Lung Cancer 109 (2017) 117–123

Contents lists available at ScienceDirect

Lung Cancer

journal homepage: www.elsevier.com/locate/lungcan

Trends, practice patterns and underuse of surgery in the treatment of early stage small cell lung cancer

E. Wakeam[a,b,*], T.K. Varghese Jr.[f,g], N.B. Leighl[c], M. Giuliani[d,e], S.R.G. Finlayson[f], G.E. Darling[b]

[a] Division of General Surgery, Department of Surgery, University of Toronto, Toronto, Canada
[b] Division of Thoracic Surgery, Department of Surgery, University of Toronto, Toronto, Canada
[c] Division of Medical Oncology, Department of Medicine, University of Toronto, Toronto, Canada
[d] Department of Radiation Oncology, University of Toronto, Toronto, Canada
[e] Radiation Medicine Program, Princess Margaret Cancer Centre, Toronto, Canada
[f] Department of Surgery, University of Utah, Salt Lake City, UT, United States
[g] Division of Thoracic Surgery, Department of Surgery, University of Utah, Salt Lake City, UT, United States

ARTICLE INFO

Keywords:
Small cell lung cancer
Thoracic surgery
Quality improvement
Cancer outcomes
Surgical disparities

ABSTRACT

Background: Practice guidelines from the National Comprehensive Cancer Network and the American Society of Clinical Oncology recommend pathologic mediastinal staging and surgical resection for patients with clinically node-negative T1/T2 small cell lung cancer (SCLC), but the extent to which surgery is used is unknown. We sought to assess trends and practice patterns in the use of surgery for SCLC.

Methods: T1 or T2N0M0 SCLC cases were identified in the National Cancer Database (NCDB), 2004–2013. Characteristics of patients undergoing resection were analyzed. Hierarchical logistic regression was used to identify individual and hospital-level predictors of receipt of surgery, adjusting for clinical, demographic and facility characteristics. Trends in resection rates were analyzed over the study period.

Findings: 9740 patients were identified with clinical T1 or T2 N0M0 SCLC. Of these, 2210 underwent surgery (22.7%), with 1421 (64.3%) undergoing lobectomy, 739 (33.4%) sublobar resections and 50 (2.3%) pneumonectomies. After adjustment, Medicaid patients were less likely to receive surgery (OR0.65 95% CI 0.48–0.89, $p = 0.006$), as were those with T2 tumors (OR0.25 CI0.22–0.29, $p < 0.0001$). Academic facilities were more likely to resect eligible patients (OR 1.90 CI1.45–2.49, $p < 0.0001$). Between 2004 and 2013, resection rates more than doubled from 9.1% to 21.7%. Overall, 68.7% of patients were not offered surgery despite having no identifiable contraindication. In patients not receiving surgery, only 7% underwent pathologic mediastinal staging.

Interpretation: Rates of resection are increasing, but two thirds of potentially eligible patients fail to undergo surgery. Further study is required to address the lack of concordance between guidelines and practice.

1. Introduction

Small cell lung cancer (SCLC) is a deadly malignancy impacting approximately 25 thousand people in the United States each year, comprising approximately 15% of new lung cancer diagnoses. Prognosis for the disease remains poor, with little observed improvement over the last 30 years [1]. Poor prognosis and a propensity for widespread dissemination has led many to view SCLC as a disease that is, in most cases, best treated with chemotherapy- and radiation-based strategies. Inclusion of surgery in multimodality treatment has been reported with mixed results [2,3], although early trials showed little benefit for surgery [4,5].

Since those trials were completed, much progress has been made in our ability to detect, image and accurately stage SCLC. More recent investigations using several large databases as well as a prospective cohort study have demonstrated that surgery may be beneficial in selected clinical circumstances [6–8]. Current guidelines from the National Comprehensive Cancer Network (NCCN), as well as those from the European Society of Medical Oncology, the American Society for Clinical Oncology and the American College of Chest Physicians recommend invasive mediastinal staging for all T1 and T2 patients with no evidence of metastatic disease [9–11]. Guidelines then recommend subsequent lobectomy for medically fit patients who are found to be node-negative. Prior work has shown that the subset of resectable patients has a 5-year survival rate of about 40–50% at 5 years [6]. Adjuvant chemotherapy in all cases and radiation in certain cases,

* Corresponding author at: Division of General Surgery, University of Toronto, 30 Bond St, Rm 3073, Queen Wing North Toronto, ON M5W 1W8, Canada.
E-mail address: Elliot.wakeam@utoronto.ca (E. Wakeam).

http://dx.doi.org/10.1016/j.lungcan.2017.05.004
Received 17 October 2016; Received in revised form 22 April 2017; Accepted 6 May 2017

including those found to be pathologically node-positive, can further lead to prolonged survival [12,13]. Despite this, surgery is not commonly incorporated in multimodality treatment and the rates at which patients are offered resection is unknown. Further, it is unknown whether certain populations are more or less likely to receive surgical resection, and trends over time in the use of surgery in SCLC have not been defined.

The goals of this investigation are threefold. First, we sought to define predictors for the receipt of surgical therapy amongst clinical T1 and T2 N0M0 patients with SCLC, including hospital and patient characteristics. Secondly, we wanted to examine trends over time in the rates of surgical resection for potentially eligible patients. Lastly, we wanted to explore reasons for not receiving surgery, which are contained within the National Cancer Database [14].

2. Methods

2.1. Population and data sources

The National Cancer Data Base (NCDB) is a national cancer registry administered jointly through the American College of Surgeons' Commission on Cancer and the American Cancer Society [15]. The database contains approximately 26 million patients from over 1500 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 [15]. The NCDB collects data on patient and hospital characteristics, cancer diagnosis, staging, treatments, and outcomes. The data used in this study are derived from a de-identified NCDB participant user file. The American College of Surgeons and the Commission on Cancer have not verified and are neither responsible for the analytic or statistical methodology employed nor the conclusions drawn from these data by the investigators.

The study population included patients 18 years of age or older diagnosed between 2004 and 2013. Patients were restricted to histologic diagnosis of invasive small-cell bronchogenic carcinoma confirmed by microscopic examination of tissue specimen or cytologic specimen, and International Classification of Diseases for Oncology, Third Edition (ICD-0–3) codes 8041–8045. Clinical and pathological stages are reported according to the 7th edition of AJCC's tumor, node, metastases (TNM) staging criteria.

Patients were included if they were classified as clinical stage T1 or T2, N0M0. Patients were excluded if they were classified as palliative, or if they had missing information on whether a surgical procedure had been performed. The main outcome of interest was the receipt of surgical resection, which included anatomic lobectomy, sublobar resections, which included anatomic segmentectomy and non-anatomic wedge resections, and pneumonectomy. Patients undergoing undefined or ablative procedures were excluded. Patients with missing or erroneous data for clinical stage were also excluded. A study flow diagram is shown in Fig. 1. This left a final cohort of 9740 clinical stage T1 or T2N0M0 patients. Reasons for not receiving surgical therapy were classified by the NCDB and can be found in the NCDB data dictionary [14].

2.2. Population characteristics

Population characteristics for those patients treated operatively and non-operatively were examined. Patients were compared in terms of age, education, insurance, income, race, ethnicity and rural residence. Tumour T stage, histology and patient Charlson-Deyo score was also compared.

Hospital characteristics were also examined and included facility type, as defined by the NCDB. This variable describes academic, comprehensive community, community and integrated cancer treatment systems. Hospital volume was defined as the total case volume for SCLC cases during the study period. Because we were examining receipt of surgical therapy as the primary outcome, surgical volumes were not examined, as they are co-linear with the outcome. Facility location was defined by region. The hospitals in the top quartile of patients on Medicaid were designated as hospitals with a high Medicaid burden. Similarly, the proportion of patients who were low-income or belonging to a racial minority was also defined by hospital, with those hospitals in the top quartile being defined as hospitals with a high-proportion of low income patients or minority-serving, respectively.

Student's T-test and Wilcoxon Test were used to compare continuous variables and Chi square test was used for categorical variables.

2.3. Risk factors for receipt of surgery

Univariate analysis was performed to identify significant predictors of receipt of surgery. Unadjusted hierarchical models, which accounted for clustering by hospital, were used to identify significant predictors. A strategy of purposive selection was used to construct the final models. Patient characteristics such as age, race, sex, income, insurance, rural residence, Spanish-speaking ethnicity, and education were included. Tumor T-stage was also included, as was Charlson-Deyo score to account for patient comorbidity. Hospital characteristics such as academic status, total volume of SCLC cases, facility location, Medicaid burden, proportion of minority and low-income patients were all analyzed. Any predictor with p value < 0.1 was included in the final models.

Multilevel, hierarchical models were constructed which included all the variables identified with p-value < 0.1 in univariate analyses. Models included a random effect for hospital to account for clustering of patient outcomes within a given hospital.

2.4. Pathologic nodal staging

The NCCN guidelines recommend invasive mediastinal lymph node evaluation for any SCLC patient with clinical stage T1 or T2 N0M0. We evaluated rates of pathologic nodal evaluation for patients meeting potential resectability criteria.

2.5. Time trends

Year of diagnosis was analyzed in univariate and multivariate models as a covariate predictor of receipt of surgery. The proportion of T1/T2N0M0 patients resected by year was examined. Due to the fact that patient covariates also vary by year of diagnosis, the adjusted rate of resection was calculated using generalized estimating equations with values for other covariates set to their population averages. In order to determine whether trends in receipt of surgical therapy were due to changes in the incidence of potentially resectable disease, the proportion resected was also compared to the number of cases of T1/T2N0M0 SCLC diagnosed in a given year as a proportion of total SCLC cases. Although definitive intent of surgery (diagnostic versus curative resection) cannot be ascertained in the NCDB data, we also examined trends in the use of sublobar excisions, which are presumed to be diagnostic, as opposed to lobectomy, which is presumed to be curative. We also examined the use of preoperative biopsy over time. Lastly, the reasons for patients not undergoing or being offered surgery were examined by year of diagnosis. Contraindication to surgery included advanced age or other medical comorbidities precluding resection.

All analyses were done using Stata Version 14 (StataCorp, College Station, TX, USA). P-values of < 0.05 were used as the cut-off for statistical significance.