Non-examination of lymph nodes in early-stage non-small cell lung cancer is associated with resections and underutilization of adjuvant chemotherapy

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Abstract 

Background: Lymph nodes are an essential component of the treatment of lung cancer and are recommended as standard of care, given that the detection of the correct ‘N’ stage is important for disease staging, which in turn determines the appropriate adjuvant therapy. 

Methods: This retrospective observational cohort study used SEER cancer registry data linked with Medicare claims data from 2006-2017. The primary outcome was receipt of adjuvant treatment (including chemotherapy, targeted therapy, immunotherapy and radiation). The primary exposure was lymph node examination status (pNX, pN0, pN1, pN2, pN3). The primary exposure was compared across study subgroups, time to adjuvant treatment, and survival outcomes. 

Results: Among 19,360 patients with eNSCLC and available lymph node examination status, 60% received lymph node examination. After adjusting for patient characteristics, lymph node examination was associated with receipt of adjuvant treatment (pN0 vs. pNX; HR 0.77, 95% CI 0.67-0.89, p<0.001; pN1 vs. pNX; HR 0.71, 95% CI 0.60-0.84, p<0.001). The receipt of adjuvant treatment was further decreased in patients with pN2/pN3 status (pN2 vs. pNX; HR 0.55, 95% CI 0.48-0.62, p<0.001; pN3 vs. pNX; HR 0.48, 95% CI 0.37-0.64, p<0.001). The association between lymph node examination and receipt of adjuvant treatment was stronger and more significant in the more recent study years (2010-2017). 

Conclusions: There are many resections in which lymph nodes are not examined, and patients without lymph node examination are less likely to receive adjuvant treatment. Given recent advancements in the adjuvant treatment of eNSCLC, due to the availability of immunotherapy, there is an increased importance in understanding whether the prevalence of lymph node examination has improved in recent years and whether lymph node examination improves outcomes in patients with non-small cell lung cancer.

Figure 1. Patient selection

Figure 2. Lymph node examination across study period

Figure 3. Median (IQR) number of lymph node examined (112,132)

Figure 4. Distribution of number lymph node examined

Table 1. Patient characteristics

Table 2. Receipt of adjuvant treatment and time to adjuvant treatment (%)

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REFERENCES

1. European Society for Medical Oncology (ESMO) Annual Meeting 2022, 9-13 September 2022, Paris, France and Virtual

1. METHODS

The distribution of the number of lymph nodes examined is shown in Figure 4. 

1. RESULTS

Lymph Node Examination

The proportion of pN2 patients decreased from 16% in 2010 to 8% in 2017, this trend was statistically significant (p<0.001) (Figure 2). 

Time to adjuvant treatment was calculated as the number of days between surgery date and adjuvant treatment start date. 

Statistical Analysis

Patient characteristics were assessed using descriptive statistics including mean (sd) for continuous variables and frequencies and percentages for categorical variables. 

Characteristics are seen presented overall and by pNX, pN0, and pN1/pN2/pN3 groups. 

Differences in patient characteristics were assessed using Kruskal-Wallis or ANOVA for continuous variables and chi-square tests for categorical variables. 

Prevalence of lymph node examination was assessed overall and by year of diagnosis, including testing for trends by year of diagnosis. 

Number of lymph nodes evaluated was assessed using the median (interquartile range (IQR)) and distribution of patients. 

Receipt of adjuvant treatment and time to adjuvant treatment (among those treated) were assessed overall and by lymph node examination status. 

Treatment differences were tested using Wilcoxon rank sum tests for time to treatment and treatment-free survival tests for categorical treatment variables. 

All results were summarized with descriptive statistics using R, version 4.1 (2021-11-11 release). 

CONCLUSIONS

Lymph node examination and receipt of adjuvant therapy (including chemotherapy, targeted therapy, immunotherapy and radiation) were identified in Medicare Parts A, B and D for ≥6 months post-surgery or up to 2010 and December 2017. 

Prevalence of lymph node examination was analyzed overall and by year of diagnosis, including testing for trends by patient diagnosis year. 

- Differences in patient characteristics were tested using Kruskal-Wallis or Wilcoxon rank sum tests for continuous variables. 

- Statistical Analysis

- METHODS

- RESULTS

- CONCLUSIONS

- REFERENCES

- DISCLOSURES

- ACKNOWLEDGMENTS

- BACKGROUND

- Surgery is the primary treatment for patients with early-stage non-small cell lung cancer (eNSCLC), and patients with stage IA-IIIA disease who meet the National Comprehensive Cancer Network (NCCN) guidelines for resection by thoracotomy, video-assisted thoracoscopic surgery ( VATS), or robotic-assisted thoracoscopic surgery (RATS).

- Adjuvant treatment is recommended for all patients following resection, regardless of lymph node status, based on the potential impact of occult metastases and the benefit of adjuvant chemotherapy in prolonging survival.

- The prevalence of lymph node examination has increased in recent years, but lower than for pN1 and pN2 patients (pN1 vs. pNX; HR 0.71, 95% CI 0.60-0.84, p<0.001; pN2 vs. pNX; HR 0.55, 95% CI 0.48-0.62, p<0.001). The receipt of adjuvant treatment was further decreased in patients with pN2/pN3 status (pN2 vs. pNX; HR 0.55, 95% CI 0.48-0.62, p<0.001; pN3 vs. pNX; HR 0.48, 95% CI 0.37-0.64, p<0.001). The association between lymph node examination and receipt of adjuvant treatment was stronger and more significant in the more recent study years (2010-2017). 

- These findings suggest a need for continued education of the clinical community on the importance of lymph node evaluation, and the need for further research to determine the optimal number of nodes to examine and the impact of lymph node examination on survival outcomes.

- The distribution of the number of lymph nodes examined is shown in Figure 4. 

- Among those patients included in the adjuvant treatment cohort (2010-2017), 31% received adjuvant treatment during the identification period (pNX). 

- The proportion of patients who received adjuvant treatment was higher among pN0 (58%) and pN1 (74%) patients compared to pN2 and pN3 patients. Adverse prognostic factors for pN0 (58%) patients were higher than for pN2 patients but higher than for pN3 patients (Figure 4).