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Investigation of postoperative pulmonary complications in patients undergoing surgical lung biopsy with a preliminary diagnosis of interstitial lung disease

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Abstract:

BACKGROUND AND AIM: Interstitial lung disease (ILD) includes a spectrum of lung disorders with various causes, pathological changes, treatment strategies, and prognoses. Lung biopsy is often crucial for diagnosing ILD subtypes, especially in complex cases. However, biopsy procedures carry significant risks due to potential postoperative complications. This study aimed to assess the rate and types of postoperative complications in ILD patients following lung biopsy and to examine their relationship with patient demographics, lung function, and comorbidities.

METHODS: We conducted a retrospective, cross-sectional review of ILD patients who underwent surgical lung biopsy at Akdeniz University Hospital between January 1, 2017 and December 31, 2022. Data collected included demographics, comorbidities, pulmonary function tests (forced expiratory volume in one second [FEV_1] and forced vital capacity [FVC]), type of surgery (video-assisted thoracoscopic surgery [VATS] or thoracotomy), biopsy location, hospital stay duration, and postoperative complications (pneumonia, prolonged air leak, hypoxia, pneumothorax, subcutaneous emphysema, pleural effusion, and mortality). Statistical analyses were performed to identify factors associated with complication rates.

RESULTS: Among the 140 patients analyzed, the mean age was 56.9±11.1 years, with 50.7% female. Postoperative complications occurred in 22.1% of patients, with hypoxia, pneumonia, and prolonged air leak being the most frequent. Lower FEV_1 was significantly associated with higher complication rates ($p=0.018$), while hospital stays longer than five days were also associated with increased complication rates ($p<0.001$). Sex, body mass index (BMI), and comorbidities showed no significant associations with complication rates.

CONCLUSIONS: Our findings reveal an increased risk of complications in ILD patients undergoing lung biopsy, particularly among those with lower FEV_1 and longer hospital stays. These results underscore the importance of thorough preoperative evaluation and suggest that VATS may be preferable to more invasive methods for ILD diagnosis.

Keywords:

Interstitial lung disease, postoperative complications, pulmonary function tests, surgical lung biopsy, video-assisted thoracoscopic surgery

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Introduction

Interstitial lung disease (ILD) encompasses a range of lung conditions with diverse etiologies, pathological changes, treatment options, and prognoses.[1,2] Accurate diagnosis and classification of ILD are therefore critical for determining appropriate treatment and prognosis. In ILD patients with complex clinical presentations, current guidelines recommend diagnostic surgical lung biopsy to differentiate among ILD subtypes. However, with advancements in high-resolution computed tomography (HRCT) and the associated high morbidity and mortality of surgical lung biopsy, its routine use in ILD diagnosis remains a topic of debate.[3]

The incidence of postoperative complications in ILD patients varies according to the surgical approach used. While thoracotomy was more common in previous years, current trends favor less invasive methods such as video-assisted thoracoscopic surgery (VATS) and cryobiopsy. Thoracotomy procedures are associated with higher rates of postoperative complications, whereas less invasive techniques generally reduce these risks. VATS is widely regarded as a safe procedure that provides sufficient lung tissue for a definitive histopathological diagnosis.[4] However, postoperative complications in ILD patients are a significant concern, as acute exacerbation following surgery can be life-threatening. Reported complication rates for lung biopsy range from 16% to 71%, with overall postoperative mortality between 0% and 24%.[4,5] The most common complications include hypoxia, postoperative atelectasis, pleural effusion, pulmonary thromboembolism, pneumonia, and hemorrhage.[4–6] In a study by Sigurdsson et al.,[7] the 30-day mortality and complication rates following surgical lung biopsy in 73 ILD patients were 2.7% and 16%, respectively. A comprehensive review by Nguyen et al.[8] reported that 9.6% of ILD patients undergoing VATS developed one or more postoperative complications, with an overall 30-day mortality rate of 2.1%. Patients with a predicted diffusing capacity for carbon monoxide (DLCO) of less than 50%, those requiring mechanical ventilation, or those with immunosuppression or pulmonary hypertension may have an increased risk of mortality after lung biopsy.[9,10] Given the limited research on this topic in Türkiye, this study aims to share clinical experience from a Turkish population by evaluating postoperative complications occurring within one week to one month after lung biopsy in patients diagnosed with ILD.

Materials and Methods

Interstitial lung diseases represent a heterogeneous group of disorders that pose diagnostic challenges. Different clinical, radiological, and pathological diagnoses may be considered. Therefore, a multidisciplinary approach will undoubtedly yield the most accurate diagnosis. In our study, decisions regarding surgical lung biopsy were made by committees comprising pulmonologists, radiologists, and thoracic surgeons, and the patients underwent surgical lung biopsies.

Study type

This is a descriptive, cross-sectional study.

Study location, sample, and time period

A retrospective review was conducted of patients who underwent lung biopsy with a preliminary diagnosis of ILD at the Department of Thoracic Surgery, Akdeniz University Hospital, between January 1, 2017 and December 31, 2022.

Inclusion criteria

- Pathology results indicating ILD,
- Available preoperative radiological images and pulmonary function tests,
- Accessible clinical follow-up data within one week to one month post-surgery.

Exclusion criteria

- Missing clinical follow-up, pathology results, preoperative pulmonary function tests, or radiological images,
- Patients who underwent anatomical resection.

Surgical methods

Surgical lung biopsy is generally considered a last-resort option in the diagnosis of ILD patients due to the inherent risks of the procedure. At this stage, all available treatment options are explored before considering surgical lung biopsy. Given the inherent risks of surgical lung biopsy, efforts were made to minimize and standardize both operative and biopsy times in all cases, in order to reduce potential complications and variability.

Data collection

Patient demographics (age, sex, Body Mass Index, smoking status, and smoking pack-years), smoking

history, comorbidities (hypertension, coronary artery disease, type 2 diabetes mellitus [T2DM], chronic obstructive pulmonary disease [COPD], and malignancy), pulmonary function test results (forced expiratory volume in one second [FEV_1] and forced vital capacity [FVC]), type of surgery (video-assisted thoracoscopic surgery [VATS] or thoracotomy), biopsy location, hospital length of stay, and postoperative complications were recorded. To better capture complications related to the underlying ILD rather than to immediate technical issues of the surgery, we specifically evaluated pulmonary complications that occurred between the first postoperative week and the end of the first postoperative month. The most frequent postoperative complications included dyspnea, pneumothorax, prolonged air leak, pneumonia, pleural effusion, subcutaneous emphysema, and mortality, with a primary focus on pulmonary complications.

Ethical approval and data usage permission

The study was approved by Akdeniz University Faculty of Medicine Clinical Research Ethics Committee (Approval Number: KAEK-452, Date: 07.06.2023), and was granted permission by Akdeniz University Hospital for a six-month data usage period. Informed consent was obtained from all subjects, and the study was conducted in accordance with the Declaration of Helsinki.

Statistical analysis

Statistical analyses were performed using IBM SPSS Statistics for Windows, Version 28.0 (Released 2021; IBM Corp., Armonk, New York, USA). Continuous variables were presented as mean±standard deviation, and categorical variables as frequency (n) and percentage (%). The Shapiro-Wilk test was used to assess the normality of data distribution. For comparisons of normally distributed data, the Independent Samples t-test was used, while the Mann-Whitney U test was applied for non-normally distributed data. Correlations between variables were analyzed using the Pearson correlation test. Statistical significance was set at $p<0.05$.

Results

During this period, surgical biopsy was performed on 145 patients diagnosed with ILD. Of these, four patients were excluded due to missing data and one due to lung malignancy, leaving 140 patients for analysis. The final cohort included 140 patients, with a mean age of 56.9±11.1 years. The group consisted of 50.7% females (n=71) and 49.3% males (n=69). The mean Body Mass Index (BMI) was 28.89±5.33, with 24.3% (n=34) classified as underweight/normal, 36.4% (n=51) as overweight, 29.3% (n=41) as obese class I, and 10% (n=14) as obese class II/morbidly obese. Regarding comorbidities, 25.7% (n=36) had none, while 74.3% (n=104) had at least one. The most common comorbidities were hypertension (32.1%, n=45), diabetes mellitus (21.4%, n=30), chronic obstructive pulmonary disease (20.7%, n=29), and coronary artery disease (27.9%, n=39). Postoperative complications occurred in 22.1% of patients (n=31). Three patients died in the postoperative period due to an exacerbation of ILD. The baseline characteristics of the patients are presented in Table 1.

Table 1: Baseline characteristics of the patients

	n	%
Age/years (mean±SD)	56.9±11.1	
Sex		
Female	71	50.7
Smoking status		
Never smoker	70	50
Current/former smoker	70	50
Smoking (pack-years)	16.5±23.6	
BMI (kg/m²)	28.8±5.3	
Comorbidities		
Hypertension	45	32.1
Coronary artery disease	39	27.9
Type 2 diabetes mellitus (T2DM)	30	21.4
COPD	29	20.7
Malignancy	4	2.9
PFT		
FVC (L)	2.3±0.8	
FVC (%)	80.0±0.9	
FEV_1 (L)	2.1±0.7	
FEV_1 (%)	71.9±1.2	
DLCO (%)	63.6±18.3	
Hospital LOS (days)	5.9±3.6	
Operation type		
VATS	56	40
Thoracotomy	71	51
VATS+Thoracotomy	13	9
Postoperative complications		
Pneumonia	10	7.1
Prolonged air leak	9	6.4
Hypoxia	7	5
Pneumothorax	4	2.9
Subcutaneous emphysema	4	2.9
Pleural effusion	3	2.1
Mortality	3	2.1

SD: Standard deviation, BMI: Body mass index, COPD: Chronic obstructive pulmonary disease, FVC: Forced vital capacity, FEV_1: Forced expiratory volume in one second, DLCO: Diffusing capacity for carbon monoxide, LOS: Length of stay, VATS: Video-assisted thoracoscopic surgery

Biopsy locations were primarily from all three lobes of the right lung (71%, n=99), with others from the middle and lower lobes of the right lung (11%, n=15), both lobes of the left lung (10%, n=14), and various other lobe combinations (8%, n=12). Most biopsies (88%, n=123) were taken from the right lung. When selecting a lobe for surgical lung biopsy, the extent of disease involvement was primarily considered. If the disease was bilateral and widespread, as is often the case, biopsies were obtained from all three lobes of the right lung, including healthy lung tissue. If disease involvement was not homogeneous but more pronounced in specific lobes, biopsy was performed on the affected side and corresponding lobe. To facilitate and increase the likelihood of diagnosis, biopsies were performed to include healthy lung tissue from all lobes of the selected lung side. The goal was to include healthy lung tissue in the biopsy specimen to facilitate diagnosis by allowing clearer distinction between normal and diseased lung tissue. Although obtaining biopsies from all lobes of the affected lung increases the likelihood of diagnosis, some patients could not undergo biopsy from all lobes of the same lung, and only one or two lobes were available due to factors such as difficulty tolerating the biopsy intraoperatively, exacerbation of disease secondary to the biopsy, inability to achieve effective single-lung ventilation, and intolerance to single-lung ventilation.

Pathological diagnoses included usual interstitial pneumonia (UIP) (26.4%, n=37), hypersensitivity pneumonitis (HP) (17.9%, n=25), nonspecific interstitial pneumonia (NSIP) (15.7%, n=22), respiratory bronchiolitis–associated interstitial lung disease (RB-ILD) (9.3%, n=13), and cryptogenic organizing pneumonia (COP) (7.9%, n=11). Other less frequent diagnoses included desquamative interstitial pneumonia (DIP) (3.6%, n=5), sarcoidosis (1.4%, n=2), and tuberculosis (2.1%, n=3). Among patients, 62.9% (n=88) stayed for five days or less, while 37.1% (n=52) stayed longer.

Sex and BMI were not significantly associated with complication development (p=0.769 and p=0.368, respectively). Comorbidities including hypertension, diabetes mellitus, obstructive lung disease, coronary artery disease, chronic kidney disease, hyperlipidemia, thyroid disease, neurologic disease, and malignancy showed no significant association with complication rates (all p-values >0.05). Smoking history and age also had no significant association with postoperative complications (p=0.541 and p=0.635, respectively).

UIP, COP, NSIP, RB-ILD, HP, DIP, and other granulomatous diseases were not significantly associated with complications (all p-values >0.05). Neither the surgical approach (VATS vs. thoracotomy) nor biopsy side (right vs. left lung) was significantly associated with complication rates (p=0.489 and p=0.533, respectively).

Patients with an FEV_1 below 80% had a higher rate of complications compared to those with an FEV_1 of 80% or higher, which was statistically significant (p=0.018). Although patients with an FVC below 80% experienced complications more frequently, this association was not statistically significant (p=0.144). Patients with hospital stays longer than five days were significantly more likely to experience complications compared to those with shorter stays (p<0.001), suggesting that prolonged hospital stay was likely related to the development of a postoperative complication. Conversely, patients without complications had significantly shorter hospital stays (p<0.001).

The Mann-Whitney U test showed that complication-free patients had significantly higher FEV_1 (p=0.018) and FVC (p=0.023) compared to those who developed complications. The relationship between the presence of postoperative pulmonary complications and patient characteristics is summarized in Table 2.

Discussion

This study aimed to evaluate postoperative complications in patients undergoing lung biopsy for ILD at a Turkish center, contributing to the limited data available on this topic in Türkiye. The findings indicated that among the 140 ILD patients analyzed, 22.1% experienced postoperative complications, with prolonged air leak, hypoxia, and pneumonia being the most frequent. These results align with prior studies reporting significant postoperative risks in ILD patients, highlighting the vulnerability of this patient population to acute exacerbations and other adverse events post-biopsy. We did not find a significant association between baseline patient characteristics, such as sex, BMI, and comorbidities, and the occurrence of postoperative complications. This finding is consistent with existing literature in which predictors of complications in ILD remain difficult to establish due to disease heterogeneity. However, a notable observation in this study was that patients with lower FEV_1 (<80%) exhibited higher complication rates, suggesting that reduced lung

Table 2: Evaluation of patient characteristics and complication development status in patients

	No complication (n=109)		Complication (n=31)		p
	n	%	n	%	
Age/years					
<60	58	53.2	15	48.4	0.635
≥60	51	46.8	16	51.6	
Smoking status					
Never smoker	56	51.4	14	45.2	0.541
Current/former smoker	53	48.6	17	54.8	
Sex					
Female	56	51.4	15	48.4	0.769
Male	53	48.6	16	51.6	
BMI					
<25	23	21.1	11	35.5	0.368
≥25	86	78.9	20	64.5	
Comorbidities					
No	30	27.5	6	19.4	0.358
Yes	79	72.5	25	80.6	
PFT					
FVC (%) <80	65	59.6	23	74.2	0.144
FVC (%) ≥80	44	40.4	8	25.8	
FEV_1 (%) <80	41	37.6	19	61.3	**0.018**
FEV_1 (%) ≥80	68	62.4	12	38.7	
DLCO	65.1±18.6		58.4±16.5		0.075
Hospital LOS					
≤5 (days)	78	71.6	10	32.3	**0.001**
>5 (days)	31	28.4	21	67.7	
Operation type					
VATS	42	38.5	14	45.2	0.489
Thoracotomy	58	53.2	13	41.9	
VATS+thoracotomy	9	8.3	4	12.9	

BMI: Body mass index, FVC: Forced vital capacity, FEV_1: Forced expiratory volume in one second, DLCO: Diffusing capacity for carbon monoxide, VATS: Video-assisted thoracoscopic surgery

function may predispose individuals to greater postoperative risk. This is in agreement with previous studies indicating that impaired lung function, particularly FEV_1, correlates with increased perioperative morbidity.

To enhance diagnostic efficiency, biopsy locations are carefully selected based on findings from high-resolution computed tomography (CT) scans, particularly targeting regions with the highest histopathologic abnormalities. Aydoğdu et al.[11] prioritized the right hemithorax for bilaterally homogenous lesions and selected the area with the highest lesion concentration in cases with non-homogenous distribution. In a study by Cilli et al.,[12] biopsies were obtained from the right lung in 68.8% of cases. In our study, 71% (n=99) of patients had biopsies from all three lobes of the right lung, 11% (n=15) from the right middle and lower lobes, 10% (n=14) from both lobes of the left lung, and 8% (n=12) from other lobe combinations. This suggests, consistent with the literature, that for patients with bilateral, homogenous parenchymal involvement, right lung biopsies are prioritized, whereas in cases of non-homogeneous involvement, biopsies target the most affected areas.

The development and increased use of VATS have led most thoracic surgeons to favor this approach over open lung biopsy. Morris and Zamvar[13] reported multiple biopsies in 42.2% of cases, most commonly from the left lower lobe (44%), left upper lobe (41%), and right lower lobe (28%). In the study by Sigurdsson et al.,[7] open minithoracotomy was the preferred method in 62% of cases. By contrast, in 85% of VATS procedures, biopsies were predominantly from the right lung (66%) compared to the left (34%), with statistical significance (p=0.01). In our study, 40% (n=56) of cases were performed using VATS, while 51% (n=71) involved thoracotomy. Additionally, 9% (n=13) of cases began with VATS but required conversion to thoracotomy due to intolerance to single-lung ventilation. Among the 71 thoracotomy cases, 58 occurred before 2019, highlighting our shift toward VATS as it became more widely available.

Since ILDs are progressive, timely diagnosis and treatment are crucial for prognosis. Miller et al.[14] compared the diagnostic yield of lung biopsies obtained via VATS and thoracotomy in ILD cases, reporting diagnostic biopsies in all patients (20 via VATS and 22 via thoracotomy). Similarly, Aydoğdu et al.[11] found no significant difference in diagnostic yield between the two methods. Morris and Zamvar[13] reported definitive diagnoses in 74.2% of cases following VATS biopsy, while Sigurdsson et al.[7] achieved a histopathological diagnosis in 83% of patients post-procedure. In our study, except for two cases via VATS, four cases initiated as VATS but converted to thoracotomy, and one case performed by thoracotomy, definitive pathological diagnoses were achieved for all patients, showing no difference in diagnostic yield between VATS and thoracotomy. In clinical practice, we aim to improve diagnostic rates by performing biopsies from at least two lung lobes in each patient, achieving this goal in 95.8% of cases. Despite these high diagnostic rates, ILD remains challenging to diagnose, as reflected in the literature.

Aydoğdu et al.[11] reported that the most common postoperative pathological diagnosis was UIP (30.7%), fol-

lowed by NSIP (28.2%). Morris and Zamvar[13] noted hypersensitivity pneumonitis (31.8%) and UIP (28.8%) as the most frequent diagnoses, followed by connective tissue disease (13.6%), NSIP (12.1%), and sarcoidosis (10.6%). Sigurdsson et al.[7] also reported UIP as the most common pathological diagnosis (32%). In our study, the most frequent diagnoses were UIP (26.4%), followed by hypersensitivity pneumonitis (17.9%), NSIP (15.7%), RB-ILD (9.3%), and COP (7.9%), with frequencies comparable to those reported in the literature.

Regarding postoperative hospital stays, Hutchinson et al.[15] reported a mean stay of five days (range: 0–308 days), while Morris and Zamvar[13] and Sigurdsson et al.[7] reported average stays of 3.5 and four days, respectively. In the study by Cilli et al.,[12] the average stay was 5.47±3.16 days. Our study found a mean hospital stay of 5.9±3.62 days, with 62.9% of patients discharged within five days and 37.1% requiring longer stays. These findings are consistent with prior reports.

Given the frequent impairment in lung function among ILD patients, surgical biopsy carries inherent risks. Reported 30-day mortality rates vary widely in the literature, ranging from 0% to 24% (336). Morbidity and mortality also vary significantly, with complication rates of 9% for VATS and 19% for open biopsy in Bensard et al.'s study,[16] and 15% and 17%, respectively, in Kadokura et al.'s study.[17] Aydoğdu et al.[11] reported a total complication rate of 5.1%, including minor postoperative apical expansion defects, with no operative mortality. Hutchinson et al.[15] observed that elective surgical lung biopsies for ILD had a hospital mortality rate of 1.7%, which increased to over 15% in unplanned procedures. Higher mortality was associated with factors such as male sex, pulmonary hypertension, and pre-existing conditions.

The limitations of our study include its retrospective nature, which may introduce bias and limit the generalizability of the findings. Additionally, the relatively small sample size may have affected the statistical power of certain analyses. While our center has a dedicated team for diagnosing and managing ILD, further prospective studies with larger cohorts are needed to validate our findings and improve understanding of the epidemiology and outcomes of ILD patients undergoing surgical lung biopsy.

Conclusion

In conclusion, our study contributes valuable insights into the demographics, clinical characteristics, and outcomes of patients with suspected ILD who underwent surgical lung biopsy. We observed no significant differences in diagnostic yield between VATS and thoracotomy, and our overall complication rate was low. These findings reinforce the importance of timely and accurate diagnosis in the management of ILDs, as well as the efficacy of surgical lung biopsy as a critical tool in the diagnostic algorithm for these complex conditions. Future research should focus on establishing standardized protocols for biopsy procedures and enhancing multidisciplinary approaches to improve patient outcomes in ILD management.

Ethics Committee Approval

The study was approved by the Akdeniz University Faculty of Medicine Clinical Research Ethics Committee (No: 452, Date: 07/06/2023).

Informed Consent

Informed consent was obtained from all subjects.

Conflicts of Interest

The authors have no conflicts of interest to declare.

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The authors did not use artificial intelligence (AI) technologies for the creation of the scientific content or data interpretation in this study. However, AI-assisted tools (specifically a large language model) were used solely for the purpose of translating and proofreading text from Turkish to English to improve readability and language quality.

Author Contributions

Concept – F.Ü., H.K.; Design – E.Ü., F.Ü., H.K.; Supervision – F.Ü., H.K.; Resource – E.Ü., A.G.Ç., F.Ü., H.K.; Materials – E.Ü., F.Ü., H.K.; Data Collection and/or Processing – E.Ü.; Analysis and/or Interpretation – E.Ü., A.G.Ç., F.Ü.; Literature Review – E.Ü., A.G.Ç.; Writing – E.Ü., F.Ü., H.K.; Critical Review – F.Ü., H.K.

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