Surgical Treatment of Non-Small Cell Lung Cancer

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Abstract:
Surgical resection remains the best treatment option for patients with limited stage non-small cell lung cancer (NSCLC). Stage I and Stage II lung cancer, where there is no lymph node involvement or the involvement is limited to the peribronchial and hilar lymph nodes (NI), can be completely resected with good five-year survival rates (50 to 90 percent). Controversy remains regarding surgery's role in treating more regionally advanced lung cancers involving mediastinal or subcarinal nodes (N2). These tumors (Stage IIIA) have poor survival with surgery, and there has been an advancing role for chemotherapy and/or radiation in their treatment. Surgery is rarely indicated in Stage IIIB or IV lung cancer.

Stages of Lung Cancer

Lung cancer is staged based on the TNM system, which was updated based on new survival rate data in 2009 (See Tables 1 and 2). Few changes in the surgical approach to lung cancer will result from this update. Large tumors (>7 cm) with local lymph node involvement (N1) were upstaged to IIIA, secondary to poor survival rates. Many of these tumors appear clinically NO on positive emission tomography (PET) and will still be approached surgically. T4 disease, based on same-lobe nodules, was downstaged. These historically have been operated on, based on the hope that that they represented synchronous primary lung cancers. All other major groups of surgical patients had no stage changes.

Present day staging involves the routine use of computed tomography (CT) and PET scanning. These studies are very accurate and have significantly decreased the number of patients who will have a disparity between clinical and pathological stages. A recent study shows that only 3 percent of patients were upstaged by mediastinoscopy from the PET/CT stage.[1]

Resectable Lung Cancer

Stage I and Stage II lung cancers are limited to the lung, adjacent resectable structures (T3) and hilar lymph nodes

(NI). The majority of these tumors get excellent local control with lobectomy. Mediastinal lymphodectomy should be a routine part of lobectomy for cancer to provide accurate staging and possibly provide some survival benefit.[2] Lesser resections (wedge excision and segmentectomy) have been studied on multiple occasions, but in general should not be used on a patient with adequate pulmonary reserve, as they provide inferior local control.[3]

More difficult localized tumors are represented in the T3 group. These tumors invade the chest wall, diaphragm or mediastinum but remain Stage II due to no lymph node involvement. Prognosis in these patients is related to completeness of resection, which should be performed in an en bloc fashion. Unfortunately, five-year survival falls significantly to the 30 percent range when adjunct structures are involved, even with clean lymph nodes.[4] T3 also includes tumors in a main stem bronchus but less than 2 cm from the carina. This group requires pneumonectomy or sleeve lobectomy for complete tumor removal. These more complex procedures involve higher morbidity/mortality rates but are justified when compared with the very poor non-surgical outcomes. It is important to note that even N1 involvement in a T3 tumor classifies the patient as a Stage IIIA, and any advantage to surgery is probably lost.[5]

Potentially Resectable Lung Cancer

Stage IIIA lung cancer represents involvement of ipsilateral mediastinal and/or subcarinal lymph nodes (N2). The majority of Stage IIIA patients will have preoperatively recognized (via CT or PET scan) advanced nodal involvement. At present, a multidisciplinary approach, using neoadjuvant chemotherapy or chemoradiation is the first line of therapy.[6] Depending on the location and extent of disease, subsets of the patients may be considered for restaging and surgery following initial treatment. Unfortunately, clear-cut data to show improved survival, regardless of treatment strategy, is lacking and prognosis remains poor with five-year survivals less than 30 percent.[7]

Patients with "minimal" N2 disease, which is not found by CT or PET scan preoperatively but discovered in the lymph node samples, fare only slightly better. Five-year survival of single-station N2 patients approaches 40 percent, but multi-station N2 patients follow the usual Stage IIIA course.[8]

Patient Selection

After proper staging, less than 30 percent of lung cancer patients will be considered for surgical resection. Assessment of cardiopulmonary reserve is the final step in the preoperative evaluation. Before proceeding with lung resection, patients with good performance status need a forced expiratory volume in one second (FEV1) of >60 percent of predicted with or without a cardiac stress test (depending on age and risk factors for coronary artery disease). In general, patients who tolerate normal daily activities will tolerate resection well and, by six months after surgery, most will show little if any change from preoperative pulmonary function tests.[9] Patients whose postoperative predicted FEV1 is less than 30 percent of normal, should undergo additional testing to determine their carbon monoxide diffusion capacity (DLCO) and arterial blood gases (ABG). For patients with very borderline pulmonary function, oxygen consumption studies and quantitative ventilation-perfusion scans will usually give the information needed to determine suitability for lobectomy or pneumonectomy.

Table 1: ANATOMIC STAGE/PROGNOSTIC GROUPS

Occult Carcinoma	TX, N0, M0
Stage 0	Tis, N0, M0
Stage IA	T1a, N0, M0
	T1b, N0, M0
Stage IB	T2a, N0, M0
Stage IIA	T2b, N0, M0
	T1a, N1, M0
	T1b, N1, M0
	T2a, N1, M0
Stage IIB	T2b, N1, M0
	T3, N0, M0
Stage IIIA	T1a, N2, M0
	T1b, N2, M0
	T2a, N2, M0
	T2b, N2, M0
	T3, N1, M0
	T3, N2, M0
	T4, N0, M0
	T4, N1, M0
Stage IIIB	T1a, N3, M0
	T1b, N3, M0
	T2a, N3, M0
	T2b, N3, M0
	T3, N3, M0
	T4, N2, M0
	T4, N3, M0
Stage IV	Any T, Any N, M1a
	Any T, Any N, M1b

Source: Edge SB, Byrd DR, Compton CC, Fritz AG, Greene FL, Trotti A, editors. AJCC Cancer Staging Manual. 7th ed. New York, Dordrecht, Heidelberg, London: Springer; 2010.

Table 2: TNM DEFINITIONS

Primary Tumor (T)

TX Primary tumor cannot be assessed, or tumor proven by the presence of malignant cells in sputum or bronchial washings but not visualized by imaging or bronchoscopy

T0 No evidence of primary tumor

Tis Carcinoma in situ

T1 Tumor 3 cm or less in greatest dimension, surrounded by lung or visceral pleura, without bronchoscopic evidence of invasion more proximal than the lobar bronchus (i.e., not in the main bronchus)*

- T1a Tumor more than 2 cm but 3 cm or less in greatest dimension
- T1b Tumor more than 2 cm but 3 cm or less in greatest dimension

T2 Tumor more than 3 cm but 7 cm or less or tumor with any of the following features (T2 tumors with these features are classified T2a if 5 cm or less); Involves main bronchus, 2 cm or more distal to the carina; invades visceral pleura (PL1 or PL2); Associated with atelectasis or obstructive pneumonitis that extends to the hilar region but doe not involve the entire lung

- T2a Tumor more than 3 cm but 5 cm or less in greatest dimension
- T2b Tumor more than 5 cm but 7 cm or less in greatest dimension

T3 Tumor more than 7 cm or one that directly invades any of the following: parietal pleural (PL3) chest wall (including superior sulcus tumors), diaphragm, phrenic nerve, mediastinal pleura, parietal pericardium; or tumor in the main bronchus (less than 2 cm distal to the carina but without involvement of the carina; or associated atelectasis or obstructive pneumonitis of the entire lung or separate tumor nodule(s) in the same lobe.

T4 Tumor of any size that invades any of the following: mediastinum, heart, great vessels, trachea, recurrent laryngeal nerve, esophagus, vertebral body, carina, separate tumor nodule(s) in a different ipsilateral lobe

Regional Lymph Nodes (N)

NX Regional lymph nodes cannot be assessed

N0 No regional lymph node metastases

N1 Metastasis in ipsilateral peribronchial and/or ipsilateral hilar lymph nodes and intrapulmonary nodes, including involvement by direct extension

N2 Metastasis in ipsilateral mediastinal and/or subcarinal lymph nodes(s)

N3 Metastasis in contralateral mediastinal, contralateral hilar, ipsilateral or contralateral scalene, or suprclavicular lymph nodes(s)

Distant Metastasis (M)

M0 No distant metastasis

M1 Distant metastasis

M1a Separate tumor nodule(s) in a contralateral lobe tumor with pleural nodules or malignant pleural (or pericardial) effusion**

M1b Distant metastasis

*The uncommon superficial spreading tumor of any size with its invasive component limited to the bronchial wall, which may extend proximally to the main bronchus, is also classified as T1a.

**Most pleural (and pericardial) effusions with lung cancer are due to tumor. In a few patients, however, multiple cytopathologic examinations of pleural (pericardial) fluid are negative for tumor, and the fluid is nonbloody and is not an exudate. Where these elements and clinical judgment dictate that the effusion is not related to the tumor, the effusion should be excluded as a staging element and the patient should be classified as M0.

Source: Edge SB, Byrd DR, Compton CC, Fritz AG, Greene FL, Trotti A, editors. AJCC Cancer Staging Manual. 7th ed. New York, Dordrecht, Heidelberg, London: Springer; 2010.

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