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# Low albumin-to-creatinine ratios (ACR) are associated with poor outcomes in cancer patients

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## Abstract

**Background** The albumin-to-creatinine ratio (ACR) is known to predict prognosis in liposarcoma patients, but its role in other tumors remains unclear. This study aimed to evaluate the prognostic relationship between ACR and common solid tumors.

**Methods** Data from the Investigation on Nutrition Status and Clinical Outcome of Common Cancers (INSCOC) between 2013 and 2022 were used to analyze patients under 65 years old with solid tumors. Patients were divided into a training cohort (n = 12,027) and a validation cohort (n = 7,985) using simple random sampling. Correlation analysis, Kaplan–Meier method, and restricted cubic spline analysis were conducted to explore ACR's relationship with overall survival (OS). Multivariable logistic regression assessed associations between ACR and Patient—Generated Subjective Global Assessment (PG-SGA), Length of Stay (LOS), and Karnofsky Performance Status (KPS).

**Results** In Cox regression, higher ACR levels were associated with better OS in solid tumor patients. Specifically, when using the cutoff value with low ACR as the reference, higher ACR levels were significantly associated with improved OS. For nasopharyngeal carcinoma (HR = 0.49, 95% CI: 0.35–0.67, $P < 0.001$), gastrointestinal tract tumors (HR = 0.84, 95% CI: 0.74–0.95, $P = 0.007$), and urogenital neoplasms (HR = 0.55, 95% CI: 0.43–0.71, $P < 0.001$), higher ACR levels were linked to better OS. When ACR was categorized into tertiles, the results were consistent with those observed using the cutoff value. In gastrointestinal tract tumor patients, higher ACR levels were linked to lower PG-SGA scores and improved KPS scores ($P < 0.05$). In urogenital neoplasm patients, higher ACR levels were associated with improved KPS scores ($P < 0.05$).

**Conclusion** Elevated ACR levels were significantly associated with improved OS in cancer patients, particularly in nasopharyngeal carcinoma, gastrointestinal tract tumors, and urogenital neoplasms. ACR was also linked to better nutritional and functional status, suggesting its potential as a prognostic biomarker.

**Keywords** Cancer, Albumin, Creatinine, Survival, Nutrition

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## Introduction

Cancer is a global and growing problem and the leading cause of human death in the world [1, 2]. Young and middle-aged people are the main force of world economic development. An aging population is bad for the economy [3]. There is a lot of research on the prognosis of cancer in the elderly [4]. However, it is also important to explore indicators that affect cancer prognosis in young and middle-aged adults.

Albumin, creatinine and the ratio of albumin to creatinine are common biochemical indicators, which are widely used to assess nutritional status and renal function. Recent studies have shown that these indicators have important clinical significance in predicting sarcoma-specific survival prognosis in myofibroblastic and fibroblastic sarcoma patients [5].

Albumin is the most abundant protein in human serum and is often used as an indicator of clinical nutritional status [6, 7]. Low albumin predicted poorer survival in cancer patients, while high albumin levels were associated with better survival [8]. Serum albumin is often combined with other hematological indicators to predict the prognosis of patients with non-small cell lung cancer and gastric cancer after surgical resection [9, 10]. Creatinine is a muscle metabolite that is excreted through the kidneys [11]. Serum creatinine (SCr) is a standard marker of kidney injury [12].

Creatinine and albumin are important biomarkers for health monitoring [13]. The ratio of albumin to creatinine has been shown in studies in liposarcoma patients that elevated serum creatinine, decreased albumin, and decreased albumin-creatinine ratio (ACR) are negative prognostic factors that lead to poor disease-specific survival [14]. In clinical practice, albumin is often combined with other indicators to predict disease prognosis. An elevated neutrophil percentage-to-albumin ratio (NPAR) is associated with the 1-year mortality rate in patients with advanced atrial fibrillation [15]. The fibrinogen-to-albumin ratio (FAR) and the blood urea nitrogen-to-albumin ratio (BAR) are associated with adverse clinical outcomes in COVID-19 patients [16]. In this study, we combined albumin and creatinine to explore their relationship with clinical outcomes in patients with solid tumors.

## Materials and methods

### Study population characteristics

The Investigation on Nutrition Status and Clinical Outcome of Common Cancers (INSCOC) is a national survey that explores the link between nutritional health and clinical outcomes in patients with malignant tumors [17]. The project was conceived and implemented by the Professional Committee of Tumor Nutrition and Support of the Chinese Cancer Society. We used the INSCOC data to screen 20,212 eligible young and middle-aged cancer patients in China between 2012 and 2022. The inclusion and exclusion criteria for this study were outlined in Table 1. Demographic and clinicopathological data were collected within 48 h after admission. The standard definition of smoking is more than 20 cigarettes in a lifetime. Alcohol consumption is defined as regular drinking in the past year. Hypertension is defined as having a history of high blood pressure or using antihypertensive drugs or having a systolic or diastolic blood pressure of more than 140 mmHg or 90 mmHg. Estimated glomerular filtration rate (eGFR) was calculated based on the Cockcroft-Gault formula [18]. ACR is defined as the ratio of albumin (g/L) to creatinine (mg/dl).

### Statistical analysis and methods

All solid tumor patients were randomly divided into training and validation cohorts at a 6:4 ratio using R software. Data were presented as simple percentages or medians with interquartile ranges (IQR). Spearman's method was used to calculate the correlations between albumin, creatinine, ACR, and age. The absolute value of the Spearman correlation coefficient reflects the strength of the correlation, with higher values indicating stronger correlations and lower values indicating weaker correlations. Restricted cubic spline regression was employed to analyze the relationship between ACR and survival in solid tumor patients, while Kaplan–Meier curves and log-rank tests were used to validate time-to-survival trends. ACR was analyzed both as a cutoff value and tertiles using Cox regression to explore its association with cancer patient survival. Additionally, ACR tertiles were examined using multivariable logistic regression to investigate their relationships with other clinical outcomes. Subgroup analyses were conducted for different cancer types, and sensitivity analyses were performed to confirm the robustness of the results. All analyses and

**Table 1** Ethical approval, informed consent, and inclusion/exclusion criteria for solid tumor patients

All participating review bodies gave ethical approval to the study, and all participants provided written informed consent.

The inclusion criteria were as follows: (1) Patients with a pathological diagnosis of solid tumors, including nasopharyngeal cancer, gastrointestinal tract tumors (esophageal cancer, gastric cancer, colorectal cancer, liver cancer, carcinoma of the biliary tract, pancreatic cancer), lung cancer, breast cancer, and urogenital neoplasms (cervical cancer, endometrial cancer, ovarian cancer, prostate cancer, carcinoma of the bladder); (2) Age $\geq$ 18 years.

The exclusion criteria included: (1) Hematological malignancies such as leukemia, lymphoma, and myeloma; (2) Patients with severe comorbidities, acute infections, or pregnancy; (3) Patients who are critically ill, difficult to assess, or unwilling to cooperate with the investigation, including HIV/AIDS patients and organ transplant recipients.

visualizations were conducted in R version 4.3.0, and a two-sided $P<0.05$ was considered statistically significant.

### Clinical outcomes and covariates

The primary outcome was overall survival (OS), defined as the time from cancer diagnosis to all-cause death or the last follow-up. Secondary outcomes included Patient-Generated Subjective Global Assessment (PG-SGA) scores, length of stay (LOS), and physical status assessments measured by Karnofsky Performance Status (KPS) scores. In this study, the adjusted covariates included sex, age, BMI, Tumor, Node, Metastasis (TNM) stage, surgery, chemotherapy, radiotherapy, liver cirrhosis, chronic hepatitis, chronic kidney disease, ALT, and cancer diagnosis.

## Results

### Baseline characteristics of study participants

Initially, the INSCOC study screened 20,100 solid tumor patients. After excluding patients with missing data, a total of 20,012 patients were included and randomly divided into a training cohort (n = 12,027) and a validation cohort (n = 7,985) at a 6:4 ratio (Fig. 1). In the training cohort (Table 2), 6,108 patients (50.8%) were male, and 5,919 patients (49.2%) were female, while in the validation cohort, 4,105 patients (51.4%) were male, and 3,880 patients (48.6%) were female, with no significant difference between the groups ($P=0.396$). The median age in both cohorts was 53.00 years (IQR: 47.00–59.00) ($P=0.673$). The proportions of non-smokers and smokers were 60.9% and 39.1% in the training cohort and 60.4% and 39.6% in the validation cohort, respectively, with no significant difference ($P=0.557$). Similarly, the proportions of non-drinkers and drinkers were 81.3% and 18.7% in the training cohort and 80.6% and 19.4% in the validation cohort, respectively ($P=0.253$). The prevalence of liver cirrhosis (0.8% vs. 1.1%, $P=0.068$), chronic hepatitis (4.4% vs. 4.4%, $P=0.991$), hypertension (12.6% vs. 12.3%, $P=0.528$), and chronic kidney disease (0.1% vs. 0.2%, $P=0.168$) showed no significant differences between the training and validation cohorts. The median ALT levels were 19.80 U/L (IQR: 13.00–30.80) in the training cohort and 19.00 U/L (IQR: 13.00–30.00) in the validation cohort (P = 0.192). Median eGFR was slightly higher in the validation cohort (88.41 vs. 89.29 mL/

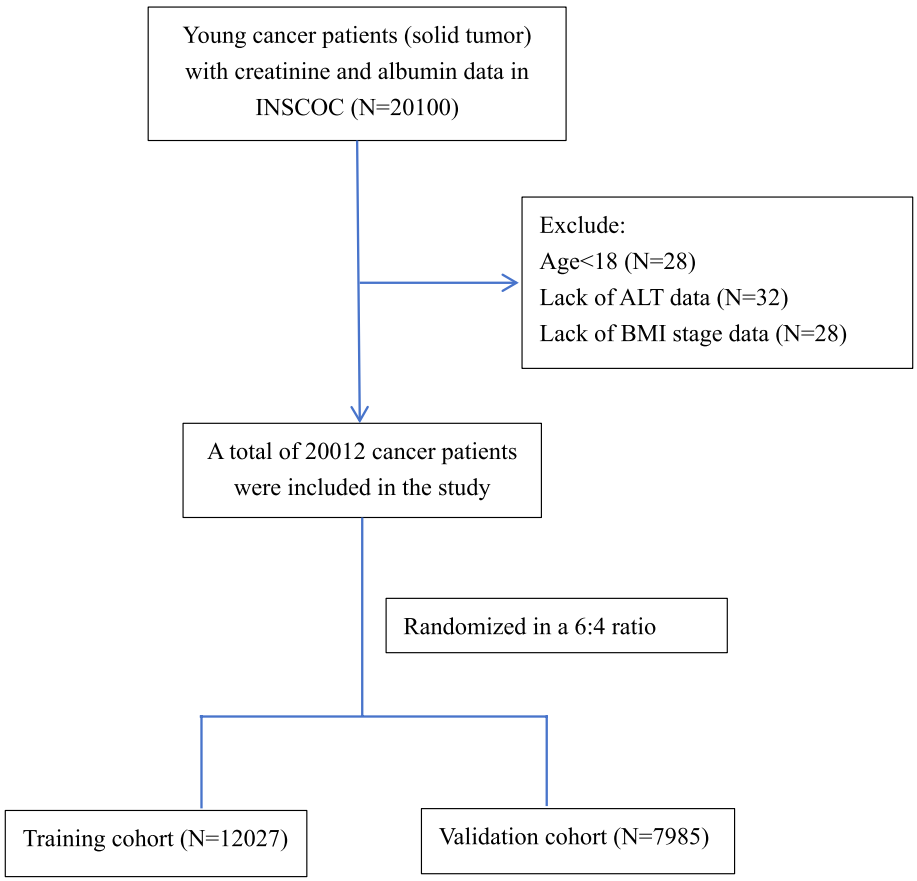


**Fig. 1** Flow Chart

**Table 2** Baseline characteristics of patients with solid tumor cancers in relation to ACR in the training and validation cohorts

| Variable | Training cohort (n = 12,027) | Validation cohort (n = 7985) | *P*-value |
|---|---|---|---|
| Sex | | | |
| Male | 6108 (50.8) | 4105 (51.4) | 0.396 |
| Female | 5919 (49.2) | 3880 (48.6) | |
| Age, y | 53.00 [47.00, 59.00] | 53.00 [47.00, 59.00] | 0.673 |
| Smoking | | | |
| No | 7320 (60.9) | 4826 (60.4) | 0.557 |
| Yes | 4707 (39.1) | 3159 (39.6) | |
| Drinking | | | |
| No | 9773 (81.3) | 6436 (80.6) | 0.253 |
| Yes | 2254 (18.7) | 1549 (19.4) | |
| Liver cirrhosis | | | |
| No | 11,925 (99.2) | 7896 (98.9) | 0.068 |
| Yes | 102 ( 0.8) | 89 ( 1.1) | |
| Chronic hepatitis | | | |
| No | 11,500 (95.6) | 7634 (95.6) | 0.991 |
| Yes | 527 ( 4.4) | 351 ( 4.4) | |
| Hypertension | | | |
| No | 10,515 (87.4) | 7006 (87.7) | 0.528 |
| Yes | 1512 (12.6) | 979 (12.3) | |
| Chronic kidney disease | | | |
| No | 12,011 (99.9) | 7967 (99.8) | 0.168 |
| Yes | 16 ( 0.1) | 18 ( 0.2) | |
| ALT (U/L) | 19.80 [13.00, 30.80] | 19.00 [13.00, 30.00] | 0.192 |
| eGFR (mL/min per 1·73 $m^2$) | 88.41 [71.08, 109.60] | 89.29 [71.83, 110.13] | 0.041 |
| Cancer diagnosis | | | |
| Nasopharyngeal carcinoma | 1097 ( 9.1) | 723 ( 9.1) | 0.316 |
| Cancer of digestive system | 4821 (40.1) | 3294 (41.3) | |
| Lung cancer | 3050 (25.4) | 1946 (24.4) | |
| Breast Cancer | 1781 (14.8) | 1146 (14.4) | |
| Urogenital neoplasms | 1278 (10.6) | 876 (11.0) | |
| TNM[a] | | | |
| I + II | 3758 (37.4) | 2473 (37.3) | 0.549 |
| III + IV | 6291 (62.6) | 4154 (62.7) | |
| Surgery | | | |
| No | 9116 (75.8) | 6074 (76.1) | 0.672 |
| Yes | 2911 (24.2) | 1911 (23.9) | |
| Chemotherapy | | | |
| No | 5329 (44.3) | 3460 (43.3) | 0.177 |
| Yes | 6698 (55.7) | 4525 (56.7) | |
| Radiotherapy | | | |
| No | 10,519 (87.5) | 6995 (87.6) | 0.786 |
| Yes | 1508 (12.5) | 990 (12.4) | |
| BMI | 22.43 [20.24, 24.66] | 22.49 [20.27, 24.84] | 0.083 |
| creatinine (mg/dl) | 0.74 [0.62, 0.86] | 0.74 [0.63, 0.86] | 0.834 |
| Albumin (g/L) | 40.20 [36.80, 43.40] | 40.20 [36.80, 43.30] | 0.426 |
| ACR | 53.85 [45.31, 64.34] | 53.85 [45.31, 63.93] | 0.538 |
| ACR | | | |
| T1[b] | 3311 (27.5) | 2155 (27.0) | 0.354 |
| T2[c] | 4215 (35.0) | 2877 (36.0) | |

**Table 2** (continued)

| Variable | Training cohort (n = 12,027) | Validation cohort (n = 7985) | *P*-value |
|---|---|---|---|
| T3[d] | 4501 (37.4) | 2953 (37.0) | |
| PG-SGA | | | |
| < 4 | 5760 (47.9) | 3789 (47.5) | 0.551 |
| ≥ 4 | 6267 (52.1) | 4196 (52.5) | |
| Los | 11.00 [7.00, 19.00] | 11.00 [7.00, 19.00] | 0.58 |
| KPS | 90.00 [80.00, 90.00] | 90.00 [90.00, 90.00] | 0.459 |

TNM[a]: 3336 data missing

T1[b], T2[c], T3[d]: The tertile value according to the ACR

The summary statistics present N% for categorical variables and median [IQR] deviation for continuous variables

min/1.73 $m^2$, $P=0.041$). The most common cancer type in both cohorts was gastrointestinal tract tumors (40.1% in the training cohort and 41.3% in the validation cohort, $P=0.316$), followed by lung cancer, breast cancer, urogenital neoplasms, and nasopharyngeal carcinoma. TNM staging distributions were also similar, with 37.4% and 37.3% of patients in stages I + II and 62.6% and 62.7% in stages III + IV in the training and validation cohorts, respectively ($P=0.549$). The proportions of patients receiving surgery, chemotherapy, and radiotherapy were comparable between the training and validation cohorts (all $P>0.05$). PG-SGA scores ≥ 4 were observed in 52.1% of patients in the training cohort and 52.5% in the validation cohort ($P=0.551$). Median LOS was 11.00 days (IQR: 7.00–19.00) in both cohorts ($P=0.58$), and the median KPS score was 90.00 in both cohorts ($P=0.459$).

### Study correlations between variables

Correlation analysis (Figs. 2 and 3) revealed the relationships between albumin, creatinine, ACR, and age. Albumin was negatively correlated with age ($\rho=-0.13$), but positively correlated with creatinine ($\rho=0.18$) and ACR ($\rho=0.37$). Creatinine showed a positive correlation with age ($\rho=0.06$) and a strong negative correlation with ACR ($\rho=-0.81$). The validation cohort results were almost consistent with those of the training cohort.

### Association between ACR and OS of cancer patients

We analyzed the association between ACR index and OS risk (HR) in solid tumor patients. Multivariable-adjusted restricted cubic spline regression demonstrated a negative correlation between ACR index and OS when analyzed as a continuous variable (Fig. 4), indicating that patients with lower ACR levels had worse OS. Using the maximal selected rank statistics method, the optimal cutoff point for ACR in the training cohort was identified as 56.75 (Fig. 5). Kaplan–Meier survival curve analysis based on this cutoff showed that patients with higher ACR levels had significantly better OS compared to those with lower ACR levels ($P<0.0001$; Fig. 6). The results were consistent between the training and validation cohorts (Fig. 6).

As shown in Table 3, the ACR index was significantly associated with all-cause mortality in solid tumor patients. In Model 1, without adjustment for covariates, patients with high ACR levels had significantly reduced all-cause mortality risk compared to those with low ACR levels (HR = 0.65, 95% CI: 0.61–0.69, $P<0.001$). After adjusting for sex, age, BMI, and TNM stage in Model 2, the association remained significant (HR = 0.79, 95% CI: 0.73–0.86, $P<0.001$). In Model 3, which further adjusted for clinical factors including surgery, chemotherapy, radiotherapy, liver cirrhosis, chronic hepatitis, chronic kidney disease, ALT levels, and cancer diagnosis, the association persisted (HR = 0.78, 95% CI: 0.71–0.84, $P<0.001$). Trend analysis across ACR categories revealed a significant inverse relationship between ACR levels and all-cause mortality risk (P for trend < 0.001). Specifically, compared to the lowest tertile (T1), patients in the middle tertile (T2) showed a significantly reduced mortality risk in Model 3 (HR = 0.88, 95% CI: 0.81–0.96, $P=0.004$), with an even greater reduction observed in the highest tertile (T3) (HR = 0.71, 95% CI: 0.64–0.79, $P<0.001$). Similar results were observed in the validation cohort.

### Association of ACR with PG-SGA Scores, LOS, and KPS

The association between ACR levels and PG-SGA scores, LOS, and KPS scores showed consistent trends in both the training and validation cohorts (Table 4). Compared to the T1, patients in the T2 and T3 had significantly lower risks of PG-SGA scores ≥ 4 in the training cohort (T2: OR = 0.85, 95% CI: 0.76–0.94, $P=0.003$; T3: OR = 0.78, 95% CI: 0.7–0.87, $P<0.001$). Similar trends were observed in the validation cohort (T2: OR = 0.78, 95% CI: 0.69–0.9, $P<0.001$; T3: OR = 0.72, 95% CI: 0.62–0.84, $P<0.001$). For LOS, patients in the T3 group of the training cohort had a significantly reduced Los compared to the T1 group (OR = 0.85, 95% CI: 0.76–0.96,

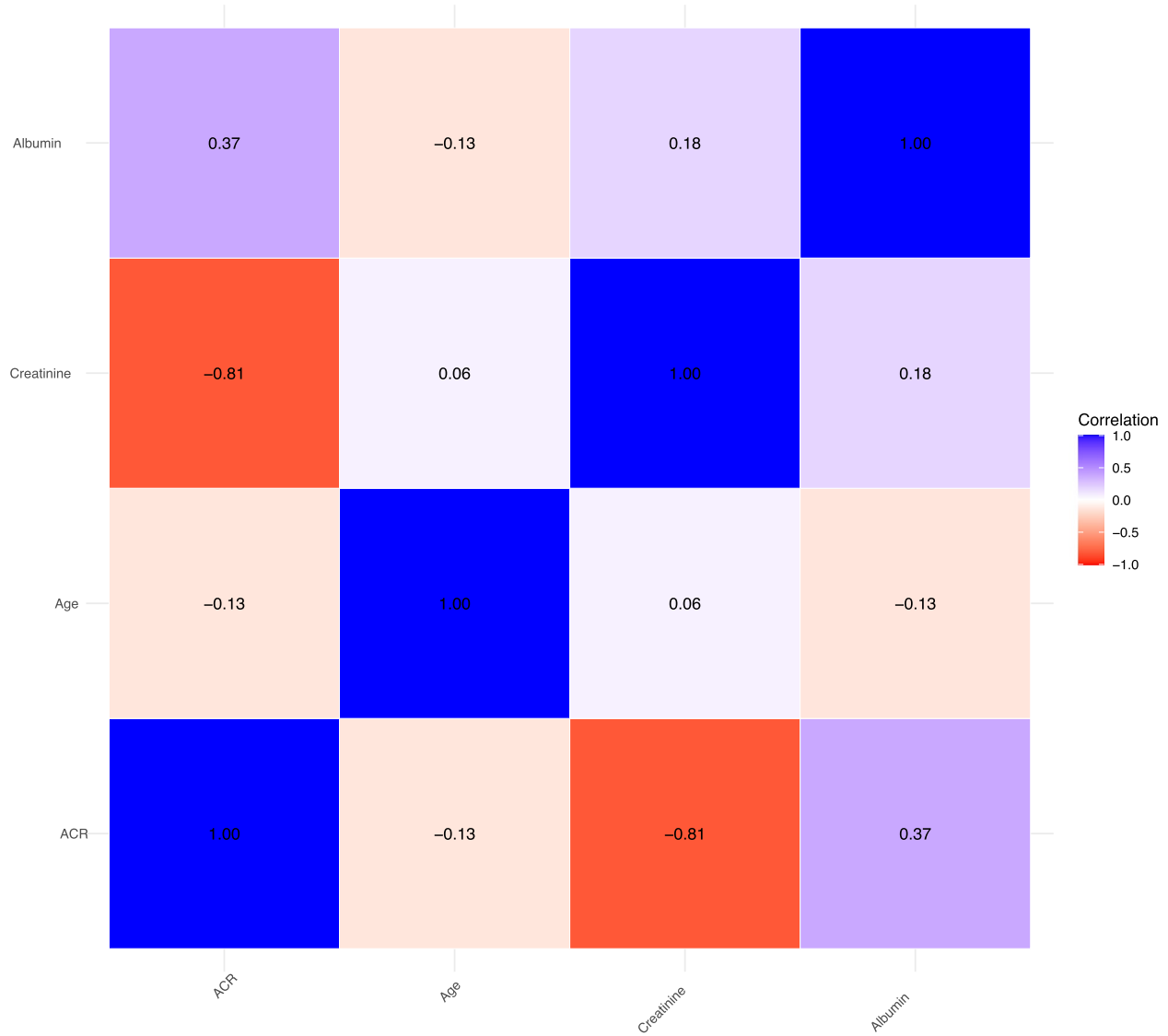


**Fig. 2** Spearman correlation coefficient between ACR, albumin, creatinine and age in training cohort

$P=0.008$), while the T2 group showed no significant difference (OR = 0.95, 95% CI: 0.85–1.07, $P=0.389$). No significant associations between ACR levels and LOS were observed in the validation cohort (T2: OR = 1.02, 95% CI: 0.89–1.18, $P=0.742$; T3: OR = 0.99, 95% CI: 0.85–1.16, $P=0.941$). For KPS scores, the risk of poor KPS scores was significantly reduced in both the T2 and T3 groups compared to the T1 group in the training cohort (T2: OR = 0.76, 95% CI: 0.68–0.86, $P<0.001$; T3: OR = 0.74, 95% CI: 0.65–0.83, $P<0.001$). The validation cohort showed a similar pattern, with the T3 group demonstrating the largest reduction in risk (T2: OR = 0.79, 95% CI: 0.67–0.93, $P=0.005$; T3: OR = 0.56, 95% CI: 0.47–0.67, $P<0.001$).

### Subgroup analysis

Figure 7 illustrated the distribution of tumor types in the training and validation cohorts. Supplementary Table 1 showed the baseline clinical characteristics of nasopharyngeal carcinoma, with no significant differences between the training and validation cohorts. After adjusting for multiple covariates, the high ACR group in the training cohort had a significantly lower risk of all-cause mortality compared to the low ACR group (HR = 0.49, 95% CI: 0.35–0.67, $P<0.001$). Trend analysis revealed that as ACR levels increased, the risk of all-cause mortality decreased significantly (P for trend < 0.001). Specifically, compared to T1, the T3 group had a significantly reduced mortality risk (HR = 0.41, 95% CI: 0.28–0.61,

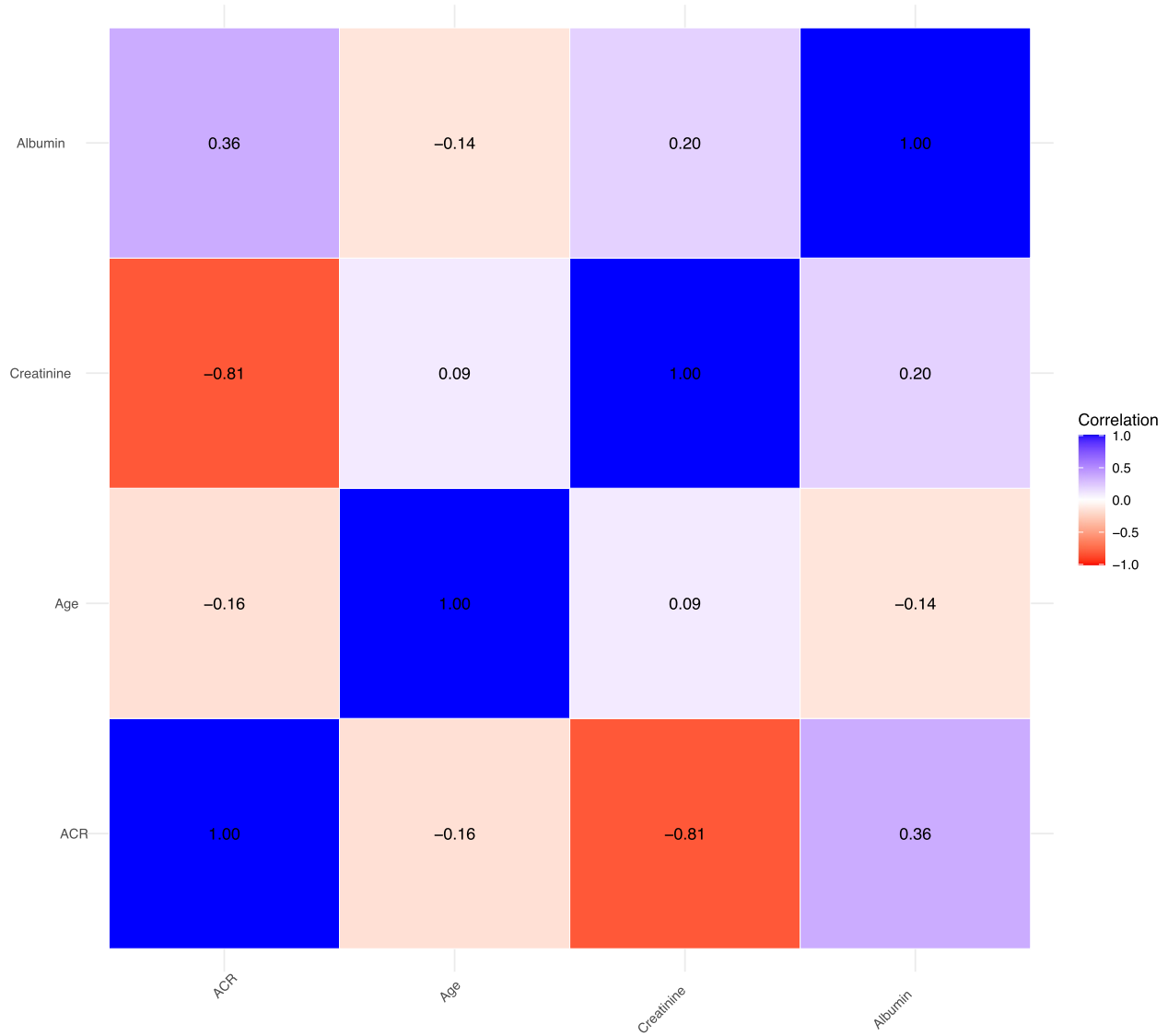


**Fig. 3** Spearman/Pearson correlation coefficient between ACR, albumin, creatinine and age in validation cohort

$P<0.001$). The validation cohort demonstrated results consistent with the training cohort. No significant associations were observed between ACR levels and PG-SGA scores, LOS, or KPS scores in nasopharyngeal carcinoma patients based on multivariable logistic regression analysis (Supplementary Table 7).

In gastrointestinal tract tumors, the median eGFR in the training cohort was 87.83 mL/min/1.73 $m^2$ (IQR: 70.72–108.99), while in the validation cohort, it was 89.89 mL/min/1.73 $m^2$ (IQR: 72.12–110.80), with a statistically significant difference ($P=0.005$; Supplementary Table 2). In the training cohort, patients with higher ACR levels had a significantly lower risk of all-cause mortality compared to those with lower ACR levels (HR = 0.84, 95% CI: 0.74–0.95, $P=0.007$). Trend analysis showed a significant decrease in mortality risk with increasing ACR levels (P for trend = 0.002). Specifically, compared to T1, patients in T2 had a slightly reduced risk of mortality (HR = 0.87, 95% CI: 0.77–0.99, $P=0.035$), while those in T3 exhibited a more pronounced reduction (HR = 0.78, 95% CI: 0.67–0.91, $P=0.002$). Similar results were observed in the validation cohort. Regarding nutritional and functional status, in the training cohort, patients in T2 and T3 had significantly lower risks of PG-SGA scores ≥ 4 compared to T1 (T2: OR = 0.84, 95% CI: 0.7–0.99, $P=0.04$; T3: OR = 0.78, 95% CI: 0.64–0.95, $P=0.014$). No significant association was observed between ACR levels and LOS. However, patients in T2

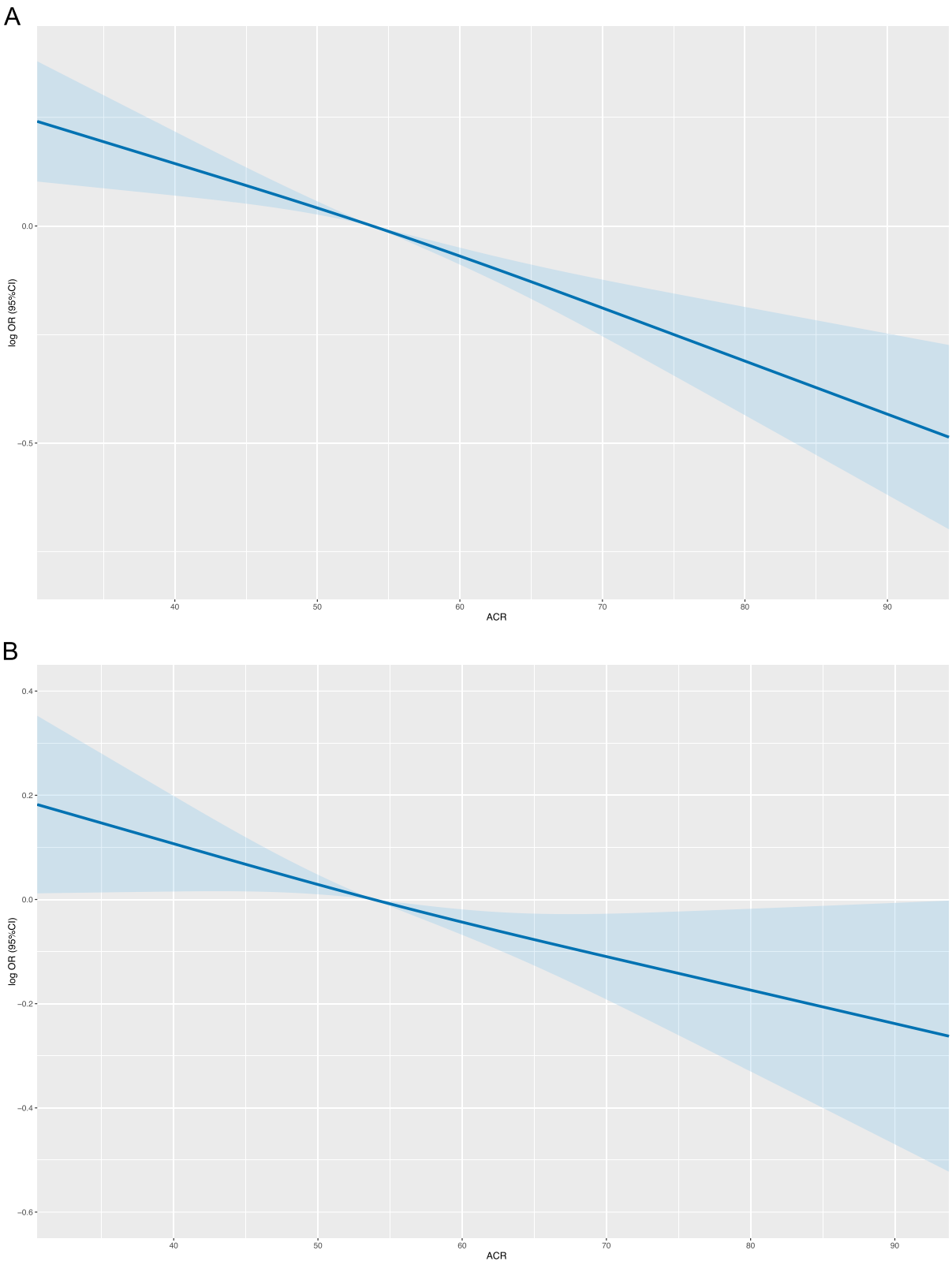


**Fig. 4** Association Between ACR and All-Cause Mortality in patients with solid tumor cancers Using a Restricted Cubic Spline Regression Model in (**A**) training cohort and (**B**) validation cohort. Model adjusted for Sex, Age, BMI, TNM, Surgery, Chemotherapy, Radiotherapy, Liver cirrhosis, Chronic hepatitis, Chronic kidney disease, ALT, Cancer diagnosis

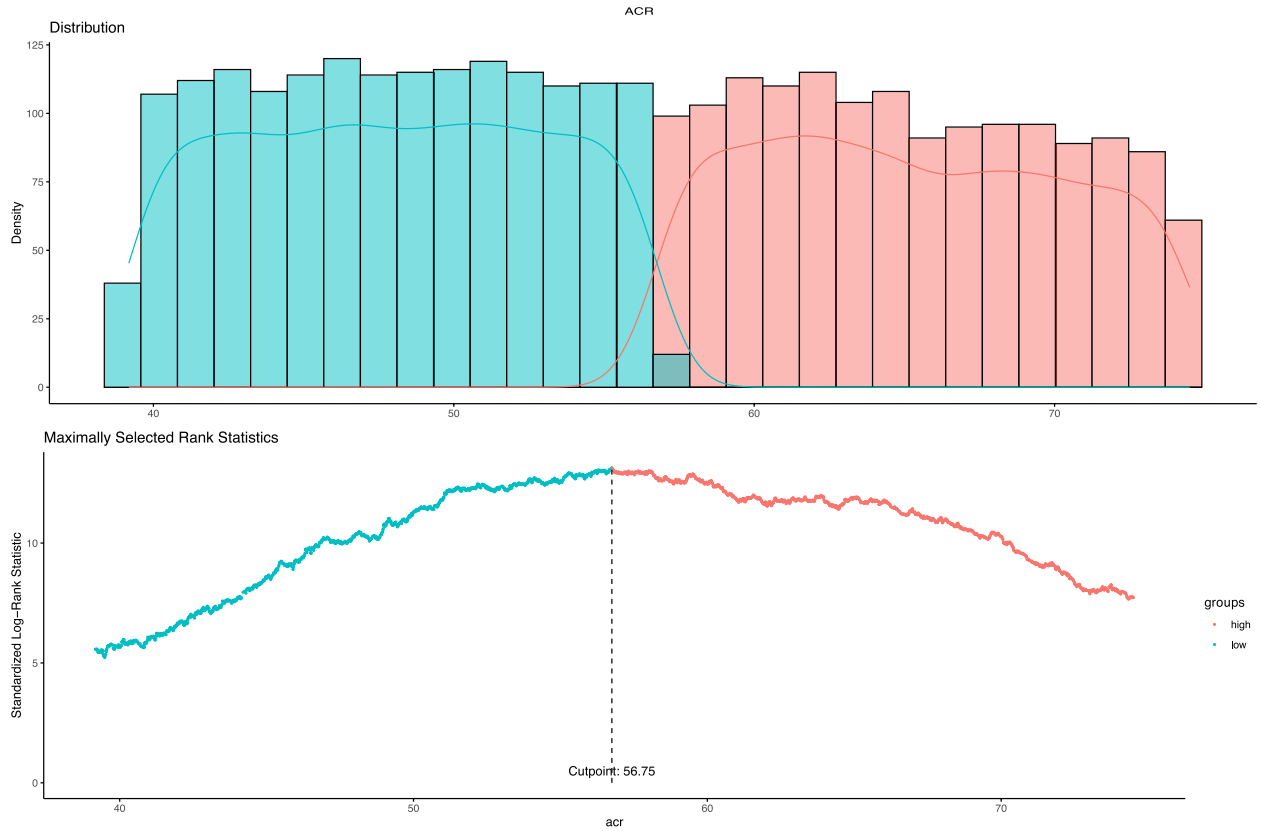


**Fig. 5** Receiver operating characteristic curve for determining the cut - off point of the ACR index in solid tumor patients within the training cohort

and T3 had significantly lower risks of poor KPS scores compared to T1 (T2: OR = 0.72, 95% CI: 0.61–0.85, $P < 0.001$; T3: OR = 0.72, 95% CI: 0.59–0.87, $P = 0.001$). Similar trends were found in the validation cohort.

In lung cancer patients, the median ACR in the validation cohort (HR = 52.71, IQR: 45.00–61.88) was significantly higher than that in the training cohort (HR = 51.57, IQR: 44.20–60.70) ($P = 0.024$). After adjusting for covariates, the training cohort showed that the risk of all-cause mortality was not significantly reduced in the high ACR group compared to the low ACR group (HR = 0.87, 95% CI: 0.75–1.02, $P = 0.079$). However, subgroup analysis revealed that patients in the T3 group had a significantly lower risk of all-cause mortality compared to the T1 group (HR = 0.83, 95% CI: 0.7–0.99, $P = 0.043$), with trend analysis indicating a significant inverse relationship between ACR levels and mortality risk (P for trend = 0.032). In the validation cohort, no significant reduction in mortality risk was observed in the high ACR group compared to the low ACR group (HR = 1.03, 95% CI: 0.86–1.23, $P = 0.757$). Subgroup analysis also showed no significant difference in mortality risk between the T3 and T1 groups (HR = 1.03, 95% CI: 0.83–1.28, $P = 0.779$), and trend analysis did not reveal a significant association (P for trend = 0.717). No significant associations were observed between ACR levels and PG-SGA scores, LOS, or KPS scores in the training cohort, with similar findings in the validation cohort.

In breast cancer patients, no significant differences were observed in the baseline variables between the training and validation cohorts (Supplementary Table 4). After adjusting for multiple covariates, ACR levels were not significantly associated with all-cause mortality in either the training or validation cohorts. In the training cohort, the high ACR group did not show a statistically significant reduction in mortality risk compared to the low ACR group (HR = 0.94, 95% CI: 0.71–1.24, $P = 0.655$). Subgroup analysis indicated no significant differences in mortality risk between the T2 or T3 groups and the T1 group (T2: HR = 1.2, 95% CI: 0.63–2.28, $P = 0.578$; T3: HR = 1.04, 95% CI: 0.56–1.94, $P = 0.903$). Trend analysis also did not reveal a significant association (P for trend = 0.735). No significant associations were observed between ACR levels and PG-SGA scores, LOS, or KPS scores in the training cohort, with similar findings in the validation cohort.

In urogenital neoplasms, there were no significant differences in the baseline pathological characteristics

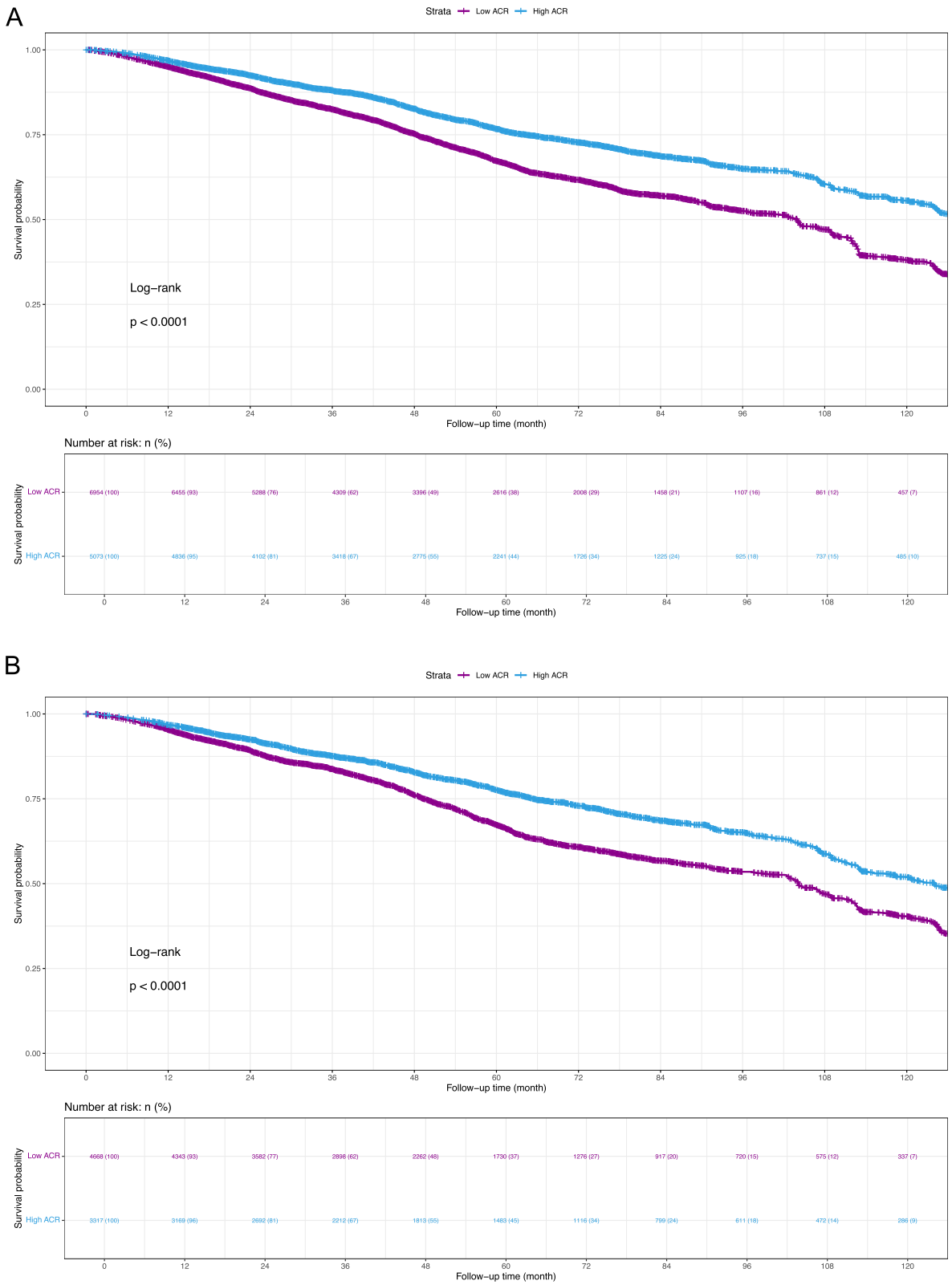


**Fig. 6** Kaplan–Meier curve of the ACR index in solid tumor cancers in (**A**) training cohort and (**B**) validation cohort

**Table 3** Association of ACR with all-cause mortality in patients with solid tumor cancers

| | Training cohort | | | | | | | Validation cohort | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Model 1 a | | Model 2 b | | Model 3 c | | | Model 1 a | | Model 2 b | | Model 3 c | | |
| ACR index | HR (95% CI) | P value | HR (95% CI) | P value | HR (95% CI) | P value | ACR index | HR (95% CI) | P value | HR (95% CI) | P value | HR (95% CI) | P value | |
| Low | Ref | | Ref | | Ref | | Low | Ref | | Ref | | Ref | | |
| High | 0.65 (0.61, 0.69) | < 0.001 | 0.79 (0.73, 0.86) | < 0.001 | 0.78 (0.71, 0.84) | < 0.001 | High | 0.69 (0.64, 0.75) | < 0.001 | 0.86 (0.78, 0.95) | 0.003 | 0.85 (0.76, 0.94) | 0.002 | |
| T1 | Ref | | Ref | | Ref | | T1 | Ref | | Ref | | Ref | | |
| T2 | 0.87 (0.81, 0.94) | < 0.001 | 0.9 (0.82, 0.98) | 0.011 | 0.88 (0.81, 0.96) | 0.004 | T2 | 0.87 (0.79, 0.95) | 0.003 | 0.95 (0.85, 1.05) | 0.326 | 0.94 (0.84, 1.05) | 0.254 | |
| T3 | 0.6 (0.56, 0.65) | < 0.001 | 0.73 (0.66, 0.81) | < 0.001 | 0.71 (0.64, 0.79) | < 0.001 | T3 | 0.66 (0.6, 0.73) | < 0.001 | 0.85 (0.75, 0.96) | 0.011 | 0.84 (0.74, 0.95) | 0.005 | |
| P for trend | | < 0.001 | | < 0.001 | | < 0.001 | P for trend | | < 0.001 | | 0.012 | | 0.001 | |

Model 1[a] was not adjusted for any covariates

Model 2[b] was adjusted for Sex, Age, BMI, TNM

Model 3[c] was adjusted for Sex, Age, BMI, TNM, Surgery, Chemotherapy, Radiotherapy, Liver cirrhosis, Chronic hepatitis, Chronic kidney disease, ALT, Cancer diagnosis

**Table 4** Associations between ACR and PG-SGA, Los and KPS among all participants

| Characteristic | Training cohort | | Validation cohort | | |
|---|---|---|---|---|---|
| | OR (95% CI) | P | Characteristic | OR (95% CI) | P |
| PG-SGA | | | PG-SGA | | |
| T1 | Ref | | T1 | Ref | |
| T2 | 0.85 (0.76,0.94) | 0.003 | T2 | 0.78 (0.69,0.9) | < 0.001 |
| T3 | 0.78 (0.7,0.87) | < 0.001 | T3 | 0.72 (0.62,0.84) | < 0.001 |
| Los | | | Los | | |
| T1 | Ref | | T1 | Ref | |
| T2 | 0.95 (0.85,1.07) | 0.389 | T2 | 1.02 (0.89,1.18) | 0.742 |
| T3 | 0.85 (0.76,0.96) | 0.008 | T3 | 0.99 (0.85,1.16) | 0.941 |
| KPS | | | KPS | | |
| T1 | Ref | | T1 | Ref | |
| T2 | 0.76 (0.68,0.86) | < 0.001 | T2 | 0.79 (0.67,0.93) | 0.005 |
| T3 | 0.74 (0.65,0.83) | < 0.001 | T3 | 0.56 (0.47,0.67) | < 0.001 |

Multivariable logistic regression model adjusted for Sex, Age, BMI, TNM, Surgery, Chemotherapy, Radiotherapy, Liver cirrhosis, Chronic hepatitis, Chronic kidney disease, ALT, Cancer diagnosis

between the training and validation groups (Supplementary Table 5). However, ACR levels were significantly associated with all-cause mortality in urogenital neoplasm patients. In the training cohort, patients with high ACR levels had a significantly lower risk of all-cause mortality compared to those with low ACR levels (HR = 0.55, 95% CI: 0.43–0.71, $P < 0.001$). Subgroup analysis revealed that the T3 group had a significantly reduced mortality risk compared to the T1 group (HR = 0.51, 95% CI: 0.36–0.72, $P < 0.001$), while the T2 group did not show a significant difference (HR = 0.8, 95% CI: 0.55–1.15, $P = 0.232$). Trend analysis indicated a significant inverse association between ACR levels and mortality risk (P for trend < 0.001). Similar results were observed in the validation cohort. In the training cohort, ACR levels were significantly associated with better nutritional and functional status. Compared to the T1 group, patients in the T2 and T3 groups had a significantly reduced risk of PG-SGA scores ≥ 4 (T2: OR = 0.44, 95% CI: 0.28–0.68, $P < 0.001$; T3: OR = 0.41, 95% CI: 0.27–0.62, $P < 0.001$). LOS was also significantly shorter in the T2 and T3 groups compared to the T1 group (T2: OR = 0.47, 95% CI: 0.29–0.74, $P = 0.001$; T3: OR = 0.44, 95% CI: 0.28–0.68, $P < 0.001$). Similarly, the risk of poor KPS scores was significantly lower in the T2 and T3 groups compared to the T1 group (T2: OR = 0.47, 95% CI: 0.3–0.75, $P = 0.001$; T3: OR = 0.31, 95% CI: 0.2–0.48, $P < 0.001$). In the validation cohort, no significant associations were observed for PG-SGA scores, and LOS.

### Sensitivity analysis

After excluding patients with eGFR < 60 mL/min/1.73 $m^2$(Supplementary Table 16–17), the association between ACR levels and all-cause mortality remained significant. In the training cohort, patients with high ACR levels had a significantly reduced risk of all-cause mortality compared to those with low ACR levels (HR = 0.77, 95% CI: 0.68–0.86, $P < 0.001$). Subgroup analysis indicated that patients in the T3 group had a significantly lower mortality risk compared to the T1 group (HR = 0.74, 95% CI: 0.64–0.85, $P < 0.001$). Trend analysis confirmed a significant inverse relationship between increasing ACR levels and mortality risk (P for trend < 0.001). Similar results were observed in the validation cohort. In the training cohort, higher ACR levels were associated with improved nutritional status. Compared to the T1 group, the risk of PG-SGA scores ≥ 4 was significantly lower in the T2 (OR = 0.86, 95% CI: 0.74–1, $P = 0.047$) and T3 groups (OR = 0.79, 95% CI: 0.66–0.93, $P = 0.005$). In the validation cohort, similar reductions were observed (T2: OR = 0.84, 95% CI: 0.73–0.97, $P = 0.016$; T3: OR = 0.77, 95% CI: 0.66–0.9, $P = 0.001$). For LOS, in the training cohort, patients in the T3 group had significantly shorter Los compared to those in the T1 group (OR = 0.74, 95% CI: 0.62–0.88, $P = 0.001$). However, no significant associations were found between ACR levels and LOS in the validation cohort (T2: OR = 0.98, 95% CI: 0.84–1.14, $P = 0.788$; T3: OR = 0.95, 95% CI: 0.81–1.12, $P = 0.565$). For KPS scores, in the training cohort, patients in the T2 and T3 groups had significantly lower risks of poor KPS scores compared to those in the T1 group (T2: OR = 0.73, 95% CI: 0.62–0.86, $P < 0.001$; T3: OR = 0.73, 95% CI: 0.61–0.87, $P = 0.001$). In the validation cohort, the T2 group also showed a significant reduction in risk (OR = 0.75, 95% CI: 0.63–0.89, $P = 0.001$), with an even

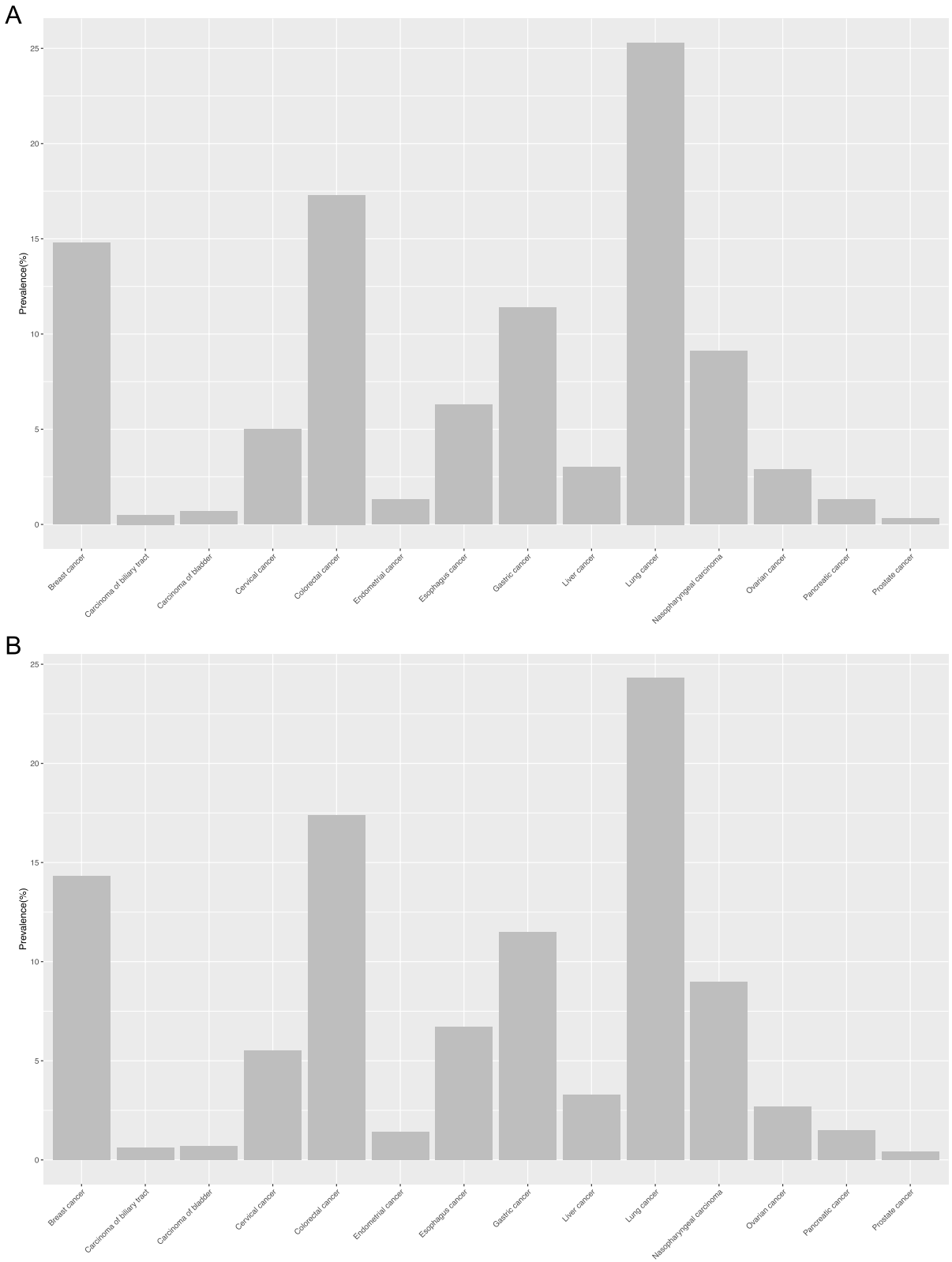


**Fig. 7** Prevalence rate in patients of different cancer types in (**A**) training cohort and (**B**) validation cohort

greater reduction in the T3 group (OR = 0.56, 95% CI: 0.46–0.67, $P < 0.001$).

After excluding patients who died within one year(Supplementary Table 18–19), ACR levels remained significantly associated with all-cause mortality in the training cohort. Compared to the low ACR group, the high ACR group showed a significantly reduced risk of all-cause mortality (HR = 0.76, 95% CI: 0.69–0.83, $P < 0.001$). Subgroup analysis indicated that patients in the T3 group had a significantly lower mortality risk compared to the T1 group (HR = 0.69, 95% CI: 0.62–0.77, $P < 0.001$), while the T2 group also exhibited a significant reduction in risk (HR = 0.87, 95% CI: 0.79–0.95, $P = 0.003$). Trend analysis further confirmed a significant inverse relationship between increasing ACR levels and mortality risk (P for trend < 0.001). In the training cohort, higher ACR levels were associated with better nutritional status. Compared to the T1 group, the risk of PG-SGA scores ≥ 4 was significantly reduced in both the T2 group (OR = 0.85, 95% CI: 0.76–0.95, $P = 0.005$) and the T3 group (OR = 0.76, 95% CI: 0.67–0.86, $P < 0.001$). For LOS, patients in the T3 group had significantly shorter hospital stays compared to the T1 group (OR = 0.82, 95% CI: 0.72–0.94, $P = 0.004$). However, no significant difference was observed between the T2 and T1 groups (OR = 0.93, 95% CI: 0.82–1.05, $P = 0.249$). For KPS scores, the risk of poor KPS scores was significantly lower in the T2 group (OR = 0.76, 95% CI: 0.67–0.85, $P < 0.001$) and the T3 group (OR = 0.68, 95% CI: 0.6–0.79, $P < 0.001$) compared to the T1 group. The validation cohort demonstrated similar results to those observed in the training cohort.

After excluding malnourished patients(Supplementary Table 20–21), ACR levels remained significantly associated with all-cause mortality. In the training cohort, the high ACR group had a significantly lower risk of all-cause mortality compared to the low ACR group (HR = 0.67, 95% CI: 0.58–0.76, $P < 0.001$). Subgroup analysis showed that patients in the T3 group had a markedly reduced mortality risk compared to the T1 group (HR = 0.6, 95% CI: 0.51–0.7, $P < 0.001$), while the T2 group exhibited a smaller but statistically significant reduction (HR = 0.87, 95% CI: 0.76–0.99, $P = 0.037$). Trend analysis confirmed a significant inverse relationship between increasing ACR levels and mortality risk (P for trend < 0.001). The validation cohort produced similar results. In the training cohort, higher ACR levels were associated with shorter hospital stays. Compared to the T1 group, the T2 group had a slightly reduced LOS (OR = 0.83, 95% CI: 0.69–1, $P = 0.044$), while the T3 group showed a more substantial reduction (OR = 0.64, 95% CI: 0.52–0.78, $P < 0.001$). However, in the validation cohort, no significant associations were observed between ACR tertiles and LOS (T2: OR = 1.12, 95% CI: 0.9–1.4, $P = 0.306$; T3: OR = 1.01, 95% CI: 0.79–1.29, $P = 0.932$). For KPS scores, in the training cohort, the risk of poor KPS scores was significantly lower in both the T2 group (OR = 0.79, 95% CI: 0.63–1, $P = 0.045$) and the T3 group (OR = 0.73, 95% CI: 0.56–0.94, $P = 0.014$) compared to the T1 group. In the validation cohort, no significant difference in KPS scores was observed between the T2 and T1 groups (OR = 0.91, 95% CI: 0.72–1.15, $P = 0.414$), but the T3 group showed a significantly lower risk of poor KPS scores (OR = 0.61, 95% CI: 0.48–0.78, $P < 0.001$).

## Discussion

This study investigated the association between the ACR and clinical outcomes in solid tumor patients, including OS, PG-SGA, LOS, and KPS scores. The results demonstrated that higher ACR levels were significantly associated with improved OS and better clinical outcomes. This association was consistently validated across multiple analyses, even after excluding patients with impaired renal function, those who died within one year of follow-up, or those with malnutrition. Subgroup analyses further supported these findings. Higher ACR levels were significantly associated with lower mortality risk in patients with nasopharyngeal carcinoma, gastrointestinal tract tumors, and urogenital neoplasms. However, no significant associations were observed in lung and breast cancer patients. Regarding the relationship between ACR and PG-SGA, higher ACR levels were associated with the absence of malnutrition in patients with gastrointestinal cancers. For the relationship between ACR and KPS, higher ACR levels were associated with better KPS scores in patients with gastrointestinal and urogenital cancers.

Malignancy is a major global public health problem [19]. Although the urinary albumin-to-creatinine ratio (UACR) has been studied before, most of it has been in cardiovascular disease [20, 21]. Both albumin and creatinine are easily obtained hematological indicators in clinical practice, and their application in cancer patients should also be paid attention to. Regarding the ACR, this paper explored its application in common tumors for the first time. Albumin and creatinine were readily accessible hematological markers in clinical practice, and their application in cancer patients warranted attention. This study was the first to explore the utility of the ACR in common cancers. The findings revealed that among patients with common cancers, higher ACR values, whether analyzed as a cutoff or tertiles, were associated with better OS. However, the analysis results showed no statistically significant association between ACR and OS in lung and breast cancers. For lung cancer, this may be attributed to its pronounced heterogeneity, including different subtypes such as non-small cell lung cancer (NSCLC) and small cell lung cancer (SCLC).

These subtypes differ significantly in pathological characteristics, proliferation rates, and treatment responses [22]. This heterogeneity may weaken the ability of ACR to serve as a unified prognostic indicator. The lungs were a site prone to recurrent or chronic inflammatory damage [23]. Albumin levels may be significantly affected. For breast cancer, this may be due to its highly heterogeneous molecular subtypes, which exhibit significant differences in prognosis [24, 25]. For women with non-metastatic breast cancer, obesity is associated with an increased risk of developing a second cancer, as well as higher overall and cancer-specific mortality rates [26–30]. Albumin levels are closely related to nutritional status [7]. Nutritional deficiencies are more commonly observed in patients with gastrointestinal tract tumors [31], This may partly explain the close association between ACR and PG-SGA, as well as KPS, in patients with gastrointestinal tract tumors. Medical conditions and medical resources are different in different regions [32], this may be the reason why ACR fails to respond to Los.

Albumin is a protein that performs a variety of functions in the body, including maintaining colloid osmotic pressure and binding and transporting molecules. It is the most abundant plasma protein [33, 34]. Studies have identified many possible roles for albumin in regulating acid–base balance, altering inflammation, maintaining vascular endothelial integrity, and binding endogenous and exogenous compounds [35]. Hypoalbuminemia is associated with high mortality in patients with nephropathy [36]. Malnutrition is a common but underrecognized problem among hospitalized patients [37]. Albumin is an index that simply reflects the nutritional status of hospitalized patients. Cancer-associated nutrition is characterized by muscle loss, malnutrition, and cachexia [38]. Malnutrition is common in cancer patients, which adversely affects patients' survival and quality of life [22].

Serum creatinine is undoubtedly one of the most commonly used biological parameters [39]. Serum creatinine is the product of muscle catabolism. Cancer cachexia is a multifactorial syndrome characterized by skeletal muscle loss leading to progressive sexual dysfunction, which is strongly associated with increased mortality [40]. Tumor cytokine induced inflammation can alter endothelial/vascular function in the kidney, leading to elevated serum creatinine values and diminished renal function [41].

Increased creatinine, low albumin, and ACR have been shown to be tumor stage independent prognostic factors for sarcoma-specific survival [5]. This study analyzed the use of the ratio of albumin to creatinine in patients with common tumors. ACR is an easily accessible and cost-effective biomarker that can aid in prognostic assessment in oncology. ACR was significantly negatively associated with the risk of death in multiple cancer subtypes, such as nasopharyngeal cancer, gastrointestinal tract tumors, and urogenital neoplasms. This suggests that ACR can be used as an independent prognostic indicator to help clinicians stratify patient management based on risk. Higher ACR levels reflect better nutritional and functional status and are associated with better survival outcomes for patients. This is particularly important for gastrointestinal tract tumors, which have a high incidence of malnutrition, and for urogenital neoplasms, which reflect a dynamic response to renal function and overall health. Based on commonly used clinical indicators (serum albumin and creatinine), ACR is a simple tool that is easy to use in clinical Settings. However, there are some limitations in this analysis. The values of albumin and creatinine are also affected by diabetes, and we failed to analyze the relationship between ACR and cancer prognosis in diabetic cancer patients. In addition, the study in this paper has only been verified internally, and has not been verified externally in other populations. Whether it can be extended to other populations is unknown. In addition, the association between ACR and disease-free survival was not explored due to the absence of relevant data. Finally, the relevant biological mechanisms need to be further explored.

#### Abbreviations

| | |
|---|---|
| ACR | Albumin-to-creatinine ratio |
| INSCOC | Investigation on Nutrition Status and Clinical Outcome of Common Cancers |
| OS | Overall Survival |
| PG-SGA | Patient—Generated Subjective Global Assessment |
| LOS | Length of Stay |
| KPS | Karnofsky Performance Status |

## Supplementary Information

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Supplementary Material 1.

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#### Authors' contributions

H.Z. and X.R.L. wrote the main manuscript text. H.Z. and X.R.L. performed the data analysis and interpretation. X.Y.L., C.A.L., and X.Z. were involved in data collection and statistical analysis. Y.C. and J.Y.S. contributed to the writing of the manuscript and provided critical revisions. Q.T.L. and Z.T.B. were responsible for data management and quality control. H.P.S. supervised the study, provided guidance on the interpretation of the results, and reviewed the manuscript. All authors reviewed the manuscript.

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**Data availability**
The datasets used and/or analysed in the current study are available from the corresponding author upon reasonable request.

## Declarations

**Ethics approval and consent to participate**
This study was approved by the ethics committee of Beijing Shijitan Hospital and adhered to the Declaration of Helsinki. Informed consent forms were signed by the participants.

**Consent for publication**
Not Applicable.

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

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