



P1.131: Preoperative predictors of surgical complexity after neoadjuvant immunochemotherapy in non-small-cell lung cancer

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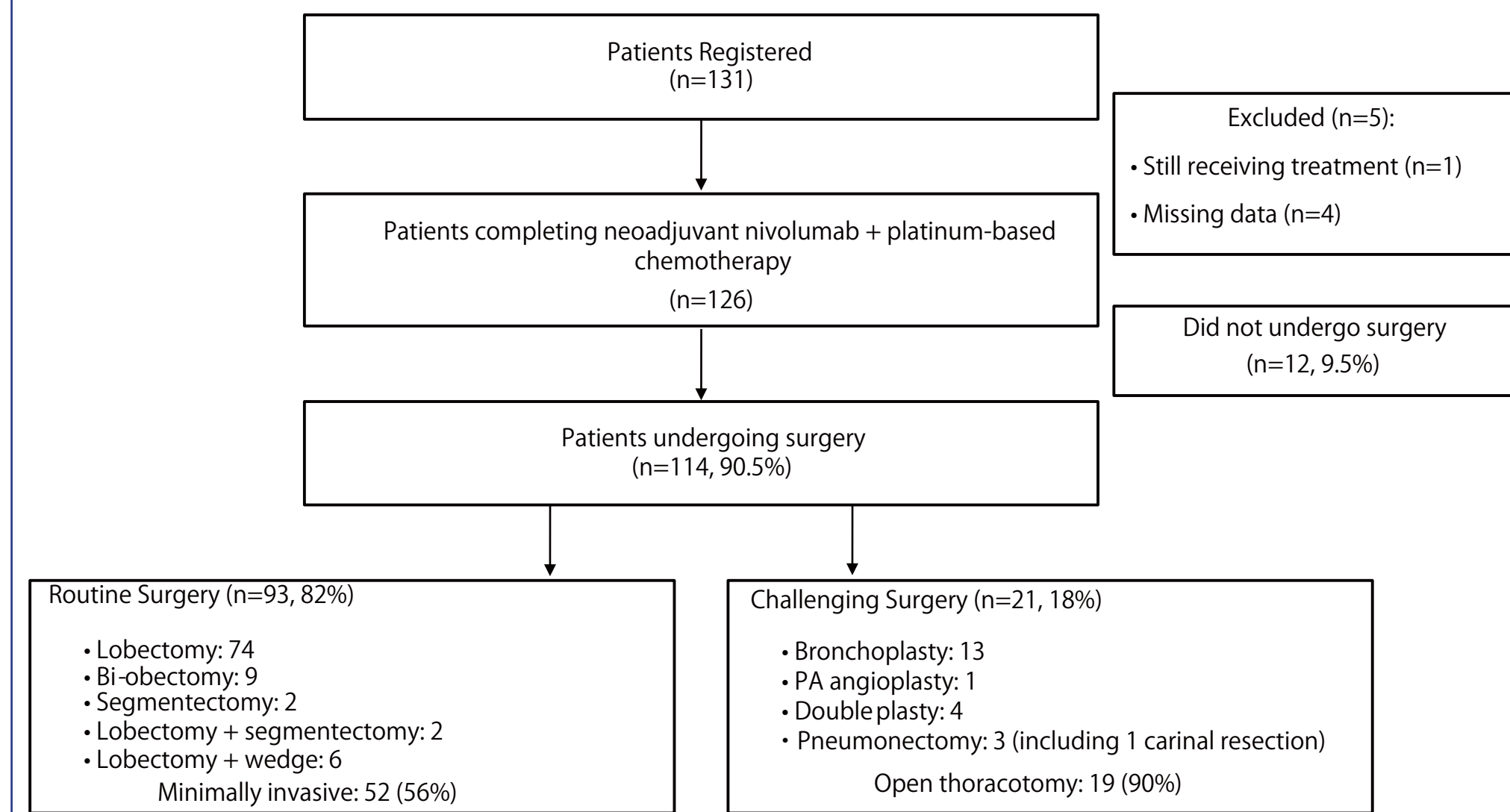
INTRODUCTION

Neoadjuvant immunochemotherapy combining immune checkpoint inhibitors with platinum-based chemotherapy has emerged as a standard-of-care strategy for resectable non-small cell lung cancer (NSCLC). While this approach improves pathological response and potentially long-term outcomes, it induces pronounced immune-driven inflammatory reactions and tissue fibrosis that may substantially increase intraoperative technical complexity and the need for so-called challenging surgery, including bronchoplastic or vascular reconstructive procedures. Identifying reliable preoperative predictors of surgical difficulty is essential for optimizing operative planning and patient counseling in this evolving treatment paradigm.

METHODS

This multicenter retrospective study (CReGYT-04 Neo-Venus) enrolled 114 patients with clinical stage IIA–IIIB NSCLC who underwent surgical resection following neoadjuvant nivolumab plus platinum-based chemotherapy across 29 institutions between March 2023 and July 2024. Challenging surgery was defined as any procedure requiring bronchoplasty, pulmonary artery angioplasty, double-sleeve resection, or unplanned pneumonectomy. Radiological extranodal extension (ENE) was evaluated by contrast-enhanced CT both before (pre-treatment) and after (post-treatment) neoadjuvant therapy. Univariable logistic regression analyses were performed to identify preoperative predictors of surgical complexity. Conventional clinical parameters, including T and N classification, PD-L1 expression, and RECIST-based radiological response, were also assessed.

Patient flow in the CReGYT-04 Neo-Venus study



RESULTS

Twenty-one patients (18.4%) required challenging surgeries, comprising 13 bronchoplasties, 4 double-sleeve resections, 1 pulmonary artery angioplasty, and 3 unplanned pneumonectomies. Compared with routine resections, challenging surgeries were associated with significantly longer operative times (340 ± 118 vs. 267 ± 98 min; p < 0.001), greater intraoperative blood loss (median 179 vs. 55 mL; p = 0.006), and higher rates of open thoracotomy (90.5% vs. 44.0%; p < 0.001). Postoperative complication rates were higher in the challenging surgery group (47.6% vs. 33.3%, p=0.22), with one perioperative death (4.8%) attributable to respiratory failure. While pre-treatment ENE showed no significant association in the univariable analysis (odds ratio [OR] 2.33, 95% CI: 0.71–7.62, p=0.17), post-treatment ENE identified on preoperative CT was the strongest independent predictor of challenging surgery (odds ratio 7.06; 95% confidence interval: 1.45–34.41; p = 0.009). Notably, conventional predictors such as clinical T/N stage, PD-L1 tumor proportion score, and objective radiological response per RECIST criteria were not significantly associated with surgical complexity. Pathological analysis demonstrated that post-treatment ENE correlated with perinodal fibrosis and inflammatory changes rather than residual nodal metastasis, as pathological ENE was confirmed in only 14.3% of post-treatment ENE-positive cases, comparable to the ENE-negative group (14.7%).

CONCLUSION

Unlike conventional predictors, post-treatment ENE may predict surgical complexity after neoadjuvant immunochemotherapy. ENE may be a potential marker of treatment-induced anatomical complexity rather than residual tumor burden, enabling evidence-based surgical planning in the immunotherapy era.

REFERENCES & ACKNOWLEDGHMENTS

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Tables and Figures

Table 1. Comparisons between challenging and routine surgeries

		Challenging surgery (n=21)	Routine surgery (n=93)	p-value
Sex (M/F)		19/2	77/16	0.52
Age (years), mean ± standard deviation		69.7±7.1	68.4±8.1	0.73
Smoking (%)		5 (23.8)	23 (24.7)	0.84
FEV1.0(%), mean ± standard deviation		72.7±13.3	72.7±13.9	0.32
cT status (%)	T1	3 (14.3)	20(21.5)	0.86
	T2	8 (38.1)	29 (31.2)	
	T3	5 (23.8)	20 (21.5)	
	T4	5 (23.8)	24 (25.8)	
cN status (%)	N0	5 (23.8)	24 (25.8)	0.73
	N1	7 (33.3)	24 (25.8)	
	N2 single station	9 (42.9)	41 (44.0)	
	N2 multiple stations	0	4 (4.3)	
Histology (%)	AD	5 (23.8)	46 (49.4)	0.085
	SQ	13 (61.9)	35 (37.6)	
	Others	3 (14.3)	12 (12.9)	
PD-L1 expression (TPS) (%)	<1%	1 (4.8)	15 (16.1)	0.22
	1–49%	12 (57.1)	34 (36.6)	
	≥50%	4 (19.0)	29 (31.2)	
	Unknown	4 (19.0)	14 (15.1)	
RECIST	CR	0 (0)	6 (6.5)	0.48
	PR	14 (66.7)	60 (64.5)	
	SD	7 (33.3)	27 (29.0)	
	PD	0 (0)	0 (0)	
Duration from neoadjuvant therapy to operation (>6 weeks) (%)		12 (57.1)	57 (61.3)	0.81

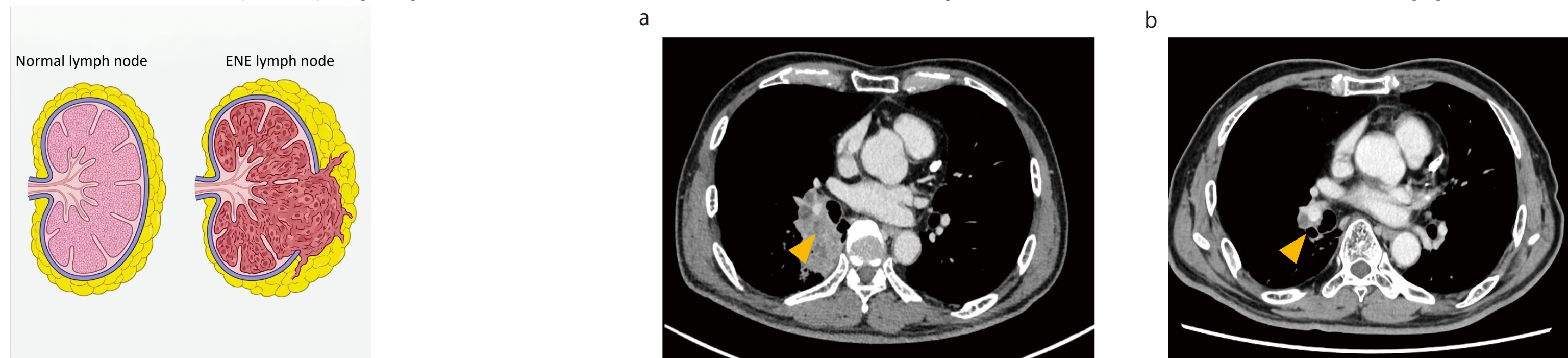
M, male; F, female; FEV1.0, forced expiratory volume in 1 s; FVC, forced vital capacity; AD, adenocarcinoma; SQ, squamous cell carcinoma; PD-L1, programmed death-ligand 1 assessed by tumor proportion score (TPS); RECIST, Response Evaluation Criteria in Solid Tumors; CR, complete response; PR, partial response; SD, stable disease; PD, progressive disease; ICI, immune checkpoint inhibitor

Table 2. Surgical outcomes between challenging surgery and routine surgery

		Challenging surgery (n=21)	Routine surgery (n=93)	p-value
Approach (%)	Thoracotomy	19 (90.5)	41 (44.0)	<0.001
	MIS	2 (9.5)	52 (55.9)	
Conversion to thoracotomy (%)		1 (50)	3 (5.8)	0.14
Extent of resection (%)	Lobectomy	12 (57.1)	74 (79.6)	<0.001
	Lobectomy+segmentectomy	3 (14.3)	2 (2.2)	
Plasty (%)	Lobectomy+wedge	1 (4.8)	6 (6.5)	<0.001
	Segmentectomy	0 (0)	2 (2.2)	
	Bi-lobectomy	2 (9.5)	9 (9.7)	
	Pneumonectomy	3 (14.3)	0 (0)	
	Bronchoplasty	14 (66.7)	0 (0)	
	PA plasty	1 (4.8)	0 (0)	
Operation time, mean ± SD (min).		340±118	267±98	<0.001
Blood loss volume, (median, IQR) (mL)		179 (100–577)	55 (20–125)	0.006
Intraoperative transfusion (%)		5 (23.8)	2 (2.2)	0.002
Complication (%)		10 (47.6)	31 (33.3)	0.22

MIS, minimally invasive surgery; PA, pulmonary artery

Extranodal extension (ENE) lymph node before and after neoadjuvant immunochemotherapy



Representative contrast-enhanced CT images of a case with persistent radiological extranodal extension (ENE) before and after neoadjuvant immunochemotherapy (a and b), without pathological nodal metastasis. This cases required challenging surgery.

Table 3. Univariate analysis for challenging surgery

Variables	Univariate		
	OR	95% CI	p-value
Sex (male)	1.97	0.42–9.33	0.39
Age (>70 years)	1.13	0.33–2.19	0.74
Histology (adenocarcinoma)	0.31	0.10–0.94	0.039
Clinical N1/N2	1.11	0.36–3.36	0.84
ENE-positive before ICI	2.33	0.71–7.62	0.17
ENE-positive after ICI	7.06	1.45–34.41	0.009
PD-L1 status (TPS ≥1%)	1.44	0.48–4.33	0.50
Response (CR+PR)	0.83	0.31–2.28	0.72
Duration from neoadjuvant therapy to surgery (>6 weeks)	0.84	0.32–2.19	0.79

OR, hazard ratio; CI: confidence interval; ENE, extranodal extension; ICI, immune checkpoint inhibitor; PD-L1, programmed death-ligand 1 assessed by tumor proportion score (TPS); CR, complete response; PR, partial response

While pre-treatment ENE showed no significant association in univariate analysis post-treatment ENE was strongly associated with challenging surgery: 4 of 7 patients (57.1%) with post-ENE positivity vs. 15 of 107 (14.0%) with post-ENE negativity required challenging surgery (univariable OR 7.06, 95% CI: 1.45–34.41, p=0.009).

Table 4. The flow analysis of ENE patterns from pre-treatment through post-treatment to pathological findings.

ENE before ICI	ENE after ICI	n (%)	CS (%)	Pathological nodal metastasis in CS	Pathological nodal metastasis in RS
Positive	Positive	4 (3.5)	2 (50.0)	0/2	0/2
Positive	Negative	12 (10.5)	3 (25.0)	1/2	1/10
Negative	Positive	3 (2.6)	2 (66.7)	1/2	0/1
Negative	Negative	95 (83.3)	14 (14.7)	6/14	8/82

ENE, extranodal extension; ICI, immune checkpoint inhibitor; CS, challenging surgery; RS, routine surgery.

Among the four patients with persistent ENE positivity (positive both pre- and post-treatment), two (50.0%) required challenging surgery; however, none showed pathological ENE metastasis (0/4, 0%). Post-treatment ENE demonstrated a substantially higher positive predictive value for challenging surgery (57.1%, 4/7) compared with its predictive value for pathological ENE metastasis (14.3%, 1/7). These findings strongly support the hypothesis that posttreatment ENE positivity is a marker of treatment-induced anatomical complexity contributing to surgical difficulty, rather than an indicator of true residual tumor with extranodal invasion.