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Original Research

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Quality Gaps and Comparative Effectiveness in Lung Cancer Staging and Diagnosis

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Background: **Guidelines recommend mediastinal lymph node sampling as the first invasive test in patients with suspected lung cancer with mediastinal lymphadenopathy without distant metastases, but there are no comparative effectiveness studies on how test sequencing affects outcomes. The objective was to compare practice patterns and outcomes of diagnostic strategies in patients with lung cancer.**

Methods: **The study included a retrospective cohort of 15,316 patients with lung cancer with regional spread without distant metastases in the Surveillance, Epidemiology, and End Results or Texas Cancer Registry Medicare-linked databases. If the first invasive test involved mediastinal sampling, patients were classified as receiving guideline-consistent care; otherwise, they were classified as receiving guideline-inconsistent care. We used propensity matching to compare the number of tests performed and multivariate logistic regression to compare the frequency of complications.**

Results: **Twenty-one percent of patients had guideline-consistent diagnostic evaluations. Among patients with non-small cell lung cancer, 44% never had mediastinal sampling. Patients who had guideline-consistent care required fewer tests than those with guideline-inconsistent care ($P < .0001$), including thoracotomies (49% vs 80%, $P < .001$) and CT image-guided biopsies (9% vs 63%, $P < .001$), although they had more transbronchial needle aspirations (37% vs 4%, $P < .001$). The consequence was that patients with guideline-consistent care had fewer pneumothoraxes (4.8% vs 25.6%, $P < .0001$), chest tubes (0.7% vs 4.9%, $P < .001$), hemorrhages (5.4% vs 10.6%, $P < .001$), and respiratory failure events (5.3% vs 10.5%, $P < .001$).**

Conclusions: **Guideline-consistent care with mediastinal sampling first resulted in fewer tests and complications. We found three quality gaps: failure to sample the mediastinum first, failure to sample the mediastinum at all in patients with non-small cell lung cancer, and overuse of thoracotomy.**

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Abbreviations: EBUS = endobronchial ultrasound; NSCLC = non-small cell lung cancer; SEER = Surveillance, Epidemiology, and End Results; TBNA = transbronchial needle aspiration; TCR = Texas Cancer Registry

In patients with suspected lung cancer without distant metastases, assessment of the mediastinal lymph nodes is important because the status of the lymph nodes will help the physician to determine whether the disease is surgically resectable.[1] Because of the limited accuracy of both CT and PET scanning, current evidence-based guidelines recommend that patients with mediastinal adenopathy by CT or PET scan undergo lymph node sampling to ensure accurate staging.[1-4]

However, significant discordance may exist between what is recommended in evidence-based guidelines and what is actually done in practice. Previous studies of patients with non-small cell lung cancer (NSCLC) found that mediastinoscopy is infrequently performed, and even then, lymph nodes are biopsied in < 50% of cases.[5,6] Alternative methods of mediastinal lymph node sampling, such as transbronchial needle aspiration (TBNA), have also been underused partly because of inadequate fellowship training.[7-10]

Although these studies demonstrate that mediastinal sampling techniques have been underused, an equally important question is how mediastinal sampling techniques are used in practice. Multiple evidence-based guidelines recommend mediastinal lymph node sampling as the first invasive diagnostic procedure in patients

with suspected lung cancer with mediastinal adenopathy without distant metastases because the procedure can be used for both diagnosis and staging.[2-4,11-16] However, to our knowledge, only one single-center comparative effectiveness study has evaluated how test sequencing affects outcomes.[17]

The goal of the present study was to compare practice patterns and outcomes of diagnostic and staging strategies in patients with lung cancer with mediastinal lymph node involvement without distant metastasis. We hypothesized that peripheral lung mass biopsy often occurs prior to sampling of the mediastinal lymph nodes, contrary to guidelines. We further hypothesized guideline-inconsistent care would result in unnecessary procedures and more complications.

Materials and Methods

Data Source

We performed a retrospective cohort analysis of two datasets: the National Cancer Institute Surveillance, Epidemiology, and End Results (SEER) database and the Texas Cancer Registry (TCR). The registry data have been linked to Medicare claims and 2000 US Census data. We compared the registries and analyzed practice patterns and outcomes. This study was approved by institutional review board 4, and a waiver of informed consent was obtained.

Study Participants

The cohort comprised patients with lung cancer with regional spread to the hilar or mediastinal lymph nodes without distant metastases. The algorithms and search results are shown in Figure 1 (see e-Table 1 for additional details). For patients entered into SEER prior to 2004 and for all patients in the TCR, American Joint Committee on Cancer nodal staging was not recorded; therefore, it was not possible to further stratify patients into N1 vs N2 vs N3 status. For patients in SEER from 2004 or later, precise TNM staging could be obtained.

Diagnostic and Staging Strategy

The type and sequencing of invasive tests used for diagnosis and staging were determined by Current Procedural Terminology and *International Classification of Diseases, Ninth Edition*, codes (e-Table 1). Invasive tests were defined as CT image-guided needle biopsy, bronchoscopy, endoscopy with ultrasound-guided needle aspiration, mediastinoscopy, or thoracotomy. Only tests done within the 6 months preceding the initiation of treatment were considered. Patients were placed into groups based on their diagnostic testing sequence: (1) evaluation consistent with guidelines, some form of mediastinal sampling done first; (2) evaluation inconsistent with guidelines, NSCLC present, mediastinal sampling performed on the second or later biopsy; (3) evaluation inconsistent with guidelines, NSCLC present, mediastinal sampling never done; and (4) evaluation inconsistent with guidelines, small cell lung cancer. Mediastinal sampling procedures were defined as bronchoscopy with TBNA or endobronchial ultrasound (EBUS)-guided TBNA, endoscopy with ultrasound-guided needle aspiration, mediastinoscopy, thoracoscopy, or thoracotomy with mediastinal lymph node sampling (see e-Appendix 1 for details on categories and criteria).

Outcomes

The primary outcome was whether the evaluation strategy was consistent with guidelines. Secondary outcomes were whether mediastinal lymph node sampling was ever performed prior to treatment in patients with NSCLC, complications related to the diagnostic evaluation, and the number of invasive diagnostic tests performed. We used a methodology similar to that previously published to identify complications, including pneumothorax, hemorrhage, and respiratory failure.[18] For thoracotomy, any hemorrhage or respiratory failure occurring within 14 days of surgery was considered a complication. For all other procedures, complications were only counted if they occurred up to 1 day after the procedure. We conducted a subset analysis of patients in SEER from 2004 and later to assess the impact of T and N stage on practice patterns. We also conducted an exploratory analysis to assess the relationship among diagnostic practice patterns, subsequent treatment modalities used, and survival.

Statistical Analysis

Characteristics of patients and outcomes were compared using χ^2 test for categorical variables; *t* tests for continuous, normally distributed variables; and Wilcoxon rank sum test for nonnormally distributed variables. We used multivariate logistic regression to analyze factors associated with complications due to diagnostic testing. We decided a priori that variables significantly associated with outcomes at the 0.2 level in univariate analysis would be considered candidate variables for multivariate analysis. Backward selection was used to retain only variables with a level of significance $< .05$. The number of invasive tests performed was not normally distributed, so we used propensity scores to match patients who had guideline-consistent care with mediastinal sampling first with counterparts who had mediastinal sampling performed second or later. The conditional probability to have guideline-consistent care was estimated by logistic regression analysis incorporating the following variables: age, sex, race, year of diagnosis, Charlson comorbidity index, T stage, geographic region, and cancer type. All statistical analyses were performed at a significance level of .05. All

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