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Ipsilateral pleural recurrence after diagnostic transthoracic needle biopsy in pathological stage I lung cancer patients who underwent curative resection

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ABSTRACT

Objectives: The relationship between transthoracic needle biopsy (TTNB) and pleural recurrence of cancer after curative lung resection remains unclear. We aimed to assess whether TTNB increases the ipsilateral pleural recurrence (IPR) rate and identify other potential risk factors for pleural recurrence after surgery.

Materials and methods: This retrospective study included 392 patients with p-stage I non-small cell lung cancer with solid or part-solid nodules after curative lung resection in 2009–2010. Imbalances among the characteristics were adjusted using an inverse probability-weighted method based on propensity scoring. Multivariate Cox's regression analysis and the Kaplan-Meier method were used to determine independent risk factors for IPR.

Results: A total of 243 (62%) patients received TTNB, while 149 (38%) underwent an alternate, or no, diagnostic technique. IPR was significantly more frequent in the TTNB group (p = 0.004), while total recurrence was similar between the groups (p = 0.098). After applying the weighted model, diagnostic TTNB (hazard ratio [HR], 5.27; 95% confidence interval [CI], 1.49–18.69; p = 0.010), microscopic visceral pleural invasion (HR, 2.76; 95% CI, 1.08–7.01; p = 0.033) and microscopic lymphatic invasion (HR, 3.25; 95% CI, 1.30–8.10; p = 0.012) were associated with an increased frequency of IPR. Among patients who received TTNB, microscopic lymphatic invasion was a risk factor for IPR (HR, 2.74; 95% CI, 1.10–6.79; p = 0.030).

Conclusions: The diagnostic TTNB procedure is associated with pleural recurrence but may be unrelated to overall recurrence-free survival in early lung cancer. Moreover, microscopic lymphatic invasion could be a risk factor for pleural recurrence. TTNB should be carefully considered before lung resection and close follow-up to detect if pleural recurrence is needed.

1. Introduction

Transthoracic needle biopsy (TTNB), one of the most widely used tools for the diagnosis of lung nodules, is valuable in distinguishing among neoplastic, focal infectious and inflammatory lesions [1–3]. In evaluations of indeterminate pulmonary nodules, TTNB has shown high accuracy and safety for detection of malignancy [1–4]. Therefore, TTNB is an important alternative to invasive surgery for histologic diagnosis, especially for patients who have a higher risk of surgical complications and those who wish to confirm malignancy before surgery [1,2,5].

Despite the usefulness of TTNB, several complications associated with this diagnostic tool have been reported [3,5–7]. The most frequent complication is pneumothorax with a reported rate of approximately 20%, followed by pulmonary hemorrhage and, rarely, air embolism, which is a life-threatening complication [3–6]. In addition, tumor seeding after TTNB performed for a malignant lesion is an extremely rare complication [4,7,8]. Recently, several reports have suggested that TTNB increases the frequency of pleural recurrence in completely resected early-stage lung cancer [9–11]. However, this is inconclusive, because other studies have indicated that diagnostic TTNB is not associated with pleural recurrence [12,13].

In light of this, we conducted a retrospective study to assess whether

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TTNB increases the rate of ipsilateral pleural recurrence (IPR) and to identify other potential risk factors for IPR in patients with pathologic stage I non-small cell lung cancer after curative lung resection. In addition, we investigated the relevant factors associated with pleural recurrence in patients who had undergone TTNB.

2. Materials and methods

2.1. Study population

Between January 2009 and December 2010, 538 patients with pathologic stage I NSCLC underwent curative surgical resection at the Samsung Medical Center (a 1979-bed referral hospital in Seoul, South Korea). After excluding patients with patients with ground-glass opacity lesions which is diagnosed by lung wedge resection rather than TTNB (n = 76), patients who received adjuvant chemotherapy at the physician's discretion (n = 44), and patients lost to follow-up after surgery (n = 26), the remaining 392 patients with pathologic stage I NSCLC with solid or part-solid nodules who underwent follow-up after curative lung resection without adjuvant treatment were enrolled in this study. Of these 392 patients, those who received TTNB as a diagnostic procedure were categorized as the "TTNB" group and those who underwent bronchoscopic biopsy, lung wedge resection, or no treatment before curative lung resection were classified as the "non-TTNB" group (Fig. 1).

This retrospective study was approved by the Institutional Review Board of the Samsung Medical Center (IRB No. 2016-07-144). Informed consent for the use of medical data was waived, because patient information was anonymized and de-identified prior to analysis.

2.2. Diagnostic evaluation

The diagnostic procedures performed were considered in all patients to obtain a histologic diagnosis. All patients underwent bronchoscopic evaluation before lung resection, and if a diagnostic specimen was not obtained by bronchoscopic biopsy, fluoroscopy or computed tomography (CT)-guided TTNB was performed using a detachable 18- or 20-gauge automated cutting needle (Acecut, TSK Laboratory) depending on the tumor size and location. If TTNB could not be performed, or if the diagnosis was indeterminate, lung resection was performed as a diagnostic procedure or as curative therapy for the suspicion of malignancy. Tumors were classified into five groups based on the greatest tumor dimension, I (≤1 cm), II (> 1–≤2 cm), III (> 2–≤3 cm), IV (> 3—≤4 cm), and V (> 4–≤5 cm).

2.3. Assessment of recurrence after curative lung resection

After successful performance of lung resection, imaging tests including a contrast chest CT scan or proton emission tomography were performed every 3 months during the first year, every 6 months during the second year, and annually thereafter for at least 5 years after surgery to detect recurrence. Local recurrence was defined as recurrence in the ipsilateral thorax including IPR whereas distant recurrence was defined as recurrence that developed in contralateral thorax or extrapulmonary involvement. Pleural recurrence was defined as new development of pleural nodules or pleural effusion found in chest CT scan. The pleural recurrence was confirmed by pleural biopsy or pleural fluid cytology. If they were not available, increased numbers and size of pleural nodules or extent of nodularity in CT, or hypermetabolism in proton emission tomography were regarded as pleural recurrence.

2.4. Statistical analysis

All data are described as means ± standard deviation for continuous variables and numbers (percentage) for categorical variables. Data were compared using the *t*-test for continuous variables and Pearson's χ^2 test or Fisher's exact test for categorical variables. An inverse probability-weighted (IPW) method was used to overcome possible patient selection bias. A logistic regression model was used to calculate the probability or propensity score of IPR for each patient based on clinicopathological variables. The IPW Cox model was used to investigate independent predictors of IPR. In addition, Cox's regression analysis was performed to identify the risk factors associated with IPR after TTNB. The Kaplan-Meier method with log-rank tests was used to estimate the difference in time-to-event outcomes between the TTNB and non-TTNB groups using two-sided *P*-values. A two-sided *P*-value of < 0.05 was considered to indicate a statistically significant difference in all analyses. All statistical analyses were executed using R version 3.2.0 (R Development Core Team, Vienna, Austria; http://www.R-project.org).

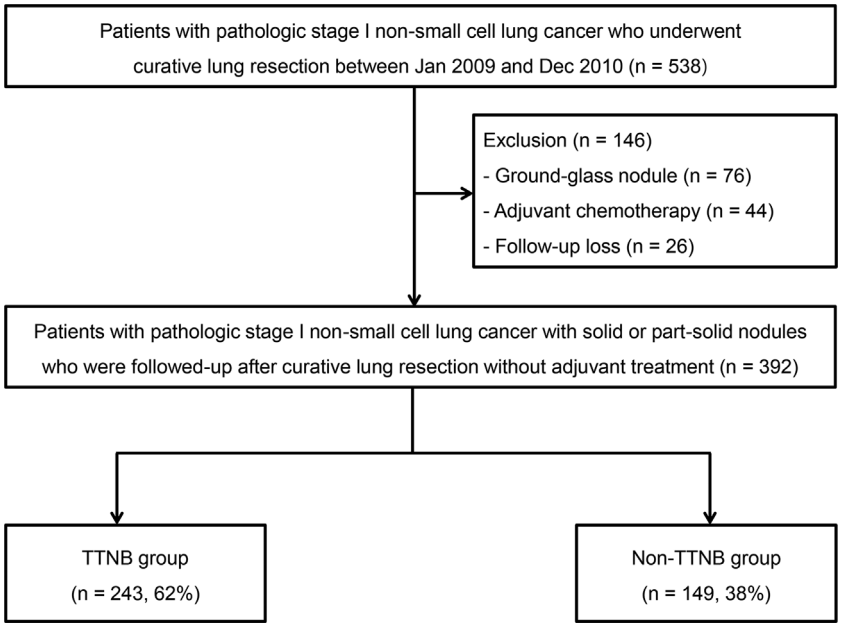

Fig. 1. Study population.

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