Surgery for Small Cell Lung Cancer

Alberto de Hoyos, MD, Malcolm M. DeCamp, MD*

KEYWORDS

• Small cell lung cancer • Early-stage small cell lung cancer • Lobectomy • Lung resection

KEY POINTS

- Evidence-based guidelines recommend that patients with newly diagnosed SCLC undergo a complete medical history and physical examination, a pathologic review of biopsy specimens, laboratory studies, imaging studies, and if appropriate, mediastinal nodal staging.
- Surgery can be offered to selected patients with early-stage SCLC as part of a multimodality treatment plan.
- With adequate patient selection, rigorous preoperative staging, and combined multimodality therapy, high rates of local control and satisfying long-term outcomes similar to equivalent-stage NSCLC can be achieved.

The American Cancer Society estimated that 222,500 new cases of lung cancer occurred in the United States in 2010.[1] Of these, small cell lung cancer (SCLC) accounted for 14% or 30,000 of these. More than 90% of these patients will die of their disease. The incidence of SCLC has decreased from 25% of all lung cancers in 1993 to approximately 10% to 14% in 2012.[2,3] SCLC is distinct from non–small cell lung cancer (NSCLC) both biologically and clinically. SCLC is also distinguished from NSCLC by its rapid doubling time and early development of widespread intrathoracic lymph node and distant metastases. Small cell carcinoma is exceedingly rare in nonsmokers, and is more common in men. The percentage of women with SCLC has been rising steadily since the 1970s, likely due to trends in smoking behavior. The average age at diagnosis is 65 to 70 years and it is the variety of lung cancer most commonly associated with paraneoplastic syndromes. Although it is the lung cancer most sensitive to chemotherapy and thoracic radiotherapy (TRT), SCLC has a generally poor prognosis.

Approximately two-thirds of patients presenting with SCLC have clinical evidence of hematogenous metastases (M1) or extensive stage (ES) disease, and chemotherapy is the standard of care. Of the remaining one-third of patients with limited-stage (LS) disease, most have clinical evidence of extensive nodal involvement in the hilar (N1), mediastinal (N2-3), or supraclavicular regions (N3). For this reason, surgical resection is seldom offered in LS-SCLC and instead, 4 to 6 cycles of systemic chemotherapy, with concurrent or sequential TRT, has been typically accepted as the cornerstone of therapy. If a complete remission is achieved, prophylactic cranial irradiation (PCI) improves both overall survival and the incidence of brain metastases. Only 4% to 12% of patients with SCLC have very early stage (VES) disease localized to the lung in the form of a solitary pulmonary nodule (T1-2, N0, M0).[4]

We should no longer equate every diagnosis of SCLC with inoperability. The immortalization of old randomized trials demonstrating lack of benefit of surgery carried out in an era using outdated staging tools and methodology and less effective

The authors have nothing to disclose.
Division of Thoracic Surgery, Northwestern Memorial Hospital, Northwestern University Feinberg School of Medicine, 676 North Saint Clair Street, Suite 650, Chicago, IL 60611, USA
* Corresponding author.
E-mail address: mdecamp@nmh.org

Thorac Surg Clin ■ (2014) ■–■
http://dx.doi.org/10.1016/j.thorsurg.2014.07.005
1547-4127/14/$ – see front matter

drugs has no validity in the present era and should not influence the current management of patients diagnosed with VES-SCLC. Unfortunately, the National Cancer Institute (NCI) Web site attributes a 1A level of evidence to a trial by the Lung Cancer Study Group performed 20 years ago to make recommendations regarding the role of surgery in LS-SCLC (http://www.cancer.gov/cancertopics/pdq/treatment/small-cell lung/healthprofessional/Page5#Section_110). Moreover, the Web site fails to mention more recent prospective trials or larger studies derived from national data bases that show a benefit of surgery in well-selected patients with SCLC. Continuously over the past several years, data have been gathering in support of surgery for early-stage SCLC. Sadly a pessimistic view about the prognosis of all patients with SCLC prevails. Surgery is often not even addressed in review publications.[5] The American College of Surgeons Oncology Group has proposed a prospective trial to verify the role of surgery plus adjuvant chemotherapy for early-stage (IA-IB) SCLC. This trial will include patients who either are found after resection to have early stage or who have biopsy-proven SCLC. The primary end points will be 3-year survival and recurrence patterns.

Although there are no recent randomized trials or meta-analyses supporting the role of surgery in selected early-stage SCLC, with adequate patient selection (good performance status), rigorous preoperative staging (T1-2, N2-3 disease excluded, M0) and combined multimodality therapy (surgery, chemotherapy ± TRT, and PCI), high rates of local control and satisfying long-term outcomes similar to equivalent-stage NSCLC can be achieved. The most current evidence is derived from small prospective or retrospective studies and analysis of large data bases (levels II–IV evidence).

STAGING OF SCLC

For more than 50 years, SCLC has been staged differently from NSCLC. Because most patients with SCLC present with advanced, metastatic disease, the TNM staging system was thought to be clinically irrelevant and the Veterans Administration Lung Cancer Study Group (VALSG) proposed a simplified staging system for use in their randomized clinical trials and focused on the importance of radiation therapy for local control.[6] This dichotomous system divided SCLC into 2 subgroups termed “limited-stage” (LS) and “extensive stage “ (ES). The VALSG system defined LS disease as (1) disease confined to one hemithorax, although local extension may be present; (2) no extrathoracic metastases except for ipsilateral supraclavicular lymph nodes; and (3) primary tumor and regional lymph nodes that can be encompassed adequately in a safe radiation portal. Tumors with ipsilateral pleural effusion not proven malignant, left recurrent laryngeal nerve involvement, or superior vena cava involvement were still included. ES disease was defined as disease that cannot be classified as LS disease, including malignant pleural or pericardial effusions, contralateral hilar or supraclavicular lymph nodes, and hematogenous metastases. In 1989, the International Association for the Study of Lung Cancer (IASLC) modified the VALSG staging including all nonmetastatic patients in the LS group. The consensus report recommended that LS should be expanded to include patients with contralateral hilar, ipsilateral and contralateral mediastinal, and ipsilateral and contralateral supraclavicular node involvement as well as those with ipsilateral pleural effusions, both positive and negative on cytologic examination. This conclusion was based on the observation that the prognosis of patients with contralateral adenopathy and ipsilateral pleural effusions was superior to those with distant metastases and more closely parallel to that of those with LS disease. In practice, most physicians and clinical trials blend the VALSG and the IASLC criteria by considering contralateral mediastinal and ipsilateral supraclavicular lymph node involvement to be LS. Determining the classification of contralateral supraclavicular or hilar node involvement remained controversial, with treatment usually determined individually based on the ability to include these regions in a safe radiation portal.

Because the TNM staging system requires accurate mediastinal lymph node sampling (either by mediastinoscopy or endobronchial ultrasound) and pathologic confirmation at the time of surgery, and most patients with SCLC seldom present at a stage for which surgery is appropriate (2%–6%), the TNM system has not been routinely applied to SCLC. However, in small surgical series of patients with SCLC, the TNM staging system can identify subgroups of patients with distinct prognoses from within the broad definition of LS.

In the 2007 proposal of the seventh edition of the IASLC staging classification system, it was recommended that the TNM system be applied to SCLC to stratify patients with LS disease.[7,8] This was formally adopted in 2010. The recommendation was based on a prognostic analysis of 12,620 patients with SCLC in the IASLC database, 8088 of whom had TNM staging available. Mediastinal lymph node metastases can be found in up to 50% of patients with clinical N1 disease.[9,10] These data emphasize the importance