European Radiology (2019) 29:270–278
https://doi.org/10.1007/s00330-018-5561-5

CHEST

Risk of pleural recurrence after percutaneous transthoracic needle biopsy in stage I non-small-cell lung cancer

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Received: 8 February 2018 / Revised: 4 May 2018 / Accepted: 23 May 2018 / Published online: 15 June 2018

Abstract

Objectives To determine whether percutaneous transthoracic needle biopsy (PTNB) increased the risk of pleural recurrence in stage I non-small-cell lung cancer (NSCLC).

Methods In this retrospective study, we reviewed 830 consecutive patients with stage I NSCLC who underwent curative resection between 2004 and 2010. Cox regression analyses with propensity score matching were performed to identify risk factors for pleural recurrence.

Results Of 830 patients, 540 (65.1%) underwent PTNB before surgery, while 290 (34.9%) underwent preoperative bronchoscopic biopsy or intraoperative wedge resection for a pathological diagnosis. Concomitant pleural recurrence occurred in 42 patients (5.1% [95% CI, 3.8–6.8]; 34 [6.3%] PTNB patients and eight [2.8%] non-PTNB patients) and isolated pleural recurrence took place in 26 patients (3.1% [95% CI, 2.1–4.6]; 20 [3.7%] PTNB patients and 6 [2.1%] non-PTNB patients). On multivariate analysis after matching, only visceral pleural invasion was associated with concomitant pleural recurrence (hazard ratio [HR]=3.367; 95% CI, 1.262–8.986; p=0.015) and isolated pleural recurrence (HR=3.216; 95% CI, 1.037–9.978; p=0.043), while PTNB was associated with neither concomitant nor isolated pleural recurrence (p=0.605 and p=0.963, respectively). Among 540 patients undergoing PTNB, the transfissural approach did not have a significant association with pleural recurrence (p=0.539 and p=0.313, respectively); instead, visceral pleural invasion and microscopic lymphatic invasion were significantly associated with concomitant pleural recurrence, and microscopic lymphatic invasion was associated with isolated pleural recurrence (p<0.05).

Conclusion PTNB did not significantly increase the risk of pleural recurrence in stage I NSCLC, whereas visceral pleural invasion was responsible for pleural recurrence.

Key Points

- *PTNB did not significantly increase the risk of pleural recurrence in stage I NSCLC, whereas visceral pleural invasion was responsible for pleural recurrence.*
- *The transfissural approach in PTNB did not increase the risk of pleural recurrence.*
- *PTNB can be performed for the confirmatory diagnosis of peripheral stage I lung cancer without concern for the risk of pleural recurrence.*

Keywords Non-small-cell lung cancer · Biopsy, needle · Neoplasm recurrence, local

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Abbreviations

HR	Hazard ratio
NSCLC	Non-small-cell lung cancer
PSM	Propensity score matching
PTNB	Percutaneous transthoracic needle biopsy

Introduction

When nodules are detected on computed tomography (CT), the management strategy depends on their size and the likelihood of malignancy [1]. Nonsurgical biopsy is recommended when the clinical probability and imaging findings are discordant and when the probability of malignancy is low to moderate. Percutaneous transthoracic needle biopsy (PTNB) is an indispensable tool for evaluating pulmonary lesions; it has a high diagnostic accuracy for detecting malignancy, and is safe when performed by experienced interventionists [2, 3]. The most common complication of PTNB is pneumothorax, followed by pulmonary hemorrhage and, rarely, air embolism [4]. Tumor seeding of the lung, pleura, and chest wall has been also reported as a rare but possible complication of PTNB in the literature, with an incidence of 0.01%-0.06% [5, 6].

No consensus exists regarding whether pleural recurrence occurs more frequently after preoperative PTNB in early lung cancer [7–12]. According to a recent meta-analysis, PTNB did not raise the risk for pleural recurrence in early-stage lung cancer, but it did increase pleural recurrence for subpleural lesions, indicating that PTNB should not be recommended for those lesions [12]. However, the finding of increased pleural recurrence after PTNB for subpleural lesions was based on the results of two studies, which only included 227 patients. Moreover, other important confounding factors relevant for pleural recurrence, such as visceral pleural invasion, were not considered in their analysis. Furthermore, the possible association between the transfissural approach and pleural recurrence has not been studied. Therefore, we conducted a study to determine whether PTNB increased the risk of pleural recurrence in stage I non-small-cell lung cancer (NSCLC) in a large population.

Materials and methods

Patients

This study was approved by the Institutional Review Board of our institution with a waiver of the requirement for patients' informed consent.

Between January 2004 and December 2010, 914 patients with pathological stage I lung cancer underwent curative surgical resection at our institution. After reviewing their electronic medical records, 84 patients were excluded, as follows: 23 patients who received preoperative chemotherapy (n=21) or underwent a previous operation for a lung malignancy (n=2), 33 patients without follow-up CT images, 11 patients with small-cell lung cancer, 11 patients who had already had metastatic lesions before surgery when retrospectively reviewed (ten patients with lung nodules and one patient with bone metastasis), and six patients with suspected recurrence or metastasis on postoperative follow-up CT, but no further follow-up, making it impossible to confirm their outcomes. Ultimately, a total of 830 patients (473 men and 357 women; mean age, 62.3 ± 9.9 years) were enrolled in our study population.

Of the 830 patients with surgically resected stage I NSCLC, 540 (65.1%) underwent PTNB before surgery, and these patients were categorised as the PTNB group, while the remaining 290 patients underwent bronchoscopic biopsy (n=90, 10.8%) or wedge resection for intraoperative pathological diagnosis during the thoracotomy (n=200, 24.1%), and were categorised as the non-PTNB group (Fig. 1). Tumour staging was determined using the seventh edition of the American Joint Committee on Cancer TNM Staging manual [13].

Diagnostic approach

Our routine practice for the management of nodules was as follows. Bronchoscopic biopsy was performed for nodules with an endobronchial lesion. If the nodule was located in the periphery, PTNB was performed under the guidance of fluoroscopy, CT or cone-beam CT with virtual navigation guidance. PTNB was usually performed with either an 18- or 20-gauge semiautomated cutting needle with a 17- or 19-gauge coaxial introducer (Stericut; TSK Laboratory, Tochigi, Japan), or with an 18- or 20-gauge automated cutting needle (Acecut; TSK Laboratory, Tochigi, Japan). Aspiration with a 22-gauge Westcott needle (MD TECH, Gainesville, FL, USA) was occasionally performed if the nodule had a high risk of complications. If the nodule remained undetermined or highly suspicious for malignancy, wedge resection for an intraoperative pathological diagnosis was performed. If the nodule was diagnosed as lung cancer, the surgeons subsequently performed complete resection of the nodule.

Assessment of recurrence

Postoperative chest CT was performed every 6–12 months to screen for recurrence for at least 5 years after surgery. Pleural recurrence was defined as newly developed pleural nodules or malignant pleural effusion of the ipsilateral hemithorax at the first recurrence. It was confirmed by pleural nodule biopsy or pleural fluid cytology. If these modalities were not available, an increase in the size and number of pleural nodules on follow-up CT was considered to indicate pleural recurrence.

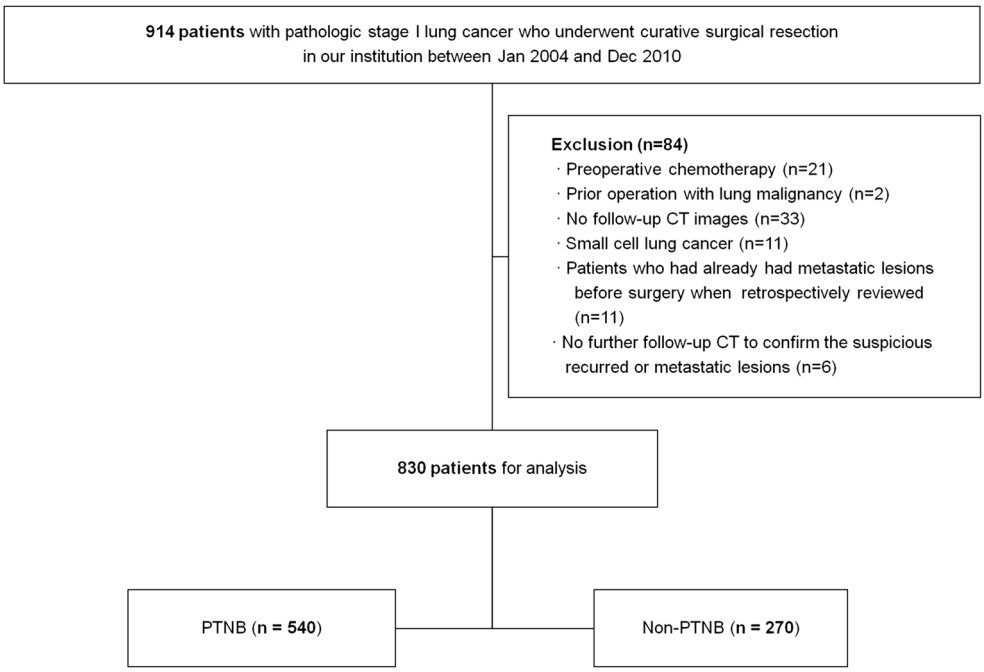

Fig. 1 Flowchart of patient inclusion process

Concomitant pleural recurrence was defined when pleural recurrence occurred with any other type of recurrence.

Statistical analysis

Continuous and categorical variables were compared using the independent-samples t-test and Pearson's chi-square test or Fisher's exact test, respectively. Progression-free survival curves were estimated using the Kaplan-Meier method with the log-rank test. Cox regression models were used to identify the risk factors associated with recurrence. Variables with $p<0.10$ in the univariate analysis were used as input variables for the Cox regression analysis. In addition, to reduce possible selection bias, propensity score matching (PSM) analysis was performed. The propensity score was calculated using a multiple logistic regression model with the variables of age, sex, tumour size, nodule type, pleural contact and visceral pleural invasion. A standardised difference < 0.10 was used to support the balance assumption between the PTNB and non-PTNB groups [14]. All statistical analyses were performed using SPSS version 23.0 (IBM Corp., Armonk, NY, USA) and SAS software (version 9.4; SAS, Institute, Inc., Cary, NC, USA). *P*-values < 0.05 were considered to indicate significant differences.

Results

Clinical and histopathological characteristics

The clinical and histopathological characteristics of the PTNB and non-PTNB groups are summarised in Table 1. The patients in the PTNB group were older (62.8 vs. 61.3 years, $p=0.033$), had a larger tumour size (2.6 vs. 2.0 cm, $p<0.001$), were more likely to have solid tumours (70.7% vs. 50.0%, $p<0.001$) and had more tumours with pleural contact (51.7% vs. 43.8%, $p=0.031$) than the non-PTNB group. The distribution of histological types was significantly different between the two groups ($p=0.004$). Visceral pleural invasion and microscopic lymphatic invasion were more common in the PTNB group (37.8% vs. 20.3%, $p<0.001$; 10.2% vs. 5.2%, $p=0.013$, respectively).

Recurrence pattern after surgical resection

The postoperative follow-up periods were 59.9 ± 35.9 months in the PTNB group and 67.0 ± 33.6 months in the non-PTNB group ($p=0.004$). There were three patients with less than 1 month of follow-up without evidence of recurrence; two were in the PTNB group and one was in the non-PTNB group.

Before PSM, the overall recurrence rate was higher in the PTNB group (n=145, 26.9%) than in the non-PTNB group (n=45, 15.5%) ($p< 0.001$). Local recurrence or regional lymph node metastasis were the most common sites of recurrence in both groups (n=92, 63.4% and n=35, 77.8%, respectively). The concomitant pleural recurrence rate was higher in the PTNB group (n=34, 6.3%) than in the non-PTNB group (n=8, 2.8%) ($p=0.027$). However, the isolated pleural recurrence rate showed no significant differences between the PTNB (n=20, 3.7%) and non-PTNB (n=6, 2.1%) groups.

Table 1 Clinical and histopathological characteristics in the percutaneous transthoracic needle biopsy (PTNB) and non-PTNB groups

	PTNB (n=540)	Non-PTNB (n=290)	Bronchoscopic biopsy (n=90)	Wedge resection (n=200)	*p*-value†
Age (years)*	62.8 ± 9.8	61.3 ± 10.1	63.2 ± 8.7	60.4 ± 10.5	0.033‡
Sex					0.084
Male	296 (54.8)	177 (61.0)	85 (94.4)	92 (46.0)	0.084
Female	244 (45.2)	113 (39.0)	5 (5.6)	108 (54.0)	
Tumour size (cm)*	2.6 ± 1.0	2.0 ± 1.2	2.8 ± 1.3	1.6 ± 0.9	<0.001‡
Tumour consistency					
Solid	382 (70.7)	145 (50.0)	84 (93.3)	61 (30.5)	<0.001
Subsolid	158 (29.3)	145 (50.0)	6 (6.7)	139 (69.5)	
Pleural contact	279 (51.7)	127 (43.8)	95 (47.5)	32 (35.6)	0.031
Histological subtype					
Adenocarcinoma	401 (74.3)	192 (66.2)	13 (14.4)	179 (89.5)	0.004
Squamous cell carcinoma	96 (17.8)	80 (27.6)	62 (68.9)	18 (9.0)	
Others	43 (8.0)	18 (6.2)	15 (16.7)	3 (1.5)	
Visceral pleural invasion	204 (37.8)	59 (20.3)	12 (13.3)	47 (23.5)	<0.001
Microscopic vascular invasion	+9 (1.7)	6 (2.1)	2 (1.0)	4 (4.4)	0.678
Microscopic lymphatic invasion	55 (10.2)	15 (5.2)	8 (8.9)	7 (3.5)	0.013
Stage					
IA	266 (49.3)	178 (61.4)			0.001
IB	274 (50.7)	112 (38.6)			

Unless otherwise indicated, data are numbers of patients, and data in parentheses are percentages

*Data are mean ± standard deviation

† *p*-value for comparison of characteristics between PTNB and non-PTNB groups

‡ *p*-value was calculated with the independent samples t-test

Propensity score-matching analysis

Of the 830 patients, 235 were extracted from the PTNB and non-PTNB groups, respectively, using PSM. After matching using the estimated propensity score, the mean and prevalence of variables were well balanced between the PTNB and non-PTNB groups (Table 2).

The 5-year overall concomitant and isolated pleural recurrence-free survival rates were 95.0% and 97.1%, respectively, in the PTNB group, and the corresponding rates in the

Table 2 Characteristics of percutaneous transthoracic needle biopsy (PTNB) and non-PTNB groups matched by propensity score

	PTNB (n = 235)	Non-PTNB (n = 235)	*p*-value
Age (years)*	62.5 ± 9.6	62.3 ± 10.3	0.821†
Sex			0.924
Male	148 (63.0)	147 (62.6)	
Female	87 (37.0)	88 (37.4)	
Size (cm)*	2.3 ± 1.1	2.1 ± 1.2	0.173†
Tumour consistency			0.85
Solid	141 (60.0)	143 (60.9)	
Subsolid	94 (40.0)	92 (39.1)	
Pleural contact	105 (44.7)	106 (45.1)	0.926
Visceral pleural invasion	54 (23.0)	57 (24.3)	0.745
Follow-up (months)	63.7± 36.6	64.1 ± 34.3	0.908

Unless otherwise indicated, data are numbers of patients, and data in parentheses are percentages

*Data are mean ± standard deviation

† *p*-value was calculated with the independent samples t-test

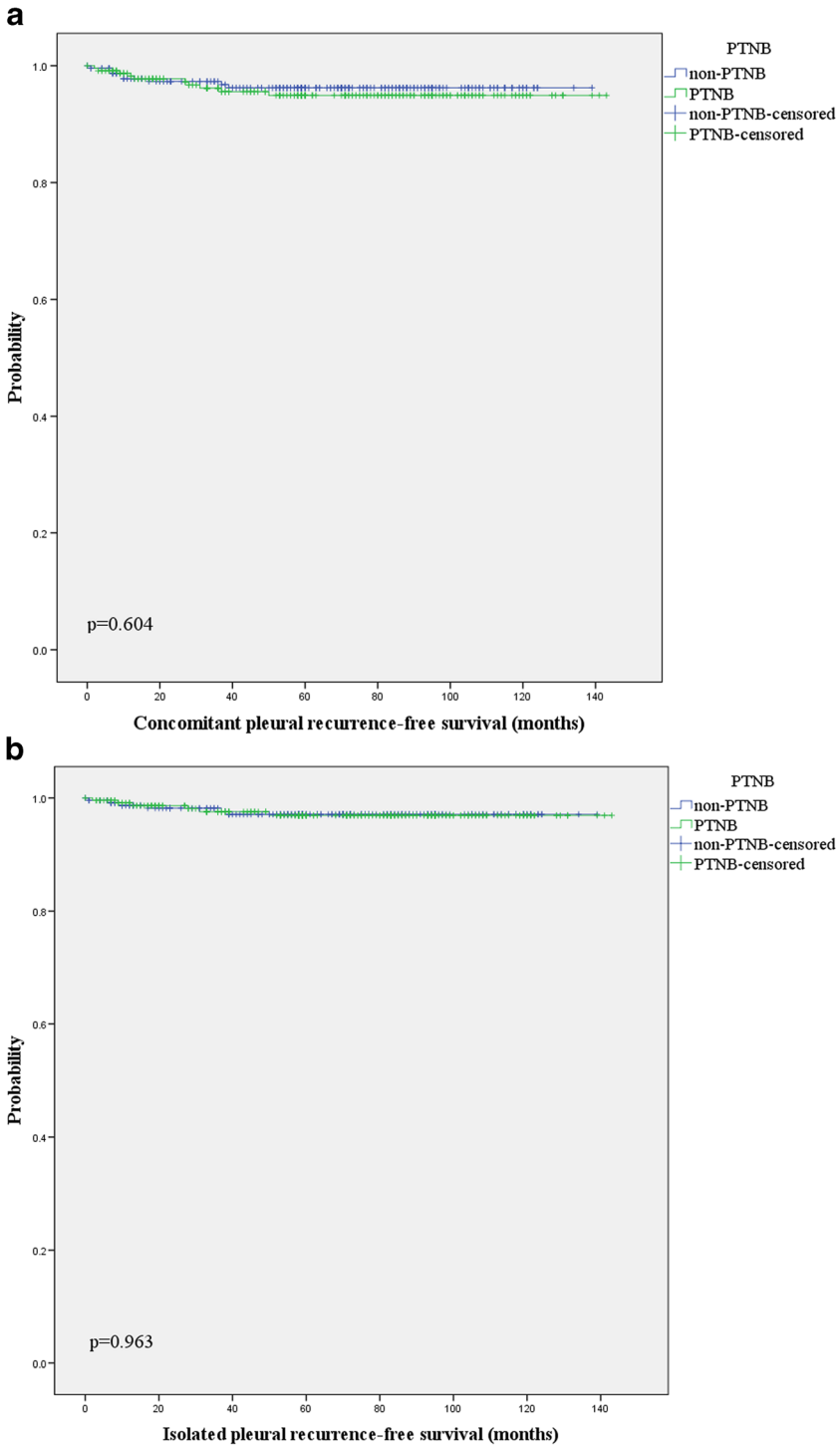

Fig. 2 Kaplan-Meier plot of concomitant and isolated pleural recurrence-free survival according to percutaneous transthoracic needle biopsy (PTNB) after propensity-matching analysis. PTNB did not influence concomitant (p=0.604) and isolated pleural recurrence (p=0.963)

non-PTNB group were 96.2% and 96.9%, respectively. There were no significant differences between the groups regarding survival (p=0.604 and p=0.963, respectively) (Fig. 2).

For concomitant pleural recurrence, prior to PSM, a solid nodule, tumour size, visceral pleural invasion, microscopic lymphatic invasion, pleural contact and PTNB were associated with concomitant pleural recurrence in the univariate analysis (p=0.004, 0.001, <0.001, 0.001, 0.004 and 0.003, respectively). The Cox regression analysis revealed that visceral pleural invasion (hazard ratio [HR]=3.002; 95% CI, 1.680–5.364; p<0.001) and microscopic lymphatic invasion (HR=2.168; 95% CI, 1.075–4.371; p=0.031) increased the risk of pleural recurrence. When analysed with PSM, a solid nodule and visceral pleural invasion were associated with concomitant pleural recurrence (p=0.038 and p=0.003, respectively) and the multivariate Cox regression analysis revealed that visceral pleural invasion was

the only significant risk factor for concomitant pleural recurrence (HR=3.367; 95% CI, 1.262–8.986; p=0.015).

For isolated pleural recurrence, three variables (visceral pleural invasion, microscopic lymphatic invasion and pleural contact) were identified as statistically significant predictors in the univariate analysis before PSM (p=0.001, 0.005 and 0.034, respectively). Visceral pleural invasion (HR=3.298; 95% CI, 1.483–7.334; p=0.003) and microscopic lymphatic invasion (HR=3.016; 95% CI, 1.197–7.603; p=0.019) were predictors of isolated pleural recurrence in the multivariate analysis. When PSM was applied, only visceral pleural invasion was associated with isolated pleural recurrence (p=0.037), and it remained a significant risk factor in the multivariate analysis (HR=3.216; 95% CI, 1.037–9.978; p=0.043) (Table 3, Fig. 3).

Transfissural approach as a risk factor for pleural recurrence in the PTNB group

We performed a further analysis to identify whether the transfissural approach raised the risk of pleural recurrence in the 540 patients in whom PTNB was performed. The transfissural approach, which involves three visceral pleural punctures, was additionally evaluated, along with other variables. There were 26 cases of transfissural approach in the PTNB group. In the univariate analysis, the transfissural approach was not associated with concomitant (p=0.539) or isolated pleural recurrence (p=0.313). Tumour size (p=0.011), pleural contact (p=0.004), visceral pleural invasion (p<0.001) and microscopic lymphatic invasion (p=0.001) increased the risk of concomitant pleural recurrence. Pleural contact (p=0.032), visceral pleural invasion (p=0.014) and microscopic lymphatic invasion (p=0.002) increased the risk of isolated pleural recurrence. In the multivariate analysis, visceral pleural invasion (HR=2.432; 95% CI, 1.265–4.674; p=0.008) and microscopic lymphatic invasion (HR=2.557; 95% CI, 1.248–5.238; p=0.010) were found to be risk factors for concomitant recurrence. Microscopic lymphatic invasion was associated with an increased risk of isolated pleural recurrence (HR=3.511; 95% CI, 1.325–9.304; p=0.012) (Table 4).

Discussion

Our large, retrospective, propensity score-matched study confirmed that PTNB did not significantly increase the risk of concomitant or isolated pleural recurrence in stage I NSCLC

Table 3 Results of Cox's regression analysis for risk factors for concomitant and isolated pleural recurrence after propensity score matching analysis

	Concomitant pleural recurrence			Isolated pleural recurrence		
	HR	95% CI	p-value	HR	95% CI	p-value
Univariate analysis						
PTNB	1.278	0.504–3.239	0.605	1.027	0.331–3.185	0.963
Age (years)*	0.989	0.946–1.034	0.624	0.999	0.944–1.058	0.974
Male	1.320	0.495–3.518	0.579	1.330	0.400–4.422	0.641
Tumour size (cm)*	1.385	0.982–1.952	0.063	1.153	0.728–1.824	0.544
Solid	3.723	1.077–12.870	0.038	3.760	0.823–17.179	0.087
Pleural contact	2.545	0.955–6.782	0.062	2.544	0.766–8.449	0.127
Visceral pleural invasion	4.167	1.644–10.558	0.003	3.334	1.075–10.338	0.037
Microscopic lymphatic invasion	2.554	0.739–8.828	0.138	1.167	0.151–9.046	0.882
Tumour histology						
Adenocarcinoma	1.000		reference	1.000		reference
Squamous cell carcinoma	0.625	0.180–2.176	0.460	1.105	0.293–4.170	0.882
Others	0.694	0.091–5.280	0.724	1.219	0.152–9.751	0.852
Multivariate analysis						
Tumour size (cm)*	1.200	0.821–1.752	0.346	N/A	N/A	N/A
Pleural contact	1.585	0.559–4.494	0.387	N/A	N/A	N/A
Solid	3.155	0.894–11.134	0.074	3.624	0.793–16.566	0.097
Visceral pleural invasion	3.367	1.262–8.986	0.015	3.216	1.037–9.978	0.043

HR hazard ratio, *CI* confidence interval, *PTNB* percutaneous transthoracic needle biopsy, *N/A* not applicable

Unless otherwise indicated, data are numbers of patients, and data in parentheses are percentages

*Data are mean ± standard deviation

† p-value was calculated with the independent samples t-test

‡ p-value was calculated with Fisher's exact tes.

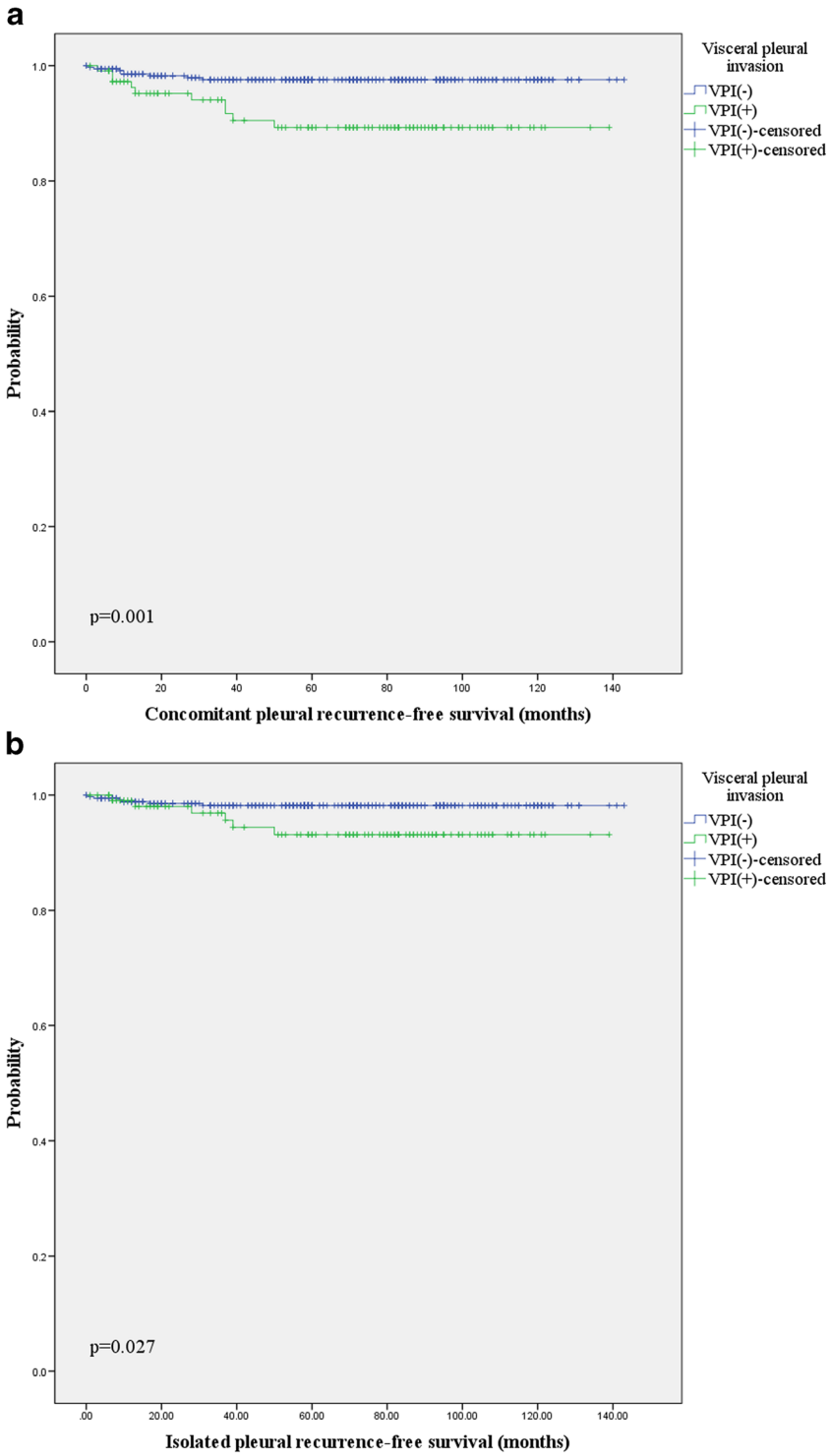

Fig. 3 Kaplan-Meier plot of concomitant and isolated pleural recurrence-free survival according to visceral pleural invasion after propensity matching analysis. Visceral pleural invasion increased the risk of concomitant and isolated pleural recurrence (p=0.001 and 0.027, respectively)

and that the transfissural approach likewise did not increase the risk of pleural recurrence during a median follow-up of longer than 5 years.

It was natural that the PTNB and non-PTNB groups had lung cancers with different characteristics, potentially affecting the likelihood of ipsilateral pleural recurrence. In particular, in the PTNB group, more cancers had a peripheral location, pleural contact was more common and visceral pleural invasion was more frequent. A bronchoscopic approach is recommended for the pathological diagnosis of central lesions, while PTNB is preferable for that of peripheral lesions. In addition, wedge resection was preferentially performed for small ground-glass lesions in this study. To resolve these fundamental differences originating from the different indications

Table 4 Results of Cox's regression analysis for risk factors for concomitant and isolated pleural recurrence after percutaneous transthoracic needle biopsy (PTNB)

	Concomitant pleural recurrence			Isolated pleural recurrence		
	HR	95% CI	*p*-value	HR	95% CI	*p*-value
Univariate analysis						
Transfissural approach	1.444	0.447–4.668	0.539	2.120	0.492–9.137	0.313
Age (years)*	0.982	0.953–1.012	0.244	0.985	0.942–1.029	0.495
Male	1.203	0.659–2.198	0.547	1.397	0.571–3.419	0.464
Tumour size (cm)*	1.395	1.079–1.802	0.011	1.241	0.837–1.841	0.283
Solid	1.595	0.786–3.239	0.196	1.092	0.419–2.844	0.858
Pleural contact	2.644	1.358–5.150	0.004	3.032	1.102–8.344	0.032
Visceral pleural invasion	3.236	1.728–6.060	<0.001	3.185	1.270–7.984	0.014
Microscopic vascular invasion	1.817	0.250–13.206	0.555	3.967	0.530–29.659	0.179
Microscopic lymphatic invasion	3.202	1.577–6.503	0.001	4.394	1.686–11.451	0.002
Tumour histology						
Adenocarcinoma	1		reference	1		reference
Squamous cell carcinoma	0.739	0.289–1.894	0.529	0.961	0.278–3.321	0.950
Others	1.802	0.703–4.619	0.220	1.578	0.361–6.904	0.545
Multivariate analysis						
Tumour size (cm)*	1.197	0.907–1.581	0.204	N/A	N/A	N/A
Pleural contact	1.796	0.882–3.655	0.106	2.235	0.781–6.397	0.134
Visceral pleural invasion	2.432	1.265–4.674	0.008	2.320	0.887–6.066	0.086
Microvascular lymphatic invasion	2.557	1.248–5.238	0.010	3.511	1.325–9.304	0.012

HR hazard ratio, *CI* confidence interval, *PTNB* percutaneous transthoracic needle biopsy

Unless otherwise indicated, data are numbers of patients, and data in parentheses are percentages

*Data are mean ± standard deviation

† *p*-value was calculated with the independent samples t-test

‡ *p*-value was calculated with Fisher's exact test

for these procedures, we balanced the PTNB and non-PTNB groups using PSM, with the consideration of important confounding factors for ipsilateral pleural recurrence, such as pleural contact and visceral pleural invasion.

Our results are in good agreement with those of a recently published meta-analysis [12] that demonstrated that PTNB did not increase the risk of pleural recurrence compared with non-PTNB strategies in patients with early-stage lung cancer. Even though some studies [9–12] have reported an increased risk of pleural recurrence after PTNB in early-stage lung cancer, PTNB does not affect overall or recurrence-free survival [9, 12, 15]. Taken together, we believe that PTNB is an appropriate diagnostic procedure for peripheral early lung cancer, with no need for concern about effects on survival outcomes associated with procedure-related pleural recurrence.

Pleural contact was not associated with an increased risk of pleural recurrence in this population after adjustment for visceral pleural invasion. On the contrary, subpleural nodules have been associated with pleural recurrence in some studies [9, 10, 12]. We assume that this discrepancy between our results and those of other studies originates from the association between subpleural location and visceral pleural invasion; specifically, subpleural lesions are more likely to have visceral pleural invasion [16], but the presence of visceral pleural invasion was not incorporated in their analyses. Visceral pleural invasion was a significant risk factor for pleural recurrence after complete resection in pathological stage I lung adenocarcinoma [17–19]. Indeed, after adjustment for visceral pleural invasion, pleural contact was not found to be a meaningful factor in predicting pleural recurrence, which is in agreement with the results of Moon et al. [12].

We also investigated the risk of pleural recurrence after PTNB and demonstrated that the transfissural approach did not increase pleural recurrence. Theoretically, an additional pleural puncture may increase the risk of pleural recurrence; however, this possible mechanism has not yet been studied. The presence of visceral pleural invasion and microscopic lymphatic invasion were significant risk factors for pleural recurrence in patients who had undergone PTNB, which is consistent with the results of Moon et al. [12]. Nevertheless, the baseline characteristics of our study showed some discrepancies with previous studies. In most previous studies, patients

in the non-PTNB group had larger tumours, but in our study, patients in the PTNB group had larger tumours, which can lead to a higher incidence of recurrence. Kashiwabara et al. [10] reported that pleural recurrence did not occur in part-solid nodules; however, there were eight (2.9%) cases of pleural recurrence in the 279 part-solid nodules analysed this study, whereas recurrence was not observed in the 24 pure ground-glass nodules, in accordance with their findings. More patients underwent PTNB than procedures other than PTNB, in contrast to previous studies [7, 9–11]. This discrepancy may reflect institutional differences.

Our study has several limitations. First, there are the inherent limitations of a retrospective study design. In addition, fundamental differences were inevitably present in the characteristics of patients and nodules between the PTNB and non-PTNB groups. However, we tried to overcome selection bias by covariance adjustments with PSM, while maintaining sufficient numbers of patients after matching. Nevertheless, a further prospective study in a larger population is warranted to confirm that PTNB does not increase the risk of pleural recurrence. Second, procedural factors other than the transfissural approach, such as the needle size, number of tissue samples, the use of aspiration or biopsy, or the use of the coaxial technique could not be analysed in this study because detailed data for these variables were not available, particularly in older medical records.

In conclusion, PTNB did not significantly increase the risk of concomitant or isolated pleural recurrence in stage I NSCLC; instead, visceral pleural invasion was responsible for pleural recurrence. PTNB can be performed for the confirmatory diagnosis of peripheral early-stage lung cancer without concern for the risk of concomitant or isolated pleural recurrence.

Funding The authors state that this work has not received any funding.

Compliance with ethical standards

Guarantor The scientific guarantor of this publication is Soon Ho Yoon.

Conflict of interest The authors of this article declare no relationships with any companies whose products or services may be related to the subject matter of the article.

Statistics and biometry One of the authors has significant statistical expertise.

Informed consent Written informed consent was waived by the Institutional Review Board.

Ethical approval Institutional Review Board approval was obtained.

Methodology
- Retrospective
- Observational
- Performed at one institution

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