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## **Diagnosis and Management of Lung Cancer Executive Summary : ACCP Evidence-Based Clinical Practice Guidelines (2nd Edition)**

W. Michael Alberts

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## Diagnosis and Management of Lung Cancer Executive Summary\*

### ACCP Evidence-Based Clinical Practice Guidelines (2nd Edition)

W. Michael Alberts, MD, FCCP, Chair

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**Key words:** diagnosis; guidelines; lung cancer; management

**Abbreviations:** ACCP = American College of Chest Physicians; BAC = bronchioloalveolar carcinoma; CIS = carcinoma *in situ*; DLCO = diffusion capacity of the lung for carbon monoxide; EBUS-NA = endobronchial ultrasound-needle aspiration; EUS-NA = endoscopic ultrasound-needle aspiration; FDG = fluorodeoxyglucose; NSCLC = non-small cell lung cancer; PET = positron emission tomography; PS = performance status; SCLC = small cell lung cancer; SPN = solitary pulmonary nodule; SVC = superior vena cava; TBNA = transbronchial needle aspiration; TTNA = transthoracic needle aspiration

In the 19th century, lung cancer was an unusual tumor; so much so that single case reports of the rare cancer were published in the scientific literature of the day. Things have changed. Other than skin cancer, lung cancer is now the most common cancer and is the most frequent cause of death from cancer in both men and women.

In recognition of the importance of lung cancer in the population and with the rise of evidence-based medicine as a basis for diagnosing the disease and managing those afflicted, in the year 2000 the American College of Chest Physicians (ACCP), through its Health and Science Policy Committee, commissioned the development of evidence-based guidelines on the diagnosis and management of lung cancer. The goal was to assist physicians in achieving the best possible outcomes given the knowledge and capabilities available at the time. The size of the task

was daunting, but the goal was laudable and the guidelines were successfully published as a Supplement to *CHEST* in January of 2003.

Fortunately, the pace of discovery in the diagnosis and management of lung cancer has quickened. As a result, the ACCP found it prudent to commission the development of a second edition of the guidelines. This guideline Supplement is the result of that effort and represents the work of nearly 100 voluntary faculty and ACCP staff.

The methodology and grading system used to develop the second edition of the guidelines may be found in a separate chapter. Rigorous adherence to formal guideline methodology was stressed. This attention to process detail and the use of the newly developed ACCP grading system has produced a valid, yet clinically useful document.

In response to suggestions made after the first edition, several new chapters have been added, such as “Diagnostic Surgical Pathology in Lung Cancer,” “Bronchioloalveolar Lung Cancer,” and “Complementary Therapies and Integrative Oncology in Lung Cancer.” A number of chapters have been extensively reworked to encompass recent knowledge; for example, “Screening for Lung Cancer, Management of Patients with Pulmonary Nodules: When is it lung cancer?” (*ie*, the chapter previously termed the “Solitary Pulmonary Nodule”), “Bronchial Intraepithelial

\*From H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL.

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Correspondence to: W. Michael Alberts, MD, MBA, FCCP, Chief Medical Officer, H. Lee Moffitt Cancer Center and Research Institute, Professor of Medicine, University of South Florida College of Medicine, 12902 Magnolia Dr, Tampa, FL 33612; e-mail: [Michael.Alberts@moffitt.org](mailto:Michael.Alberts@moffitt.org)

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Neoplasia/Early Central Airways Lung Cancer” (ie, the chapter previously termed “The Treatment of Early Stage Non-small Cell Lung Cancer”), and “Palliative Care Consultation,” “Quality of Life Measurement,” and “Bereavement for End-of-Life Care in Patients with Lung Cancer.” All of the chapters have incorporated information and knowledge gleaned from the literature published since 2002.

Recommendations from each of the chapters are listed below under their respective chapter titles. For an in-depth discussion or clarification of each recommendation, readers are encouraged to read the specific chapter in question in its entirety.

#### SUMMARY OF RECOMMENDATIONS

##### *Lung Cancer Chemoprevention*

**1. For individuals with a > 20-pack-year history of smoking or with a history of lung cancer, the use of beta-carotene supplementation is not recommended for primary, secondary, or tertiary chemoprevention of lung cancer.** Grade of recommendation, 1A

**2. For individuals at risk for lung cancer and for patients with a history of lung cancer, the use of vitamin E, retinoids, N-acetylcysteine, and aspirin is not recommended for primary, secondary, or tertiary prevention of lung cancer.** Grade of recommendation, 1A

**3. For individuals at risk for lung cancer or with a history of lung cancer, budenonide, cyclooxygenase-2 inhibitors, 5-lipoxygenase inhibitors, and prostaglandin analogs are not recommended for use for primary, secondary, or tertiary lung cancer chemoprevention outside of the setting of a well-designed clinical trial.** Grade of recommendation, 2C

**4. In individuals at risk for lung cancer or with a history of lung cancer, the use of oltipraz as a primary, secondary, or tertiary chemopreventive agent of lung cancer is not recommended.** Grade of recommendation, 1B

**5. For individuals at risk for lung cancer or with a history of lung cancer, the use of selenium, and anethole dithiolethione, for primary, secondary, or tertiary lung cancer chemoprevention is not recommended outside of the setting of a well-designed clinical trial.** Grade of recommendation, 1B

**6. For individuals at risk for lung cancer or with a history of lung cancer, there are not yet sufficient data to recommend the use of any agent either alone or in combination for primary, secondary, or tertiary lung cancer chemoprevention outside of a clinical trial.** Grade of recommendation, 1B

##### *Screening for Lung Cancer*

**1. We do not recommend that low-dose helical CT be used to screen for lung cancer except in the context of a well-designed clinical trial.** Grade of recommendation, 2C

**2. We recommend against the use of serial chest radiographs to screen for the presence of lung cancer.** Grade of recommendations, 1A

**3. We recommend against the use of single or serial sputum cytologic evaluation to screen for the presence of lung cancer.** Grade of recommendation, 1A

##### *Diagnostic Surgical Pathology in Lung Cancer*

**1. When pathologically diagnosing lung cancer, the reporting of histologic type, tumor size and location, tumor grade (if appropriate), lymphovascular invasion, involvement of pleura, surgical margins, and status and location of lymph nodes by station is recommended.** Grade of recommendation, 1B

**2. In individuals at risk for lung cancer but without symptoms or history of cancer, utilization of single or serial sputum cytologic examinations to screen for the presence of lung cancer is of insufficient clinical benefit and is not recommended.** Grade of recommendation, 1A

**3. In individuals with pleural-based tumors, when distinguishing between pleural adenocarcinoma and malignant mesothelioma, a structured approach utilizing a limited panel of histochemical and immunohistochemical assays is recommended to increase the diagnostic accuracy. More challenging cases may need additional studies, including ultrastructural analysis.** Grade of recommendation, 1B

**4. In individuals with parenchymal-based tumors, distinguishing between small cell carcinoma and non-small cell carcinoma of the lung is recommended. For challenging cases, a diagnostic panel of immunohistochemical assays is recommended to increase**

diagnostic accuracy. More challenging cases may need additional studies, including ultrastructural analysis. Grade of recommendation, 1B

**5. For individuals with glandular producing tumors, distinguishing pure bronchioloalveolar carcinoma (BAC) from adenocarcinoma with or without BAC component is recommended.** Grade of recommendation, 1C

**6. For individuals with lung tumors whose differential includes primary lung carcinoma vs metastatic carcinoma, a directed panel of immunohistochemical assays is recommended to increase the diagnostic accuracy.** Grade of recommendation, 1C

**7. For individuals with lung tumors who have had an assessment of pathologic features and staging parameters, the evaluation of pathobiological and molecular markers is appropriate for protocol investigations and is not routinely recommended for clinical management.** Grade of recommendation, 1C

**8. For individuals with lung tumors who have had an assessment of pathologic features and staging parameters, the determination of occult or micrometastatic disease, utilizing enhanced pathologic or molecular techniques, is not of sufficient clinical utility and is not recommended.** Grade of recommendation, 1C

#### *Management of Patients With Pulmonary Nodules: When Is It Lung Cancer?*

**1. In every patient with a solitary pulmonary nodule (SPN), we recommend that clinicians estimate the pretest probability of malignancy either qualitatively by using their clinical judgment or quantitatively by using a validated model.** Grade of recommendation, 1C

**2. In every patient with an SPN that is visible on chest radiography, we recommend that previous chest radiographs and other relevant imaging tests be reviewed.** Grade of recommendation, 1C

**3. In patients who have an SPN that shows clear evidence of growth on imaging tests, we recommend that tissue diagnosis should be obtained unless specifically contraindicated.** Grade of recommendation, 1C

**4. In a patient with an SPN that is stable on imaging tests for at least 2 years, we suggest that no additional diagnostic evaluation be**

**performed, except for patients with pure ground-glass opacities on CT, for whom a longer duration of annual follow-up should be considered.** Grade of recommendation, 2C

**5. In a patient with an SPN that is calcified in a clearly benign pattern, we recommend that no additional diagnostic evaluation is necessary.** Grade of recommendation, 1C

**6. In every patient with an indeterminate SPN that is visible on chest radiography, we recommend that CT of the chest should be performed, preferably with thin sections through the nodule.** Grade of recommendation, 1C

**7. In every patient with an indeterminate SPN that is visible on chest CT, we recommend that previous imaging tests should be reviewed.** Grade of recommendation, 1C

**8. In a patient with normal renal function and an indeterminate SPN on chest radiograph or chest CT, we recommend that CT with dynamic contrast enhancement be considered in centers with experience performing this technique.** Grade of recommendation, 1B

**9. In patients with low-to-moderate pretest probability of malignancy (5 to 60%) and an indeterminate SPN that measures at least 8 to 10 mm in diameter, we recommend that fluorodeoxyglucose (FDG)-positron emission tomography (PET) imaging should be performed to characterize the nodule.** Grade of recommendation, 1B

**10. In patients with an SPN that has a high pretest probability of malignancy (> 60%), or patients with a subcentimeter nodule that measures < 8 to 10 mm in diameter, we suggest that FDG-PET not be performed to characterize the nodule.** Grade of recommendation, 2C

**11. In every patient with a SPN, we recommend that clinicians discuss the risks and benefits of alternative management strategies and elicit patient preferences.** Grade of recommendation, 1C

**12. In patients with an indeterminate SPN that measures at least 8 to 10 mm in diameter and who are candidates for curative treatment, observation with serial**

**CT scans is an acceptable management strategy in the following circumstances:**

- When the clinical probability of malignancy is very low (< 5%)



- When clinical probability is low (< 30 to 40%) and the lesion is not hypermetabolic by FDG-PET or does not enhance > 15 Hounsfield units on dynamic contrast CT
- When needle biopsy is nondiagnostic and the lesion is not hypermetabolic by FDG-PET
- When a fully informed patient prefers this nonaggressive management approach.

Grade of recommendation, 2C

13. In patients with an indeterminate SPN that measures at least 8 to 10 mm in diameter who undergo observation, we suggest that serial CT scans be repeated at least at 3, 6, 12, and 24 months. Grade of recommendation, 2C

14. In patients with an indeterminate SPN that measures at least 8 to 10 mm in diameter and who are candidates for curative treatment, it is appropriate to perform transthoracic needle biopsy or bronchoscopy in the following circumstances:

- When clinical pretest probability and findings on imaging tests are discordant; for example, when the pretest probability of malignancy is high and the lesion is not hypermetabolic by FDG-PET
- When a benign diagnosis requiring specific medical treatment is suspected
- When a fully informed patient desires proof of a malignant diagnosis prior to surgery, especially when the risk of surgical complications is high.

In general, we suggest that transthoracic needle biopsy be the first choice for patients with peripheral nodules unless the procedure is contraindicated or the nodule is inaccessible. We suggest that bronchoscopy be performed when an air bronchogram is present or in centers with expertise in newer guided techniques. Grade of recommendation, 2C

15. In surgical candidates with an indeterminate SPN that measures at least 8 to 10 mm in diameter, surgical diagnosis is preferred in most circumstances, including:

- When the clinical probability of malignancy is moderate to high (> 60%)
- When the nodule is hypermetabolic by FDG-PET imaging
- When a fully informed patient prefers undergoing a definitive diagnostic procedure.

Grade of recommendation, 1C

16. In patients with an indeterminate SPN in the peripheral third of the lung who chose surgery, we recommend that thoracoscopy be performed to obtain a diagnostic wedge resection. Grade of recommendation, 1C

17. In a patient who chooses surgery with an indeterminate SPN that is not accessible by thoracoscopy, bronchoscopy, or transthoracic needle aspiration (TTNA), we recommend that a diagnostic thoracotomy should be performed. Grade of recommendation, 1C

18. In patients with a SPN who undergo thoracoscopic wedge resection that is found to be cancer by frozen section, we recommend that anatomic resection with systematic mediastinal lymph node sampling or dissection be performed during the same anesthetic. Grade of recommendation, 1C

19. In patients with an SPN who are judged to be marginal candidates for lobectomy, we recommend definitive treatment by wedge resection/segmentectomy (with systematic lymph node sampling or dissection). Grade of recommendation, 1B

20. For the patient with an SPN who is not a surgical candidate and who prefers treatment, we recommend that the diagnosis of lung cancer be confirmed by biopsy, unless contraindicated. Grade of recommendation, 1C

21. For the patient with a malignant SPN who is not a surgical candidate and who prefers treatment, we recommend referral for external beam radiation or to a clinical trial of an experimental treatment such as stereotactic radiosurgery or radiofrequency ablation. Grade of recommendation, 2C

22. For surgical candidates with subcentimeter nodules who have no risk factors for lung cancer, the frequency and duration of follow-up (preferably with low-dose CT) should depend on the size of the nodule. We suggest that:

- Nodules measuring up to 4 mm in diameter need not be followed up, but the patient must be fully informed of the risks and benefits of this approach
- Nodules measuring > 4 to 6 mm should be re-evaluated at 12 months without the need for additional follow-up if unchanged
- Nodules measuring > 6 to 8 mm should be followed up sometime between 6 months and 12 months, and then again between

18 months and 24 months if unchanged.

Grade of recommendation, 2C

**23. For surgical candidates with subcentimeter nodules who have one or more risk factors for lung cancer, the frequency and duration of follow-up (preferably with low-dose CT) should depend on the size of the nodule. We suggest that:**

- Nodules measuring up to 4 mm in diameter should be re-evaluated at 12 months without the need for additional follow-up if unchanged
- Nodules measuring > 4 to 6 mm should be followed up sometime between 6 months and 12 months, and then again between 18 months and 24 months if unchanged
- Nodules measuring > 6 to 8 mm should be followed up initially sometime between 3 months and 6 months and then subsequently between 9 months and 12 months, and again at 24 months if unchanged.

Grade of recommendation, 2C

**24. For surgical candidates with subcentimeter nodules that display unequivocal evidence of growth during follow-up, we recommend that definitive tissue diagnosis should be obtained, either by surgical resection, transthoracic needle biopsy, or bronchoscopy.** Grade of recommendation, 1C

**25. For individuals with subcentimeter nodules who are not candidates for curative treatment, we recommend limited follow-up (in 12 months) or follow-up when symptoms develop.** Grade of recommendation, 1C

**26. In patients who are candidates for curative treatment with a dominant SPN and one or more additional small nodules, we recommend that each nodule be evaluated individually, as necessary, and curative treatment should not be denied unless there is histopathologic confirmation of metastasis.** Grade of recommendation, 1C

**27. In surgical candidates with a solitary pulmonary metastasis, we recommend that pulmonary metastasectomy be performed if there is no evidence of extrapulmonary malignancy and there is no better available treatment.** Grade of recommendation, 1C

**28. In surgical candidates with an SPN that has been diagnosed as small cell lung cancer (SCLC), we recommend surgical resection with adjuvant chemotherapy, provided that noninvasive and invasive staging exclude the presence of regional or distant metastasis.** Grade of recommendation, 1C

**29. In patients with an SPN in whom SCLC is diagnosed intraoperatively, we recommend anatomic resection (with systematic mediastinal lymph node sampling or dissection) under the same anesthetic if there is no evidence of nodal involvement and if the patient will tolerate resection. Surgery should be followed by adjuvant chemotherapy.** Grade of recommendation, 1C

*Initial Diagnosis of Lung Cancer*

**1. In patients suspected of having SCLC based on radiographic and clinical findings, it is recommended that the diagnosis be confirmed by the easiest method (sputum cytology, thoracentesis, fine-needle aspirate, bronchoscopy including transbronchial needle aspiration [TBNA] and endobronchial ultrasound-needle aspiration [EBUS-NA], endoscopic ultrasound-needle aspiration [EUS-NA]), as dictated by the patient's presentation.** Grade of recommendation, 1C

**2. In patients suspected of having lung cancer who have an accessible pleural effusion, thoracentesis is recommended to diagnose the cause of the pleural effusion.** Grade of recommendation, 1C

**3. In a patients suspected of having lung cancer who have an accessible pleural effusion, if pleural fluid cytology is negative (after at least two thoracenteses), thoracoscopy is recommended as the next step if establishing the cause of the pleural effusion is believed to be clinically important.** Grade of recommendation, 1C

**4. In patients suspected of having lung cancer who have a solitary extrathoracic site suspicious for metastasis, it is recommended that tissue confirmation of the metastatic site be obtained if a fine-needle aspirate or biopsy of the site are feasible.** Grade of recommendation, 1C

**5. In patients suspected of having lung cancer who have lesions in multiple distant sites suspected of metastases but in whom biopsy of a metastatic site would be technically difficult, it is recommended that diagnosis of the primary lung lesion be obtained by the easiest method (sputum cytology, bronchoscopy with TBNA or EBUS-NA, EUS-NA, or TTNA).** Grade of recommendation, 1C

**6. In patients suspected of having lung cancer who have extensive infiltration of the mediastinum based on radiographic studies,**

it is recommended that the diagnosis of lung cancer be established by the easiest and safest method (bronchoscopy with TBNA, EBUS-NA, EUS-NA, TTNA, or mediastinoscopy). Grade of recommendation, 1C

7. In patients suspected of having lung cancer who present with a central lesion with or without radiographic evidence of metastatic disease, in whom a semiinvasive procedure such as bronchoscopy or TTNA might pose a higher risk, sputum cytology is recommended as an acceptable method of establishing the diagnosis. However, the sensitivity of sputum cytology varies by location of the lung cancer. It is recommended that further testing be performed with a nondiagnostic sputum cytology if suspicion of lung cancer remains. Grade of recommendation, 1C

8. In patients suspected of having lung cancer who have a central lesion, bronchoscopy is recommended to confirm the diagnosis. However, it is recommended that further testing be performed if bronchoscopy results are nondiagnostic and suspicion of lung cancer remains. Grade of recommendation, 1C

9. In expert hands, radial probe ultrasound device can increase the diagnostic yield of flexible bronchoscopy while dealing with peripheral lesions < 20 mm in size. Its use can be considered prior to referring the patient for TTNA. Grade of recommendation, 2B

10. In patients suspected of having lung cancer who have a small (< 2 cm) peripheral lesion, and who require tissue diagnosis before further management can be planned, TTNA is recommended. However, it is recommended that further testing be performed if TTNA results are nondiagnostic and suspicion of lung cancer remains. Grade of recommendation, 1B

11. In a patient suspected of having lung cancer, the diagnosis of non-small cell lung cancer (NSCLC) made on cytology (sputum, TTNA, or bronchoscopic specimens) is highly reliable and can be accepted with a high degree of certainty. Grade of recommendation, 1B

12. The possibility of an erroneous diagnosis of SCLC on a cytology specimen must be kept in mind if the clinical presentation or clinical course is not consistent with that of SCLC. In such a case, it is recommended that

further testing (biopsy for histologic evaluation) be performed to establish a definitive cell type. Grade of recommendation, 1B

*Initial Evaluation of the Patient With Lung Cancer: Symptoms, Signs, Laboratory Tests and Paraneoplastic Syndromes*

1. It is recommended that patients with known or suspected lung cancer receive timely and efficient care. Grade of recommendation, 1B

2. It is recommended that all patients with known or suspected lung cancer have a thorough history, physical examination, and standard laboratory tests as a screen for metastatic disease. Grade of recommendation, 1C

3. It is recommended that patients with lung cancer and a paraneoplastic syndrome not be precluded from potentially curative therapy on the basis of these symptoms alone. Grade of recommendation, 2C

*Physiologic Evaluation of the Patient With Suspected Lung Cancer Being Considered for Resection Surgery*

1. It is recommended that patients with lung cancer be assessed for curative surgical resection by a multidisciplinary team, which includes a thoracic surgeon specializing in lung cancer, medical oncologist, radiation oncologist, and pulmonologist. Grade of recommendation, 1C

2. It is recommended that patients with lung cancer not be denied lung resection surgery on the grounds of age alone. Grade of recommendation, 1B

3. It is recommended that patients with lung cancer being evaluated for surgery who have major factors for increased perioperative cardiovascular risk undergo a preoperative cardiologic evaluation. Grade of recommendation, 1C

4. In patients being considered for lung cancer resection, spirometry is recommended. If the FEV<sub>1</sub> is > 80% of predicted normal or > 2 L and there is no evidence of either undue dyspnea on exertion or interstitial lung disease, the patient is suitable for resection including pneumonectomy without further physiologic evaluation. If the FEV<sub>1</sub> is > 1.5 L and there is no evidence of either undue dyspnea on exertion or interstitial lung disease, the patient is suit-



able for a lobectomy without further physiologic evaluation. Grade of recommendation, 1C

5. In patients being considered for lung cancer resection, if there is evidence of either undue dyspnea on exertion or interstitial lung disease, even though the FEV<sub>1</sub> might be adequate, measuring diffusion capacity of the lung for carbon monoxide (DLCO) is recommended. Grade of recommendation, 1C

6. In patients being considered for lung cancer resection, if either the FEV<sub>1</sub> or DLCO are < 80% of predicted, it is recommended that postoperative lung function be predicted through additional testing. Grade of recommendation, 1C

7. In patients with lung cancer being considered for surgery, either a percentage of predicted postoperative FEV<sub>1</sub> < 40% or a percentage of predicted postoperative DLCO < 40% indicate an increased risk for perioperative death and cardiopulmonary complications with standard lung resection. It is recommended that these patients undergo exercise testing preoperatively. Grade of recommendation, 1C

8. In patients with lung cancer being considered for surgery, either a product of percentage of predicted postoperative FEV<sub>1</sub> and percentage of predicted postoperative DLCO < 1,650 or a percentage of predicted postoperative FEV<sub>1</sub> < 30% indicate an increased risk for perioperative death and cardiopulmonary complications with standard lung resection. It is recommended that these patients be counseled about nonstandard surgery and nonoperative treatment options for their lung cancer. Grade of recommendation, 1C

9. In patients with lung cancer being considered for surgery, a maximum oxygen uptake < 10 mL/kg/min indicates an increased risk for perioperative death and cardiopulmonary complications with standard lung resection. These patients should be counseled about nonstandard surgery and nonoperative treatment options for their lung cancer. Grade of recommendation, 1C

10. Patients with lung cancer being considered for surgery who have a maximum oxygen uptake < 15 mL/kg/min and both a percentage of predicted postoperative FEV<sub>1</sub> and DLCO < 40 are at increased risk for perioperative death and cardiopulmo-

nary complications with standard lung resection. It is recommended that these patients be counseled about nonstandard surgery and nonoperative treatment options for their lung cancer. Grade of recommendation, 1C

11. Patients with lung cancer being considered for surgery who walk < 25 shuttles on two shuttle walks or less than one flight of stairs are at increased risk for perioperative death and cardiopulmonary complications with standard lung resection. These patients should be counseled about nonstandard surgery and nonoperative treatment options for their lung cancer. Grade of recommendation, 1C

12. In patients with lung cancer being considered for surgery, a PaCO<sub>2</sub> > 45 mm Hg is not an independent risk factor for increased perioperative complications. However, it is recommended that these patients undergo further physiologic testing. Grade of recommendation, 1C

13. In patients with lung cancer being considered for surgery, an arterial oxygen saturation < 90% indicates an increased risk for perioperative complications with standard lung resection. It is recommended that these patients undergo further physiologic testing. Grade of recommendation, 1C

14. In patients with very poor lung function and lung cancer in an area of upper-lobe emphysema, it is recommended that combined lung volume reduction surgery and lung cancer resection be considered if both the FEV<sub>1</sub> and DLCO are > 20% of predicted. Grade of recommendation, 1C

15. It is recommended that all patients with lung cancer be counseled regarding smoking cessation. Grade of recommendation, 1C

#### *Noninvasive Staging of NSCLC*

1. For patients with either a known or suspected lung cancer who are eligible for treatment, a CT scan of the chest with contrast including the upper abdomen (liver and adrenal glands) should be performed. Grade of recommendation, 1B

2. In patients with enlarged discrete mediastinal lymph nodes on CT (> 1 cm in short axis) and no evidence of metastatic disease, further evaluation of the mediastinum should be made prior to definitive treatment of the primary tumor. Grade of recommendation, 1B



**3. PET to evaluate for mediastinal and extrathoracic staging should be considered in patients with clinical IA lung cancer being treated with curative intent.** Grade of recommendation, 2C

**4. Patients with clinical IB-IIIB lung cancer being treated with curative intent should undergo PET (where available) for mediastinal and extrathoracic staging.** Grade of recommendation, 1B

**5. In patients with an abnormal result on FDG-PET, further evaluation of the mediastinum with sampling of the abnormal lymph node should be performed prior to surgical resection of the primary tumor.** Grade of recommendation, 1B

**6. For patients with either known or suspected lung cancer who are eligible for treatment, MRI of the chest should not routinely be performed for staging the mediastinum. MRI may be useful in patients with NSCLC when there is concern for involvement of the superior sulcus or brachial plexus involvement.** Grade of recommendation, 1B

**7. For patients with either known or suspected lung cancer, a thorough clinical evaluation similar to that listed in Table 4 in this chapter should be performed.** Grade of recommendation, 1B

**8. Patients with abnormal clinical evaluations should undergo imaging for extrathoracic metastases. Site-specific symptoms warrant directed evaluation of that site with the most appropriate study (eg, head CT/MRI plus either whole-body PET or bone scan plus abdominal CT).** Grade of recommendation, 1B

**9. Routine imaging for extrathoracic metastases (eg, head CT/MRI plus either whole-body PET or bone scan plus abdominal CT) should be performed in patients with clinical stage IIIA and IIIB disease (even if they have a negative clinical evaluation).** Grade of recommendation, 2C

**10. Patients with imaging studies consistent with distant metastases should not be excluded from potentially curative treatment without tissue confirmation or overwhelming clinical and radiographic evidence of metastases.** Grade of recommendation, 1B

### *Invasive Mediastinal Staging of Lung Cancer*

**1. For patients with extensive mediastinal infiltration of tumor (and no distant metastases), radiographic (CT) assessment of the mediastinal stage is usually sufficient without invasive confirmation.** Grade of recommendation, 2C

**2. For patients with discrete mediastinal lymph node enlargement (and no distant metastases), invasive confirmation of the radiographic stage is recommended (regardless of whether a PET finding is positive or negative in the mediastinal nodes).** Grade of recommendation, 1B

**3. For patients with discrete mediastinal lymph node enlargement (and no distant metastases), many invasive techniques for confirmation of the N2,3 node status are suggested as reasonable approaches (mediastinoscopy, EUS-NA, TBNA, EBUS-NA, TTNA), given the appropriate experience and skill.** Grade of recommendation, 1B

**4. For patients with discrete mediastinal lymph node enlargement (and no distant metastases), a nonmalignant result from a needle technique (EUS-NA, TBNA, EBUS-NA, TTNA) should be further confirmed by mediastinoscopy (regardless of whether a PET finding is positive or negative in the mediastinal nodes).** Grade of recommendation, 1C

**5. For patients with a radiographically normal mediastinum (by CT) and a central tumor or N1 lymph node enlargement (and no distant metastases), invasive confirmation of the radiographic stage is recommended (regardless of whether a PET finding is positive or negative in the mediastinal nodes).** Grade of recommendation, 1C

**6. For patients with a central tumor or N1 lymph node enlargement (and no distant metastases), invasive staging is recommended. In general, mediastinoscopy is suggested, but EUS-NA or EBUS-NA may be a reasonable alternative if nondiagnostic results are followed by mediastinoscopy.** Grade of recommendation, 2C

**7. For patients with a peripheral clinical stage I tumor in whom a PET scan shows uptake in mediastinal nodes (and not distant metastases), invasive staging is recom-**

mended. In general, mediastinoscopy is suggested, but EUS-NA or EBUS-NA may be a reasonable alternative if nondiagnostic results are followed by mediastinoscopy. Grade of recommendation, 1C

8. For patients with a peripheral clinical stage I tumor, invasive confirmation of the mediastinal nodes is not needed if a PET scan result is negative in the mediastinum. Grade of recommendation, 1C

9. For the patients with a left upper lobe cancer in whom invasive mediastinal staging is indicated as defined by the previous recommendations, it is suggested that invasive mediastinal staging include assessment of the aortopulmonary window nodes (via Chamberlain, thoracoscopy, extended cervical mediastinoscopy, EUS-NA or EBUS-NA) if other mediastinal node stations are found to be uninvolved. Grade of recommendation, 2C

#### *Bronchial Intraepithelial Neoplasia/Early Central Airways Lung Cancer*

1. For patients with severe dysplasia, carcinoma *in situ* (CIS), or carcinoma in sputum cytology but with chest imaging studies showing no localizing abnormality, standard white light bronchoscopy is recommended. Autofluorescence bronchoscopy should be used when available. Grade of recommendation, 1B

2. For patients being considered for curative endobronchial therapy to treat CIS in centers where it is available, autofluorescent bronchoscopy may be considered to guide therapy. Grade of recommendation, 2C

3. For patients with known severe dysplasia or CIS in the central airways, standard white light bronchoscopy is recommended at periodic intervals (3 to 6 months) for follow-up. Autofluorescence bronchoscopy should be used when available. Grade of recommendation, 2C

4. For patients with superficial squamous cell carcinoma who are not surgical candidates, photodynamic therapy, electrocautery, cryotherapy, and brachytherapy are recommended as treatment options. Use of Nd:YAG laser therapy is not recommended because of the risk of perforation. Grade of recommendation, 1C

#### *Treatment of NSCLC Stage I and II*

1. For patients with clinical stage I and II NSCLC and no medical contraindication to operative intervention, surgical resection is recommended. Grade of recommendation, 1A

2. For patients with clinical stage I and II NSCLC, it is recommended that they be evaluated by a thoracic surgical oncologist with a prominent part of his/her practice focused on lung cancer, even if the patients are being considered for nonsurgical therapies such as percutaneous ablation or stereotactic body radiation therapy. Grade of recommendation, 1B

3. In patients with stage I and II NSCLC who are medically fit for conventional surgical resection, lobectomy or greater resection are recommended rather than sublobar resections (wedge or segmentectomy). Grade of recommendation, 1A

4. In patients with stage I NSCLC who may tolerate operative intervention but not a lobar or greater lung resection due to comorbid disease or decreased pulmonary function, sublobar resection is recommended over nonsurgical interventions. Grade of recommendation, 1B

5. In patients with stage I NSCLC who are considered appropriate candidates for thoracoscopic anatomic lung resection (lobectomy or segmentectomy), the use of video-assisted thoracic surgery by surgeons experienced in these techniques is an acceptable alternative to open thoracotomy. Grade of recommendation, 1B

6. In patients undergoing resection for stage I and II NSCLC, it is recommended that intraoperative systematic mediastinal lymph node sampling or dissection be performed for accurate pathologic staging. Grade of recommendation, 1B

7. For patients with centrally or locally advanced NSCLC in whom a complete resection can be achieved with either technique, sleeve lobectomy is recommended over pneumonectomy. Grade of recommendation, 1B

8. For patients with N1 lymph node metastases (stage II NSCLC) in whom a complete resection can be achieved with either technique, sleeve lobectomy is recommended over pneumonectomy. Grade of recommendation, 1B

9. For patients with completely resected stage IA NSCLC, the use of adjuvant chemotherapy is not recommended for routine use outside the setting of a clinical trial. Grade of recommendation, 1A

10. For patients with completely resected stage IB NSCLC, the use of adjuvant chemotherapy is not recommended for routine use. Grade of recommendation, 1B

11. For patients with completely resected stage II NSCLC and good performance status (PS), the use of platinum-based adjuvant chemotherapy is recommended. Grade of recommendation, 1A

12. For patients with stage I or II NSCLC who are not candidates for surgery (“medically inoperable”) or who refuse surgery, curative intent fractionated radiotherapy is recommended. Grade of recommendation, 1B

13. For patients with completely resected stage IA or IB NSCLC, postoperative radiotherapy is associated with a decreased survival and is not recommended. Grade of recommendation, 1B

14. For patients with completely resected stage II NSCLC, postoperative radiotherapy decreases local recurrence but a survival benefit has not been clearly shown, and therefore postoperative radiotherapy is not recommended. Grade of recommendation, 1B

#### *Treatment of NSCLC Stage IIIA: Incidental (Occult) N2 Disease Found at Thoracotomy (Stage IIIA1–2)*

##### *Surgical Considerations*

1. In patients with NSCLC who have incidental (occult) N2 disease (IIIA2) found at surgical resection and in whom complete resection of the lymph nodes and primary tumor is technically possible, completion of the planned lung resection and mediastinal lymphadenectomy is recommended. Grade of recommendation, 2C

2. In patients with NSCLC undergoing surgical resection, systematic mediastinal lymph node sampling or complete mediastinal lymph node dissection is recommended. Grade of recommendation, 1B

##### *Adjuvant Chemotherapy*

3. In patients with resected NSCLC who were found to have incidental (occult) N2

disease (IIIA1–2) and who have good PS, adjuvant platinum-based chemotherapy is recommended. Grade of recommendation, 1A

##### *Adjuvant Radiotherapy*

4. In patients with resected NSCLC who were found to have incidental (occult) N2 disease (IIIA1–2), adjuvant postoperative radiotherapy should be considered after adjuvant chemotherapy to reduce local recurrence. Grade of recommendation, 2C

##### *Adjuvant Chemoradiotherapy*

5. In patients with resected NSCLC who were found to have incidental (occult) N2 disease (IIIA1–2), combined postoperative concurrent chemotherapy and radiotherapy is not recommended except as part of a clinical trial. Grade of recommendation, 1B

#### *Treatment of NSCLC Stage IIIA: Potentially Resectable N2 Disease (Stage IIIA3)*

6. In NSCLC patients with N2 disease identified preoperatively (IIIA3), referral for multidisciplinary evaluation (which includes a thoracic surgeon) is recommended before embarking on definitive treatment. Grade of recommendation, 1C

7. In NSCLC patients with N2 disease identified preoperatively (IIIA3), induction therapy followed by surgery is not recommended except as part of a clinical trial. Grade of recommendation, 1C

8. In NSCLC patients with N2 disease identified preoperatively (IIIA3) who do receive induction chemoradiotherapy as part of a clinical trial, pneumonectomy is not recommended. The subsequent surgical resection in this setting should be limited to a lobectomy. If after induction chemoradiotherapy it appears that a pneumonectomy will be needed, it is recommended that pneumonectomy not be performed and treatment should be continued with full-dose radiotherapy. Grade of recommendation, 1B

9. In NSCLC patients with N2 disease identified preoperatively (IIIA3), primary surgical resection followed by adjuvant therapy is not recommended except as part of a clinical trial. Grade of recommendation, 1C



**10. In NSCLC patients with N2 disease identified preoperatively (IIIA3), surgery alone is not recommended.** Grade of recommendation, 1A

**11. In NSCLC patients with N2 disease identified preoperatively (IIIA3), platinum-based combination chemoradiotherapy is recommended as primary treatment.** Grade of recommendation, 1B

#### *Surgical Considerations*

**12. In NSCLC patients with N2 disease identified preoperatively (IIIA3), surgical debulking procedures are not recommended.** Grade of recommendation, 1A

**13. In NSCLC patients with N2 disease identified preoperatively (IIIA3) who have incomplete resections, postoperative platinum-based chemoradiotherapy is recommended.** Grade of recommendation, 1C

#### *Treatment of NSCLC Stage IIIA: Unresectable, Bulky N2 Disease (Stage IIIA4)*

**14. In patients with NSCLC who have bulky N2 disease (IIIA4) and good PS, radiotherapy alone is not recommended.** Grade of recommendation, 1A

**15. In patients with NSCLC who have bulky N2 disease (IIIA4) and good PS, combination platinum-based chemotherapy and radiotherapy are recommended.** Grade of recommendation, 1A

**16. In patients with NSCLC who have bulky N2 disease (IIIA4), good PS, and minimal weight loss, concurrent chemoradiotherapy is recommended over sequential chemoradiotherapy.** Grade of recommendation, 1A

#### *Treatment of NSCLC Stage IIIB*

**1. In selected patients with clinical T4N0-1 NSCLC due to satellite tumor nodule(s) in the same lobe, carinal involvement, or superior vena cava (SVC) invasion, it is recommended that evaluation be performed by a multidisciplinary team that includes a thoracic surgeon with lung cancer expertise to determine if the patient is operable. Surgery is not recommended if there is N2 involvement.** Grade of Recommendation, 1C

**2. For patients with stage IIIB NSCLC due to N3 disease, treatment with neoadju-**

**vant (induction) chemotherapy or chemoradiotherapy followed by surgery is not recommended.** Grade of recommendation, 1C

**3. For patients with stage IIIB disease without malignant pleural effusions, PS of 0 or 1, and minimal weight loss ( $\leq 5\%$ ), platinum-based combination chemotherapy is recommended.** Grade of recommendation, 1A

**4. In patients with stage IIIB NSCLC and PS of 2 or those with substantial weight loss ( $> 10\%$ ), chemoradiotherapy is recommended only after careful consideration.** Grade of recommendation, 1C

**5. For stage IIIB NSCLC patients with PS of 0 or 1 and minimal weight loss ( $\leq 5\%$ ), concurrent chemoradiotherapy is recommended.** Grade of recommendation, 1A

**6. The most efficacious chemotherapy drugs to be combined with thoracic radiotherapy and the number of cycles of chemotherapy needed to yield the best results is currently uncertain. No one combination chemotherapy regimen can be recommended.** Grade of recommendation, 2C

**7. For patients with stage IIIB NSCLC, once-daily thoracic radiotherapy plus chemotherapy is recommended.** Grade of recommendation, 1B

**8. For stage IIIB patients and either poor PS or disease too extensive to treat with curative intent and symptoms due to chest disease, palliative radiotherapy is recommended. The fractionation pattern should be chosen based on the physician's judgment and patient's needs.** Grade of recommendation, 1A

#### *Treatment of NSCLC Stage IV*

**1. In patients with stage IV NSCLC and a good PS, two-drug combination chemotherapy is recommended. The addition of a third cytotoxic chemotherapeutic agent is not recommended because it provides no survival benefit and may be harmful.** Grade of recommendation, 1A

**2. Bevacizumab improves survival combined with carboplatin and paclitaxel in a clinically selected subset of the good PS, stage IV NSCLC (nonsquamous histology, lack of brain metastases, and no hemoptysis). In these patients, bevacizumab added to carboplatin and paclitaxel should be considered a therapeutic option.** Grade of recommendation, 1A



**3. In patients with stage IV NSCLC who are elderly ( $\geq 70$  to 79 years) single-agent chemotherapy is recommended for most patients. Grade of recommendation, 1A**

**4. However, in patients with stage IV NSCLC who are elderly ( $\geq 70$  to 79 years) and have a good PS and lack significant comorbidities, two-drug combination chemotherapy is recommended as an option. Grade of recommendation, 1B**

**5. In patients with stage IV NSCLC who are  $\geq 80$  years old, the benefit of chemotherapy is unclear and should be decided on based on individual circumstances. Grade of recommendation, 2C**

**6. In patients with stage IV NSCLC and a PS of 2, chemotherapy is recommended based on defined response rates and symptom palliation. Grade of recommendation, 1B**

**7. In patients with stage IV NSCLC and a PS of 2, no specific recommendation can be given with regard to the optimal chemotherapeutic strategy. A single phase III trial showed a survival benefit to a carboplatin-based doublet compared to a single agent in a prospectively planned subset analysis. Grade of recommendation, 2C**

**8. It is recommended that patient-reported health-related quality of life be measured using the FACT-L or European Organization for Research and Treatment of Cancer QLQ-C30 questionnaire because it is a significant prognostic factor for survival. Grade of recommendation, 1A**

**9. It is recommended that patients with stage IV NSCLC receive adequate education about the risks and benefits of chemotherapy to enable active participation in the decision-making process regarding treatment selection. Grade of recommendation, 1C**

#### *Special Treatment Issues in Lung Cancer*

**1. In patients with a Pancoast tumor, it is recommended that a tissue diagnosis be obtained prior to the initiation of therapy. Grade of recommendation, 1C**

**2. In patients with a Pancoast tumor being considered for curative intent surgical resection, an MRI of the thoracic inlet and brachial plexus to rule out tumor invasion of unresectable vascular structures or the extradural space is recommended. Grade of recommendation, 1C**

**3. In patients with a Pancoast tumor involving the subclavian vessels or vertebral column, it is suggested that resection be undertaken only at a specialized center. Grade of recommendation, 2C**

**4. In patients with a Pancoast tumor being considered for curative resection, invasive mediastinal staging and extrathoracic imaging (head CT/MRI plus either whole-body PET or abdominal CT plus bone scan) is recommended. Involvement of mediastinal nodes and/or metastatic disease represent a contraindication to resection. Grade of recommendation, 1C**

**5. In patients with a potentially resectable, nonmetastatic Pancoast tumor (and good PS), it is recommended that preoperative concurrent chemoradiotherapy be administered prior to resection. Grade of recommendation, 1B**

**6. In patients undergoing resection of a Pancoast tumor, it is recommended that every effort be made to achieve a complete resection. Grade of recommendation, 1A**

**7. It is recommended that resection of a Pancoast tumor consist of lobectomy (instead of a nonanatomic wedge resection) as well as the involved chest wall structures. Grade of recommendation, 1C**

**8. In patients with either a completely or incompletely resected Pancoast tumor, postoperative radiotherapy is not recommended because of lack of demonstrated survival benefit. Grade of recommendation, 2C**

**9. In patients with an unresectable, but nonmetastatic Pancoast tumor who have good PS, definitive concurrent chemotherapy and radiotherapy is recommended. Grade of recommendation, 1C**

**10. In patients with Pancoast tumors who are not candidates for curative intent treatment, palliative radiotherapy is recommended. Grade of recommendation, 1B**

**11. In patients with a clinical T4N0,1M0 NSCLC being considered for curative resection, it is recommended that invasive mediastinal staging, and extrathoracic imaging (head CT/MRI plus either whole-body PET or abdominal CT plus bone scan) be undertaken. Involvement of mediastinal nodes and/or metastatic disease represent a contraindication to resection. Grade of recommendation, 1C**

**12. In patients with a T4N0,1M0 NSCLC, it is recommended that resection be undertaken only at a specialized center. Grade of recommendation, 1C**

**13. In patients with suspected or proven lung cancer and a satellite nodule within the same lobe, it is recommended that no further diagnostic workup of a satellite nodule is undertaken. Grade of recommendation, 1B**

**14. In patients with a satellite lesion within the same lobe as a suspected or proven primary lung cancer, evaluation of extrathoracic metastases and confirmation of the mediastinal node status should be performed as dictated by the primary lung cancer alone, and not modified due to the presence of the satellite lesion. Grade of recommendation, 1C**

**15. In patients with NSCLC and a satellite focus of cancer within the same lobe (and no mediastinal or distant metastases), resection via a lobectomy is the recommended treatment. Grade of recommendation, 1B**

**16. In patients with two synchronous primary NSCLCs being considered for curative surgical resection, invasive mediastinal staging and extrathoracic imaging (head CT/MRI plus either whole-body PET or abdominal CT plus bone scan) are recommended. Involvement of mediastinal nodes and/or metastatic disease represent a contraindication to resection. Grade of recommendation, 1C**

**17. In patients suspected of having two synchronous primary NSCLCs, a thorough search for an extrathoracic primary cancer to rule out the possibility that both of the lung lesions represent metastases is recommended. Grade of recommendation, 1C**

**18. In patients not suspected of having a second focus of cancer who are found intraoperatively to have a second cancer in a different lobe, resection of each lesion is recommended, provided the patient has adequate pulmonary reserve and there is no N2 nodal involvement. Grade of recommendation, 1C**

**19. In patients with a metachronous NSCLC being considered for curative surgical resection, invasive mediastinal staging and extrathoracic imaging (head CT/MRI plus either whole-body PET or abdominal CT plus bone scan) are recommended. Involvement of**

**mediastinal nodes and/or metastatic disease represent a contraindication to resection. Grade of recommendation, 1C**

**20. In patients with an isolated brain metastasis from NSCLC being considered for curative resection of a stage I or II lung primary tumor, invasive mediastinal staging and extrathoracic imaging (head CT/MRI plus either whole-body PET or abdominal CT plus bone scan) are recommended. Involvement of mediastinal nodes and/or metastatic disease represent a contraindication to resection. Grade of recommendation, 1C**

**21. In patients with no other sites of metastases and a synchronous resectable N0,1 primary NSCLC, resection or radiosurgical ablation of an isolated brain metastasis are recommended (as well as resection of the primary tumor). Grade of recommendation, 1C**

**22. In patients with no other sites of metastases and a previously completely resected primary NSCLC (metachronous presentation), resection or radiosurgical ablation of an isolated brain metastasis is recommended. Grade of recommendation, 1B**

**23. In patients who have undergone a curative resection of an isolated brain metastasis, adjuvant whole-brain radiotherapy is suggested, although there is conflicting and insufficient data regarding a benefit with respect to survival or the rate of recurrent brain metastases. Grade of recommendation, 2B**

**24. In patients who have undergone curative resections of both the isolated brain metastasis and the primary tumor, adjuvant chemotherapy may be considered. Grade of recommendation, 2C**

**25. In patients with an isolated adrenal metastasis from NSCLC being considered for curative intent surgical resection, invasive mediastinal staging, and extrathoracic imaging (head CT/MRI plus either whole-body PET or abdominal CT plus bone scan) are recommended. Involvement of mediastinal nodes and/or metastatic disease represent a contraindication to resection. Grade of recommendation, 1C**

**26. In patients with a synchronous resectable N0,1 primary NSCLC, with no other sites of metastases, resection of the primary tumor and an isolated adrenal metastasis is recommended. Grade of recommendation, 1C**

27. In patients with no other sites of metastases and a previously completely resected primary NSCLC (metachronous presentation), resection of an isolated adrenal metastasis is the recommended treatment of choice if the disease-free interval is > 6 months and complete resection of the primary NSCLC has been achieved. Grade of recommendation, 1C

28. In patients with a NSCLC invading the chest wall who are being considered for curative intent surgical resection, invasive mediastinal staging and extrathoracic imaging (head CT/MRI plus either whole-body PET or abdominal CT plus bone scan) are recommended. Involvement of mediastinal nodes and/or metastatic disease represent a contraindication to resection, and definitive chemoradiotherapy is recommended for these patients. Grade of recommendation, 2C

29. At the time of resection of a tumor invading the chest wall, we recommend that every effort be made to achieve a complete resection. Grade of recommendation, 1B

#### *BAC*

1. We recommend the use of the term *BAC* be reserved for those lung cancers that meet the criteria established in the revised World Health Organization classification system for lung tumors. Grade of recommendation, 1B

2. For patients with suspected *BAC*, we recommend a surgical biopsy be used to establish a histopathologic diagnosis. Grade of recommendation, 1C

3. For patients unable to undergo surgical biopsy, the diagnosis of *BAC* should be made only with compatible histopathologic pattern on transbronchial or core needle biopsy, and a CT demonstrating a pure ground-glass or pneumonic appearance. Grade of recommendation, 1C

4. For patients whose CT scans show ground-glass attenuation or pneumonic consolidation (suggesting *BAC*), PET scan results are often false negative, and therefore we recommend that a negative PET scan result be followed by additional diagnostic testing to exclude the presence of cancer. Grade of recommendation, 1C

5. In patients with suspected *BAC* who are good surgical candidates, a sublobar resection may be appropriate, provided the

CT shows a pure ground-glass appearance, intraoperative pathologic consultation confirms pure *BAC* without evidence of invasion, and surgical margins are free of disease. Grade of recommendation, 1B

6. For patients with good PS and unresectable *BAC*, we recommend the use of standard chemotherapy. The use of first-line epidermal growth factor receptor-targeted agents should be reserved for patients with poor PS, or those enrolled in clinical trials. Grade of recommendation, 2C

#### *Management of SCLC*

1. Routine staging of SCLC includes the following: history and physical examination, CBC counts and comprehensive chemistry panel, CT scan of the chest and abdomen or CT of the chest with cuts going through the entire liver and adrenal glands, CT or MRI of the brain, and bone scan. Grade of recommendation, 1B

2. PET scanning is not recommended in the routine staging of SCLC. Grade of recommendation, 2B

3. Patients with extensive-stage disease should receive four to not more than six cycles of cisplatin- or carboplatin-based combination chemotherapy. Cisplatin could be combined with either etoposide or irinotecan. Grade of recommendation, 1B

4. After chemotherapy, patients achieving a complete response outside the chest and a complete or partial response in the chest could be offered consolidative thoracic radiation therapy in the chest. Grade of recommendation, 2C

5. Outside of a clinical trial, maintenance treatment for patients with extensive-stage or limited-stage disease achieving a partial or complete remission is not recommended. Grade of recommendation, 1B

6. Relapsed or refractory patients with SCLC should be offered further chemotherapy. Grade of recommendation, 1B

7. Elderly patients with good PS (Eastern Cooperative Oncology Group PS of 0 or 1) with intact organ function should be treated with platinum-based chemotherapy. Grade of recommendation, 1A

8. Elderly patients with poor prognostic factors such as poor PS or medically significant concomitant comorbid disease may

still be considered for chemotherapy. Grade of recommendation, 2C

**9. Outside of a clinical trial, there is no role for either dose dense/intense initial/induction or maintenance treatment for extensive-stage or limited-stage SCLC.** Grade of recommendation, 1A

**10. Patients with limited-stage SCLC should be treated with combined concurrent chemoradiotherapy. Patients require referral to a radiation oncologist and a medical oncologist for the consideration of combined modality treatment.** Grade of recommendation, 1A

**11. If the PS and comorbid illnesses allow, patients with limited-stage disease should be treated with chemotherapy and radiation therapy administered concurrently.** Grade of recommendation, 1C

**12. In patients eligible to receive early concurrent chemoradiotherapy, patients should be treated with accelerated hyperfractionated radiation therapy concurrently with platinum-based chemotherapy.** Grade of recommendation, 1B

**13. Patients with limited-stage SCLC achieving a complete remission or resected patients with stage I disease should be offered PCI.** Grade of recommendation, 1B

**14. Patients with extensive stage SCLC achieving a complete remission should be offered PCI.** Grade of recommendation, 1C

**15. In patients with SCLC and stage I disease who are being considered for curative intent surgical resection, invasive mediastinal staging and extrathoracic imaging (head CT/MRI, abdominal CT plus bone scan) followed by a platinum-based chemotherapy should be offered.** Grade of recommendation, 1A

**16. In patients with stage I SCLC who have undergone curative intent surgical resection, platinum-based adjuvant chemotherapy is recommended.** Grade of recommendation, 2C

**17. Patients with mixed SCLC/NSCLC histology should be treated the same as patients with SCLC. All treatment recommendations made for SCLC should apply to this category of patients.** Grade of recommendation, 2C

### *Complementary Therapies and Integrative Oncology in Lung Cancer*

**1. It is recommended that all patients with lung cancer be specifically asked about the use of complementary and alternative therapies.** Grade of recommendation, 1C

**2. It is recommended that all patients with lung cancer be given guidance about the advantages and disadvantages of complementary therapies in an open, evidence-based, and patient-centered manner by a qualified professional.** Grade of recommendation, 1C

**3. In lung cancer patients, mind-body modalities are recommended as part of a multimodality approach to reduce anxiety, mood disturbances, or chronic pain.** Grade of recommendation, 1B

**4. In lung cancer patients with anxiety or pain, massage therapy delivered by an oncology-trained massage therapist is recommended as part of a multimodality treatment approach.** Grade of recommendation, 1C

**5. The application of deep or intense pressure is not recommended near cancer lesions or anatomic distortions, such as postoperative changes, as well as in patients with a bleeding tendency.** Grade of recommendation, 2C

**6. For lung cancer patients, therapies based on putative manipulation of bioenergy fields are not recommended.** Grade of recommendation, 1C

**7. Acupuncture is recommended as a complementary therapy when pain is poorly controlled or when side effects, such as neuropathy or xerostomia from other modalities, are clinically significant.** Grade of recommendation, 1A

**8. Acupuncture is recommended as a complementary therapy when nausea and vomiting associated with chemotherapy are poorly controlled.** Grade of recommendation, 1B

**9. Electrostimulation wristbands are not recommended for managing chemotherapy-induced nausea and vomiting.** Grade of recommendation, 1B

**10. When the lung cancer patient does not stop smoking despite use of other options, a trial of acupuncture is recommended to assist in smoking cessation.** Grade of recommendation, 2C



11. In patients with lung cancer suffering from symptoms such as dyspnea, fatigue, chemotherapy-induced neuropathy, or postthoracotomy pain, a trial of acupuncture is recommended. Grade of recommendation, 2C

12. In patients with a bleeding tendency, it is recommended that acupuncture be performed by qualified practitioners and used cautiously. Grade of recommendation, 1C

13. It is recommended that dietary supplements, in particular herbal products, be evaluated for side effects and potential interaction with other drugs. Those that are likely to interact with other drugs, such as chemotherapeutic agents, should not be used concurrently during chemotherapy or radiation, or prior to surgery. Grade of recommendation, 1B

14. In lung cancer patients who either fail or decline antitumor therapies, it is recommended use of botanical agents occur only in the context of clinical trials. Grade of recommendation, 1C

15. It is recommended that patients be advised to avoid therapies promoted as “alternatives” to mainstream care. Grade of recommendation, 1A

#### *Follow-up and Surveillance of the Lung Cancer Patient Following Curative Intent Therapy*

1. In lung cancer patients treated with curative intent therapy, follow-up for complications related to the curative intent therapy should be managed by the appropriate specialist and should probably last at least 3 to 6 months. At that point, the patient should be reevaluated by the multidisciplinary tumor board for entry into an appropriate surveillance program for detecting recurrences and/or metachronous tumors. Grade of recommendation, 2C

2. In lung cancer patients treated with curative intent therapy, and those having adequate performance and pulmonary functions, surveillance with a history, physical examination, and imaging study (either chest radiography or CT) is recommended every 6 months for 2 years and then annually. All patients should be counseled on symptom recognition and be advised to contact their physician if worrisome symptoms were recognized. Grade of recommendation, 1C

3. Ideally, surveillance for recognition of a recurrence of the original lung cancer and/or development of a metachronous tumor should be coordinated through a multidisciplinary team approach. If possible, the physician who diagnosed the primary lung cancer and initiated the curative intent therapy should remain as the health-care provider overseeing the surveillance process. Grade of recommendation, 2C

4. In lung cancer patients following curative intent therapy, use of blood tests, PET scanning, sputum cytology, tumor markers, and fluorescence bronchoscopy is not currently recommended for surveillance. Grade of recommendation, 2C

5. Lung cancer patients who smoke should be strongly encouraged to stop smoking, and offered pharmacotherapeutic and behavioral therapy, including follow-up. Grade of recommendation, 1A

#### *Palliative Care in Lung Cancer*

1. All lung cancer patients and their families must be reassured that pain can be relieved safely and effectively. All patients should be questioned regularly about their pain, using the patient's self-report of pain and a simple rating scale as the primary source of assessment. Grade of recommendation, 1A

2. For all patients, individualize medications that are used to control pain. Administer medications regularly, and treat pain appropriately. Document the effectiveness of pain management at regular intervals during treatment. Grade of recommendation, 1A

3. For all patients with mild-to-moderate pain, manage the pain initially with acetaminophen or a nonsteroidal antiinflammatory drug, assuming there are no contraindications to their use. Use opioids when pain is more severe or when it increases. Grade of recommendation, 1B

4. For any patient, if it is anticipated that there will be a continuous need for opioid medication, meperidine is not recommended. It has a short duration of action, and its metabolite normeperidine is toxic and can cause CNS stimulation resulting in dysphoria, agitation, and seizures. Grade of recommendation, 1B

5. For patients whose pain is not controlled by pure analgesic medications, adjunctive medications such as tricyclic antidepressants, anticonvulsants, and neuroleptic agents will often augment the effects of pure analgesic medications. Grade of recommendation, 1C

6. For all patients, administer medications by mouth because of convenience and cost-effectiveness. In patients with lung cancer who cannot take pain medications by mouth, rectal and transdermal administration are recommended. Administration of analgesics by the IM route is not recommended because of pain, inconvenience, and unreliable absorption. Grade of recommendation, 1C

7. For all patients receiving opioids, because constipation is common anticipate it, treat it prophylactically, and constantly monitor it. Grade of recommendation, 1B

8. Encourage all patients to remain active and to care for themselves whenever possible. Avoid prolonged immobilization whenever possible. Grade of recommendation, 1B

9. In patients who have pain associated with muscle tension and spasm, it is recommended that complimentary methods for pain relief such as cutaneous stimulation techniques (heat and cold applications), acupuncture, psychosocial methods of care, and pastoral care be incorporated into the pain management plan, but not as a substitute for analgesics. Grade of recommendation, 1C

10. For patients with advanced lung cancer, provide palliative radiation therapy to control pain. Palliative chemotherapy to decrease pain and other symptoms is recommended, even though the increase in survival may be only modest. Grade of recommendation, 1B

11. In patients with lung cancer who have pain unresponsive to standard methods of pain control, referral to a specialized pain clinic or palliative care consultant is recommended. Grade of recommendation, 1C

12. For all lung cancer patients who complain of dyspnea, it is recommended that they be evaluated for potentially correctable causes, such as localized obstruction of a major airway, a large pleural effusion, pulmonary emboli, or an exacerbation of coexisting COPD or congestive heart failure. If one of these problems is identified, treat-

ment with appropriate methods is recommended. Grade of recommendation, 1C

13. For all lung cancer patients whose dyspnea does not have a treatable cause, opioids are recommended. Also recommended are other pharmacologic approaches such as oxygen, bronchodilators, and corticosteroids. Grade of recommendation, 1C

14. For all lung cancer patients with dyspnea, it is recommended that nonpharmacologic and noninterventional treatments be considered, such as patient and family education, breathing control, activity pacing, relaxation techniques, fans, and psychosocial support. Grade of recommendation, 2C

15. For all lung cancer patients who have troublesome cough, it is recommended that they be evaluated for treatable causes. Grade of recommendation, 1B

16. For all lung cancer patients who have troublesome cough without a treatable cause, it is recommended that opioids be used to suppress the cough. Grade of recommendation, 1B

17. For patients with lung cancer who have pain due to bone metastases, external radiation therapy is recommended for pain relief. A single fraction of 8 Gy is as effective as higher fractionated doses of external radiation therapy for immediate relief of pain. Grade of recommendation, 1A

18. For patients with lung cancer who have pain due to bone metastases, higher fractionated doses of radiation therapy provide a longer duration of pain relief, less frequent need for retreatment, and fewer skeletal-related events than does a single fraction. Grade of recommendation, 1A

19. For patients with lung cancer who have painful bone metastases, bisphosphonates are recommended together with external radiation therapy for pain relief. Grade of recommendation, 1A

20. For patients with lung cancer who have painful bone metastases refractory to analgesics, radiation, and bisphosphonates, radiopharmaceuticals are recommended for pain relief. Grade of recommendation, 1B

21. In patients with lung cancer who have painful bone metastases to long bones and/or weight-bearing bones and a solitary well-defined lytic lesion circumferentially involving > 50% of the cortex and an expected survival > 4 weeks with satisfactory health status,

surgical fixation is recommended to minimize the potential for a fracture. Intramedullary nailing is the preferred approach, especially for the femur or the humerus. Grade of recommendation, 1C

**22. In patients with lung cancer who have symptomatic brain metastases, dexamethasone at 16 mg/d is recommended during the course of definitive therapy with a rapid taper and discontinuation within 6 weeks of completion of definitive therapy (either surgery or radiation therapy).** Grade of recommendation, 1B

**23. Patients with NSCLC and an isolated solitary brain metastasis should be considered for a curative resection of the lung primary tumor, as long as a careful search for other distant metastases or mediastinal lymph nodes has been performed and results are negative.** Grade of recommendation, 1C

**24. In patients with no other sites of metastases and a synchronous resectable N0,1 primary NSCLC, resection or radiosurgical ablation of an isolated brain metastasis should be undertaken (as well as resection of the primary tumor). Resection of the isolated solitary brain metastases should be followed by whole-brain radiotherapy.** Grade of recommendation, 1B

**25. For cancer patients with lung cancer who have new onset of back pain, sagittal T1-weighted MRI of the entire spine is recommended for diagnostic purposes. Other diagnostic studies such as plain radiographs, bone scans, or CT myelograms are not recommended.** Grade of recommendation, 1C

**26. For patients with lung cancer and epidural spinal cord metastases who are not paraparetic and ambulatory, prompt treatment with high-dose dexamethasone and radiotherapy is recommended.** Grade of recommendation, 1B

**27. When there is symptomatic radiographically confirmed compression of the spinal cord, neurosurgical consultation must be sought and, if appropriate, surgery should be performed immediately and should then be followed by radiation for patients with metastatic epidural spinal cord compression and generally good PS.** Grade of recommendation, 1A

**28. For all lung cancer patients with large-volume hemoptysis, bronchoscopy is recommended to identify the source of bleeding,**

**followed by endobronchial management options such as argon plasma coagulators, Nd-YAG laser, and electrocautery.** Grade of recommendation, 1C

**29. In lung cancer patients with symptomatic malignant pleural effusions, thoracentesis is recommended as the first drainage procedure for symptom relief.** Grade of recommendation, 1C

**30. In lung cancer patients with symptomatic pleural effusions that recur after thoracentesis, chest tube drainage and pleurodesis are recommended.** Grade of recommendation, 1B

**31. In patients with SVC obstruction from suspected lung cancer, definitive diagnosis by histologic or cytologic methods is recommended before treatment is started.** Grade of recommendation, 1C

**32. In patients with symptomatic SVC obstruction due to SCLC, chemotherapy is recommended.** Grade of recommendation, 1C

**33. In patients with symptomatic SVC obstruction due to NSCLC, stent insertion and/or radiation therapy are recommended. Stents are also recommended for SCLC or NSCLC symptomatic patients with SVC obstruction who do not respond to chemotherapy or radiation therapy.** Grade of recommendation, 1C

**34. For patients with a malignant tracheoesophageal or bronchoesophageal fistula, stenting of esophagus, airway, or both should be considered for symptomatic relief. Attempts at curative resection or esophageal bypass of the involved airway and/or the esophagus are not recommended.** Grade of recommendation, 1C

**35. It is recommended that all patients with lung cancer be evaluated for the presence of depression and, if present, treated appropriately.** Grade of recommendation, 1C

*Palliative Care Consultation, Quality of Life Measurements, and Bereavement for End-of-Life Care in Patients With Lung Cancer*

**1. For all patients with advanced lung cancer (and their families), it is recommended that palliative care be integrated into their treatment, including those pursuing curative or life-prolonging therapies.** Grade of recommendation, 1C

**2. For patients with advanced lung cancer, it is recommended that palliative and end-of-life care include involvement of a palliative care consultation team, which should be made available.** Grade of recommendation, 1C

**3. For patients with advanced lung cancer, it is recommended that standardized evaluations with symptom assessment and abbreviated disease-specific health-related quality-of-life questionnaires should be administered by the responsible member of the health-care team at the appropriate frequency.** Grade of recommendation, 1B

**4. It is recommended that clinicians of patients who die from lung cancer extend communication with the bereaved family and friends after death.** Grade of recommendation, 1C

**5. For patients with lung cancer, proactive interventions, such as those listed below, are recommended to improve grief outcomes:**

- a. Informing the patient and family of foreseeable death within weeks
- b. Forewarning family of impending death
- c. Enabling effective palliative care, focused on spiritual, existential, physical, and practical concerns.

Grade of recommendation, 1C

**6. It is recommended that clinicians of dying patients with lung cancer encourage caregivers to maintain a healthy lifestyle during the period of caregiver burden, as well as during bereavement.** Grade of recommendation, 1C

**7. It is recommended that clinicians of patients dying from lung cancer honor rituals of death and mourning in a culturally sensitive manner.** Grade of recommendation, 1C



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