Surgical Treatment for Early Small Cell Lung Cancer: Variability in Practice and Impact on Survival

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Background. **Surgical resection with lobectomy is recommended for T1/T2 N0 small cell lung cancer (SCLC) patients after negative mediastinal staging. We sought to characterize variation in surgical therapy for early SCLC and determine the effect of a hospital's practice patterns on patient survival.**

Methods. **The National Cancer Database was examined from 2004 to 2013. Risk- and reliability-adjusted hierarchical logistic regression was used to estimate the adjusted odds of resection by hospital. Hospitals were then grouped into quartiles by observed-to-expected rates of surgical treatment. Patient, tumor, and hospital characteristics were compared across quartiles. Kaplan-Meier plots and Cox proportional hazard models were built to compare patient survival as a function of a hospital's tendency to use surgical intervention.**

Results. **We identified 5,079 patients with T1/T2 N0 SCLC in 317 hospitals, and 1,260 underwent resection. Analysis after adjusting for demographic, comorbidity, and tumor factors showed patients treated at hospitals in the highest quartile of surgical use were 17 times more likely to undergo surgical resection than those in the lowest quartile (44.8% vs 7.6%; odds ratio, 16.7l; 95% confidence interval, 12.59 to 22.18). Hospitals in the highest quartile were more likely to be academic centers (48% vs 21%), more likely to perform lobectomy (28.3% vs 5.0%), and treated more mixed-histology tumors (11.1% vs 4.5%). Survival was significantly longer for patients treated at hospitals most likely to use surgical therapy (median, 25.3 vs. 18.8 months; $p < 0.0001$). Hazard ratio differences in mortality persisted in multivariate Cox models (hazard ratio, 0.80; 95% confidence interval, 0.72 to 0.89; $p < 0.0001$).**

Conclusions. **Large variation exists in the use of surgical therapy for early SCLC in the United States, which may represent a significant quality improvement opportunity for patients with early SCLC.**

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Small cell lung cancer (SCLC) is a common pulmonary malignancy accounting for 25,000 cases yearly [1]. Despite advances in the treatment of this disease, primarily with chemotherapy and radiotherapy, the 5-year survival rate remains low [2, 3]. Surgical therapy is not widely used because of a propensity for early development of distant metastatic disease and because nearly all patients initially present with in locally advanced and metastatic stages (IIIA, IIIB, and IV). However, there is a population of patients with early (stage I and II) disease that may benefit from surgical therapy [4–7]. Furthermore, surgical treatment is a key part of multimodality therapy for the approximately 5% of patients presenting with very early disease (T1/T2).

There is a growing body of evidence that surgical resection, in particular lobectomy, is associated with longer survival and approaches 40% to 50% at 5 years with adjuvant chemotherapy [4, 6, 8–10]. Adjuvant radiotherapy can further improve survival in node-positive patients, especially those found to have pathologic N2 disease, and in patients receiving wedge excisions [11, 12].

In fact, most major oncology guidelines, including those from the American Society of Clinical Oncology (ASCO), the European Society for Medical Oncology, and the National Comprehensive Cancer Network recommend surgical resection for localized (clinical T1/T2 N0 M0) disease if invasive staging of mediastinal lymph nodes reveals no evidence of mediastinal spread on pathologic evaluation [13–15]. Previous evaluation of practice patterns has shown surgical resection is vastly underused in this population of very early SCLC [16, 17], but the scope of variation in the use of surgical therapy is

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unknown. Further, how delivery of guideline-concordant treatment affects overall survival in this population has not been investigated.

For this reason, we set out to characterize variability in practice patterns between hospitals in the use of surgical management for early-stage SCLC because such variations may represent significant quality improvement opportunities. Lastly, associations between the use of resection and overall survival are important to understand because they may point to actionable strategies to improve patient care and survival for a high-risk but potentially treatable group of lung cancer patients.

Patients and Methods

Study Design and Objectives

This was a retrospective study of patients with early-stage SCLC in the National Cancer Data Base (NCDB) from 2004 to 2013. This study had three objectives: (1) to examine the national trends and variation in the use of surgical management for early (clinical T1/T2 N0 M0 with negative pathologic mediastinal evaluation) SCLC between hospitals; (2) to examine patient and hospital characteristics as they relate to hospital tendency for use of surgical management; and (3) to determine the effect of hospital use of surgical management on patient survival.

Data Source

Data were derived from the NCDB participant user file. The NCDB is a national cancer registry administered jointly through the American College of Surgeons Commission on Cancer and the American Cancer Society [18]. The database contains approximately 26 million patients from more than 1,500 participating institutions and captures approximately 70% of newly diagnosed cancer cases in the United States annually. Standardized collection and data definitions have been previously described [18]. The NCDB collects data on patient and hospital characteristics, cancer diagnosis, staging, treatments, and outcomes. The American College of Surgeons Commission on Cancer has not verified and is not responsible for the analytic methods used or the conclusions drawn by the investigators in this study. The University of Utah Institutional Review Board exempted the study from review.

Study Population

The study population included adult patients (aged ≥18 years) with a histologic diagnosis of invasive small-cell bronchogenic carcinoma confirmed by microscopic examination of a tissue specimen or cytologic specimen. Diagnoses for SCLC were identified using International Classification of Diseases for Oncology, Third Edition codes 8041 to 8045. Clinical and pathologic stages are reported according to the Seventh Edition of American Joint Committee on Cancer tumor, node, metastases (TNM) staging criteria.

Derivation of the study cohort is outlined in Figure 1. Patients were excluded if they had missing information on whether a surgical procedure had been performed, if they underwent undefined or ablative procedures, of if data for clinical stage were missing. Our goal was to create a population of patients who would be eligible for

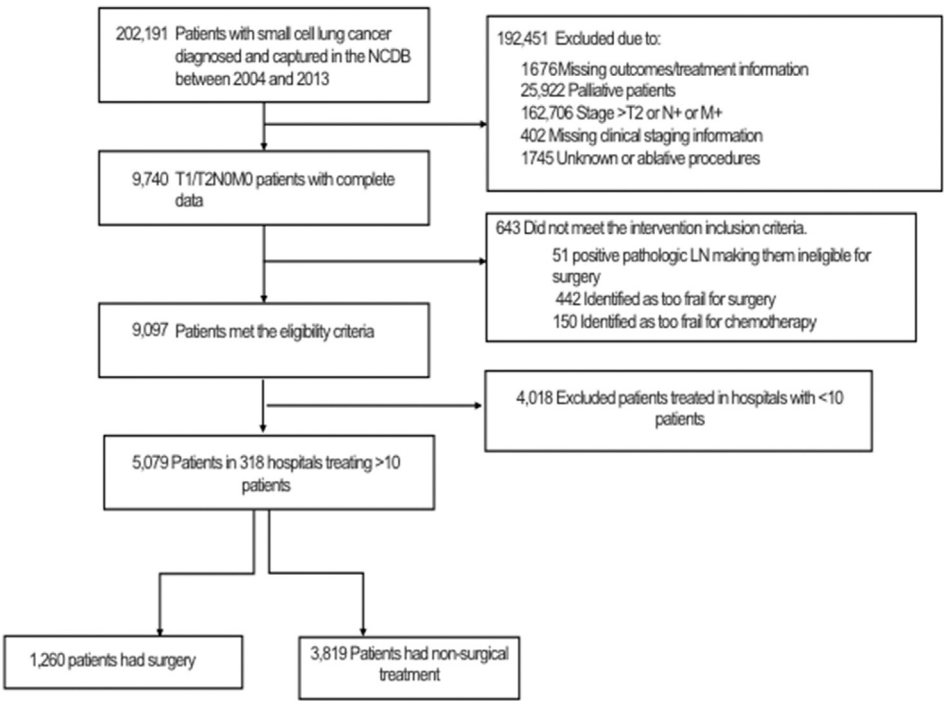

Fig 1. Study flow diagram. (LN = lymph node; NCDB = National Cancer Database.)