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INTRODUCTION

Neoadjuvant therapies have revolutionized the treatment of stage II/III NSCLC. Their efficacy and safety have been demonstrated in many RCTs¹⁻⁵.

Here, we show the evolution of treatment and assess the impact of neoadjuvant therapies on operative management of resectable NSCLC in a real-world cohort.

METHODS

Data of all patients undergoing resection for stage II/III NSCLC between 01/2015 and 12/2024 were obtained from a prospectively maintained institutional registry.

Primary outcome was postoperative complications in patients treated with neoadjuvant therapy (NAT) compared to upfront surgery (S); exploratory analyses were performed for OS.

DISCUSSION AND CONCLUSION

Consistent with RCT data¹⁻⁵, CxIO achieved greater downstaging-, pCR- and MPR-rates than Cx alone.

Although NAT was associated with more extended lobectomy, minimally-invasive surgery remained feasible and NAT did not increase complications or mortality. Higher rates of extended lobectomies and fewer pneumonectomies after NAT suggest that tumor downstaging may facilitate parenchymal-sparing resections.

Postoperative complications were more closely associated with comorbidity and operative complexity than with NAT.

RESULTS

PATIENTS' CHARACTERISTICS

	Neoadjuvant treatment (N=301)	Upfront surgery (N=470)	p-value
Age, median (range)	66 (29-83)	68 (26-87)	<0.001
Sex, N (%)			
male	133 (44.2)	235 (50.0)	0.115
female	168 (55.8)	235 (50.0)	
BMI, mean±SD	26±5.1	26±5.3	0.473
CCI, mean±SD	3.7±1.5	4.7±1.6	<0.001
Histology, N (%)			
AdenoCa	197 (65.4)	289 (61.5)	0.267
SCC	83 (27.6)	148 (31.5)	0.247
other	21 (7.0)	33 (7.0)	0.981
Clinical stage, N (%)			
UICC IIA	20 (6.6)	129 (27.4)	<0.001
UICC IIB	78 (25.9)	209 (44.5)	<0.001
UICC IIIA	162 (53.8)	116 (24.7)	<0.001
UICC IIIB	36 (12.0)	14 (3.0)	<0.001
UICC IIIC	5 (1.7)	2 (0.4)	0.117

Table 1. Patients' characteristics: Patients receiving NAT were younger than those undergoing S, had fewer comorbidities, and more frequently presented with clinical stage III NSCLC.

EVOLUTION OF TREATMENT

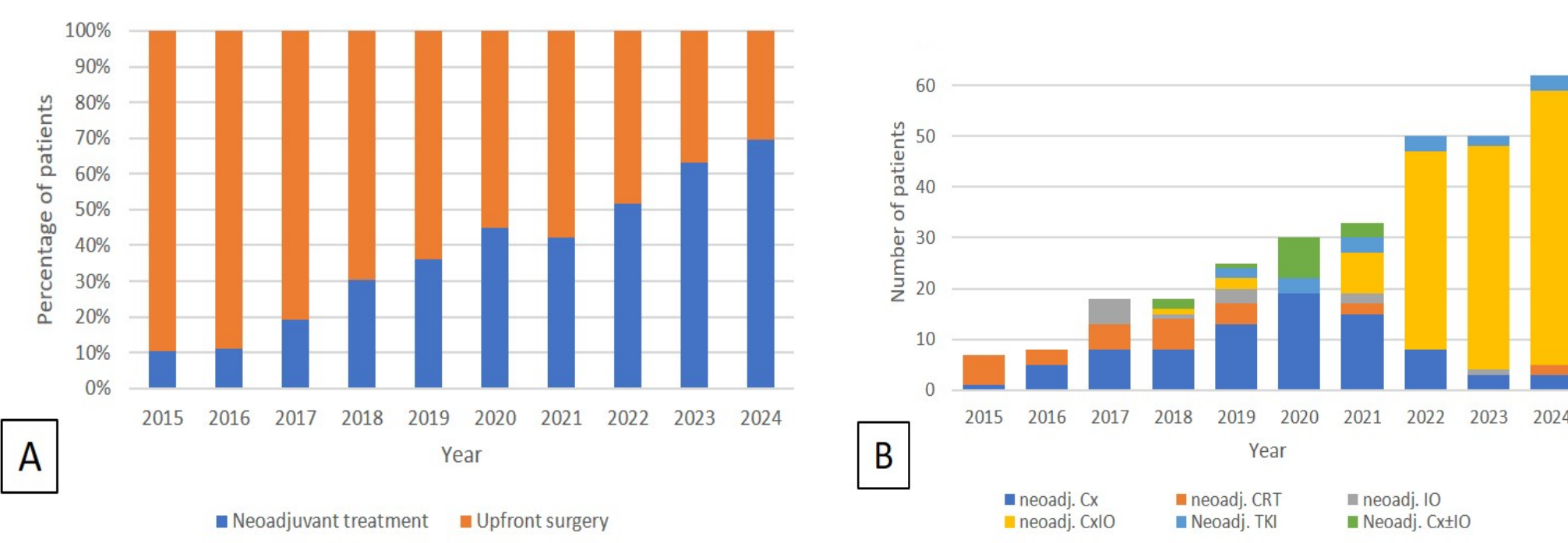


Figure 3. Evolution of treatment: The proportion of NAT increased from 10.4% in 2015 to 69.7% in 2024 (A). After regulatory approval in 2020, neoadjuvant CxIO replaced Cx as predominant modality. Administration of CRT, IO and TKI declined over time (B).

SURGICAL OUTCOME

	Neoadjuvant treatment (N=301)	Upfront surgery (N=470)	p-value
Duration of surgery, mean±SD (min)	174±85	162±71	0.102
Extent of resection, N (%)			
Standard lobectomy	151 (50.2)	293 (62.3)	0.001
Extended lobectomy	126 (41.9)	105 (22.3)	<0.001
Pneumonectomy	17 (5.6)	43 (9.1)	0.098
Other	7 (2.3)	29 (6.2)	0.014
Surgical approach, N (%)			<0.001
Minimally invasive	202 (67.1)	321 (49.1)	
Open	99 (32.9)	239 (50.9)	
IntraOP morbidity, N (%)	49 (16.3)	58 (12.3)	0.123
Conversion	29 (9.6)	36 (7.7)	0.336
postOP morbidity, N (%)	146 (48.5)	242 (51.5)	0.402
Minor (CDI-II)	101 (33.6)	169 (36.0)	0.892
Major (CD III-V)	45 (15.0)	73 (15.5)	0.827
LOS, mean±SD (days)	5.9±7.5	7.0±9.4	0.030
Readmission, N (%)	23 (7.6)	38 (8.1)	0.824
30-day mortality, N (%)	2 (0.7)	6 (1.3)	0.493
90-day mortality, N (%)	7 (2.3)	10 (2.1)	0.855

Table 2. Surgical outcome: After NAT, more patients underwent extended lobectomies. Pneumonectomy rate was numerically lower in NAT-patients. Complication rate was comparable in both cohorts.

DOWNSTAGING

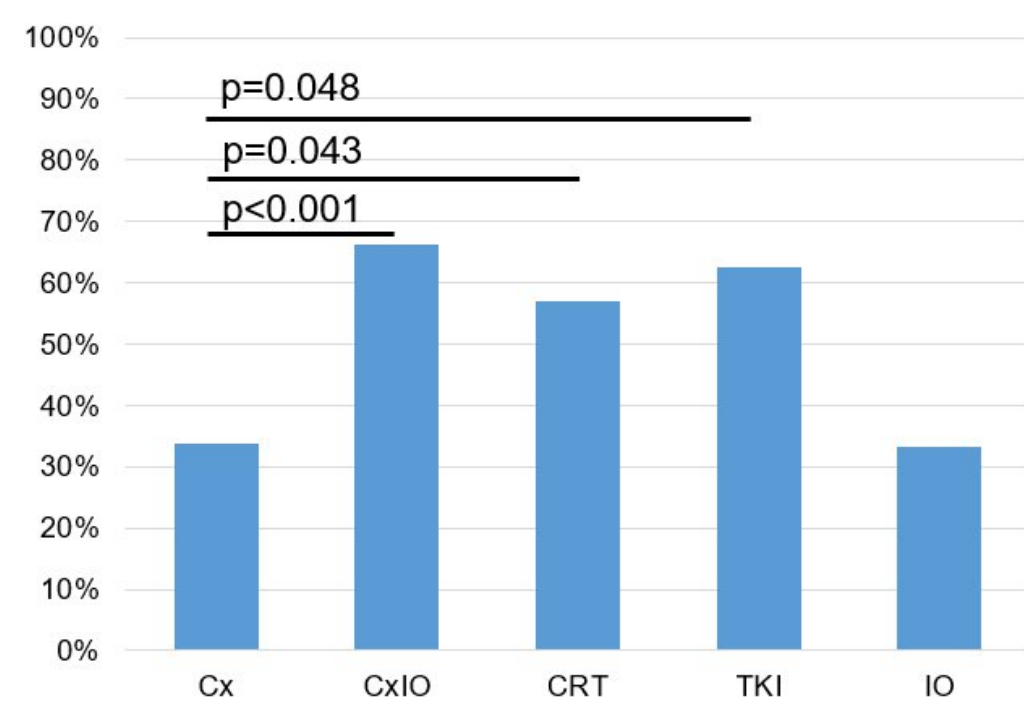


Figure 4. Tumor downstaging: Downstaging rates were significantly higher following CxIO, CRT, and TKI compared with Cx alone. pCR- and MPR-rates were consistent with downstaging results.

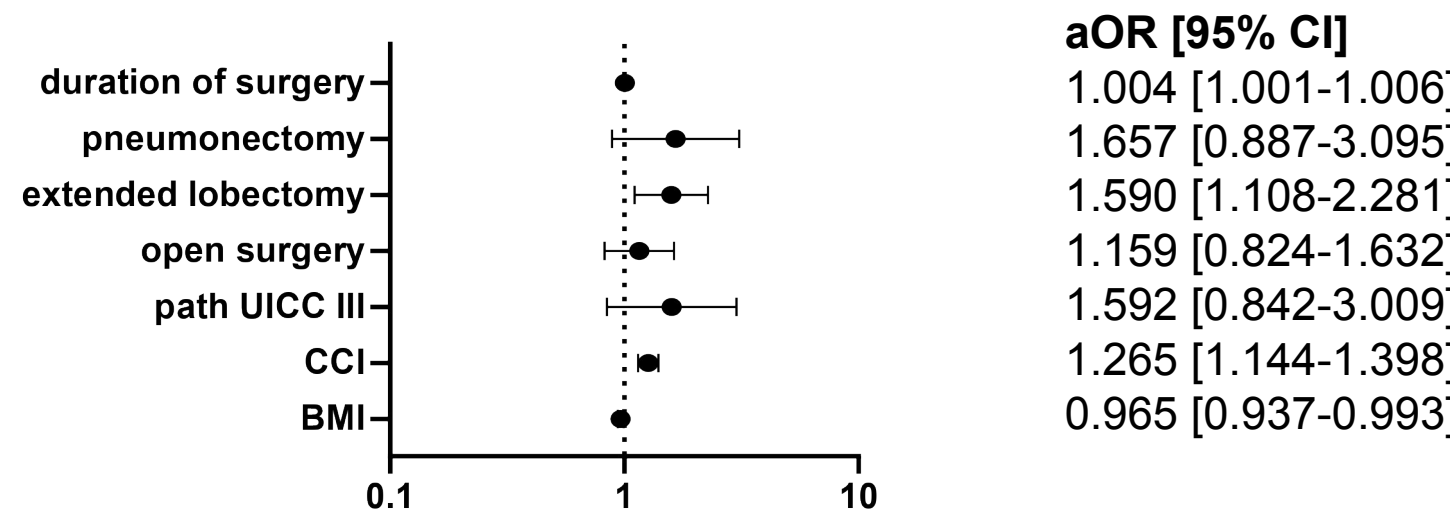


Figure 1. Multivariable regression for postoperative complications: Higher CCI, lower BMI, extended lobectomy, and longer operative duration were independently associated with postoperative complications.

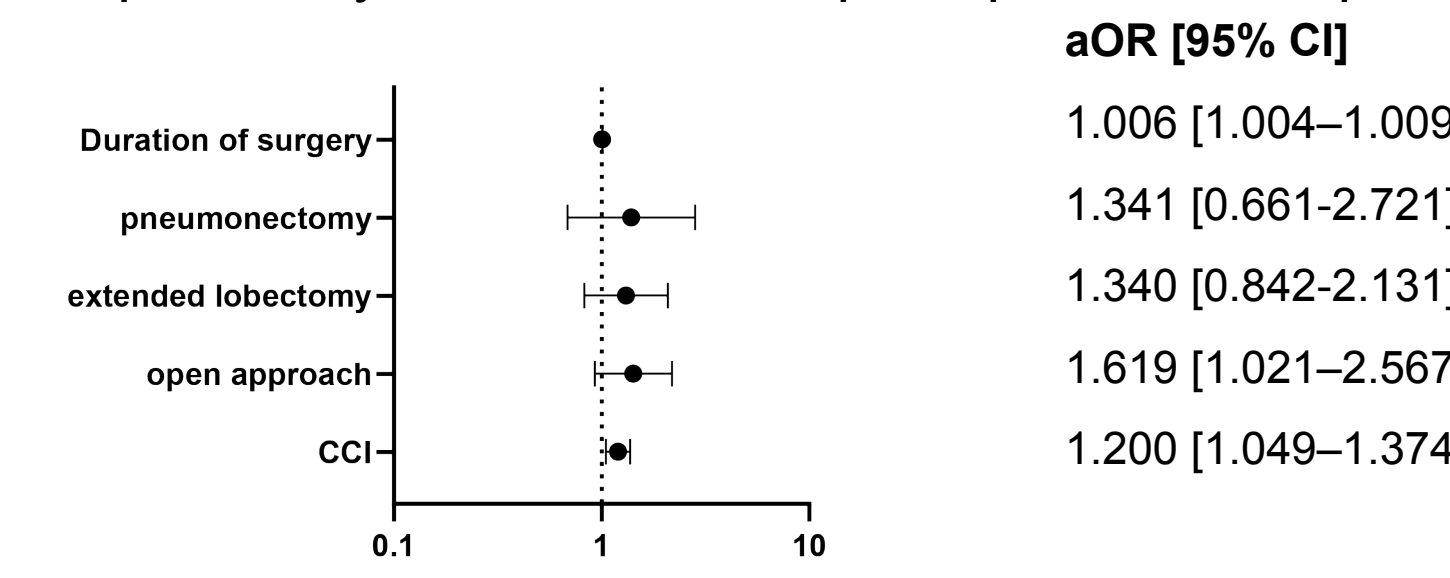


Figure 2. Multivariable regression for major complications: Higher CCI, open approach, and longer operative duration were independently associated with major postoperative complications.

OVERALL SURVIVAL

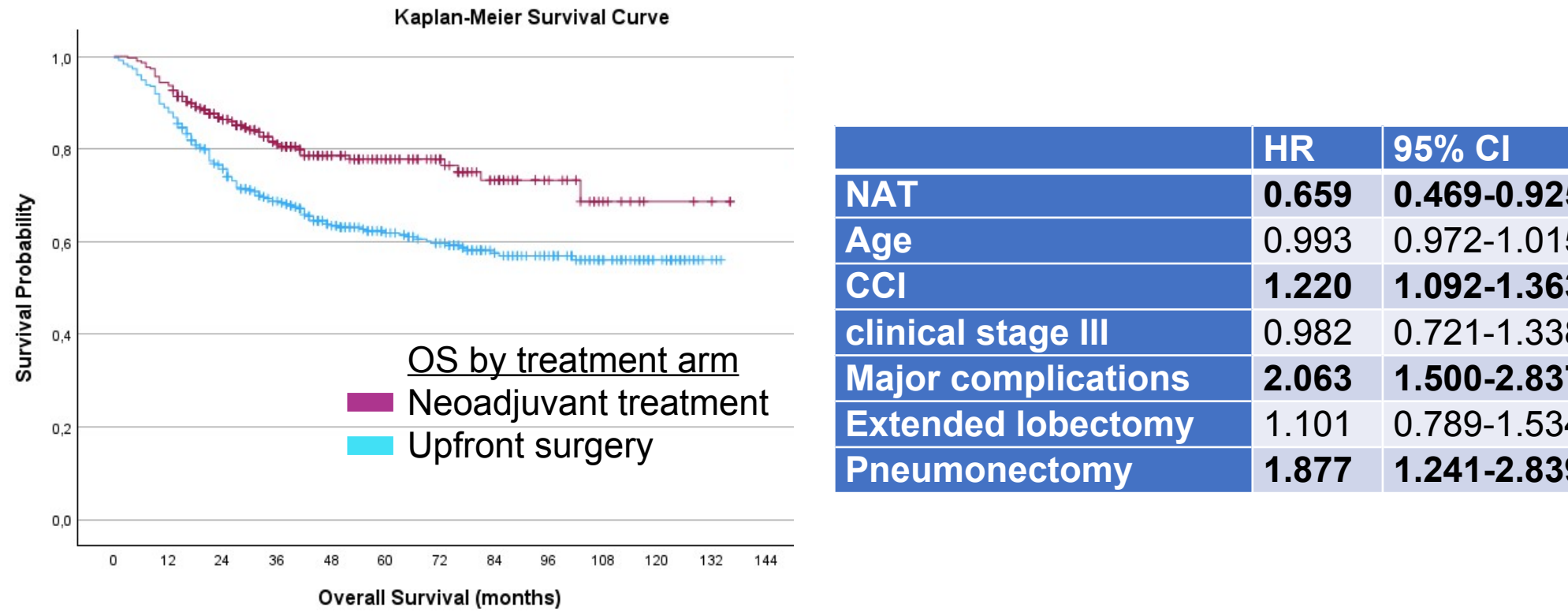


Figure 5. Survival analysis: Kaplan-Meier analysis showed superior OS in patients with NAT [106.514±3.586 months (NAT) vs 87.860±2.982 (S), p<0.001, log-rank]. On Cox regression, NAT remained associated with improved OS. Higher CCI, major complications and pneumonectomy were associated with worse OS.

Limitations:

- Retrospective single-center design: risk of selection bias and residual confounding
- Temporal heterogeneity: evolution of therapies, surgical techniques, and perioperative care over study period
- Incomplete follow-up: postoperative oncologic care often provided by external institutions, limiting data on adjuvant treatment and recurrence
- Limited follow-up for recently introduced neoadjuvant CxIO

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