Guidelines for the Management of Lung Cancer

Full Version
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Objective:
This guideline reviews the overall management (from initial presentation and diagnosis through referral, treatment and follow up) of adult lung cancer in Nova Scotia. This guideline was written for an audience of general practitioners and medical students, not necessarily lung cancer specialists. As such, it is a synthesis of knowledge and evidence, and reflects the practice policies of the Thoracic Cancer Site Team in Nova Scotia (see Appendix I).

Other interested physicians (especially family physicians) and health professionals may find the algorithms a useful summary of the management of lung cancer. Patients, family members and other non-health professionals are encouraged to review materials written specifically for them. The Canadian Cancer Society Information Service (1-888-939-3333 or www.cancer.ca) is one source for this type of information.

Preamble Note:
Practice guidelines are intended to assist health care professionals with decisions throughout the spectrum of the cancer experience. Guidelines should never replace specific decisions for individual patients, and do not substitute for the shared decisions between any patient and doctor (or other health professional) which are unique to each circumstance. However, guidelines do provide evidence-based background information, consensus-based recommendations for similar problems, and a context for each individual decision. This guideline will be revised, from time to time, as new evidence becomes available. Current versions of this guideline will be available on the Cancer Care Nova Scotia website (www.cancercare.ns.ca). The development of this guideline is described in Appendix II.

Comment on Clinical Research:
An important component of treatment decision-making for any patient is the potential for enrollment in relevant clinical research. The Thoracic Cancer Site Team is committed to advancing patient care, through participation in clinical trials and other clinical research projects. At any point in time, there may be a clinical trial or other clinical research opportunity related to any component of this guideline. As specific trials or clinical research projects become available, eligible patients may be offered the opportunity to enroll in the relevant trial or research project. Every effort will be made to accommodate patients for clinical research participation, but there will be eligibility restrictions for each trial. Patients are encouraged to discuss clinical trials opportunities with their cancer specialist. Other researchers may also contact patients to offer participation in relevant trials. Current clinical trials are listed on the Cancer Care Nova Scotia website (www.cancercare.ns.ca).

Acknowledgements:
This guideline was written by a collaborative effort of the Thoracic Cancer Site Team, and was sponsored by Cancer Care Nova Scotia. Portions of this practice guideline have been adapted from guidelines prepared by the British Columbia Cancer Agency. The guidelines also incorporate knowledge of current evidence by the cancer experts in Nova Scotia.

For further information on this, or any other Practice Guideline, please contact the CST Co-Chairs, or members of the Guidelines Resource Team, Cancer Care Nova Scotia (contact person Michele Moore, Tel. 902-473-3152 or by email michele.moore@ccns.nshealth.ca).
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**Appendices**

| Appendix I | Thoracic Cancer Site Team Members                     | A1   |
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**Guideline Approvals:**
- Thoracic Cancer Site Team-
  - Initial date approved- 9 Jun 2004
  - Revision with Community Reviewer Input- 13 Jan 2005
  - Cancer Care Nova Scotia, Commissioner- 10 Mar 2005

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Thoracic Cancer Site Team, Cancer Care Nova Scotia, 2005

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Part 1. Introduction

1.1 Epidemiology
Lung cancer is the leading cause of cancer deaths in men and women\(^1\). Age-standardized mortality is rapidly increasing in women, but has peaked in men and is now slowly declining. Because the population is aging, it is expected that absolute rates of lung cancer will increase significantly—at least for the next decade. In Nova Scotia, lung cancer incidence and mortality are above the national average, presumably reflecting higher historic levels of tobacco consumption than most other provinces in Canada. It is estimated that there were 850 cases of lung cancer in Nova Scotia in 2002. By 2005 this is expected to increase to 985 cases, and by 2010 to 1160 cases.

In 2002, it is estimated that there were 20,800 new cases of lung cancer and 18,400 lung cancer deaths in Canada. These accounted for 15% of all cases of cancer and 27.8% of cancer deaths in that year. Lung cancer is the second most common type of cancer in both males and females, and the leading cause of cancer deaths in both genders in Nova Scotia (Figure 1). In Nova Scotia, lung cancer incidence and mortality is well above the national average (age-standardized incidence rates are 95/56 per 100,000 in NS vs. 74/47 for Canada, males and females respectively; age-standardized mortality rates are 84/33 per 100,000 in NS vs. 67/38 for Canada).

1.2. Presentation
Patients with lung cancer may present without clinical symptoms, just an abnormal chest x-ray. These patients often have the best prognosis, and careful evaluation and follow-up of these patients is crucial.

Patients may present with various symptoms, that mimic other pulmonary disorders. Typically, a change in pulmonary symptoms is the most suspicious sign of lung cancer. Common presenting symptoms include cough, chest pain, rust-coloured or purulent sputum, hemoptysis or dyspnea. Symptoms of lung cancer can be divided into central airway obstructive symptoms, symptoms of a peripheral mass, or symptoms of metastatic disease.

**Symptoms of Bronchial Obstruction**
- Patients who have hemoptysis, a change in their cough, or persistent pneumonia require further investigations for malignancy.

**Symptoms of a Peripheral Tumour Mass**
- These patients can present with chest wall pain, the Pancoast syndrome with pain in their arm or shoulder, and a Horner syndrome, or with recurrent pleural effusions. Intrathoracic lymph node involvement can lead to superior vena cava (SVC) syndrome and recurrent nerve paralysis on the left side.

**Metastatic Disease**
- Lung cancer patients occasionally present with seizures representing cerebral metastases or bone metastases manifested by localized bone pain or pathologic fractures.
Figure 1

Trends in age-standardised incidence (A) and mortality (B) rates for common tumour sites, females, Nova Scotia 1971-1999.

FEMALES
Age-Standardised Incidence Rate per 100,000

<table>
<thead>
<tr>
<th>Year</th>
<th>Breast</th>
<th>Colorectal</th>
<th>Lung</th>
</tr>
</thead>
<tbody>
<tr>
<td>1971</td>
<td>30</td>
<td>45</td>
<td>60</td>
</tr>
<tr>
<td>1975</td>
<td>45</td>
<td>30</td>
<td>15</td>
</tr>
<tr>
<td>1980</td>
<td>60</td>
<td>15</td>
<td>30</td>
</tr>
<tr>
<td>1985</td>
<td>90</td>
<td>60</td>
<td>45</td>
</tr>
<tr>
<td>1990</td>
<td>120</td>
<td>90</td>
<td>60</td>
</tr>
<tr>
<td>1995</td>
<td>150</td>
<td>120</td>
<td>90</td>
</tr>
</tbody>
</table>

Note that the observed increase in the rate of lung cancer incidence and mortality for the years 1998-1999 appears greater than that reported at the national level. However, preliminary analyses for the year 2000 and 2001 show important declines in the rate of invasive lung cancer incidence.

MALES
Age-Standardised Incidence Rate per 100,000

<table>
<thead>
<tr>
<th>Year</th>
<th>Prostate</th>
<th>Colorectal</th>
<th>Lung</th>
</tr>
</thead>
<tbody>
<tr>
<td>1971</td>
<td>30</td>
<td>45</td>
<td>60</td>
</tr>
<tr>
<td>1975</td>
<td>45</td>
<td>30</td>
<td>15</td>
</tr>
<tr>
<td>1980</td>
<td>60</td>
<td>15</td>
<td>30</td>
</tr>
<tr>
<td>1985</td>
<td>90</td>
<td>60</td>
<td>45</td>
</tr>
<tr>
<td>1990</td>
<td>120</td>
<td>90</td>
<td>60</td>
</tr>
<tr>
<td>1995</td>
<td>150</td>
<td>120</td>
<td>90</td>
</tr>
</tbody>
</table>

Reference:

Guidelines for the Management of Lung Cancer - 2
Part 2. Histologic Classification of Lung Tumours

Lung cancers are divided into two broad categories: small cell (SCLC) and non-small cell lung cancer (NSCLC). About 80% of lung cancers are non-small cell. Characteristically, squamous cell carcinomas are about 40% of NSCLC cases and involve the central airways. Adenocarcinomas are typically peripheral carcinomas, and represent about 40% of NSCLC cases1.

Table 2.1 Histopathologic Types of Lung Cancer

<table>
<thead>
<tr>
<th>Squamous cell carcinoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Variants:</td>
</tr>
<tr>
<td>Papillary</td>
</tr>
<tr>
<td>Clear cell</td>
</tr>
<tr>
<td>Small cell</td>
</tr>
<tr>
<td>Basiloid</td>
</tr>
<tr>
<td>Adenocarcinoma</td>
</tr>
<tr>
<td>Acinar</td>
</tr>
<tr>
<td>Papillary</td>
</tr>
<tr>
<td>Bronchioloaveolar carcinoma*</td>
</tr>
<tr>
<td>Non-mucinous</td>
</tr>
<tr>
<td>Mucinous</td>
</tr>
<tr>
<td>Mixed or indeterminate cell types</td>
</tr>
<tr>
<td>Solid adenocarcinoma with mucin</td>
</tr>
<tr>
<td>Mixed subtypes</td>
</tr>
<tr>
<td>Variants:</td>
</tr>
<tr>
<td>Well-differentiated fetal adenocarcinoma</td>
</tr>
<tr>
<td>Mucinous (colloid) adenocarcinoma</td>
</tr>
<tr>
<td>Mucinous cystadenocarcinoma</td>
</tr>
<tr>
<td>Signet-ring adenocarcinoma</td>
</tr>
<tr>
<td>Clear cell adenocarcinoma</td>
</tr>
<tr>
<td>Small cell carcinoma</td>
</tr>
<tr>
<td>Variant:</td>
</tr>
<tr>
<td>Combined small cell carcinoma</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Carcinoid tumor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Typical carcinoid</td>
</tr>
<tr>
<td>Atypical carcinoid</td>
</tr>
<tr>
<td>Large cell carcinoma</td>
</tr>
<tr>
<td>Variants</td>
</tr>
<tr>
<td>Large cell neuroendocrine carcinoma</td>
</tr>
<tr>
<td>Basaloid carcinoma</td>
</tr>
<tr>
<td>Lymphoepithelioma-like carcinoma</td>
</tr>
<tr>
<td>Clear cell carcinoma</td>
</tr>
<tr>
<td>Large cell carcinoma with rhabdoid phenotype</td>
</tr>
<tr>
<td>Adenosquamous carcinoma</td>
</tr>
<tr>
<td>Carcinomas with pleomorphic, sarcomatoid or sarcomatous elements</td>
</tr>
<tr>
<td>Carcinomas with spindle and / or giant cells</td>
</tr>
<tr>
<td>Pleomorphic carcinoma</td>
</tr>
<tr>
<td>Spindle cell carcinoma</td>
</tr>
<tr>
<td>Giant cell carcinoma</td>
</tr>
<tr>
<td>Carcinosarcoma</td>
</tr>
<tr>
<td>Pulmonary blastoma</td>
</tr>
<tr>
<td>Others</td>
</tr>
<tr>
<td>Carcinomas of salivary-gland type</td>
</tr>
<tr>
<td>Mucoepidermoid carcinoma</td>
</tr>
<tr>
<td>Adenoid cystic carcinoma</td>
</tr>
<tr>
<td>Others</td>
</tr>
<tr>
<td>Unclassified carcinoma _</td>
</tr>
</tbody>
</table>

Reference:
Part 3. Diagnosis and Staging

3.1 Diagnostic Pathology

**Definitive Diagnosis of Lung Cancer**

A definitive histological diagnosis\(^1\) is the standard for all patients suspected of having lung cancer.

A pathological diagnosis may be obtained histologically or cytologically. It is particularly important to distinguish small cell carcinoma from non-small cell carcinoma since treatment is radically different for each of these cancers. In rare situations where the patient is moribund or diagnosis requires major surgery, the decision to pursue a diagnosis is based on the best judgment of the clinician.

Methods of obtaining a diagnosis include bronchoscopy, mediastinoscopy, fine needle aspirate (FNA) of the lung lesion, FNA of metastatic nodes, aspiration of pleural fluid for cytology, pleuroscopy, FNA of liver or adrenal gland\(^2\).

In early operable stage carcinoma, surgical excision of the nodule is often done for diagnosis of suspicious lesions.

3.2 Staging

3.2.1 Classification Criteria for Non-Small Cell Lung Cancer

Non-small cell lung cancer patients should be staged using the TNM staging criteria\(^3,4\).

The staging definitions and stage groups are as follows:

<table>
<thead>
<tr>
<th>(T)</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>(TX)</td>
<td>Tumour proved by the presence of malignant cells in sputum or bronchial washings but not visualized by imaging or bronchoscopy or any tumour that cannot be assessed.</td>
</tr>
<tr>
<td>(TO)</td>
<td>No evidence of a primary tumour.</td>
</tr>
<tr>
<td>(TIS)</td>
<td>Carcinoma in situ.</td>
</tr>
<tr>
<td>(T1)</td>
<td>Tumour is 3 cm or less in greatest dimension, surrounded by lung or visceral pleura without bronchoscopic evidence of invasion more proximal than the lobar bronchus(^1) (i.e., not in the main bronchus).</td>
</tr>
<tr>
<td>(T2)</td>
<td>Tumour with any of the following features of size or extent: a) &gt;3 cm in greatest dimension. b) involves the main bronchus, &gt;2 cm distal to the carina. c) invades the visceral pleura. d) associated with atelectasis or obstructive pneumonitis that extends to the hilar region but does not involve the entire lung.</td>
</tr>
<tr>
<td>(T3)</td>
<td>Tumour of any size that directly invades any of the following: the chest wall (including superior sulcus tumours), diaphragm, mediastinum pleura, parietal pericardium (no invasion of the heart, great vessels, trachea, esophagus or vertebral body) or tumour involving a main bronchus less than 2 cm distal to the tracheal carina but not involving the carina, or associated atelectasis or obstructive pneumonitis of the entire lung.</td>
</tr>
<tr>
<td>(T4)</td>
<td>Tumour of any size which invades any of the following: mediastinum, heart, great vessels, trachea, esophagus, vertebral body, carina; or tumour associated with a malignant pleural or pericardial effusion(^2) or with satellite tumour nodule(s) within the ipsilateral primary-tumour lobe of the lung.</td>
</tr>
</tbody>
</table>
Table 3.2.2 N (Node) Definitions

<table>
<thead>
<tr>
<th>Stage</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>NX</td>
<td>Regional lymph nodes cannot be assessed.</td>
</tr>
<tr>
<td>N0</td>
<td>No metastasis to regional lymph nodes.</td>
</tr>
<tr>
<td>N1</td>
<td>Metastasis to lymph nodes in the ipsilateral peribronchial and/or the ipsilateral hilar lymph nodes, and intrapulmonary nodes involved by direct extension of the primary tumour.</td>
</tr>
<tr>
<td>N2</td>
<td>Metastasis to ipsilateral mediastinal lymph nodes and/or subcarinal lymph nodes.</td>
</tr>
<tr>
<td>N3</td>
<td>Metastasis to contralateral hilar or mediastinal lymph nodes, ipsilateral or contralateral scalene, or supraclavicular lymph node(s).</td>
</tr>
</tbody>
</table>

Table 3.2.3 M (Metastasis) Definitions

<table>
<thead>
<tr>
<th>Stage</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>MX</td>
<td>Presence of distant metastasis cannot be assessed.</td>
</tr>
<tr>
<td>M0</td>
<td>No known distant metastasis.</td>
</tr>
<tr>
<td>M1</td>
<td>Distant metastasis present.</td>
</tr>
</tbody>
</table>

Notes:
1. The uncommon superficial tumour of any size with its invasive component limited to the bronchial wall, which may extend proximal to the main bronchus, is also classified as T1.
2. Most pleural effusions associated with lung cancer are due to tumour. However, there are a few patients in whom multiple cytopathologic examinations of pleural fluid show no tumour. In these cases, the fluid is non-bloody and is not an exudate. Thoracoscopy assessment of the pleura should be considered. If these factors and clinical judgement indicate that the effusion is not related to the tumour, the effusion should be excluded as a staging element and the patient’s disease should be staged as T1, T2, or T3. Pericardial effusion is classified according to the same rules.
3. Separate metastatic tumour nodules(s) in the ipsilateral non primary-tumour lobe(s) of the lung also are classified M1.

Stage Groupings: TNM Subsets

<table>
<thead>
<tr>
<th>Occult carcinoma: TX</th>
<th>N0 M0</th>
<th>Stage IIIA</th>
<th>T3</th>
<th>N1</th>
<th>M0</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 0: TI N0 M0</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage IA: T1 N0 M0</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage IB: T2 N0 M0</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage IIA: T1 N1 M0</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage IIB: T2 N1 M0</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Stage IV: Any T Any N M1

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Stage 0</th>
<th>Stage I A</th>
<th>Stage I B</th>
<th>Stage II A</th>
<th>Stage II B</th>
<th>Stage III A</th>
<th>Stage III B</th>
<th>Stage IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary Tumour (T)</td>
<td>Tis (T0)</td>
<td>T1a</td>
<td>T1b</td>
<td>T1c</td>
<td>T2a</td>
<td>T2b</td>
<td>T2c</td>
<td>T3a, b, c or d</td>
</tr>
<tr>
<td>Local Invasion</td>
<td>Endobronchial location</td>
<td>Any</td>
<td>Any</td>
<td>Any</td>
<td>&gt;3cm</td>
<td>Any</td>
<td>&gt;3cm</td>
<td>Any</td>
</tr>
<tr>
<td>Location</td>
<td>Mediastinum/ trachea/ heart/ great vessels/ esophagus/ vertebral body/ carina</td>
<td>Any</td>
<td>Any</td>
<td>Any</td>
<td>Any</td>
<td>Any</td>
<td>Any</td>
<td>Any</td>
</tr>
<tr>
<td>Endo-bronchial location</td>
<td>Main bronchus (&lt;2cm distal to the carina)</td>
<td>Any</td>
<td>Any</td>
<td>Any</td>
<td>Any</td>
<td>Any</td>
<td>Any</td>
<td>Any</td>
</tr>
<tr>
<td>Size</td>
<td>&lt;3cm</td>
<td>Any</td>
<td>Any</td>
<td>Any</td>
<td>Any</td>
<td>Any</td>
<td>Any</td>
<td>Any</td>
</tr>
</tbody>
</table>

**Lymph Node (N)**

- N0: None
- N1: Any
- N2: Any
- N3: Any

**Metastases (M)**

- M0: Absent
- M1: Present

**Stage Definitions**

- **Stage 0**: Carcinoma in situ (Tis, N0, M0)
- **Stage I A**: T1a (N0, M0)
- **Stage I B**: T1b (N0, M0)
- **Stage II A**: T1c (N0, M0)
- **Stage II B**: T2a (N0, M0)
- **Stage III A**: T2b (N0, M0)
- **Stage III B**: T2c (N0, M0)
- **Stage IV**: T3a, b, c or d (N0, M0)

3.2.2 Staging Definitions for Small Cell Lung Cancer (SCLC)

Small cell lung cancer patients are staged as either limited or extensive stage\(^6-8\).

Approximately 25-40% of small cell lung cancer patients have limited stage disease. Limited stage small cell lung cancer is equivalent to stages I to IIIB in the TNM staging system. Limited stage small cell lung cancer patients fit enough to receive combined modality therapy are treated with curative intent.

Extensive stage small cell lung cancer is equivalent to stage IV disease by the TNM system, with the addition of pleural effusions. Extensive stage patients are generally treated with palliative intent.

References:
Part 4. Referral Information for the New Patient Visit

A letter of referral is the minimal requirement for a referral. A referral need not be delayed due to delays in scheduling tests or delayed reporting of tests (either due to test scheduling delays or waiting time for test results).

**Referral to the QEII Health Sciences Centre**

Referrals to the QEII Health Sciences Centre- Cancer Care Program may be faxed to the Nova Scotia Cancer Centre referrals office at 902-473-6079 (tel. 902-473-5140 or 902-473-6098). For urgent or emergent referrals, please page the appropriate specialist on call through the QEII HSC Locating service (902-473-2220) to discuss the referral.

**Referral to the Cape Breton Cancer Centre**

Referrals to the Cape Breton Cancer Centre may be directed to the referrals/booking office at 902-567-7774 (fax 902-567-7911). For urgent or emergent referrals, please page the appropriate specialist on call through the Cape Breton Regional Hospital locating service (902-567-8000) to discuss the referral.

**Referral Information**

**Letter of Referral***

A legible referral or consultation letter highlighting presenting signs and symptoms

**Pathology Reports***

a. Any cytology reports (if done)*

b. Needle biopsy
c. Bronchoscopy
d. Mediastinoscopy
e. Any other diagnostic procedure where a biopsy is taken

**Operative Reports** (relevant to the cancer)*

a. Bronchoscopy
b. Endoscopy
c. Mediastinoscopy
d. Thoracotomy

**Diagnostic Imaging Reports***

a. All relevant chest radiographs, including old images.*
b. Thoracic and any other CT scans.*
c. Bone scans.*
d. Any other relevant diagnostic imaging.

**Other Information**

a. Any relevant consultation reports.
b. Pulmonary function test results (if done)*.
c. Relevant bloodwork (if done)*.
d. Detailed information on any previous chemotherapy or radiotherapy of current malignancy.
e. Any information on previous malignancies.
f. Information on co-existing medical conditions and allergies.

* Specific information which is necessary for proper triage of referrals

Note: If the referring physician would like to discuss a case with a specialist, feel free to call the appropriate specialist (Radiation Oncology, Medical Oncology, or Thoracic Surgery, by calling 902-473-2220 at QEII HSC or 902-567-8000 at CBCC- ask for the specialist on call or a specific physician at this number).

If any tests or reports are pending, the date of the procedure, and the location of the procedure should be noted, so that the reports may be obtained when available. Send in the referral while awaiting these results, to facilitate a timely appointment for your patient.
Part 5. Treatment of Non-Small Cell Lung Cancer (NSCLC)

Contemporary management of lung cancer patient care requires a collaborative approach, with a free interchange of information among the medical specialties, nursing, supportive and palliative care. Patient management in a collaborative group setting will result in superior patient outcomes.

5.1 Clinical Stage I and II (Early Stage) NSCLC

For patients with clinically operable NSCLC, surgical resection is the treatment with the best potential for cure\(^1\)\(^-\)\(^6\). Approximately \(20-30\%\) of NSCLC patients have clinically operable disease. This is the only category of lung cancer patients who are routinely cured of their disease.

The diagnostic work-up of these patients is discussed in investigations and consists of a search for metastatic disease, based on history, physical examination, and imaging, and an assessment of fitness for surgery. With current anaesthetic techniques, surgical options have been extended to patients who are more frail and elderly. Since lung cancer incidence increases with age and the disease contributes to greater frailty, this allows more patients the option of surgery.

The optimal management of early-stage lung cancer is surgery alone for low risk patients, or surgery with adjuvant chemotherapy for high risk patients. The five-year disease-free survival rate in this group ranges from 40 to 75 percent depending on stage grouping. Two-thirds of these patients fail from distant metastatic spread. High-risk patients who may benefit from adjuvant chemotherapy include those with NSCLC (excluding mixed NSCLC/SCLC histology or non-solitary bronchoalveolar carcinomas), Stage Ib/II (excluding T3N0M0) following complete resection, and favorable organ functions and performance status. Adjuvant platinum-based chemotherapy starting 4-8 weeks after surgery has been demonstrated to improve survival by 12-14%.

5.1.1 Conduct of Surgery

Patients without a diagnosis, but with a high clinical suspicion for malignancy, may be offered surgical resection. The risk of not finding a malignancy must be balanced against the potential benefit of earlier resection of a tumour and avoidance of progression to advanced disease. Smaller tumours have a better cure rate than larger tumours, even within the T1 category. For patients with suspicious nodules, and who are fit to receive surgery, current practice has moved towards an expedited surgical procedure, rather than waiting. Needle biopsies have a significant false negative rate and can mislead the surgeon to delay surgery. Earlier access to surgery has been assisted by the use of thoracic CT scanning. The management of tiny pulmonary nodules in smokers will become an increasingly common clinical approach.

At the time of thoracotomy, an attempt should be made to excise the nodule for histologic confirmation of malignancy. Central nodules may be excised as a lobectomy, especially if they are clinically compatible with malignancy. Pneumonectomies should not be routinely done without histology.

The smallest unit of the lung that should be resected for malignancy is a lobe. Wedge resections and segmental
resections are reserved for high-risk patients who cannot tolerate larger resections. During the operation, hilar and mediastinal lymph nodes should be excised for pathological staging.

5.1.2 Non-Operative Management of Stage I and II Non-Small Cell Lung Cancer

Radiotherapy in Early Stage Non-Small Cell Lung Cancer

Radiotherapy is considered in two situations in early-stage non-small cell lung cancer:
(a) following resection, or
(b) in patients who are not suitable candidates for surgery.

A. Adjuvant Radiotherapy Postoperatively

Radiotherapy is only offered in rare circumstances following surgical resection. The most common indication for radiotherapy is microscopic involvement of the resection margin. Patients with stage II cancer in which the chest wall is also involved may be considered for adjuvant radiotherapy of the chest wall.

B. Non-Surgical Early-Stage Non-Small Cell Lung Cancer

Radical radiotherapy alone should be considered in patients who are not candidates for surgery. Depending on the location and size of the tumour, the cure rates with radical radiotherapy may be 15 to 20 percent. The radiotherapy approach must be individualized, since there can be significant reduction in pulmonary function (similar to functional reduction from a lobectomy in most cases). If radiotherapy does not cure the patient, this treatment may still be beneficial, by significant reduction of local recurrence.

C. Combined Modality Therapy for Inoperable Patients with Early Stage Non-Small Cell Lung Cancer

In selected patients the benefits of radiotherapy may be enhanced by concurrent chemotherapy with a cisplatin-based regimen. These patients are assessed on an individualized basis and constitute a small percentage of lung cancer patients.

5.2 Clinical Stage III (Locally Advanced) Non-Small Cell Lung Cancer

About 60 percent of non-small cell lung cancer patients present in this category. These patients form a heterogeneous group ranging from patients with “minimal” stage III disease (discovered at resection) to patients with clearly incurable disease (manifesting as a malignant effusion on their initial presenting chest x-ray). The majority of these patients do not receive surgery; treatment considerations involve radiotherapy, chemotherapy and palliative therapy.

5.2.1 Diagnosis of Stage III Non-Small Cell Lung Cancer

In most circumstances, unless the patient is moribund, it is necessary to obtain a pathologic diagnosis. Diagnostic modalities include bronchoscopy, mediastinoscopy, pleuroscopy, pleural fluid cytology, radiologically-guided FNA. Elderly patients will be considered for treatment without a diagnosis when every reasonable attempt at diagnosis has been made. It is not unusual for patients with locally advanced disease to have small cell lung cancer. Since the treatment of small cell lung cancer is different than for non-small cell lung cancer, it is important to obtain a pathologic diagnosis, if possible.
5.2.2 Radiotherapy
Radiotherapy is commonly offered to this group of patients for palliation\textsuperscript{21,22} or as part of a combined modality protocol in highly selected patients for cure\textsuperscript{11,23-26}. Radical radiotherapy alone may be given to selected patients who may have a more favourable outcome\textsuperscript{11}. Although radiotherapy may significantly reduce local recurrence, radiotherapy alone only results in a 5-year survival of about 5 percent.

For patients with symptomatic chest disease or impending complications, radiotherapy can be of great benefit. Actual or impending SVC obstruction, central airway obstruction, direct invasion of the chest wall, and impending recurrent nerve paralysis with sub-aortic nodal disease are all situations where palliative radiotherapy can be of great benefit to the patient.

5.2.2 Combined Modality Radiotherapy + Chemotherapy
Combined modality therapy for unresectable stage III non-small cell lung cancer may be offered to selected stage III patients (ECOG Performance Status = 0-1*; less than 10 percent weight loss; acceptable Pulmonary Function Tests; and suitable distribution of intrathoracic disease). Patients may receive treatment with combined cisplatin-based chemotherapy and thoracic irradiation\textsuperscript{13,17,27-36}. Combined modality therapy may result in a cure rate up to 20 percent of patients\textsuperscript{37}. Combined modality therapy is quite toxic, so patients must carefully consider the risks and benefits before a decision is made to accept this treatment-intense regimen.

5.3 Stage IV (Advanced/Metastatic) Non-Small Cell Lung Cancer
Twenty to thirty percent of patients present with stage IV disease. Almost all of these patients have incurable disease, and survival is usually short. There are rare circumstances where patients may receive surgery with curative intent, including patients with resectable brain metastases or isolated adrenal metastases. The use of CT scans may help to identify those few patients with potentially resectable metastatic disease.

The majority of stage IV non-small cell lung cancer patients are treated with the goal of palliation (i.e., symptom relief or prevention of impending complications).

The prognosis is poor, with a median survival of 6 to 10 months. Patients with minimal stage IV disease rarely survive beyond 1 to 2 years after treatment.

5.3.1 Surgery for Advanced Non-Small Cell Lung Cancer
Surgery in advanced non-small lung cancer patients is used almost exclusively for obtaining diagnosis and managing complications. Bronchoscopy, pleuroscopy, and mediastinoscopy are often done in the diagnosis and initial treatment of advanced non-small cell lung cancer. Surgery or endoscopy may also be useful for endobronchial manipulations, such as laser therapy, stent insertion, and brachytherapy catheter insertion\textsuperscript{38}. These procedures are almost exclusively done on centrally obstructing tumours for the management of infection, hemoptysis or major airway obstruction, which may cause a significant loss of lung function.

\textsuperscript{*} See Page 37 for ECOG Performance Status Scale
5.3.2 Radiotherapy for Advanced Non-Small Cell Lung Cancer

Radiotherapy has a significant role to play in the management of patients with advanced non-small cell lung cancer. Radiotherapy may result in significant improvement of the quality of life for patients with advanced disease, and can be given with minimal morbidity. Radiotherapy may be used for treatment of patients with or without symptoms, as follows:

a. Symptomatic Patients

Palliative radiotherapy should be considered for all symptomatic patients. Urgent treatment should be considered in cases of:

a) Multiple brain metastases, especially metastasis to brain stem (in small solitary brain metastasis as the only site of relapse, surgical excision followed by radiotherapy may be considered).

b) Spinal cord/cauda equina compression.

c) Radiculopathy.

d) Metastasis to orbital region.

e) Skull base metastasis with cranial nerve(s) involvement.

f) Severe pain.

g) Fungating cutaneous lesion.

h) Main stem bronchus obstruction.

i) Hemoptysis.

b. Asymptomatic patients

Some patients with metastatic lung cancer are asymptomatic or have only mild symptoms. However, palliative radiation should be considered in cases of:

a) Paraspinal mass.

b) Large lytic lesion in a weight-bearing bone. Surgical consultation regarding prophylactic stabilization may be necessary as well.

c) Asymptomatic multiple brain metastasis.

c. Palliative radiotherapy generally has no role in managing:

a) Widespread intrapulmonary metastasis.

b) Carcinomatous leptomeningeal metastasis.

c) Liver metastasis.

5.3.3 Palliative Chemotherapy for Advanced Non-Small Cell Lung Cancer

Chemotherapy is an option for palliative therapy of patients with non-small cell lung cancer (ECOG performance status 0-2, where symptom control and quality-of-life are the outcomes of interest), provided there is a full discussion of the benefits, limitations and toxicities of the treatment.

a. Patient Selection for Palliative Chemotherapy

Palliative chemotherapy patients should have ambulatory performance status (ECOG PS = 0, 1, or 2)*. Extensive previous radiotherapy is associated with increased chemotherapy toxicity and symptomatic disease within a previous radiotherapy volume may be less chemosensitive. Renal, hematologic and hepatic function must be adequate.

Active patient participation in decision-making is crucial. Outcome measurements should reflect more than just the selected disease measures (e.g. survival), but other concerns as well, including symptom control and quality-of-life, patients’ value or meaning of life, their feelings about themselves, and their perceptions and attitudes about a specific treatment.

b. Chemotherapy Duration

There is no evidence that continuing chemotherapy beyond 3-4 months in responding patients prolongs survival and cumulative toxicity should be minimized.
b. Second-line Chemotherapy

Patients who fail to respond to a standard first line regimen, or who progress within less than 3 months after completion of chemotherapy have resistant tumours which are unlikely to respond to second line therapy. Patients with good performance status who had obtained a good response or stable disease for at least 3-6 months after completion of first-line chemotherapy may benefit from additional chemotherapy.

References:
20. Keller SM, Adak S, Wagner H, et al. Prospective randomized trial of postoperative adjuvant...


6.1 Treatment of Limited Stage Disease
Less than half of small cell lung cancer patients have limited stage disease, which is defined as tumour confined to one side of the chest and mediastinum, excluding malignant pleural effusions but including involved ipsilateral supraclavicular nodes as long as all disease can be encompassed in a reasonable-sized radiotherapy field.

Of these, most patients may be offered a combination of chemotherapy and radiotherapy\(^2\)\(^-\)\(^13\). With this combination, survival time may be tripled, quality of life is generally improved, and there is a small chance (20 to 25%) of cure\(^14\)\(^-\)\(^16\). The current chemotherapy regimen is a combination of cisplatin and etoposide\(^4\)\(^,\)\(^5\), although other options may be offered to patients with reduced renal function. Thoracic radiation is usually given early in the course of chemotherapy. The standard chemotherapy regimen extends over a period of about 4 months. The radiotherapy extends over a period of about 3 weeks.

Prophylactic cranial irradiation (PCI) may also be administered to patients in complete remission\(^17\)\(^,\)\(^18\). This therapy is based on the rationale that the chemotherapeutic agents do not cross the blood/brain barrier, and the administration of PCI reduces the probability of brain metastases from 25-30% to 5-10%. Prophylactic cranial irradiation may cause neurotoxicity in a small percentage of long-term survivors (e.g. dementia, ataxia).

6.2 Treatment of Extensive Stage Disease
About two-thirds of patients have extensive stage small cell lung cancer at presentation. Palliative chemotherapy is the primary treatment, usually comprised of 4 cycles of cisplatin-etoposide\(^8\)\(^,\)\(^9\)\(^,\)\(^12\)\(^,\)\(^19\)\(^-\)\(^25\). Radiotherapy may be used for refractory disease, or to manage metastases in sanctuary sites such as the spinal cord or central nervous system\(^1\)\(^,\)\(^17\)\(^,\)\(^26\)\(^,\)\(^27\). Seventy to ninety percent of patients respond to chemotherapy with a median survival of 6-12 months (median survival is only 5 to 6 weeks without chemotherapy). Unfortunately almost all patients relapse, and less than 5% are alive in 2 years.

Second-line chemotherapy is occasionally used particularly in patients who develop a relapse more than 6 months following initial treatment\(^24\)\(^,\)\(^28\)\(^-\)\(^34\).

References:
8. Turrisi AT 3rd, Kim K, Blum R, et al. Twice-daily compared with once-daily thoracic...
Guidelines for the Management of Lung Cancer - 18


Part 7. Surveillance and Follow-up

7.1 Follow-up of Patients Treated with Curative Intent

There are no evidence-based guidelines for follow-up of lung cancer patients. It is known that patients who have had a lung cancer have an increased risk of developing a second lung cancer, at a rate of about 1% (non-smokers) to 2% (smokers). Therefore, patients should be considered for surveillance, based on their increased risk of a new cancer developing.

Follow-up is also done to detect recurrent disease. Lung cancers characteristically recur in the bones, brain, adrenals, and liver. There is no benefit in detecting asymptomatic metastases. The follow-up examination is based on an assessment of symptoms and evaluation of physical findings including weight loss and cervical adenopathy and plain film radiologic investigation. The frequency of visits may vary between patients, but are generally scheduled at 3-6 month intervals for the first 2 years, and then every 6-12 months thereafter. Most recurrences occur within 3 years of treatment. One strategy for follow-up is illustrated in Table 7.1.

7.2 Follow-up of Patients Treated with Palliative Intent

Patients initially treated with palliative intent require systematic, careful follow-up. These patients are much more likely to be symptomatic again, and should be monitored by the oncologist to detect treatable symptomatic disease.

Symptoms detected on follow-up may benefit from a variety of modalities, including chemotherapy, radiotherapy to painful metastases, other pain management strategies, and psychosocial support.

<table>
<thead>
<tr>
<th>Year</th>
<th>Frequency</th>
<th>Investigations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-2</td>
<td>q 3-6 months</td>
<td>history &amp; physical (symptoms), weight change, chest X-ray</td>
</tr>
<tr>
<td>3+</td>
<td>q 6-12 months</td>
<td>history &amp; physical (symptoms), weight change, chest X-ray</td>
</tr>
</tbody>
</table>

May be followed by family physician or cancer specialist
(clarify most responsible physician for follow-up at completion of treatment)

Reference:
8.1 Psychosocial Needs
Lung cancer patients, like all cancer patients, may have a number of supportive care needs, often including the need for psychosocial support. Sometimes the need may be for help to cope with the cancer experience; other times there may be need for mental health support. It is the responsibility of the attending health caregivers to provide basic support through the continuum of disease.

If there are specific needs beyond the abilities of the front-line caregivers, a referral to the Psychosocial Oncology Team at either of the Cancer Centres, or an appropriate local resource, may be considered. Specialized psychosocial support may be offered by psychosocial counsellors, psychologists, psychiatrists, social workers, clinical nurse specialists, or other trained professionals.

Further information on psychosocial care and support will be available in future in the Guidelines for the Management of Distress in Cancer Patients, under development at present. Other standards for the supportive care of cancer patients are under development by the Supportive Care Cancer Site Team.

8.2 Symptom Management
During the course of treatment, cancer patients often have symptom management and psychosocial needs. The responsible oncologist(s) and/or community specialist(s) should monitor patients who are undergoing treatment with radiotherapy and/or chemotherapy.

Esophagitis is common during the final days of thoracic radiation and may be managed with diet modification, analgesics, and topical anesthetics (such as Mucaine suspension). Gastric acid suppression with proton pump inhibitors or H₂ antihistamine may also be considered. In rare situations, severe radiation esophagitis requires hospitalization and intravenous support.

Physicians should watch for radiation pneumonitis in the first 3 to 4 months after completion of treatment. This is an uncommon delayed side effect.

During the course of chemotherapy, patients may develop neutropenia with fever, often 10 to 14 days after their treatment. Most of these patients require empiric antibiotics, and the oncologist should be contacted as soon as possible.

Guidelines for the management of symptoms are under development by the Supportive Care Cancer Site Team. As these guidelines are completed, they are posted on the Cancer Care Nova Scotia website (www.cancercare.ns.ca). Current CCNS symptom management guidelines are:
- Management of Oral Complications from Cancer Therapy (2005-06)
Part 9. Practice Pathways

Presentation
Lung cancer is the third most common cancer in Canada, and the leading cause of cancer deaths. Patients with lung cancer may present with various symptoms that mimic other pulmonary disorders, and often mimic the 'smoker's cough' that precedes cancer in many smokers. Typically, a change in pulmonary symptoms is the most suspicious sign of lung cancer. Common presenting symptoms include cough, chest pain, rust-coloured or purulent sputum, hemoptysis or dyspnea. Some patients may present without clinical symptoms, just an abnormal chest x-ray. These patients often have the best prognosis, and careful evaluation and follow-up of these patients is crucial.

Management
Management of lung cancer begins with referral from the family physician to the local surgeon or surgical oncologist for appropriate surgery (for patients who are reasonable surgical candidates with early stages of the disease). Patients who have hemoptysis, a change in their cough, or persistent pneumonia require further investigations for malignancy. Clinical staging of non-small cell lung cancer is integral to management decisions. Staging may be achieved during surgical resection (for continuing management decisions in earlier stage cancers), or may be achieved by clinical examination and diagnostic imaging (for more advanced disease). Radiation therapy and/or chemotherapy may be considered for initial treatment or later if the cancer relapses. Small cell lung cancer is generally split into limited or extensive stages based upon the clinical decision of the radiation oncologist. Staging is a clinical decision, not based upon disease pathology.

Supportive care of lung cancer patients can be as important as managing the tumour. Local management of bronchial obstruction, superior vena cava (SVC) syndrome and dyspnea may be achieved through good tumour control. Other cancer-related symptoms also require good management as they occur. For information on management of symptoms and distress, please visit the Cancer Care Nova Scotia website (www.cancercare.ns.ca) for appropriate supportive care guidelines.

Guidelines
To follow the guideline care pathways in the following pages, begin with the staging of a patient, then go to the appropriate treatment page(s) for the stage of disease. Recurrences, metastases and surveillance are also discussed in the pages noted below. Management of non-small cell lung cancer precedes management of small cell lung cancer in these care pathways.

Practice guidelines are intended to assist health care professionals with decisions throughout the spectrum of the cancer experience. Guidelines should never replace specific decisions for individual patients, and do not substitute for the shared decisions between any patient and doctor (or other health professional) which are unique to each circumstance. However, guidelines do provide evidence-based background information, consensus-based recommendations for similar problems, and a context for each individual decision. A full-text version of this guideline is also available on the Cancer Care Nova Scotia website. Both versions of this guideline will be revised, from time to time, as new evidence becomes available.
Signs & symptoms of Lung Cancer
- Identified by Primary Care Physician
- Consider performance status\(^a\) & weight loss in patient evaluation

Chest X-ray
(include review of old X-ray films)

Lesion or abnormality

Referral to surgeon, or lung specialist\(^b\) (Suspicion of lung cancer)

Pathology Review:
Confirm histology and/or cytology

SCLC or inoperable NSCLC

Resectable NSCLC

Pathologic Evaluation (staging)

Reaccession if indicated

Referral to: Medical Oncology, Radiation Oncology, Internal Medicine, Palliative Care as appropriate

Footnotes:
- ECOG Performance Status criteria- See Page 33
- Referral to local thoracic surgeon or thoracic surgical oncologist at Cancer Centre
- Clear boxes may be performed by family doctor; grey boxes will occur at the hospital with a cancer care program

See Treatment for each stage (Pages 21 to 32)
**Referral Information:**
A letter of referral is the minimal requirement for a referral. A referral need not be delayed due to delays in scheduling tests or delayed reporting of tests.

**QEI Health Sciences Centre:**
- Fax referrals to the Nova Scotia Cancer Centre Referrals Office at 902-473-6079 (tel. 902-473-5140 or 902-473-6098).
- For urgent referrals, page the appropriate specialist on call through the Locating service (902-473-2220).

**Cape Breton Cancer Centre:**
- Direct referrals to the Referrals/Booking office at 902-567-7774 (fax 902-567-7911).
- For urgent referrals, page the appropriate specialist on call through the Locating service (902-567-8000).

**Referral Information:**
- Letter of Referral*
- Pathology Reports*
- Operative Reports (relevant to the cancer)*
- Diagnostic Imaging Reports*
- Specific information which is necessary for proper triage of referrals

**Assess for pain & symptoms, distress, and other psychosocial needs throughout continuum of care (diagnosis to treatment to follow-up).**
**Address supportive care needs as they are identified.**

**Investigations for the Diagnosis and Staging of Lung Cancer**
- May be arranged by lung cancer specialist

**For clinical staging of Small Cell Lung Cancer, see Page 31**
- Pathology Review
- History & Physical (include performance status + weight loss)
- Chest X-ray
- CT scan of chest and upper abdomen (including adrenal glands)
- CBC, Serum chemistry profile
- Pulmonary Function Tests
  
  *May be performed by the Primary Care physician or referred to be done by the lung cancer specialist*

**For clinical staging of Non-Small Cell Lung Cancer, see Pages 4-6 & Page 20**

**For Treatment of Metastatic Lung Cancer, see Page 30 for NSCLC or Page 32 for SCLC**

**Symptomatic for brain mets**
- Brain scan

**Symptomatic for bone mets or elevated alk phos**
- Bone scan

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*Specific information which is necessary for proper triage of referrals*
Staging of Non-Small Cell Lung Cancer- Nodal Status

REGIONAL NODAL STATIONS FOR LUNG CANCER STAGING

**Lung Cancer Staging**

**N1 Nodes**
All nodes are ipsilateral

- Hilar (ipsilateral)
- Interlobar
- Lobar
- Segmental
- Subsegmental

**Diagram 1.**

**N2 Nodes**
(inside mediastinal pleura)

- Superior Mediastinal Nodes (ipsilateral)
  - Highest mediastinal
  - Upper Paratracheal
  - Pre- and Retrotracheal
  - Lower Paratracheal (including Azygos Nodes)
- Aortic Nodes
  - Subaortic (A_P Window)
  - Para-aortic (ascending aorta or phrenic)
- Inferior Mediastinal Nodes (ipsilateral)
  - Subcarinal
  - Paraesophageal (below carina)
  - Pulmonary Ligament

**Diagram 2.**

**N3 Nodes**
Supraclavicular
Scalene
Mediastinal (contralateral)
Hilar (contralateral)

**Diagram 3.**
Treatment of Non-Small Cell Lung Cancer—Clinical Stage I & IIA

Stage I
(T1-2, N0)
Stage IIA
(T1-2, N1)

- Bronchoscopy
- CT scan of chest/upper abdomen
- Mediastinoscopy (at discretion of surgeon)
- See Page 19 for other investigation(s)

Stage I
(T1-2, N0)

- Negative mediastinal nodes
  • Surgical exploration
  • Resectable
  • Margins positive (R1,R2) or Positive mediastinal nodes
  • Margins negative (R0)a

Stage IIA
(T1-2, N1)

- Negative mediastinal nodes
  • See Treatment Stage IIA
- Positive mediastinal nodes
  • Surgical exploration
  • Resectable
  • Margins positive (R1,R2) or Positive mediastinal nodes
  • Margins negative (R0)a

Assess for pain & symptoms, distress, and other psychosocial needs
Address supportive care needs as they are identified

Margins positive (R1,R2)a OR
Positive mediastinal nodes

Refer to Radiation Oncology and/or Medical Oncology

Margins negative (R0)a

Refer to Surgical Oncology

Margins positive (R1,R2)a OR
Consider re-resection

Referral to Medical Oncology (high risk Stage IB-II NSCLC)
for adjuvant chemotherapy

Refer to Radiation Oncology

See Surveillance—Page 29

Footnote:
a. R0 = no residual tumour, R1 = microscopic residual tumour, R2 = macroscopic residual tumour

Diagram 4.

Diagram 5.

Stage I* - Examples

T1,N0,M0
(No lymph node involvement)

T2,N0,M0
(Involved bronchus)

T2,N0,M0
(Involved visceral pleura)

Stage II A - Examples

T2,N1,M0
(>3cm involving bronchus and hilar lymph nodes)

T1,N1,M0
(<3cm involving peribronchial lymph nodes)

No lymph node involvement

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Footnote:
a. R0 = no residual tumour, R1 = microscopic residual tumour, R2 = macroscopic residual tumour

Guidelines for the Management of Lung Cancer
Treatment of Non-Small Cell Lung Cancer - Clinical Stage IIB & IIIA

Stage IIB (T3,N0)  
Stage IIIA (T3, N1)

- Bronchoscopy
- CT chest/upper abdomen
- MRI of spine & thoracic inlet for superior sulcus lesions as indicated
- See Page 19 for other investigation(s)

Deemed resectable

Deemed unresectable

Surgery

Pre-op Chemo-radiotherapy (superior sulcus tumour)

Margins negative (R0)α

Margins positive (R1,R2)α

Observe

Referral to Radiotherapy (OR Consider Re-resection)

Consider surgery (if resectable)

Observe

Chemo-radiotherapy OR Radiotherapy

Assess for pain & symptoms, distress, and other psychosocial needs
Address supportive care needs as they are identified

Symptomatic Progression- see Surveillance Page 29

Stage IIIB (T3,N0-2,M0)
Superior sulcus tumor with or without lymph node involvement

Stage IIIA (T3,N1,M0)
Peripheral tumor >3cm involving chest wall and hilar lymph nodes

Footnote:
α. R0 = no residual tumour, R1 = microscopic residual tumour, R2 = macroscopic residual tumour

Guidelines for the Management of Lung Cancer -26

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Treatment of Non-Small Cell Lung Cancer—Clinical Stage IIIA (cont’d)

Stage IIIA (T1-3, N2)

- CT chest/ upper abdomen
- Bronchoscopy
- Mediastinoscopy
- See Page 19 for other investigations

Mediastinal Biopsy Findings

Positive N2 → Chemotherapy and/or Radiotherapy

Observe

Negative N2, N3 → See Treatment Stage I & II- Page 21

Assess for pain & symptoms, distress, and other psychosocial needs
Address supportive care needs as they are identified

Diagram 7.

Stage IIIA - Example

T3,N2,M0
Involvement of ipsilateral hilar and mediastinal lymph nodes.

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Treatment of Non-Small Cell Lung Cancer—Clinical Stage IIIB

Stage IIIB (T4, N0-1)

- Bronchoscopy
- CT scan of chest/upper abdomen
- Consider Mediastinoscopy
- See Page 19 for other investigations

Potentially Resectable

Consider pre-operative Chemotherapy and/or Radiotherapy

Reassess resectability

Margins negative (R0)\(^a\)

Surgery

Margins positive (R1,R2)\(^a\)

Observe

Not resectable upon surgical exploration

Unresectable

Referral for Radiotherapy and/or Chemotherapy

Assess for pain & symptoms, distress, and other psychosocial needs
Address supportive care needs as they are identified

---

Footnote:
\(a\) R0 = no residual tumour, R1 = microscopic residual tumour, R2 = macroscopic residual tumour

Diagram 8.

Stage IIIB - Example

T4,N1,M0
Involving pleural membrane and ipsilateral hilar nodes (with pleural effusion)

Pleural effusion

Diagram by Monique Guilderson 04

Guidelines for the Management of Lung Cancer -28
Treatment of Non-Small Cell Lung Cancer—Clinical Stage IIIB (cont’d)

Stage IIIB (T1-3, N3)

Pathologic confirmation of N3 disease by:
- Mediastinoscopy
- Supraclavicular lymph node biopsy
- Thoracoscopy
- Needle biopsy
- Mediastinoscopy

N3 Nodes

- Negative
  - See treatment of Stage I-IIIA- Pages 21-23
- Positive
  - Brain MRI
  - Bone Scan
  - Chemotherapy/Radiotherapy
  - Positive
    - See treatment of metastatic disease-Page 29

Assess for pain & symptoms, distress, and other psychosocial needs
Address supportive care needs as they are identified.

Diagram 9.

Stage IIIB - Example

T3,N3,M0 involving pericardium and both ipsilateral nodes (N2,2) and contralateral nodes (N3)

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- Guidelines for the Management of Lung Cancer
Treatment of Non-Small Cell Lung Cancer - Clinical Stage IIIB (cont'd)

Stage IIIB (T4, N2-3)

Pathologic confirmation of T4, N2-3 disease by:
- Mediastinoscopy
- Supraclavicular lymph node biopsy
- Thoracoscopy
- Needle biopsy
- Mediastinoscopy
- Bone scan
- Brain MRI

N3 Nodes

Contralateral Node Negative

Contralateral Node Positive

Ipsilateral Node Negative

Ipsilateral Node Positive

Chemotherapy/Radiotherapy

Chemotherapy/Radiotherapy

Assess for pain & symptoms, distress, and other psychosocial needs
Address supportive care needs as they are identified

Stage IIIB - Example

T4, N3, M0
Involving great vessels, ipsilateral and contralateral lymph nodes with satellite ipsilateral nodule

Diagram 10.
Treatment of Non-Small Cell Lung Cancer—
Clinical Stage IIIB & IV

Stage IIIB
(T4: pleural effusion)

Thoracentesis +/- thoracoscopy
if thoracentesis indeterminate

Stage IV
(M1: solitary site)

If Positive

Local therapy if necessary
(e.g. pleurodesis)

Pathologic & clinical confirmation of M1
disease by:
- Mediastinoscopy
- Bronchoscopy
- Bone scan
- Brain MRI
- CT scan of chest and upper abdomen (including adrenal glands)

Stage IV
(M1: disseminated)

Referral for Chemotherapy and/or Radiotherapy

Assess for pain & symptoms, distress, and other psychosocial needs
Address supportive care needs as they are identified

Referral for Chemotherapy and/or Radiotherapy

See treatment of recurrence and metastasis (Pages 28, 29)

Footnote:
a. Most pleural effusions associated with lung cancer are due to tumour. There are few patients in whom multiple cytopathologic examinations of pleural fluid are negative for tumour. Fluid is non-bloody and not an exudate. When these elements and clinical judgement dictate the effusion is not related to the tumour, the effusion should be excluded as a staging element and the patient should be staged T1, T2 or T3.
Surveillance and Treatment of Recurrent Non-Small Cell Lung Cancer

**Surveillance**

- In asymptomatic patients, clinical assessment + chest X-ray every 6 mo for 3 yr, then annually
- Smoking cessation counselling

Assess for pain & symptoms, distress, and other psychosocial needs
Address supportive care needs as they are identified

**Locoregional recurrence:**
- Endobronchial obstruction:
  - External-beam Radiotherapy
  - Laser/stent/other surgery
  - Brachytherapy
- Resectable local recurrence:
  - Re-resection
  - External-beam Radiotherapy
- Superior vena cava (SVC) obstruction:
  - External-beam Radiotherapy
  - Stent
- Severe hemoptysis:
  - Bronchoscopy (to assess for intervention)
  - External-beam Radiotherapy
  - Brachytherapy
  - Laser
  - Embolization
  - Surgery

**Evidence of disseminated disease**

See treatment of recurrence and metastasis (Page 29)

**Solitary metastasis**

See treatment of recurrence and metastasis (Page 29)

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Diagram 12.

Lung Cancer Recurrence - Examples

- Obstructed bronchus
- Brain metastasis
- Bone or spinal metastasis
- SVC syndrome

(C)Ronikie Guilberson 04

Guidelines for the Management of Lung Cancer -32
Treatment of Non-Small Cell Lung Cancer - Metastases

Treatment for Recurrence and Metastasis

- Performance status 0-2\textsuperscript{a,b}
  - Consider Radiotherapy
  - Observation
  - Tumour response evaluation
  - Progression
  - See below for salvage treatment

- Chemotherapy (usually 2 cycles)
  - Response or stable disease
    - 2 more cycles of chemotherapy
      - Response or stable disease
        - Consider 2 more cycles chemotherapy (total of 6 cycles)
        - Observation
        - See CCNS Guidelines for management of specific symptoms, where appropriate
      - Progression
      - Observation
  - Consider Radiotherapy
  - Best supportive care

Performance status 3, 4

- Referral to Medical and/or Radiation Oncology

- Consider chemotherapy
- Consider Radiotherapy
- Clinical trial
- Observation

Relapsed Non-Small Cell Lung Cancer

- Relapsed disease
  - Referral to Medical and/or Radiation Oncology
  - Assess for pain & symptoms, distress, and other psychosocial needs
  - Address supportive care needs as they are identified
  - Performance status 3, 4
    - Relapse performance status 3, 4
      - Best supportive care
    - Consider chemotherapy
      - OR
      - Consider Radiotherapy
      - OR
      - Clinical trial
      - OR
      - Observation

Footnotes:

a. ECOG Performance Status criteria - See Page 35
b. Performance status (PS) 2 patients have greater toxicity and potential for lower benefit than PS 0-1 patients
Staging of Small Cell Lung Cancer

Referral to Medical Oncology

Clinical Staging for Small Cell Lung Cancer

Limited Stage
- Disease in hemithorax only AND
- Can be encompassed within a reasonable radiation port (assessed by radiation oncologist)

Additional evaluations:
- MRI or CT scan of the head
- Bone scan

Positive findings

Extensive Stage
- Disease in contralateral lung AND/OR
- Pleural Effusion AND/OR
- Any disseminated disease

Negative findings

See treatment of extensive stage disease (Page 31)

See treatment of limited stage disease (Page 31)

Assess for pain & symptoms, distress, and other psychosocial needs
Address supportive care needs as they are identified

NOTE: SCLC can be staged using the same TNM Staging criteria applied to NSCLC; however, clinicians generally use the simpler classification of Limited vs. Extensive Disease. Treatment decisions are usually based upon this simple classification system.
Footnote:

- Radiotherapy for limited disease:
  - Radiotherapy over 3-5 weeks concurrent with chemotherapy
  - Prophylactic Cranial Irradiation (PCI) treatment over about 2 weeks

Assess for pain & symptoms, distress, and other psychosocial needs
Address supportive care needs as they are identified
Follow-up after Treatment of Small Cell Lung Cancer

Response Assessment Following Initial Treatment

- History & physical exam (including weight loss)
- Chest X-ray
- Consider CT scan of chest (baseline post-treatment)

Complete response or radiation scarring on chest imaging studies

Partial response

Progressive disease or relapse

- Oncology follow-up visits every 3-6 mo for 2 yr, then every 6-12 mo
- New pulmonary nodule after 2 yr follow-up should initiate work-up for potential new primary
- At every visit: H&P, chest X-ray, bloodwork as clinically indicated
- Smoking cessation counselling

See below

Assess for pain & symptoms, distress, and other psychosocial needs
Address supportive care needs as they are identified

Relapsed or Progressive Small Cell Lung Cancer

Relapse or progressive disease

- Consider second-line chemotherapy and/or palliative radiotherapy

Relapse or refractory to second-line therapy

Consider third-line chemotherapy

OR

Best supportive care

See CCNS Guidelines for management of specific symptoms, where appropriate

Assess for pain & symptoms, distress, and other psychosocial needs
Address supportive care needs as they are identified

OR

Best supportive care
Chemotherapy Regimens

Non-Small Cell Lung Cancer

**Docetaxel Chemotherapy**
Docetaxel IV- Day 1
Repeat every three weeks

**Docetaxel-Carboplatin Chemotherapy**
Docetaxel IV- Day 1
Carboplatin IV- Day 1
Repeat every three weeks

**Docetaxel-Cisplatin Chemotherapy**
Docetaxel IV- Day 1
Cisplatin IV- Day 1
Repeat every three weeks

**Docetaxel-Gemcitabine Chemotherapy**
Docetaxel IV- Day 1
Gemcitabine IV- Days 1, 8, and 15
Repeat every three weeks

**Gemcitabine-Cisplatin Chemotherapy**
Gemcitabine IV- Days 1, 8, and 15
Cisplatin IV- Day 1
Repeat every four weeks

NB. The role of EGFR Inhibitors (e.g. Erlotinib, Geftinib) are under review by the Thoracic CST

Small Cell Lung Cancer

**Cisplatin-Etoposide Chemotherapy**
Etoposide IV- Days 1 to 3
Cisplatin IV- Days 1 to 3
Repeat every 3 weeks for 4 cycles

**Carboplatin-Etoposide Chemotherapy**
Etoposide IV- Days 1 to 3
Carboplatin IV- Day 1
Repeat every 3 weeks for 4 cycles

**CAV Chemotherapy**
Cyclophosphamide IV- Day 1
Doxorubicin IV- Day 1
Vincristine IV- Day 1
Repeat every 3 weeks for 4 cycles

**Etoposide Chemotherapy**
Etoposide PO- daily for 14-21 days

**Topotecan Chemotherapy**
Topotecan IV- Days 1-5
Repeat every 3 weeks for 4 cycles

See the Systemic Therapy Manual for Cancer Patients for further details.

**ECOG Performance Status Scale**

0 Fully active, able to carry on all predisease activities without restriction. (Karnofsky 90-100)

1 Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, for example, light housework or office work. (Karnofsky 70-80)

2 Ambulatory and capable of all self-care but unable to carry out work activities. Up and about more than 50% of waking hours. (Karnofsky 50-60)

3 Capable of only limited self-care, confined to bed or chair 50% or more of waking hours. (Karnofsky 30-40)

4 Completely disabled, cannot carry on any self-care, totally confined to bed or chair. (Karnofsky 10-20)

ECOG = Eastern Cooperative Oncology Group
Lung Cancer Prognosis by Stage

Reference:
APPENDIX I  Thoracic Cancer Site Team Members

Drew Bethune, Surgical Oncology Lead Capital Health (Co-Chair)
Liam Mulroy, Radiation Oncology Lead Capital Health (Co-Chair)

Anthony Atkinson, Internist, South Shore Regional Hospital
Marsha Avery, Oncology Nurse, Capital Health
Larry Broadfield, CCNS Systemic Therapy Program
Ralph Burnett, Surgeon, Valley Regional Hospital
Yannick Cartier, Radiology, Capital Health
Alan Casson, Surgical Oncology, Capital Health
Lynn Coulter, Oncology Nurse ERN, Capital Health
Slawa Cwajna, Radiation Oncology, Capital Health
Mary Davis, Medical Oncology, Capital Health
Kendra Dill, Oncology Nurse, Capital Health
Paul Dubois, Surgeon, Moncton, New Brunswick
Rex Dunn, Surgeon, Cape Breton Regional Hospital
Linda Eastham, Oncology Nurse, Capital Health
Jill Flinn, Health Services Manager, Capital Health
Heather Gage, Clinical Trials Nurse, Capital Health
Paul Gardner, Surgeon, St. John’s, Newfoundland
Donna Grant, Nurse Educator, Capital Health
Harry Henteleff, Surgical Oncology, Capital Health
Robert Horton, Palliative Care, Capital Health
Ken Johnson, Palliative Care, Capital Health
Cheryl Lahey, Oncology Nurse, Capital Health
Cheryl Lamkey, Oncology Nurse, Capital Health
Ron MacCormick, Medical Oncology, Cape Breton Cancer Centre
Heather MacKenzie, Capital Health (Site Team Secretary)
Jo-Ann Martin, Oncology Nurse, Capital Health
Kathy McIntyre, Surgical Oncology Nurse, Capital Health
Leslie McLean, Nursing Department, Capital Health
Wojciech Morzycki, Medical Oncology, Capital Health
Lorraine Parkin, Oncology Pharmacy, Capital Health
Jill Petrella, CCNS Quality Co-ordinator
Mal Rajaraman, Radiation Oncology, Capital Health
Dorianne Rheaume, Radiation Oncology, Capital Health
Rob Rutledge, Radiation Oncology, Capital Health
David Smith, Oncology Nurse, Capital Health
Jorge Sanson, Surgeon, Valley Regional Hospital
Marlene Sellon, Oncology Pharmacy, Capital Health
Tara Shaw, Clinical Trials Nurse, Capital Health
Vickie Sullivan, Director, Capital Health Cancer Care Program
Veronica Tanner, Oncology Nurse, Capital Health
Kiran Virik, Medical Oncology, Capital Health
Karen Woodworth, Oncology Nurse, Capital Health
Zhaolin Xu, Pathology, Capital Health
Tallal Younis, Medical Oncology, Capital Health

There are no known conflicts of interest by this team relevant to this guideline
Guideline Development Process

This guideline was written by Members of the Thoracic Cancer Site Team, headed by Dr. D. Bethune and supported by L. Broadfield. Specific recommendations were based upon evidence routinely reviewed by the expert members of the CST and by consensus development among the CST members. Upon completion of an initial draft, the guideline was reviewed by the entire Thoracic CST for critical appraisal. Format issues were resolved in collaboration with the Guidelines Resource Team of Cancer Care Nova Scotia.

This guideline was written for an audience of general practitioners and medical students, not necessarily lung cancer specialists. As such, it is a synthesis of knowledge and evidence, and reflects the practice policies of the Thoracic Cancer Site Team in Nova Scotia. The written text on management is supported by the graphic flowcharts in the ‘Practice Pathways’ section.

Once the draft document was approved by the CST, it was distributed to a group of community reviewers. The draft guidelines were also presented to a meeting of oncology pharmacists from Atlantic Canada (who did not complete the review questionnaire and are removed from the analysis of data). Community reviewers included identified internists, pathologists, radiologists, medical and radiation oncologists and selected oncology nurses and oncology pharmacists from health care districts in Nova Scotia, New Brunswick, Newfoundland, and Prince Edward Island. 145 copies of the guideline were distributed for review, of which 49 were sent to pharmacists who had attended an earlier presentation of this topic. All responses were anonymous.

Responses to the draft review were collected on a standard guideline review questionnaire. Results are presented on the next page. The adjusted response rate (adjusted for removal of the pharmacist group) was 23%.

Upon review of the feedback from the community reviewers, and incorporation of appropriate comments, the guidelines were subsequently presented to the Family Practice Council of Capital Health for their collective feedback (no questionnaires were received from this group). The guideline was returned to the Thoracic Cancer Site Team (CST) for final review and approval. The CST-approved document was reviewed by the Guidelines Resource Team against the AGREE tool for guideline evaluation. A number of changes were incorporated into the final guideline document, in better compliance with the AGREE tool domains.

The approved guideline is published in both a Full Version and a Quick Reference Version (just the Practice Pathways). The full version will be circulated in hard copy to all lung cancer specialists (from multiple disciplines) as well as to the cancer chemotherapy clinics and regional hospital pharmacies in Nova Scotia. The Quick Reference Version will be circulated to all health care professional subscribers to the CCNS newsletter (all physicians, pharmacies, oncology nurses and others in Nova Scotia). Copies of either version will also be made available to healthcare professionals in Prince Edward Island, Newfoundland, and New Brunswick. Others who are interested may request hard copies by contacting Cancer Care Nova Scotia (CCNS) at 1-866-599-2267 or download from the CCNS website (www.cancercare.ns.ca).

The guideline will be reviewed three years after approval or revised as new evidence becomes available. The development of this guideline was funded indirectly by CCNS via a stipend for the Thoracic Cancer Site Team’s operations. CCNS staff also support the guideline development process. CCNS directly funded the design, printing and dissemination of the guideline survey as well as the approved guideline. The views and interests of CCNS have not influenced the Thoracic CST’s recommendations in this guideline.
Summary of Reviewers for Lung Cancer Guideline - By Profession and Province

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<th>Sent to Reviewers: By Specialty:</th>
<th>By Province:</th>
<th>Responses</th>
<th>Number</th>
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Total Responses 24 17%
Response Rate (excluding Pharmacists) 23%

1. Is this guideline relevant to your practice? Yes = 20 No = 3 N. A. = 1
2. A guideline on this topic will be useful to clinicians.

<table>
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3. You agree with the guideline.

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4. The format of the guideline is easy to use.

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5. The illustrations make this guideline easier to understand.

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7. Would you use this guideline in your own practice? Yes = 18

Comments:
* Decision aid when caring for a lung cancer patient = 12
* Better understanding about how lung cancer is detected and managed = 9
* Aid for patient education about lung cancer = 12

8. This guideline should be disseminated to all appropriate practitioners in Nova Scotia.

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9. This guideline should be disseminated to all appropriate practitioners in Atlantic Canada.

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If NO or UNSURE
* Not the mandate of Cancer Care Nova Scotia to distribute guidelines outside NS = 2

11. How should CCNS guidelines be disseminated once they are approved?

* paper copy = 15
* Palm Pilot/PDA = 8
* Website = 18
* CME = 10
Cancer Care Nova Scotia

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5th floor Bethune Building
Halifax, Nova Scotia  B3H 2Y9

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