Percutaneous transthoracic needle biopsy of lung lesions is a safe method associated with a very low risk of pleural recurrence

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Aim. Percutaneous transthoracic needle biopsy (PTNB), an alternative to bronchoscopic confirmation of lung lesions, is today being associated with a risk of pneumothorax and hemorrhage. Further, there are no data on the possible risk of malignant disease spreading to the pleura at the site of the PTNB. Previous studies have dealt with this risk in stage I non-small cell lung cancer only. The aim of this study was thus to assess the risk of pleural recurrence for all types of lung lesions. Secondary objectives included assessment of diagnostic yield and safety with respect to the incidence of pneumothorax and hemorrhage.

Methods. Clinical data of all patients from the University Hospital in Pilsen who had undergone PTNB of lung lesions between 1.1.2018 and 31.12.2022 were included in this retrospective study.

Results. Following PTNB, ipsilateral pleural effusion occurred in 4.8% of patients without prior pleural infiltration. The effusion was confirmed as malignant in one patient (0.7%). Diagnostic yield of the method was 86.6%. We recorded pneumothorax or hemorrhage in the lung parenchyma or pleural space requiring medical intervention in 3.4% and 1.1% of patients, respectively.

Conclusion. In our study, percutaneous transthoracic needle biopsy of lung lesions showed high sensitivity and low degree of acute complications requiring an invasive solution. The risk of pleural recurrence after a biopsy was very low. Consequently, we continue to consider this method to be an alternative to bronchoscopy biopsies.

Key words: NSCLC, percutaneous transthoracic needle biopsy, recurrence, pneumothorax, bleeding into the lung parenchyma

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INTRODUCTION

Percutaneous transthoracic needle biopsy (PTNB) is an alternative to bronchoscopic verification of lung lesions. In particular, this method is used for peripheral lung lesions and is not limited to those in contact with the pleura. The specificity is >90%. However, false negative rate is relatively high (about 20–30%) (ref.[1]). Therefore, although PTNB is useful for the definitive diagnosis of malignancy, it cannot be used to exclude the diagnosis. Complications are more common with PTNB than with bronchoscopy – they generally occurred in nearly 40% of patients[1]. However, the frequency of clinically significant complications (requiring active medical management) is low (about 5% of all biopsies) (ref.[2]). The complications include air embolism, hemorrhage (including subsequent hemoptysis) and pneumothorax[1,2]. Some studies also indicate risk of pleural recurrence in connection with the biopsy[3]. However, there is no consensus on this topic between different publications, and pleural recurrence has only been investigated in biopsies of early stages of lung cancer[1,4]. These studies then show that the risk of recurrence may relate mainly to subpleural lesions[1,4]. Studies assessing the risk of recurrence after biopsy in unselected types of lesions are lacking.

For these reasons, the aim of this study was to assess the risk of pleural recurrence (here examined as the occurrence of ipsilateral pleural effusion) in patients with any type of lung lesion diagnosed using the PTNB under computed tomography (CT) control. Secondary objectives were to evaluate diagnostic yield and to assess safety with respect to the incidence of pneumothorax and bleeding.

PATIENTS AND METHODS

Patients

Clinical data of all patients from the University Hospital in Pilsen who underwent lung lesion PTNB under CT control between 1.1.2018 and 31.12.2022 were included in this retrospective study. Patients who had undergone PTNB of a lesion outside of the lung were excluded. Occurrence of possible complications was monitored with a follow-up CT scan immediately after

the biopsy, clinically during a 24-hour hospitalization and with an x-ray of the lungs 24 hours after the biopsy. All pneumothoraxes and hemorrhages were recorded, including the cases requiring medical intervention as well as the cases in whom observation was the only means of management. The data were drawn from the hospital system of the University Hospital in Pilsen. All patients had given their informed consent.

Ethics Statement

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved Ethics Committee of University hospital in Pilsen, number 298/2020. Individual consent for this retrospective analysis was waived.

Percutaneous transthoracic needle biopsy technique

CT-guided PTNB was performed according to routine standards. PTNB was started with accurate positioning of the patient and local anesthesia. A CT scan was then performed to precisely locate the lesion and plan the needle trajectory, ensuring accurate and safe needle placement. Under repeated CT guidance, a core needle was inserted in the lesion and sample extracted. Confirmatory CT scan was performed to assess the occurrence or extent of pneumothorax.

Statistical methods

Standard descriptive statistics and frequencies were used to characterize the data set. Comparisons of ordinal and quantitative variables between two categories were carried out using the Mann-Whitney U test. Associations between two categorical variables were analyzed by cross-tabulation followed by Fisher's exact test. The level of statistical significance was set at $\alpha = 0.05$ and all reported p-values are two-tailed. The statistical analysis was performed using STATISTICA (Version 12; StatSoft, Inc., TuIsa, OK, USA) and SISA (Simple Interactive Statistical Analysis, https://www.quantitativeskills.com/sisa/).

RESULTS

Patient characteristics

A total of 179 patients were included in the study. Median age was 70 years (range 22 to 89 years). Median lesion size was 47 mm (range 10 to 164 mm). Other patient characteristics are summarized in Table 1.

Incidence of pleural effusion following the biopsy of the lesion

Pleural effusion preceding the biopsy on the ipsilateral side was present in 33 (18.4%) patients. These patients were excluded from the evaluation of the formation of post-puncture pleural effusion. Therefore, 146 patients were included in further analyses. We noted the formation of a pleural effusion following the biopsy in 13 (8.9%) patients. Of these, it was ipsilateral in 11 (7.5%) patients. Seven (4.8%) patients developed a pleural effusion without prior known malignant pleural infiltration according to CT. The pleural effusion was minimal in 5 patients, and required thoracentesis in 2 patients. One patient had a paramalignant effusion (with no evidence of metastatic pleural disease) and one patient (i.e. 0.7%) had a malignant pleural effusion. Detailed characteristics of patients with ipsilateral pleural effusion arising after biopsy are summarized in Table 2.

There was no statistically significant association between the occurrence of ipsilateral pleural effusion after biopsy and distance of the lesion from the pleura (P=0.248), diameter of the lesion (P=0.159), stage of the tumor (P=0.507), age of the patient (P=0.080), gender (P=0.516) or smoking habits (P=0.252).

Incidence of pneumothorax and intrapulmonary hemorrhage

Pneumothorax after biopsy was identified in 55 (30.7%) patients. However, in most cases (49 patients with pneumothorax, i.e. 27.4%), it did not require any specific treatment and was pneumothorax resolved with a conservative procedure. Chest tube insertion was necessary in 6 (3.4%) patients.

We demonstrated a significant relationship between the distance of the lesion from the pleura and the incidence of pneumothorax (P<0.001, higher distance is associated with a greater risk). The size of the lesion was associated with a non-significant trend in the incidence of pneumothorax (P=0.082, trend towards more pneumothoraxes in smaller lesions). Neither gender nor smoking habits played a role in the incidence of pneumothorax (P=0.738 and P=0.113, respectively).

We observed intrapulmonary hemorrhage from a punctured lesion in 56 (31.3%) patients. However, in 54 patients (30.2%) this was a self-limiting radiological finding, without any clinical symptoms. Two (1.1%) patients had clinically significant hemorrhage associated with hemoptysis and requiring hemostatic therapy (during the 5 years of follow-up, there was one case of severe bleeding, associated with the development of haemothorax and requiring immediate surgical treatment).

Greater distance of the lesion from the pleura and decreasing size of the lesion were significantly associated with an increased risk of hemorrhage (P=0.001 and P<0.001, respectively). Neither gender nor smoking habits played a role in the incidence of hemorrhage (P=0.620 and P=0.467, respectively).

No patient had permanent consequences or died as a result of the procedure.

Diagnostic yield of the method

PTNB enabled verification of a lesion etiology in 155 (86.4%) patients. The lesion was malignant in 135 (75.4%) and benign in 20 (11.2%) patients, respectively. The biopsy did not lead to a diagnosis in 24 (13.2%) patients.

We did not record a significant relationship between the size of the lesion or its distance from the pleura and the yield of the biopsy (P=0.288 and P=0.685, respectively).

Table 1. Patient characteristics.

Parameter	Category	n (%)
Sex	Male	113 (63.1)
	Female	66 (36.9)
Smoking status	Smoker	65 (36.3)
	Ex-smoker	74 (41.3)
	Non-smoker	37 (20.7)
	Unknown	3 (1.7)
Stage of lung cancer	IA1	0 (0.0)
	IA2	9 (5.0)
	IA3	8 (4.5)
	IB	12 (6.7)
	IIA	4 (2.2)
	IIB	13 (7.3)
	IIIA	13 (7.3)
	IIIB	15 (8.4)
	IIIC	12 (6.7)
	IVA	35 (19.6)
	IVB	16 (8.9)
	Unknown	5 (2.8)
	Other tumors / lesions of unclear origin	17 (9.5)
	Benign	20 (11.2)
Distance of the lesion from the pleura	0 cm	73 (40.8)
	0–1 cm	45 (25.1)
	1–2 cm	35 (19.6)
	>2 cm	26 (14.5)
Size of the lesion	0–1 cm	1 (0.6)
	1–2 cm	18 (10.1.)
	2–3 cm	30 (16.8)
	3–4 cm	28 (15.6)
	4–5 cm	27 (15.1)
	>5 cm	74 (41.3)
	Cannot be measured	1 (0.6)

DISCUSSION

To the best of our knowledge, in our retrospective study, we are the first to demonstrate a very low potential risk of malignant ipsilateral pleural effusion after PTNB in unselected population. We observed this phenomenon in only one (0.7%) patient from our group of 146 patients without ipsilateral pleural effusion before PTNB. At the same time, PTNB showed a high diagnostic yield and a low risk of serious complications.

The diagnostic yield of PTNB in our study was 86.4%. Yen et al. had a similar result (91.5%) in their group of 2556 patients[5]. Correspondingly, Borelli et al. demonstrated diagnostic yield of 82.0% (ref.[6]). Other studies also showed diagnostic accuracy in the range of 82.0–98.2% (ref.[7,8]). Yen et al. reported a significant difference in diagnostic yield between tumors smaller or greater than 3 cm (ref.[5]). We did not observe the same relationship. However, this result could have been influenced by the lower number of small (up to 2 cm) lesions in our study. We found lesions smaller than 2 cm correlated significantly with the lower diagnostic yield shown by Borelli et al.[6].

In their large retrospective study with 16,971 patients, Vachani et al. found the frequency of pneumothorax after PTNB to be 25.3% and the rate of chest tube insertions of 8.1% (ref.[9]). Two large meta-analyses reported a pneumothorax rate of about 25% and the need for chest tube insertions of about 6% (ref.[2,10]). However, for example, in the study by Hajjar et al. the frequency of pneumothorax reached almost 70% (ref.[11]). These differences may be due to different methodology of recording pneumothorax. For example, Chiu et al. (REF) included pneumothoraxes larger than 1 cm only. With this definition, the frequency of pneumothorax was 17.9% (ref.[12]). In addition, inclusion or exclusion of delayed pneumothorax might have also affected study results, as shown by Bae et al.[13]. In our case,

Table 2. Characteristics of patients with ipsilateral pleural effusion arising after biopsy.

Patient	Time from biopsy (months)	Type of effusion	Cytology	Comment
1	9	Unknown	×	Unpunctuated – atelectasis + poor condition of patient, pleural infiltration before biopsy
2	13	Unknown	×	Small – unpunctuated
3	17	Unknown	×	Small – unpunctuated, 1 year stable
4	1	Unknown	×	Small – unpunctuated, pleural infiltration before biopsy
5	0.5	Unknown	×	Small – unpunctuated, tumor infiltrating the chest wall
6	4	Exudate	Neutrophils + tumor cells	Pleural infiltration before biopsy
7	52	Exudate	Tumor cells	×
8	11	Unknown	×	Small – unpunctuated
9	7	Exudate	Macrophages	×
10	2	Unknown	×	Small – unpunctuated
11	4	Unknown	×	Small – unpunctuated, patient with mesothelioma

we counted all pneumothoraxes occurring within 24 hours post biopsy, so the frequency of this complication does not deviate from those reported by other authors.

We have noted the effect of the lesion distance from the pleura and the trend in the relationship between the size of the lesion and the frequency of pneumothorax. A number of other studies reported the relationship between a greater depth of puncture through the lung parenchyma and the frequency of pneumothorax[12-14]. In contrast, Weon et al. reported that greater distance of lesions led to a reduction in the number of pneumothoraxes[15]. However, a meta-analysis by Huo et al. showed, in accordance with other results, greater risk of pneumothorax in the deeper lesions[10]. Higher frequency of pneumothorax in patients with smaller lesions has been evidenced by several studies, including the meta-analysis by Huo et al. (ref.[10,11,13,16]).

The frequency of intrapulmonary hemorrhage after PTNB reported in the literature is in the range of 2.9–54.5% and the frequency of hemoptysis of 0.5–14.4% (ref.[17]). Here too, the method of how the complications are counted is likely to affect the results. If, as in our study, hemorrhage is defined on the basis of radiological evidence only and not on the basis of the patient's symptoms, its frequency increases[9]. In addition, some authors only record bleeding exceeding a defined size on CT (ref.[12]). Again, in this context, our results do not deviate from the current literature.

In accordance with our study, several other authors have demonstrated the effect of the lesion distance from the pleura and its size on the frequency of intrapulmonary hemorrhage[14,17,18].

A review by Cheng et al. found 7 studies exploring the incidence of pleural recurrence after biopsy in early stage non-small cell lung cancer (NSCLC) (ref.[3]). Four of the 7 studies indicated a possible association between biopsy and pleural recurrence, while the other three studies did not confirm this[3]. A meta-analysis by Hong et al. analyzed data of 2,394 individual patients from 6 studies[19]. PTNB was associated with increased pleural recurrence in early stage NSCLC and reduced survival in patients younger than 55 years. In contrast, a meta-analysis by Wang et al. (including 1242 patients from 5 studies) showed no increased risk of pleural recurrence after biopsy in early stage NSCLC (ref.[4]). The discrepant results could be due to the different sampling technique (e.g. different type of needles, single-use vs. multiple sampling etc.), although this assumption is contradicted by Kim et al., who found no differences in recurrence based on the biopsy technique[4,20]. Pleural invasion/lymphatic invasion in subpleural lesions at the time of biopsy could be a more important factor[4,20-22]. In our study, we excluded patients with pleural involvement evident at the time of the biopsy and this could have led to the low risk of possible recurrence on the pleura across all lesions. This conclusion would be consistent with the study by Ahn et al., where only lesions with visceral pleural invasion increased the risk of malignant pleural effusion[21]. Based on these data, we believe that the risk of pleural recurrence after PTNB in patients without pleural invasion is very low.

Our study has several limitations. We conducted a retrospective study, where some variation in the course of the procedure in specific patients, and the possible effect of this variation on the rate of complications, cannot be ruled out. Furthermore, it cannot be reliably determined whether the ipsilateral effusion was related to the tumor itself or could result from the biopsy. However, the effusion had to be punctured in two patients only with an ipsilateral effusion without previous pleural metastases, and in one patient only, the effusion was found to be malignant. Therefore, the risk of clinically significant recurrence is low. As other diagnostic modalities are also burdened by specific risks, we suggest there is a need for prospective comparative study to, for example, compare PTNB with navigated bronchoscopy.

CONCLUSION

PTNB of lung lesions is a method with high diagnostic potential and a low degree of acute complications requiring an invasive solution. The majority of acute complications in our group were resolved by observation only. The risk of pleural recurrence after PTNB is very low. We thus continue to consider this method as an alternative for bronchoscopic biopsies.

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