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Efficacy and safety of surgical lung biopsy for interstitial disease. Experience of 161 consecutive patients from a single institution in Italy

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Abstract. *Background:* The role of surgical biopsy for interstitial lung disease (ILD) is controversial, because of possible postoperative morbidity and mortality. We aimed to assess the efficacy and safety of surgical biopsy for ILD. *Methods:* We retrospectively analysed the diagnostic performance and the postoperative complications of 161 consecutive surgical lung biopsy procedures carried out in suspected ILD cases that were undefined after multidisciplinary clinico-radiological evaluation. In 151 cases (93.8%) the biopsy was performed by video-assisted thoracoscopic surgery (VATS), in 6.2% by limited thoracotomy. *Results:* A specific histological diagnosis was obtained in 154 (95.7%) of the surgically biopsied patients, while 4.3% remained histologically unclassified. The predominant histological patterns were granulomatous inflammation (29.8 %), usual interstitial pneumonia/idiopathic pulmonary fibrosis (UIP/IPF) (24.2%), organizing pneumonia (18.6%) and nonspecific interstitial pneumonia (8.1%). The postoperative course was uneventful in 142 cases. In 19 patients (11.8%) we observed postoperative complications, predominantly prolonged air leakage (5.0% of all cases). Thirty-day postoperative mortality was 3.1%, mostly due to acute exacerbation of respiratory insufficiency. Postoperative mortality independently correlated with preoperative need of oxygen therapy (OR, 5.21; 95% CI, 1.19-22.95) and with UIP/IPF histology (OR, 5.67; 95% CI, 1.27-25.25). *Conclusions:* Lung biopsy was performed mostly by VATS, with limited morbidity, and was effective in yielding a specific histological diagnosis in the vast majority of undefined ILD cases. Postoperative mortality was low, predominantly due to exacerbation of respiratory failure in patients with UIP/IPF *(Sarcoidosis Vasc Diffuse Lung Dis 2015; 32: 251-258)*

Key words: interstitial lung disease, idiopathic interstitial pneumonia, surgical lung biopsy, video assisted thoracoscopic surgery, VATS complications

Introduction

The diagnosis of interstitial lung disease (ILD) is initially based on patient history, clinical symptoms and chest radiological imaging. In patients with suspected ILD the chest X-ray findings are generally nonspecific, and conventional computed tomography (CT) imaging of the chest frequently does not yield a confident diagnosis. Therefore, high resolution computed tomography (HRCT) is the investigation of choice (1). Bronchoalveolar lavage (BAL) is also one of the initial procedures for ILD

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diagnosis, but examination of BAL fluid provides additional information that usually does not yield a final diagnosis. Typical BAL cellular profiles however may allow an alternative diagnosis in patients with infection, malignancy or acute exacerbations (2). When clinico-radiological findings and BAL are inconclusive and a definitive diagnosis of the specific type of ILD cannot be established, lung biopsy may be necessary (1).

Typically for usual interstitial pneumonia/idiopathic pulmonary fibrosis (UIP/IPF), and for some other ILD entities, HRCT imaging may be sufficiently characteristic to avert the need for lung biopsy (3-5); this is especially true in a clinical setting where all the suspected ILD cases are evaluated for consensus by an expert multidisciplinary team (6-8).

Transbronchial lung biopsy or transthoracic needle biopsy can be considered as diagnostic options in selected cases, but their role in the ILD diagnosis process remains marginal because tissue samples are often insufficient to yield a precise diagnosis (6,9). Moreover, needle biopsy of the lung is not without complications, such as pneumothorax and haemothorax (10). Recent studies documented that transbronchial cryobiopsy allows to obtain large quantities of lung tissue, and this new technique is currently investigated as an alternative to surgical lung biopsy (11,12). Surgical lung biopsy is currently considered the gold standard for accurate diagnosis of non-IPF/UIP disease, and when clinico-radiological data result in an uncertain ILD diagnosis (6,13,14).

When surgical lung biopsy is deemed necessary in patients with suspected ILD, the approach of choice is by video-assisted thoracoscopic surgery (VATS), a minimally invasive technique that has largely substituted biopsy by conventional limited thoracotomy (6,15-17). While VATS biopsy is generally considered a safe procedure to provides an adequate lung tissue sample for definitive pathologic diagnosis, in compromised ILD patients the risk of complications may be substantial and may outweigh the potential benefits of biopsy (1,17,18).

Therefore patients referred for surgical biopsy must be carefully evaluated for operative risk factors. Nguyen and Meyer recently reviewed the literature and recommendations for optimizing the outcome of surgical lung biopsy for the diagnosis of ILD (19). In this paper we aimed to assess the diagnostic performance and the complication of surgical biopsy for ILD in the experience of 161 consecutive patients from a single institution in Italy.

Methods

The case files of all patients with suspected ILD undergoing surgical lung biopsy between January 1997 and September 2014 at the Center for Thoracic Surgery of the University of Insubria-Varese, Italy were retrospectively analysed. The study cohort, consisting of 161 consecutive patients (men, 57.8%) had mean age of 55 years ± 13.4 standard deviation (SD). In 138 patients (85.7% of cases) the initial diagnosis of ILD was based on clinical symptoms and chest X-ray (CXR) or computed tomography (CT) exams. In 23 cases (14.3%) the diagnosis was incidental, after radiological imaging performed for unrelated reasons. HRCT scan was obtained in 93% of patients, while bronchoscopy with BAL was carried out in all cases. After evaluation of these exams, in the patients of this study a confident specific diagnosis of ILD could not be reached and the indication to perform surgical lung biopsy was given by consensus of our multidisciplinary team including a pulmonologist, a radiologist, a pathologist and a thoracic surgeon.

Surgical lung biopsy

VATS biopsy by lung wedge resection was the technique of choice, generally with three-port access (10-12 mm), under general anaesthesia with double-lumen endotracheal ventilation. The procedures were performed by the same surgical team, with uniform surgical technique over the 17-year period of study. Preferably the biopsy was made in the right lung, as the two pleural fissures facilitate wedge resections. The thoracoscope was initially placed in the 7th or 8th intercostal space in the posterior axillary line, while the other accesses were in the intercostal positions most suitable in each case for lung grasper and endoscopic stapler placement, based on thoracoscopic findings. CT imaging guided the surgeon to sample the active disease areas adjacent to normal lung, avoiding areas of greatest involvement such as advanced honeycombing fibrosis.

For each patient candidate to lung biopsy the following data were recorded: age, sex, smoking history, symptoms at the time of diagnosis, lung function pattern, need of preoperative long-term oxygen therapy (LTOT). The database inherent to the surgical procedure included: length of hospital stay, surgical biopsy technique, biopsy site, number of wedge resections and histopathological diagnosis. Post-operative complications occurring within 30 days from surgery were recorded. To this effect all patients were followed up with a clinical examination after one week from hospital discharge and at 30 days postoperatively. Case files of patients experiencing one or more complications were analyzed to assess the correlation of risk factors with postoperative mortality.

The local Institutional Review Board approved this study.

Outcome definitions

The term "postoperative complication" included: prolonged air leak (> 7 days), wound infection, pleural effusion, acute respiratory failure requiring mechanical ventilation or admission to Intensive Care Unit (ICU), and cardiovascular events.

All complications occurred within 30 days from surgery were grouped and named "morbidity". Mortality was defined as 30-day postoperative death from all causes.

Statistical analysis

Data were expressed as mean value and standard deviation, or range. Differences between proportions were analyzed with chi square test or Fisher exact test. Continuous, normally distributed variables were compared by Student *t* test; variables with non-normal distribution were compared by Mann-Whitney U-test. A p value <0.05 was considered statistically significant. Univariate analysis was performed by logistic regression to identify preoperative risk factors associated with postoperative mortality. Risk factors with p<0.05 significance underwent multivariate analysis. Odds ratio (OR) and 95% confidence interval (CI) were estimated. Statistical analysis was performed using MedCalc 13.2.2 (MedCalc Software, Ostend, Belgium).

Results

Patient characteristics are summarized in Table 1. At the time of hospital admission, 51.3% patients had a history of smoking, with median pack-years of 27 (range: 3-75). Current smokers were 23.4% of cases, former smokers 27.9%, never smokers 48.7%.

Lung function was preoperatively assessed in the 145 patients who could undergo spirometry; among these, normal lung function was found in 48.3%, restrictive pattern in 32.4 %, obstructive in 17.9%, combined obstructive/restrictive pattern in 1.4%. The diffusion lung CO (DLCO) values were available only for 8.7% of patients in our series, therefore we did not asses DLCO mean values.

On admission, 23 patients (14.3%) were on LTOT and 3 patients (1.9%) were pre-operatively admitted to ICU for acute respiratory failure requiring mechanical ventilation.

Surgical procedure

In 154 patients (95.6%) the initial approach for lung biopsy was by VATS. In 7 patients (4.3%) single-lung ventilation was not tolerated, and the procedure started with limited thoracotomy. In all cases the biopsies consisted of lung wedge resections performed with mechanical staplers and were predominantly done in the right lung (80.1%). In the initial 50 patients of our series one biopsy sample only was obtained; thereafter, 2 wedges were made per patient (69% of cases) or 3 wedges (31% of cases). In the 154 cases approached by VATS, 3 (1.9%) were converted to limited thoracotomy because of extensive pleural adhesions, thus lung biopsy was performed by VATS in 151 cases (93.8%) overall. The mean operative time was 58 minutes ± 25 SD, and the mean postoperative stay was 7 days ± 9 SD.

Histology

A specific histological diagnosis was obtained in 154 patients (95.7%). The predominant histological patterns were granulomatous inflammation (29.8 %), UIP/IPF (24.2%), organizing pneumonia (OP) (18.6%) and nonspecific interstitial pneumonia (NSIP) (8.1%). In 7 patients (4.3%) the pathologist made only a descriptive diagnosis, not attributable to a specific disease (Table 1).

Table 1. Demographic data of patients undergoing surgical lung biopsy for interstitial disease, by histological diagnosis

	Histological diagnosis							
	Granulomatous Inflammation n=48 (29.8)	UIP/IPF n=39 (24.2)	OP n=30 (18.6)	NSIP n=13 (8.1)	Pneumoconiosis n=10 (6.2)	DIP n=8 (5.0)	Other[#] n=13 (8.1)	Total n=161
Gender								
Male	29 (60.4)	20 (51.3)	17 (56.7)	8 (61.5)	6 (60.0)	6 (75.0)	7 (53.8)	93 (57.8)
Female	19 (39.6)	19 (48.7)	13 (43.3)	5 (38.5)	4 (40.0)	2 (25.0)	6 (46.2)	68 (42.2)
Mean age, years ± SD	45 ± 11	61 ± 11	59 ± 14	56 ± 13	60 ± 12	59 ± 12	52 + 12	55 ± 13
Main symptom on admission*								
Cough	16 (33.3)	13 (33.3)	9 (30.0)	5 (38.5)	2 (20.0)	4 (50.0)	2 (18.2)	51 (31.9)
Dyspnoea	10 (20.8)	17 (43.6)	8 (26.7)	5 (38.5)	4 (40.0)	2 (25.5)	2 (18.2)	44 (27.5)
Chest pain	5 (10.4)	1 (2.6)	3 (10.0)	1 (7.7)	0	0	0	11 (6.9)
Fever	3 (6.3)	1 (2.6)	5 (16.7)	1 (7.7)	1 (10.0)	0	3 (27.3)	14 (8.7)
Weight loss	2 (4.2)	0	0	0	1 (10.0)	1 (12.5)	0	4 (2.5)
Haemoptysis	0	0	0	0	0	1 (12.5)	2 (18.2)	3 (1.9)
Other symptom	2 (4.2)	2 (5.1)	0	1 (7.7)	0	0	0	5 (3.1)
No symptoms	10 (20.8)	4 (10.3)	5 (16.7)	0	2 (20.0)	0	2 (18.2)	23 (14.4)
Smoking status**								
Never smoker	30 (62.5)	15 (42.9)	13 (43.3)	5 (38.5)	5 (55.6)	3 (37.5)	4 (36.4)	75 (48.7)
Former smoker	7 (14.6)	12 (34.3)	10 (33.3)	6 (46.2)	3 (33.3)	2 (25.0)	3 (27.3)	43 (27.9)
Current smoker	11 (22.9)	8 (22.9)	7 (23.3)	2 (15.4)	1 (11.1)	3 (37.5)	4 (36.4)	36 (23.4)
Lung function pattern**								
Normal	25 (54.3)	12 (35.3)	14 (50.0)	4 (36.4)	5 (55.6)	4 (57.1)	6 (60)	70 (48.3)
Restrictive	11 (23.9)	16 (47.1)	8 (28.4)	5 (45.5)	3 (33.3)	3 (42.9)	1 (10)	47 (32.4)
Obstructive	9 (19.6)	6 (17.6)	6 (21.4)	1 (9.1)	1 (11.1)	0	3 (30)	26 (17.9)
Combined restrictive/ obstructive	1 (2.2)	0	0	1 (9.1)	0	0	0	2 (1.4)
FEV_1[##]	90% ± 18	85% ± 21	93% ± 26	75 ± 34	85 ± 37	84% ± 15	100 ± 18	88 ± 24
Long term oxygen therapy	2 (4.2)	8 (20.5)	4 (13.3)	5 (38.5)	1 (10.0)	1 (12.5)	2 (15.4)	23 (14.3)

Numbers indicate patients, % within parentheses.
SD: standard deviation
*available in 160 patients; ** available in 154 patients, ***available in 145 patients
[#] Other included: Wegener's granulomatosis 2; Langerhans' cell histiocytosis 2; Emphysema 2; Descriptive diagnosis, nonspecific 7, .
[##]available in 144 patients
UIP = usual interstitial pneumonia; IPF = idiopatic pulmonary fibrosis; OP = organizing pneumonia; NSIP= nonspecific interstitial pneumonia; DIP = desquamative interstitial pneumonia

Outcomes

The postoperative course was uneventful in 142 cases (88.2%). In the 19 patients (11.8%) who developed complications (Table 2), the most frequent problem was postoperative air leakage for >7 days, recorded in 8 patients (5.0%). There were no hospital readmissions. Five patients died within 30 days after lung biopsy (acute respiratory failure, 4; myocardial infarction, 1, accounting for 3.1% mortality rate (Table 3). The clinical course of the 5 patients who died was as follows.

Patient 1: 64 year old female who presented at the emergency medicine department with acute onset dyspnea and fatigue, requiring tracheal intubation and ICU treatment with mechanical ventilation. This patient was previously unknown to our hospital and details of her medical history were not available. On admission, HRCT scan showed ILD with large areas of ground glass opacity. Due to unresponsiveness to medical therapy (cortisone, antibiotics), after multidisciplinary consultation VATS lung biopsy was performed. In the early postoperative period the patient's pulmonary function worsened and death ensued from respiratory failure on the 8th postoperative day. Histological diagnosis was : severe UIP.

Patient 2: 74 year old female, with history of arterial hypertension, diabetes, colon diverticulosis and episode of ischemic colitis. She presented at the emergency department with progressive dyspnea,

Table 2. Postoperative complications in 161 surgical lung biopsies

Events	Patients, n (%)*
Prolonged air leak (> 7 days)	8 (5.0)
Acute respiratory failure	4 (2.5)
Wound infection	3 (1.9
Pleural effusion	2 (1.2)
Atrial fibrillation, myocardial infarction	2 (1.2)
Overall postoperative morbidity	19° (11.8)
Mortality (acute respiratory failure, 4; myocardial infarction, 1)	5 (3.1)

* percent of all biopsies
° minor pneumothorax and fever were also recorded in 2 patients

nausea and abdominal pain; her respiratory insufficiency did not respond to medical treatment (cortisone, antibiotics) and she required invasive ventilation in ICU. Chest HRTC showed pulmonary fibrosis with reticular pattern and ground glass areas. VATS lung biopsy was carried out to clarify the diagnosis. Due to exacerbation of respiratory failure, the patient died on the 6th postoperative day. Histological diagnosis was: end stage IPF.

Patient 3: 24 year old male previously treated for testicular cancer (surgery + chemotherapy with cisplatin-etoposide-bleomycin). On presentation the patient was on LTOT because he had developed combined obstructive/restrictive lung dysfunction. He underwent VATS lung biopsy without intraoperative complications. However, on the 4th postoperative day his respiratory conditions rapidly worsened and the patient required mechanical ventilation; he died on the 12th postoperative day from acute respiratory failure, with radiological imaging suggestive of bilateral pneumonia. Histological diagnosis was: pulmonary fibrosis with OP aspects, attributable to bleomycin chemotherapy.

Patient 4: 72 year old male with history of arterial hypertension and diabetes. He had recently undergone diagnostic workup for persistence of dyspnea, and the diagnosis was ILD, suspected IPF. One month later he presented with worsening of dyspnea, fever, productive cough, and was diagnosed with acute respiratory failure and right pneumonia. He did not respond to medical treatment (cortisone, antibiotics) and after one day he required artificial ventilation in ICU. To clarify the diagnosis, VATS lung biopsy was performed, but the patient died on the first postoperative day due to the exacerbation of respiratory failure. Histological diagnosis was: severe ILD, not specified.

Patient 5: 59 year old male with arterial hypertension, on LTOT. He presented with productive cough, chest pain and dyspnea and his lung function tests showed severe restrictive disease and chronic respiratory failure. Chest CT indicated pulmonary fibrosis and multiple lung micronodules; after multidisciplinary team evaluation, VATS lung biopsy was performed. On the 2nd postoperative day the patient

Table 3. Patients who died within 30 days after surgical lung biopsy

Patient	Age	Gender	Lung function tests	Therapy before lung biopsy	ICU*	Postop. day of death	Cause of death	Histological pattern
1	64	F	NA	Cortisone Antibiotics	Yes	8	*Exacerbation of respiratory failure*	UIP
2	74	F	NA	Cortisone Antibiotics	Yes	6	*Exacerbation of respiratory failure*	IPF
3	24	M	Restrictive/obstructive mixed pattern	LTOT, Cortisone Antibiotics Antifungal	No	12	*Exacerbation of respiratory failure due to bleomycin chemotherapy for testicular cancer*	IPF and areas of OP
4	72	M	NA	Cortisone Antibiotics	Yes	1	*Exacerbation of respiratory failure*	Descriptive diagnosis of ILD, non specific
5	59	M	Severe restrictive disease	LTOT	No	2	*Acute myocardial infarction*	NSIP

* Lung biopsy performed in patients undergoing treatment in intensive care unit (ICU)
UIP: usual interstitial pneumonia; IPF: idiopathic pulmonary fibrosis; LTOT: long-term oxygen therapy; OP: organizing pneumonia; ILD: interstitial lung disease; NSIP: non-specific interstitial pneumonia

Table 4. Analysis of mortality risk factors

	OR	95% CI	*p* value
Univariate analysis			
Age (+ 1 year)	1.04	0.98-1.10	0.189
Smoker (yes vs no)	0.46	0.08-2.59	0.380
Gender (male vs female)	0.91	0.23-3.52	0.890
Pre-op LTOT (yes vs no)	5.60	1.38-22.71	0.016
UIP/IPF histology (yes vs no)	7.21	1.71-30.40	0.007
Multivariate analysis			
Age (+ 1 year)	1.03	0.96-1.09	0.416
Pre-op LTOT (yes vs no)	5.21	1.19-22.95	0.029
UIP/IPF histology (yes vs no)	5.67	1.27-25.25	0.023

LTOT = long-term oxygen therapy; UIP = usual interstitial pneumonia; IPF = idiopathic pulmonary fibrosis

developed acute myocardial infarction and died shortly thereafter. Histological diagnosis was: NSIP.

Of the 4 patients who died of acute exacerbation of respiratory disease, 2 had pathologic diagnosis of UIP/IPF, 1 had histological pattern of IPF with areas of OP, 1 had a descriptive nonspecific diagnosis. Notably, 3 of these patients had severe respiratory failure at the time of their surgical lung biopsy, as they were being treated in ICU (Table 3). Unfortunately, lung function test were not available in 3 of the 5 cases with fatal postoperative outcome, because these patients were brought to our attention for the first time as emergency cases with acute respiratory failure, without documentation of previous lung function tests.

As there were only 5 postoperative deaths, the characteristics of survivors and nonsurvivors could not be statistically compared.

Analysis of mortality risk factors

For the following variables we performed univariate analysis to assess the correlation with 30-day postoperative mortality: age, smoking history, gender, preoperative LTOT, restrictive lung function pattern, obstructive pattern, UIP/IPF histology. The latter histological pattern was tested as risk factor because an increased mortality rate was reported following surgical lung biopsy for UIP/IPF (20,21).

Preoperative LTOT and UIP/IPF histology were the only variables with significant correlation ($p<0.05$) at univariate analysis. Multivariate analysis results, shown in Table 4, indicate that postoperative mortality independently correlated with preoperative LTOT (OR, 5.21; 95% CI, 1.19-22.95) and with UIP/IPF histology (OR, 5.67; 95% CI, 1.27-25.25).

Discussion

In spite of increased quality of chest HRCT, of bronchoscopy and of non-surgical biopsy procedures, about one-third of patients with suspected IPF require surgical lung biopsy (SLB) to achieve a confident and specific diagnosis (14,22). It is likely that the repertoire of "classical" clinical and radiological ILD profiles not requiring surgical biopsy will expand in the future; however at this time lung biopsy remains the most effective method for ILD definitive diagnosis in patients with inconclusive clinico-radiological findings (1).

Historically, open thoracotomy was the standard access for lung biopsy in ILD, but this procedure was associated with 20-30% postoperative morbidity and 1.8-70% mortality, depending on the severity of patient condition (23-25).

With the minimally invasive VATS approach to lung biopsy, widely used since the early 1990's (15,16), postoperative pain and distress are significantly reduced compared to open thoracotomy. In addition, the VATS technique offers excellent view of the entire lung parenchyma, allowing to perform targeted biopsies. Only rarely the initial VATS approach needs to be converted to mini-thoracotomy, due to extensive pleural adhesions or stiff lung. VATS conversion occurred in 1.9% of our ILD biopsies, and in 1.5%-20% of cases reported in the literature (26,27). In our experience the contraindication to VATS lung biopsy arose in few patients (4.3%), who could not have the endotracheal double-lumen ventilation tube correctly positioned or did not tolerate single lung ventilation. In such cases a muscle-sparing mini-thoracotomy was made to rapidly complete lung biopsy. In our series of 151consecutive VATS biopsies, the 30-day postoperative morbidity rate (11.8%) was consistent with the average complication rate of 9.6% (range: 2-25%) reported in the last decade series (19). Prolonged air leak was the commonest postoperative complication (5.0%), reflecting the prevailing frequency of this problem after VATS procedures (28). The postoperative mortality rate in our cohort was 3.1%, within the range reported in the ILD literature for VATS lung biopsy. Due

Table 5. Outcomes of surgical lung biopsy for interstitial lung disease

Authors	Patients, n	Rate of VATS conversion to thoracotomy	30-day mortality	Postop. morbidity	Diagnostic yield
Zegdi et al, 1998 (32)	64	15.6%	4.7%	10.9%	92%
Rena et al, 1999 (27)	58	1.7%	0%	3.4%	86%
Lettieri et al., 2005 (33)	83	n.s.	4.8%	8.4%	100%
Kreider et al, 2007 (21)	68	n.s.	4.4%	19%	76.5%
Sigurdsson et al., 2009 (34)	73	10.7.	2.7%	16%	81%
Fibla et al, 2012 (17)	311	8.7%	10.6%	11.5%	74.6%
Fibla et al., 2012 (28)	224	n.s.	0%	5.4%	87%
Present study, 2014	161	1.9%	3.1%	11.8%	95.7%

VATS= video-assisted thoracoscopic surgery; n.s.=not specified

to different patient selection criteria, very likely the proportion of severely compromised patients undergoing surgical lung biopsy varied widely among the published series, as suggested by the different postoperative mortality rates ranging from 0% (27,28) to 10.6% (17) (Table 5).

The results obtained from our experience of surgical lung biopsies confirm the value of this procedure for ILD diagnosis. In agreement with other literature reports, we observed a high diagnostic yield (95.7%) of VATS lung biopsy for ILD, and low perioperative morbidity and mortality.

In our series the most frequent histological diagnoses were granulomatous inflammation (29.8%) and UIP/IPF (24.2%), reflecting the prevalence of these interstitial diseases in the Italian RIPID registry (29) and in other European registries (30). A high diagnostic efficacy of surgical biopsy for ILD, ranging from 74.6% to 100 %, was reported by most literature studies on this subject (Table 5); only one study recorded a markedly lower rate (42%) of definitive specific diagnoses (18). It must be noted that a recent study reported unclassifiable ILD after multidisciplinary review in 10% of an ongoing longitudinal cohort of 1370 patients (31). Focusing on risk factors that may assist in deciding whether surgical lung biopsy for ILD is justified, we found that postoperative mortality independently correlated with respiratory illness requiring oxygen therapy preoperatively, and with UIP/IPF histology.

Studies have been carried out to identify a subgroup of ILD patients at particularly high risk of postoperative complications. For predicting mortality after surgical lung biopsy, a simple aggregate risk score of individual patient parameters has been developed; this can be used to evaluate the procedure risk/benefit ratio (17).

Our study has limitations, as it is retrospective and the clinical outcome indicators in our surgical lung biopsy series are biased by patient selection. In fact it has been our multidisciplinary group's policy to exclude surgical lung biopsy in patients with end-stage disease or with severe co-morbidities, as the risk of complications from the biopsy procedure may outweigh the potential benefits (1,18). Strong points in our study are the management of lung biopsy by the same team, with uniform surgical technique over a long period, and the consecutive series of patients examined. Many clinicians are reluctant to refer patients for surgical lung biopsy, as they are uncertain whether the benefits outweigh the risks of the procedure. The 2005 report of the Italian register for infiltrative lung disorders showed that in the 79 surveyed centers surgical lung biopsy was performed on average in 20.3% of ILD cases (29), a rather high proportion that likely reflects patient selection in participating centres. In everyday clinical practice of our institutional experience however the proportion of ILD cases undergoing surgical biopsy is only 10-15%, as reported also by others in Italy (12).

In conclusion, in our experience lung biopsy was predominantly carried out by VATS and was especially useful in ILD cases with undefined clinical and radiological characteristics, achieving a specific histological diagnosis in the vast majority (95.7%) of undetermined interstitial diseases. Lung biopsy was carried out with low postoperative morbidity and mortality in ILD patients who were not overly ill. Our results confirm that in order to optimize the outcome of surgical biopsy for the specific diagnosis of ILD, this procedure should be performed only exceptionally in patients with critical respiratory illness, as postoperative mortality risk in these subjects is exceedingly high.

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