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Original Article

Concurrent chemoradiotherapy plus immunotherapy for locally advanced non-small-cell lung cancer: clinical efficacy and prognostic analysis

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Abstract: Objective: To evaluate the efficacy of concurrent chemoradiotherapy (CCRT) combined with immunotherapy (IT) for locally advanced non-small-cell lung cancer (LA-NSCLC). Short-term treatment outcomes during the two-year follow-up were recorded, and 2-year survival data were collected to analyze prognosis and identify factors affecting short-term outcome. Additionally, a predictive model was developed. Methods: We conducted a retrospective analysis of 90 LA-NSCLC patients admitted between February 2018 and February 2020. Patients were grouped according to their treatment regimens: 45 patients treated with 4-6 cycles of CCRT followed by 1 year of Sintilimab therapy were assigned to the observation group, and 45 patients treated with cisplatin/carboplatin + albumin-bound paclitaxel for 4-6 cycles after CCRT were assigned to the control group. Short-term adverse reactions were recorded for both groups. Patients were followed up after 4-6 cycles of IT or chemotherapy, and short-term efficacy and toxicity were evaluated. During the 2-year follow-up, overall survival (OS) and progression-free survival (PFS) were recorded, and survival curves were plotted. The Cox proportional hazards model was used to identify factors influencing PFS in the observation group, and a predictive model was developed. The predictive value of relevant indicators for prognosis was assessed using receiver operating characteristic (ROC) curves. Results: The observation group showed superior short-term efficacy, with higher objective response rates (ORR) and disease control rates (DCR) compared to the control group (both $P < 0.05$). Regarding toxicity, the control group exhibited more severe adverse effects, particularly grade III and higher gastrointestinal reactions, leukopenia, thrombocytopenia, and anemia (all $P < 0.05$). The PFS was significantly higher in the observation group than that of the control group ($P < 0.05$). Additionally, the incidence of pneumonia was higher in the observation group, but it demonstrated better 2-year OS ($P < 0.05$). Cox multivariate analysis revealed that factors influencing PFS in the observation group included distant metastasis, tumor differentiation, platelet-to-lymphocyte ratio (PLR), and prealbumin (PAB). ROC analysis showed that the areas under the curve (AUC) for predicting prognosis based on PLR and PAB were 0.662 and 0.774, respectively, and the combined AUC of these indicators was 0.812. Conclusions: CCRT combined with IT is an effective treatment for LA-NSCLC, improving survival outcomes. The predictive model developed may help assess prognosis and guide early clinical intervention. Attention should be given to pneumonia prevention and management during IT. Moreover, the combination of PLR and PAB enhances prognostic prediction for NSCLC patients undergoing CCRT plus IT.

Keywords: Non-small-cell lung cancer, concurrent chemoradiotherapy, overall survival

Introduction

Non-small-cell lung cancer (NSCLC) accounts for approximately 85% of lung cancer (LC) cases, a leading cause of cancer-related death worldwide. Pathologically, NSCLC includes adenocarcinoma, squamous cell carcinoma, and large cell carcinoma [1, 2]. For patients diagnosed with early-stage NSCLC, surgical resection can provide a cure, and chemotherapy may be added to improve survival and reduce recurrence [3]. However, due to nonspecific early symptoms and insufficient screening techniques, most NSCLC patients are diagnosed at

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a locally advanced (LA) stage (stage III) or with distant metastasis (stage IV), at which point surgery is no longer curative [4]. Concurrent chemoradiotherapy (CCRT) is the preferred treatment for LA-NSCLC and can also effectively alleviate symptoms in stage IV NSCLC patients [5, 6]. Sakin et al. [7] reported that, compared to chemotherapy or sequential chemoradiotherapy, CCRT in elderly patients with LA-NSCLC leads to the highest survival rates, indicating that CCRT can significantly improve patient outcomes.

Despite its benefits, CCRT has limited potential to improve the cure rate and prognosis of LA-NSCLC patients and is associated with toxic side effects that can severely affect patients' quality of life [8]. Thus, optimizing treatment strategies for these patients remains a critical need. Immunotherapy (IT) enhances the body's immune response against tumors and has been shown to improve prognosis and prolong survival compared to standard chemotherapy, although it also carries some side effects [9]. The cytotoxic T lymphocyte-associated antigen 4 (CTLA-4) and programmed cell death protein 1 (PD-1) pathways are key immune checkpoints exploited by tumor cells to evade immune surveillance. Consequently, inhibitors of CTLA-4 and PD-1 pathways have become standard options in IT [10]. Sintilimab, a PD-1 inhibitor, blocks the interaction between PD-1 and its ligands, enhancing the body's endogenous anti-tumor T-cell response. It has shown effectiveness in treating LA-NSCLC patients [11]. Zhang et al. [12] demonstrated that Sintilimab is more effective and safer for treating non-squamous NSCLC compared to other PD-1 inhibitors.

Currently, there are limited studies on the combination of CCRT and IT (Sintilimab) for treating LA-NSCLC or distant metastatic NSCLC. This study aims to compare this combination therapy with CCRT plus cisplatin-based chemotherapy (albumin-bound paclitaxel, TP, or carboplatin + albumin-bound paclitaxel, TC) to optimize clinical treatment options for LA or metastatic NSCLC patients.

Patients and methods

General information

This study was approved by the Ethics Committee of Changzhou Wujin People's Hospital. A total of 90 LA-NSCLC patients admitted between February 2018 and February 2020 were enrolled and grouped according to their treatment protocols. The observation group (n=45) received 4-6 cycles of CCRT followed by 1 year of Sintilimab immunotherapy. The control group (n=45) underwent the same CCRT treatment, followed by 4-6 cycles of TP or TC chemotherapy.

Inclusion and exclusion criteria

Patients included in the study were diagnosed with stage III-IVA NSCLC based on pathologic and imaging evaluations [13], and were able to tolerate radiotherapy and chemotherapy. All patients had a Karnofsky Performance Scale (KPS) score > 70 [14], normal liver and renal function, coagulation function, and bone marrow reserve. Additionally, they all had a programmed cell death-ligand 1 (PD-L1) expression > 10% as indicated by immune checkpoint analysis, with a life expectancy > 3 months.

Exclusion criteria included: moderate-to-severe respiratory dysfunction, acute myocardial infarction, heart failure, active tuberculosis, severe pneumonia or high fever, lymph node metastasis, and mental illness or communication disorders.

Clinical response and toxicity evaluation

Efficacy was assessed according to the RECIST (Response Evaluation Criteria in Solid Tumors) [15].

Complete response (CR): Complete disappearance of the tumor or all target lesions. Partial response (PR): No new lesions and tumor regression ≥ 50%. Stable disease (SD): Tumor growth ≤ 25% or tumor regression < 50%. Progressive disease (PD): New lesions or tumor growth > 25%. Objective response rate (ORR) was defined as the percentage of CR and PR cases among all patients. Disease control rate (DCR) was the percentage of CR, PR, and SD cases.

Toxicity and side effects were evaluated according to the Common Terminology Criteria for Adverse Events (CTCAE) v4.03 [16], and classified into grades I-V.

Treatment methods

Both groups received CCRT (conformal intensity-modulated radiotherapy [IMRT] + chemo-

therapy [cisplatin + etoposide]). A Varian TrueBeam Linear Accelerator (6 MV X-ray energy) was used for IMRT. Patients were positioned in the supine position and immobilized using thermoplastic film for CT simulation (scanning thickness: 5 mm). Routine segmentation was performed with the Eclipse system (60 Cy, 2 Gy/f, 30 sessions in total). Radiotherapy was given five times a week for 4-6 cycles, or 20-30 sessions based on the patient's condition. No radiotherapy was administered for 2 years after treatment.

Chemotherapy: 50 mg/m^2 cisplatin (Qilu Pharmaceutical, H37021358) was administered on days 1, 8, 29, and 36. Also, 50 mg/m^2 etoposide (Qilu Pharmaceutical, H37023183) was given intravenously on days 1-5 and 29-33 (28-day interval).

For the observation group, Sintilimab (200 mg; Innovent Biologics, S20180016) was administered intravenously on day 1, followed by 3-week intervals for 1 year.

For the control group, patients received 4-6 cycles of TP or TC chemotherapy. TP regimen: 130 mg/m^2 albumin-bound paclitaxel (Jiangsu Hengrui Pharmaceuticals, H20183378) was administered intravenously over 1 hour on day 1, followed by administration every 7 days. Cisplatin (25 mg/m^2) was given intravenously over 2 hours on days 2-4. TC regimen: Carboplatin (300 mg/m^2; Qilu Pharmaceutical, H200-20180) was given on day 2. Both regimens had a 21-day cycle, with 4-6 cycles depending on the patient's recovery.

Follow-up

Follow-up was conducted quarterly through pathologic data review, telephone interviews, and return visits to record overall survival (OS) and progression-free survival (PFS). OS was defined as the time from the first day of treatment to death from any cause or the last follow-up. PFS was defined as the time from the first day of treatment to disease progression or death.

Statistical processing

Data were processed using SPSS 26.0. A *P*-value of < 0.05 was considered significant. Quantitative data were expressed as mean ± SEM and analyzed using t-tests (inter-group) and paired t-tests (pre- and post-treatment). Categorical data were described by frequency (percentage), and group comparisons were performed using the χ^2-test. Survival was assessed using Kaplan-Meier curves, with inter-group differences identified by the Log-Rank test. Multivariate regression analysis was performed using the Cox model. The predictive value of relevant indicators for prognosis in the observation group was analyzed using receiver operating characteristic (ROC) curves.

Results

General information

The control group consisted of 28 males and 17 females, with a mean age of 57.11 ± 7.76 years and a BMI of 23.00 ± 2.28. In the observation group, the male-to-female ratio was 25:20, with an average age of 58.15 ± 11.31 years and a BMI of 22.78 ± 2.55. The clinical data were comparable between the two groups (all P > 0.05). See **Table 1**.

Efficacy

Efficacy evaluation showed that the ORR and DCR for the observation group were 73.33% and 93.33%, respectively, while the ORR and DCR for the control group were 53.33% and 77.77%, respectively. Significant differences were observed between the groups for both ORR and DCR (both P < 0.05). See **Table 2**.

Toxicity

The safety evaluation (**Table 3**) showed a significantly higher incidence of grade I-II pneumonia in the observation group compared to the control group (13.33% vs. 2.22%, P < 0.05). The control group had notably higher incidences of grade III-IV gastrointestinal reactions, leukopenia, thrombocytopenia, and anemia compared to the observation group (44.44% vs. 13.32%, P < 0.05). Overall, the total incidence of toxic and side effects was significantly lower in the observation group compared to the control group (46.67% vs. 26.67%, P < 0.05).

Survival curves

Follow-up was completed for all 90 LA-NSCLC patients, and survival was evaluated by plotting survival curves (**Figure 1**). The 2-year OS and 2-year PFS were significantly higher in the

Table 1. Comparison of general information

Factor	n	Control group (n=45)	Observation group (n=45)	χ^2/t	P
Gender				0.413	0.520
Male	53	28 (62.22)	25 (55.56)		
Female	37	17 (37.78)	20 (44.44)		
Mean age (years)	90	57.11±7.76	58.15±11.31	0.509	0.612
Body mass index (kg/m^2)	90	23.00±2.28	22.78±2.55	0.431	0.667
Clinical staging (stage)				0.476	0.490
III	63	33 (73.33)	30 (66.67)		
IVa	27	12 (26.67)	15 (33.33)		
Pathological type				0.963	0.327
Adenocarcinoma	68	36 (80.00)	32 (71.11)		
Adenosquamous carcinoma	22	9 (20.00)	13 (28.89)		

Table 2. Comparison of therapeutic effects [n (%)]

Group	n	CR	PR	SD	PD	ORR (%)	DCR (%)
Control group	45	4 (8.89)	20 (44.44)	11 (24.44)	10 (22.23)	24 (53.33)	35 (77.77)
Observation group	45	11 (24.44)	22 (48.89)	9 (20.00)	3 (6.67)	33 (73.33)	42 (93.33)
χ^2 value	-	-	-	-	-	3.876	4.406
P value	-	-	-	-	-	0.049	0.036

Note: LA-NSCLC, locally advanced - non-small-cell lung carcinoma; CR, complete response; PR, partial response; SD, stable disease; PD, progressive disease; ORR, objective response rate; DCR, disease control rate.

Table 3. Comparison of Toxicity [n (%)]

Grade	Category	Control group (n=45)	Observation group (n=45)	χ^2 value	*P* value
I-II	Pneumonia	1 (2.22)	6 (13.33)	3.873	0.049
III-IV	Gastrointestinal reactions	6 (13.33)	2 (4.44)	11.905	< 0.001
	Leukopenia	6 (13.33)	2 (4.44)		
	Thrombocytopenia	5 (11.11)	1 (2.22)		
	Anemia	3 (6.67)	1 (2.22)		
Total		21 (46.67)	12 (26.67)	3.876	0.049

Note: LA-NSCLC, locally advanced - non-small-cell lung carcinoma.

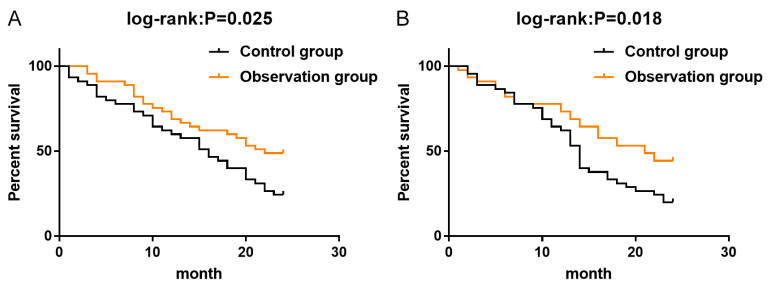

Figure 1. Survival curves of two groups of LA-NSCLC patients. A. The observation group had a significantly higher two-year OS than the control group. B. The observation group had a significantly higher two-year PFS than the control group. Note: LA-NSCLC, locally advanced - non-small-cell lung carcinoma; OS, overall survival; PFS, progression-free survival.

observation group compared to the control group (P < 0.05). The 2-year OS and 2-year PFS for the observation group were 48.89% and 44.44%, respectively, while those of the control group were 24.44% and 20.00%, respectively.

Univariate and multivariate analyses of prognosis of LA-NSCLC patients in the observation group

Patients in the observation group were grouped according to their outcome. The 2-year PFS for patients in the observation group was 44.44%. Patients without disease progression within 2 years were classified into the good prognosis

Table 4. Univariate analysis of prognosis of LA-NSCLC patients in observation group (n [%], mean ± SEM)

Factor	n	Good prognosis (n=20)	Poor prognosis (n=25)	χ^2/t	P
Sex				0.450	0.502
Male	25	10 (50.00)	15 (60.00)		
Female	20	10 (50.00)	10 (40.00)		
Age (years)				0.218	0.641
< 60	23	11 (55.00)	12 (48.00)		
≥ 60	22	9 (45.00)	13 (52.00)		
BMI (kg/m^2)				0.288	0.592
< 23	25	12 (60.00)	13 (52.00)		
≥ 23	20	8 (40.00)	12 (48.00)		
Pathologic classification				3.246	0.197
Adenocarcinoma	28	10 (50.00)	18 (72.00)		
Squamous-cell carcinoma	14	9 (45.00)	5 (20.00)		
Others	3	1 (5.00)	2 (8.00)		
Disease stage				1.401	0.237
III	29	11 (55.00)	18 (72.00)		
IVA	16	9 (45.00)	7 (28.00)		
Distant metastasis				6.000	0.014
Yes	18	4 (20.00)	14 (56.00)		
No	27	16 (80.00)	11 (44.00)		
Differentiation degree				6.790	0.009
Moderate and high differentiation	24	15 (75.00)	9 (36.00)		
Low differentiation	21	5 (25.00)	16 (64.00)		
PLR	45	120.18±50.27	166.99±86.11	2.152	0.037
NLR	45	2.48±1.26	5.57±2.76	4.628	< 0.001
PAB (g/dl)	45	239.79±45.83	153.07±41.39	6.659	< 0.001
LDH (U/L)	45	399.66±122.31	425.34±227.41	0.454	0.652

Note: LA-NSCLC, locally advanced - non-small-cell lung carcinoma; BMI, body mass index; PLR, platelet-to-lymphocyte ratio; NLR, neutrophil-to-lymphocyte ratio; PAB, prealbumin; LDH, lactate dehydrogenase.

Table 5. Assignments

Indicator	Variable	Assignment
Distant metastasis	X1	Without =0, with =1
Differentiation degree	X2	Moderate and high differentiation =0, low differentiation =1
PLR	X3	Continuous variable
NLR	X4	Continuous variable
PAB	X5	Continuous variable
Prognosis	Y	Favorable prognosis =0, unfavorable prognosis =1

Note: PLR, platelet-to-lymphocyte ratio; NLR, neutrophil-to-lymphocyte ratio; PAB, prealbumin.

group (n=20), while those with relapse were assigned to the poor prognosis group (n=25). Univariate analysis showed that distant metastasis, degree of differentiation, platelet-to-lymphocyte ratio (PLR), neutrophil-to-lymphocyte ratio (NLR), and prealbumin (PAB) were significantly associated with poor prognosis in LA-NSCLC patients (all P < 0.05). Cox regression analysis revealed that distant metastasis [HR: 3.830 (1.491-9.843), P=0.005], degree of differentiation [HR: 3.583 (1.335-9.614), P= 0.011], PLR [HR: 1.009 (1.003-1.014), P= 0.001], and PAB [HR: 0.981 (0.972-0.991), P < 0.001] were significantly and independently associated with poor prognosis in the observation group. See **Tables 4**-**6**.

Table 6. Multivariate Cox regression analysis of prognosis of LA-NSCLC patients in the observation group

Factor	β	S.E.	Wald	P	HR	95% CI
Distant metastasis	1.343	0.482	7.777	0.005	3.830	1.491-9.843
Differentiation degree	1.276	0.504	6.421	0.011	3.583	1.335-9.614
PLR	0.009	0.003	10.145	0.001	1.009	1.003-1.014
NLR	0.095	0.088	1.174	0.279	1.100	0.926-1.306
PAB	-0.019	0.005	15.228	< 0.001	0.981	0.972-0.991

Note: LA-NSCLC, locally advanced - non-small-cell lung carcinoma; PLR, platelet-to-lymphocyte ratio; NLR, neutrophil-to-lymphocyte ratio; PAB, prealbumin.

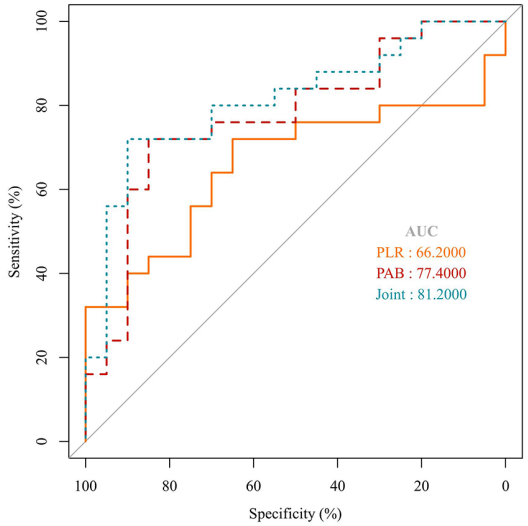

Figure 2. The ROC curves of PLR and PABfor predicting the prognosis of patients with LA-NSCLC in the observation group. Note: ROC, receiver operating characteristic; PLR, platelet-to-lymphocyte ratio; PAB, prealbumin; LA-NSCLC, locally advanced non-small-cell lung carcinoma; AUC, area under the curve.

Prognostic value of PLR and PAB in LA-NSCLC patients in the observation group

ROC analysis showed that the area under the curve (AUC) for PLR in predicting the prognosis of LA-NSCLC patients in the observation group was 0.662, with a specificity of 65.00% and sensitivity of 72.00%. The optimal cut-off value was 117.2. For PAB, the AUC was 0.774, with a specificity of 85.00% and sensitivity of 72.00%, and an optimal cut-off value of 187.0. After combining PLR and PAB, the resulting AUC was 0.812, with a specificity of 90.00% and sensitivity of 72.00%, and an optimal cut-off value of 0.593. See **Figure 2** and **Table 7**.

Discussion

A total of 90 patients with stage III-IVA NSCLC were included in this study, consisting of 63 stage III patients and 27 stage IVA patients. LA-NSCLC refers primarily to stage III NSCLC, characterized by advanced local lesions that cannot be surgically resected, regional lymph node invasion, but no distant metastasis [17]. Stage IVA NSCLC is marked by oligometastasis, and induction immune (chemo) therapy for stage III NSCLC patients has been shown to improve both cure rates and prognosis [18].

Our findings indicated a significantly higher ORR and DCR in the observation group compared to the control group, consistent with the results reported by Sun et al. [19]. This suggests that late-stage IT is more effective than late-stage TP or TC regimens for improving the clinical outcome of NSCLC patients. The CCRT regimen used in our study involved IMRT combined with chemotherapy (cisplatin + etoposide). IMRT offers high precision and safety, ensuring both target area dose conformity and minimizing harm to surrounding tissues [20]. Wang et al. [21] demonstrated that IMRT significantly prolongs local PFS and reduces pulmonary toxicity compared to three-dimensional conformal radiotherapy (3DCRT) in LA-NSCLC patients. Moreover, various chemotherapy schemes in CCRT were compared, with cisplatin + etoposide proving to have a superior chemotherapy induction effect [22].

Rui et al. [23] found that Sintilimab outperformed Camrelizumab in treating LA- or metastatic non-squamous NSCLC, showing higher clinical efficacy and lower medical cost.

Regarding safety, both groups primarily experienced grade I-II pneumonia, along with grade III-IV gastrointestinal reactions, leukopenia, thrombocytopenia, and anemia, which is in line with the findings of Zhang et al. [24]. Notably, the observation group had a significantly lower overall incidence of toxic and side effects compared to the control group but exhibited a high-

Table 7. Value of PLR and PAB for predicting the prognosis of patients with LA-NSCLC in the observation group

Indicator	AUC	S.E.	95% CI	Specificity	Sensitivity	Optimal cut-off
PLR	0.662	0.083	0.500-0.825	65.00	72.00	117.2
PAB	0.774	0.072	0.633-0.915	85.00	72.00	187.0
Joint detection	0.812	0.065	0.684-0.940	90.00	72.00	0.593

Note: PLR, platelet-to-lymphocyte ratio; PAB, prealbumin; LA-NSCLC, locally advanced non-small-cell lung carcinoma; AUC, area under the curve; CI, confidence interval.

er incidence of pneumonia. This indicates that while CCRT + IT offers better overall safety than CCRT + TP/TC, attention should be paid to the prevention and treatment of pneumonia in the IT regimen. Pneumonia is the most serious and life-threatening adverse reaction associated with IT, with its occurrence closely related to immune checkpoint blockade. In addition to Sintilimab, other immune agents such as Durvalumab and Sugemalimab can also induce pneumonia events [25, 26].

Although CCRT is the standard therapy for LA-NSCLC patients, it results in a 5-year OS rate of only 15-20%. Therefore, CCRT is often combined with other therapies to improve survival outcome [27]. CCRT combined with IT using Durvalumab has been reported to significantly improve OS and PFS in LA-NSCLC patients compared to placebo [28, 29]. In our study, after 2 years of follow-up, we found that the observation group had significantly higher 2-year OS and 2-year PFS compared to the control group, which is consistent with the findings of Gennen et al. [30] and Wang et al. [31]. These results suggest that CCRT combined with Sintilimab leads to better survival outcome in LA-NSCLC patients.

Cox multivariate analysis identified that distant metastasis, degree of differentiation, PLR and PAB levels were independent predictors of poor prognosis in the OG. In contrast, distant metastasis, low differentiation, high PLR, and low PAB levels were also identified as poor prognostic factors for patients receiving CCRT + IT. Chen et al. [32] identified distant metastasis and differentiation degree as adverse prognostic indicators for NSCLC patients, which aligns with our findings.

The systemic inflammatory response is a known predictor of prognosis in solid tumors. High PLR levels are associated with poor prognosis in NSCLC patients undergoing IT [33] and have also been identified as a predictor of brain metastases in LA-NSCLC patients [34]. Furthermore, Kawai et al. [35] emphasized that low perioperative PAB is a predictor of poor prognosis, which is consistent with our results.

We further quantified the prognostic predictive value of PLR and PAB in LA-NSCLC patients treated with CCRT + Sintilimab. The AUC for predicting prognosis using PLR and PAB was 0.662 and 0.774, respectively. When both markers were combined for joint prediction, the AUC increased to 0.812, with relatively high specificity and sensitivity. This suggests that use of PLR and PAB together as prognostic markers in LA-NSCLC patients following CCRT + Sintilimab treatment enhances diagnostic efficacy.

This study's innovation lies in demonstrating that CCRT combined with IT offers superior clinical efficacy compared to CCRT plus TP/TC chemotherapy in the management of LA-NSCLC patients. Beyond efficacy, CCRT combined with IT also shows improved clinical safety, particularly regarding grade I-II pneumonia, grade III-IV gastrointestinal reactions, leukopenia, thrombocytopenia, and anemia. Notably, patients receiving CCRT plus IT exhibited significantly higher 2-year OS and PFS rates, reflecting a more marked improvement in prognosis.

Our study identifies independent prognostic factors for patients receiving CCRT plus IT, namely distant metastasis, degree of differentiation, PLR, and PAB. Moreover, the study quantitatively validates the prognostic potential of PLR and PAB in these patients.

However, there are several limitations. First, long-term prognostic evaluation was not performed. Incorporating long-term follow-up data (spanning 5-10 years or more) would be invaluable in assessing the prolonged effect of CCRT combined with IT on the survival of LA-NSCLC patients. Second, the factors influencing treat-

ment efficacy in LA-NSCLC patients were not comprehensively investigated. Additional analyses in this area could yield targeted strategies to optimize treatment. Finally, assessing measurements such as pulmonary function and quality of life would enhance the understanding of the clinical benefits of CCRT combined with IT for LA-NSCLC patients. We plan to address these limitations through in-depth analyses in future studies.

In conclusion, CCRT combined with IT demonstrates superior efficacy and safety compared to CCRT plus TP/TC chemotherapy for LA-NSCLC patients, significantly extending patients' OS and PFS. The prognostic model developed for patients receiving CCRT plus IT identifies distant metastasis, differentiation degree, PLR, and PAB as key predictors of poor prognosis. Additionally, the combination of PLR and PAB was shown to be effective for prognostic prediction in LA-NSCLC patients undergoing CCRT plus Sintilimab treatment. Our findings provide a solid foundation for prognosis estimation and clinical decision-making in LA-NSCLC patients.

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Disclosure of conflict of interest

None.

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References

[1] Chen P, Liu Y, Wen Y and Zhou C. Non-small cell lung cancer in China. Cancer Commun (Lond) 2022; 42: 937-970.

[2] Gyorffy B. Transcriptome-level discovery of survival-associated biomarkers and therapy targets in non-small-cell lung cancer. Br J Pharmacol 2024; 181: 362-374.

[3] Takenaka T, Yano T, Yamazaki K, Okamoto T, Hamatake M, Shimokawa M and Mori M; Kyushu University Lung Surgery Study Group Japan. Survival after recurrence following surgical resected non-small cell lung cancer: a multicenter, prospective cohort study. JTCVS Open 2022; 10: 370-381.

[4] Miao D, Zhao J, Han Y, Zhou J, Li X, Zhang T, Li W and Xia Y. Management of locally advanced non-small cell lung cancer: State of the art and future directions. Cancer Commun (Lond) 2024; 44: 23-46.

[5] Kim YH, Ahn SJ, Moon SH, Kim JH, Kim YC, Oh IJ, Park CK, Jeong JU, Yoon MS, Song JY, Suh CO, Cho KH and Park SH. Randomized, multicenter, phase 3 study of accelerated fraction radiation therapy with concomitant boost to the gross tumor volume compared with conventional fractionation in concurrent chemoradiation in patients with unresectable stage III non-small cell lung cancer: The Korean Radiation Oncology Group 09-03 Trial. Int J Radiat Oncol Biol Phys 2023; 115: 873-885.

[6] Zheng Q, Min S and Zhou Y. A network meta-analysis for efficacies and toxicities of different concurrent chemoradiotherapy regimens in the treatment of locally advanced non-small cell lung cancer. BMC Cancer 2022; 22: 674.

[7] Sakin A, Sahin S, Atci MM, Sakin A, Yasar N, Geredeli C, Aksaray F and Cihan S. The effect of different treatment modalities on survival in elderly patients with locally advanced non-small cell lung cancer. Pulmonology 2021; 27: 26-34.

[8] Abe T, Iino M, Saito S, Aoshika T, Ryuno Y, Ohta T, Igari M, Hirai R, Kumazaki YU, Miura YU, Kaira K, Kagamu H, Noda SE and Kato S. Comparison of the efficacy and toxicity of concurrent chemoradiotherapy and durvalumab and concurrent chemoradiotherapy alone for locally advanced non-small cell lung cancer With N3 lymph node metastasis. Anticancer Res 2023; 43: 675-682.

[9] Franzi S, Mattioni G, Rijavec E, Croci GA and Tosi D. Neoadjuvant chemo-immunotherapy for locally advanced non-small-cell lung cancer: a review of the literature. J Clin Med 2022; 11: 2629.

[10] Huang Y, Chen Z, Shen G, Fang S, Zheng J, Chi Z, Zhang Y, Zou Y, Gan Q, Liao C, Yao Y, Kong J and Fan X. Immune regulation and the tumor

microenvironment in anti-PD-1/PDL-1 and anti-CTLA-4 therapies for cancer immune evasion: a bibliometric analysis. Hum Vaccin Immunother 2024; 20: 2318815.
[11] Zhang L, Mai W, Hao B, Jiang W and Geng Q. Promising response to a PD-1 inhibitor (sintilimab) in non-small cell lung cancer: a case report. Medicine (Baltimore) 2020; 99: e19790.
[12] Zhang L, Qian Y, Li J, Cui C, Chen L, Qu S and Lu S. Indirect comparison of sintilimab and other PD-L1 inhibitors for first-line treatment of nonsquamous non-small-cell lung cancer. Future Oncol 2022; 18: 1896-1905.
[13] Alduais Y, Zhang H, Fan F, Chen J and Chen B. Non-small cell lung cancer (NSCLC): a review of risk factors, diagnosis, and treatment. Medicine (Baltimore) 2023; 102: e32899.
[14] McNair KM, Zeitlin D, Slivka AM, Lequerica AH and Stubblefield MD. Translation of Karnofsky Performance Status (KPS) for use in inpatient cancer rehabilitation. PM R 2023; 15: 65-68.
[15] Hu Q, Wang S, Ma L, Sun Z, Liu Z, Deng S and Zhou J. Radiological assessment of immunotherapy effects and immune checkpoint-related pneumonitis for lung cancer. J Cell Mol Med 2024; 28: e17895.
[16] Guberti M, Schiroli D, Marraccini C, Mazza G, Iotti C, Baricchi R, Iotti B and Merolle L. Homologous platelet gel on radiation-induced dermatitis in a patient receiving head and neck radiotherapy plus cetuximab: a case report. Medicine (Baltimore) 2023; 102: e34779.
[17] Wei Y, Qin X, Liu X, Zheng J, Luan X, Zhou Y, Yu J and Yuan S. Tumor angiogenesis at baseline identified by (18)F-Alfatide II PET/CT may predict survival among patients with locally advanced non-small cell lung cancer treated with concurrent chemoradiotherapy. J Transl Med 2022; 20: 63.
[18] Jongbloed M, Bartolomeo V, Steens M, Dursun S, van de Lisdonk T, De Ruysscher DKM and Hendriks LEL. Treatment outcome of patients with synchronous oligometastatic non-small cell lung cancer in the immunotherapy era: analysis of a real-life intention-to-treat population. Eur J Cancer 2023; 190: 112947.
[19] Sun C, Liu Y, Zhang P, Wang X, Xu Y, Lin X, Ma X, Guo Y, Qiu S, Shao G, Yang Z and Ma K. Interim analysis of the efficiency and safety of neoadjuvant PD-1 inhibitor (sintilimab) combined with chemotherapy (nab-paclitaxel and carboplatin) in potentially resectable stage IIIA/IIIB non-small cell lung cancer: a single-arm, phase 2 trial. J Cancer Res Clin Oncol 2023; 149: 819-831.
[20] Abe T, Iino M, Saito S, Aoshika T, Ryuno Y, Ohta T, Igari M, Hirai R, Kumazaki Y, Miura Y, Kaira K, Kagamu H, Noda SE and Kato S. Feasibility of intensity modulated radiotherapy with involved field radiotherapy for Japanese patients with locally advanced non-small cell lung cancer. J Radiat Res 2021; 62: 894-900.
[21] Wang J, Zhou Z, Liang J, Feng Q, Xiao Z, Hui Z, Wang X, Lv J, Chen D, Zhang H, Ji Z, Cao J, Liu L, Jiang W, Men Y, Xu C, Dai J, Yin W and Wang L. Intensity-modulated radiation therapy may improve local-regional tumor control for locally advanced non-small cell lung cancer compared with three-dimensional conformal radiation therapy. Oncologist 2016; 21: 1530-1537.
[22] Ai X, Qiu B, Zhou Y, Li S, Li Q, Huan J, Li J, Hu N, Chen N, Liu F, Wang D, Chu C, Wang B, Chen L, Jiang H, Huang S, Huang X, Bi N and Liu H. Comparison and quantification of different concurrent chemotherapy regimens with radiotherapy in locally advanced non-small cell lung cancer: clinical outcomes and theoretical results from an extended LQ and TCP model. Radiother Oncol 2022; 167: 34-41.
[23] Rui M, Fei Z, Wang Y, Zhang X, Ma A, Sun H and Li H. Cost-effectiveness analysis of sintilimab + chemotherapy versus camrelizumab + chemotherapy for the treatment of first-line locally advanced or metastatic nonsquamous NSCLC in China. J Med Econ 2022; 25: 618-629.
[24] Zhang L, He Y, Yi C and Huang M. Systematic evaluation meta-analysis of the efficacy of recombinant human endostatin combined with gemcitabine and cisplatin in non-small-cell lung cancer. J Healthc Eng 2022; 2022: 3208780.
[25] Naidoo J, Nishino M, Patel SP, Shankar B, Rekhtman N, Illei P and Camus P. Immune-related pneumonitis after chemoradiotherapy and subsequent immune checkpoint blockade in unresectable stage III non-small-cell lung cancer. Clin Lung Cancer 2020; 21: e435-e444.
[26] Zhou Q, Chen M, Jiang O, Pan Y, Hu D, Lin Q, Wu G, Cui J, Chang J, Cheng Y, Huang C, Liu A, Yang N, Gong Y, Zhu C, Ma Z, Fang J, Chen G, Zhao J, Shi A, Lin Y, Li G, Liu Y, Wang D, Wu R, Xu X, Shi J, Liu Z, Cui N, Wang J, Wang Q, Zhang R, Yang J and Wu YL. Sugemalimab versus placebo after concurrent or sequential chemoradiotherapy in patients with locally advanced, unresectable, stage III non-small-cell lung cancer in China (GEMSTONE-301): interim results of a randomised, double-blind, multicentre, phase 3 trial. Lancet Oncol 2022; 23: 209-219.
[27] Honglian M, Zhouguang H, Fang P, Lujun Z, Dongming L, Yujin X, Yong B, Liming X, Yirui Z, Xiao H, Jin W, Yue K, Lvhua W and Ming C. Different administration routes of recombinant human endostatin combined with concurrent chemoradiotherapy might lead to different efficacy and safety profile in unresectable stage

III non-small cell lung cancer: updated follow-up results from two phase II trials. Thorac Cancer 2020; 11: 898-906.

[28] Antonia SJ, Villegas A, Daniel D, Vicente D, Murakami S, Hui R, Yokoi T, Chiappori A, Lee KH, de Wit M, Cho BC, Bourhaba M, Quantin X, Tokito T, Mekhail T, Planchard D, Kim YC, Karapetis CS, Hiret S, Ostoros G, Kubota K, Gray JE, Paz-Ares L, de Castro Carpeno J, Wadsworth C, Melillo G, Jiang H, Huang Y, Dennis PA and Ozguroglu M; PACIFIC Investigators. Durvalumab after chemoradiotherapy in stage III non-small-cell lung cancer. N Engl J Med 2017; 377: 1919-1929.

[29] Antonia SJ, Villegas A, Daniel D, Vicente D, Murakami S, Hui R, Kurata T, Chiappori A, Lee KH, de Wit M, Cho BC, Bourhaba M, Quantin X, Tokito T, Mekhail T, Planchard D, Kim YC, Karapetis CS, Hiret S, Ostoros G, Kubota K, Gray JE, Paz-Ares L, de Castro Carpeno J, Faivre-Finn C, Reck M, Vansteenkiste J, Spigel DR, Wadsworth C, Melillo G, Taboada M, Dennis PA and Ozguroglu M; PACIFIC Investigators. Overall survival with durvalumab after chemoradiotherapy in stage III NSCLC. N Engl J Med 2018; 379: 2342-2350.

[30] Gennen K, Kasmann L, Taugner J, Eze C, Karin M, Roengvoraphoj O, Neumann J, Tufman A, Orth M, Reu S, Belka C and Manapov F. Prognostic value of PD-L1 expression on tumor cells combined with CD8+ TIL density in patients with locally advanced non-small cell lung cancer treated with concurrent chemoradiotherapy. Radiat Oncol 2020; 15: 5.

[31] Wang J, Xia TY, Wang YJ, Li HQ, Li P, Wang JD, Chang DS, Liu LY, Di YP, Wang X and Wu WZ. Prospective study of epidermal growth factor receptor tyrosine kinase inhibitors concurrent with individualized radiotherapy for patients with locally advanced or metastatic non-small-cell lung cancer. Int J Radiat Oncol Biol Phys 2011; 81: e59-65.

[32] Chen WJ, Zhang EN, Zhong ZK, Jiang MZ, Yang XF, Zhou DM and Wang XW. MicroRNA-153 expression and prognosis in non-small cell lung cancer. Int J Clin Exp Pathol 2015; 8: 8671-8675.

[33] Liu N, Mao J, Tao P, Chi H, Jia W and Dong C. The relationship between NLR/PLR/LMR levels and survival prognosis in patients with non-small cell lung carcinoma treated with immune checkpoint inhibitors. Medicine (Baltimore) 2022; 101: e28617.

[34] Sert F, Cosgun G, Yalman D and Ozkok S. Can we define any marker associated with brain failure in patients with locally advanced non-small cell lung cancer? Cancer Radiother 2021; 25: 316-322.

[35] Kawai H and Ota H. Low perioperative serum prealbumin predicts early recurrence after curative pulmonary resection for non-small-cell lung cancer. World J Surg 2012; 36: 2853-2857.