

# Preoperative SUVmax Stratifies Prognosis in cStage IB NSCLC : High Uptake Mirrors the Prognosis of Stage II Disease

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## INTRODUCTION

### Background

- Perioperative treatment strategies have been increasingly adopted for pathologic stage II-III NSCLC, whereas their role in stage IB disease remains poorly defined.<sup>1-3</sup>
- Current guidelines recommend adjuvant therapy for stage IB patients only in the presence of specific high-risk histopathologic features identified after surgery.<sup>4</sup>
- However, these features do not fully capture the prognostic heterogeneity within stage IB disease.
- A potential complementary marker is preoperative SUVmax on <sup>18</sup>F-FDG PET-CT, which reflects tumor metabolic activity and has been associated with adverse pathologic features, recurrence, and survival.<sup>5-6</sup>
- To our knowledge, no study has directly compared oncologic outcomes between high SUVmax stage IB and stage II NSCLC using a stage-specific cutoff.

### Objective

To determine whether clinical stage IB NSCLC with high SUVmax has oncologic outcomes comparable to those of clinical stage II disease, potentially supporting similar perioperative treatment strategies.

## METHOD

### Study Design & Population

- This single-center retrospective study included patients with clinical tage IIB NSCLC (8<sup>th</sup> TNM) who underwent upfront curative-intent surgery between 2018 and 2023.
- A total of 931 patients were included in the final analysis. Patients with a previous cancer history, neoadjuvant treatment, or missing preoperative PET-CT SUVmax data or incomplete resection were excluded.

### Statistical analysis

- The prognostic SUVmax cutoff was determined within cStage IB using maximally selected log-rank statistics with adjustment for cut-point selection.
- Patients were classified as low uptake cStage IB, high-uptake cStage IB, cStage IIA, or cStage IIB.
- RFS and OS were evaluated using Kaplan-Meier analysis and multivariable Cox regression with prespecified clinical covariates.
- To compare high-SUVmax cStage IB with cStage II, multivariable Cox regression was performed with clinical stage II as the reference group, using a prespecified equivalence margin (HR 0.75-1.33).
- All statistical analyses were performed using R version 4.4, with a two-sided p-value of less than 0.05 considered statistically significant.

### Discussion & Conclusion

- Preoperative SUVmax identified a clinically relevant high-risk subgroup within cStage IB NSCLC.
- Clinical stage IB tumors with high-uptake on PET CT showed more frequent pathologic upstaging than low uptake tumors, including a higher incidence of pathologic nodal involvement.
- High preoperative SUVmax on PET CT identified a biologically high-risk cStage IB adenocarcinoma subgroup characterized by survival outcomes approaching those of cStage IIB disease.
- Prospective validation in larger cohort is warranted.

### Limitations

- Retrospective, single-center design with potential selection bias and residual confounding.
- Differences in PET scanners and acquisition protocols may affect the reproducibility and comparability of SUVmax measurements.

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## RESULTS

Figure1. Preoperative SUVmax by Clinical Stage and Histology

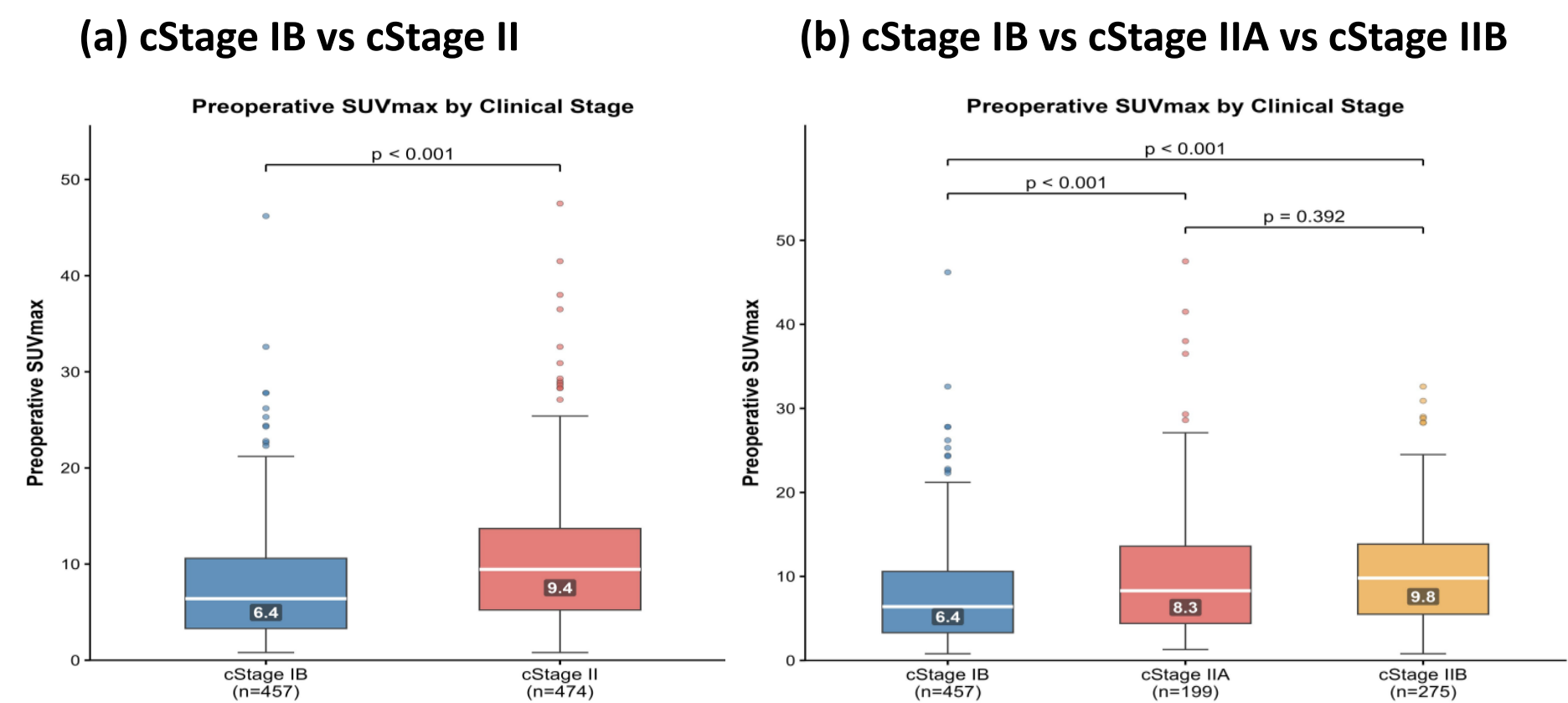


Figure3. Pathologic stage migration

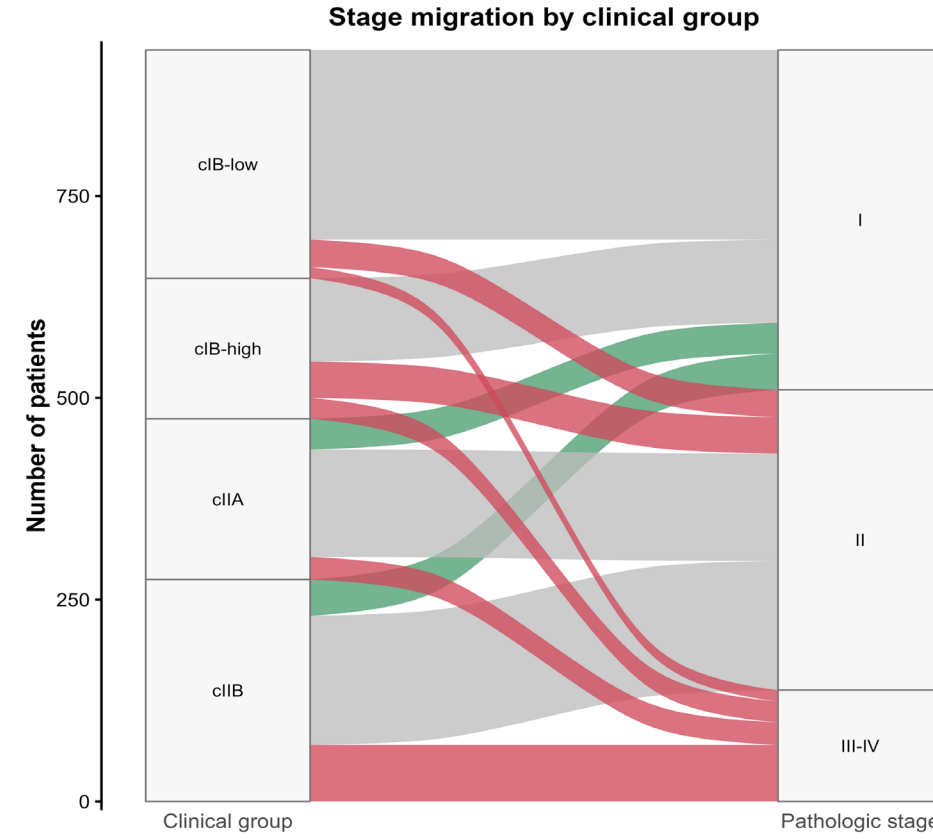
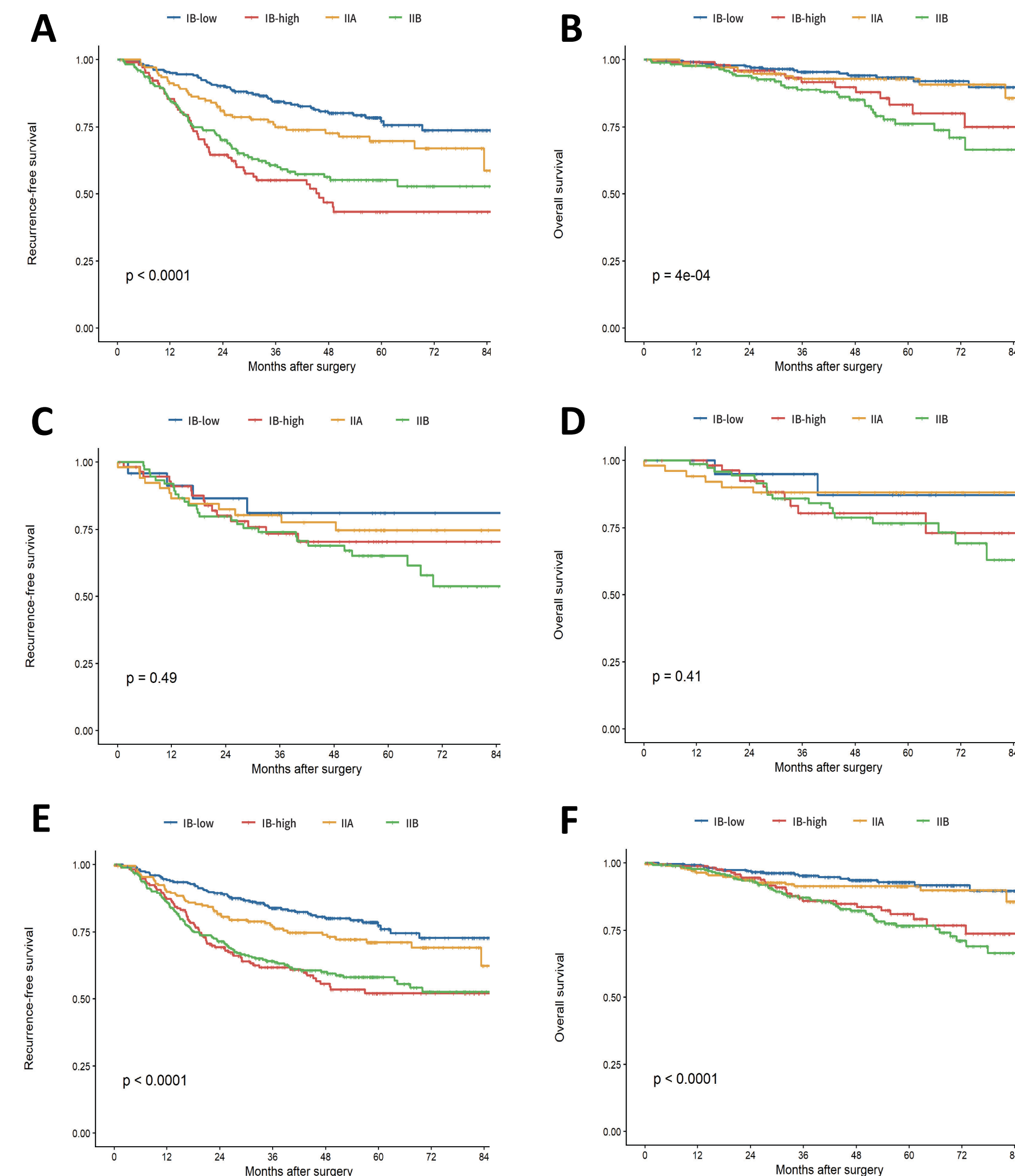


Figure4. Kaplan–Meier curves for recurrence-free survival (RFS) and overall survival (OS) according to clinical stage and SUVmax category.



Kaplan–Meier curves for recurrence-free survival (RFS) and overall survival (OS) according to clinical stage and SUVmax category. (A) RFS in the overall cohort; (B) OS in the overall cohort; (C) RFS in the adenocarcinoma subgroup; (D) OS in the adenocarcinoma subgroup; (E) RFS in the squamous cell carcinoma subgroup; and (F) OS in the squamous cell carcinoma subgroup.

Figure2. Determination of the Preoperative SUVmax Cutoff value by maximally log-rank statistics

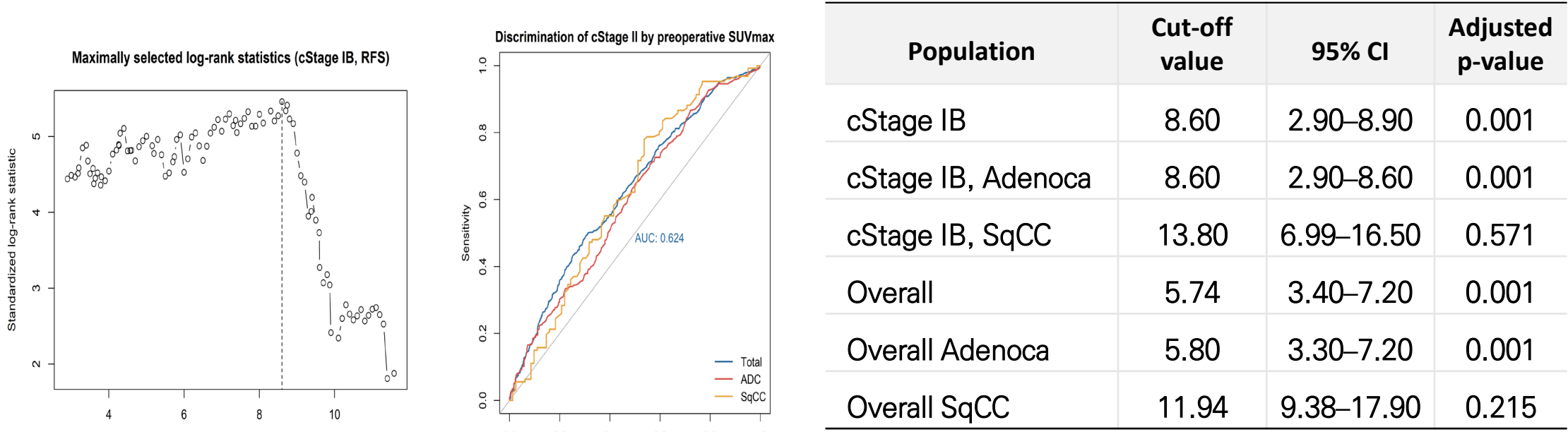


Table 1. Pathologic stage migration and nodal involvement in cStage IB NSCLC

| Variables                             | Low-uptake group (n=283) | High-uptake group (n=174) | P-value |
|---------------------------------------|--------------------------|---------------------------|---------|
| <b>Stage Migration, n (%)</b>         |                          |                           | 0.001   |
| Downstaging                           | 73 (25.8)                | 13 (7.5)                  |         |
| No Change                             | 162 (57.2)               | 90 (51.7)                 |         |
| Upstaging                             | 48 (17.0)                | 71 (40.8)                 | 0.001   |
| <b>Pathologic Nodal Status, n (%)</b> |                          |                           |         |
| pN1/N2                                | 17 (6.0)                 | 51 (29.5)                 |         |

Table 2. Five-year survival and adjusted HRs according to clinical stage and SUVmax

| Group                             | N          | 5year RFS (%) | adjusted HR (95% CI) | 5year OS (%) | adjusted HR (95% CI) |
|-----------------------------------|------------|---------------|----------------------|--------------|----------------------|
| <b>In Total Cohort</b>            | <b>931</b> |               |                      |              |                      |
| Low uptake cStage IB              | 283        | 77.3          | 1.00 (Ref.)          | 92.9         | 1.00 (Ref.)          |
| High uptake cStage IB             | 174        | 52.1          | 2.89 (2.01–4.15)     | 80.9         | 2.27 (1.25–4.13)     |
| cStage IIA                        | 199        | 71.1          | 1.55 (1.05–2.28)     | 91.4         | 1.16 (0.61–2.21)     |
| cStage IIB                        | 275        | 58.1          | 2.56 (1.83–3.59)     | 76.6         | 2.60 (1.52–4.45)     |
| <b>In Adenocarcinoma group</b>    | <b>661</b> |               |                      |              |                      |
| Low uptake cStage IB              | 244        | 77.1          | 1.00 (Ref.)          | 93.4         | 1.00 (Ref.)          |
| High uptake cStage IB             | 103        | 43.4          | 3.40 (2.27–5.09)     | 83.2         | 2.08 (1.01–4.31)     |
| cStage IIA                        | 139        | 69.7          | 1.55 (1.01–2.39)     | 92.9         | 1.12 (0.52–2.42)     |
| cStage IIB                        | 175        | 55.2          | 2.63 (1.81–3.82)     | 76.1         | 2.88 (1.58–5.27)     |
| <b>In Squamous cell ca. group</b> | <b>209</b> |               |                      |              |                      |
| Low uptake cStage IB              | 24         | 81.1          | 1.00 (Ref.)          | 87.1         | 1.00 (Ref.)          |
| High uptake cStage IB             | 58         | 70.4          | 1.22 (0.39–3.83)     | 80.4         | 1.49 (0.31–7.13)     |
| cStage IIA                        | 52         | 74.7          | 1.06 (0.33–3.39)     | 88.0         | 0.93 (0.18–4.78)     |
| cStage IIB                        | 75         | 65.1          | 1.48 (0.50–4.37)     | 76.6         | 1.63 (0.36–7.37)     |

The RFS was adjusted for age, sex, BMI, smoking status, ECOG, histologic subtype, extent of resection, and number of resected lymph nodes. The OS was adjusted for age, sex, ECOG, and histologic subtype. The median follow-up duration was 53.5 months (IQR, 33.0–68.7 months). For adenocarcinoma, the RFS was adjusted for age, sex, BMI, smoking status, ECOG, extent of resection, and number of lymph nodes removed, whereas the OS was adjusted for age, sex, and ECOG. For squamous cell carcinoma, owing to the limited number of events and complete separation, the RFS was adjusted for age, ECOG, and extent of resection, whereas the OS was adjusted for age only.

Table 3. Post hoc pairwise log-rank tests for RFS and OS with Benjamini-Hochberg adjustment

| In Total Cohort                               | Pairwise log-rank<br>p-value for RFS | Pairwise log-rank<br>p-value for OS |
|-----------------------------------------------|--------------------------------------|-------------------------------------|
| High uptake cStage IB vs Low uptake cStage IB | 0.001                                | 0.003                               |
| High uptake cStage IB vs cStage IIA           | 0.002                                | 0.049                               |
| High uptake cStage IB vs cStage IIB           | 0.583                                | 0.464                               |
| cStage IIA vs cStage IIB                      | 0.003                                | 0.003                               |

RFS, recurrence-free survival; OS, overall survival; HR, hazard ratio. The RFS model was adjusted for age, sex, BMI, smoking status, ECOG, histologic subtype, extent of resection, and number of lymph nodes removed (291 events; n=928). Owing to the limited number of deaths (120 events), the OS was adjusted for age, sex, ECOG, and histologic subtype. The median follow-up duration was 53.5 months (IQR, 33.0–68.7 months).