

Multimodality Approach to Management of Stage III Non–Small Cell Lung Cancer

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KEYWORDS

• Non–small cell lung cancer • Neoadjuvant treatment • Multimodality approach

KEY POINTS

- Non–small cell lung cancer is a serious health condition requiring multidisciplinary input from surgical oncology, radiation oncology, and medical oncology.
- Appropriate staging studies are required to develop the optimal strategy for an individual patient. This strategy includes positron emission tomography/computed tomography scan and endobronchial ultrasonography or mediastinoscopy for locally advanced disease to determine resectability.
- Chemoradiation is the standard approach in stage III lung cancer, with surgery as an option in some cases. Concurrent chemoradiation has been proved to be superior to sequential therapy.
- Cisplatin doublet therapy is considered standard for chemotherapy selection.
- Pathologic review of biopsy samples now includes testing for EGFR gene mutations and EML4-ALK gene rearrangements.

INTRODUCTION

According to the American Cancer Society, there were an estimated 222,520 new cases of lung cancer in 2010. It is the second most prevalent cancer in men and women, behind prostate cancer and breast cancer, respectively. It is responsible for the most cancer-related deaths in both men and women. Lung cancer was responsible for 157,300 deaths in 2010.¹ The mortality data are impressive when compared with other cancers (**Table 1**).

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Cancer	Incidence	Mortality
Lung	222,520	157,300
Colorectal	142,570	51,370
Breast	209,060	40,230
Prostate	217,730	32,050
Pancreatic	43,140	36,800
Colorectal, breast, prostate, pancreatic combined	612,500	160,450

There are nearly as many deaths from lung cancer yearly as there are from the combined total of colorectal, breast, prostate, and pancreatic cancers. As a contributing factor to the high mortality, many patients present with advanced disease. According to the National Cancer Database report on lung cancer, 30% of patients with non-small cell lung cancer (NSCLC) present with locally advanced, stage IIIA/B disease, and 40% of patients present with metastatic disease at diagnosis.²

This article reviews staging and clinical evaluation of patients with lung cancer, with a focus on those with locally advanced disease. Patients should have routine staging studies, including pathology review, history, and physical examination, computed tomography (CT) of the chest and upper abdomen (including adrenals), positron emission tomography (PET) or integrated PET-CT, bronchoscopy, evaluation of the mediastinum by mediastinoscopy or endobronchial ultrasonography (EBUS)/endoscopic ultrasonography as recommended by National Comprehensive Cancer Network (NCCN) guidelines plus brain magnetic resonance imaging (MRI). In addition, for some locally advanced, but potentially resectable cancer, chest MRI may delineate the depth of invasion better (Pancoast tumor, pericardial invasion, involvement of vertebral bodies).

Most patients with stage III disease are recognized based on clinical staging, especially because the addition of integrated PET-CT to the staging armamentarium has increased the accuracy of preoperative evaluation. A few patients are found on pathologic review to have unsuspected N2 or N3 disease; this usually constitutes microscopic metastasis that is too small to be fluorodeoxyglucose (FDG)-avid and, therefore, PET-negative. Once the pretreatment clinical staging has been completed, patients should be discussed at a multidisciplinary tumor board, which includes but is not limited to medical oncology, radiation oncology, and a dedicated thoracic surgeon. In addition, it improves patient care and communication if representatives from pulmonary medicine, pathology, social services, and radiology are present.

SURGICAL EVALUATION

Advanced local and regional cancer includes the following: any T stage with ipsilateral (N2; stage IIIA) or contralateral (N3; stage IIIB) or any scalene or supraclavicular node involvement (N3; stage IIIB). In addition, tumors that are more than 5 cm (T2b, T3>7.0 cm) or any tumor that directly invades resectable structures (T3 invasion) should be considered locally advanced and require a multimodality approach to increase the cure rate. Some tumors that invade the mediastinum, heart, great vessels, trachea, recurrent laryngeal nerve, esophagus, vertebral body, or carina (all T4) may be resectable. Some lobe nodules (formerly considered T4; *TNM Classification of Malignant Tumours, Sixth Edition*) are now surgical disease (T3; stage IIB if node-negative).

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