# Exploring Diagnostic Pathways and Factors for Early Detection of Lung Cancer in Small and Large Nodule Patients

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## OBJECTIVE

- Lung cancer is frequently diagnosed at advanced stages.
- Early detection significantly improves outcomes.
- This study investigates the characteristics and diagnostic pathways of patients with small nodules (SN) versus large nodules (LN) to identify factors that could improve early diagnosis.

## METHODS

- A retrospective analysis was conducted using the Japanese Medical Data Vision (MDV) from 2008 to 2023.
- Patients with T1a or T1b lung cancer were classified as SN, while those with more advanced T stages were categorized as LN.
- Patients without any diagnostic procedures before cancer confirmation, those with TX, T0, or Tis stages, and those with incomplete records were excluded.
- Patient characteristics, biopsy and imaging rate, and time to cancer confirmation were compared between SN and LN groups.
- Logistic regression was used to identified factors influencing biopsy decisions.

## RESULTS

- The cohort included 11,989 SN and 31,278 LN patients. Only 20.2% of SN and 20.7% of LN patients received biopsy.
- SN patients were younger, more likely to be female, less likely to smoke, and had higher obesity rates.

**Table1. Patients baseline characteristics**

| Characteristics | Small Nodule* (n = 11989) | T1c-T4 (n = 31278) | p-value | ASMD |
|---|---|---|---|---|
| Sex | | | <0.001 | |
| Female (n, %) | 4739 (39.53%) | 8992 (28.75%) | | 0.023 |
| Male (n, %) | 7250 (60.47%) | 22286 (71.25%) | | 0.023 |
| Age (mean, SD) | 70.97 (9.64) | 73.59 (10.13) | <0.001 | 0.265 |
| BMI * | | | <0.001 | |
| Normal (n, %) | 8032 (66.99%) | 19836 (63.42%) | | 0.075 |
| Obese (n, %) | 2748 (22.92%) | 4898 (15.66%) | | 0.185 |
| Underweight (n, %) | 1209 (10.08%) | 6544 (20.92%) | | 0.303 |
| Smoking index | | | <0.001 | |
| Nonsmoker (n, %) | 4765 (39.74%) | 9585 (30.64%) | | 0.191 |
| <400 (n, %) | 1123 (9.37%) | 2293 (7.33%) | | 0.074 |
| 400~799 (n, %) | 1808 (15.08%) | 4951 (15.83%) | | 0.021 |
| ≥800 (n, %) | 4293 (35.81%) | 14449 (46.20%) | | 0.212 |
| CCI (mean, SD) | 1.23 (1.99) | 1.03 (2.05) | <0.001 | 0.099 |
| COPD (n, %) | 1637 (13.65%) | 2689 (8.6%) | <0.001 | 0.161 |
| Chronic Kidney Disease (n, %) | 174 (1.45%) | 300 (0.96%) | <0.001 | 0.045 |
| Diabetes Mellitus (n, %) | 1763 (14.71%) | 2870 (9.18%) | <0.001 | 0.017 |
| Coronary Artery Disease (n, %) | 39 (0.33%) | 50 (0.16%) | 0.001 | 0.34 |
| Myocardial Infarction (n, %) | 122 (1.02%) | 214 (0.68%) | 0.001 | 0.036 |
| Arterial Hypertension (n, %) | 1604 (13.38%) | 3034 (9.7%) | <0.001 | 0.115 |
| Metastatic Cancer (n, %) | 505 (4.21%) | 1845 (5.9%) | <0.001 | 0.077 |
| Care setting | | | <0.001 | |
| Inpatient (n, %) | 11138 (92.9%) | 28604 (91.45%) | | 0.054 |
| Outpatient (n, %) | 851 (7.1%) | 2674 (8.55%) | | 0.054 |
| Hospital Scale (Beds) | | | <0.001 | |
| <200 (n, %) | 509 (4.25%) | 1912 (6.11%) | | 0.084 |
| 200~499 (n, %) | 6334 (52.83%) | 18078 (57.8%) | | 0.100 |
| ≥500 (n, %) | 5146 (42.92%) | 11288 (36.09%) | | 0.140 |

ASMD: absolute standardized mean difference; SD: standard deviation; BMI: body mass index; CCI: Charlson comorbidity index; COPD: Chronic Obstruction Pulmonary Disease.

*Small Nodule: T1a and T2b stage patients according to the eighth edition TNM stage classification for lung cancer.

†The Japan Society for the Study of Obesity (JASSO) defines BMI classifications as follows: underweight, <18.5 kg/m2; normal, 18.5 to <25 kg/m2; obese, ≥25 kg/m2.

- Among SN patients who received biopsies, 37.7% had multiple biopsies and was higher than LN patients (29.2%, p <.001). SN patients experienced longer time to cancer confirmation: 90 days longer from first procedure to confirmation, and 45 days longer from first suspected diagnosis to confirmation (p < 0.001).

**Table2. Procedures before lung cancer confirmation**

| Characteristics | Small Nodule* (n = 11989) | T1c-T4 (n = 31278) | p-value |
|---|---|---|---|
| Received Biopsy (n, %) | 2423 (20.2%) | 6482 (20.7%) | 0.242 |
| Multiple (n, %) | 913 (37.7%) | 1891 (29.2%) | <0.001 |
| Single (n, %) | 1510 (62.3%) | 4591 (70.8%) | |
| Average Biopsy numbers including 0 (mean, SD) | 0.29 (0.63) | 0.28 (0.60) | 0.154 |
| Average Biopsy numbers excluding 0 (mean, SD) | 1.42 (0.60) | 1.34 (0.58) | <0.001 |
| Average Biopsy numbers excluding 0&1 (mean, SD) | 2.10 (0.43) | 2.15 (0.48) | 0.012 |
| First Biopsy Type | | | <0.001 |
| EBUS-TBNA (n, %) | 223 (9.2%) | 787 (12.1%) | |
| TB Cryobiopsy (n, %) | 10 (0.4%) | 39 (0.6%) | |
| TB Navigation (n, %) | 56 (2.3%) | 117 (1.8%) | |
| TB Virtual Broncoscpoe (n, %) | 69 (2.8%) | 117 (1.8%) | |
| TBLB (n, %) | 1742 (71.9%) | 4636 (71.5%) | |
| TTNA (n, %) | 323 (13.3%) | 786 (12.1%) | |
| Received imaging (n, %) | 11971 (99.8%) | 31162 (99.6%) | <0.001 |
| Received imaging number (mean, SD) | 8.09 (9.96) | 6.29 (9.29) | <0.001 |
| First Procedure Type | | | <0.001 |
| Biopsy (n, %) | 147 (1.2%) | 664 (2.1%) | |
| Imaging (n, %) | 11842 (98.8%) | 30614 (97.9%) | |
| Days from 1st Procedure to lung cancer confirmation (mean, SD) | 498.83 (785.28) | 409.91 (778.53) | <0.001 |
| Days from 1st Biopsy to lung cancer confirmation (mean, SD) | 85.38 (248.23) | 52.16 (219.46) | <0.001 |
| Days from 1st Imaging to lung cancer confirmation (mean, SD) | 499.54 (785.66) | 411.16 (789.39) | <0.001 |
| Days from lung cancer suspected to confirmation (mean, SD) | 197.76 (441.10) | 152.93 (440.66) | <0.001 |

EBUS-TBNA: endobronchial ultrasound transbronchial needle aspiration; TB: tuberculous; TBLB: transbronchial lung biopsy; TTNA: transthoracic needle aspiration

*Small Nodule: T1a and T2b stage patients according to the eighth edition TNM stage classification for lung cancer.

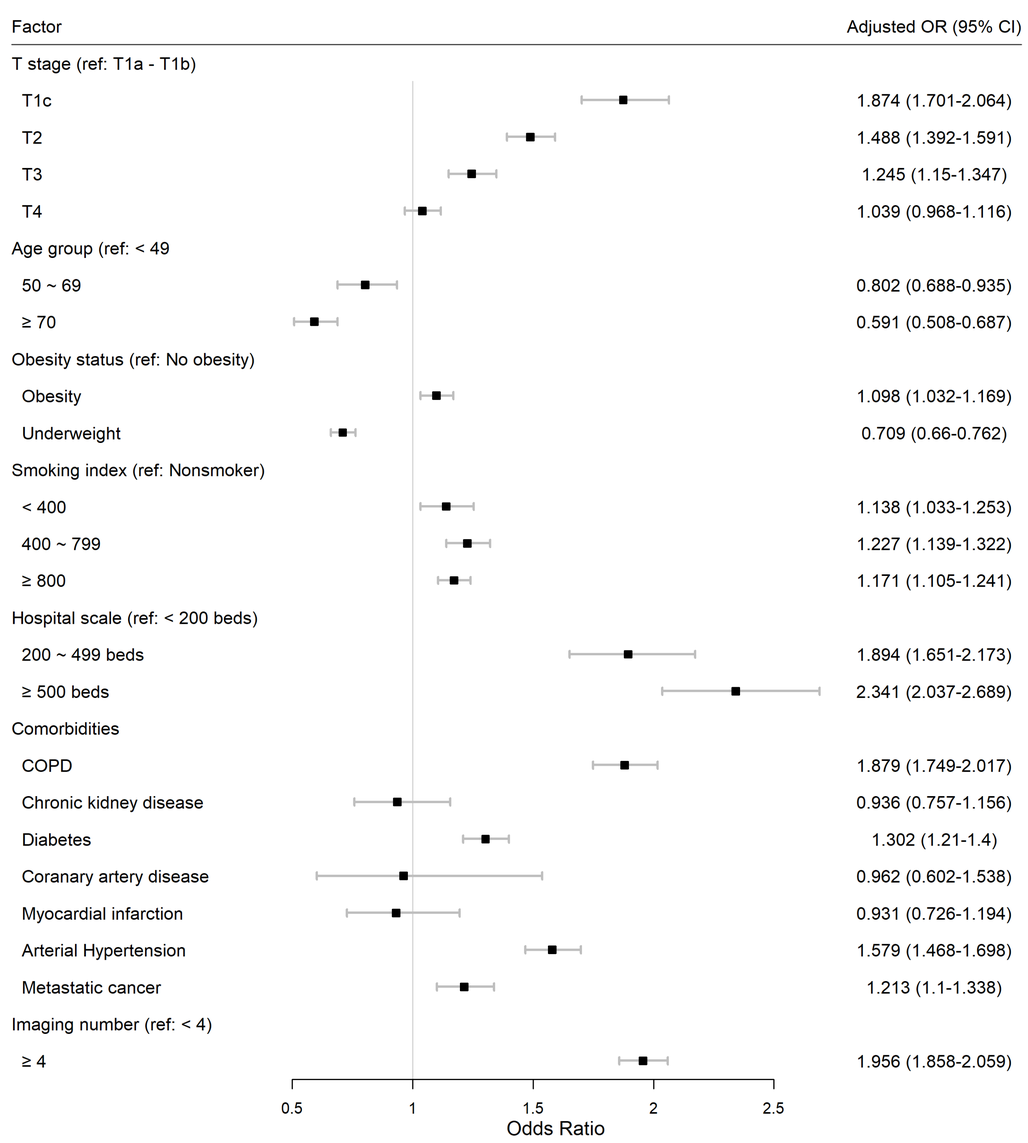


**Figure 1. Forest Plot of Multivariate Logistic Regression in Lung Cancer Patients**

- Biopsy before cancer confirmation was more common in patients with smaller nodules, but rare in SN patients with T1a or T1b tumors (< 2 cm). Factors associated with a higher likelihood of pre-diagnosis biopsy included younger age, obesity, smoking, larger hospital size, frequent imaging, COPD, hypertension, diabetes, and metastatic disease.

## CONCLUSIONS

- This study highlights the diagnostic challenges of SN lung cancer in Japan and identifies factors for early diagnosis. Addressing low biopsy rates and improving biopsy technology may enhance early detection and patient outcomes.

INTUITIVE