scientific reports

Check for updates

OPEN

Optimizing tissue sampling during medical pleuroscopy for diagnosis of malignant pleural effusion due to lung cancer

Irene Lojo-Rodríguez[1,2], Maribel Botana-Rial[3]✉, Ana González-Piñeiro[4], Enrique Cases-Viedma[5], Almudena González-Montaos[1], Cristina Ramos-Hernández[1], Manuel Nuñez-Delgado[1] & Alberto Fernández-Villar[3]

Cryobiopsy has emerged in recent years as a tool of growing interest in the diagnosis of non-small cell lung cancer (NSCLC). We first conducted the study with the primary objective to compare the quality of cryobiopsies versus conventional forceps biopsies, including diagnostic yield and the feasibility of histological characterization and molecular testing, of malignant pleural effusion (MPE). Prospective study including 14 caucasian patients with MPE due to NSCLC who underwent semirigid pleuroscopy with cryobiopsies. The median biopsy size for conventional flexible forceps and cryoprobe was 2.5 mm (1.5–3.2 mm) and 5.5 mm (3.8–7.6 mm), respectively ($p = 0.07$). The number of biopsies also differed: flexible forceps: 5 (4–6.25) biopsies vs cryoprobe: 3 (3–4) biopsies($p = 0.01$). The tumor/non-tumor ratio in the conventional forceps sample was 2.4 (1.2–5.9), while in the cryoprobe sample, it was 3.6 (1.2–10) ($p = 0.09$). Only in one case, the samples obtained during semirigid pleuroscopy were insufficient for molecular diagnosis. The incorporation of cryobiopsy into semirigid pleuroscopy has been demostrated to be a effective and safe diagnostic tool. This technique could shortening procedure time and facilitating tissue collection without increasing procedural risks.

Keywords Biomarker, Diagnostic, Cryobiopsy, Semirigid pleuroscopy, Histology, Pathological finding

Lung adenocarcinoma is the most common cause of malignant pleural effusion (MPE), representing an advanced disease at the time of diagnosis[1,2]. In order to improve the prognosis of patients; a complete characterization of the tumor needs to performed, with the determination of all the molecular alterations that can be targeted by novel therapies. Therefore, using a biopsy method that provides safe and adequate lung tissue sampling is very imporantant. Medical pleuroscopy is the main procedure for the diagnosis of MPE[1,2].

Cryobiopsy has emerged in recent years as a tool of growing interest in the diagnosis of non-small cell lung cancer (NSCLC)[3,4]. Two recently published systematic reviews, about the diagnostic yield and safety of pleural cryobiopsy during medical thoracoscopy to diagnose pleural effusion, one of them by our group, demonstrated that it is a safe and effective technique[5,6]. Early studies, which included a small number of patients, showed that pleural cryobiopsy had a high diagnostic yield, in some cases to 100%[7–10]. Another aspect of increasing interest is going be that the obtained samples may also allow for the molecular characterization of the tumor. So far, only two publications have analyzed this aspect[8,10]. A limitation of both studies were that only a single specific molecular determination was performed on the samples obtained with the cryoprobe, specifically the *EGFR* gene mutation.

Optimizing the diagnosis of lung cancer represents a challenge, as well as a necesary, for improving the low survival of patients with MPE. When performing semirigid pleuroscopy and comparing it with rigid pleuroscopy, a greater number of biopsies is required to achieve a diagnosis due to the small size of the forceps[2].

[1]Pulmonary Department, PneumoVigoI+I Research Group, Alvaro Cunqueiro Hospital, Sanitary Research Institute Galicia Sur (IISGS), Vigo, Spain. [2]Predoctoral Student of Santiago de Compostela University, A Coruña, Spain. [3]Pulmonary Department, PneumoVigoI+I Research Group, Alvaro Cunqueiro Hospital, Sanitary Research Institute Galicia Sur (IISGS), CIBERES-ISCIII, Street Clara Campoamor, 341, 36312 Vigo, Spain. [4]Pathology Department, PneumoVigoI+I Research Group, Alvaro Cunqueiro Hospital, Sanitary Research Institute Galicia Sur (IISGS), Vigo, Spain. [5]Pulmonary Department, Hospital Universitario y Politécnico La Fe, Valencia, Spain. ✉email: maria.isabel.botana.rial@sergas.es

In the era of personalized medicine, molecular diagnosis is especially relevant, making it essential to improve biopsy techniques. Therefore, we first conducted the study with the primary objective to compare the quality of cryobiopsies versus conventional forceps biopsies, including diagnostic yield and the feasibility of histological characterization and molecular testing, of MPE due to NSCLC.

Results

Data from 19 patients who underwent semirigid pleuroscopy with conventional forceps and cryoprobe biopsies were analyzed. The baseline characteristics of the patients are shown in Table 1.

Regarding the procedural characteristics, the drainage amount (ml) was 1900 ml (1050–2400).

The pleural abnormalities found during pleuroscopy were: plaques in 12 patients (63.2%), nodules in 2 patients (10.5%) and polyps in 5 patients (26.3%). The duration of subsequent chest drainage (days) was 3 (2–3) days and the length of stay after the procedure (days) was 6 (4–10) days.

The dose of sedative drugs used during the procedure was 6 (5–7) micrograms of midazolam and 100 (50–100) micrograms of fentanyl. The 30-day mortality was 2 cases (10.5%), and the overall survival was 4.5 (2–31.5) months.

There not were severe complications observed during the procedure, nor minor bleeding that required hemostatic control. Pain was reported in 2 patients (10.5%).

The patients with MPE due to NSCLC included in the study were 14 cases. The Table 2 presents some of their clinical, histological, and TNM characteristics.

In this group, the median biopsy size for conventional flexible forceps and cryoprobe was 2.5 mm (1.5–3.2 mm) and 5.5 mm (3.8–7.6 mm), respectively ($p = 0.07$). The number of biopsies also differed: flexible forceps: 5 (4–6.25) biopsies vs cryoprobe: 3 (3–4) biopsies($p = 0.01$). The percentage of viable tumor in samples obtained by flexible forceps and cryoprobe was 55% (15–80%) and 55% (10–80%), respectively ($p = 0.9$). The tumor/

Characteristics	Value
Age (year)	68 (63–789)
Sex	
Female	6 (31.6%)
Male	13 (68.4%)
Smoking status	
Current smoker	6 (31.6%)
Ex-smoker	7 (36.8%)
Non-smoker	6 (31.6%)
Smoking (pack-year)	29 (0–40)
ECOG ≥ 2	4 (21.1%)
LDH < 1500 (UI/L)	4415 (242.2–885.2)
NLR < 9	16 (84.2%)
NLR (median)	4.4 (2.9–5.8)
Etiology	
Lung cancer	14
Lung adenocarcinoma	13 (68.4%)
Lung large cell carcinoma	1 (5.3%)
Others cancer	5
Breast cancer	2 (10.5%)
Mesothelioma	1 (5.3%)
Ovarian	1 (5.3%)
Sarcoma	1 (5.3%)
Radiological characteristics	
Pleural effusion size chest radiograph	
Massive (˃2/3)	9 (47.4%)
Medium	8 (42.1%)
Small (≤ 2/3)	2 (10.5%)
Findings in CT	
Nodal thickening	10 (52.6%)
Circumferential thickening	2 (10.5%)
Pleural masses	2 (10.5%)
No pleural thickening	5 (26.3%)

Table 1. Baseline characteristics. Definition of abbreviation = Eastern Cooperative Oncology Group (ECOG), High lactate dehydrogenase (LDH), Neutrophil-to-lymphocyte ratio (NLR), Computed tomography (CT).

Patient	Age (years)	Sex	Histology	TNM
1	69	Male	ADC	T3N0
2	65	Male	ADC	T3N1
3	65	Male	ADC	TxN0
4	78	Female	ADC	T3N2
5	79	Male	ADC	TxN0
6	60	Male	ADC	T4N3
7	63	Male	ADC	TxN3
8	80	Male	ADC	T4N3
9	73	Male	ADC	T1N3
10	70	Female	ADC	T2aN2
11	63	Male	ADC	T4N0
12	68	Male	ADC	TxN1
13	61	Male	Large cell carcinoma	T1N2
14	60	Male	ADC	TxN0

Table 2. Clinical, histological, and prognostic characteristics of patients with malignant pleural effusion due to NSCLC. Definition of abbreviation = Adenocarcinoma (ADC).

non-tumor ratio in the conventional forceps sample was 2.4 (1.2–5.9), while in the cryoprobe sample, it was 3.6 (1.2–10) ($p = 0.09$).

In all patients, a morphological and immunohistochemical diagnosis was possible using both conventional forceps and cryoprobe biopsies. Only in one case, the samples obtained during semirigid pleuroscopy with both cryoprobe and forceps were insufficient for molecular diagnosis, requiring a surgical video-assisted thoracoscopic surgery. In this case, the pleuroscopy revealed plaque-like lesions.

Discussion

Our study is the first published Spanish study to analyze the quality of cryoprobe obtained samples to optimize the molecular diagnosis of MPE due to NSCLC. When pleural biopsies were obtained using a cryoprobe, although there were no differences in the percentage of viable tumor cells, the sample size was significantly larger, as was the tumor/non-tumor ratio.

A difference between semi-rigid and rigid pleuroscopy is the size and flexibility[1,2]. Although the semirigid pleuroscope is more manageable than the rigid one, its smaller diameter limits the ability to obtain larger biopsies, potentially affecting the amount of tissue available for molecular studies. Furthermore, its lower rigidity can make biopsy collection more challenging.

In a small study conducted by our group on the diagnostic performance of semirigid pleuroscopy for the molecular characterization of MPD due to NSCLC, molecular testing was performed in 14 adenocarcinomas. Sufficient and adequate material was obtained to determine *EGFR* mutation status in 100% of cases, but only in 90% of cases for ALK translocation[11]. *EGFR* mutations were identified in two patients, while no cases of *ALK* translocation were detected. *EGFR* mutation detection was possible in all cases, but the yield for *ALK* translocation analysis was lower[11]. Many revolutionary advances have recently been made in the management of NSCLC. There have been a number of approvals of molecular-targeted therapy for subgroups of NSCLC patients with sensitizing *EGFR, ALK, ROS1, RET, BRAF V600E, MET,* or *NTRK* alterations[12]. In addition to genetic examination, NSCLC are usually subjected to the analysis of PD-L1 protein expression in order to direct the use of immune checkpoint inhibitors[12,13].

Cryobiopsy, a relatively novel bronchoscopic technique, has gained prominence in recent years due to its ability to procure larger, higher-quality tissue samples with fewer crush artifacts compared to traditional forceps biopsies[3–5]. This method has demonstrated promising diagnostic yields in lung cancer[3].

However, none of the published studies on MPE and lung cancer have primarily focused on analyzing the effectiveness of pleural cryobiopsies for mutation studies and other molecular alterations. In studies where this aspect was analyzed secondarily, only *EGFR* gene mutations had been investigated[8,10]. In one study including 14 cases of MPE, four of which were lung adenocarcinomas, obtaining pleural biopsies with a cryoprobe allowed DNA isolation for *EGFR* mutation analysis in all samples using a commercially available kit[8]. In another study, samples were valid for *EGFR* mutation testing, but these results were not compared with the molecular diagnostic yield of biopsies obtained using conventional forceps[10].

Another study conducted in an Asian population included six patients with NSCLC, all of whom underwent genetic panel testing to detect driver gene mutations. Sufficient specimens were obtained for appropriate genetic analysis in all cases[14]. However, a limitation of this study was the lack of specification regarding which molecular alterations were analyzed. In our study, all the necessary molecular analyses, including PDL1 expression, were successfully performed. Regarding the molecular alterations identified, three patients presented a specific mutation in the *EGFR, BRAF*, and *KRAS* genes, respectively. Only two patients showed a PD-L1 expression greater than 50%.

However, the diagnostic yield for medical thoracoscopy in MPEis very hight (91–99%). Importantly, it has been proven to be safe procedure, morbidity (1.8%) and mortality (0.3%) rates are low[2,15,16]. The results represent

evidence for comparative diagnostic yields of the semi-rigid and rigid thoracoscopy for pleural effusions of unknow aetiology[2,17,18]. There is ongoing debate regarding the ideal instrument for pleuroscopy[19]. Bansal S et al. compared rigid mini-thoracoscopy with semirigid thoracoscopy and found that biopsy size was larger in the mini-thoracoscopy group (16.1 ± 4.5 mm vs. 8.3 ± 2.9 mm; $p < 0.001$)[20]. However, the diagnostic yield of pleural biopsy was similar between the two groups.

When comparing rigid versus semirigid thoracoscopy, differences have been observed. In 2016, Wurps H et al. conducted a prospective study with 80 patients to compare parietal pleural biopsies obtained using rigid forceps, flexible forceps, and a cryoprobe during pleuroscopy[21]. Rigid biopsies were significantly larger than both cryobiopsies and flexible biopsies ($p < 0.001$), while cryobiopsies were significantly larger than flexible biopsies ($p < 0.01$). The diagnostic yield of cryobiopsies was lower than that of rigid biopsies but not inferior to flexible biopsies[22]. In our study, although the tumor percentage was similar in both biopsy types, cryobiopsies were larger, and fewer samples were required with cryobiopsy.

It is important to consider that tissue remains the standard material for NSCLC diagnosis, and there is a continuous search for new molecular markers in MPE, with the primary limiting factor being the availability of viable samples.

Studies comparing the diagnostic yield of cryobiopsy by radial endobronchial ultrasound with that of conventional biopsy have shown that cryobiopsy improves diagnostic yield and obtains larger samples in patients with peripheral pulmonary lesions due to lung cancer[22,23].

As discussed earlier, the main limitation of semirigid pleuroscopy is the small sample size, which necessitates obtaining more biopsies. Additionally, when using flexible forceps, it can be difficult to biopsy lesions located tangentially to the instrument[1,2,5]. However, a notable advantage of the semirigid pleuroscope is that it is a less complex procedure compared to the rigid pleuroscopy, making it a favorable option for Interventional Pulmonology Units. The incorporation of cryobiopsy into semirigid pleuroscopy could reduce the number of biopsies required, thereby shortening procedure time and facilitating tissue collection without increasing procedural risks.

Pleural cryobiopsy has been shown to be a technique with a low complication rate, as reported in recent systematic reviews on its efficacy and safety[5,6]. In our study, despite performing biopsies with both a cryoprobe and conventional flexible forceps, no major complications were observed, nor were there increases in hospital stays or chest drainage duration. These findings are consistent with those reported in the literatura[24].

An additional consideration is the cost: while both techniques showed comparable diagnostic yield, conventional forceps are less expensive than the cryoprobe. This economic factor should be taken into account in clinical decision-making.

The primary limitation of this study is the small number of patients with MPE due to NSCLC, although it is the first study conducted in a Caucasian population for this purpose. Additionally, as previously mentioned, this is an innovative technique that will require further standardization for integration into clinical practice. Incorporating this technique into semirigid pleuroscopy could enhance procedural methodology, but it would be of interest to analyze the number of biopsies required to achieve a specific molecular diagnosis and the time spent with conventional biopsies and cryobiopsies, as this could reduce the procedure time, and do so without increasing complication rates.

Pleural cryobiopsy has been demonstrated to be a safe and effective diagnostic tool during semirigid pleuroscopy, providing adequate samples for all molecular testing and for the histological characterization of patients with MPE due to lung cancer.

Methods

Study population

Prospective study including all patients with a diagnosis or high suspicion of MPE due to NSCLC who underwent semirigid pleuroscopy with cryobiopsies between November 1, 2019, and November 30, 2024, at the Bronchopleural Techniques Unit of Hospital in Spain. The present work corresponds to the CRIOPLEURA study.

The inclusion criteria were: age > 18 years; caucasian population and patients with MPE due to NSCLC confirmed by cytology or histology.

Exclusion criteria included were: patients with benign pleural effusion; patients with paramalignant pleural effusion without evidence of malignant cells in the pleural cavity; other etiologies different from MPE and contraindication for pleural biopsy.

Semirigid pleuroscopy procedure and pleural biopsy

All procedures were performed according to clinical practice guideline recommendations[2,15]. Pleuroscopy was conducted under aseptic conditions in the endoscopy suite, with the patient under spontaneous respiration, conscious sedation (midazolam ± fentanyl), and local anesthesia (2% mepivacaine). The semirigid pleuroscope (LTF-160 autoclave, Olympus, Tokyo, Japan) was used for the procedures. Ultrasound was performed on all patients before trocar insertion to determine the entry point. The pleural fluid was drained at the beginning, and the pleural cavity was inspected under direct visualization. All pleural biopsies were performed on parietal pleural lesions. Before biopsy collection, 5 ml of 2% lidocaine was applied under direct visualization through the working channel of the pleuroscope to the selected area. Initially, 4 to 8 pleural biopsies were taken using flexible conventional forceps (biopsy forceps with an external diameter of 1.9 mm (Olympus EndoJaw FB-231D Disposable Biopsy Forceps (Oval Fenestrated, SwingJaw). Subsequently, biopsies were collected using a flexible cryoprobe (ERBOCRYOCA, ERBE, Tübingen, Germany) with an external diameter of 1.7 mm (2 to 5 biopsies). The probe tip, which froze tissue using CO_2 gas, was placed on the lesion and frozen for 5–7 s. The adhered sample was then extracted.

Samples obtained by both conventional forceps and cryoprobe were placed in separate formalin containers and sent to the Pathology Department for histological analysis. Following the procedure, a 24Fr chest drain was placed.

Study variables

The following variables were recorded: epidemiological characteristics of patient (age, sex, smoking history), functional characteristics (general health status using the ECOG performance scale), radiological characteristics (size of pleural effusion on chest radigraphic, and characteristics of pleural lesions and/or thickening on CT).

Others variables were also analyzed as tumor classification: Histological tumor type and TNM classification[25] at the time of DPM diagnosis or at the time of primary tumor diagnosis in cases of disease progression.

The prognostic and survival variables were the predictive variables from the LENT prognostic scale[26]. We recorded the 30-day mortality rate and overall survival.

The procedure-related variables were: volume of pleural fluid drained, pleural findings during pleuroscopy, duration of chest drainage (days) and the length of hospital stay (days).

About the procedure safety, we classified bleeding complications as follows: mild (self-limiting), moderate (requiring topical vasoconstrictors such as adrenaline) and severe (requiring intervention with electrocautery or argon plasma). Other complications, including pain.

We analized the diagnostic yield and molecular analysis as follows: comparison of histological diagnostic yield between cryobiopsy and conventional forceps biopsies. The pathological findings in both biopsy samples, including: number, sample size (mm) and percentage of viable vs. non-viable tumor cells. To determine the proportion of viable and non-viable tumor cells, the evaluation was carried using standard pathological techniques, and the percentage of viable tumor cells was recorded. The results of molecular studies were also analyzed (detection of genomic alterations *EGFR, ROS1,BRAF, ALK, RET, MET, NTRK* and PD-L1 expression).

Ethical aspects

The study was conducted following the Helsinki Declaration guidelines. The data were pseudonymized for biomedical research purposes. The study has been approved by the provincial research Ethics Committee of Galicia (Pontevedra-Vigo-Ourense code: 2019/293). All participants provided written informed consent to participate in this study and to allow the publication of their data and sample results.

Statistical analyses

Categorical variables were presented as counts and percentages, and continuous variables were presented as mean and standard derivation (SD). Statistical analyses were performed using SPSS Statistic 21 (IBM Corp., Armonk, NY). Pearson's chi-square or Fisher exact test was used to compare proportions, as appropriate. For continuous data, differences between groups were determined using Students t-test or Mann–Whitney U test for parametric or non-parametric data, respectively. $p < 0.05$ was considered statistically significant.

Data availability

The datasets used and/or analysed during the current study available from the corresponding author (maria.isabel.botana.rial@sergas.es) on reasonable request.

Received: 11 July 2025; Accepted: 19 September 2025
Published online: 27 October 2025

References

1. Kapp, C. M. & Lee, H. J. Malignant pleural effusions. *Clin. Chest Med.* **42**, 687–696 (2021).
2. Avasarala, S. K., Lentz, R. J. & Maldonado, F. Medical thoracoscopy. *Clin. Chest Med.* **42**, 751–766 (2021).
3. Simon, M., Simon, I., Andrei Tent, P., Adina Todea, D. & Haranguș, A. Cryobiopsy in lung cancer diagnosis—A literature review. *Medicina* **19**(57), 393 (2021).
4. Botana-Rial, M. et al. Is the diagnostic yield of mediastinal lymph node cryobiopsy (cryoEBUS) better for diagnosing mediastinal node involvement compared to endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA)? A systematic review. *Respir. Med.* **218**, 10738 (2023).
5. Rial, M. B. et al. Diagnostic yield and safety of pleural cryobiopsy during medical thoracoscopy to diagnose pleural effusion. A systematic review and meta-analysis. *Arch. Bronconeumol.* **56**, 784–791 (2020).
6. Shafiq, M. et al. Pleural cryobiopsy: A systematic review and meta-analysis. *Chest* **157**, 223–230 (2020).
7. Thomas, R. et al. Pleuroscopic cryoprobe biopsies of the pleura: A feasibility and safety study. *Respirology* **20**, 327–332 (2015).
8. Rozman, A., Camlek, L., Marc Malovrh, M., Kern, I. & Schönfeld, N. Feasibility and safety of parietal pleural cryobiopsy during semi-rigid thoracoscopy. *Clin. Respir. J.* **10**, 574–578 (2016).
9. Pathak, V., Shepherd, R. W., Hussein, E. & Malhotra, R. Safety and feasibility of pleural cryobiopsy compared to forceps biopsy during semirigid pleuroscopy. *Lung* **195**, 371–375 (2017).
10. Tousheed, S. Z. et al. Cryobiopsy of the pleura: An improved diagnostic tool. *J. Bronchol. Interv. Pulmonol.* **25**, 37–41 (2018).
11. Botana-Rial, M., Mouronte-Roibás, C., González-Piñeiro, A. & Fernández-Villar, A. Rendimiento diagnóstico de la toracoscopia semirrígida para la caracterización molecular de derrames pleurales malignos de origen pulmonar. *Arch. Bronconeumol.* **54**, 489–491 (2018).
12. Alexander, M., Kim, S. Y. & Cheng, H. Update 2020: Management of non-small cell lung cancer. *Lung* **198**, 897–907 (2020).
13. Alduais, Y., Zhang, H., Fan, F., Chen, J. & Chen, B. Non-small cell lung cancer (NSCLC): A review of risk factors, diagnosis, and treatment. *Medicine* **102**, e32899 (2023).
14. Kamatani, M. et al. Diagnostic yields and safety of thoracoscopic cryobiopsies in Japan: A single-center retrospective observational study. *Respir. Investig.* **62**, 617–622 (2024).
15. Shaikh, F., Lentz, R. J., Feller-Kopman, D. & Maldonado, F. Medical thoracoscopy in the diagnosis of pleural disease: A guide for the clinician. *Expert Rev. Respir. Med.* **14**, 987–1000 (2020).
16. So, M., Chaddha, U., Shojaee, S. & Lee, P. Medical thoracoscopy for pleural diseases. *Curr. Opin. Pulm. Med.* **30**, 84–91 (2024).

17. Yap, K. H., Phillips, M. J. & Lee, Y. C. G. Medical thoracoscopy: Rigid thoracoscopy or flexi-rigid pleuroscopy?. *Curr. Opin. Pulm. Med.* **20**, 358–365 (2014).
18. Rozman, A., Camlek, L., Marc-Malovrh, M., Triller, N. & Kern, I. Rigid versus semi-rigid thoracoscopy for the diagnosis of pleural disease: A randomized pilot study. *Respirology* **18**, 704–710 (2013).
19. Puchalski, J. Advances and controversies in thoracentesis and medical thoracoscopy. *Semin. Respir. Crit. Care Med.* **40**, 410–416 (2019).
20. Bansal, S. et al. Rigid mini-thoracoscopy versus semirigid thoracoscopy in undiagnosed exudative pleural effusion: The MINT randomized controlled trial. *J. Bronchol. Interv. Pulmonol.* **27**, 163–171 (2020).
21. Wurps, H. et al. Intra-patient comparison of parietal pleural biopsies by rigid forceps, flexible forceps and cryoprobe obtained during medical thoracoscopy: A prospective series of 80 cases with pleural effusion. *BMC Pulm. Med.* **16**, 98 (2016).
22. Udagawa, H. et al. Feasibility and utility of transbronchial cryobiopsy in precision medicine for lung cancer: Prospective single-arm study. *Cancer Sci.* **111**, 2488–2498 (2020).
23. Arimura, K. et al. Cryobiopsy with endobronchial ultrasonography using a guide sheath for peripheral pulmonary lesions and DNA analysis by next generation sequencing and rapi don-site evaluation. *Respir. Investig.* **57**, 150–156 (2019).
24. Shujaat, A., Bajwa, A. A., Usman, F., Jones, L. & Cury, J. D. Safety and accuracy of semirigid pleuroscopy performed by pulmonary fellows at a major university hospital: our initial experience. *J. Bronchol. Interv. Pulmonol.* **20**(3), 213–223 (2013).
25. Goldstraw, P. et al. The IASLC lung cancer staging project: Proposals for revision of the TNM stage groupings in the forthcoming (eighth) edition of the TNM Classification for lung cancer. *J. Thorac. Oncol.* **11**, 39–51 (2016).
26. Clive, A. O. et al. Predicting survival in malignant pleural effusion: development and validation of the LENT prognostic score. *Thorax* **69**, 1098–1104 (2014).

Author contributions

All authors should have made sustancial contributions to all of the folllowing (the concepcion and design of the study, or acquisition of data, or analysis and interpretation of data, drafting the article and revising it critically for impostant intellectual concept. Author contributions—conception and design: MBR, AFV—analysis, acquisition, analysis, interpretation of the data: MBR, ILR, AGP, AGM, CRH, ECV—the drafting of the paper or revising it critically for intellectual content: AFV, MND, ECV—The final approval of the versión: all authors All authors agree to be accountable for all aspects of the work.

Funding

This research received a specific grant from public agency: Spanish Society of Pulmonology (SEPAR) and Integrated Research Projects of Interventional Pulmonology (PII NI) in 2019.

Declarations

Competing interests

The authors declare no competing interests.

Additional information

Correspondence and requests for materials should be addressed to M.B.-R.

Reprints and permissions information is available at www.nature.com/reprints.

Publisher's note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Open Access This article is licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License, which permits any non-commercial use, sharing, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if you modified the licensed material. You do not have permission under this licence to share adapted material derived from this article or parts of it. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit http://creativecommons.org/licenses/by-nc-nd/4.0/.

© The Author(s) 2025