Original Article

A single center retrospective study assessing the prognostic significance of pre-treatment neutrophil/lymphocyte ratio in locally advanced nasopharyngeal carcinoma

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Background: In light of the growing evidence suggesting the impact of inflammatory parameters on the survival of individuals with cancer, this research assessed the prognostic significance of the neutrophil-to-lymphocyte ratio (NLR) in individuals diagnosed with locally advanced nasopharyngeal carcinoma (NPC) prior to undergoing intensity-modulated radiation therapy (IMRT).

Methods: A total of 163 individuals diagnosed with locally advanced NPC treated with IMRT at our hospital between January 2012 and December 2017 were included in this research. For each patient, the absolute counts of neutrophils and lymphocytes were recorded, and the NLR was calculated at the first diagnosis. To determine the optimal cut-off values for NLR, receiver operating characteristic (ROC) curve analysis was conducted. The effects of the determined cut-off value on local failure-free survival (LFFS), overall survival (OS), progression-free survival (PFS), and distant failure-free survival (DFFS) were evaluated employing the Cox regression model.

Results: The median follow-up duration for the individuals in this study was 15 months (ranging from 6 to 79 months). According to the determined NLR cut-off value of 3.27, individuals were classified into two groups (high NLR and low NLR). Individuals in the high-NLR group had remarkably poorer 3-year OS (62.8% *vs.* 91.7%), PFS (51.4% *vs.* 82.4%), and DFFS (70.7% *vs.* 89.6%) compared to the low-NLR group. Furthermore, the outcomes of univariate and multivariate survival analyses revealed that NLR served as an independent predictor of DFFS (HR: 2.81, 95% CI: 1.195–6.608, P=0.018), OS (HR: 3.1, 95% CI: 1.211–7.935, P=0.018), and PFS (HR: 2.21, 95% CI: 1.133–4.292, P=0.02).

Conclusions: Elevated NLR exhibited a significant correlation with reduced OS, DFFS, and PFS. These findings suggest that NLR holds promise as a cost-effective and reliable marker for the prediction of clinical outcomes among patients with locoregionally advanced nasopharyngeal carcinoma (LANPC). Furthermore, incorporating NLR into clinical decision-making regarding LANPC treatment strategies may contribute to a more targeted approach aimed at reducing the risk of distant failure.

Keywords: Nasopharyngeal carcinoma (NPC); neutrophil-to-lymphocyte ratio (NLR); prognostic factor

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Introduction

Nasopharyngeal carcinoma (NPC) is a relatively rare malignancy around the globe. However, it is endemic in southern China, northern Africa, and southeastern Asia. There are more than 130 thousand newly diagnosed NPC cases worldwide per year, and more than 70% of these cases are locoregionally advanced (1-3). The current preferred treatment approach for locoregionally advanced nasopharyngeal carcinoma (LANPC) involves concurrent chemoradiotherapy (CCRT) and CCRT combined with adjuvant chemotherapy or induction chemotherapy (4-7). Locoregional recurrence and distant metastases are the primary failure patterns in LANPC patients (5). In the current clinical practice, tumor-node-metastasis (TNM) classification is the most reliable prognostic tool that can effectively guide treatment (8,9). However, previous study has reported that the prognosis can vary among individuals with similar staging in LANPC (10). This emphasizes the necessity of identifying additional biomarkers that can augment the current traditional staging system.

Prior research has provided evidence highlighting the crucial contribution of the systemic inflammatory response to the onset and progression of the tumor (11,12). Inflammatory markers, including platelet-lymphocyte ratio (PLR), neutrophil-to-lymphocyte ratio (NLR), monocyte-lymphocyte ratio (MLR), and systemic immune-inflammation index (SII), have been identified as independent prognostic indicators for individuals with non-small cell lung cancer (13), pancreatic cancer (14), breast cancer (15,16), multiple myeloma (17,18) and NPC (19-21). The measurement of peripheral NLR through routine blood examinations is a simple and cost-effective method. Research has revealed that elevated NLR prior to the commencement of therapy served as an independent risk factor for poorer clinical outcomes (17). However, the underlying molecular mechanisms need further understanding. One crucial factor could be the association of elevated NLR with a tumor microenvironment that promotes tumor progression, potentially contributing to an unfavorable prognosis. Prior reports have revealed that higher pre-treatment NLR was linked to poorer overall survival (OS) or progression-free survival (PFS) among individuals diagnosed with NPC (22,23).

However, the role of NLR as a prognostic marker of local-regional recurrence survival or distant failure-free survival (DFFS) LANPC is rarely reported. The potential effect of NLR in local or distant failure patterns still needs further investigation.

The current study collected baseline data of pre-treatment NLR in patients with LANPC to observe the prognostic risk factors affecting OS, PFS, DMFS, and local failure-free survival (LFFS). This article is presented in accordance with the REMARK reporting checklist (available at https://tcr.amegroups.com/article/view/10.21037/tcr-23-528/rc).

Highlight box

Key findings

- This research found that an increased pre-treatment NLR was considerably linked to reduced OS and DFFS, and PFS in LANPC.

What is known and what is new?

- NLR has gradually been proven to be related to OS and PFS in NPC with stage I–IV.
- NLR was an independent predictive factor for distant metastases in LANPC.

What is the implication, and what should change now?

- Incorporating NLR into clinical decision-making regarding LANPC treatment strategies may contribute to a more targeted approach aimed at reducing the risk of distant failure.

Methods

Study design and eligibility

This retrospective study was based on a consecutive cohort of patients diagnosed with LANPC who underwent IMRT and chemotherapy from January 2012 to December 2017 at Ruijin Hospital of Shanghai Jiaotong University, China. The inclusion criteria were as follows: (I) individuals diagnosed with stage III–IVA NPC as per the 8th edition of the American Joint Committee on Cancer (AJCC) staging system, verified by histological and radiographic evaluations; (II) patients undergoing treatment with or without induction chemotherapy; (III) individuals undergoing radical intensity-modulated radiotherapy with or without weekly/triweekly platinum-based concurrent chemotherapy, (IV) availability of pre-treatment NLR; (V) absence of any chronic inflammatory disease. The NLR was measured by dividing the absolute neutrophil counts by the lymphocyte counts obtained from routine blood tests conducted at the time of diagnosis. This study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This research was approved by the Institutional Review Board of Ruijin Hospital of Shanghai Jiaotong University (ID:

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2022-194). Written informed consent for this retrospective analysis was waived.

Treatment plan and delivery procedure

All enrolled individuals were positioned in a supine posture and immobilized by means of a customized head-shoulder thermoplastic mask. Subsequently, a CT simulation was performed utilizing a Brilliance Big Bore CT scanner (Phillips, Amsterdam, Netherlands) with a slice thickness of 3–5 mm, covering the region from the head to 5 cm below the sternoclavicular joint. Target volumes were delineated in a slice-by-slice manner following the guidelines set forth in reports 50 and 62 of the International Commission on Radiation Units and Measurements.

For this cohort of individuals, the treatment plan included concurrent chemotherapy +/– induction chemotherapy or adjuvant chemotherapy. Induction chemotherapy involved the administration of paclitaxel (135 mg/m^2) or docetaxel (75 mg/m^2) and cisplatin (75 mg/m^2), administered every three weeks for two to three cycles. Concurrent chemotherapy involved the administration of cisplatin either every three weeks (100 mg/m^2) or on a weekly basis (40 mg/m^2) throughout radiotherapy.

Follow-up procedures

The follow-up procedures included an interview on call and outpatient follow-up. The follow-up schedule comprised assessments 3 months after the completion of the treatment, followed by evaluations every 3 months for 3 years, every 6 months for an additional 4 to 5 years, and annually thereafter. During each follow-up visit, various examinations were conducted, including nasopharyngeal magnetic resonance imaging, measurement of blood biochemical indicators, thoracoabdominal computed tomography, and bone scan as required.

Statistical analyses

The duration of all events was determined from the completion of the radiation therapy until either documented treatment failure or the last follow-up visit. The study assessed various survival outcomes, with LFFS indicating the persistence or recurrence of the disease in the nasopharynx or/and neck, OS representing death from any cause, PFS indicating the absence of disease progression after radiotherapy, and DMFS reflecting the occurrence of disease metastasis at distant sites. To assess these outcomes, the Kaplan-Meier (KM) analysis was conducted to measure the rates of LFFS, OS, PFS, and DMFS. The variation between these rates was determined by means of a log-rank test, and the optimal cut-off values for each of the above-mentioned endpoints were determined based on the receiver operating characteristic (ROC) curves. The sample size was determined to be ten times greater than the number of variables. The Cox regression model was utilized to find independent risk factors. A forward stepwise method was utilized to enter new terms into the model, with a significance level of $P<0.05$ for term entry and the most significant term being entered first.

All statistical analyses were two-sided, and P values of 0.05 or less denoted the statistical significance. The data analyses were carried out with the aid of BM SPSS for Mac (SPSS 26.0, Chicago, IL, USA).

Results

Patient characteristics and therapeutic results

In total, 163 patients participated in this retrospective study, including 126 males and 37 females aged 13–73 years, with a median age of 52. *Table 1* summarizes the baseline characteristics of all participants in the study. The median follow-up period of the whole cohort was 15 months (6–79 months). During the follow-up time, 21 patients developed distant metastases, including five with lung metastases, three with bone metastases, eight with liver metastases, and five patients with metastases in more than two organs. Ten patients developed local-regional recurrence, and a total of 18 patients died, nine of whom died of distant metastasis and seven due to recurrence. Two patients did not experience disease progression, but the cause of their death remains unidentified. The 3-year OS rate for the entire cohort was 85.1%, and the 3-year LFFS, DFFS, and PFS rates were 92.0%, 83.0%, and 68.7%, respectively.

The prognostic value of NLR in NPC

The median value of NLR was 2.92 (1.0–17.5) (see *Table 1*). The ROC curve confirmed 3.28 to be the optimal cut-off point to distinguish between the survival and death of individuals. Moreover, the NLR of 3.27 was the optimal cut-off value to differentiate between the occurrence of metastasis and no metastasis, as well as between disease

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Table 1 Baseline characteristics of 163 patients with locally advanced nasopharyngeal carcinoma

Characteristics	N (%)
Age (years), median [range]	52 [13–73]
<52	70 (42.9)
≥52	93 (57.1)
Gender	
Male	126 (77.3)
Female	37 (22.7)
T stage	
T1	12 (7.4)
T2	38 (23.3)
T3	62 (38.0)
T4	51 (31.3)
N stage	
N0–1	40 (24.5)
N2	94 (57.7)
N3	29 (17.8)
TNM stage	
III	89 (54.6)
IVA	74 (45.4)
Induction chemotherapy	
No	25 (15.3)
Yes	138 (84.7)
Adjuvant chemotherapy	
No	124 (76.1)
Yes	39 (23.9)
NLR, median [range]	2.92 [1.0–17.5]

TNM, tumor-node-metastasis; NLR, neutrophil-to-lymphocyte ratio.

progression and no progression (see *Table 2*). Participants were classified into two groups as per the cut-off value of 3.27: high NLR (>3.27) and low NLR (≤3.27).

The KM survival analysis revealed that individuals in the high-NLR group exhibited poorer OS as opposed to the low-NLR group. The 3-year OS, DFFS, and PFS in the high-NLR and low-NLR were 62.8% *vs.* 91.7% (P<0.001), 70.7% *vs.* 89.6% (P=0.03) and 51.4% *vs.* 82.4% (P=0.02), respectively. However, this cut-off value was not able to make a statistical difference in the LFFS (89.5% *vs.* 93.9%, P=0.43) (see *Figure 1A-1D*).

Univariate and multivariate Cox regression analyses were conducted to predict OS, LFFS, DFFS, and PFS in the entire cohort. Variables that met the prespecified significance threshold (P<0.05) for predicting OS, DFFS, and PFS in the univariate and multivariate Cox models were the N stage and NLR (*Tables 3-5*). Additionally, patients with high NLR had approximately 3.1 times higher risk of mortality (HR: 3.1, 95% CI: 1.211–7.935, P=0.018) than those with low NLR. Moreover, higher NLR also had a 1.8 times higher risk of distant metastasis (HR: 2.81, 95% CI: 1.195–6.608, P=0.018) and 1.2 times higher risk of disease progression (HR: 2.206, 95% CI: 1.133–4.292, P=0.02) than those with low NLR. However, no significant difference was recorded in LFFS between high- and low-NLR groups (*Table 6*). N stage was another independent prognostic factor for OS (N3 *vs.* N0-1: HR: 5.823, 95% CI: 1.374–24.671, P=0.017), DFFS (N3 *vs.* N0-1: HR: 7.689, 95% CI: 1.92–30.791, P=0.004) and PFS (N3 *vs.* N0-1: HR: 3.305, 95% CI: 1.214–9.003, P=0.019).

Discussion

In the current study, an optimal cut-off value of 3.27 for the NLR was determined to classify individuals with LANPC into two groups; one with low and one with high NLR. The outcomes of this research highlighted that individuals in the high-NLR group had a remarkably poorer prognosis in contrast with the individuals in the low-NLR group. Furthermore, through multivariate Cox regression analysis, it was revealed that a high NLR level at diagnosis remained an independent predictor of poor OS, DFFS, and PFS in individuals with locally advanced NPC treated with chemoradiotherapy. However, there were no notable statistically significant differences in terms of LFFS based on NLR in these patients.

Currently, the TNM stage is the primary determinant for treatment decisions and prognostic prediction in NPC. However, it has been observed in clinical practice that patients with the same stage can exhibit different prognoses, suggesting the need to incorporate other prognostic factors in the pre-treatment evaluation. While the NLR is not currently a part of the clinical staging of NPC, numerous reports have highlighted that elevated NLR before treatment is strongly linked to poor survival outcomes in individuals with NPC following radiotherapy (24-26).

The underlying mechanisms of correlation between NLR

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Table 2 ROC curve analysis of optimal NLR cutoff value for OS, LFFS, DFFS and PFS

Analysis variables	OS	LFFS	DFFS	PFS
Area under the ROC curve	0.616	0.552	0.569	0.578
Standard error	0.0683	0.0851	0.0647	0.0565
95% confidence interval	0.529–0.698	0.385–0.718	0.443–0.696	0.467–0.689
z statistic	1.698	0.606	1.073	1.382
Significance level P (area =0.5)	0.0895	0.5445	0.2833	0.1671
Youden index	0.3221	0.2047	0.2656	0.2636
95% confidence interval	0.1503–0.5112	0.1543–0.2228	0.1489–0.4514	0.1392–0.4219
Associated criterion	>3.28	>2.07	>3.27	>3.27
95% confidence interval	>1.47 to <3.46	>1.86 to <2.16	>2.65 to <4.95	>2.06 to <4.12
Sensitivity (%)	66.67	100	61.9	60
Specificity (%)	65.55	20.47	64.66	66.36

ROC, receiver operative characteristics; NLR, neutrophil-to-lymphocyte ratio; OS, overall survival; LFFS, local failure-free survival; DFFS, distant failure-free survival; PFS, progression-free survival.

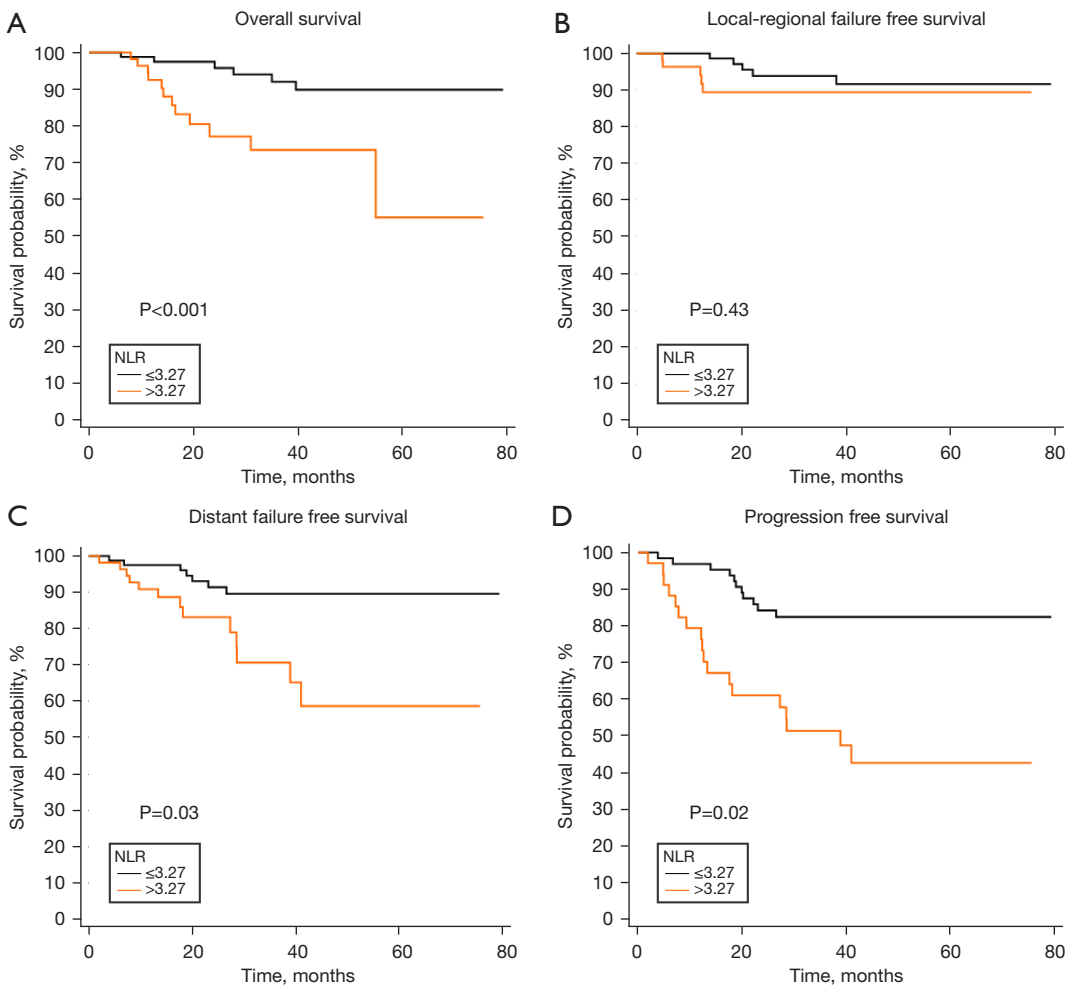

Figure 1 Three-year survival of patients with NLR ≤3.27 and >3.27 (A-D). NLR, neutrophil-to-lymphocyte ratio.

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Table 3 Univariate and multivariate Cox regression analyses of OS

Variables	Univariate analysis		Multivariate analysis	
	Hazard ratio (95% CI)	P	Hazard ratio (95% CI)	P
Gender				
Female	1		1	
Male	1.823 (0.539–6.163)	0.334	1.734 (0.488–6.164)	0.395
Age (years)				
≥52	1		1	
<52	0.39 (0.144–1.058)	0.064	0.408 (0.145–1.152)	0.091
T stage				
1	1	0.068	1	0.151
2	0.921 (0.095–8.896)	0.943	1.2 (0.12–12.019)	0.877
3	1.084 (0.13–9.038)	0.94	1.651 (0.187–14.573)	0.652
4	3.227 (0.419–24.855)	0.261	4.016 (0.506–31.842)	0.188
N stage				
0–1	1	0.035	1	0.033
2	1.662 (0.469–5.894)	0.432	2.018 (0.551–7.39)	0.289
3	4.764 (1.212–18.72)	0.025	5.823 (1.374–24.671)	0.017
NLR				
≤3.27	1		1	
>3.27	4.414 (1.785–10.915)	0.001	3.1 (1.211–7.935)	0.018

Hazard ratios estimated by Cox proportional hazards regression. All statistical tests were two-sided. OS, overall survival; CI, confidence interval; NLR, neutrophil-to-lymphocyte ratio.

and poor prognosis of tumor are not fully understood. However, an elevated NLR is indicative of either an enhanced neutrophil count and/or a reduced lymphocyte count. Neutrophils are a type of inflammatory cells that contribute to various stages of tumor development by producing cytokines, including oncostatin M, hepatocyte growth factor, and transforming growth factor-β (TGF-β) (27). Furthermore, neutrophils enhance tumor angiogenesis by releasing angiogenic factors, including angiopoietin-1, vascular endothelial growth factor, and fibroblast growth factor-2 (28,29). Furthermore, lymphocytes mediate immune surveillance and help in the elimination of tumor cells.

The majority of previous studies focused on the role of NLR in OS or PFS. This is the first research in the IMRT era that explores the prognostic value of NLR in predicting survival outcomes, particularly focusing on the link to distant failure among individuals with LANPC after definitive IMRT. Distant metastasis was found to be the most prevalent mode of treatment failure and the leading cause of mortality in individuals with LANPC (30,31). This research suggests that NLR was important for predicting distant failure, which dramatically affects clinical outcomes, including OS and PFS. Both univariate and multivariate analyses highlighted that NLR was important in predicting the OS, DFS, and DFFR (*Tables 3-5*). NLR was an independent predictive factor for distant metastases (HR: 3.1, 95% CI: 1.211–7.935, P=0.018). Higher NLR (exceeding 3.27) was closely related to adverse prognosis in LANPC, mainly associated with distant metastasis, which consequently resulted in decreased OS and PFS statistically. The identification of distant metastases as the primary mode of treatment failure in individuals with LANPC is crucial for making informed decisions regarding treatment strategies. These data provide valuable insights into the need for more aggressive neoadjuvant or adjuvant chemotherapy in certain patients to effectively target and

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Table 4 Univariate and multivariate Cox regression analyses of DFFS

Variables	Univariate analysis		Multivariate analysis	
	Hazard ratio (95% CI)	P	Hazard ratio (95% CI)	P
Gender				
Female	1		1	
Male	0.482 (0.514–4.367)	0.459	1.737 (0.572–5.276)	0.33
Age (years)				
≥52	1		1	
<52	0.482 (0.572–5.276)	0.101	0.501 (0.202–1.247)	0.138
T stage				
1		0.495	1	0.441
2	1.415 (0.165–12.155)	0.752	1.602 (0.181–14.19)	0.672
3	1.704 (0.216–13.478)	0.613	2.917 (0.354–24.048)	0.32
4	2.801 (0.358–21.915)	0.326	3.495 (0.441–27.67)	0.236
N stage				
0–1	1	0.004	1	0.003
2	1.742 (0.496–6.116)	0.386	1.988 (0.555–7.119)	0.291
3	5.996 (1.613–22.296)	0.008	7.689 (1.92–30.791)	0.004
NLR				
≤3.27	1		1	
>3.27	3.228 (1.437–7.254)	0.005	2.81 (1.195–6.608)	0.018

Hazard ratios estimated by Cox proportional hazards regression. DFFS, distant failure-free survival; CI, confidence interval; NLR, neutrophil-to-lymphocyte ratio.

prevent distant metastasis. The current treatment regimens for LANPC offer modest benefits while being associated with significant toxicities. These toxicities often lead to reduced quality of life, particularly in patients receiving adjuvant chemotherapy. It was observed in a phase III randomized trial that individuals who were treated with CCRT in combination with AC in locally advanced NPC showed improved distant metastasis survival compared to the standard CCRT group (2-y DFS: 88% *vs.* 86%, P=0.12) (31). Acute toxicities were similar between the two groups during CCRT, but grade 3–4 toxicities, including oral mucositis, nausea, and vomiting, were seen in 42% of individuals during AC. Moreover, it was found that grade 3–4 leukopenia or neutropenia occurred in 17% of individuals, with the second most commonly observed events being thrombocytopenia and anemia. Induction chemotherapy (IC) is more advantageous in alleviating early symptoms, reducing tumor volume, and eliminating micro-metastases (32). Large-scale multicenter randomized clinical trials conducted in endemic areas found that IC combined with CCRT gave better outcomes regarding OS, PFS, and DFS when compared to CCRT alone (6,7,33,34). Due to the incidence and severity of toxicity associated with adjuvant or induction chemotherapy, NLR as a marker for predicting distant failure can significantly improve patient selection for comprehensive treatment. The main implication of NLR is to risk stratify patients and help clinicians and patients make informed decisions about treatment options. Pan *et al.* reported that high-level NLR was linked to an unfavorable locoregional-recurrence-free survival in stage II NPC patients (35). However, this research highlighted no statistically significant differences in this regard, suggesting the need for further investigation to determine the correlation between NLR and local failure among locally advanced individuals.

Different research institutions have used different

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Table 5 Univariate and multivariate Cox regression analyses of PFS

Variables	Univariate analysis		Multivariate analysis	
	Hazard ratio (95% CI)	P	Hazard ratio (95% CI)	P
Gender				
Female	1		1	
Male	1.337 (0.591–3.022)	0.486	1.312 (0.564–3.052)	0.528
Age (years)				
≥52	1		1	
<52	0.69 (0.36–1.321)	0.263	0.82 (0.418–1.606)	0.563
T stage				
1	1	0.062	1	0.093
2	1.749 (0.21–14.559)	0.605	1.996 (0.236–16.866)	0.526
3	2.935 (0.387–22.243)	0.297	4.423 (0.566–34.544)	0.156
4	5.104 (0.681-38.259)	0.113	5.751 (0.76–43.528)	0.09
N stage				
0–1	1	0.049	1	0.031
2	1.091 (0.486–2.451)	0.833	1.277 (0.556–2.932)	0.564
3	2.527 (1.01–6.43)	0.048	3.305 (1.214–9.003)	0.019
NLR				
≤3.27	1		1	
>3.27	2.649 (1.414–4.965)	0.002	2.206 (1.133–4.292)	0.02

Hazard ratios estimated by Cox proportional hazards regression. PFS, progression free survival; CI, confidence interval; NLR, neutrophil-to-lymphocyte ratio.

thresholds for NLR, ranging from 2.0 to 3.5 (25,36,37). Sun *et al.* highlighted that NLR ≥2.7 was linked to shorter PFS in individuals with NPC across stages I to IV (23). Yin *et al.* obtained NLR =3.0 for stages I to IV patients (37), and Yao *et al.* set NLR =2.5 for individuals across stages II to IVA (25). The slight differences among those studies can be attributed to the varied stages of enrolled patients. In the current study, the optimal cut-off value of 3.27 for NLR was obtained in survival analysis. Multivariate analysis highlighted that increasing NLR >3.27 was considerably linked to poor OS (HR: 3.1, 95% CI: 1.211–7.935, P=0.018) and PFS (HR: 2.21, 95% CI: 1.133–4.292, P=0.02). This cut-off value was consistent with those reported in the previously published studies that assessed the link between NLR and clinical outcomes.

Despite being regarded as a convenient, cost-effective, and reliable biomarker associated with clinical outcomes in LANPC, there are still unresolved questions regarding the NLR. One such question pertains to the need for longitudinal evaluations throughout the treatment period to enhance accuracy. Additionally, comparing this ratio with other markers of inflammation and the EBV-DNA load in the blood may contribute to improving its prognostic significance.

In a report by Chua *et al.*, high NLR (≥3.0) was reported to be linked to an enhanced pre-treatment EBV DNA titer (P=0.001) (19). Moreover, along with their study on NLR, Sun *et al.* also compared platelet to lymphocyte ratio (23). Using multiple serum biomarkers as confounding factors will provide clinicians with more accurate prognostic information for NPC. The results showed that NLR ≥2.7 (P=0.005) and PLR ≥167.2 (P=0.001) were considerably linked to poor PFS, and PLR ≥163.4 (P=0.011) was related to worse OS. The incorporation of NLR into NCCN guidelines or refining treatment strategies and predicting prognosis is constrained at present by the variability and lack of uniformity in the

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Table 6 Univariate and multivariate Cox regression analyses of LFFS

Variables	Univariate analysis		Multivariate analysis	
	Hazard ratio (95% CI)	P	Hazard ratio (95% CI)	P
Gender				
Female	1		1	
Male	0.714 (0.224–2.277)	0.569	0.627 (0.188–2.086)	0.446
Age (years)				
≥52	1		1	
<52	1.025 (0.356–2.957)	0.963	1.468 (0.49–4.401)	0.493
T stage				
1	1	0.209	1	0.241
2	3,132.344 (0–3.326E+89)	0.937	3,066.652 (0–1.15E+90)	0.937
3	9,584.262 (0–1.01E+90)	0.928	8,418.469 (0–3.136E+90)	0.929
4	21,930.262 (0–2.309E+90)	0.921	20,610.515 (0–7.667E+90)	0.922
N stage				
0–1	1	0.298	1	0.513
2	0.408 (0.132–1.267)	0.121	0.493 (0.148–1.649)	0.251
3	0.576 (0.116–2.862)	0.5	0.726 (0.123–4.281)	0.724
NLR				
≤3.27	1		1	
>3.27	0.654 (0.226–1.894)	0.434	1.324 (0.41–4.276)	0.639

Hazard ratios estimated by Cox proportional hazards regression. LFFS, Local failure-free survival; CI, confidence interval; NLR, neutrophil-to-lymphocyte ratio.

published research. Due to the heterogeneity of the study population, sufficient research with supportive results is needed. This will help establish unified methods, such as comparing critical dichotomy or subgroup thresholds, to determine a practical optimal ratio and attain standardization in the field. In conclusion, additional efforts should be directed toward investigating the prognostic significance of NLR in patients eligible for LANPC treatment. Moreover, it is important to conduct subgroup analyses to identify the specific populations that would benefit the most from individualized treatment approaches.

There were several limitations in the current study. Firstly, this study only focused on patients with LANPC. The population selected for this study was relatively single and did not cover NPC in all stages. Therefore, the prognostic value of NLR might vary across individuals at other stages of the disease. Furthermore, there may be unmeasured confounding factors because of the retrospective study design. In addition, potential inflammatory conditions may affect the composition of complete blood count (CBC), such as asymptomatic infection, possible effects of underlying diseases, smoking status, etc. Other shortcomings of this research are the relatively small sample size and the short follow-up time (average of 31 months).

Conclusions

In conclusion, an increased NLR was considerably linked to reduced OS and DFFS, and PFS. The NLR can serve as a promising and cost-effective marker for predicting clinical outcomes among individuals with LANPC and making improved clinical decisions regarding LANPC treatment strategies to further decrease distant failure. Patients with higher baseline NLR may need more aggressive systemic therapy.

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Footnote

Reporting Checklist: The authors have completed the REMARK reporting checklist. Available at https://tcr.amegroups.com/article/view/10.21037/tcr-23-528/rc

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://tcr.amegroups.com/article/view/10.21037/tcr-23-528/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. This study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This research was approved by the Institutional Review Board of Ruijin Hospital of Shanghai Jiaotong University (ID: 2022-194). Written informed consent for this retrospective analysis was waived.

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