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Evaluating the Role of Advanced Age and Risk Factors in Postoperative Outcomes Following Major Lung Cancer Resection

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ABSTRACT

Background: The incidence of lung cancer increases with age. On average, patients diagnosed with lung cancer are about 70 years. It is known that older patients are more prone to complications after major lung resection due to physiological changes; however, there is still a lack of knowledge of predictive factors associated with a higher complication risk.

Aims: In this study the association of age and postoperative complication rates in lung cancer patients is analyzed. Further, predictors of postoperative complications in the era of minimally invasive surgery in older patients are identified.

Methods: We retrospectively analyzed 180 consecutive patients with pathologically proven lung adenocarcinoma and squamous cell carcinoma. Patients were categorized into septuagenarians and octogenarians. Univariate and multivariate analyses were conducted to detect risk factors of postoperative morbidity.

Results: There were 141 (78.33%) and 39 patients (21.67%) in the septuagenarian group and octogenarian group, respectively. 67 (37.2%) patients experienced postoperative complications. The thirty-day mortality rate was 1.6%. The groups did not differ in terms of postoperative complications. Upon multivariate analysis, ECOG score ≥ 1 ($p = 0.032$), lowered FEV1/FVC ($p = 0.029$), and hypoalbuminemia ($p = 0.027$) were significant predictors for the development of major complications after lung cancer surgery.

Conclusion: Age over 80 years was not found to be an independent risk factor for the complication rates after lung cancer surgery. However, ECOG performance status ≥ 1, reduced FEV1/FVC, and lower serum albumin levels were independently associated with major postoperative complications.

1 | Introduction

Lung cancer continues to be the foremost cause of cancer mortality, with non-small cell lung cancer (NSCLC) comprising nearly 80% of all instances [1]. The risk to develop lung cancer increases with age. Indeed, the average age of lung cancer patients at the time of diagnosis is approximately 70 years [2] and 44% of individuals diagnosed with lung cancer in Europe are aged

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over 70 years [3]. As the elderly population continuously grows, the annual number of new cancer cases further increases. By 2050, it is projected that approximately 6.9 million new cancer cases will be diagnosed globally in individuals over the age of 80 [4]. As ongoing improvements in perioperative management and the use of minimally invasive surgical techniques continuously increased the number of operations performed in older individuals, also the frequency of major surgery in elderly NSCLC patients will further rise [5]. Nevertheless, treatment of older NSCLC patients remains challenging, as age-related physiological changes and limitations, the presence of comorbidities, and a relatively shorter life expectation have to be considered [6]. In fact, following lung surgery, Detillon et al. detected a higher postoperative mortality rate in octogenarians compared to patients aged 60–79 years [7]. However, another study found no significant difference in the occurrence of complications after minimally invasive lung surgery between patients above and below 70 years of age [8]. The inconsistent data has created some uncertainty in making appropriate treatment decisions for older adults with NSCLC.

Up to now, study cohorts of older patients undergoing cancer-related major lung surgery reported in the literature usually comprise a relatively small number of individuals [8–11]. Furthermore, studies on older lung cancer patients undergoing major lung resections encompassed nearly all NSCLC subtypes, including very rare histological findings, thus reducing the specificity of the findings [8–11]. Therefore, analyzing larger and more specific patient cohorts, including lung adenocarcinoma and squamous cell carcinoma, could help to improve the evidence on age and comorbidity-related complications following major lung surgery.

The aim of this study was to evaluate the association between advanced age and postoperative complication rates following major lung cancer resection. In particular, we analyzed whether patients aged ≥ 80 years have a higher risk of postoperative morbidity compared with septuagenarians undergoing lung cancer surgery. Furthermore, we sought to identify clinical predictors of postoperative complications in elderly patients by analyzing perioperative parameters, including laboratory findings, pulmonary function, radiological characteristics, and relevant comorbidities.

The safety of surgery was evaluated based on postoperative morbidity, mortality, and hospital stay.

2 | Methods

2.1 | Study Population

This retrospective cohort study, conducted at a single institution, received approval from the Ethics Committee of Ludwig Maximilian University of Munich (LMU), Germany (file number 24-0114), and adhered to the principles of the Declaration of Helsinki and the STROBE guidelines for clinical research.

Patient recruitment and treatment were carried out at the Department of Thoracic Surgery, Robert Bosch Hospital (Stuttgart, Germany) between January 1, 2019, and December 31, 2023.

The study included patients aged over 70 years with resectable primary malignant lung tumors who underwent major surgical procedures—segmentectomy, lobectomy, bilobectomy, or pneumonectomy—with intraoperative histological confirmation of lung adenocarcinoma or squamous cell carcinoma.

Patients with rare histological subtypes (e.g., carcinoid tumors, adenoid cystic carcinoma, pleomorphic carcinoma, or sarcomatoid carcinoma) identified intraoperatively, despite receiving similar surgical treatment, were excluded from the analysis. Other exclusion criteria were age below 70 years, nonanatomical lung resections, palliative lung tumor resections, and neoadjuvant-treated patients.

2.2 | Data Assessments and Sources

Clinical data were extracted from a retrospectively maintained institutional database. Tumor classification followed the 8th edition of the TNM staging system [12], and histopathological findings were interpreted according to the World Health Organization (WHO) classification of lung tumors [13].

Collected variables included demographic characteristics (age, sex, Body Mass Index (BMI), smoking status, comorbidities), laboratory values measured within 1 to 5 days before surgery (complete blood count, C-reactive protein [CRP], creatinine, lactate dehydrogenase [LDH], and serum albumin), and preoperative pulmonary function tests (FVC, FEV1, DLCO, and FEV1/FVC ratio). Tumor staging was assessed radiologically (cTNM), and histological details were recorded. Surgerical safety in older patients was evaluated based on postoperative morbidity, 30-day mortalitiy, and length of hospital stay.

Major postoperative complications were defined as Clavien-Dindo grade 3b or higher [14]. All patient data were anonymized prior to analysis.

2.3 | Assessment of Comorbidities

Cardiovascular comorbidities comprised conditions such as myocardial infarction, valvular heart disease, heart failure, cardiomyopathy, atrial fibrillation, and presence of peripheral arterial disease. Liver comorbidities included liver cirrhosis, chronic liver virus infections such as hepatitis B and C, and steatosis hepatis. Respiratory comorbidities include COPD, asthma, and idiopathic lung disorders. Renal comorbidities included renal insufficiency. Neurological comorbidities included cerebrovascular conditions such as stroke and transient ischemic attack (TIA), dementia, as well as Parkinson's disease. Diabetes mellitus Types 1, 2, and 3 were included. Other malignancies included all previous malignancies of patients. Based on the comorbidities, a Charlson Comorbidity Index (CCI) was calculated for each patient [15].

2.4 | Perioperative Management and ERAS Elements

Several elements of the Enhanced Recovery After Surgery (ERAS) protocol were implemented in our department as part of

the standard perioperative management for patients undergoing lung cancer resection.

Preoperative management included dedicated patient counseling and encouragement to discontinue smoking and alcohol consumption at least 4 weeks prior to surgery whenever possible.

Pre-anesthetic management followed current fasting recommendations. Patients were allowed to consume clear fluids up to 2 h and solid food up to 6 h before surgery.

Intraoperative management included antibiotic prophylaxis administered within 60 min prior to skin incision. General anesthesia was performed with strategies to prevent intraoperative hypothermia and with lung-protective ventilation. Regional analgesia was routinely applied: during thoracotomy procedures via epidural catheter and during thoracoscopic surgery via intercostal nerve block catheter. Fluid therapy aimed to maintain euvolemia. Surgical techniques followed minimally invasive principles whenever feasible, with uniportal video-assisted thoracoscopic surgery (uVATS) as the preferred approach. When thoracotomy was required, an anterolateral muscle-sparing approach was used.

Postoperative management focused on early recovery and mobilization. Intravenous fluids were minimized, and early oral intake of fluids and diet was encouraged. Multimodal analgesia consisted of oral acetaminophen and non-steroidal anti-inflammatory drugs (NSAIDs), combined with regional analgesia via intercostal nerve block catheter or epidural catheter. Early physiotherapy with mobilization within 24 h after surgery was encouraged. Chest tube management aimed for the use of a single chest drain whenever feasible, connected to a digital drainage system. Pharmacological thromboembolism prophylaxis was routinely administered using low-molecular-weight heparin.

2.5 | Outcomes

The objective of this study was to assess the influence of advanced age on immediate perioperative outcomes following major lung cancer resection and to identify potential risk factors associated with increased morbidity and mortality.

To this end, we conducted a comprehensive analysis encompassing demographic characteristics, laboratory findings, pulmonary function, radiological and histopathological parameters, as well as comorbid conditions. The correlation between these parameters was analyzed concerning the age groups of patients (septuagenarians vs. octogenarians) and complications according to Clavien-Dindo classification (<3b vs. ≥ 3b).

2.6 | Data Analysis

Statistical analysis was performed in R software (Version 4.2.2). Continuous data, if normal distribution was observed, were compared using an unpaired *t*-test; otherwise, Mann–Whitney *U*-test was used. Comparison of categorical variables was performed using Chi-square or, where applicable, Fisher's exact test. To control for the increased risk of Type I errors associated with multiple comparisons in the univariate analyses, *p*-values were adjusted using the Benjamini-Hochberg false discovery rate (FDR) method. Visualization of data was performed with ggplot and ggpubr packages. Univariate and multivariate analyses were performed with the "glm()" function of base R, and forest plots were generated with the SjPlot package [16]. Receiver Operating Characteristic (ROC) curves were generated with the pROC package, and cutoff values were calculated with the Youden index [17]. *p*-values <0.05 were considered statistically significant.

3 | Results

3.1 | Study Population

Based on the age, 141 patients (78.33%) and 39 patients (21.67%) were included in the septuagenarian and octogenarian groups, respectively.

The analyzed cohort included patients with a mean age of 74.8 years (interquartile range 72.2–77.6) in the septuagenarian group and 82.5 years (interquartile range 80.9–83.5) in the octogenarian group. Tables 1 and 2 display some clinical data, surgical and tumor characteristics of the cohort.

Septuagenarians were admitted with significantly better ECOG PS in comparison to the octogenarians (ECOG PS 0: $p=0.04$). Patients in the octogenarian group presented both with a significantly larger clinically estimated tumor size in CT scan ($p=0.006$) and tumor size as measured by histopathology ($p=0.03$) (Table 2). Despite larger tumor manifestations, the octogenarians were more likely to undergo video-assisted thoracoscopic surgery; however, without significant difference between groups (38.4% vs. 28.3%, $p=0.58$). No significant differences regarding side, lobar distribution, surgical approach, as well as laboratory parameters were reported between age groups (Table 1 and Figure S1).

Whereas the octogenarian group included more patients undergoing lobectomies (37 patients (94.8%) vs. 117 patients (82.9%), $p=0.64$), the septuagenarian group comprised more patients undergoing segmental resections (Table 1).

In the comparison between patients aged 70–79 years and those aged ≥ 80 years, the most prevalent comorbidities were pulmonary diseases (30.4% vs. 17.9%, $p=0.15$), cardiac conditions (39.7% vs. 30.7%, $p=0.352$), and diabetes mellitus (21.2% vs. 20.5%, $p=1.00$). No statistically significant differences in the distribution of comorbidities were observed between the two age groups. However, CCI was significantly higher in octogenarians ($p=0.00001$). Figure 1 displays the distribution of comorbidities among the age groups.

Table 3 provides a summary of the main postoperative characteristics in the two groups of patients. Hospital length of stay (LOS, $p=0.21$) and readmission rate ($p=0.21$) were slightly longer in octogenarians compared to septuagenarians. Additionally, the duration of drainage tended to be longer in octogenarians ($p=0.21$).

TABLE 1 | Demographics and clinico-surgical aspects of patients.

Variables	Age: 70–79 $n = 141$	Age: ≥ 80 $n = 39$	p (adjusted)
Age, years, median (IQR)	74.8 (72.2–77.6)	82.5 (80.9–83.5)	0.0004
Sex [male], *n* (%)	88 (62.4)	22 (56.4)	0.80
BMI [kq/m^2], median (IQR)	26.3 (23.1–28.9)	26.4 (23–27.4)	0.80
Alcohol and tobacco use [yes], *n* (%)	108 (76.5)	30 (76.9)	1
Smoking status [ever smoker], *n* (%)	107 (75.8)	26 (66.6)	0.60
Alcohol consumption [yes], *n* (%)	26 (18.4)	13 (33.3)	0.22
ASA [3 or 4], *n* (%)	104 (73.7)	31 (79.4)	0.81
ECOG PS			0.04
0, *n* (%)	135 (95.7)	32 (82)	
1, *n* (%)	6 (4.25)	6 (15.3)	
2, *n* (%)	0 (0)	1 (2.5)	
CCI, Median (IQR)	6.23 (5–7)	8.03 (7–9)	< 0.0001
Chronic diseases N of organs [≥ 2], *n* (%)	50 (35.4)	12 (30.7)	0.90
Lung function parameters			
FEV1, Median (IQR)	84 (69.5–97)	90.2 (81–102)	0.28
DLCO SB, Median (IQR)	68.6 (54.25–79)	69.9 (58.25–81.75)	0.89
FVC, Median (IQR)	88.9 (77.5–100)	92.9 (83.25–104.75)	0.31
FEV1/FVC, Median (IQR)	94.3 (87.5–103)	95.8 (89.5–103.75)	0.82
Tumor size in CT, Median (IQR)	2.87 (1.5–3.8)	4.05 (2.45–5)	0.06
Tumor localization			0.85
LLL, *n* (%)	28 (19.8)	5 (12.8)	
LMB, *n* (%)	1 (0.7)	0 (0)	
LUL, *n* (%)	39 (27.6)	8 (20.5)	
RLL, *n* (%)	25 (17.7)	8 (20.5)	
RML, *n* (%)	5 (3.5)	2 (5.1)	
RUL, *n* (%)	43 (30.4)	16 (41)	
Surgical approach			0.58
Thoracotomy, *n* (%)	101 (71 0.6)	24 (61.5)	
Minimally invasive, *n* (%)	40 (28.3)	15 (38.4)	
Surgical resection			0.64
Segmentectomy, *n* (%)	16 (11.3)	1 (2.5)	
Lobectomy, *n* (%)	117 (82.9)	37 (94.8)	
Bilobectomy, *n* (%)	6 (4.2)	1 (2.5)	
Pneumonectomy, *n* (%)	2 (1.4)	0 (0)	
Surgery time (min), Median (IQR)	226 (167–276)	225 (156–242)	0.76

Note: For continuous variables, a non-parametric Mann–Whitney *U* test was performed. For binary variables, the Pearson Chi-square test or Fisher's exact test was performed. p-values < 0.05 are statistically significant.

Abbreviations: ASA, American Society of Anesthesiologists; BMI, body mass index; CCI, Charlson comorbidity index; DLCO SB, diffusion capacity of the lung for carbon monoxide in single breath; ECOG PS, eastern cooperative oncology group performance status; FEV1, forced expiratory volume in 1 s; FVC, functional vital capacity; LLL, left lower lobe; LMB, left main bronchus; LUL, left upper lobe; RLL, right lower lobe; RML, right middle lobe; RUL, right upper lobe.

TABLE 2 | Tumor characteristics in patients undergoing surgical resection classified by age groups.

Variables	Age: 70–79 $n=141$	Age: ≥80 $n=39$	p (adjusted)
Tumor histology			0.83
Adenocarcinoma, *n* (%)	107 (75.8)	29 (74.3)	
Squamous cell carcinoma, *n* (%)	34 (24.1)	10 (25.6)	
UICC			0.03
I, *n* (%)	98 (69.5)	19 (48.7)	
II, *n* (%)	28 (19.8)	9 (23)	
III, *n* (%)	15 (10.6)	11 (28.2)	
Pathological *T* stage			0.06
1, *n* (%)	88 (62.4)	15 (38.4)	
2, *n* (%)	28 (19.8)	11 (28.2)	
3, *n* (%)	18 (12.7)	8 (20.5)	
4, *n* (%)	7 (4.9)	5 (12.8)	
Pathological *N* stage			0.18
0, *n* (%)	121 (85.8)	31 (79.4)	
1, *n* (%)	12 (8.5)	2 (5.1)	
2, *n* (%)	7 (4.9)	4 (10.2)	
3, *n* (%)	1 (0.7)	2 (5.1)	
Tumor grade			0.48
1, *n* (%)	1 (0.7)	1 (2.5)	
2, *n* (%)	91 (64.5)	27 (69.2)	
3, *n* (%)	49 (34.7)	11 (28.2)	
Tumor size in pathology, Median (IQR)	3.08 (1.5–4.1)	3.97 (2.35–5.05)	0.03
Pleura visceralis infiltration, *n* (%)	47 (33.3)	12 (30.7)	0.95

Note: For continuous variables, a non-parametric Mann–Whitney *U* test was performed. For binary variables, the Pearson Chi-squared test or Fisher's exact test was performed. *p*-values < 0.05 are statistically significant.
Abbreviation: UICC, Union for International Cancer Control.

Notably, there was no significant difference in the 30-day mortality rate between the two age groups (1.4% vs. 2.5%, $p=0.60$).

3.2 | Logistic Regression Analysis of Risk Factors

By trend, the overall postoperative morbidity rate was higher in octogenarians compared to septuagenarians (48.7% vs. 34%, $p=0.13$). However, the rate of major complications was slightly lower in octogenarians (10.2% vs. 14.1%, $p=0.60$). In the univariate analysis of the entire cohort, preoperative laboratory variables associated with major postoperative complications included lower levels of erythrocytes (OR = 0.31 CI (0.12–0.73), $p=0.009$), hemoglobin (OR = 0.96, CI (0.94–0.99), $p=0.014$), and serum albumin (OR = 0.24, CI (0.09–0.56), $p=0.001$), as well as higher levels of leucocytes (OR = 1.23, CI (1.03–1.46), $p=0.018$) and C-reactive protein (OR = 1.41, CI (1.11–1.86), $p=0.010$). Additional variables associated with major complications were ECOG performance score of ≥1 (OR = 4.70, CI (1.30–15.6), $p=0.012$), larger tumor size (OR = 1.23, CI (1.01–1.49), $p=0.028$), a lower Tiffenaeu index (FEV1/FVC) (OR = 0.95, CI (0.91–0.98), $p=0.008$), and reduced DLCO (OR = 0.97, CI (0.93–0.99), $p=0.012$) (Figure 2A).

To identify meaningful parameters that independently predict major complications, a binary regression analysis was performed. The analysis identified the following factors as statistically significant: decreased serum albumin levels (OR = 0.32, CI (0.11–0.87), $p=0.02$), ECOG PS ≥1 (OR = 4.4, CI (1.04–16.7), $p=0.03$), and a reduced Tiffeneau index (OR = 0.95, CI (0.91–0.99), $p=0.02$). The logistic regression model is summarized in Figure 2B (displaying only statistically significant variables).

The serum albumin levels had an area under the curve (AUC) of 0.70 (95%—CI 0.59–0.81) with a cut-off serum albumin of

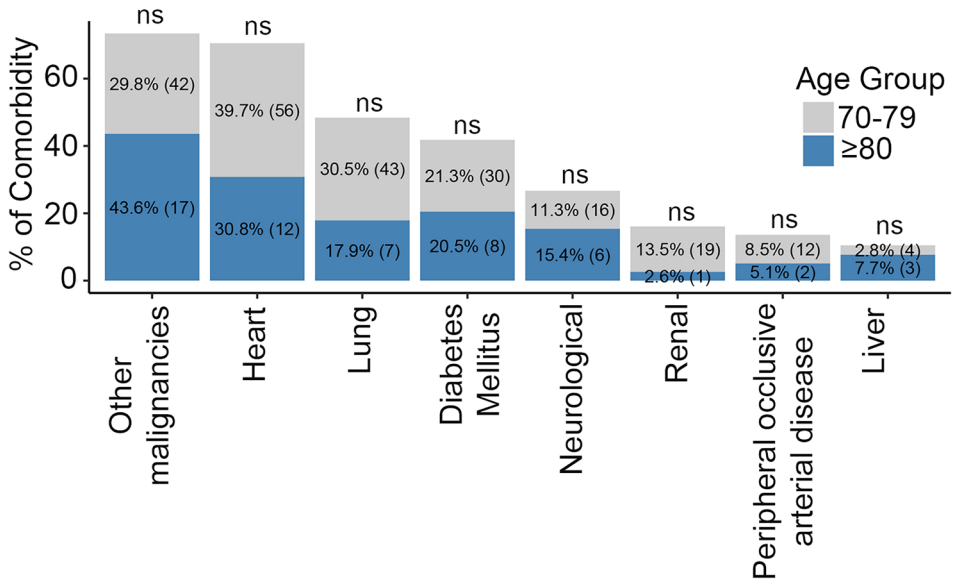

FIGURE 1 | Stacked barplot, distribution of comorbidities in age groups.

TABLE 3 | Postoperative characteristics of patients undergoing surgical resection classified by age groups.

Variables	Age: 70–79 *n* = 141	Age: ≥ 80 *n* = 39	*p* (adjusted)
ICU stay, days, (IQR)	2.43 (1–1)	2.03 (1–3)	0.23
LOS, days, Median (IQR)	13 (7–14)	14.5 (8–17)	0.21
Duration of drainage, days, Median (IQR)	9.55 (5–10)	10.5 (5.5–14)	0.25
Complications till discharge, *n* (%)	48 (34)	19 (48.7)	0.22
Readmission in 30 days, *n* (%)	20 (14.1)	10 (25.6)	0.21
Clavien – Dindo classification [≥ 3b], *n* (%)	20 (14.1)	4 (10.2)	0.80
Mortality in 30 days, *n* (%)	2 (1.4)	1 (2.5)	0.80

Note: For continuous variables, a non-parametric Mann–Whitney *U* test was performed. For binary variables, the Pearson Chi-squared test or Fisher's exact test was performed. *p*-values < 0.05 are statistically significant.
Abbreviations: ICU, intermediate care unit; LOS, length of hospital stay.

3.85 g/dL. If the level of serum albumin was < 3.85 mg/dL the sensitivity and specificity in predicting of postoperative complications were 54% and 72%, respectively. The AUC of Tiffenaeu index was 0.66 with a cut-off 90.5% (95%—CI 0.51–0.79). If the Tiffeneau index was < 90.5% the sensitivity and specificity in predicting of postoperative complications were 62% and 75%, respectively. The ROC curve based on the serum albumin levels as well as Tiffeneau index is shown in Figure 2C.

4 | Discussion

Non-small cell lung cancer primarily affects an older population. However, in our cohort, age was not identified as a factor associated with the occurrence of postoperative complications after major resection for resectable NSCLC. The overall 30-day postoperative mortality rate in the cohort was 1.6%, consistent with the findings reported by Safi et al. and Stamenovic et al. [10, 18]. Several studies have indicated that 30-day mortality after major lung resection in elderly NSCLC patients ranges from 1.8% to 9% [19–24]. The differences in reported mortality rates may be explained by the heterogeneity of the study populations and the variability in the extent of surgical resections. Evidence from several studies suggests that advanced age is associated with increased perioperative mortality, emphasizing its role in influencing surgical risk [7, 20, 25].

In our study, by trend a higher complication rate in the octogenarians' group compared to the septuagenarians' group was reported (48.7% vs. 34%, the overall complication rate for the whole cohort 37.2%). In previous reports, varied rates of postoperative complications among older patients undergoing lung cancer surgery, ranging from 13% to 50% were reported [7, 8, 10, 11, 18, 21, 22, 26]. The observed range in postoperative complication rates is likely influenced by inconsistencies in complication definitions and variability in patient inclusion criteria.

Indeed, in the present study several preoperative factors were associated with a higher complication rate in the univariate

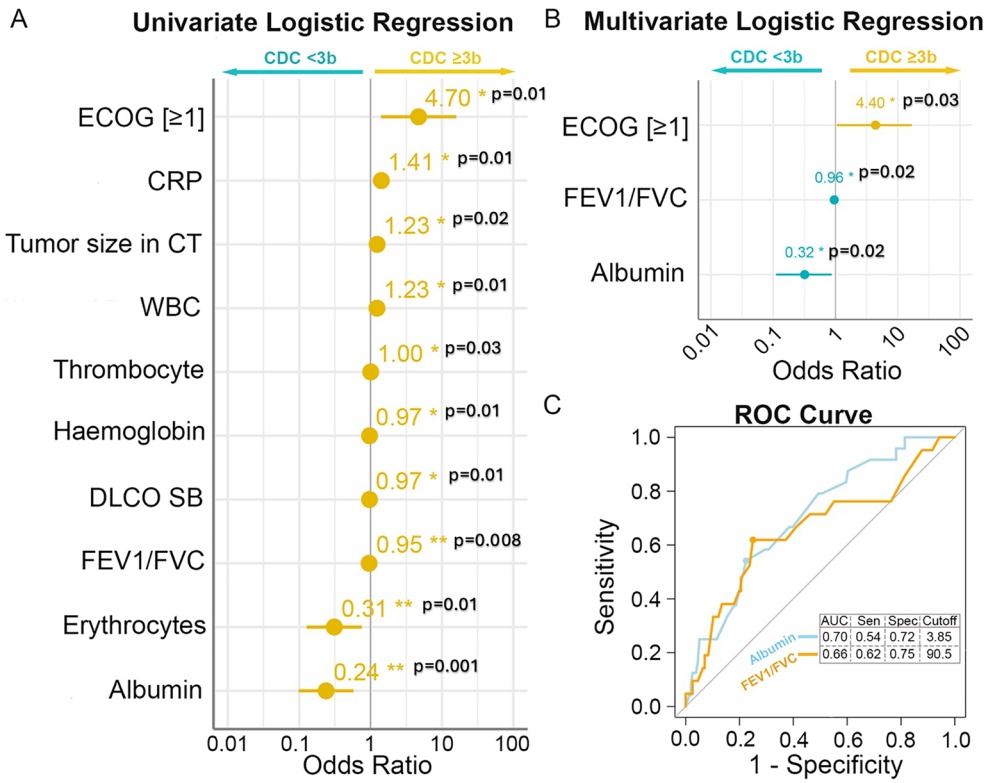

FIGURE 2 | Univariate and multivariate logistic regression analyses and receiver operating characteristic (ROC) curves for significant predictors of major postoperative complications. (A) Forest plot showing odds ratios (OR) with 95% confidence intervals from the univariate logistic regression analysis. (B) Forest plot showing independent predictors identified in the multivariate logistic regression analysis. Only variables that remained statistically significant in the multivariate model are displayed. (C) Receiver operating characteristic (ROC) curves demonstrating the diagnostic performance of serum albumin and the tiffeneau index for predicting major postoperative complications. Abbreviations: CRP, C-reactive protein; CT, computer tomography; DLCO SB, diffusion capacity of the lung for carbon monoxide in single breath; ECOG, Eastern cooperative oncology group; FEV1/FVC, Tiffenaeu index; WBC, leucocytes.

analysis. These included ECOG PS ≥1, lung function parameters (FEV1/FVC and DLCO), complete blood count (CRP, WBC, hemoglobin, erythrocytes), serum albumin levels, and tumor size. However, most of these variables did not remain significant predictors in the multivariate logistic regression analysis. This may be explained by potential confounding and intercorrelations between clinical variables reflecting patients' overall health status and physiological reserve. For example, ECOG performance status and comorbidity burden may capture overlapping aspects of functional impairment. Consequently, when analyzed together in a multivariate model, only the strongest independent predictors remained statistically significant. Furthermore, the relatively limited number of patients in the octogenarian group may have reduced the statistical power to detect independent associations for some variables. In our analysis, ECOG PS ≥1, reduced FEV1/FVC, and lower serum albumin levels remained significant predictors of major postoperative complications.

Patients with ECOG PS greater than 1 constitute a significant proportion of the cancer population [27]. Most studies exclude patients with poor ECOG PS (ECOG PS >1) for radical treatment [28]. The risk of aggressive treatment causing severe complications in NSCLC patients with poor ECOG PS is significant. In their study involving 2133 patients aged 60 and older, Detillon et al. reported significantly increased rates of postoperative complications and mortality in patients with impaired ECOG performance status undergoing major lung cancer surgery [7]. This finding is in line with our results. Based on this information, future older NSCLC patients with poor ECOG PS must be better evaluated for possible surgery to avoid severe complications.

In the multivariate analysis results, reduced FEV1/FVC was also an independent predictor of postoperative complications in lung cancer patients. We further identified FEV1/FVC < 90.5% (AUC = 0.68) as the optimal cutoff point through ROC analysis, providing clinicians with a more refined risk stratification tool than the traditional FEV1% < 60% [29, 30]. Our findings align with those of other researchers, who have also reported a significant correlation between reduced FEV1 or FEV1/FVC ratios and the occurrence of postoperative complications in older NSCLC patients undergoing surgical treatment [10, 22, 26, 31].

This study demonstrates an association between reduced serum albumin levels and the occurrence of major postoperative complications in older patients undergoing lung cancer surgery. Low serum albumin levels, often observed in malnourished patients, are linked to various physiological impairments that can contribute to postoperative complications. Hypoproteinemia has previously been identified as an

independent predictor of complications during lung cancer treatment. For example, a retrospective study by Lee et al. investigating post-chemotherapy pulmonary complications in patients with locally advanced NSCLC indicated that hypoproteinemia of grade ≥ 1 was significantly associated with the occurrence of these complications [32]. One important contributing factor to hypoalbuminemia is impaired nutritional status. Experimental models of lung cancer cachexia have demonstrated profound metabolic alterations characterized by weight loss and adipose tissue atrophy, which may contribute to reduced serum protein levels [33].

In addition to nutritional deficiency, dysregulated inflammation may play a relevant role. A recent meta-analysis including 28 high-quality trials identified hypoalbuminemia as an independent risk factor associated with elevated inflammatory markers such as C-reactive protein and leukocyte counts, suggesting that systemic inflammation may contribute to the development of complications, including pneumonia [34].

Despite these associations, the precise pathophysiological mechanisms linking hypoalbuminemia to adverse clinical outcomes remain incompletely understood. As highlighted in a review article by Kim et al., a direct causal relationship between low serum albumin levels and postoperative morbidity has not been conclusively established. Moreover, interventions aimed solely at correcting perioperative hypoalbuminemia, such as intravenous albumin administration, appear to have limited impact on the overall clinical course of hospitalized patients [35].

Direct evidence linking hepatic dysfunction to hypoalbuminemia is also limited. Florez et al. reported hypoalbuminemia as a frequent adverse event during amivantamab treatment for advanced NSCLC, potentially related to Mesenchymal-Epithelial Transition factor-Gen (MET) inhibition and impaired hepatic protein synthesis; however, the underlying biological mechanisms remain unclear [36].

In addition, ROC analysis in our study identified a serum albumin cut-off value of 3.85 g/dL for predicting major postoperative complications. This threshold may help to identify older patients at increased perioperative risk. Similar to other clinical studies evaluating albumin as a prognostic marker, these cut-off values should not be interpreted as absolute diagnostic thresholds but rather as indicators for risk stratification. In clinical practice, serum albumin reflects nutritional status, systemic inflammation, and overall physiological reserve, which may influence postoperative recovery. Previous studies have also used albumin-based stratification approaches to identify patient subgroups with different risks for postoperative complications. For example, stratification according to preoperative albumin levels has been applied in surgical cohorts to evaluate the association between albumin status and postoperative outcomes [37]. Therefore, the albumin threshold identified in our cohort may serve as a practical parameter for perioperative risk assessment and for identifying patients who may benefit from closer perioperative monitoring and optimization of nutritional status.

Taken together, these findings suggest that low serum albumin levels may reflect an impaired physiological and metabolic reserve rather than acting as a direct causal factor. In clinical practice, therefore, serum albumin at admission may primarily serve as a prognostic indicator for perioperative risk assessment in older patients undergoing lung cancer surgery.

Recently, enhanced recovery after surgery (ERAS) guidelines were introduced to improve the quality-of-care following surgery and reduce perioperative morbidity and mortality [38]. Since their recommendation, many aspects of the ERAS-based perioperative treatment protocol have been partially or fully adopted in numerous thoracic surgery units worldwide. The ERAS concept also appears to provide benefits for older patients following major lung resections [39], offering the potential for improved outcomes.

Although compliance with ERAS protocols was not systematically audited in this retrospective cohort, several ERAS-related perioperative measures were implemented in our department and may have influenced postoperative outcomes. In particular, the increasing use of minimally invasive surgical techniques, such as video-assisted thoracoscopic surgery (VATS), may reduce surgical trauma and postoperative pain, which could be especially advantageous for older patients. Furthermore, optimized perioperative fluid management and early postoperative mobilization are key ERAS components that may contribute to lower rates of cardiopulmonary complications, venous thromboembolism, and pulmonary infections.

Nevertheless, due to the retrospective nature of this study, the degree of adherence to individual ERAS elements could not be systematically quantified. Future prospective studies should incorporate standardized ERAS compliance assessments, for example using the ERAS checklist [38], to better evaluate the impact of individual ERAS components on postoperative outcomes in older patients undergoing lung cancer surgery.

This study has several notable limitations. First, its retrospective design results in incomplete data sets. Second, the cohort of octogenarians and some older patients at the end of their septuagenarian years undergoing major surgery tends to be more selectively chosen compared to other younger patient collectives. Moreover, the sample size was not large enough to deliver stronger conclusions regarding postoperative complications; however, according to the ROC curve (Figure 2C), our findings appear to be valid and might help to improve patients' selection for advanced lung surgery. In addition, screening for hypoalbuminemia and obstructive disease enables a targeted preconditioning of the patients to improve nutrition status and establish anti-obstructive therapy. Prospective randomized studies may offer more answers to the questions.

In conclusion, advancements in medicine have made it possible to offer major surgery to older lung cancer patients, even those with significant comorbidities, while maintaining acceptable perioperative morbidity and mortality rates. No significant differences were observed between septuagenarians and octogenarians in terms of postoperative complications, length of hospital stay, readmission rates, perioperative mortality, or detrimental habits such as smoking and alcohol consumption. ECOG PS ≥ 1, reduced Tiffenaeu index, and lower serum albumin levels were associated with major postoperative complications.

Author Contributions

Javad Karimbayli: software, formal analysis, visualization, methodology. **Fuad Damirov:** conceptualization, investigation, writing – original draft, methodology, writing – review and editing, resources, validation, visualization. **Junli Ke:** investigation, writing – review and editing. **Mircea Gabriel Stoleriu:** software, formal analysis, visualization. **Enole Boedeker:** resources. **Sascha Dreher:** resources. **Ughur Aghamaliyev:** methodology. **Sibylle Gerz:** resources. **Gerhard Preissler:** conceptualization, methodology, validation, data curation, supervision, resources, writing – review and editing. **Rudolf Alexander Hatz:** data curation.

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Ethics Statement

The study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of the Ludwig Maximilian University of Munich (LMU), Munich, Germany, file number 24–0114.

Consent

Patient consent was waived due to the retrospective and anonymized nature of the study by the Ethics Committee of the Ludwig Maximilian University of Munich (LMU).

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

References

1. R. L. Siegel, K. D. Miller, N. S. Wagle, and A. Jemal, "Cancer Statistics, 2023," *CA: A Cancer Journal for Clinicians* 73, no. 1 (2023): 17–48.

2. B. C. Bade and C. S. Dela Cruz, "Lung Cancer 2020: Epidemiology, Etiology, and Prevention," *Clinics in Chest Medicine* 41, no. 1 (2020): 1–24.

3. I. Saftic, A. Bille, N. Asemota, et al., "Risks and Rewards of the Surgical Treatment of Lung Cancer in Octogenarians," *Interactive Cardiovascular and Thoracic Surgery* 33, no. 6 (2021): 905–912.

4. S. Pilleron, E. Soto-Perez-de-Celis, J. Vignat, et al., "Estimated Global Cancer Incidence in the Oldest Adults in 2018 and Projections to 2050," *International Journal of Cancer* 148, no. 3 (2021): 601–608.

5. A. J. Fowler, T. E. F. Abbott, J. Prowle, and R. M. Pearse, "Age of Patients Undergoing Surgery," *British Journal of Surgery* 106, no. 8 (2019): 1012–1018.

6. R. Blanco, I. Maestu, M. G. de la Torre, A. Cassinello, and I. Nunez, "A Review of the Management of Elderly Patients With Non-Small-Cell Lung Cancer," *Annals of Oncology* 26, no. 3 (2015): 451–463.

7. D. Detillon and E. J. Veen, "Postoperative Outcome After Pulmonary Surgery for Non-Small Cell Lung Cancer in Elderly Patients," *Annals of Thoracic Surgery* 105, no. 1 (2018): 287–293.

8. M. Zaatar, T. Stork, D. Valdivia, et al., "Minimal-Invasive Approach Reduces Cardiopulmonary Complications in Elderly After Lung Cancer Surgery," *Journal of Thoracic Disease* 12, no. 5 (2020): 2372–2379.

9. N. Panagopoulos, K. Grapatsas, V. Leivaditis, M. Galanis, and D. Dougenis, "Are Extensive Open Lung Resections for Elderly Patients With Lung Cancer Justified?," *Current Oncology* 30, no. 6 (2023): 5470–5484.

10. D. Stamenovic, A. Messerschmidt, and T. Schneider, "Surgery for Lung Tumors in the Elderly: A Retrospective Cohort Study on the Influence of Advanced Age (Over 80 Years) on the Development of Complications by Using a Multivariate Risk Model," *International Journal of Surgery* 52 (2018): 141–148.

11. A. Kaprin, O. Pikin, A. Ryabov, O. Aleksandrov, D. Larionov, and A. Garifullin, "Surgical Intervention for Lung Cancer in Patients Aged 75 and Above: Potential Associations With Increased Mortality Rates-a Single-Center Observational Study," *Journal of Cardiothoracic Surgery* 19, no. 1 (2024): 471.

12. F. C. Detterbeck, K. Chansky, P. Groome, et al., "The IASLC Lung Cancer Staging Project: Methodology and Validation Used in the Development of Proposals for Revision of the Stage Classification of NSCLC in the Forthcoming (Eighth) Edition of the TNM Classification of Lung Cancer," *Journal of Thoracic Oncology* 11, no. 9 (2016): 1433–1446.

13. W. D. Travis, E. Brambilla, A. G. Nicholson, et al., "The 2015 World Health Organization Classification of Lung Tumors: Impact of Genetic, Clinical and Radiologic Advances Since the 2004 Classification," *Journal of Thoracic Oncology* 10, no. 9 (2015): 1243–1260.

14. D. Dindo, N. Demartines, and P. A. Clavien, "Classification of Surgical Complications: A New Proposal With Evaluation in a Cohort of 6336 Patients and Results of a Survey," *Annals of Surgery* 240, no. 2 (2004): 205–213.

15. M. E. Charlson, P. Pompei, K. L. Ales, and C. R. MacKenzie, "A New Method of Classifying Prognostic Comorbidity in Longitudinal Studies: Development and Validation," *Journal of Chronic Diseases* 40, no. 5 (1987): 373–383.

16. D. Lüdecke, "Sjplot - Data Visualization for Statistics in Social Science. (Version 2.6.1) (Computer Software)," Zenodo, (2018).

17. X. Robin, N. Turck, A. Hainard, et al., "pROC: An Open-Source Package for R and S+ to Analyze and Compare ROC Curves," *BMC Bioinformatics* 12 (2011): 77.

18. S. Safi, M. R. Gysan, D. Weber, et al., "Peri- and Postoperative Morbidity and Mortality in Older Patients With Non-Small Cell Lung Cancer: A Matched-Pair Study," *World Journal of Surgical Oncology* 22, no. 1 (2024): 213.

19. M. F. Berry, J. Hanna, B. C. Tong, et al., "Risk Factors for Morbidity After Lobectomy for Lung Cancer in Elderly Patients," *Annals of Thoracic Surgery* 88, no. 4 (2009): 1093–1099.

20. C. Rivera, P. E. Falcoz, A. Bernard, P. A. Thomas, and M. Dahan, "Surgical Management and Outcomes of Elderly Patients With Early Stage Non-Small Cell Lung Cancer: A Nested Case-Control Study," *Chest* 140, no. 4 (2011): 874–880.

21. K. Baldvinsson, G. N. Oskarsdottir, A. W. Orrason, et al., "Resection Rate and Operability of Elderly Patients With Non-Small Cell Lung Cancer: Nationwide Study From 1991 to 2014," *Interactive Cardiovascular and Thoracic Surgery* 24, no. 5 (2017): 733–739.

22. A. Dell'Amore, M. Monteverde, N. Martucci, et al., "Early and Long-Term Results of Pulmonary Resection for Non-Small-Cell Lung Cancer in Patients Over 75 Years of Age: A Multi-Institutional Study," *Interactive Cardiovascular and Thoracic Surgery* 16, no. 3 (2013): 250–256.

23. H. Hino, T. Karasaki, Y. Yoshida, et al., "Risk Factors for Postoperative Complications and Long-Term Survival in Lung Cancer Patients

Older Than 80 Years," *European Journal of Cardio-Thoracic Surgery* 53, no. 5 (2018): 980–986.

24. H. Rostad, A. Naalsund, T. E. Strand, R. Jacobsen, O. Talleraas, and J. Norstein, "Results of Pulmonary Resection for Lung Cancer in Norway, Patients Older Than 70 Years," *European Journal of Cardio-Thoracic Surgery* 27, no. 2 (2005): 325–328.

25. A. K. E. Elfrink, A. J. Alberga, M. I. van Berge Henegouwen, et al., "Outcomes After Major Surgical Procedures in Octogenarians: A Nationwide Cohort Study," *World Journal of Surgery* 46, no. 10 (2022): 2399–2408.

26. A. C. Kutluk, H. Akin, A. Ceritoglu, et al., "Is the Outcome of Pulmonary Resections due to Non-Small Cell Lung Cancer in Octogenarian Patients Worse?," *Annals of Thoracic and Cardiovascular Surgery* 25, no. 2 (2019): 95–101.

27. D. Mojsak, B. Kuklinska, M. Debczynski, and R. M. Mroz, "Immunotherapy in Patients With Non-Small Cell Lung Cancer With ECOG PS 2," *Contemporary Oncology* 25, no. 1 (2021): 53–56.

28. R. C. Lilenbaum, J. Cashy, T. A. Hensing, S. Young, and D. Cella, "Prevalence of Poor Performance Status in Lung Cancer Patients: Implications for Research," *Journal of Thoracic Oncology* 3, no. 2 (2008): 125–129.

29. X. Mao, W. Zhang, Y. Q. Ni, Y. Niu, and L. Y. Jiang, "A Prediction Model for Postoperative Pulmonary Complication in Pulmonary Function-Impaired Patients Following Lung Resection," *Journal of Multidisciplinary Healthcare* 14 (2021): 3187–3194.

30. R. Wang, D. Gao, W. Gong, and Z. Liang, "Value of Modified POSSUM Scoring System on Predicting Operation Risk in Elderly NSCLC Patients," *Zhongguo Fei Ai Za Zhi* 17, no. 9 (2014): 669–673.

31. M. F. Berry, M. W. Onaitis, B. C. Tong, D. H. Harpole, and T. A. D'Amico, "A Model for Morbidity After Lung Resection in Octogenarians," *European Journal of Cardio-Thoracic Surgery* 39, no. 6 (2011): 989–994.

32. T. H. Lee, B. H. Kang, H. J. Kim, H. G. Wu, and J. H. Lee, "Predictors of Post-Chemoradiotherapy Pulmonary Complication in Locally Advanced Non-Small Cell Lung Cancer," *Cancer Research and Treatment* 55, no. 3 (2023): 865–874.

33. H. Wang, Y. L. Chan, Y. H. Chiu, T. H. Wu, S. Hsia, and C. J. Wu, "Supplementation With Fish Oil and Selenium Protects Lipolytic and Thermogenic Depletion of Adipose in Cachectic Mice Treated With an EGFR Inhibitor," *Cells* 13, no. 17 (2024): 1485.

34. X. Zhou, Y. Xu, Y. Ying, R. Chen, Z. Wang, and X. Lv, "Risk Factors for Checkpoint Inhibitor Pneumonitis in Lung Cancer Patients Treated With Immune Checkpoint Inhibitors: A Systematic Review and Meta-Analysis," *Frontiers in Immunology* 16 (2025): 1607170.

35. S. Kim, S. A. McClave, R. G. Martindale, K. R. Miller, and R. T. Hurt, "Hypoalbuminemia and Clinical Outcomes: What Is the Mechanism Behind the Relationship?," *American Surgeon* 83, no. 11 (2017): 1220–1227.

36. N. Florez, N. R. LeBoeuf, J. Rotow, et al., "Mitigation and Management of Adverse Events Associated With Amivantamab Therapy," *Oncologist* 30, no. 7 (2025): 1–16.

37. H. Zhang, S. Yan, L. Bian, et al., "Intraoperative 20% Albumin Infusion and Acute Kidney Injury in On-Pump Cardiac Surgery: A Focus on Preoperative Albumin Levels," *Renal Failure* 47, no. 1 (2025): 2522327.

38. T. J. P. Batchelor, N. J. Rasburn, E. Abdelnour-Berchtold, et al., "Guidelines for Enhanced Recovery After Lung Surgery: Recommendations of the Enhanced Recovery After Surgery (ERAS(R)) Society and the European Society of Thoracic Surgeons (ESTS)," *European Journal of Cardio-Thoracic Surgery* 55, no. 1 (2019): 91–115.

39. F. Mazza, M. Venturino, D. Turello, et al., "Enhanced Recovery After Surgery: Adherence and Outcomes in Elderly Patients Undergoing VATS Lobectomy," *General Thoracic and Cardiovascular Surgery* 68, no. 9 (2020): 1003–1010.

Supporting Information

Additional supporting information can be found online in the Supporting Information section. **Figure S1:** Laboratory parameters between age groups.