and systemic inflammatory responses may contribute to higher baseline ANLR levels, thereby reducing the discriminatory capacity of ANLR for risk stratification within this cancer subtype. For the majority of solid tumors, including lung, esophageal, and colorectal cancers, ANLR demonstrated stable prognostic performance, supporting its potential utility as a pan-cancer biomarker. Compared with tumor-specific biomarkers restricted to individual malignancies, ANLR may have broader clinical applicability. We also observed that the prognostic discriminative capacity of ANLR was significantly stronger in advanced-stage disease (stages III and IV) than in early-stage disease (stages I and II). One possible explanation is that, in the early stages of cancer, the tumor burden is relatively limited and systemic inflammatory stress and nutritional depletion may not yet be clinically evident. Consequently, although ANLR remained statistically significant, its ability to discriminate long-term survival was weaker than that observed in advanced disease. This finding suggests that even in the absence of clinically apparent muscle wasting or overt inflammatory activation, subclinical reductions in albumin reserve and neutrophil-lymphocyte immune imbalance may adversely influence the long-term survival trajectory of patients with cancer. In advanced disease, the release of proinflammatory mediators such as IL-6 and TNF- α contributes to a simultaneous increase in systemic inflammatory burden and muscle catabolic stress. As the vicious cycle between inflammation and malnutrition

intensifies, ANLR may become increasingly effective in quantitatively capturing and discriminating the severity of this imbalance^{41–44}.

Further stratified analyses showed that ANLR consistently remained an independent prognostic factor for overall survival, regardless of age, sex, comorbidities, or receipt of different antitumor treatments, including surgery, chemotherapy, and radiotherapy. Although previous studies have documented sex-related differences in physiological serum albumin levels, innate immune-inflammatory response patterns, and lymphocyte subset composition, ANLR demonstrated highly consistent prognostic performance in both male and female patients. ANLR may serve as a broadly applicable biomarker for assessing the overall host reserve in patients with cancer. Although albumin levels may be influenced by hepatic or renal comorbidities and fluid status, and NLR may fluctuate in response to treatment-related bone marrow suppression or infection, the prognostic association of ANLR remained stable in the presence of these potential sources of variation. These findings further support the value of ANLR as a composite indicator of nutritional and inflammatory status that may better capture pathophysiological heterogeneity and facilitate more accurate prognostic stratification in patients with cancer.

The reliability and stability of ANLR as a prognostic biomarker were further supported by sensitivity analyses and RCS dose–response analyses. To minimize the potential influence of early mortality bias, all regression analyses were repeated after excluding 693 patients who died within the first 3 months of follow-up. Regardless of whether ANLR was analyzed as a continuous, dichotomous, or quartile-based variable, its independent association with overall survival remained statistically significant across all three adjusted models. These findings suggest that the prognostic value of ANLR was not solely driven by acute inflammatory exacerbation or severe nutritional depletion in patients with terminal disease, and that substantial reverse-causation bias was unlikely. The results support the clinical reproducibility and potential generalizability of the prognostic association between ANLR and survival.

At the dose–response level, RCS analysis provided more refined quantitative evidence. In the discovery cohort, the unadjusted, partially adjusted, and fully adjusted models consistently demonstrated a significant inverse nonlinear association between ANLR and all-cause mortality. Overall, the log hazard ratio declined continuously as ANLR increased. Notably, when ANLR was below the critical threshold, mortality risk increased rapidly with further decreases in ANLR, whereas the rate of risk reduction attenuated slightly at higher ANLR levels, yielding a characteristic curvilinear dose–response pattern. This pattern was fully reproduced in the validation cohort, further supporting the cross-cohort stability of the observed association. Consistent with these findings, quartile-stratified analyses demonstrated a clear risk gradient. This continuous and graded dose–response relationship suggests that increasing ANLR reflects the synergistic effects of improved nutritional reserve and reduced inflammatory burden, which may translate progressively into survival benefits and provide direct quantitative evidence for clinical risk assessment. The cutoff value of 10 derived in this study should be regarded as a cohort-derived exploratory stratification threshold rather than a definitive dichotomous clinical decision point. In clinical practice, ANLR may be more appropriately used as a complementary tool alongside TNM staging, treatment planning, and structured nutritional assessment, thereby supplementing traditional

oncologic indicators. Its dichotomized form may facilitate rapid initial risk stratification, whereas its continuous value may support dynamic monitoring of changes in the host inflammatory–nutritional state.

Structured nutritional assessment tools, such as PG-SGA and NRS 2002, can systematically evaluate nutritional status based on dietary intake, weight change, physical function, and related parameters. However, they do not incorporate objective inflammatory biomarkers. They may fail to capture the amplifying effect of tumor-driven chronic inflammation on nutritional depletion or the contribution of inflammation to tumor progression and treatment resistance, thereby limiting their ability to predict long-term survival^{45–47}. In the present study, ANLR independently predicted overall survival after adjustment for traditional prognostic factors, including age, TNM stage, and treatment modality, and was also significantly associated with clinically important outcomes such as cancer cachexia and severe malnutrition. Unlike biomarkers that focus primarily on survival endpoints, the clinical associations of ANLR span the continuum from long-term survival to short-term nutritional complications. This broad association profile is consistent with the biological basis of its components: albumin reflects visceral protein reserves and overall nutritional status, whereas NLR reflects neutrophil-mediated proinflammatory burden and the balance between neutrophil activity and lymphocyte-mediated antitumor immunity. Their combination therefore captures both the host's nutritional reserve and the degree of systemic immune-inflammatory imbalance, allowing ANLR to reflect survival prognosis and the risk of nutritional complications simultaneously. Patients with extremely low ANLR may already have substantial depletion of nutritional reserves and marked systemic inflammatory activation and may therefore be at particularly high risk of developing cachexia. These patients may benefit from comprehensive management involving intensified nutritional assessment and support, appropriate treatment of underlying inflammatory or disease-related drivers, and multidisciplinary cachexia management. In contrast, patients with relatively high ANLR may have more stable nutritional and immune-inflammatory profiles and may be managed according to standard antitumor treatment pathways, avoiding unnecessary interventions.

Despite the strengths of this study, several limitations should be acknowledged. First, as a retrospective cohort study, it cannot completely exclude residual confounding from unmeasured variables. Although we adjusted as comprehensively as possible for known confounders, including demographic characteristics, tumor stage, pathological type, comorbidities, and antitumor treatment modality, information on out-of-hospital nutritional support, anti-inflammatory medication use, daily physical activity, and socioeconomic status was incompletely documented in the retrospective medical records and could not be incorporated into the adjustment models. Second, ANLR was calculated from a single baseline measurement obtained at admission. Longitudinal changes in albumin, neutrophil count, lymphocyte count, and ANLR throughout antitumor treatment were not assessed. Compared with a static baseline value, biomarker trajectories may more sensitively reflect disease progression, treatment response, and changes in host reserve and may have greater clinical utility. Future prospective studies should investigate whether treatment-related changes in ANLR are associated with chemotherapy sensitivity, recurrence risk, and long-term survival, thereby supporting dynamic risk assessment. Third,

the ANLR cutoff value of 10 was determined by maximizing the Youden index on the ROC curve and should therefore be considered an exploratory, cohort-derived threshold applicable primarily to risk stratification within the present study population. Because ANLR demonstrated a continuous nonlinear dose–response relationship with mortality risk, dichotomization inevitably resulted in some loss of quantitative information. Fourth, the strength of the association between ANLR and cachexia or severe malnutrition should be interpreted cautiously. ANLR incorporates albumin, a core nutritional marker, and NLR, a core inflammatory marker. Cancer cachexia itself is defined partly by features such as weight loss and systemic inflammation, while PG-SGA-based assessment of severe malnutrition is closely related to albumin levels and muscle depletion. Therefore, the observed associations may partly reflect overlap in construct composition rather than a completely independent predictive effect. ANLR may thus be more appropriately used as a complementary tool for nutritional risk screening and prognostic stratification than as an independent diagnostic criterion for cachexia or malnutrition. Fifth, we did not conduct systematic head-to-head comparisons of ANLR with established inflammation- and nutrition-related prognostic markers, including PNI, and PLR. Therefore, the incremental predictive value of ANLR relative to traditional indices could not be quantified. Future comparative diagnostic or prognostic studies should evaluate the relative and incremental performance of ANLR within existing clinical assessment frameworks. Sixth, the generalizability of the findings requires further evaluation. Both the training and validation cohorts were derived from the same multicenter INSCOC database, and the study population consisted predominantly of Chinese patients with solid tumors. Independent external validation across different ethnicities, geographic regions, and healthcare systems was not available. Because populations may differ in baseline albumin synthesis, immune-inflammatory response patterns, and tumor-type distribution, the prognostic performance and optimal cutoff value of ANLR may vary across populations. Its global applicability therefore requires confirmation in multinational and multiethnic cohorts.

Conclusion

In conclusion, this multicenter cohort study has confirmed that ANLR is an independent prognostic factor for the overall survival of cancer patients, and is significantly associated with cancer cachexia, severe malnutrition, and impaired performance status. Therefore, it can serve as a simple and objective tool for assessing prognostic risks, helping to identify high-risk patients at an early stage and having potential clinical application value.

Declarations

Ethical approval and consent to participate

This study was conducted in accordance with the Helsinki Declaration. All participants signed an informed consent form and this study was approved by the Institutional Review Board of The First Affiliated Hospital of Guangxi Medical University (Ethical number: NO.2022-KY-(043)). The study was approved by the INSCOC's institutional review board (Name of the ethic committee: Medical Ethics Committee of First Affiliated Hospital of Sun yat-sen University; Registration number:

ChiCTR1800020329; Registration Date: December 24, 2018; Registration website: <http://www.chictr.org.cn>).

Consent to publish

Not applicable.

Availability of data and materials

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

Declaration of competing interests

There are no competing interests.

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Author contributions

NX: Conceptualization, Investigation, Formal analysis, Writing – original draft. SW: Data curation, Conceptualization, Formal analysis, Methodology. CX: Methodology, Supervision, Investigation. SL: Data curation, Investigation. YC: Data curation, Formal analysis. CC: Methodology, Supervision, Investigation. HX: Conceptualization, Supervision, Funding acquisition, Writing – review & editing. HS: Conceptualization, Methodology, Visualization, Supervision, Writing – review & editing.

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Figures

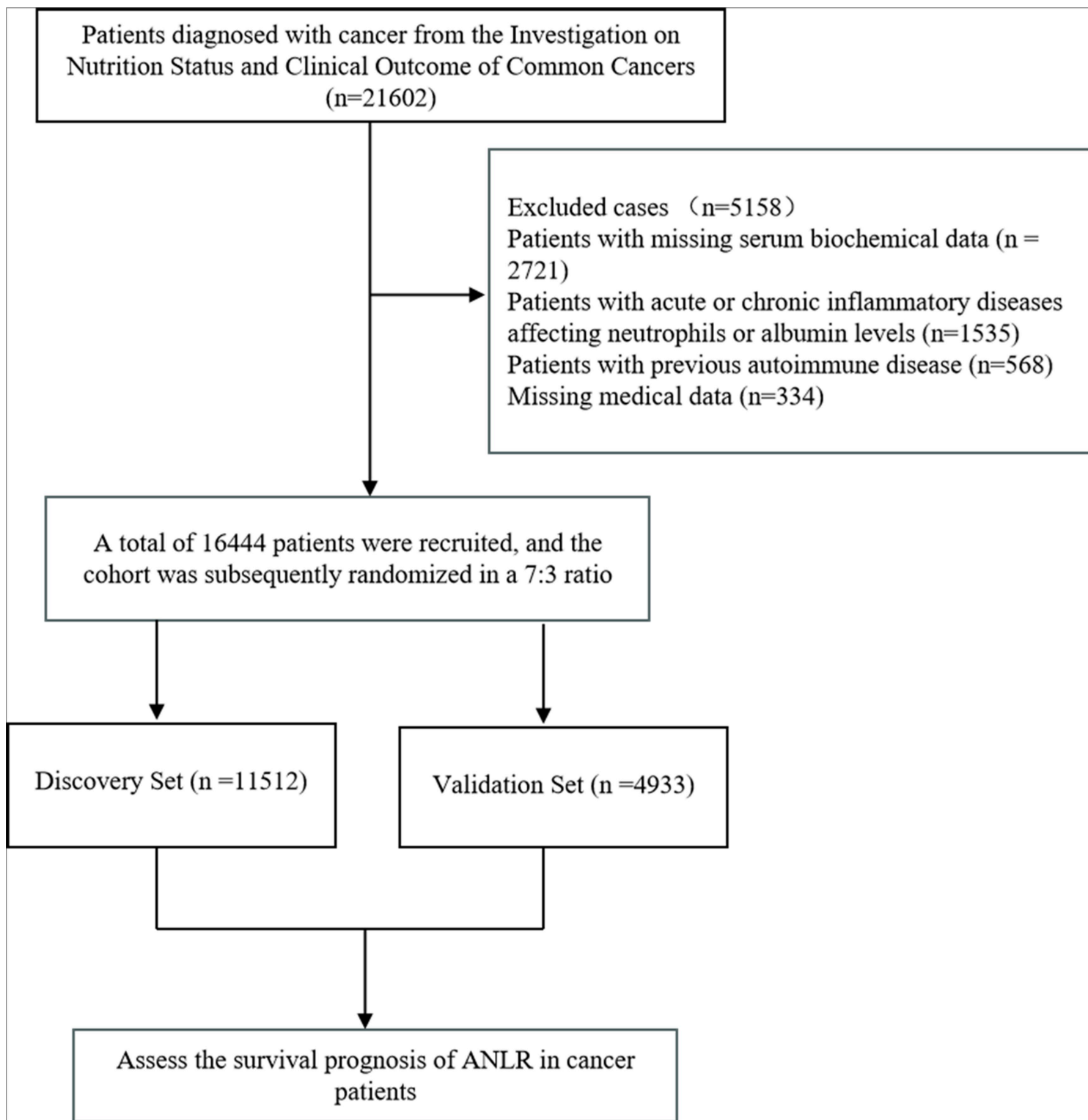


Figure 1

Study design and flow chart.

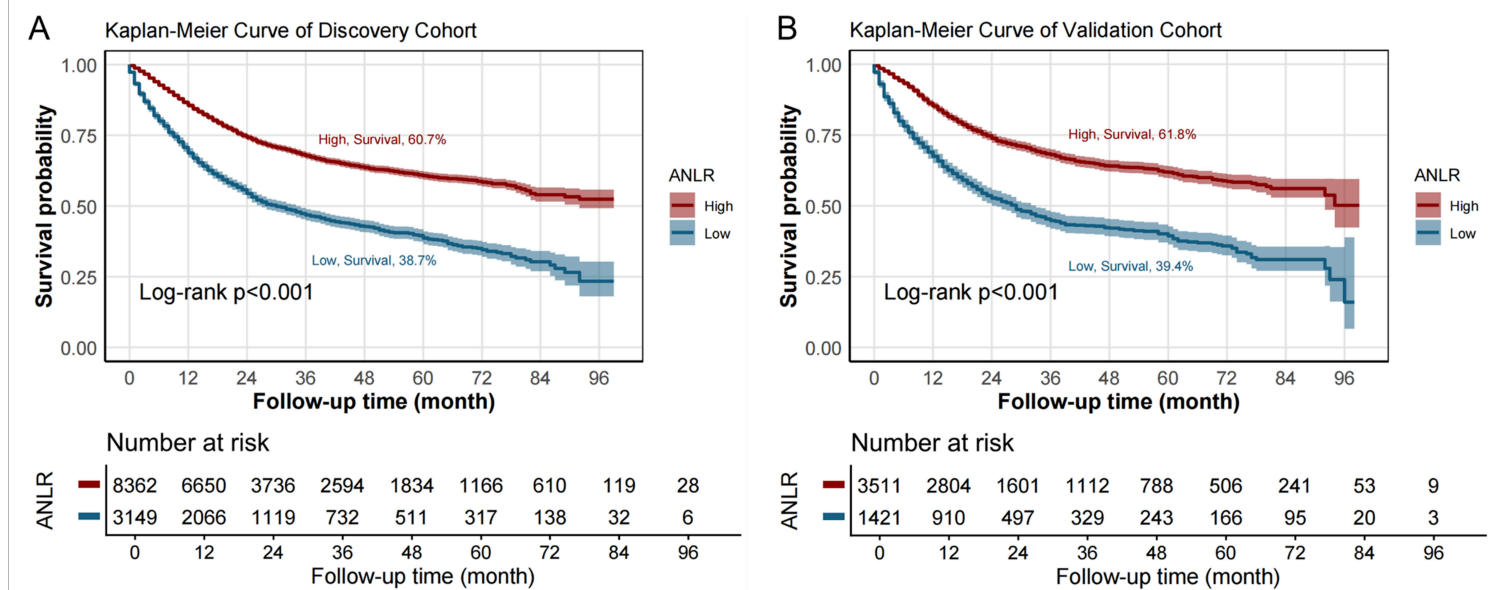


Figure 2

Kaplan-Meier curve of ANLR in patients with cancer.

Notes: A, discovery cohort; B, validation cohort.

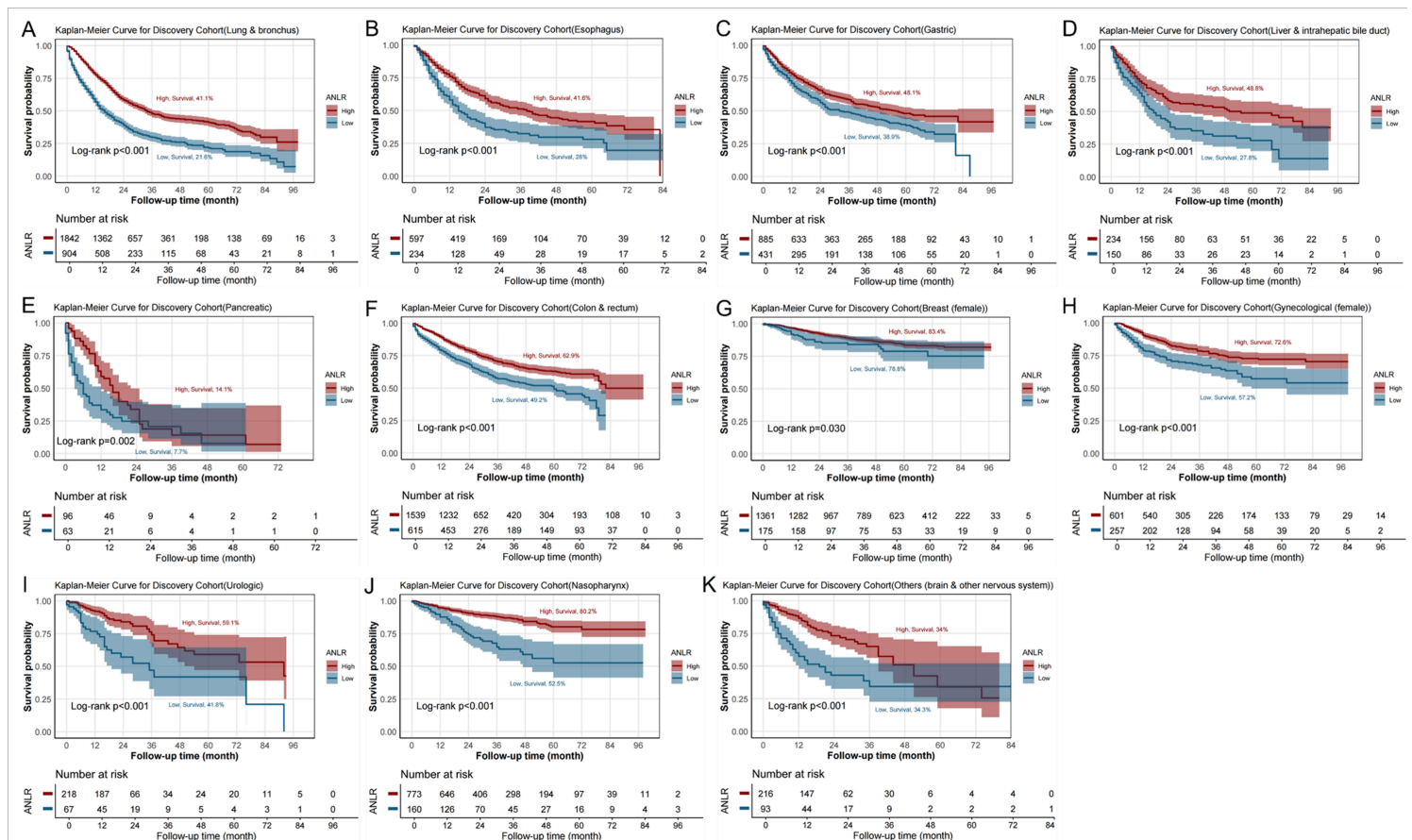


Figure 3

Subgroup survival analysis of ANLR of different cancers at discovery cohort.

Notes: A, Lung & bronchus; B, Esophagus; C, Gastric; D, Liver & intrahepatic bile duct; E, Pancreatic; F, Colon & rectum; G, Breast (female); H, Gynecological (female); I, Urologic; J, Nasopharynx; K, Others (brain & other nervous system).

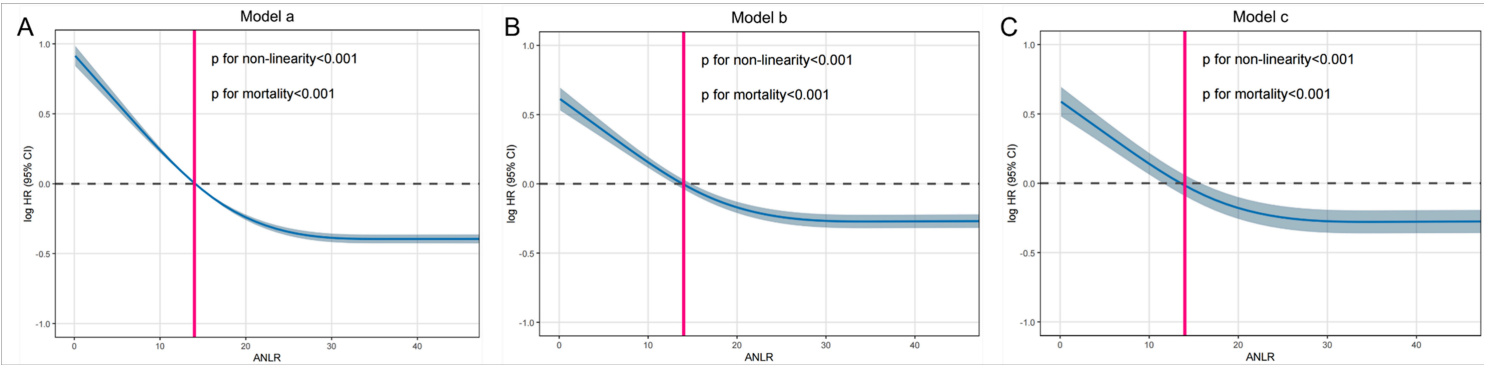


Figure 4

The association between ANLR and survival in patients with cancer at discovery cohort.

Notes:

Model a: No adjusted.

Model b: Adjusted for age, sex, BMI, TNM stage, tumor type.

Model c: Adjusted for age, sex, BMI, TNM stage, tumor type, chronic hepatitis, diabetes, hypertension, cardiovascular disease, chronic nephrosis, family history, smoking, drinking, education level, marital status, surgery, chemotherapy, radiotherapy.

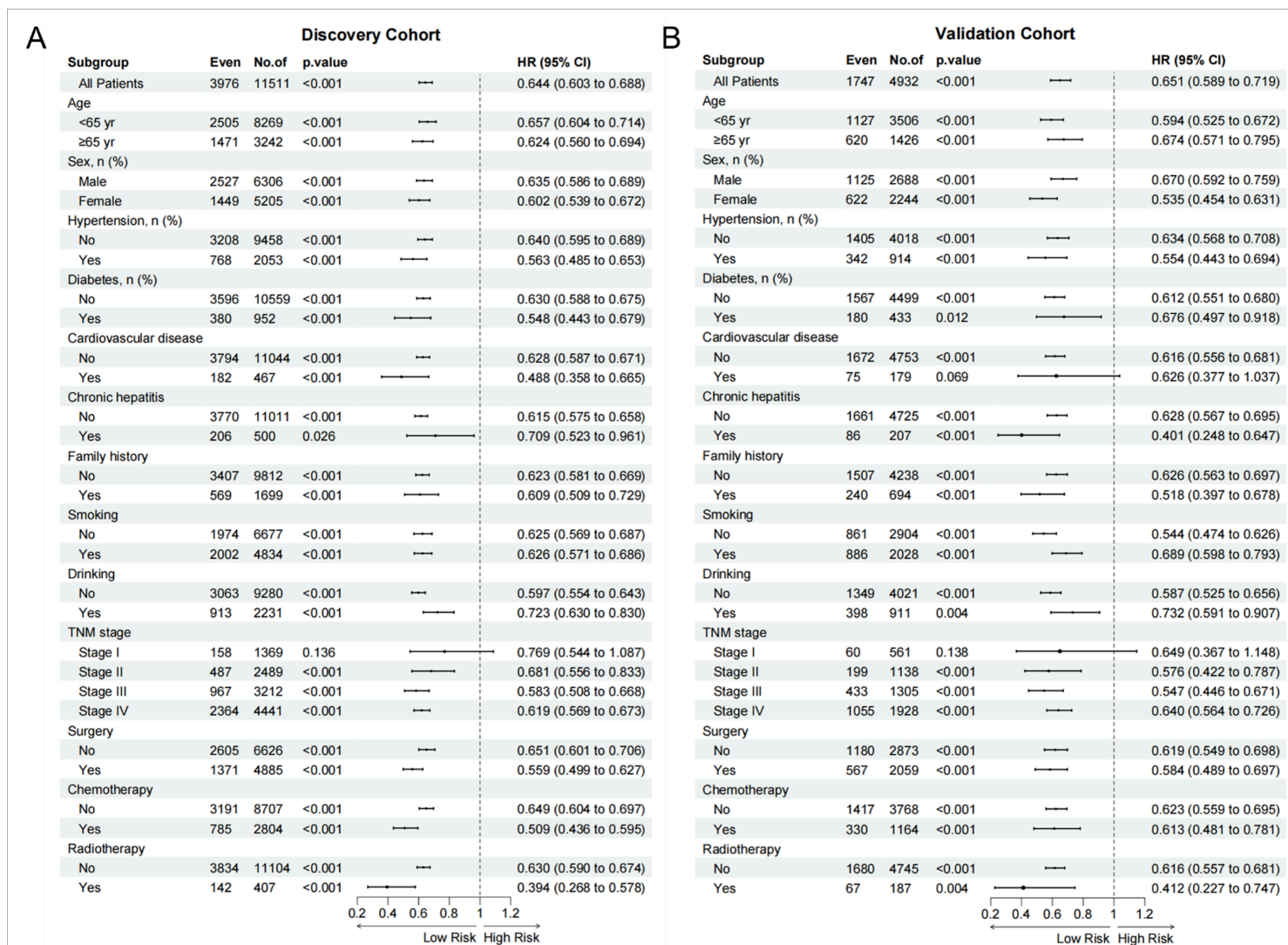


Figure 5

The association between ANLR and hazard risk of survival in various subgroups.

Notes: The model was adjusted for multivariate factors except for its own subgroup factors. A, discovery cohort; B, validation cohort.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [Supplementarymaterials.docx](#)