

2023 대한심장혈관흉부외과학회

# 제55차 추계학술대회 & APELSO 2023

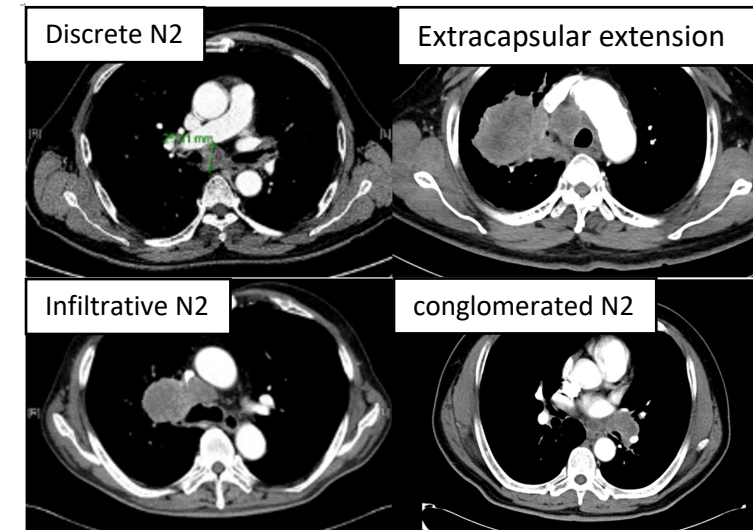
2023. 11. 02 (Thu) - 11. 04 (Sat), 그랜드 인터컨티넨탈 파르나스 서울

## Radiologic Features of *Lymph Node* *Margins* and Mortality in Stage III-N2 Non-small Cell Lung Cancer



- During the evolution of various neoadjuvant treatments for stage III-N2 NSCLC, defining resectability has become an important issue, as it is the primary determinant for the inclusion of neoadjuvant therapy.
- The definition of resectability might include complete resection of the primary tumor and metastatic regional lymph nodes. However, resectability regarding lymph node status is not well defined due to the heterogeneous nature of N2 presentation in terms of the number of metastatic stations, size, and various relationships to surrounding tissues (e.g. extracapsular extension).
- Therefore, we aimed to classify N2 lymph nodes by their radiologic margin status and compare survival outcomes in patients with N2 NSCLC who underwent neoadjuvant concurrent chemoradiotherapy followed by surgery.

- **Design:** A cohort study using the institutional thoracic surgery registry
- **Study population:** Patients with histologically confirmed clinical stage III (T1-T3) non-small cell lung cancer who initiated neoadjuvant concurrent chemoradiotherapy (N=1060)
- **Period:** January 2003 – February 2019
- **Exclusion criteria:** Patients who had not undergone 1) invasive mediastinal examination (n=85); and whose smoking status is missing (n=66)
- **Final study sample, N=909**
- **Classification of radiologic features**
  - 1) Discrete N2
  - 2) Extracapsular extension of N2
  - 3) Infiltrative N2
  - 4) Conglomerate N2
- **Study outcome:** all-cause mortality
- **Statistical analysis:** Survival analysis by **Kaplan-Meier method** and **log-rank test**. Hazard ratios were estimated using **Cox proportional hazard model** and **adjusted** for age, sex, smoking history, Charlson comorbidity index, and histology. Subgroup analysis was performed by extent of clinical N2 and histology. Sensitivity analysis restricting the study population to those who completed trimodality therapy

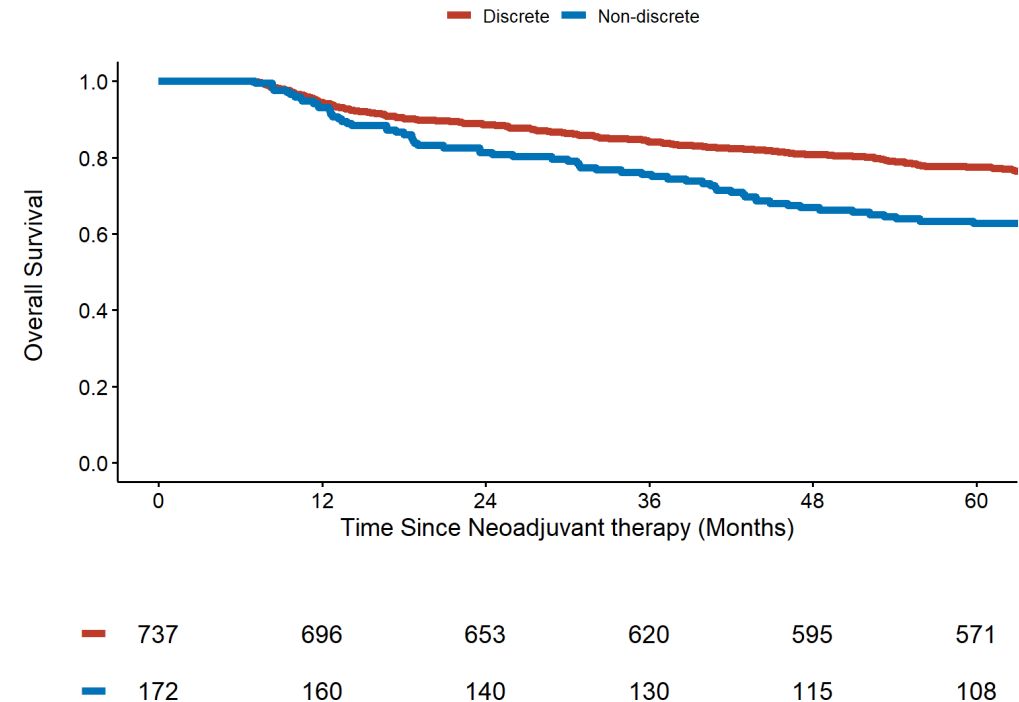


**Table 1.** Participant characteristics.

Characteristics	Overall (n = 909)	Radiologic features		P-value
		Discrete (N = 737)	Non-discrete (N = 172)	
Age, years	60.8 (8.7)	60.8 (8.8)	61.1 (8.2)	0.67
Sex, male	660 (72.6)	514 (69.7)	146 (84.9)	<0.001
Smoking status				<0.001
Never smokers	258 (28.4)	231 (31.3)	27 (15.7)	
Ever smokers	651 (71.6)	506 (68.7)	145 (84.3)	
CCI				0.86
0	604 (66.4)	494 (67.0)	110 (64.0)	
1	190 (20.9)	152 (20.6)	38 (22.1)	
≥2	103 (11.3)	84 (11.4)	19 (11.0)	
FEV1 % predicted (%)	92.8 (17.0)	93.8 (16.9)	88.9 (17.0)	0.02
DLCO (%)	74.4 (15.9)	75.4 (16.2)	70.8 (14.2)	0.04
Clinical tumor size (mm)	39.9 (17.3)	39.5 (17.3)	41.9 (17.2)	0.10
Clinical T category				0.02
T1	262 (28.8)	219 (29.7)	43 (25.0)	
T2	380 (41.8)	312 (42.3)	68 (39.5)	
T3	193 (21.2)	156 (21.2)	37 (21.5)	
T4	71 (8.1)	50 (6.8)	24 (14.0)	
Clinical N category				0.09
N2a1	193 (21.2)	257 (21.0)	58 (22.1)	
N2a2	317 (34.9)	304 (36.5)	77 (27.9)	
N2b	399 (43.9)	169 (42.5)	32 (50.0)	
Completed trimodality therapy	897 (98.7)	730 (99.1)	167 (97.1)	0.10
Resection extent				<0.001
Lobectomy	816 (89.8)	681 (92.4)	135 (78.5)	
Pneumonectomy	75 (8.3)	45 (6.1)	30 (17.4)	
Sublobar	6 (0.7)	4 (0.5)	2 (1.2)	
Total number of LN removed	19.1 (9.0)	19.4 (9.0)	17.7 (8.9)	0.03
Histology				<0.001
ADC	542 (59.6)	469 (63.6)	73 (42.4)	
SCC	301 (33.1)	219 (29.7)	82 (47.7)	
Others <sup>1</sup>	54 (5.9)	42 (5.7)	12 (7.0)	

Values in the table are number (%) or mean (SD).

Abbreviations: ADC, adenocarcinoma; CCI, Charlson Comorbidity Index; DLCO, diffusing capacity of the lungs for carbon monoxide; FEV<sub>1</sub>, forced expiratory volume in 1 second; LN, lymph nodes; SCC, squamous cell carcinoma.



Hazard ratios (95% confidence intervals) for overall survival by radiologic features

	Overall	
	Unadjusted	Adjusted
Discrete	Reference	Reference
Non-discrete	1.28 (1.03, 1.60)	1.23 (0.98, 1.55)

Hazard ratios (95% confidence intervals) for overall survival by radiologic features and histology.

	Overall		Adenocarcinoma		Squamous cell carcinoma	
	Unadjusted	Adjusted	Unadjusted	Adjusted	Unadjusted	Adjusted
<b>Discrete</b>	Reference	Reference	Reference	Reference	Reference	Reference
<b>Non-discrete</b>	1.28 (1.03, 1.60)	1.23 (0.98, 1.55)	1.15 (0.82, 1.62)	1.01 (0.72, 1.42)	1.42 (1.01, 2.01)	1.53 (1.08, 2.18)

Adjusted model includes age, sex, smoking (never or ever), tumor size, histology, and Charlson comorbidity index. P for interaction by histology = 0.09 in the adjusted model.

	Overall		Adenocarcinoma		Squamous cell carcinoma	
	Unadjusted	Adjusted	Unadjusted	Adjusted	Unadjusted	Adjusted
<b>Discrete</b>	Reference	Reference	Reference	Reference	Reference	Reference
<b>Extracapsular</b>	1.21 (0.95, 1.55)	1.16 (0.90, 1.49)	1.10 (0.77, 1.56)	0.95 (0.66, 1.36)	1.39 (0.94, 2.05)	1.50 (1.01, 2.22)
<b>Infiltrative</b>	1.80 (1.05, 3.07)	1.87 (1.04, 3.36)	1.68 (0.23, 12.0)	1.47 (0.19, 11.5)	1.81 (0.97, 3.39)	1.95 (1.03, 3.70)
<b>Conglomerated</b>	1.38 (0.62, 3.10)	1.38 (0.61, 3.12)	2.36 (0.75, 7.38)	2.82 (0.89, 8.97)	0.81 (0.20, 3.27)	0.85 (0.21, 3.48)

Adjusted model includes age, sex, smoking (never or ever), tumor size, histology, and Charlson comorbidity index.

- Non-discrete LN had a higher risk of mortality compared to discrete LN after adjusted for age, sex, smoking, tumor size, histology, and comorbidities (HR 1.23; 95% CI 0.98, 1.55)
- Non-discrete LN feature was associated with an increased risk of mortality in squamous cell carcinoma (fully adjusted HR 1.42; 95% CI 1.01, 2.01) but not in adenocarcinoma
- In squamous cell carcinoma, both extracapsular (HR 1.50; 95% CI 1.01, 2.22) and infiltrative LNs (HR 1.95; 95% CI 1.03, 3.7-) had a higher risk of mortality compared to discrete LN
- In this study, non-discrete N2 especially squamous cell carcinoma with extracapsular and infiltrative feature may not be good candidate for neoadjuvant concurrent chemoradiotherapy followed by surgery