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Prognostic Role of Preoperative Neutrophil-to-Lymphocyte Ratio in Clinical Stage I Lung Adenocarcinoma with Ground-Glass Opacity

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**Following abstract submission, additional eligible patients were included, and all analyses were repeated using the updated cohort.*

Disclosure

Artificial Intelligence (AI) Use Disclaimer

Artificial intelligence (AI) was used for translation purposes in the preparation of this presentation.



Background

- Lung adenocarcinoma with a ground-glass opacity (GGO) component generally has a favorable prognosis, although disease recurrence occasionally occurs.

Hamada et al. *JTO Clin Res Rep*. 2022.

Hattori et al. *J Thorac Cardiovasc Surg*. 2021.

Kamigaichi et al. *Eur J Cardiothorac Surg*. 2022.

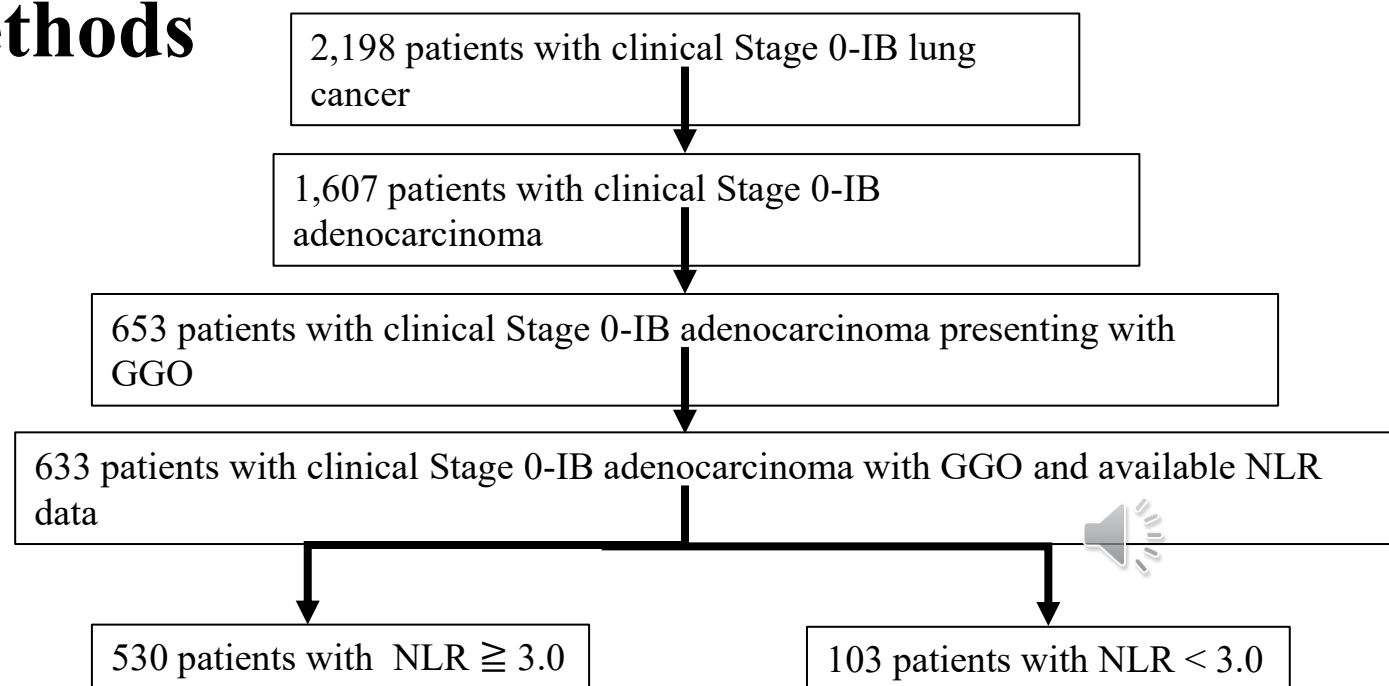
- The neutrophil-to-lymphocyte ratio (NLR) has been reported as a prognostic factor in patients with non-small cell lung cancer undergoing surgical resection.

Gu et al. *Sci Rep*. 2015.

Tomita et al. *Anticancer Res*. 2011.

- To our knowledge, no studies have specifically evaluated the prognostic significance of preoperative NLR in patients with clinical stage I lung adenocarcinoma with a GGO component on preoperative chest computed tomography (CT).
- Therefore, this study aimed to assess the prognostic impact of NLR in early-stage lung cancer with GGO.

Methods



- At Kindai University, Between September 2007 and February 2025, 2,198 patients underwent curative-intent pulmonary resection for clinical stage 0–IB lung cancer at our institution.
- Of these, 1,607 patients were diagnosed with clinical stage 0–IB adenocarcinoma.
- Among them, 653 patients presented with GGO component on preoperative chest CT.
- After excluding cases without available NLR data, 633 patients were included in the analysis.

Methods

- In our hospital, the normal values for plasma fibrinogen, Carcinoembryonic Antigen (CEA) and CRP are ≤ 4.0 g/L, < 5 ng/ml, and < 0.14 mg/dl, respectively, and these were used as the cut-off values.
- The cut-off values for NLR (3.0) and albumin (4.0 g/dl) were determined based on previous reports.

Wang et al. Zhonghua Zhong Liu Za Zhi. 2014

Zhang et al. Ann Palliat Med. 2021.

- Associations between NLR and clinical factors were assessed using the chi-square test.
- Survival curves were estimated using the Kaplan–Meier method and compared using the log-rank test.
- Univariate Cox proportional hazards regression analyses were performed to evaluate the association between each variable and RFS.
- Subsequently, all variables included in the univariate analyses were entered into a multivariate Cox proportional hazards regression model.
- Gray's test was performed using EZR (Saitama Medical Center, Jichi Medical University, Saitama, Japan) and all other statistical analyses were performed using JMP Student Edition 19.

Table 1. Patient Characteristics

Category	Sub-category	Total (n=633)
Age	< 70 years	278
	≥ 70 years	355
Sex	Male	279
	Female	354
Smoking history	Smokers	280
	Non-smokers	344
	unknown	9
Albumin	< 4.0 g/dl	70
	≥ 4.0 g/dl	563
CRP	< 0.14 g/dl	468
	≥ 0.14 g/dl	153
	unknown	12
CEA	< 5 ng/ml	549
	≥ 5 ng/ml	84
Fibrinogen	≤ 400 mg/dl	572
	> 400 mg/dl	59
cT (Clinical T stage)	is, 1mi, 1a, 1b	537
	1c, 2a	96

Category	Sub-category	Total (n=633)
Surgical procedure	Wedge resection	105
	Segmentectomy, Lobectomy	528
NLR	< 3.0	530
	≥ 3.0	103
Pathological tumor size	≤ 2.0 cm	486
	> 2.0 cm	147
Venous invasion	positive	9
	negative	377
	unknown	247
Lymphatic invasion	positive	13
	negative	374
	unknown	246
Pleural invasion	positive	21
	negative	611
	unknown	1

● A total of 633 patients from Kindai University were included in the cohort (Table 1).

● Most tumors were cTis–cT1b (84.8%), and segmentectomy or lobectomy was performed in 83.4% of patients.

● Elevated NLR (≥3.0) was present in 16.3% of cases. Additional biomarker data showed elevated CRP in 24.2%, elevated CEA in 13.3%, and elevated fibrinogen in 9.3% of patients.

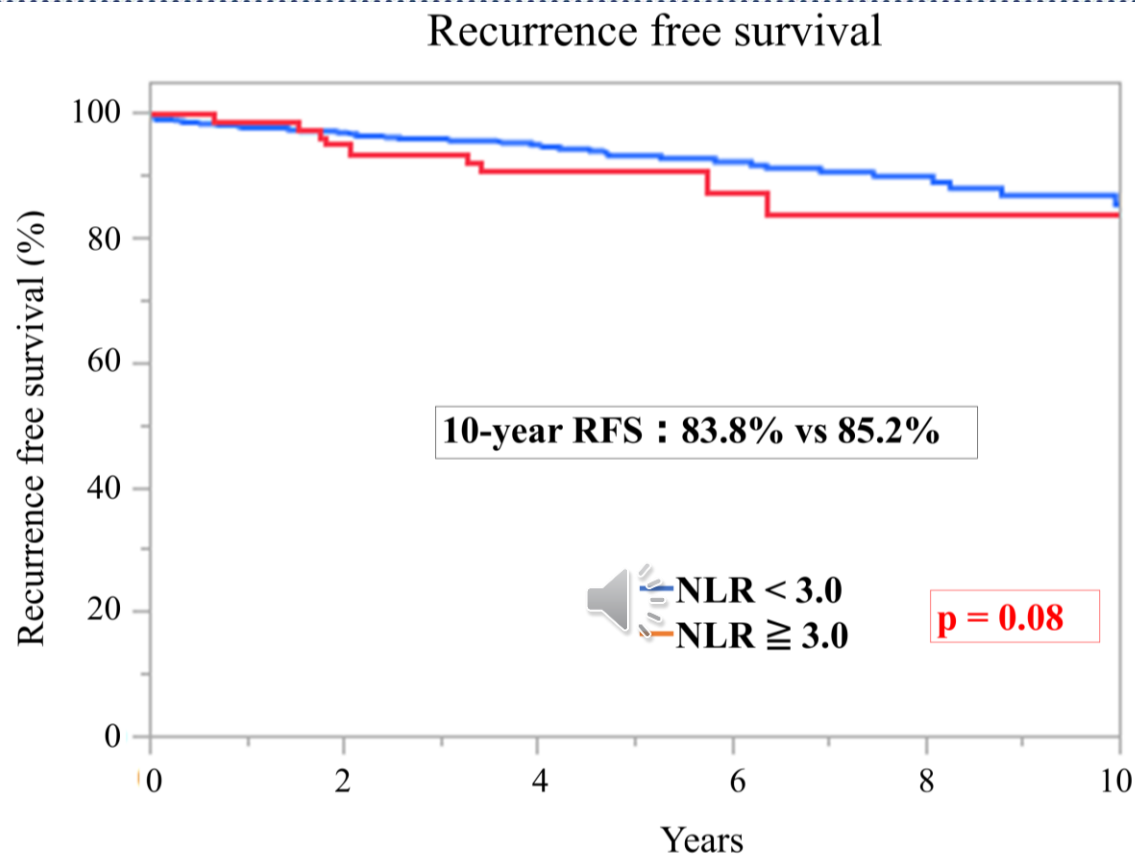
● A relatively large proportion of patients had missing data for venous and lymphatic invasion.

Table 2. Exploration of factors associated with high NLR

Variable		Univariate analysis		
		OR	95% CI	p-value
Age	≥ 70 vs. < 70 years	1.22	0.80–1.89	0.36
Sex	Male vs. Female	1.57	1.03–2.40	0.04
Smoking history	Smokers vs. Non-smokers	1.87	1.22–2.88	< 0.01
Albumin	< 4.0 vs. ≥ 4.0 g/dL	1.20	0.61–2.22	0.59
CRP	≥ 0.14 vs. < 0.14 g/dL	1.50	0.94–2.38	0.09
CEA	≥ 5 vs. < 5 ng/mL	0.84	0.42–1.56	0.59
Fibrinogen	> 400 vs. ≤ 400 mg/dL	2.07	1.09–3.78	0.03
cT	1c, 2a vs. is, 1mi, 1a, 1b	0.78	0.40–1.41	0.42
Surgical procedure	Wedge vs. Seg/Lobectomy	1.26	0.72–2.13	0.41
Pathological tumor size	> 2.0 vs. ≤ 2.0 cm	0.82	0.48–1.36	0.45
Venous invasion	positive vs. negative	0.50	0.03–2.76	0.47
Lymphatic invasion	positive vs. negative	1.80	0.48–5.70	0.36
pleural invasion	positive vs. negative	1.66	0.53–4.34	0.36

- In this cohort, male sex (OR, 1.57; 95% CI, 1.03–2.40; $p = 0.04$), smoking history (OR, 1.87; 95% CI, 1.22–2.88; $p < 0.01$), and elevated fibrinogen levels (>400 mg/dL) (OR, 2.07; 95% CI, 1.09–3.78; $p = 0.03$) were significantly associated with an elevated NLR (Table 2).
- Elevated CRP showed a trend toward association with high NLR but did not reach statistical significance (OR, 1.50; 95% CI, 0.94–2.38; $p = 0.09$).
- No significant associations were observed for age, albumin level, CEA level, clinical T stage, surgical procedure, pathological tumor size, venous invasion, lymphatic invasion, or pleural invasion.
- Of note, elevated fibrinogen was the strongest inflammatory factor associated with high NLR in this cohort, supporting a close relationship between systemic inflammation and elevated NLR.

Result 3:



NLR < 3.0	487	392	293	188	107	55
NLR ≥ 3.0	90	74	49	29	15	11

- The high NLR group tended to have worse RFS than the low NLR group.
- The 10-year RFS rates were 83.8% in the high NLR group and 85.2% in the low NLR group (log-rank $p = 0.08$)

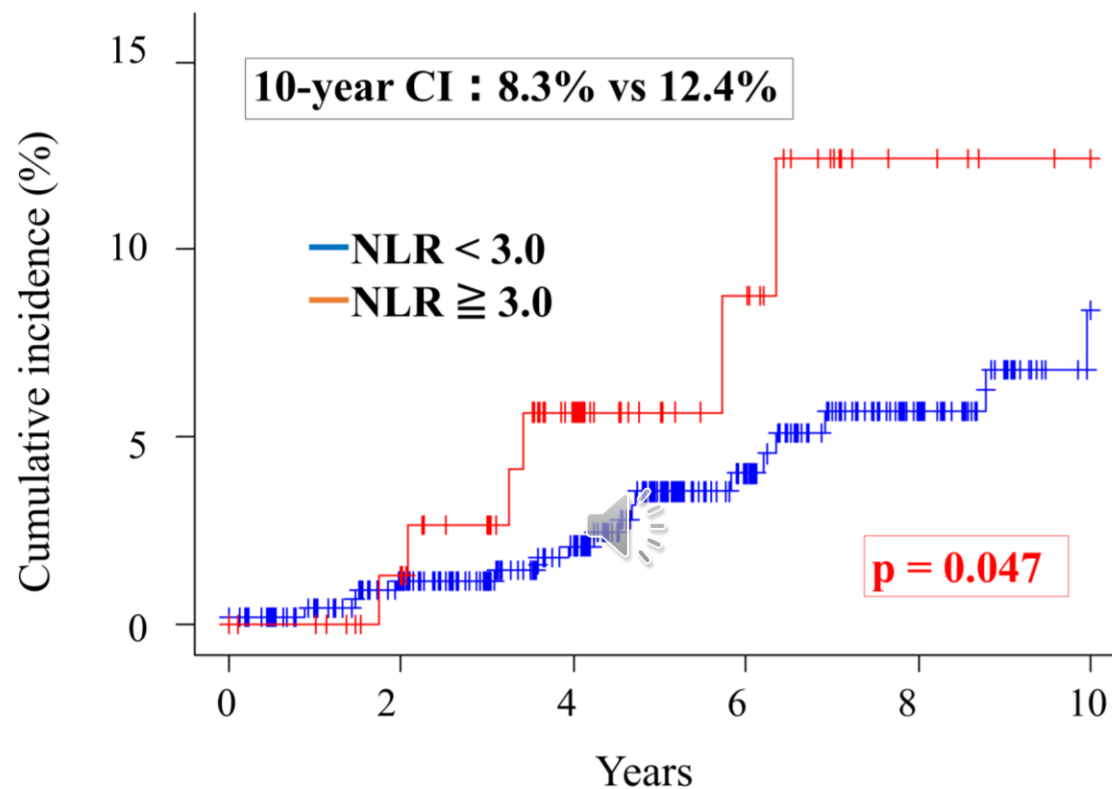
Result 4:

Table 3. Prognostic factors associated with recurrence-free survival

Variable		Univariate analysis			Multivariate analysis		
		HR	95% CI	p-value	HR	95% CI	p-value
Age	≥ 70 vs. < 70 years	2.23	1.20-4.13	0.01	1.94	1.02-3.68	0.04
Sex	Male vs. Female	1.89	1.06-3.37	0.03	1.80	0.84-3.86	0.13
Smoking history	Smokers vs. Non-smokers	1.57	0.86-2.85	0.14	0.95	0.44-2.06	0.90
Albumin	< 4.0 vs. ≥ 4.0 g/dL	2.35	1.09-5.06	0.03	2.46	1.12-5.37	0.02
cT	1c, 2a vs. 1a, 1b	2.31	1.16-4.58	0.02	1.87	0.92-3.80	0.08
Surgical procedure	Wedge vs. Seg/Lobectomy	0.73	0.31-1.72	0.47	0.74	0.31-1.79	0.51
NLR	≥ 3.0 vs. < 3.0	1.79	0.91-3.52	0.09	1.84	0.92-3.67	0.08

- Older age (≥70 years), male sex, low albumin level, and advanced clinical T stage (cT1c–2a) were associated with worse RFS in the univariate analysis (Table 3).
- In the multivariate analysis, older age (HR, 1.94; 95% CI, 1.02–3.68; p = 0.04) and low albumin level (HR, 2.46; 95% CI, 1.12–5.37; p = 0.02) remained independent prognostic factors.
- Although elevated NLR was not significantly associated with recurrence, a trend toward worse RFS was observed in patients with high NLR in both the univariate (HR, 1.79; 95% CI, 0.91–3.52; p = 0.09) and multivariate analyses (HR, 1.84; 95% CI, 0.92–3.67; p = 0.08).

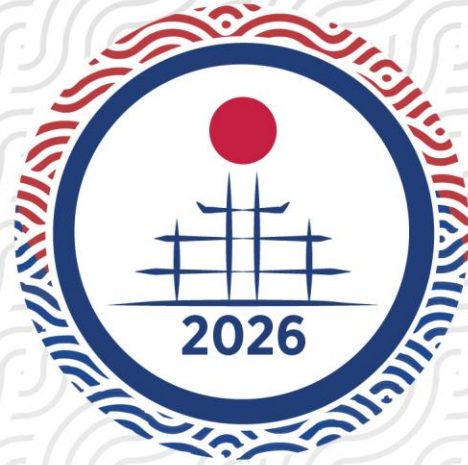
Result 5:



- Patients with a high NLR showed a significantly higher cumulative incidence of recurrence compared with those with a low NLR (10-year cumulative incidence: 12.4% vs. 8.3%, $p = 0.047$).
- In contrast, there was no statistically significant difference in the cumulative incidence of non-cancer-specific death between the two groups (10-year cumulative non-cancer death rate: 3.7% vs. 6.4%, $p = 0.73$).

Conclusions

A high preoperative NLR is a significant adverse prognostic factor even in patients with clinical stage I lung adenocarcinoma with a GGO component.



Thank You.●