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Original Article

Inflammatory and nutritional biomarker changes at postoperative days 25-34 after uniportal minimally invasive anatomical lung resection for non-small cell lung cancer

Mehlika Iscan*, Omer Yavuz, Ali Yeginsu

Department of Thoracic Surgery, Başakşehir Çam and Sakura City Hospital, İstanbul, Türkiye

ABSTRACT

Background: Blood-based inflammatory and nutritional biomarkers are increasingly used in non-small cell lung cancer (NSCLC), but their early postoperative behavior after uniportal minimally invasive anatomical lung resection remains unclear. This study evaluated perioperative changes in selected indices between the preoperative period and the standardized early postoperative outpatient assessment.

Materials and Methods: This retrospective observational study included 48 consecutive patients with histopathologically confirmed NSCLC who underwent uniportal minimally invasive anatomical lung resection between January 2024 and December 2025. Patients who underwent completion resection, had non-NSCLC histology, or lacked paired laboratory data were excluded. Preoperative laboratory values were compared with those obtained at the postoperative outpatient assessment between postoperative days 25 and 34. The primary endpoint was the change in hemoglobin, albumin, lymphocyte, and platelet score (HALP). Secondary endpoints were changes in neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio, prognostic nutritional index, C-reactive protein-to-albumin ratio, and systemic immune-inflammation index.

Results: The cohort included 37 uniportal video-assisted thoracic surgery and 11 uniportal robotic-assisted thoracic surgery patients. HALP decreased significantly, whereas platelet-to-lymphocyte ratio and C-reactive protein-to-albumin ratio increased significantly. Hemoglobin and hematocrit decreased, while platelet count and C-reactive protein increased. No significant changes were observed in neutrophil-to-lymphocyte ratio, prognostic nutritional index, systemic immune-inflammation index, white blood cell count, neutrophil count, lymphocyte count, creatinine, or albumin.

Conclusions: The standardized postoperative outpatient assessment after uniportal minimally invasive anatomical lung resection for NSCLC suggested a selective biomarker pattern that may reflect a non-uniform early postoperative recovery process after uniportal anatomical lung resection.

Keywords: carcinoma, non-small cell lung, biomarkers, thoracic surgery, video-assisted, robotic surgical procedures, hemoglobin, albumin, lymphocyte, platelet score

Corresponding Author*: Mehlika Iscan, MD. Department of Thoracic Surgery, Çam and Sakura City Hospital, Department of Thoracic Surgery, İstanbul, Türkiye.
Email: mehlikaiscan@gmail.com Phone: +902129096000
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Introduction

Non-small cell lung cancer (NSCLC) remains the predominant histological subtype of lung cancer, and surgical resection continues to be the main curative treatment for patients with resectable disease. In recent years, increasing attention has been directed toward blood-based inflammatory and nutritional biomarkers because they can be obtained from routine laboratory tests at no additional cost and may reflect the interaction between tumor biology, host immunity, systemic inflammation, and nutritional status. In resected NSCLC, markers such as the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), prognostic nutritional index (PNI), and other composite scores have been widely investigated, mostly in relation to postoperative complications or long-term oncologic outcomes [1,2].

Among these markers, several indices are of particular interest because they capture complementary biological domains. The hemoglobin, albumin, lymphocyte, and platelet (HALP) score integrates anemia, nutritional status, immune balance, and platelet-related inflammatory burden into a single composite measure [3]. The C-reactive protein-to-albumin ratio (CAR) reflects a CRP-dominant inflammatory and nutritional profile, whereas the systemic immune-inflammation index (SII) and PLR provide additional information on platelet-linked inflammatory activity [2,4,5]. These markers have been associated with prognosis in NSCLC and are increasingly viewed as practical host-related biomarkers in thoracic oncology [1].

However, most available studies have focused on preoperative values or long-term prognostic stratification rather than short-term postoperative biomarker behavior. This distinction is important because perioperative systemic changes after lung resection are influenced not only by cancer-related biology but also by surgical trauma and the subsequent recovery process. Previous work has shown that minimally invasive major lung resection is associated with a more attenuated inflammatory and immune disturbance than open surgery [6]. Recent reviews have also emphasized that perioperative systemic inflammation may itself be clinically relevant in lung cancer surgery [7]. Nevertheless, the early postoperative pattern of routinely available inflammatory and nutritional indices after uniportal minimally invasive anatomical lung resection remains insufficiently characterized, particularly at a standardized outpatient follow-up time point.

The present study was therefore designed to evaluate perioperative changes in inflammatory and nutritional indices between the preoperative period and the standardized early postoperative outpatient assessment in patients undergoing uniportal minimally invasive anatomical lung resection for NSCLC. HALP was assessed as the primary endpoint. Changes in NLR, PLR, PNI, CAR, and SII were examined as secondary indices to characterize the early postoperative biological recovery pattern after uniportal anatomical resection. We hypothesized that the standardized early postoperative follow-up after uniportal anatomical lung resection would demonstrate a selective exploratory biomarker recovery pattern, with more pronounced changes in composite and CRP/platelet-linked indices than in broader leukocyte- or albumin-based markers.

Materials and Methods

Study design and patient selection

This retrospective observational study included consecutive patients who underwent uniportal minimally invasive anatomical lung resection for NSCLC at our clinic between January 2024 and December 2025. The institutional database was reviewed to identify eligible patients.

Patients were included if they met all of the following criteria: (1) histopathologically confirmed NSCLC, including adenocarcinoma, squamous cell carcinoma, or adenosquamous carcinoma; (2) uniportal minimally invasive anatomical lung resection performed by either uniportal video-assisted thoracic surgery (UVATS) or uniportal robotic-assisted thoracic surgery (URATS); (3) anatomical resection in the form of lobectomy, segmentectomy, and pneumonectomy; and (4) availability of both preoperative and early postoperative laboratory measurements required for calculation of inflammatory and nutritional indices.

Patients were excluded if they underwent completion resection, had a non-NSCLC histology, or had missing paired laboratory data. After applying the eligibility criteria, 48 patients constituted the final study cohort. To reduce potential selection and information bias, we in-

cluded consecutive eligible patients from a single institutional database and restricted the analysis to patients with paired laboratory measurements obtained within a prespecified postoperative follow-up window.

Data collection

Demographic, clinical, operative, pathological, and laboratory data were obtained retrospectively from electronic medical records and the institutional surgical database. The following baseline variables were recorded: age, sex, body mass index, smoking history, chronic obstructive pulmonary disease, diabetes mellitus, hypertension, and forced expiratory volume in 1 second (FEV_1).

Operative and pathological variables included surgical approach (UVATS or URATS), type of resection (lobectomy, segmentectomy, and pneumonectomy), tumor size, pathological T category, pathological stage, mediastinal lymph node dissection status, and total number of harvested lymph nodes. Postoperative descriptive variables included chest tube duration, length of hospital stay, in-hospital complications, and 30-day adverse events.

Laboratory assessment and follow-up window

Preoperative laboratory values were obtained from routine blood tests performed before surgery. Early postoperative laboratory values were collected from the postoperative outpatient assessment. To ensure a relatively homogeneous follow-up interval, only patients with postoperative laboratory assessment performed between postoperative days 25 and 34 were included in the final analysis. This interval was selected to reflect the standardized outpatient postoperative review in our practice and to approximate the 1-month postoperative time point used in prior NSCLC studies evaluating postoperative immunonutritional status [8,9]. It also captures an early recovery phase in which final pathology and postoperative oncologic planning are usually available while adjuvant systemic treatment has often not yet started.

The following laboratory parameters were recorded for both the preoperative and postoperative time points: white blood cell count, hemoglobin, hematocrit, platelet count, neutrophil count, lymphocyte count, C-reactive protein, serum creatinine, and albumin.

Inflammatory and nutritional indices

The following inflammatory and nutritional indices were calculated at both time points:

- Neutrophil-to-lymphocyte ratio (NLR): neutrophil count / lymphocyte count
- Platelet-to-lymphocyte ratio (PLR): platelet count / lymphocyte count
- Prognostic nutritional index (PNI): albumin (g/L) + 5 × lymphocyte count (10^9/L)
- C-reactive protein-to-albumin ratio (CAR): C-reactive protein / albumin
- Systemic immune-inflammation index (SII): platelet count × neutrophil count / lymphocyte count
- Hemoglobin, albumin, lymphocyte, and platelet (HALP) score: 10 × hemoglobin (g/dL) × albumin (g/L) × lymphocyte count (10^9/L) / platelet count (10^9/L)

For each index, change from the preoperative assessment to the standardized early postoperative follow-up was defined as the postoperative value minus the preoperative value in order to quantify the direction and magnitude of within-patient change over time.

Study endpoints

The primary aim of the study was to evaluate perioperative changes in inflammatory and nutritional indices between the preoperative period and the early postoperative follow-up after uniportal minimally invasive anatomical lung resection for NSCLC.

The primary endpoint was the change in HALP score between the preoperative and postoperative assessments. Secondary endpoints included changes in NLR, PLR, PNI, CAR, and SII. The study was designed as a descriptive and exploratory analysis intended to characterize early postoperative biomarker behavior and to generate hypotheses for future prospective studies, rather than to establish clinically actionable thresholds.

The study protocol was approved by the Institutional Review Board (Approval Date: 24.12.2025, Approval No: KAEK/24.12.2025.396). Written informed consent was obtained from all patients prior to surgery. The study

was conducted in accordance with the ethical principles of the Declaration of Helsinki and its later amendments.

Statistical Analysis

All statistical analyses were performed using IBM SPSS Statistics for Windows, Version 29.0 (IBM Corp., Armonk, NY, USA). Data completeness was reviewed before analysis. Because all variables required for the predefined analyses were available in the final study cohort, a complete-case analysis was performed.

The distribution of continuous variables was assessed using visual inspection of histograms and the Shapiro–Wilk test. As most continuous variables, including the derived inflammatory and nutritional indices, did not follow a normal distribution, continuous data were expressed as median and interquartile range (IQR), whereas categorical variables were summarized as number and percentage.

The primary analysis of the study was based on within-patient paired comparisons between preoperative and early postoperative measurements. Changes in laboratory parameters and derived inflammatory/nutritional indices between the two time points were evaluated using the Wilcoxon signed-rank test. For paired comparisons, effect size for the Wilcoxon signed-rank test was expressed as r ($Z/\sqrt{N}$), and the magnitude of change was additionally summarized using the Hodges–Lehmann estimate of the paired difference with 95% confidence intervals. For each index, perioperative change was defined as the postoperative value minus the preoperative value.

The prespecified primary endpoint was the change in HALP score. Secondary endpoints were changes in NLR, PLR, PNI, CAR, and SII. Because the primary aim of the study was to characterize the shared early postoperative biomarker pattern after uniportal minimally invasive anatomical lung resection, operative approach was not used as a primary grouping variable for inferential analysis. Formal subgroup comparison between UVATS and URATS was not planned because of the small size of the URATS subgroup and the exploratory design of the study. Accordingly, operative approach was treated as a descriptive cohort characteristic. It was not used as a primary grouping variable for inferential analysis in order to avoid overlap with the separate perioperative outcomes study comparing URATS and UVATS.

Continuous baseline and postoperative descriptive variables were reported for the overall cohort using median (IQR), and categorical descriptive variables were reported as number (%). No predictive modeling, cutoff analysis, receiver operating characteristic analysis, or multivariable regression was performed, given the exploratory nature of the study and the limited sample size.

All tests were two-sided, and a p value of <0.05 was considered statistically significant. Because HALP change was defined a priori as the primary endpoint, analyses of the remaining indices were considered secondary and exploratory and were interpreted accordingly. No formal adjustment for multiple comparisons was applied, because HALP was prespecified as the single primary endpoint and the remaining biomarker analyses were exploratory in nature. Therefore, p values for secondary endpoints should be interpreted cautiously, with particular awareness of the increased risk of type I error.

Results

Study cohort and baseline characteristics

Among 57 preliminarily screened patients in the NSCLC biomarker cohort, 2 who underwent completion resection and 7 with missing laboratory data were excluded. The final analysis included 48 patients (Figure 1). Median age was 68.0 (IQR, 62.0–74.0) years, and 39 patients (81.2%) were male. The surgical approach was UVATS in 37 patients (77.1%) and URATS in 11 patients (22.9%). Lobectomy was performed in 35 patients (72.9%), segmentectomy in 11 patients (22.9%), and pneumonectomy in 2 patients (4.2%). Histopathology showed adenocarcinoma in 36 patients (75.0%), squamous cell carcinoma in 6 patients (12.5%), and adenosquamous carcinoma in 6 patients (12.5%). The early postoperative laboratory assessment was obtained at a median postoperative day of 29.5 (IQR, 27.0–31.0). Baseline and operative characteristics are summarized in Table 1.

Changes in routine laboratory parameters

Routine laboratory comparisons are presented in Table 2. Hemoglobin decreased from 13.85 (IQR, 11.85-

14.47) to 12.35 (IQR, 11.10-14.22) ($p < 0.001$), and hematocrit decreased from 41.25 (IQR, 36.25-43.90) to 38.05 (IQR, 33.98-41.95) ($p < 0.001$). Platelet count increased from 244.00 (IQR, 197.50-287.25) to 260.00 (IQR, 216.75-302.00) ($p = 0.038$), and C-reactive protein increased from 2.95 (IQR, 1.70-7.12) to 5.30 (IQR, 3.48–21.57) ($p = 0.005$). No significant differences were observed in white blood cell count, neutrophil count, lymphocyte count, creatinine, or albumin (all $p > 0.05$).

Changes in inflammatory and nutritional indices

Changes in inflammatory and nutritional indices are shown in Table 3, which also provides effect size estimates and Hodges-Lehmann confidence intervals for paired differences. The prespecified primary endpoint, HALP score, showed a significant decline from 44.14 (IQR, 34.48-65.76) preoperatively to 38.95 (IQR, 24.52-48.29) at early follow-up (median delta, -7.36 [IQR, -21.02 to 3.34]; $p = 0.010$; Figure 2). Figure 2 illustrates the paired within-patient decline in HALP score between the preoperative assessment and the standardized early postoperative follow-up. PLR increased significantly from 125.23 (IQR, 94.50-155.95) to 135.86 (IQR, 98.25-190.04) (median delta, 14.27 [IQR, -16.76 to 51.32]; $p = 0.047$; Figure 3), and Figure 3 demonstrates the overall upward shift in PLR values during the same interval. CAR increased from 0.067 (IQR, 0.040-0.157) to 0.121 (IQR, 0.086–0.521) (median delta, 0.039 [IQR, -0.004 to 0.262]; $p = 0.005$; Figure 4), while Figure 4 shows the postoperative increase in CAR across paired observations. In contrast, changes in NLR, PNI, and SII were not statistically significant ($p = 0.357$, $p = 0.134$, and $p = 0.065$, respectively).

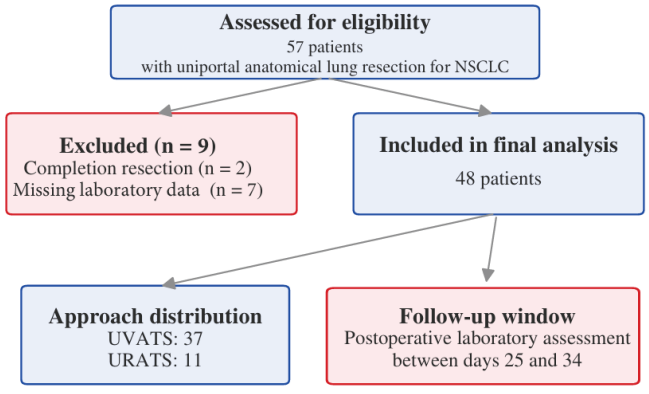


Figure 1. Study flow diagram.

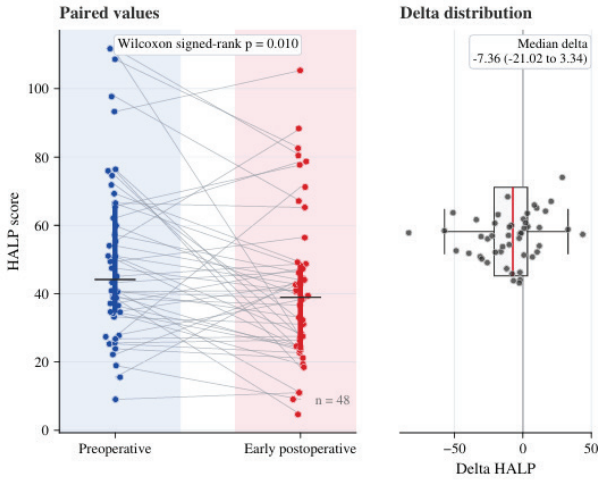


Figure 2. Paired change in HALP score between the preoperative period and the standardized postoperative outpatient assessment. Lower postoperative HALP values may reflect a less favorable early immunonutritional recovery profile.

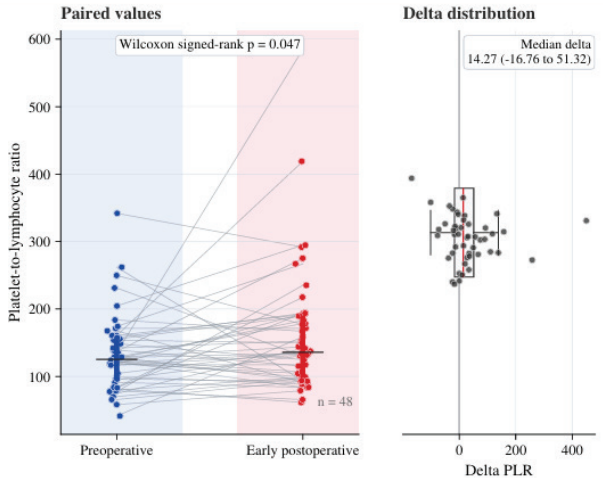


Figure 3. Paired change in platelet-to-lymphocyte ratio between the preoperative period and the standardized postoperative outpatient assessment. Higher postoperative PLR values may reflect greater platelet-predominant inflammatory activity during early recovery.

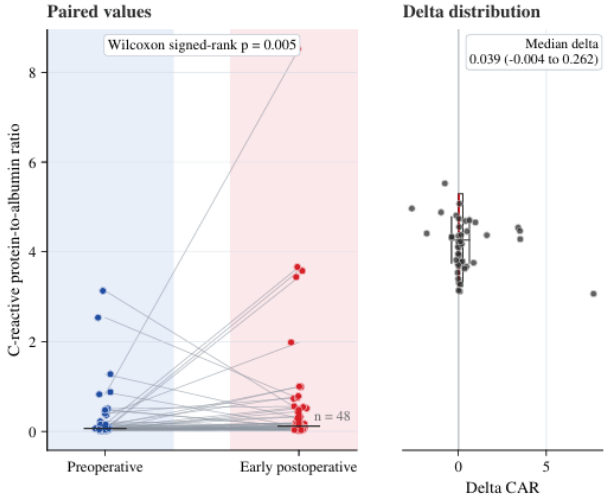


Figure 4. Paired change in C-reactive protein-to-albumin ratio between the preoperative period and the standardized postoperative outpatient assessment. Higher postoperative CAR values may reflect greater CRP-dominant inflammatory burden during early recovery.

Table 1. Baseline, operative, and pathological characteristics of the overall cohort.	
Variable	Overall cohort (n=48)
Demographic and clinical characteristics	
Age, years	68.0 (62.0-74.0)
Male sex	39 (81.2)
Body mass index, kg/m^2	26.6 (24.7-28.7)
Smoking status	
Never smoker	6 (12.5)
Current smoker	23 (47.9)
Former smoker	19 (39.6)
Pack-years	45.0 (32.2-62.5)
Chronic obstructive pulmonary disease	20 (41.7)
Diabetes mellitus	15 (31.2)
Hypertension	33 (68.8)
Forced expiratory volume in 1 second, % predicted	91.0 (78.0-104.0)
Operative and pathological characteristics	
Surgical approach	
Uniportal video-assisted thoracic surgery	37 (77.1)
Uniportal robotic-assisted thoracic surgery	11 (22.9)
Type of resection	
Lobectomy	35 (72.9)
Segmentectomy	11 (22.9)
Pneumonectomy	2 (4.2)
Tumor size on computed tomography, mm	25.5 (15.0-38.5)
Histopathology	
Adenocarcinoma	36 (75.0)
Squamous cell carcinoma	6 (12.5)
Adenosquamous carcinoma	6 (12.5)
Pathological T category	
Tis	1 (2.1)
T1	16 (33.3)
T2	22 (45.8)
T3	8 (16.7)
T4	1 (2.1)
Pathological stage	
Stage I	29 (60.4)
Stage II	16 (33.3)
Stage III	3 (6.2)
Harvested lymph nodes, total number	15.5 (10.0-22.0)
Postoperative descriptive characteristics	
Chest tube duration, days	2.0 (2.0-4.0)
Length of hospital stay, days	3.0 (2.0-5.0)
In-hospital complications	10 (20.8)
30-day adverse events	1 (2.1)
Postoperative laboratory assessment day	29.5 (27.0-31.0)

Table 2. Preoperative and early postoperative routine laboratory parameters.			
Parameter	Preoperative, median (IQR)	Early postoperative, median (IQR)	p value
White blood cell count, $\times 10^9$/L	7.790 (6.697-8.875)	7.960 (7.080-9.227)	0.369
Hemoglobin, g/dL	13.85 (11.85-14.47)	12.35 (11.10-14.22)	<0.001
Hematocrit, %	41.25 (36.25-43.90)	38.05 (33.98-41.95)	<0.001
Platelet count, $\times 10^9$/L	244.00 (197.50-287.25)	260.00 (216.75-302.00)	0.038
Neutrophil count, $\times 10^9$/L	4.770 (4.082-6.080)	4.985 (4.098-5.935)	0.988
Lymphocyte count, $\times 10^9$/L	1.965 (1.555-2.355)	1.910 (1.478-2.552)	0.562
C-reactive protein, mg/L	2.95 (1.70-7.12)	5.30 (3.48-21.57)	0.005
Creatinine, mg/dL	0.930 (0.835-1.120)	0.855 (0.808-1.005)	0.073
Albumin, g/L	43.00 (38.75-45.00)	42.00 (38.75-44.00)	0.181

Table 3. Preoperative and early postoperative inflammatory and nutritional indices.						
Index	Preoperative, median (IQR)	Early postoperative, median (IQR)	Delta (post - pre), median (IQR)	p	Effect size (r)	Hodges–Lehmann estimate (95% CI)
HALP score	44.14 (34.48–65.76)	38.95 (24.52–48.29)	-7.36 (-21.02 to 3.34)	0.010	0.367	-7.99 (-14.61 to -1.98)
Neutrophil-to-lymphocyte ratio	2.60 (1.96–3.67)	2.52 (1.63–4.08)	0.07 (-0.60 to 1.16)	0.357	0.135	0.21 (-0.19 to 0.69)
Platelet-to-lymphocyte ratio	125.23 (94.50–155.95)	135.86 (98.25–190.04)	14.27 (-16.76 to 51.32)	0.047	0.287	16.69 (0.20 to 38.46)
Prognostic nutritional index	51.98 (48.61–56.04)	51.62 (47.24–55.58)	-1.73 (-4.95 to 2.49)	0.134	0.216	-1.37 (-2.93 to 0.37)
C-reactive protein-to-albumin ratio	0.067 (0.040–0.157)	0.121 (0.086–0.521)	0.039 (-0.004 to 0.262)	0.005	0.401	0.07 (0.02 to 0.24)
Systemic immune inflammation index	584.35 (469.45–749.67)	725.13 (425.89–1117.80)	95.58 (-131.40 to 440.73)	0.065	0.266	126.94 (-11.46 to 279.68)
Data are presented as median (interquartile range). P values were obtained using the Wilcoxon signed-rank test. Effect size was expressed as r (Z/√N). The magnitude of paired change was additionally summarized using the Hodges–Lehmann estimate with 95% confidence intervals.						

Discussion

In this retrospective paired-cohort study, we found that the standardized postoperative outpatient assessment after uniportal minimally invasive anatomical lung resection for NSCLC was characterized by a biomarker pattern that appeared selective rather than global. The most relevant findings were a significant reduction in HALP score and significant increases in PLR and CAR, accompanied by lower hemoglobin and hematocrit values and higher platelet and CRP levels. In contrast, NLR, PNI, SII, total white blood cell count, neutrophil count, lymphocyte count, creatinine, and albumin did not change significantly. Overall, this pattern suggests that by postoperative days 25-34, the residual biological signal may be less consistent with a generalized leukocyte-driven inflammatory response. Instead, it appears more compatible with a selective profile marked by persistent CRP- and platelet-related activity together with incomplete hematologic recovery. This interpretation is consistent with the broader NSCLC literature showing that blood-based inflammatory and nutritional biomarkers are clinically relevant in resected disease, while perioperative systemic changes after lung surgery reflect both surgical trauma and subsequent biological recovery [1,7].

An important strength of the present study is that the evaluated biomarker panel was not assembled in an arbitrary fashion. Instead, the selected indices were predefined because they represent complementary biological domains derived from routine perioperative blood tests. HALP was chosen as the primary endpoint because it integrates anemia, nutritional status, immune balance, and platelet-related inflammatory burden into a single composite marker [3]. CAR was included as a CRP-dominant inflammation/nutrition index, whereas PLR and SII were used to reflect platelet-linked inflammatory activity [2,4,5]. NLR and PNI were retained as supportive secondary indices of immune balance and immunonutritional reserve. This selection strategy is aligned with current reviews of resected NSCLC, in which blood-based biomarkers are considered attractive

because they are simple, inexpensive, and widely available, even though most previous studies have primarily focused on baseline or prognostic value rather than short-term postoperative kinetics [1].

Among the evaluated markers, the decrease in HALP appears to be the most informative finding. HALP is driven upward by hemoglobin, albumin, and lymphocyte count and downward by platelet count. In our cohort, HALP decreased in parallel with significant reductions in hemoglobin and hematocrit and a concomitant rise in platelet count, whereas albumin and lymphocyte count remained relatively stable. This suggests that the early postoperative decline in HALP was mainly related to incomplete hematologic recovery and platelet-mediated inflammatory activity rather than to overt nutritional deterioration. This distinction is important, because HALP has mainly been studied as a prognostic marker in NSCLC, whereas our data indicate that it may also serve as a sensitive composite marker of short-term perioperative recovery after uniportal anatomical lung resection [3].

At the same time, the added value of these composite indices should be interpreted critically. The postoperative decrease in hemoglobin and the increases in CRP and platelet count observed in our cohort are expected findings after lung resection and do not, by themselves, establish the superiority of HALP, PLR, or CAR over their individual components. Rather, their potential value lies in summarizing multiple inflammatory and nutritional domains into a more integrated postoperative recovery signal. This interpretation is supported by the broader NSCLC biomarker literature and by thoracic surgical data on postoperative thrombocytosis after minimally invasive lung resection [1,10].

The increases in PLR and CAR support the same biological interpretation. In the case of CAR, the signal seems largely CRP-driven, as CRP increased significantly while albumin remained relatively stable. In the case of PLR, the increase is most plausibly explained by postoperative platelet elevation in the setting of relatively unchanged lymphocyte values. This pattern is clinically coherent, as CRP- and platelet-based indices may remain abnormal even when broader leukocyte-based measures are less disturbed. The relevance of CAR in lung cancer is supported by meta-analytic evidence showing that elevated CAR is associated with poorer survival outcomes, although our study was not designed to evaluate prognosis [4]. Therefore, our findings should not be interpreted as evidence that higher postoperative CAR or PLR predicts recurrence or survival; rather, they suggest that these indices may reflect incomplete early biological recovery and may warrant prospective evaluation in standardized postoperative follow-up windows.

Although these findings are not yet directly practice-changing, they may still have practical relevance for standardized postoperative follow-up. In routine thoracic surgical care, the outpatient postoperative review is often the time point when recovery status, final pathology, and adjuvant treatment planning are reassessed. Within this context, persistent reduction in HALP together with increases in CAR or PLR may be interpreted as candidate indicators of incomplete biological recovery rather than as immediate prognostic markers. If confirmed prospectively, such patterns may help identify patients who could benefit from closer laboratory reassessment or a more individualized early follow-up strategy. However, because the present study did not correlate biomarker changes with postoperative complications, recovery metrics, or oncologic outcomes, these findings should not yet be used to guide clinical decision-making.

Equally important are the biomarkers that did not change significantly. The lack of statistically significant shifts in NLR, SII, PNI, white blood cell count, neutrophil count, lymphocyte count, albumin, and creatinine should not be viewed as a negative result. Instead, it likely reflects the specific timing of assessment in the present study. We did not evaluate biomarkers during the immediate postoperative inflammatory surge; rather, we assessed them at a standardized follow-up visit between postoperative days 25 and 34. By that stage, leukocyte-based disturbances may already have partially resolved, particularly after minimally invasive surgery, whereas CRP, platelet, and anemia-related changes may persist for longer. This interpretation is supported by work showing that minimally invasive major lung resection is associated with a more attenuated postoperative inflammatory and immune disturbance than open surgery [6]. Recent

data also suggest that perioperative biomarker trajectories, including SII dynamics, may provide information beyond a single static postoperative measurement [8,11].

The present study should therefore be interpreted as hypothesis-generating rather than definitive. Its main contribution is to characterize the shared early postoperative biomarker profile after uniportal minimally invasive anatomical resection, rather than to establish postoperative cutoffs, predict recurrence, or compare the superiority of UVATS and URATS. Within that scope, our results support the hypothesis that early postoperative recovery after uniportal anatomical lung resection for NSCLC may follow a selective biomarker recovery pattern, with HALP reduction and increases in CAR and PLR remaining detectable at the standardized follow-up, whereas broader leukocyte-based or albumin-based changes are less prominent. If validated prospectively, this pattern may help identify which readily available biomarkers are most suitable for monitoring early recovery after minimally invasive lung cancer surgery [1]. In addition, because several secondary biomarkers were evaluated simultaneously without formal multiplicity adjustment, the observed secondary associations should be regarded as exploratory signals rather than confirmatory findings and interpreted with appropriate caution.

Limitations of the Study

Several limitations should be acknowledged. First, this was a retrospective single-center study, which limits external generalizability. In addition, the retrospective design introduces potential selection bias and information bias, particularly with respect to eligibility based on availability of paired laboratory data and the accuracy and completeness of retrospectively retrieved clinical variables. Second, the sample size was modest, and the analysis was therefore intentionally restricted to paired within-patient comparisons and descriptive cohort characterization. No formal a priori power analysis was performed because of the retrospective exploratory design of the study. Therefore, the cohort may have been underpowered to detect modest differences in secondary biomarker endpoints. Third, only one standardized early postoperative time point was evaluated; thus, we were unable to assess serial biomarker trajectories, delayed normalization patterns, or associations with long-term oncologic outcomes. In addition, we did not correlate biomarker changes with postoperative complications, recovery metrics, or other short-term clinical outcomes. Therefore, the observed biomarker shifts should not yet be interpreted as markers of clinical recovery, complication risk, or prognosis. In addition, the cohort included different extents of anatomical resection (lobectomy, segmentectomy, and pneumonectomy), which may differ in surgical stress and postoperative inflammatory response. Fourth, although both UVATS and URATS were represented in the cohort, the study was intentionally designed as a pooled uniportal analysis rather than a between-approach comparative study in order to preserve conceptual separation from our dedicated perioperative outcomes analysis. Potential differences in surgical trauma and postoperative inflammatory response between UVATS and URATS therefore cannot be excluded and should be evaluated in larger comparative cohorts. Furthermore, because multiple secondary biomarkers were analyzed without formal adjustment for multiple comparisons, the possibility of type I error should be acknowledged. Accordingly, the secondary results should be interpreted as exploratory findings that require confirmation in larger prospective cohorts. Finally, because the selected indices were derived from overlapping hematologic and inflammatory variables, the present work should be interpreted as a focused characterization of postoperative biological recovery rather than as a search for independent predictive markers. These limitations should temper interpretation, but they do not diminish the main methodological strength of the study: a homogeneous NSCLC cohort, anatomically comparable resections, and a tightly standardized postoperative laboratory window.

In conclusion, the standardized postoperative outpatient assessment after uniportal minimally invasive anatomical lung resection for NSCLC was characterized by a selective biomarker pattern, with reduced HALP and increased PLR and CAR despite stable NLR, SII, PNI, albumin, and leukocyte counts. These findings suggest that early postoperative recovery after uniportal minimally invasive anatomical lung resection may not

be biologically uniform. Among the evaluated indices, HALP, CAR, and PLR appeared to be the most responsive markers of residual postoperative biological stress and may deserve prospective evaluation in larger cohorts with serial postoperative follow-up.

Declaration of conflicting interests

The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

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Ethics approval

This study was approved by the Institutional Review Board of Başakşehir Çam and Sakura City Hospital (Approval No: KAEK/24.12.2025.396)

Authors' contribution

MI: contributed to the study's concept, design, supervision, data collection or processing, literature search, statistical analysis, writing, and critical review. OY: was involved in the design, data collection or processing, literature search, and critical review of the manuscript. AY: contributed to the study's supervision and critical review. All authors have read and approved the final version of the manuscript.

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