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Original Research

Preoperative neutrophil-to-lymphocyte ratio (preNLR) for the assessment of tumor characteristics in lung adenocarcinoma patients with brain metastasis

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ABSTRACT

Objectives: Brain metastases from lung adenocarcinoma cause significant patient mortality. This study aims to evaluate the role of preoperative Neutrophil-to-Lymphocyte ratio (preNLR) in predicting the survival and prognosis of Lung adenocarcinoma (LUAD) patients with brain metastasis (BM) and provide more references for predicting peritumoral edema.

Methods: We retrospectively reviewed 125 LUAD-BM patients who had undergone surgical resection from December 2015 to December 2020. The clinical characteristic, demographic, MRI data, and preNLR within 24–48 h before craniotomy were collected. Patients were divided into two groups based on preNLR (high NLR and low NLR), with cutoff values determined by receiver operating characteristic (ROC) analysis. Association between preoperative NLR and clinical features was determined by using Pearson chi-squared tests. Uni- and multivariate analyzes were performed to compare the overall survival (OS) of clinical features.

Results: The patients were divided into NLR-low (64 patients) and NLR-high (61 patients) groups based on receiver operating characteristic analysis of NLR area. According to correlation analysis, a high preNLR (NLR$\geq$2.8) is associated with the both supra- and infratentorial location involved ($P = 0.017$) and a greater incidence of severe peritumoral edema ($P = 0.038$). By multivariable analysis, age $\geq$ 65 years ($P = 0.011$), KPS $<$ 70 ($P = 0.043$), elevated preNLR ($P = 0.013$), extracerebral metastases ($P = 0.003$), EGFR/ALK+ ($P = 0.037$), postoperative radiotherapy ($P = 0.017$) and targeted therapy ($P = 0.007$) were independent prognostic factors. OS nomogram was constructed based on cox model and model performance was examined (AUC = 0.935).

Conclusions: PreNLR may serve as a prognosis indicator in LUAD patients with brain metastasis, and high preNLR tends to be positively associate with multiple locations and severe peritumoral edema.

Introduction

Brain metastases (BM) are the most common central nervous system tumors with significant morbidity and poor survival outcomes [1]. A recent study found that up to 50 percent of patients with advanced non-small-cell lung cancer (NSCLC) develop BM, which is a significant reason for mortality [2,3]. Despite therapeutic progress, the median survival of these patients remains poor [4]. BM occurs most frequently in patients with adenocarcinomas and tumors harboring epidermal growth factor receptor (EGFR) mutations or anaplastic lymphoma kinase (ALK) rearrangements [5]. The treatment for BM has gradually developed into comprehension treatment with the core being surgical treatment, especially the patients with a single occurrence in the brain, appropriate location, easy resection, heavy tumor/edema mass effect, and severe hydrocephalus to reduce symptoms rapidly [6–8]. In several studies, performance status [9], age, presence of extracranial metastasis, number and volume of brain lesions [10], EGFR and ALK alteration, and previous WBRT (whole-brain radiation therapy) [11] are independent prognostic factors for patients with brain metastasis. However, a paucity of studies investigating how preoperative testing and imaging are associated with OS before surgical resection of brain metastasis.

There have been studies showing that elevated preoperatively

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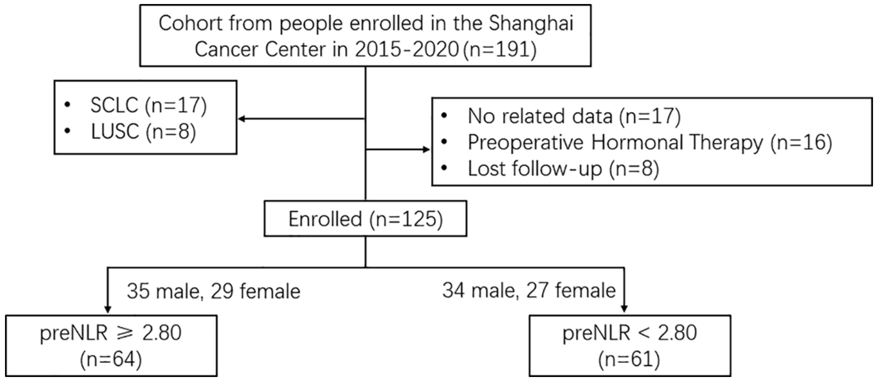

Fig. 1. Grouping flowchart of inclusion/exclusion Criteria.

neutrophil/lymphocyte ratio (preNLR) has a dominant prognostic value in brain metastases [12–14]. In addition, previous studies have shown the prognostic value of NLR in other nervous system disorders, including glioblastoma [15], traumatic brain injury [16], Meningiomas [17], Alzheimer's disease [18] and lymphoma [19]. The cutoff value of NLR reported in previous literature is around 2.0–7.0 [12,14,20-22]. However, few studies focused on the prognostic value of elevated preNLR in LUAD patients with BM. To date, few have studied the correlation between preNLR and peritumoral edema before the surgical resection of brain metastasis of LUAD and its prognostic value.

Taken together, we investigated the connections between preNLR and lesion characteristics in LUAD-BM undergoing surgical resection, and evaluated its values in the prediction of overall survival (OS). To facilitate public usage, an innovative prognostic nomogram model was developed to identify a new tool to risk-stratify patients to aid in clinical decision making.

Materials and methods

Study population

Of 191 patients,125 lung cancer patients with BM surgeries were performed from December 2015 to December 2020 at the Department of Neurosurgery, Fudan University Shanghai Cancer Center, Shanghai, China. A flowchart is presented to show the inclusion/exclusion criteria in this study. (Fig. 1). Clinicopathologic information of these patients, including age, gender, Karnofsky performance status, tumor size, tumor location, the number of tumors, peritumoral brain edema, extracerebral metastases, pathological features and postoperative treatment modalities were obtained from electronic medical records. KPS was used to assess the clinical status of the patient before each surgery on a scale from 0 to 100, with higher scores indicating better health status.

Preoperative imaging findings

Lesion characteristics were based on brain magnetic resonance imaging (MRI) according to the standard protocol. Tumor size was defined as the maximum diameter of the tumor and analyzed separately by the size criteria applicable to their category (size 3 cm for single or multiple tumors). Tumor location was divided into three groups: infratentorial, supratentorial and both supra- and infratentorial. Peritumoral cerebral edema was assessed by two experienced radiologists on MRI and graded according to the Steinhoff classification: 0 - no signs of edema; I- peritumoral cerebral edema, limited to 2 cm; II- peritumoral cerebral edema limited to one hemisphere; III - more than half of the hemisphere [23]. Since no grade 0 was found in the cases, grade I, grade II and grade III were defined as mild, moderate, and severe in this study, respectively. Positron emission tomography-computed tomography (PET-CT) was performed to determine the presence of extracranial metastasis in the diagnosis of BM.

Preoperative laboratory test

Laboratory data with differential counts were collected 48 h before receiving operation at baseline. All clinical laboratory tests were performed at the Clinical Pathology Laboratories at our main hospital. The preNLR was calculated by dividing absolute neutrophil count by total lymphocyte count. Preoperative NLR is defined as patients who received brain tumor resection within 48 h before preceding surgery. EGFR mutations and ALK rearrangements detection were evaluated using the paraffin blocks of the pathological specimens from surgical specimens.

Postoperative treatment and follow-up

Postoperative radiotherapy and targeted therapy information were abstracted from medical records. Overall survival (OS) was measured from the time of craniotomy. Patients who survived were reviewed from the date of the last follow-up. Cox regression analysis was used to evaluate the ability of clinical factors to predict overall postoperative survival. Intracranial MRI enhanced scan was performed every 3 months postoperatively. All patients had undergone surgical resection and were followed until death or up to October 3, 2021. For all patients, written informed consent was recorded by the Human Subject Protection or ethics committee.

Statistics

A pROC package for R was used to calculate the (receiver operating characteristic) ROC scores. The log-rank test was used to compare the survival distributions between 2 groups. The categorical and binary variables were analyzed in contingency tables using Fisher's exact test. A nomogram was created using the function from the rms library. All statistical analyses were performed using R software, version 4.1.3 (http://www.r-project.org). All p values reported were two-sided, and p values < 0.05 were considered statistically significant.

Results

Patient characteristics

Patients had a median age of 65 years (range, 28–76 years) at the time of surgery with the male predominance (60%, $n = 75$). More than half of the patients (70, 55%) had a KPS ≥ 70 and EGFR mutations or ALK rearrangements at diagnosis. Approximately all of the patients (105, 84%) had neurological symptoms (e.g. headache, tinnitus, blurry vision, and dizziness) at the time before resection, and the remaining patients only had space-occupying intracranial based on a screening brain. Extracranial metastasis was present in 41.6% of patients, and 76

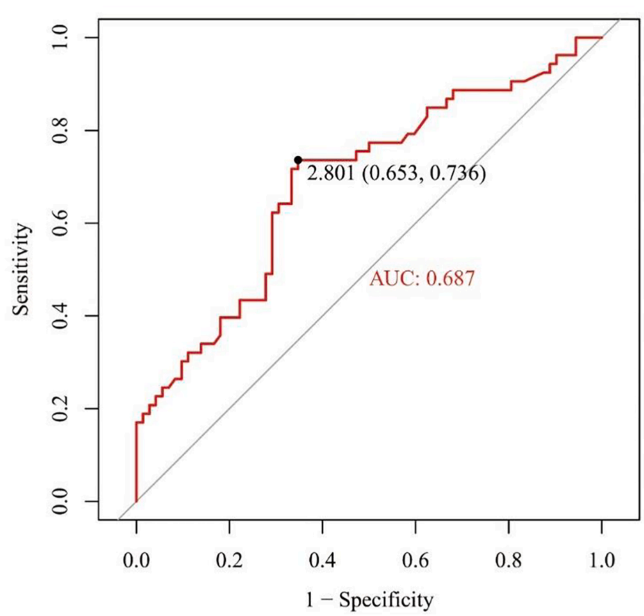

Fig. 2. Summary Receiver Operating Characteristic Curve plot of preNLR of patients.

patients (60.8%) had a single intracranial metastasis. Tumor locations were supratentorial in 100, infratentorial in 7, and 18 patients in both supra- and infratentorial. There were 30 cases with peritumor cerebral edema less than 2 cm (I Steinhoff classification), 46 cases with peritumor cerebral edema less than half of the brain (II Steinhoff classification), and 49 cases with peritumor cerebral edema more than half of the brain (III Steinhoff classification). In this paper, peritumoral brain edema was defined and graded as mild, moderate, or severe according to the international recommendations.

The brain tumor resection was well tolerated in all patients, 4 cases of active bleeding, 2 cases of post-operative infection, 1 case post-operative subcutaneous and no other significant complications or procedure-related mortality were observed. A total of 78 patients (62%) underwent postoperative targeted therapy, and 68 patients (54%) underwent postoperative radiotherapy. The median and maximum follow-up periods for survivors were 16.8 and 60.6 months, respectively. The mean postoperative survival period was 17.1 ± 12.8 months.

The ROC analysis showed that the AUC for preNLR was 0.687, the cutoff value of preNLR was 2.801, the sensitivities and specificities of diagnosing BM by preNLR were 0.653 and 0.736 (Fig. 2). Patients were divided into two groups according to preoperative NLR ≥ 2.8 and NLR < 2.8, respectively. Thirty-nine patients (61%) in high NLR and fourteen patients (23%) in low NLR had died. PreNLR < 2.8 patients had a worse prognosis than those with preNLR ≥ 2.8 ($P < 0.001$) (Fig. 3A). Patients with KPS < 70 patients had a median survival of 18.7 months compared with 59.9 months in the KPS ≥ 70 patients group ($P = 0.0017$) (Fig. 3B).

Lesion characteristics

Inspection of the survival curve reveals a strong survival advantage in single and double lesions, but a limited survival advantage in multiple brain metastasis ($P = 0.0025$) (Fig. 3C). Moreover, multiple tumors occupying both supra- and infratentorial sites had a significantly worse median survival time than supratentorial location only (supratentorial median survival 35 months; supra- and infratentorial 19 months, $P = 0.034$), showing a location-dependent effect of the BM on lifespan and multiple metastases (Fig. 3D). However, the Kaplan-Meier survival analysis did not reveal differences among the three groups (severe

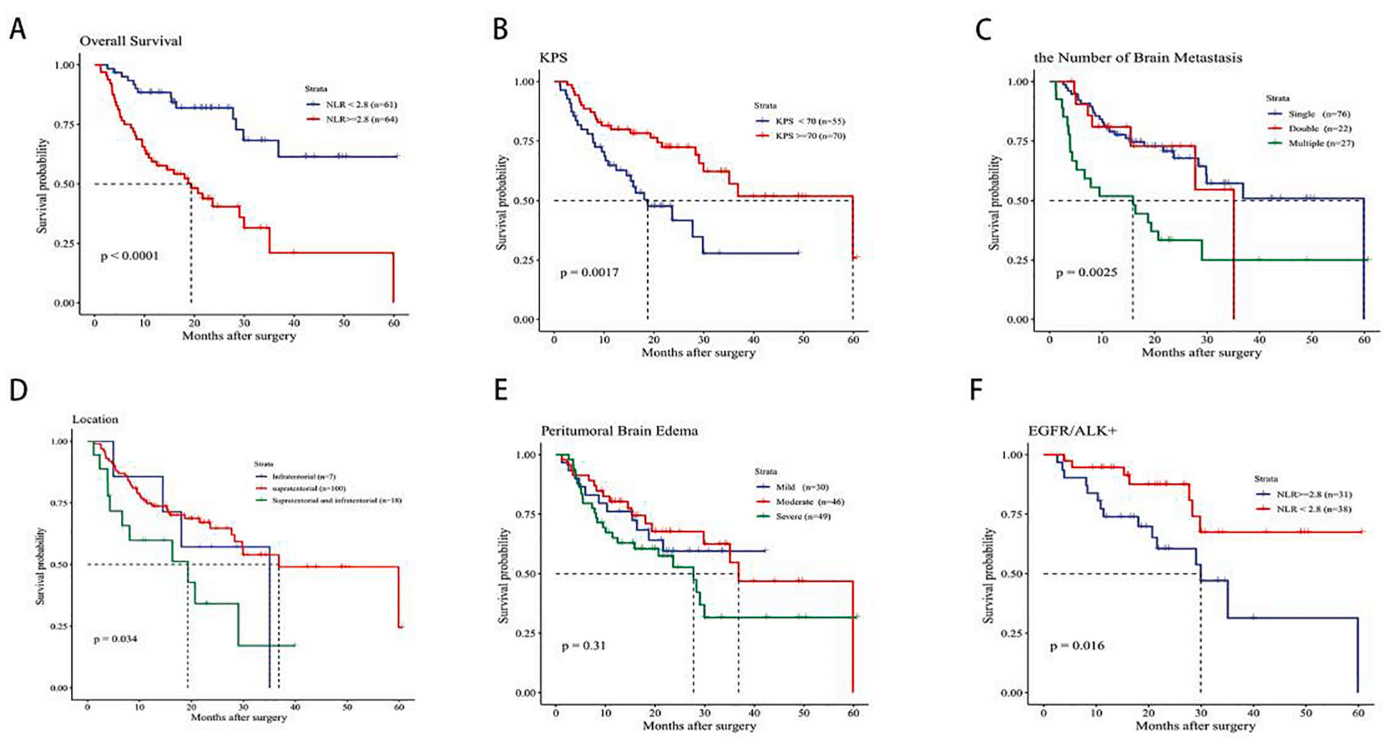

Fig. 3. Kaplan–Meier curves depict survival. (A) Univariate effect of the preoperative NLR on overall survival. (B) Kaplan–Meier curves for overall survival between high (KPS $\geq$ 70) and low (KPS $<$ 70) KPS before surgery in LUAD patients with BM. (C) Comparison of median survival time of LUAD BM patients with single, double and multiple brain lesions ($P = 0.0025$). (D) Kaplan–Meier survival curves for overall survival between the different locations of brain metastasis in LUAD patients with BM. (E) Kaplan–Meier survival curves for overall survival between different peritumoral edema of brain metastasis in LUAD patients (F) Overall survival in LUAD patients with BM of EGFR/ALK+ cases with high and low NLR levels. Abbreviation: LUAD, lung adenocarcinoma; BM, brain metastases; NLR, neutrophil-to-lymphocyte ratio; KPS, Karnofsky performance status; EGFR, epidermal growth factor receptor; ALK, anaplastic lymphoma kinase.

Table 1
Association between NLR and clinical background features in LUAD patients with BM.

Variables	NLR≥2.8 (n = 64)	NLR<2.8 (n = 61)	P value
Age			0.256
≥65	25(39%)	17(27%)	
<65	39(61%)	44(73%)	
Gender			1
male	35(55%)	34(56%)	
female	29(45%)	27(44%)	
KPS			
≥70	36(56%)	34(55%)	1
< 70	28(44%)	27(45%)	
Tumor size			0.45
< 3cm	22(34%)	26(42%)	
≥ 3cm	42(64%)	35(58%)	
Location			
supratentorial	45(70%)	55(90%)	**0.017**
infratentorial	6(9%)	1(8%)	
Supra- and infratentorial	13(21%)	5(2%)	
Number of brain metastases			0.068
1	36(56%)	40(65%)	
2	9(14%)	13(21%)	
≥3	19(30%)	8(12%)	
Peritumoral brain edema			
mild	12(18%)	18(29%)	**0.038**
moderate	20(31%)	26(42%)	
severe	32(51%)	17(29%)	
Extracerebral metastases			
Presence	32(50%)	20(32%)	0.333
Absence	32(50%)	41(68%)	
EGFR/ALK+			
No	33(51%)	23(37%)	0.168
Yes	31(49%)	38(63%)	
Postoperative radiotherapy			
yes	32(50%)	36(59%)	0.405
no	32(50%)	25(41%)	
Postoperative targeted therapy			
yes	36(56%)	42(68%)	0.204
no	28(44%)	19(32%)	

median survival = 27.7 months; moderate median survival = 36.8 months, mild median survival has not been reached, P = 0.31) (Fig. 3E). EGFR mutations or ALK rearrangements patients with a high NLR (n = 31) had a median survival of 19.5 months compared with 22.2 months in the low NLR (n = 38) group (P = 0.016). (Fig. 3F)

To explore the relationship between preNLR and clinical characteristics, the relationships between the preNLR and the clinic laboratory background features in 125 LUAD patients with BM. (Table 1). We found there were no significant differences between the two groups (NLR ≥ 2.8 and NLR < 2.8) in the clinic laboratory background features, except for the location of brain tumor lesion (χ^2 = 8.0596, P = 0.018) and the peritumoral brain edema (χ^2 = 6.5062, P = 0.038). The chi-square test was performed to compare the differences in the varying brain metastasis locations and degrees of peritumoral edema by preNLR (Fig. 4). There was a significant between-group difference in preNLR between brain metastasis locations (P = 0.02) and degrees of peritumoral edema (P = 0.04). Only patients with severe peritumoral edema have significantly higher preNLR (P=0.03). Patients with tumors in the infratentorial group and supra- and infratentorial group tend to have a higher preNLR (P = 0.06). Spearman's rank correlation between the extent of peritumoral edema in different tumor location were performed (Fig. 5A), and a mixed design 2-way ANOVA was performed on the preNLR, with peritumoral brain edema as the within-subjects variable and brain metastasis location as the between-subjects variable. The ANOVA revealed a significant interaction between brain metastasis location and peritumoral brain edema (F = 4.208; P = 0.003). However, there is no meaningful main effect emerged with both Brain metastasis location (F = 0.705; P = 0.535) and peritumoral brain edema (F = 1.053; P = 0.428), which indicated a possible trend toward severe peritumoral edema for higher preNLR. The interaction plot is summarized in Fig. 5B.

Postoperative treatment

Since most of our patients already finished chemotherapy for a long time when the brain metastasis happened, we do not directly take into account the effect of chemotherapy on preNLR. Of 125 cases, a total of 78 patients (62.4%) underwent postoperative targeted therapy, and 58 (46.4%) chose postoperative cerebral radiotherapy. Only 28 of these patients were concurrently on both treatments. We compared the

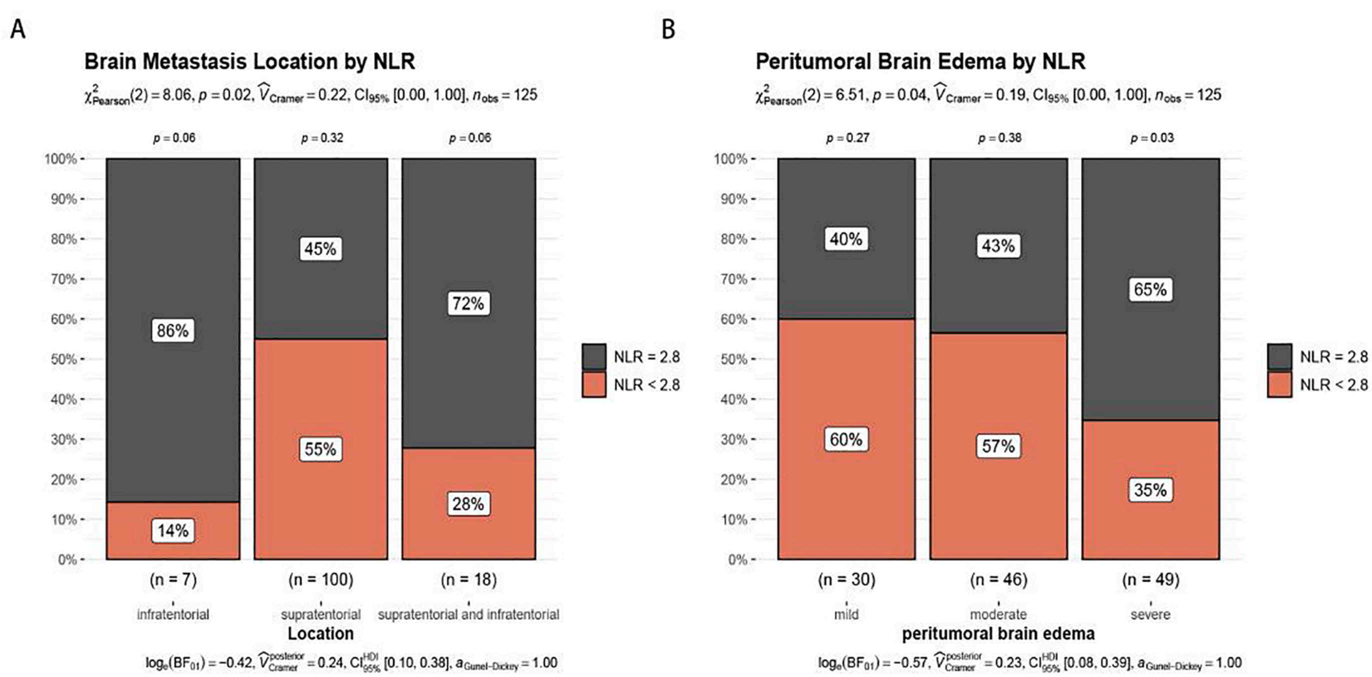

Fig. 4. Stacked histogram showing the brain metastasis locations (A) and the peritumoral edema levels (B) of both levels of NLR on the indicated day before surgery.

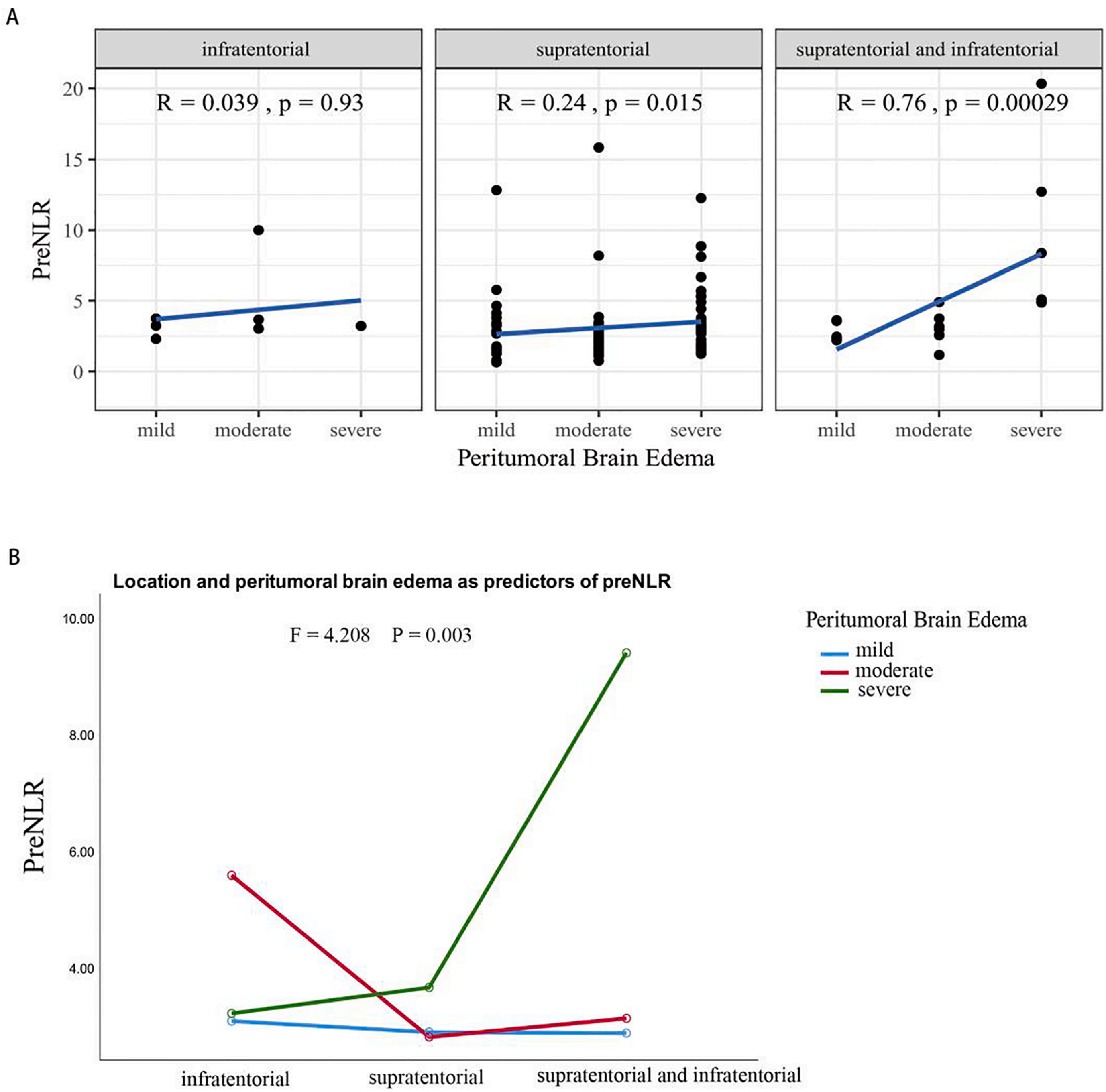

Fig. 5. The relationship of locations and peritumoral brain edema on preNLR. (A)The corresponding Spearman correlations of peritumoral brain edema and preoperative NLR between different tumor location. (B) The Interaction ANOVA plot of location and peritumoral brain edema was conducted on patients. The severe peritumoral brain edema shows a high level of preNLR when it happens to both supra- and infratentorial compared to baseline level when exposed to the location of supratentorial or infratentorial. Relative preNLR measures are represented as Mean ± SEM.

prognostic effects of postoperative radiotherapy and targeted therapy between the two groups. we found that patients with a higher preNLR received postoperative radiotherapy and targeted therapy had a significantly worse prognosis than lower preNLR patients who received the same treatment (P < 0.001, P < 0.001, respectively).

Survival analysis

All variables with statistical significance in univariate cox regression analysis ($p < 0.05$) were subjected to multivariate cox regression analysis. The age (≥65) (HR 2.403, 95% CI 1.223 to 4.723; $P = 0.011$), KPS < 70 (HR 2.019, 95% CI 1.022 to 3.989; $P = 0.043$), extracerebral metastases (HR 2.530, 95% CI 1.380 to 4.639; $P = 0.003$), elevated preNLR (HR 2.400, 95% CI 1.204 to 4.782; $P = 0.013$), EGFR/ALK+ (HR 0.485, 95% CI 0.246 to 0.956; $P = 0.037$), postoperative radiotherapy (HR 0.433, 95% CI 0.218 to 0.862; $P = 0.017$) and targeted therapy (HR 0.384, 95% CI 0.192 to 0.766; $P = 0.007$) before surgery resection were independent prognostic factors for survival. It appears that factors with

Table 2
Risk factors for LUAD patients with BM.

Characteristics	Total(N)	Univariate analysis		Multivariate analysis	
		Hazard ratio (95% CI)	P value	Hazard ratio (95% CI)	*P* value
Age	125				
<65	83	Reference			
≥65	42	3.270 (1.831–5.841)	**<0.001**	2.403 (1.223–4.723)	**0.011**
Gender	125				
male	69	Reference			
female	56	0.846 (0.487–1.469)	0.553		
KPS	125				
≥ 70	70	Reference			
< 70	55	2.396 (1.366–4.205)	**0.002**	2.019 (1.022–3.989)	**0.043**
preNLR	125				
low	61	Reference			
high	64	3.611 (1.949–6.693)	**<0.001**	2.400 (1.204–4.782)	**0.013**
Tumor size	125				
≥ 3cm	77	Reference			
< 3cm	48	0.661 (0.367–1.192)	0.169		
Location	125				
supratentorial	100	Reference			
infratentorial	7	1.453 (0.517–4.085)	0.478	1.738 (0.696–4.340)	0.237
Supra- and infratentorial	18	2.370 (1.205–4.662)	**0.012**	1.790 (0.550–5.826)	0.334
Number of brain metastases	125				
1	76	Reference			
2	22	1.128 (0.490–2.598)	0.778	1.274 (0.576–2.818)	0.549
≥3	27	2.677 (1.482–4.837)	**0.001**	1.272 (0.515–3.142)	0.602
Peritumoral brain edema	125				
severe	49	Reference			
moderate	46	0.631 (0.340–1.172)	0.145		
mild	30	0.717 (0.352–1.462)	0.360		
Extracerebral metastases	125				
Absence	73	Reference			
Presence	52	3.233 (1.833–5.701)	**<0.001**	2.530 (1.380–4.639)	**0.003**
EGFR/ALK+	125				
No	56	Reference			
Yes	69	0.379 (0.216–0.663)	**<0.001**	0.485 (0.246–0.956)	**0.037**
Postoperative radiotherapy	125				
No	57	Reference			
Yes	68	0.326 (0.184–0.579)	<**0.001**	0.433 (0.218–0.862)	**0.017**
Postoperative targeted therapy	125				
No	47	Reference			
Yes	78	0.214 (0.121–0.377)	<**0.001**	0.384 (0.192–0.766)	**0.007**

significant prognostic significance in the univariate analysis were not significant in the multivariate analysis except location and the number of brain metastasis. (Table 2).

Based on the independent predictors found in the cox regression analyses, we developed a nomogram to facilitate prognosis prediction. (Fig. 6A) Individual patients scored the value of each variable by locating the corresponding position on the variable scale and drawing a vertical line to determine the corresponding point. The total score was then tallied and a vertical line was drawn on the survival scale to calculate 1/2-year survival. We then assessed the performance of the model in 2-year by ROC curve analysis, the AUC of the nomogram was 0.935 (Fig. 6B). The calibration plot, which runs very close to the diagonal, shows excellent calibration (Fig. 6C).

Discussion

We retrospectively analyzed a large consecutive cohort of LUAD patients' laboratory tests for preNLR levels. We found that among those with BMs, high radio likely indicated a poor survival after surgery of BM in line with previous studies of brain metastasis ($P < 0.0001$) [20,24,25]. On univariate analysis of overall survival, elevated preNLR was an independent prognostic poor factor along with KPS < 70, extracerebral metastases, age ≥ 65, without postoperative radiotherapy and targeted therapy. These results have been supported by other studies [22,26]. When the high and low NLR groups are analyzed, it becomes apparent that preNLR is associated with the BM lesions of both supra- and infratentorial and the severe peritumoral edema, thereby causing severe neurological symptoms (Fig. 4).

The mechanism underlying the association between preNLR and severe peritumoral edema is complex and needs to be elucidated. Peritumoral edema has been described as a risk factor for early recurrence or progression and was the consequence of a disruption of the blood-brain barrier [27,28]. The reasons for preNLR value in predicting the occurrence and development of brain edema could be explained by neutrophil-induced neurotoxicity, increased capillary permeability, destruction of the BBB (Blood Brain Barrier), and cell swelling [29–31]. In our study, we found the location has a significant interaction with peritumoral edema, which means the effect of peritumoral edema on preNLR depends on different locations. This is quite different with other studies that NLR is independently associated with peritumoral edema [30]. However, our results indicate that the locations of the brain tumor, rather than the peritumoral edema play a vital role in postoperative outcomes. This is consistent with previous studies [32–35].

It was found that preNLR was a predictive factor of poor prognosis for patients with brain metastasis [14,36]. Still, our subject of research focused on the LUAD origin brain metastasis with different NLR values. A large prospective study of 496 NSCLC patients with mandatory baseline brain CECT and a CNS examination over 18 months period found that adenocarcinoma histology and high NLR (≥ 2.5) were predictors factors in NSCLC patients with BM. In addition, the NLR was an independent prognostic factor for overall survival [37]. However, separate analyses for adenocarcinoma lung cancer were not performed in other studies. NLR also predicts the outcome of NSCLC BM patients before radiosurgery [36]. A few studies have also successfully combined NLR with steroid use or combined platelet: lymphocyte ratio (PLR) [38,39]. This suggests NLR is a classical prognostic factor when used with

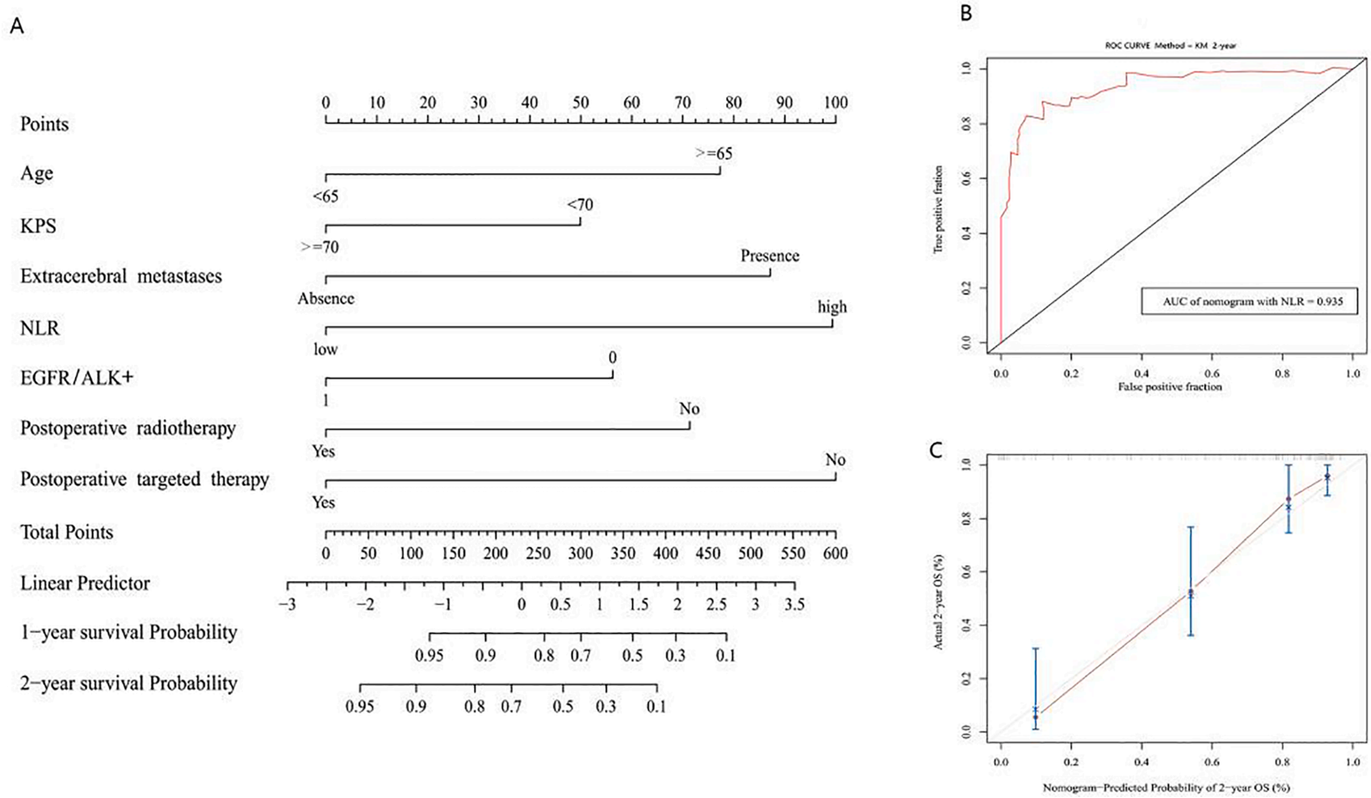

Fig. 6. Nomogram, ROC curves, calibration plots for the prediction of the prognosis at 2 years of LUAD patients with BM. (A) Nomogram for the prediction of OS at 1/2 years; To estimate the probability of 1/2 year survival for a given patient, locate the individuals' categorized age ($<$ or $\geq$ 65 years) and draw a line straight up to the Points axis to determine the score associated with that number. Repeat the process for KPS ($<$ or $\geq$ 70), extracerebral metastases, NLR, EGFR/ALK+, postoperative radiotherapy and targeted therapy; sum the scores and locate this sum on the Total Points axis. Then, draw a vertical line down to the Probability axis and read off the probability. (B) ROC curves in the discrimination ability of the nomogram. (C) The calibration plots of the nomogram. Abbreviation: OS, overall survival; ROC, receiver operating characteristic; DCA, decision curve analysis; LUAD, lung adenocarcinoma.

other predictors to benefit patients from adjusted therapy and monitored indicators. However, these studies did not focus on LUAD patients with BM. In this study, the relationship between NLR and peritumoral brain edema in LUAD patients with BM was demonstrated, which expands knowledge about the role of NLR in brain metastasis patients.

There are a few mechanisms by which the prognostic effect of NLR may be produced in the brain. NLR is considered a simple index reflecting tumor-generated inflammation status of tumor-host and is a predictor of bacterial infection [40]. Based on the findings of this and previous studies about brain metastasis [41], we tended to assume that elevated NLR in severe peritumoral edema is associated with neutrophilic activation. Much has been confirmed that neutrophils in inflammatory tumor sites cause increased NLR in the literature [42]. Furthermore, it has been recently shown that Arg1+/PD-L1+ neutrophils could be recruited into the brain by upregulating the expression of c-JUN, which suppresses the adaptive immune response in the brain to drive the metastasis [4]. Activated neutrophils incite tumor cell invasion and significantly increase the ability of aggressive tumor cells to enter the bloodstream, colonize distal organs, seed, and survive in the metastatic site. The recruitment of neutrophils by CXCL8, IL-17, the formyl peptide receptor 2/lipoxin A4 receptor, and other inflammatory cytokines were generally thought to aggravate the peritumoral edema and promote tumor progression and metastasis [43–45]. At the same time, neutrophils promoted the breakdown of the blood-brain barrier by releasing matrix metalloproteinase 9 (MMP-9) [46], which impaired BBB integrity by inhibiting neutrophils [47] and was found to associate with high levels of peritumoral brain edema [48].

Like others, we found that a high level of the preNLR predicts postsurgical survival in brain metastasis patients. In addition, the preNLR may be an essential indicator of peritumoral edema severity especially multiple tumors at both supra- and infratentorial. Although such a mechanism remains to be investigated in-depth in future studies, it can serve as valuable prognostic information to take precautions before surgical intervention. Further studies will be performed to explore the underlying roles of preNLR in tumor immune microenvironment and immune therapy.

However, there were still some limitations in this study. Firstly, due to the small sample size of our cohort, there may be a certain selection bias in the certain group focused on patients with resectable brain metastasis. which makes it difficult to draw broad conclusions. Secondly, as a retrospective study, we did not have access to information related to confounders, such as smoking, chronic obstructive pulmonary disease or other inflammatory factors. Finally, our nomogram including preNLR was only internally validated, and future studies are needed for ongoing assessment.

Conclusion

This study indicated that preNLR was an independent prognostic factor for LUAD-BM patients after surgical excision and may be associated with tumor locations and peritumoral edema extent as well.

Data availability statement

The data used to support the findings of this study are available from the corresponding author upon request.

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Authors' contributions

Conception and design: C Zhou; H Cui; **Acquisition of data:** C Zhou; Y Yang; **Analysis and interpretation of data:** H Cui, C Zhou; **Drafting the article:** H Cui, Y Yang; **Critically revising the article:** all authors; **Reviewed submitted version of manuscript:** H Cui, Y Yang, C Zhou; **Approved the final version of the manuscript on behalf of all authors:** Y Cao; **Statistical analysis:** H Cui, M Fen, Y Gao; **Administrative/technical/material support:** C Zhou, L Li; **Study supervision:** Y Cao, C Zhou.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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