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Research article

Pneumothorax risk reduction during CT-guided lung biopsy – Effect of fluid application to the pleura before lung puncture and the gravitational effect of pleural pressure

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ABSTRACT

Purpose: This study investigated strategies to reduce pneumothorax risk in CT-guided lung biopsy. The approach involved administering 10 ml of 1 % lidocaine fluid in the subpleural or pleural space before lung puncture and utilizing the gravitational effect of pleural pressure with specific patient positioning.
Method: We retrospectively analyzed 72 percutaneous CT-guided lung biopsies performed at a single center between January 2020 and April 2023. These were grouped based on fluid administration during the biopsy and whether the biopsies were conducted in dependent or non-dependent lung regions. Confounding factors like patient demographics, lesion characteristics, and procedural details were assessed. Patient characteristics and the occurrence of pneumothoraces were compared using a Kurskal-Wallis test for continuous variables and a Fisher's exact test for categorical variables. Multivariable logistic regression was used to identify potential confounders.
Results: Subpleural or pleural fluid administration and performing biopsies in dependent lung areas were significantly linked to lower *peri*-interventional pneumothorax incidence (n = 15; 65 % without fluid in non-dependent areas, n = 5; 42 % without fluid in dependent areas, n = 5; 36 % with fluid in non-dependent areas,n = 0; 0 % with fluid in dependent areas; p = .001). Even after adjusting for various factors, biopsy in dependent areas and fluid administration remained independently associated with reduced pneumothorax risk (OR 0.071, p<=.01 for lesions with fluid administration; OR 0.077, p = .016 for lesions in dependent areas).
Conclusions: Pre-puncture fluid administration to the pleura and consideration of gravitational effects during patient positioning can effectively decrease pneumothorax occurrences in CT-guided lung biopsy.

1. Introduction

The most frequent complication of CT-guided lung biopsies is pneumothorax, whereby the subatmospheric pleural pressure created by the stiff chest wall and the lung's elastic recoil force is neutralized by infiltrating air [1–3]. According to comprehensive studies involving a broader sample size and extensive data collection, pneumothorax has been found to manifest in approximately 20–25% of cases [4–10]. Most pneumothoraces caused by this procedure are small, asymptomatic and resolve spontaneously [6]. However, larger pneumothoraces require the placement of a drainage catheter (5–15%), additional imaging, and hospital admission with overnight stay [6,7,9,11–13]. In these cases, complications during lung biopsy not only jeopardize patient safety, but also increase costs by 300 to 400% and represent an economic burden for the healthcare system [14–16]. To reduce the incidence of peri-/postinterventional pneumothorax, different patient- and intervention-

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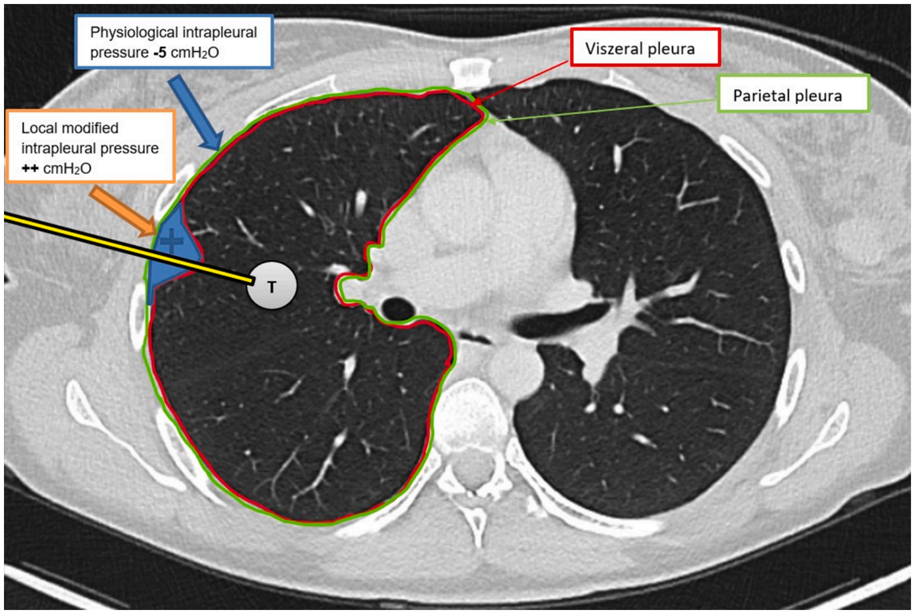

Fig. 1. Schematic illustration of percutaneous transthoracic lung biopsy with locally applied fluid in the subpleural space to increase intrapleural pressure and consequently minimize the occurrence of pneumothorax.

related factors have been identified, such as age [6], lesion size [6], lesion depth [17], needle size [9], and biopsy angle [18]. Several studies have investigated post-biopsy maneuvers to prevent pneumothorax. These have included respiratory arrest before needle removal [19] or attempting to seal the pleura with blood patches [20], sodium chloride [21,22], or embolization of the puncture channel [11,23,24]. Patient positioning during CT-guided lung biopsy has also been investigated, with conflicting results regardless of whether the patient position before or after lung puncture was taken into account: studies in which biopsy was performed in the biopsy-down position did not reduce the risk of pneumothorax [11,25], while the PEARL approach [26] postulates the opposite. Some studies showed a reduction in pneumothorax risk when the patient was moved to the dependent, biopsy-side down position after the biopsy [4–6,27]. Leger et al. [11] found no evidence for this. This discrepancy can be explained by the physiological characteristics of the pleural cavity with more substantial negative pressure in higher, nondependent lung regions [27]. In addition to patient positioning, the presence of pleural effusion resulted in a lower risk of pneumothorax, which can be explained by the increasing pleural pressure due to pleural effusion [3,28]. We therefore hypothesized that injecting a small amount of fluid to the pleura at the biopsy site may reduce the risk of pneumothoraces, in addition to the patient's positioning to allow biopsy in gravity-dependent lung areas.

This study aimed to investigate the risk of pneumothorax, focusing on the administration of fluid into the subpleural space or the pleural cavity and the gravitational effect of pleural pressure caused by specific patient positioning (Fig. 1).

2. Materials and Methods

2.1. Study population

The study was approved by the Ethics Committee of the Canton of Bern (internal registration number: BASEC ID 2023-00298) and was conducted in accordance with the principles of the Declaration of Helsinki. The authors had full access to the data and take full responsibility for the integrity of the data. Written informed consent was obtained from all patients for the biopsy procedure. This was a retrospective analysis of 97 percutaneous CT-guided lung biopsies performed at our university hospital from January 2020 to April 2023. Of these 72 met the inclusion criteria (mean age 67 ± 12 years old, range 25–86 years; Fig. 2), of whom 42 were men (58%) and 30 (42%) were women (Table 1). In order not to compromise the results by a predominant abnormal physiology in the pleural cavity, consecutive exclusion criteria were defined (Fig. 2).

2.2. Baseline evaluation and biopsy technique

All patients underwent a clinical examination prior to the procedure, including detailed medical history and standard blood tests. At least an INR value below 1.5 or a Quick value above 60%, an Hb value above 80g/L and platelet value of more than 50 x 10ˆ9/L were required for the intervention. If the biopsy was too risky with free breathing, the biopsy was rescheduled under anesthesia using jet ventilation. Two senior physicians in Interventional Radiology, each with seven years of experience, performed all lung biopsies in equal numbers. The procedures were performed with CT guidance on a Toshiba Asteion 4SL and with a 17 or 19-gauge coaxial needle and an 18 or 20-gauge semiautomated biopsy system (SemiCut side cutting; Medical Devices Lease S.A., Zug, Switzerland) or (CorVocet™ full core; Merit Medical Systems, Utah, United States). To plan the biopsy, a non-contrast chest CT was obtained and reconstructed at 1 mm increments. The needle path was planned according to the current gold standard.

The skin, subcutaneous tissues, and parietal pleura were locally anesthetized with 1% lidocaine (max. 20 ml). Breathing commands were not given, since studies have shown that phases of hyperventilation often occur as compensation after the first commands and prolong the procedure [29]. After the tissue sampling was completed, the needle was quickly removed. No sealing agent (blood patch) was used. A control CT followed and if no complications occurred, the patient was transferred to a bed in supine position. There was no transfer to the biopsy site. A drainage system (Safe-T-Centesis ™ 6 or 8F) was used when progressive pneumothorax was detected on control CT scan (immediately after needle withdrawal and 5 min later). All patients were monitored (routine vital signs) for 4 h after the procedure on the ward. If no complications were detected on the control CT and the patient was asymptomatic during the monitoring period, he was discharged home. In cases where the control CT scan showed a non-progressive pneumothorax, a chest X-ray was performed after 6 h for further assessment. If the pneumothorax exceeds 2 cm, the patient was admitted as an

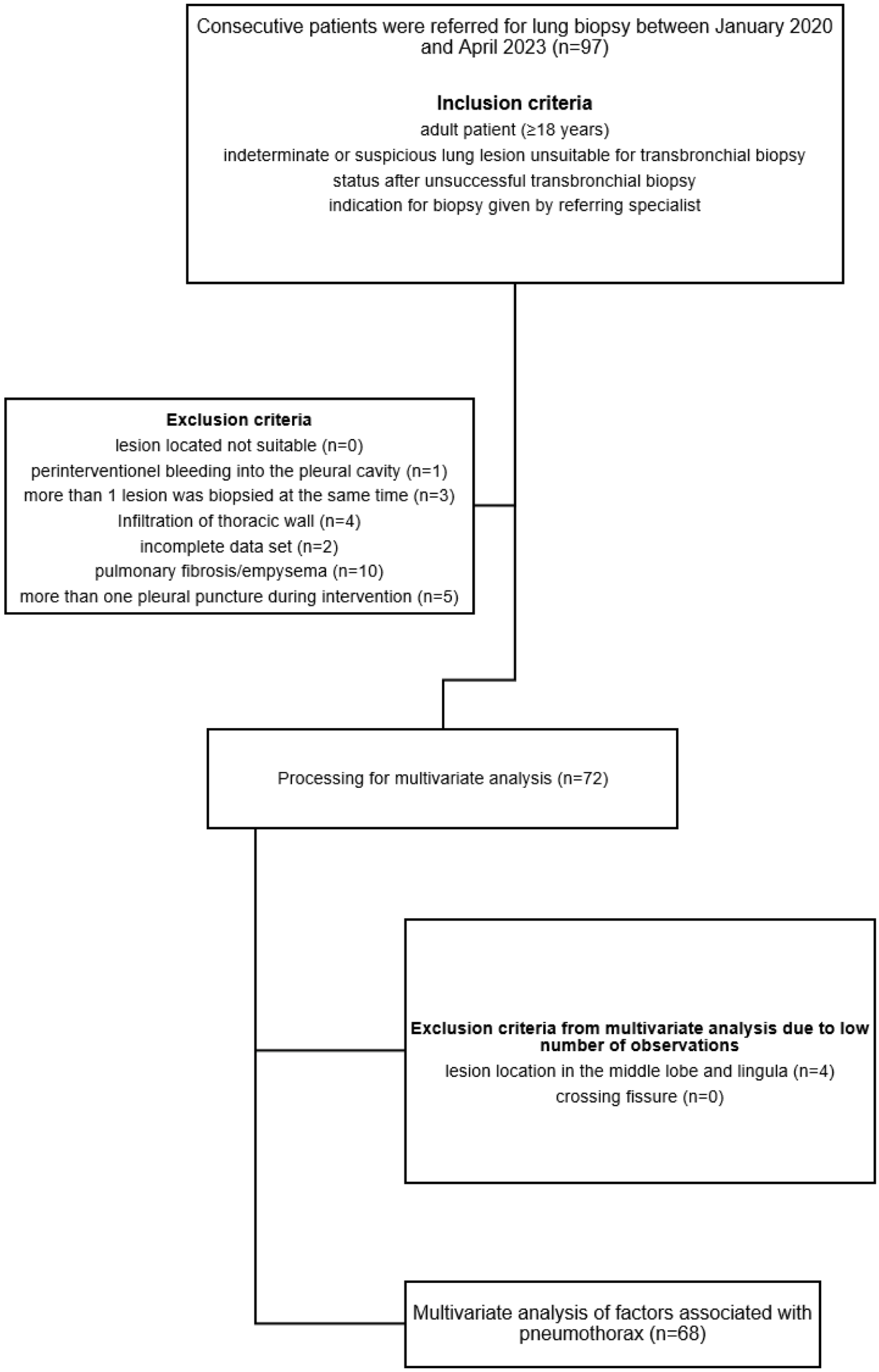

Fig. 2. Flowchart shows the study population.

inpatient for one night. In the case of fluid administration, a depot of 10 ml local anesthetic (lidocaine 1%) was created subpleurally or in the pleural cavity. The acceptance of the subpleural depot in the soft tissue directly adjacent to the parietal pleura was based on the understanding that extrapulmonary pressure in close proximity increases the pleural pressure [30]. No saline solutin was used, as the additional manipulation of the needle itself poses a risk of complications. It was done by continuous application during the usual local anesthesia without changing the needle. We used a 20-gauge needle for this. Explicit care was taken not to penetrate the visceral pleura. In order to avoid this and to ensure the correct position of the fluid administration, the final position of the needle was continuously monitored by sequential CT scanning. If the fluid diffused into the rest of the space, the needle was repositioned, and the target volume of fluid was added again. The puncture needle was then subsequently replaced by the coaxial needle.

Table 1

Patient Demographics and Lesion Characteristics. Unless stated otherwise, data are number of biopsies. X^2 (2x2), X^2 (R X 2), Fisher's exact test and the Kruskal-Wallis Test were used to calculate the statistical difference between groups of categorical, dichotomous, and continuous variables, respectively. Data are mean ± standard deviation. nFnD = non-dependent areas without fluid administration; nFD = dependent areas without fluid administration, FnD = non-depedent areas with fluid administration; FD = dependent areas with fluid administration; SL = skin to lesion; PL = pleural to lesion; M/L = Middle Lobe or Lingula; UL = Upper Lobe; LL = Lower Lobe; Pleural Base = Affection of the pleura by the lesion.

	Survey of Lung Biopsies										
	All		**nFnD**		**nFD**		**FnD**		**FD**		***P* value**
Demographic	72		23	33 %	12	17 %	14	19 %	23	32 %	
Female	30	42 %	8	35 %	2	17 %	7	50 %	13	57 %	0.111
Age (y)	67.14	± 12.48	68.3	± 8.61	66.8	± 8.64	65.29	± 16.12	67.26	± 15.29	0.718
Lesion Size (mm)	24.67	± 16.65	24.7	± 15.40	22.75	± 15.70	64.6	± 12.07	27.83	± 20.67	0.464
Pleural Base (mm)	10.00	± 20.58	7.87	± 18.38	14.25	± 22.27	7.14	± 15.5	11.65	± 24.84	0.890
Needle Size											0.480
18 G	33	46 %	9	39 %	6	50 %	7	50 %	11	48 %	
20 G	39	54 %	14	61 %	6	50 %	7	50 %	12	52 %	
Biopsy Angle (degree)	64.27	± 17.59	61.07	± 16.56	71.25	± 17.27	65.86	± 17.92	62.87	± 18.58	0.449
Distance SL (mm)	63.24	± 22.59	59.91	± 19.89	57.25	± 16.36	66.29	± 25.52	67.83	± 25.97	0.672
Distance PL (mm)	16.85	± 15.62	18.83	± 20.09	11.83	± 10.37	18.14	± 15.80	16.70	± 12.80	0.610
Pneumothorax	25	35 %	15	65 %	5	42 %	5	36 %	0	0 %	0.001
Position											0.002
Lateral	27	38 %	3	13 %	6	50 %	4	29 %	14	61 %	
Prone	18	25 %	12	52 %	2	17 %	4	29 %	0	0 %	
Supine	27	38 %	8	35 %	4	33 %	6	43 %	9	39 %	
Location											0.032
UL	32	44 %	11	48 %	1	8 %	11	79 %	9	39 %	
LL	36	50 %	11	48 %	10	83 %	3	21 %	12	52 %	
M/L	4	6 %	1	4 %	1	8 %	0	0 %	2	9 %	

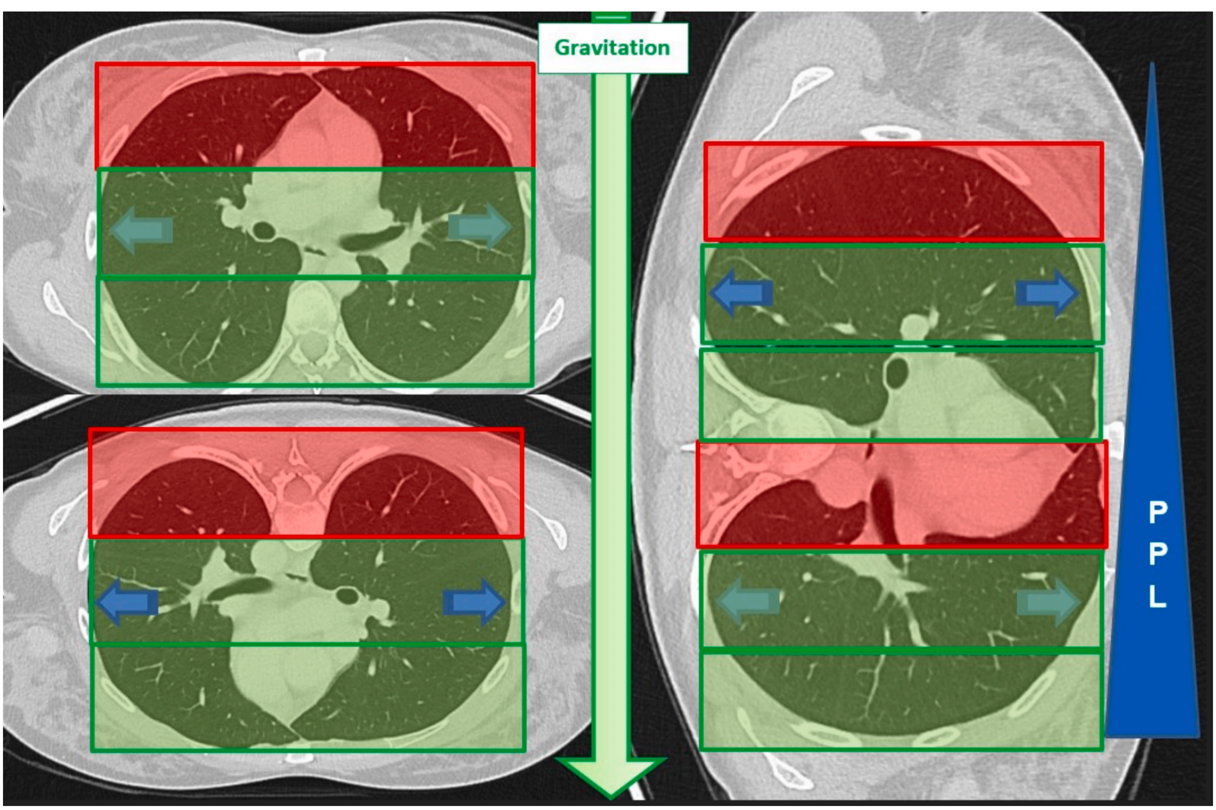

Fig. 3. Schematic illustration of the zoning used for this study according to position-dependent gravitational effect on pleural pressure (PPL). From non-dependent in the upper to dependent lung regions lower down, the PPL increases. However, in a healthy, non-intubated lung, PPL always remains negative [7,32]. The weight of the lung influences the PPL, and an additional force acts into the periphery. Consecutively and for simplification, we determined only the zone "RED" as non-dependent. For zoning, we applied the rule of thirds.

2.3. Differentiation between biopsy in dependent and non-dependent areas of the lung

We applied a simplified zoning system by dividing the axial planning images into three thirds and using non-anatomical landmarks for orientation. The red zone as the non-dependent lung area was defined as the third in which the gravitational force is strongest. We decided to evaluate the remaining two thirds as a dependent lung area (Fig. 3).

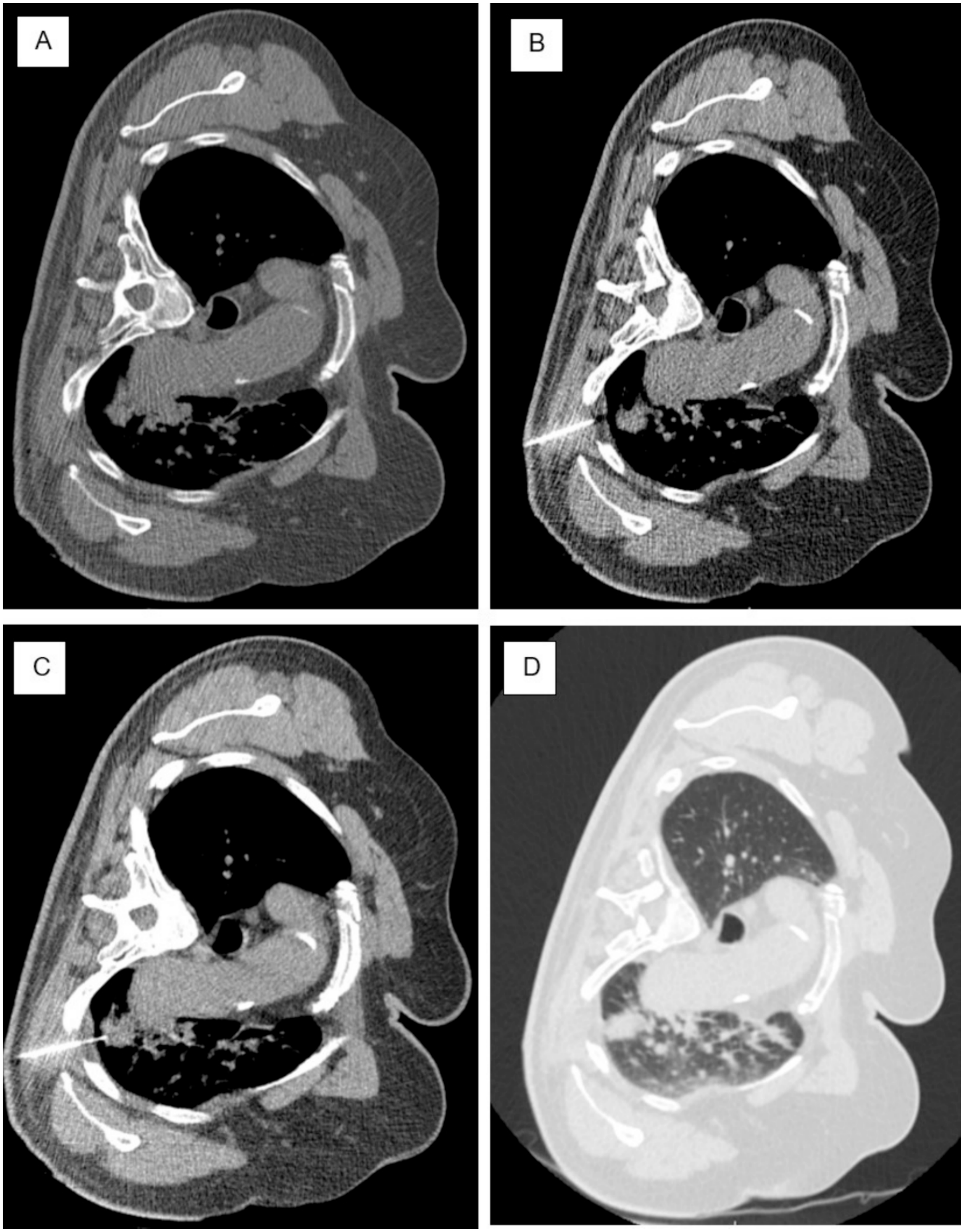

Fig. 4. Technical realization: **A)** Lesion in the left lower lobe and ipsilateral-dependent patient positioning. **B)** Application of fluid in the subpleural space during local anesthesia. **C)** Biopsy of the lesion using a coaxial needle through the prepared pleural cavity and biopsy path through the dependent lung region. **D)** Post-intervention, no evidence of pneumothorax with residual detectable fluid deposition in the pleural cavity.

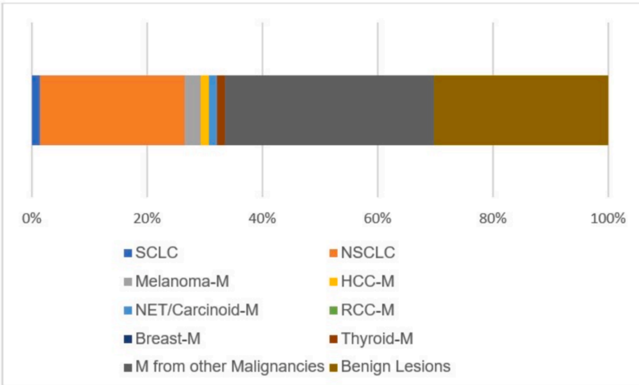

Fig. 5. Histological findings of the lung biopsies.

Based on the schematic representation of the gravitational effect on pleural pressure by Stenqvist et al [28], pleural pressure is considered positive from the middle third downwards, which is due to progressive lung collapse.

2.4. Procedures and patient groups

All procedures were reviewed by a board-certified, independent, interventional radiologist with seven years of experience. He did not perform any of these interventions. Patients were divided into four groups according to whether or not fluid was administered at the site of biopsy before the procedure and whether the biopsy was performed in the dependent or non-dependent areas of the lung. We recorded patient demographics, biopsy positioning, access route according to our zone classification (Fig. 3), lesion size, lesion location, distance from skin to the lesion (along needle pathway), pleural base (extent in mm), fluid application in or near to the pleural space (see technical realization in Fig. 4), biopsy angle, needle size, and the name of the interventionalist performing the procedure.

2.5. Statistical analysis

Patients characteristics and the occurrence of pneumothoraces were compared using a Kurskal-Wallis test for continuous variables and a Fisher's exact test for categorical variables. Multivariable logistic regression was used to assess for potential confounders of pneumothorax [31]. Goodness of fit was assessed by using the Hosmer-Lemeshow test. Statistical analyses were performed using commercially available software (IBM SPSS Statistics for Windows, version 28; IBM, Armonk, NY).

3. Results

3.1. Study population

Age and sex did not differ significantly between patients. Lesion size, lesion location, pleural base, needle size, biopsy angle, the skin-to-lesion and pleura-to-lesion distance were normally distributed in all four patient groups (Table 1). A total of 70% of the biopsied lung nodules were malignant. Most of these were metastases and about a quarter were primary lung tumors. Only 30% of all biopsies were benign lesions (Fig. 5).

3.2. Pneumothorax after CT-guided lung biopsy

Twenty-five patients (35%) had a post-biopsy pneumothorax. Overall, pneumothorax occurred most frequently in the age group between 55–69 years. In all other age groups, the proportion of biopsies without complications predominated. Most pneumothoraces occurred when lesions were biopsied in the non-dependent areas (20/37, 54%), while only 5/35 (14%) pneumothoraces occurred in dependent areas. The lowest incidence of pneumothorax was observed in patients with prior fluid administration to the pleura in both non-dependent (5/14, 36%) and dependent areas (0/23, 0%, $p<.001$).

3.3. Association lesion characteristics and technical parameters with the occurrence of pneumothorax

Multivariable logistic regression analysis showed that the administration of fluid to the pleura (OR 0.071, 95% CI 0.012–0.409, $p<.001$) and biopsy in dependent lung areas (OR 0.077, 95% CI 0.010–0.616, $p=.0016$) were independently associated with a lower incidence of pneumothorax, while there was no significant association with patient position, age, sex, larger needle size, pleural base involvement of the lesion, smaller biopsy angle, smaller distance from skin or pleura to lesion, or whether the lesion was located in the upper or lower lobe (Table 2). A good model fit with an $\chi^2(8) = 7.831$, p 0.444. Cohen's f^2 is 0.36, corresponding to a strong effect [32].

4. Discussion

Our study showed that administration of fluid into the vicinity or

Table 2
Multivariable Logistic Regression Predicting Likelihood of Pneumothorax. The total number of cases in the cohort for the multivariable analysis was n = 67. B = Regression Coefficient; S.E. = Standard Error; df = Degree of Freedom; CI = Confidence Interval; D = dependent; y = per year; mm = millimeter; g = Gauge; UL = Upper Lobe; LL = Lower Lobe; M/L = Middle Lobe or Lingula; SL = Skin to Lesion; PL = pleural to lesion. The prone position is not in the equation due to redundancies as the opposite of supine.

Variable	B	S.E.	Wald test	df	*P* Value	Odds Ratio	95 % CI −	+
Pleural fluid	−2.642	0.892	8.770	1.000	0.003	0.071	0.012	0.409
Supine	−0.274	1.122	0.060	1.000	0.807	0.760	0.084	6.855
Lateral	0.748	1.134	0.434	1.000	0.510	2.112	0.229	19.516
Access route D lung region	−2.560	1.059	5.841	1.000	0.016	0.077	0.010	0.616
Age (y)	−0.026	0.034	0.592	1.000	0.441	0.974	0.912	1.041
Sex	0.247	0.763	0.105	1.000	0.746	1.281	0.287	5.713
Lesion Size (mm)	−0.027	0.035	0.585	1.000	0.444	0.974	0.910	1.042
Pleural Base (mm)	−0.024	0.033	0.525	1.000	0.469	0.976	0.914	1.042
Needle Size (g)	−0.291	0.383	0.577	1.000	0.447	0.748	0.353	1.583
Biopsy Angle (degree)	−0.012	0.024	0.231	1.000	0.631	0.988	0.943	1.036
UL	−0.864	1.673	0.266	1.000	0.606	0.422	0.016	11.204
LL	−0.933	1.821	0.263	1.000	0.608	0.393	0.011	13.959
Distance SL (mm)	−0.020	0.038	0.275	1.000	0.600	0.980	0.911	1.055
Distance PL (mm)	−0.003	0.030	0.011	1.000	0.917	0.997	0.940	1.057
Constant	8.959	9.741	0.846	1.000	0.358	7779.158		

into the pleural cavity in the access route before lung puncture allowed a 14-fold relative risk reduction of pneumothorax ($p<.01$), while a 13-fold relative risk reduction of pneumothorax was achieved when the access route of the biopsy was performed through a dependent lung region ($p<.01$). No pneumothorax occurred in this study in 23 patients in whom both fluid administration and biopsy were performed in a dependent lung region. Both procedures maintained their independent association with a lower incidence of pneumothorax when corrected for other risk factors such as age, sex, position of the patient and size of the lesion.

The results of this study confirm and extend the current state of knowledge. Some studies, as well as part of the PEARL approach [26], showed a lower incidence of pneumothorax when saline, gelatin sponge, autologous blood clot seals were processed after lung puncture in the access route [20–22,24]. The risk reduction by prior fluid administration to the pleura can be explained by the fact that the artificial pressure in the pleural space increases, minimizing the risk of pneumothorax. This observation is supported by physiological experiments showing that pleural effusion leads to an increase in pleural pressure, called pleural liquid pressure, resulting in a vertical gradient of 1 cm H_2O/cm [3,28]. On the other hand, it can be assumed that this deposited fluid possibly minimizes the airflow into the puncture access [21].

The lower frequency of pneumothoraces in biopsies of non-dependent lung region is also in agreement with prior studies. In a study with dogs, pneumothorax progression could be stopped when the dogs were placed in the biopsy side down decubitus position [27]. An overall reduction in the rate of pneumothorax was also demonstrated by Cassel et al. [4] who placed their patients ($n = 80$) on the side of the puncture immediately after the intervention. Drumm et al. [25] and followed in particular by Najafi et al. [26] with the results from their prospective data showed that positioning the patient in the biopsy-down position (ipsilateral decubitus position) before puncture as part of the PEARL protocol reduced rates of pneumothorax. A conclusive explanation for this was provided by Zidulka et al. [27] who postulated that the dependent position may reduce the pressure difference between the alveoli and the pleura, as well as the alveolar size, both minimizing the occurrence of pneumothorax. However, there were also a few studies that did not found a lower pneumothorax with ipsilateral-dependent patient positioning during biopsy [5,11]. One possible explanation for this difference is that not the ipsilateral patient positioning is relevant, but the needle path that ultimately passes through dependent lung regions along its entire length. In contrast, it must be mentioned that this technique is based on careful patient positioning, which can sometimes have an impact on the percutaneous access to the target lesion. Thus, a horizontal or ascending needle pathway is of more difficulty, since the bed may limit the angulation. Our results suggest that each lung should be divided into dependent and non-dependent with respect to the gravitational effect and that the full needle path should traverse the dependent lung along its entire length. Our extended approach should be pursued in further studies.

We found no correlation between lesion size and the occurrence of pneumothorax, which supports the findings of Billich et al. [21], Laurent et al. [33] and Geraghty et al. [34]. In contrast, some other studies found different results in this regard [6,25,35–37]. However, we also suspect that this may be an investigator-dependent variable [33]. For example, smaller lesions are more difficult to hit and require a longer intervention time, possibly increasing the risk of pneumothorax [33,37].

We found a tendency towards a lower incidence of pneumothorax in patients aged 70 years or older, which is in accordance with findings of other colleagues such as Wiener et al. [38] and Vatrella et al. [39]. One explanation for this observation could be the decreasing elastic recoil in aged lung parenchyma [e.g. 28, 39]. Due to the reduction in elastic lung tissue and the associated effect of the lung's own weight, the pleural pressure becomes positive in dependent part of the pleural space [28]. Consequently, the risk should increase in non-dependent lung regions, whereas it decreases in the dependent lung regions with age [27]. The findings of this single-center study population need external validation. In addition, patients with pulmonary fibrosis and emphysema were excluded from the analysis and should thus be analyzed in subsequent studies. If the findings of a lower incidence of pneumothorax with biopsy in dependent lung areas and prior fluid administration to the pleura will be confirmed, these two novel technical adaptations of a CT-guided lung biopsy may be easily applicable without the need for additional resources or infrastructure.

Our study has several limitations. First it was a retrospective analysis of a single center with a relatively small number of cases. Second, a simplified model of the gravitational effect of pleural pressure in specific patient positions was used. A direct pleural manometry during the procedure was not possible due to ethical considerations, as used in different positions in animals by Zidulka et al. [27]. Thirdly, the amount of 10 ml of fluid given was always the same in this study. Based on the findings regarding the association between pleural effusion and pneumothorax risk, it can be assumed that different amounts of fluid in different positions have a different outcome regarding pneumothorax [3,28]. Finally, we studied healthy lungs and excluded patients with emphysema or fibrosis. A diseased lung parenchyma as a potential confounder should be investigated in a further study.

5. Conclusion

Administering fluid close to or into the pleura and utilising the gravitational effect of pleural pressure prior to lung puncture can preventively reduce the incidence of pneumothorax during CT-guided lung biopsy.

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CRediT authorship contribution statement

Michael P. Brönnimann: Writing – review & editing, Writing – original draft, Project administration, Methodology, Investigation, Formal analysis, Conceptualization. **Andreas Christe:** Supervision. **Johannes T. Heverhagen:** Validation, Supervision. **Bernhard Gebauer:** Supervision. **Timo A. Auer:** Supervision, Formal analysis. **Dirk Schnapauff:** Writing – review & editing, Project administration. **Federico Collettini:** Supervision. **Christophe Schroeder:** Resources, Formal analysis. **Patrick Dorn:** Supervision. **Lukas Ebner:** Supervision. **Adrian T. Huber:** Writing – review & editing, Writing – original draft, Formal analysis, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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