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► **To cite this version:**

Aude Nguyen, Timothée Jouitteau, Arnaud Bourdin, Anne-sophie Gamez, Laurence Solovei, et al.. Exploring Benefits of Non-Intubated Surgery for Lung Biopsy in Interstitial Lung Disease. *Respirology*, 2025, <10.1111/resp.70067>. <hal-05098565>

HAL Id: hal-05098565

<https://hal.science/hal-05098565v1>

Submitted on 5 Jun 2025

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Exploring Benefits of Non-Intubated Surgery for Lung Biopsy in Interstitial Lung Disease

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Keywords:

interstitial lung disease; non-intubated video-assisted thoracic surgery; respiratory function; surgical lung biopsy.

Abstract

Background and objectives:

General anaesthesia with intubation is the standard technique for video-assisted thoracic surgery (VATS). However, non-intubated VATS (NIVATS) is emerging as a less invasive alternative, particularly for lung biopsies in patients with interstitial lung disease (ILD) and impaired respiratory function. This study aims to investigate the benefits of non-intubated surgery on postoperative respiratory function and to compare operative outcomes between intubated VATS (IVATS) and NIVATS.

Methods:

We conducted a single-centre retrospective study of patients who underwent lung biopsy for ILD diagnosis via VATS between January 2020 and September 2023 at Montpellier University Hospital. Primary outcomes included the variation in pulmonary function tests after surgery (FEV₁, FVC, DLCO). Secondly, this study compares clinical postoperative outcomes and diagnostic yield between the two groups.

Results:

The study included 61 patients, with 42% (n = 26) undergoing NIVATS. The NIVATS group showed a significantly smaller decrease in postoperative FEV₁ and FVC compared to the IVATS group (p = 0.001 for both variables). Additionally, NIVATS was associated with shorter operating room time (247 min vs. 288 min, p = 0.013), reduced hospital stay duration (47.5 h vs. 65.2 h, p = 0.018), and decreased need for additional analgesics (3% vs. 15%, p = 0.001). Diagnostic yield was at least similar to IVATS. There were no significant differences in DLCO or chest tube duration between the two groups.

Conclusions:

NIVATS offers better preservation of respiratory function, a good diagnostic yield, and improved overall outcomes following surgical lung biopsy in patients with ILD and could be a preferred technique for diagnosis.

Summary

- NIVATS appears to provide better preservation of respiratory function, a satisfactory diagnostic yield, and improved overall outcomes following surgical lung biopsy in patients with ILD.
- These findings suggest that it could be a preferred technique for diagnosis and emphasise the need for randomised studies

| Introduction

General anaesthesia with intubation is the standard technique for video-assisted thoracic surgery (VATS). However, numerous studies have documented the complications associated with acute lung injury resulting from mechanical ventilation, especially with One-Lung Ventilation (OLV) [1–4]. In the context of interstitial lung disease (ILD), international guidelines recommend obtaining an accurate histopathological diagnosis by surgical lung biopsy when clinical and paraclinical evaluations are inconclusive [5–8]. In these patients, who often present with impaired respiratory function, intubated VATS (IVATS) is associated with significant morbidity and mortality rates for a diagnostic procedure (approximately 15% and 2%, respectively) [9–12]. OLV has been identified as a risk factor for acute exacerbation of ILD [13, 14]. Literature suggests that non-intubated VATS (NIVATS) lung biopsy provides comparable diagnostic yield with reduced postoperative complications and a shorter recovery period compared to IVATS [9, 15, 16]. Given these findings, NIVATS for ILD biopsies has been increasingly adopted worldwide in recent years as a less invasive alternative. This study aims to further investigate the benefits of non-intubated surgery on postoperative respiratory function. The primary objective of this study was to compare the variation in pulmonary function tests (FEV₁, FVC, DLCO) between patients undergoing IVATS and those undergoing NIVATS. Secondary outcomes were operative outcomes such as overall mortality, postoperative complications, rescue pain therapy, hospital length of stay, diagnostic yield and operating time.

2 | Materials and Methods

2.1 | Study Design

We conducted a single-centre retrospective study including all patients who underwent video-assisted surgical lung biopsy for the diagnosis of ILD between January 2020 and September 2023. All patients had an indeterminate diagnosis of ILD after discussion in a multidisciplinary team, which concluded that a surgical biopsy was required. Non-intubated thoracic surgery started in 2020 at Montpellier University Hospital. Two pre-specified subgroups were compared: patients undergoing IVATS and patients undergoing NIVATS.

The choice between intubated and non-intubated procedures was determined by a preoperative multidisciplinary discussion involving thoracic surgeons, pulmonologists, and anaesthesiologists. Decisions were based on medical and organisational factors, with non-intubated procedures performed only by a trained anaesthesia team. Two experienced anaesthetists took part in the majority of procedures. Classical anaesthetic contraindications to spontaneous ventilation, such as difficult intubation criteria, gastroesophageal reflux disease, BMI > 30, or previous thoracic surgery, prohibited the use of NIVATS. Regional anaesthesia, either epidural or paravertebral catheter, was chosen at the anaesthetist's discretion. The first procedures were preferably performed under epidural anaesthesia. All procedures were performed in a lateral decubitus position using three-port video-assisted thoracoscopy.

2.2 | Intubated VATS

The procedure was performed under general anaesthesia with selective orotracheal intubation and muscle relaxation. Regional anaesthesia was either paravertebral block or epidural anaesthesia. Blood pressure was monitored with an intermittent pressure cuff. After anaesthesia and intubation, patients were placed in the lateral decubitus position.

2.3 / Non- Intubated VATS

Anaesthesia management for a non-intubated procedure followed a precise protocol established in the department. Premedication with acetaminophen and dexmedetomidine 0.5 µg/kg was administered 30 to 60 min before the incision. Patients received 2% lidocaine aerosol for 5 min. Regional anaesthesia was performed on admission to the operating room. The practice habits of the department led to a preference for epidural over paravertebral anaesthesia in the NIVATS group. Arterial pressure was monitored invasively in the first three cases. After conditioning, a face mask was placed on the patients, who were positioned in the lateral decubitus position with their participation. Sedation was ensured with remifentanyl and propofol. The anaesthesia team systematically ensured free access to the upper airway in case of emergency conversion to general anaesthesia. Prior to incision, the surgeon and anaesthesiologist reassessed the efficacy of sedation and regional analgesia. At the end of the procedure, sedation was reduced after the chest tube placement, and positive pressure ventilation with a face mask was applied to facilitate lung re-expansion.

2.4 / Postoperative

After the procedure, all patients were directed to the recovery room for postoperative monitoring. If air leakage allowed, the chest tube was removed 2 h after surgery in the recovery room. Patients were discharged to home the day after drain removal. As part of their disease follow-up, pulmonary function tests (PFTs) were performed at 3 months, then every 6 months. Morbidity was defined as the occurrence of a postoperative complication.

2.5 / Data Collection

We collected patient characteristics, perioperative surgical and anaesthetic data, pathological findings, pre- and postoperative respiratory function, and operative outcomes. Data were obtained from patient case notes and electronic patient records, then entered into a dedicated anonymized database (Excel, Microsoft Corp, Redmond, WA). The study was approved by the local ethics committee and Institutional Review Board (No. IRB-MTP_2021_06_202100817). All patients have authorised the use of their data for research purposes.

2.6 | Statistical Analysis

Statistical analyses were performed using R Foundation (Vienna, Austria) and Excel Stat (Microsoft Corp, Redmond, WA). Continuous data are reported as mean with standard deviation (SD) or median with interquartile ranges (IQR), and categorical data are reported as numbers and percentage frequencies, as appropriate. All statistical tests were two-sided, and the confidence intervals were at 95%. The primary outcome was tested using the equality two-sided T-test for independent data and a linear regression model adjusted for the time to postoperative PFT. For binary outcomes, we performed the Chi-square test or Fisher's exact test as appropriate. A p-value of < 0.05 was considered statistically significant. No strategy was implemented to handle missing data.

TABLE 1 | Patients characteristics.

	Overall	Intubated	Non-intubated	<i>p</i>
Number of patient (<i>n</i> , %)	61	35 (57%)	26 (43%)	NS
Age (mean, years)	66.7±8.2	66.3±8.9	67.2±8.4	NS
Gender (<i>n</i> , %)				NS
Male	50 (82%)	28 (80%)	22 (85%)	
Female	11 (18%)	7 (20%)	4 (15%)	
Smoking history	49 (80%)	29 (83%)	20 (77%)	NS
Smoking cessation	40 (66%)	23 (66%)	17 (65%)	
Body mass Index (kg/m ²)	27	27.9	25.8	> 0.05
Blue color (<i>n</i> , %)	29 (46%)	17 (48)	12 (46%)	NS
NYHA (<i>n</i> , %)				NS
I	18 (30%)	10 (29%)	8 (31%)	
II	27 (44%)	14 (40%)	13 (50%)	
III	16 (26%)	11 (31%)	5 (19%)	
IV	0	0	0	
Right biopsy (<i>n</i> , %)	38 (62%)	21 (60%)	17 (65%)	NS
Preoperative oxygen therapy (<i>n</i>)	3 (5%)	1 (3%)	2 (8%)	NS
Preoperative corticosteroid therapy (<i>n</i> , %)	19 (31%)	15 (42%)	4 (15%)	<0.001
Peridural (<i>n</i> , %)	25 (41%)	3 (9%)	22 (85%)	<0.05
Paravertebral block (<i>n</i>)	33 (54%)	29 (83%)	4 (15%)	<0.05
Preoperative FEV ₁ (mean, L)	2.4	2.4	2.5	NS
Preoperative FEV ₁ (mean, %)	87	87	88	NS
Preoperative FVC (mean, %)	84	83	84	NS
Preoperative DLCO (mean, %)	54	53	56	NS

Gap index (score)			
0	2	1	1
1	4	3	1
2	8	7	1
3	19	9	10
4	16	8	8
5	12	7	5

Note: Data are presented as mean. Missing data for PFT: $n=5$.

Abbreviations: BMI, body mass index; DLCO, diffusion for carbon monoxide; FEV₁, forced expiratory volume in 1 s; FVC, forced vital capacity; NYHA, New York Heart Association; PFT, pulmonary function test.

3 | Results

Patient characteristics are described in Table 1. The cohort included 61 patients who underwent lung biopsy for ILD diagnosis between January 2020 and September 2023. Of these, 81% ($n = 50$) were male with a mean age at surgery of 66.7 years. The population studied was relatively severe with a poor prognosis as more than 50% had a GAP index ≥ 4 . The non-intubated VATS technique was performed in 42% of patients ($n = 26$). Pulmonary function tests were performed at a median of 5 months (2.9–4.1) after surgery.

Comparison of the two groups showed similar preoperative characteristics with no significant difference in the evaluated variables, except for regional anaesthesia, body mass index, and preoperative corticosteroid therapy. Patients in the NIVATS group were statistically more likely to receive epidural anaesthesia (84% vs. 8% in the IVATS group, $p < 0.05$), whereas the IVATS group received statistically more paravertebral blocks (83% vs. 15% in the NIVATS group, $p < 0.05$). The presence of preoperative corticosteroid therapy was higher in the IVATS group (43% vs. 15%, respectively, $p < 0.001$). Three (11.5%) patients in the NIVATS group required tracheal intubation after the start of surgery due to epidural anaesthesia failure. These conversions were performed during the early period of our experience, and data were treated in the NIVATS group. There was no conversion to thoracotomy.

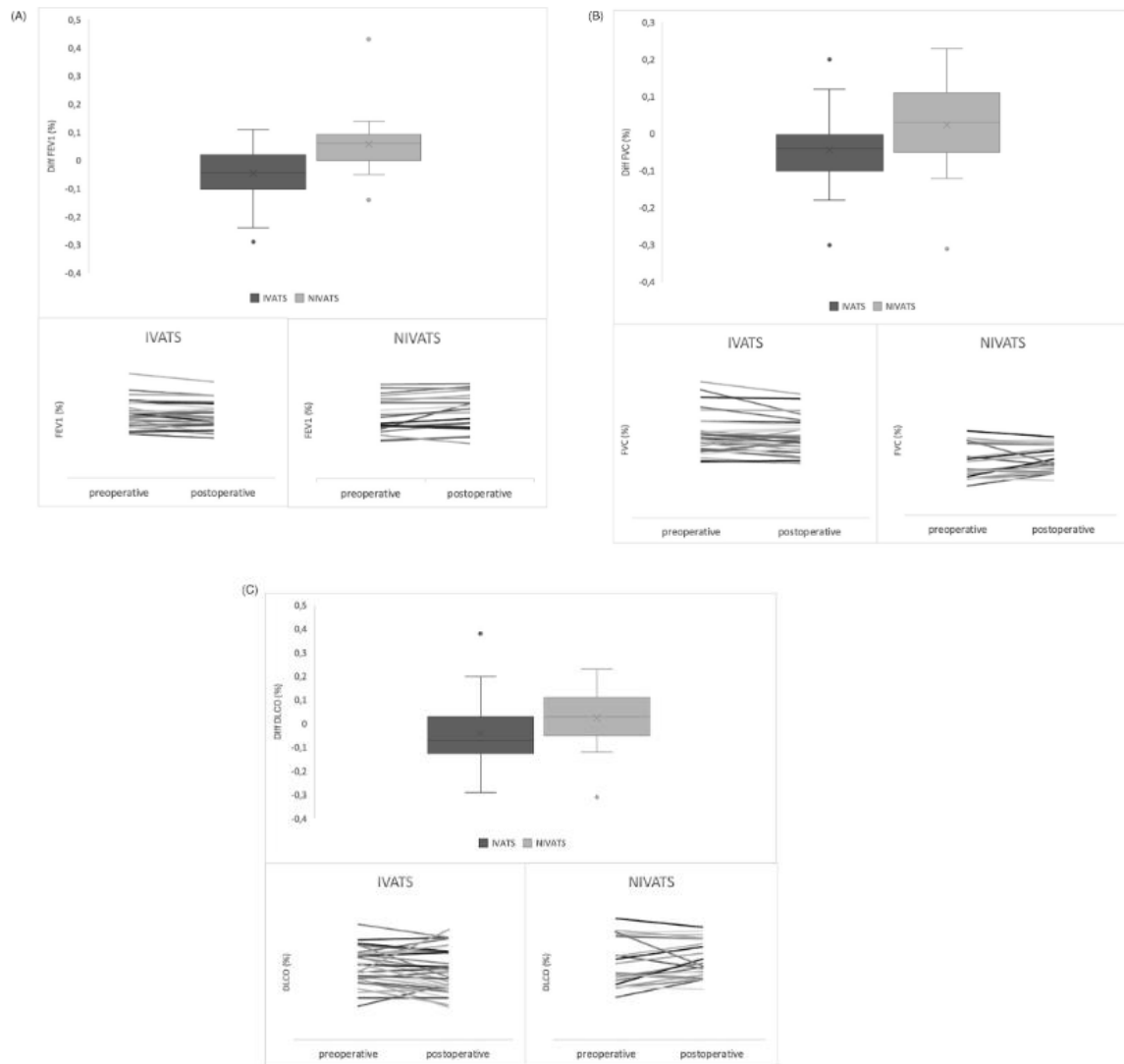


FIGURE 1 | Pre- and postoperative pulmonary function test: Intubated versus Non-intubated VATS lung biopsy comparison. (a) Comparison of FEV₁ variation in the IVATS versus NIVATS Groups ($p < 0.001$). (b) Comparison of FVC variation in the IVATS versus NIVATS Groups ($p < 0.001$). (c) Comparison of DLCO variation in the IVATS vs. NIVATS Groups ($p = 0.08$).

3.1 / Respiratory Function Results

Pulmonary function tests used for the statistical analysis were the most recent available at the date of data extraction (09.21.23), with a median of 5.1 months (2.9–14.1) after surgery. Median time to postoperative PFT was higher in IVATS group (median of 9 months (4.3–20.1)) than in the NIVATS group (median of 3.3 months (2.3–7.5)). Comparison of pre- and postoperative variation in FEV₁ (DiffFEV₁) and FVC (DiffFVC) between the two groups showed a statistically significant difference in favour of the NIVATS group. Specifically, the mean pre-/postoperative change in FEV₁ was significantly higher in the NIVATS group,

with an overall unadjusted mean difference of +10.4% (+253 mL) compared to the IVATS group ($p = 0.001$). In the NIVATS group, FEV 1 variation between the pre and postoperative period was +5.8% (+96 mL, $p = 0.009$), and -4.6% (-157 mL, $p = 0.015$) in the IVATS group (Figure 1a). After adjustment for time to PFT, the difference in favour of the NIVATS group remained statistically significant ($p < 0.01$). Regarding FVC, DiffFVC also showed a statistically significant difference in favour of the NIVATS group. The mean difference was 9.9% (+264 mL) higher in the NIVATS group compared to IVATS ($p = 0.001$). The pre-/postoperative variation was +5.5% (+149 mL, $p = 0.22$) in the NIVATS group, while it decreased by -4.4% (-115 mL, $p = 0.02$) in the IVATS group (Figure 1b). After adjustment for time to PFT, the difference in favour of the NIVATS group remained statistically significant ($p < 0.001$). However, the same analysis for DLCO did not show a statistically significant difference between the two groups ($p = 0.08$) with a mean change of +2.3% in the NIVATS group ($p = 0.04$) versus -4.1% in IVATS group ($p = 0.19$) (Figure 1c), even after a time to PFT adjustment.

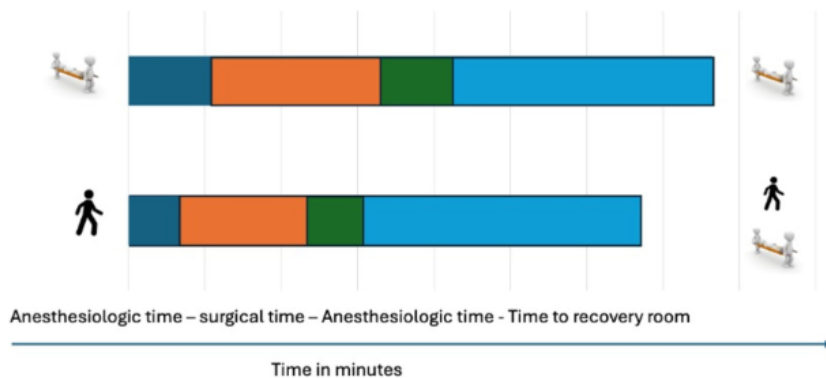


FIGURE 2 | Timeline in the operating room for intubated versus non-intubated group.

3.2 / Postoperative Outcomes

For the entire cohort, the 30-day mortality rate was zero. The overall mortality rate was 1.6% ($N = 1$) at the date of data extraction. In the NIVATS group, one patient died of acute respiratory distress syndrome following severe COVID lung disease 131 days after surgery. The overall morbidity rate was 6.5%. There were fewer postoperative complications in the NIVATS group than in the IVATS group. Compared to the IVATS group, patients in the NIVATS group showed less need for rescue pain therapy (3% vs. 15%, $p = 0.001$), a shorter hospital stay (47.5 h vs. 65.2 h, $p = 0.018$), and shorter operating room time (247 min vs. 288 min, $p = 0.013$) (Figure 2, Table 2). There was no significant difference in chest tube duration between the two groups ($p = 0.8$) with a mean of 17.9 h for the entire cohort (median of 5 h). It should be noted that 29 (47%) patients had chest tube removal within 2 h of surgery, including 15 (52%) in the NIVATS group. The most common diagnosis was usual interstitial

pneumonia (UIP) in both groups. Nine pathologies were unclassifiable in the IVATS group compared to four in the NIVATS group (Figure 3). The diagnostic yield was 88% in the NIVATS group compared with 77% in the IVATS group.

TABLE 2 | Post-operative outcomes between IVATS and NIVATS groups.

	Intubated	Non-intubated	<i>p</i>
Length of hospital stay, mean (h)	65.2	47.5	0.018
Chest tube duration (h)			
Mean	18.5	17.2	0.8
Median	24	2.5	
Post-operative rescue analgesia (<i>n</i> , %)	14 (40%)	1 (3.8%)	0.001
Postoperative complications (<i>n</i> , %)			
Prolonged air leak	0	1	
Surgical revision	1	0	
Pneumothorax requiring chest tube	2	0	
Admission to ICU	1	0	

Abbreviation: ICU, Intensive care unit.

4 | Discussion

In recent years, non-intubated thoracic surgery for lung biopsies related to ILD has evolved significantly, expanding to more complex procedures such as major resections [17–19]. Several studies have demonstrated the feasibility, efficacy, and safety of this technique for ILD biopsies [20–23]. The recent meta-analysis conducted by Patirelis et al. [24] confirms

that NIVATS in this context provides a good diagnostic yield (ranging from 84.6% to 100%) with lower morbidity and mortality compared to intubated surgery. To our knowledge, this study is the first to compare pre- and postoperative respiratory function after lung biopsy for ILD in the IVATS versus NIVATS group. The overall characteristics of the patients align with cohorts found in the literature, comprising a predominantly male smoking population with a mean age of 66.7 ± 8.2 years. However, the characteristics of the NIVATS and IVATS groups were similar in key variables, and the only statistically significant differences were primarily related to the fact that we used very rigorous selection criteria at the beginning of our NIVATS experience ($BMI < 30$). Additionally, the distribution of regional anaesthesia (epidural or paravertebral block) was statistically different because we favoured epidural catheter in the NIVATS group according to our practice habits. Postoperative outcomes were similar to those reported in the literature, with significant improvements in operating room time, hospital stay duration, and a decrease in the need for additional analgesics in the NIVATS group [24–26]. These criteria contribute to accelerated recovery after thoracic surgery, reducing the morbidity of NIVATS procedures, thus confirming the feasibility and safety of this technique in our centre. It should be noted that 85% of patients in the NIVATS group had epidural anaesthesia, likely introducing a bias in the management of postoperative analgesia. Indeed, the need for rescue pain therapy was lower in the NIVATS group. Furthermore, the lack of difference in chest drainage duration, contrary to other studies, can be explained by the shorter drainage duration in both groups in this study (less than 24 h) [27, 28]. In pulmonary surgery, it is recognised that the type of ventilation affects postoperative morbidity [4, 29]. Previous studies showed that the use of mechanical ventilation for acute respiratory failure in ILD is associated with a high mortality [30, 31]. The fear of an acute exacerbation largely limits the indications for surgical biopsy, which is sometimes essential for diagnosis and treatment [14]. Although cryobiopsies have been widely validated to obtain a diagnosis in ILD [32], their routine use remains highly controversial. Several studies have highlighted variable diagnostic concordances and an increased risk of haemorrhagic complications [26, 33–35]. Surgical biopsy is still the gold standard for the diagnosis of ILD. The NIVATS technique avoids complications related to intubation and acute ventilation lung injury caused by mechanical ventilation, as well as the adverse effects related to the accumulation of hypnotic and opioid medications [36]. This study adds additional data regarding the advantages of the NIVATS technique concerning respiratory function. It shows a statistically significant difference in pre- and postoperative FEV 1 and FVC variation in favour of the NIVATS group. Postoperative lung function tests were performed at a median of 287 days, providing sufficient follow-up to rule out immediate postoperative changes. Several factors could contribute to this observation. First, the avoidance of intubation and mechanical ventilation in the NIVATS group potentially reduces the risk of ventilator-induced lung injury and other complications such as barotrauma or volutrauma. Second, a limitation of this study is that the time to postoperative PFT differed between the groups. However, this was counterbalanced by fitting a regression model adjusted for time to PFT, and the adjusted results remained consistent. Third, the use of spontaneous breathing techniques in NIVATS may enhance the maintenance of more physiological respiratory mechanics, leading to improved postoperative lung function recovery [37]. This encouraging conclusion confirms the benefit of the NIVATS technique in ILD patients with impaired respiratory function. We

can presume NIVATS will provide a reliable histologic diagnosis [24] without the risk of exacerbating interstitial pathology. In addition, descriptive analysis of the anatomopathologic results shows a lower rate of unclassifiable pathology in the NIVATS group. This result confirms the quality of surgical biopsy, even without the need for anaesthesia and intubation. Additionally, corticosteroid therapy can reduce lung inflammation in some patients with inflammatory ILD, such as hypersensitivity pneumonitis, sarcoidosis, or nonspecific interstitial pneumonia. This reduction in inflammation can improve DLCO by decreasing damage and thickening of the alveolar walls, facilitating gas exchange [38]. Forty-two percent of the IVATS patients had preoperative corticosteroid therapy compared to 15% of the NIVATS group ($p < 0.001$). This observation may represent a confounding factor in DLCO results. Our study aligns with previous research suggesting the benefits of NIVATS in reducing perioperative respiratory complications and promoting faster recovery of pulmonary function. However, it is important to acknowledge some limitations of our study, including the relatively small sample size and the design. The retrospective nature does not allow for eliminating certain biases, notably selection bias. The NIVATS technique, innovative and under development in our centre, was performed on selected patients. For example, the NIVATS technique was not offered to obese patients, who would probably benefit in terms of postoperative complications without an increase in morbidity [39]. Future studies with larger cohorts, randomisation, and extended follow-up are warranted to confirm these findings and to better understand the long-term implications of non-intubated anaesthesia on pulmonary outcomes. To this end, a randomised trial is currently underway at our centre.

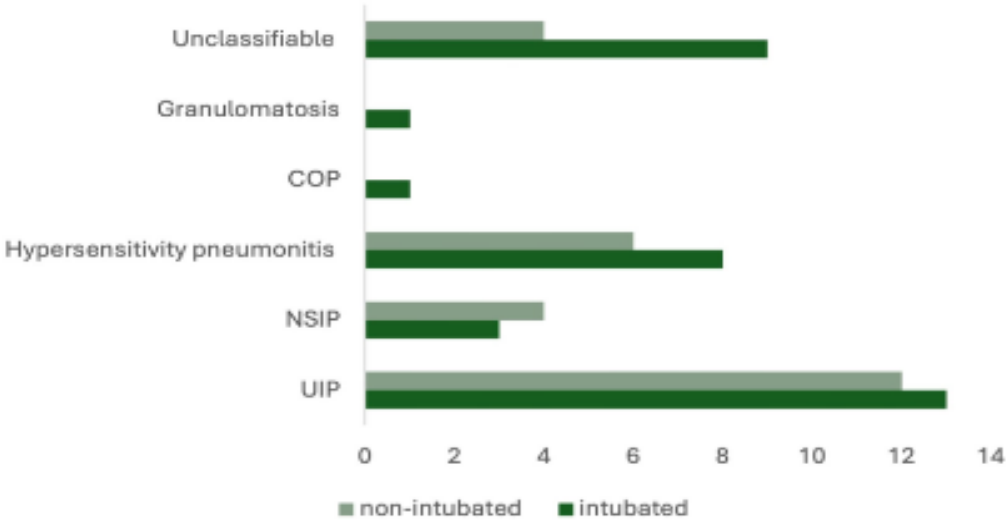


FIGURE 3 | Pathological diagnosis.

In conclusion, intubation in patients undergoing lung biopsy for ILD diagnosis could negatively impact postoperative FEV 1 and FVC. Patients who undergo the NIVATS technique have better postoperative outcomes including respiratory function recovery than those operated on using the IVATS technique. NIVATS appears to be a promising technique

with potentially lower morbidity compared to IVATS. However, larger prospective studies are needed to validate these findings.

Author Contributions

Aude Nguyen: conceptualization (equal), data curation (lead), formal analysis (lead), methodology (equal), project administration (lead), supervision (equal), validation (lead), visualization (lead), writing – original draft (lead), writing – review and editing (lead).
Timothée Jouitteau: conceptualization (lead), data curation (lead), formal analysis (supporting), investigation (lead), methodology (equal), project administration (lead), supervision (lead), validation (lead), visualization (lead), writing – original draft (equal), writing – review and editing (equal).
Arnaud Bourdin: conceptualization (lead), data curation (supporting), formal analysis (supporting), investigation (lead), methodology (lead), project administration (supporting), supervision (lead), validation (lead), visualization (equal), writing – original draft (supporting), writing – review and editing (lead).
Anne- Sophie Gamez: conceptualization (equal), data curation (supporting), formal analysis (supporting), methodology (lead), project administration (supporting), supervision (supporting), validation (lead), visualization (equal), writing – original draft (supporting), writing – review and editing (lead).
Laurence Solovei: conceptualization (supporting), data curation (supporting), formal analysis (supporting), methodology (supporting), project administration (supporting), supervision (supporting), validation (lead), visualization (equal), writing – original draft (supporting), writing – review and editing (lead).
José Molina: conceptualization (supporting), data curation (lead), formal analysis (supporting), project administration (supporting), supervision (supporting), validation (lead), visualization (equal), writing – original draft (supporting), writing – review and editing (lead).
Kheira Hireche: conceptualization (lead), data curation (lead), formal analysis (lead), investigation (lead), methodology (lead), project administration (lead), supervision (lead), validation (lead), visualization (lead), writing – original draft (lead), writing – review and editing (lead).

Ethics Statement

The study was approved by the local ethics committee and Institutional Review Board (No. IRB-MTP_2021_06_202100817). All patients have authorised the use of their data for research purposes.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

References

1. J. Lohser and P. Slinger, "Lung Injury After One-Lung Ventilation: A Review of the Pathophysiologic Mechanisms Affecting the Ventilated and the Collapsed Lung," *Anesthesia and Analgesia* 121, no. 2 (2015): 302–318.
2. J. Lohser, "Evidence-Based Management of One-Lung Ventilation," *Anesthesiology Clinics* 26, no. 2 (2008): 241–272.
3. D. Karalapillai, L. Weinberg, P. Peyton, et al., "Effect of Intraoperative Low Tidal Volume vs Conventional Tidal Volume on Postoperative Pulmonary Complications in Patients Undergoing Major Surgery," *Journal of the American Medical Association* 324, no. 9 (2020): 1–11.
4. C. Ferrando, A. Carramiñana, P. Piñeiro, et al., "Individualised, Perioperative Open-Lung Ventilation Strategy During One-Lung Ventilation (iPROVE-OLV): A Multicentre, Randomised, Controlled Clinical Trial," *Lancet Respiratory Medicine* 12, no. 3 (2024): 195–206.
5. G. Raghu, M. Remy-Jardin, L. Richeldi, et al., "Idiopathic Pulmonary Fibrosis (An Update) and Progressive Pulmonary Fibrosis in Adults: An Official ATS/ERS/JRS/ALAT Clinical Practice Guideline," *American Journal of Respiratory and Critical Care Medicine* 205, no. 9 (2022): e18–e47.
6. P. M. George, P. Spagnolo, M. Kreuter, et al., "Progressive Fibrosing Interstitial Lung Disease: Clinical Uncertainties, Consensus Recommendations, and Research Priorities," *Lancet Respiratory Medicine* 8, no. 9 (2020): 925–934.
7. A. Cilli, C. Kocaturk, K. C. Tertemiz, et al., "Morbidity and Mortality of Surgical Lung Biopsy in the Diagnosis of Usual Interstitial Pneumonia," *ANZ Journal of Surgery* 91, no. 3 (2021): 298–303.
8. J. Pastre, S. Khandhar, S. Barnett, et al., "Surgical Lung Biopsy for Interstitial Lung Disease. Safety and Feasibility at a Tertiary Referral Center," *Annals of the American Thoracic Society* 18, no. 3 (2021): 460–467.
9. J. H. Park, D. K. Kim, D. S. Kim, et al., "Mortality and Risk Factors for Surgical Lung Biopsy in Patients With Idiopathic Interstitial Pneumonia," *European Journal of Cardio-Thoracic Surgery* 31, no. 6 (2007): 1115–1119.

10. M. T. Durheim, S. Kim, B. C. Gulack, et al., "Mortality and Respiratory Failure After Thoracoscopic Lung Biopsy for Interstitial Lung Disease," *Annals of Thoracic Surgery* 104, no. 2 (2017): 465–470.
11. Q. Han, Q. Luo, J. X. Xie, et al., "Diagnostic Yield and Postoperative Mortality Associated With Surgical Lung Biopsy for Evaluation of Interstitial Lung Diseases: A Systematic Review and Meta-Analysis," *Journal of Thoracic and Cardiovascular Surgery* 149, no. 5 (2015): 1394–1401.e1.
12. C. J. Lettieri, G. R. Veerappan, D. L. Helman, C. R. Mulligan, and A. F. Shorr, "Outcomes and Safety of Surgical Lung Biopsy for Interstitial Lung Disease," *Chest* 127, no. 5 (2005): 1600–1605.
13. J. P. Hutchinson, T. M. McKeever, A. W. Fogarty, V. Navaratnam, and R. B. Hubbard, "Surgical Lung Biopsy for the Diagnosis of Interstitial Lung Disease in England: 1997-2008," *European Respiratory Journal* 48, no. 5 (2016): 1453–1461.
14. W. H. Amundson, E. Racila, T. Allen, et al., "Acute Exacerbation of Interstitial Lung Disease After Procedures," *Respirology* 150 (2019): 30–37, <https://doi.org/10.1016/j.rmed.2019.02.012>.
15. M. I. Sigurdsson, H. J. Isaksson, G. Gudmundsson, and T. Gudbjartsson, "Diagnostic Surgical Lung Biopsies for Suspected Interstitial Lung Diseases: A Retrospective Study," *Annals of Thoracic Surgery* 88, no. 1 (2009): 227–232.
16. G. Rossi, P. Spagnolo, W. A. Wuyts, et al., "Pathologic Comparison of Conventional Video-Assisted Thoracic Surgical (VATS) Biopsy Versus Non-Intubated/"Awake" Biopsy in Fibrosing Interstitial Lung Diseases," *Respiratory Medicine* 195 (2022): 106777.
17. C. Pathonsamit, A. Tantraworasin, S. Poopipatpab, and S. Laohathai, "Perioperative Outcomes of Non-Intubated Versus Intubated Video-Assisted Thoracoscopic Surgery in Different Thoracic Procedures: A Propensity Score-Matched Analysis," *BMC Anesthesiology* 22, no. 1 (2022): 154.
18. K. Zhang, H. G. Chen, W. B. Wu, et al., "Non-Intubated Video-Assisted Thoracoscopic Surgery vs. Intubated Video-Assisted Thoracoscopic Surgery for Thoracic Disease: A Systematic Review and Meta-Analysis of 1,684 Cases," *Journal of Thoracic Disease* 11, no. 8 (2019): 3556–3568.
19. G. L. Rosboch, F. Giunta, E. Ceraolo, et al., "Italian Survey on Non-Intubated Thoracic Surgery: Results From INFINITY Group," *BMC Anesthesiology* 22, no. 1 (2022): 2.
20. H. Y. Deng, Z. J. Zhu, Y. C. Wang, W. P. Wang, P. Z. Ni, and L. Q. Chen, "Non-Intubated Video-Assisted Thoracoscopic Surgery Under Loco-Regional Anaesthesia for Thoracic Surgery: A Meta-Analysis," *Interactive Cardiovascular and Thoracic Surgery* 23, no. 1 (2016): 31–40, <https://doi.org/10.1093/icvts/ivw055>.
21. E. Pompeo, P. Rogliani, C. Atinkaya, et al., "Nonintubated Surgical Biopsy of Undetermined Interstitial Lung Disease: A Multicentre Outcome Analysis," *Interactive Cardiovascular and Thoracic Surgery* 28, no. 5 (2019): 744–750.
22. E. Pompeo, P. Rogliani, B. Cristino, O. Schillaci, G. Novelli, and C. Saltini, "Awake Thoracoscopic Biopsy of Interstitial Lung Disease," *Annals of Thoracic Surgery* 95, no. 2 (2013): 445–452.
23. W. M. Hajjar, S. A. Al-Nassar, G. S. Al-Sugair, et al., "Evaluation of Safety and Efficacy of Regional Anesthesia Compared With General Anesthesia in Thoracoscopic Lung Biopsy Procedure on Patient With Idiopathic Pulmonary Fibrosis," *Saudi Journal of Anaesthesia* 12, no. 1 (2018): 46–51.

24. A. Patirelis, S. Elia, B. Cristino, et al., "Spontaneous Ventilation Thoracoscopic Lung Biopsy in Undetermined Interstitial Lung Disease: Systematic Review and Meta-Analysis," *Journal of Clinical Medicine* 13, no. 2 (2024): 374.
25. Y. Wen, H. Liang, G. Qiu, et al., "Non-Intubated Spontaneous Ventilation in Video-Assisted Thoracoscopic Surgery: A Meta-Analysis," *European Journal of Cardio-Thoracic Surgery* 57, no. 3 (2020): 428–437.
26. M. Grott, C. D. Wimmer, M. Kreuter, et al., "Surgical Lung Biopsy for Interstitial Lung Disease: A Two Center Propensity Score Matching Analysis," *Respiration* 101, no. 10 (2022): 910–917.
27. F. Guerrero, L. Costardi, G. L. Rosboch, et al., "Awake or Intubated Surgery in Diagnosis of Interstitial Lung Diseases? A Prospective Study," *ERJ Open Research* 7, no. 3 (2021): 00630-2020.
28. C. S. Jeon, D. W. Yoon, S. M. Moon, et al., "Non-Intubated Video-Assisted Thoracoscopic Lung Biopsy for Interstitial Lung Disease: A Single-Center Experience," *Journal of Thoracic Disease* 10, no. 6 (2018): 3262–3268.
29. E. Marret, R. Cinotti, L. Berard, et al., "Protective Ventilation During Anaesthesia Reduces Major Postoperative Complications After Lung Cancer Surgery: A Double-Blind Randomised Controlled Trial," *European Journal of Anaesthesiology* 35, no. 10 (2018): 727.
30. S. Gaudry, F. Vincent, A. Rabbat, et al., "Invasive Mechanical Ventilation in Patients With Fibrosing Interstitial Pneumonia," *Journal of Thoracic and Cardiovascular Surgery* 147, no. 1 (2014): 47–53.
31. R. Tonelli, S. Grasso, A. Cortegiani, et al., "Physiological Effects of Lung-Protective Ventilation in Patients With Lung Fibrosis and Usual Interstitial Pneumonia Pattern Versus Primary ARDS: A Matched-Control Study," *Critical Care* 27, no. 1 (2023): 398.
32. V. Tzilas, A. Tzouvelekis, J. H. Ryu, and D. Bouros, "2022 Update on Clinical Practice Guidelines for Idiopathic Pulmonary Fibrosis and Progressive Pulmonary Fibrosis," *Lancet Respiratory Medicine* 10, no. 8 (2022): 729–731.
33. A. Bourdin, M. Romagnoli, A. S. Gamez, et al., "Careful Consideration of the Bleeding Caused by Transbronchial Lung Cryobiopsies," *European Respiratory Journal* 55, no. 5 (2020): 1902415.
34. C. Suehs, A. Bourdin, I. Vachier, N. Molinari, and M. Romagnoli, "Transbronchial Cryobiopsy in the Diagnosis of Interstitial Lung Diseases: Methodologies and Perspectives From the Cryo-PID and COLDICE Studies," *Annals of Translational Medicine* 8, no. 20 (2020): 1330.
35. K. A. Kalverda, M. K. Ninaber, L. Wijmans, et al., "Transbronchial Cryobiopsy Followed by As-Needed Surgical Lung Biopsy Versus Immediate Surgical Lung Biopsy for Diagnosing Interstitial Lung Disease (The COLD Study): A Randomised Controlled Trial," *Lancet Respiratory Medicine* 12, no. 7 (2024): 513–522.
36. J. J. Marini, P. R. M. Rocco, and L. Gattinoni, "Static and Dynamic Contributors to Ventilator-Induced Lung Injury in Clinical Practice. Pressure, Energy, and Power," *American Journal of Respiratory and Critical Care Medicine* 201, no. 7 (2020): 767–774.
37. R. Mudannayake, G. Martinez, I. Bello, and M. Gimenez-Milà, "Non-Intubated Thoracic Surgery: A Physiological Approach," *Archivos de Bronconeumología* 59, no. 11 (2023): 699–701.
38. M. Ejima, T. Okamoto, T. Suzuki, T. Anzai, K. Takahashi, and Y. Miyazaki, "Efficacy of Treatment With Corticosteroids for Fibrotic Hypersensitivity

Pneumonitis: A Propensity Score-Matched Cohort Analysis,” *BMC Pulmonary Medicine* 21 (2021): 243.

39. R. Cherchi, P. A. Ferrari, F. Guerrera, et al., “Lung Biopsy With a Non-Intubated VATS Approach in an Obese Population: Indications and Results,” *Frontiers in Surgery* 9 (2022): 829976.