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

Gene L. Colice, MD, FCCP; Jeffrey Rubins, MD, FCCP; and Michael Unger, MD, FCCP

The following two distinctly different issues should be taken into account when planning patient care following curative-intent therapy for lung cancer: adequate follow-up to manage complications related to the curative-intent therapy; and surveillance to detect recurrences of the primary lung cancer and/or development of a new primary lung cancer early enough to allow potentially curative retreatment. Follow-up for complications should be performed by the specialist responsible for the curative-intent therapy and should last 3 to 6 months. Recurrences of the original lung cancer will be more likely during the first 2 years after curative-intent therapy, but there will be an increased lifelong risk of approximately 1 to 2% per year of developing a metachronous, or new primary, lung cancer. A standard surveillance program for these patients is recommended based on periodic visits, with chest-imaging studies and counseling patients on symptom recognition. Whether subgroups of patients with a higher risk of developing a metachronous lung cancer (e.g., those patients whose primary lung cancer was radiographically occult or central and those patients surviving for >2 years after treatment for small cell lung cancer) should have a more intensive surveillance program is presently unclear. The surveillance program should be coordinated by a multidisciplinary tumor board and overseen by the physician who diagnosed and initiated therapy for the original lung cancer. Smoking cessation is recommended for all patients following curative-intent therapy for lung cancer.

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Key words: lung cancer; metachronous tumors; recurrence; surveillance

Abbreviations: NSCLC = non-small cell lung cancer; PET = positron emission tomography

Approximately 170,000 new cases of lung cancer are diagnosed annually in the United States.1 Unfortunately, only about 50 to 55% of patients with newly diagnosed lung cancer will have localized disease and will be candidates for potentially curative treatment.2 Furthermore, some patients with localized non-small cell lung cancer (NSCLC) either may refuse potentially curative surgical therapy or may be unable to tolerate surgery because of limiting comorbid cardiopulmonary disease or other diseases. Consequently, it has been estimated that only 35,000 patients underwent curative-intent surgical resection for NSCLC in 1998.3 Smaller numbers of patients will receive curative-intent radiation therapy for localized NSCLC and some combination of curative-intent chemotherapy and radiation therapy for the treatment of localized small cell carcinoma.

Two distinctly different issues should be taken into account when planning patient care following curative-intent therapy for lung cancer. First, adequate follow-up should be ensured to manage complications related to the curative-intent therapy itself. This should be a specialist-directed process. The thoracic surgeon should be responsible for managing complications related to any surgical procedures that have been performed, as should the radiation oncologist and the oncologist be responsible for managing complications related to radiation therapy and chemotherapy, respectively. In most cases, this specialist-directed follow-up should be transient.

Second, a surveillance program should be considered to detect recurrences of the primary lung cancer and/or the development of a new primary lung cancer early enough to allow potentially curative retreatment. Numerous guidelines have been published regarding the management of lung cancer.

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Several of these guidelines include recommendations for a posttreatment surveillance program. These recommendations will be summarized and compared. Available data on rates, patterns, and diagnostic tools for identifying a recurrence of the primary lung cancer and/or the development of a second primary lung cancer will be reviewed as the basis for recommendations on an ongoing surveillance program following curative-intent therapy for lung cancer. Issues related to follow-up for palliative therapy of lung cancer will not be discussed (see article on palliative treatment in this supplement).

### Methods and Definitions

**Methods**

Published guidelines on lung cancer diagnosis and management were identified by a systematic review of the literature and were evaluated (see article on methods and grading in this supplement). Those guidelines, including recommendations that are specific to the follow-up and surveillance of patients with lung cancer after receiving curative-intent therapy, were identified for inclusion in this section. Supplemental material appropriate to this topic was obtained by a literature search of computerized database (MEDLINE) and a review of the reference lists of relevant articles. Recommendations were developed by the section editor and writing committee, were graded by a standardized method (see article on methods and grading in this supplement) and then reviewed by all section editors, the Chair of the lung cancer panel, and the Co-Chair of the lung cancer panel.

**Definitions**

A difficult issue in the surveillance of the lung cancer patient following curative-intent therapy is distinguishing between a recurrence of the original lung cancer and the identification of a new primary, or metachronous, lung cancer. Martini and Melamed proposed criteria for making this distinction in 1975. One confusing aspect of these criteria was the inclusion of synchronous lung cancers, which were described as physically distinct and separate from the primary tumor. In the original series by Martini and Melamed, 15 of the 18 patients with synchronous lung cancers were identified at the time of the initial treatment. In current lung cancer staging terminology, these cancers would have been described either as satellite tumor nodules, if they were within the same lobe as the primary tumor, or as intrapulmonary metastases, if they were not within the same lobe. With current imaging capability, synchronous lung cancer usually would be discovered prior to the performance of curative-intent surgical resection of the primary lung cancer. Hence, synchronous lung cancers should not be considered an issue in the surveillance of the lung cancer patient following curative-intent therapy.

There are also difficulties with the criteria that Martini and Melamed used for diagnosing metachronous tumors (Table 1). If the primary lung cancer had a mixed histology, the histologic pattern of a second cancer might not adequately distinguish a recurrence from a metachronous tumor. After curative-intent surgical resection, it would not be possible for a newly recognized cancer to have intrapulmonary lymphatics in common with the original lung cancer. Because systematic mediastinal lymph node sampling is included in the procedure for curative-intent lung cancer surgery, identifying mediastinal nodes in common between the new and old lung cancer also would be problematic. The choice of a tumor-free interval of 2 years for distinguishing a metachronous lung cancer from a recurrence of lung cancer with similar histology was arbitrary. Although the most appropriate tumor-free interval for making this distinction has not been defined (nor has it even been determined whether such an interval is possible to define), Detterbeck and colleagues have suggested (see article on special treatment issues in this supplement) that a 4-year interval might be more appropriate. Based on these considerations, it might be appropriate to revise the criteria of Martini and Melamed for identifying metachronous tumors (Table 1). Whichever criteria are used, Martini and Melamed remind us that the distinction between a new primary lung cancer and a recurrence of the original lung cancer is not as important as determining whether the tumor can be treated with curative intent.

### Current Guidelines

Four guidelines were identified that included specific recommendations for surveillance methods in patients with NSCLC following curative-intent therapy. Two guidelines provided specific recommendations for patients with small cell lung cancer. These guidelines were developed by a consensus of expert panels. In addition, published information is available on surveillance methods for patients following curative-intent therapy for NSCLC that have been used by two leading cancer institutes in the United States and one in Japan. The specific recommendations from the guidelines and institutional practices are summarized in Tables 2 and 3. One other guideline provided only the general recommendation that respiratory physicians should follow-up with their colleagues an explicit follow-up
policy that would be appropriate to the needs and resources of the patient and health-care providers.

The guidelines and institutional practices have remarkable similarities. Each recommends more frequent visits during the first 2 years following curative-intent therapy. Visits are less frequent for years 3 through 5 and decrease to a minimal level of annual visits after year 5. This pattern of visits is based on the expectation that recurrences of the original lung cancer will be more likely during the first 2 years after curative-intent therapy but that there will be an increased lifelong risk of developing a new primary lung cancer. Each of the guidelines and the institutional practices emphasizes symptoms that are elicited in the patient’s medical history as an extremely important indication of recurrence. The physical examination is included as an adjunctive, but less valuable, tool for identifying recurrences or new primaries. All the guidelines and institutional practices include the chest radiograph as a surveillance technique with slight variations as to how often the chest radiograph should be performed.

Most guidelines and institutional practices agree that chest CT scans should not be routinely performed during these surveillance visits. One guideline suggested that a chest CT scan should be performed at baseline, soon after curative-intent therapy, for comparison purposes if suspicion should arise either of a recurrence or a new primary tumor. Another guideline recommended an annual spiral chest CT scan as a surveillance method, although disagreement was noted within the panel about the added value of this approach. One guideline and one institutional practice incorporated regular complete blood counts and serum chemistry measurements into surveillance monitoring, but other groups found little value in performing these tests routinely. The National Kyushu Cancer Center incorporated regular complete blood counts and serum chemistry measurements into surveillance monitoring, but other groups found little value in performing these tests routinely.

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<th>Table 2—Specific Recommendations for Surveillance Methods in Patients with NSCLC Following Curative-Intent Therapy</th>
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| | *See Table 2 for abbreviations not used in the text.*

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<th>Table 3—Specific Recommendations for Surveillance Methods in Patients with Small Cell Lung Cancer Following Curative-Intent Therapy</th>
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also recommended following serial levels of tumor markers (e.g., carcinoembryonic antigen, Stialy Lewis X, and squamous cell carcinoma antigen) as an indicator of cancer recurrence, but other investigators did not find this practice helpful.12 Sputum cytology and bronchoscopy were specifically not incorporated into either guidelines or institutional surveillance practices.

**Follow-up of Complications Related to the Original Mode of Curative-Intent Therapy**

Hospital admissions following pulmonary resection are common. A recent study14 found that 19% of patients discharged from the hospital after undergoing pulmonary resection, most often for lung cancer, were readmitted within 90 days. The reasons for hospital readmission were not specifically described but were most often related to pulmonary problems, postsurgical infections, and cardiac issues.14 This high hospital readmission rate may reflect the numerous comorbid conditions that are often found in patients with lung cancer.

The most common long-term morbidities from pulmonary resection result from the loss of lung function and from chronic pain. The degree of reduction in pulmonary function after surgery is directly related to the extent of the resection performed. Six months after a patient undergoes lobectomy, FEV1 is approximately 10 to 15% lower than preoperative values, and after pneumonectomy, approximately 25 to 35% lower than preoperative values.15 Similarly, maximal exercise capacity stabilizes at 6 months after lobectomy at a 10% reduction, and after pneumonectomy at a 20% reduction, compared with preoperative values.15 Estimates of the frequency of chronic postthoracotomy pain vary widely, but pain may persist in up to 50% of patients at 18 to 24 months after resection.16 Landreneau et al17 reported that 16% of their patients required narcotic analgesia to control pain > 1 year after they underwent thoracotomy. Small numbers of patients will require more aggressive therapy, such as intercostal nerve blocks, for pain control.18 The degree of early postoperative pain may predict the occurrence of chronic pain.19 Of note, measures of quality of life return to preoperative values by 6 months after surgery.19

Unusual complications related to pulmonary resection may occur after hospital discharge. Case series from the 1960s20,21 reported that persistent air in the pleural space was noted for weeks to months following lobectomy and pneumonectomy but usually resolved without complications. An autopsy series from the same time period confirmed residual air in the pleural space after pneumonectomy in 27 of 37 cases, even though surgery had been performed years before.22 In very rare situations, empyema may develop in these spaces.20 Torsion of the mediastinum developing after pneumonectomy may lead to mainstem bronchus obstruction.23

Complications of radiation therapy with curative intent for lung cancer include early and late injury predominantly to the lungs and skin, and, much less commonly, injury to the heart, pericardium, and esophagus. Pulmonary radiation toxicity is related to the volume of the lung that was irradiated, the cumulative dose, and undefined factors determining the biological predisposition of the patient. In a large study24 using high-dose radiation therapy, acute toxicity was seen in 11% of the patients, with most injuries relating to esophageal problems and only a third to lung toxicity. Acute radiation pneumonitis may be responsive to corticosteroid therapy. In contrast, late radiation pneumonitis represents irreversible tissue damage, occurs in approximately 8% of patients treated with curative intent, and may present as early as 3 months after treatment and as late as 24 months.24 Even without producing overt pneumonitis, effective radiation therapy may result in a loss of pulmonary function. Curran et al25 described an average decrease in FEV1 of 10% after irradiation therapy, which is similar to that reported after lobectomy. However, Choi and Kanarek26 found that patients with poor lung function before treatment had little decrease in FEV1 after undergoing irradiation therapy.

Most of the complications related to the chemotherapeutic agents used for the treatment of NSCLC and small cell lung cancer are detected during the course of therapy. A long-term morbidity that is of concern in patients who have completed chemotherapy is a mild-to-moderate peripheral neuropathy, which results from multiple treatments with the commonly used platin vinca alkaloid and taxane compounds.

**Recommendation 1**

In lung cancer patients who have been treated with curative-intent therapy, the follow-up for complications related to the curative-intent therapy should be managed by the appropriate specialist and should probably last 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. Level of evidence, poor; benefit, moderate; grade of recommendation, C.
Recurrence of the Original Lung Cancer and Development of New Primary Lung Cancers

In 1973, Matthews et al.27 reported the results of autopsies performed on patients who had died within 1 month of undergoing curative-intent surgical therapy for lung cancer. Of the 202 patients autopsied, 73 (35%) had either residual local disease or systemic metastases. Certainly, our ability to image extrapulmonary metastases is much improved since the early 1970s. However, within the last decade, occult micrometastases have been found in histologically negative bone marrow and thoracic lymph nodes using immunohistochemical staining and reverse transcriptase-polymerase chain reaction techniques in lung cancer patients who were presumed to be eligible for curative-intent surgical resection.28–31 Given this information, it should not be surprising that lung cancer recurs distressingly far too often following curative-intent therapy.

Numerous studies11,32–40 have reported on recurrence rates and patterns in patients with NSCLC who have been treated with curative-intent surgical resection. In patients with stage I disease that was confirmed at surgery, 5-year recurrence rates of up to 39% have been reported.33,36,37 Most of these recurrences were distant metastases.33,36,38 Although most recurrences were detected within the first 4 years following curative-intent surgery,36,37 up to 10% of recurrences may be discovered ≥5 years following curative-intent therapy.33,36,38,39 In patients with nodal involvement, recurrence rates increase34,35,40 and recurrences probably occur earlier.32,34,40

It has been estimated from published studies on treatment outcomes that the approximate rate of developing a new primary lung cancer after undergoing curative-intent therapy for a NSCLC is 1 to 2% per patient per year.41,42 Metachronous tumors are usually of the same histology as the original lung cancer.42 A review of a regional cancer registry in Switzerland suggests that the rate may actually be slightly less than this estimate (about 0.5% per patient per year).43 Experience with long-term survivors of lung cancer has indicated that new primary lung cancers may develop up to 20 years after the original cancer had been treated.44 Although Johnson42 has suggested that the risk of developing a new lung cancer following curative-intent therapy increases with time, the available data are unclear on whether the rate of development of metachronous tumors increases or decreases over time. Pairolero et al.33 noted a lower rate of development of metachronous tumors >5 years after curative-intent therapy for the original lung cancer, but the Lung Cancer Study Group38 found an increased rate after 5 years. An important point is that following curative-intent therapy for NSCLC, patients are also at increased risk for developing other aerodigestive cancers (eg, carcinoma of the oropharynx and esophagus).43 Roentgenographically occult lung cancers detected by sputum cytology have been reported to have an especially high rate of metachronous tumors. Saito et al.45 described 13 metachronous tumors occurring in a group of 127 patients who underwent surgical resection for roentgenographically occult NSCLC. The cumulative rate at 5 years for metachronous tumors was 11%, and the incidence per patient-year of surveillance was 2.2%. Bechtel and colleagues46 reported that seven metachronous tumors were identified in a group of 27 patients following surgical resection of roentgenographically occult NSCLC. Consistent with these findings has been the observation that central lung cancers that have been treated with sleeve resection also may have a high rate of metachronous tumors. Van Schil et al.47 found that metachronous tumors developed in 11 of 145 patients undergoing sleeve resection.

Patients who have been treated for small cell lung cancer and have survived for 2 years also have been reported to have an especially high rate of developing metachronous NSCLCs. In two separate observational studies,48,49 NSCLC was diagnosed in 12 to 15% of patients who had survived for at least 2 years after undergoing therapy for small cell lung cancer (six cases in one group of 40 patients and six cases in another group of 47 patients). It has been estimated that the rate of developing NSCLC 2 years after undergoing effective therapy for small lung cancer is 2 to 13% per patient per year.50 Another study confirmed that the rate of developing NSCLC following therapy for small cell lung cancer was significantly greater than that expected from the population data.50 A more recent study51 estimated that 10% of 2-year survivors of small cell lung cancer will eventually develop NSCLC.

Curative-Intent Therapy for a Recurrence and/or for a New Primary Tumor

Most recurrences of lung cancer are found outside the thorax.11,32–36,48,50 Effective treatment of isolated metastases may be possible (see article on special treatment issues in this supplement). Locoregional intrathoracic recurrences are treated only infrequently with curative-intent surgical therapy,36,39,52 and more often are treated with radiation therapy.53,54 Regardless of the therapy, survival with locoregional recurrence of lung cancer appears to be poor. Accumulating data suggest that curative-intent surgical therapy is more likely to be possible with
metachronous tumors than with locoregional recurrences of the primary lung cancer.\textsuperscript{44,52,55–61} However, survival rates for patients with metachronous lung cancers following curative-intent surgical resection are generally not as good as for primary lung cancer (Table 4). Curative-intent surgical therapy may not be possible because patients with metachronous tumors may present with advanced-stage disease or may be unable to tolerate surgical resection due to pulmonary insufficiency.\textsuperscript{42} The limited data suggest that, even controlling for stage of disease, survival following curative-intent surgical resection of metachronous tumors may not be as favorable as that for the original lung cancer. Despite limitations in the approach to curative-intent therapy of metachronous lung cancers, 5-year survival rates of 25 to 53\% (Table 4) have been reported when surgical resection is possible.

**ISSUES IN SURVEILLANCE FOR RECURRENCE AND NEW PRIMARY TUMORS**

**Intensity of the Surveillance Program**

There may be differences in how recurrences and metachronous tumors are identified. Pairolero et al\textsuperscript{33} scheduled visits for their stage I NSCLC patients every 4 months for the first 2 years and then every 4 to 6 months thereafter following curative-intent surgery. A medical history, physical examination, chest radiograph, blood tests, urine analysis, and pooled sputum cytology were performed at each visit. Most recurrences were detected at scheduled visits (59\%), but a substantial number of recurrences were detected at unscheduled visits. Most patients with recurrences were symptomatic (53\%), and symptom assessment was the most sensitive method for detecting recurrences. The blood tests, urine analysis, physical examination, and sputum cytology added little to detecting recurrences. Ichinose\textsuperscript{11} described a similarly intensive surveillance program and also reported that most recurrences were recognized by symptoms. Neither CT scans nor standard blood tests provided appreciable additional benefit in identifying recurrences.\textsuperscript{11} In contrast, some case series\textsuperscript{60,60,61} have reported that 68 to 100\% of patients with metachronous lung cancers were asymptomatic and had the new primary lung cancer detected by radiographic methods.

More recent studies have provided an expanded view of the methods used for detecting recurrences and/or metachronous tumors by considering the costs involved in a surveillance program. Walsh et al\textsuperscript{62} retrospectively evaluated the courses of 358 patients following curative-intent surgical resection for NSCLC. There were 135 recurrences, and most (76\%) were recognized through symptoms. Although the asymptomatic patients had a longer survival time following detection of the recurrence, the authors thought that this reflected lead-time bias and was not a true survival benefit. Similar percentages of symptomatic patients (29\%) and asymptomatic patients (30\%) could be treated with curative intent. Seven metachronous lung cancers were recognized in this study, but information on therapy and survival for these patients was not provided. The authors concluded that intensive surveillance was not cost-effective and suggested a reduced surveillance approach consisting of a medical history, physical examination, and chest radiograph every 6 months for the first year following curative-intent surgery, and annually thereafter.

Virgo and colleagues\textsuperscript{63} compared two groups ret-

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*Values given as No. (%), unless otherwise indicated.
†Values in parentheses indicate 5-year survival rate after surgical resection of primary lung cancer.
‡Five-year survival comparative data following surgical resection of primary lung cancer not provided.
respective following surgery for NSCLC. One group of 120 patients had intensive surveillance, consisting of at least four visits per year, with testing of serum chemistry and a chest radiograph, and annual bronchoscopy and/or sputum cytology with CT scan.\(^6\) The other group of 62 patients underwent nonintensive surveillance with, on average, only two visits per year, with testing of serum chemistry and a chest radiograph. No differences were found between the groups in either the time to detection of recurrences or metachronous tumors or in survival time. Virgo et al\(^6\) agreed that intensive surveillance was not cost-effective and supported the surveillance schedule suggested by Walsh et al.\(^6\) Two other retrospective analyses of intensive surveillance methods provided similar results. Younes and colleagues\(^6\) found that intensive surveillance yielded no survival advantage and was more expensive than a symptom-based approach, although more patients in the symptom-based group had disease identified through emergency department visits. Gilbert and coworkers\(^6\) showed that more recurrences were found by family physicians based on a symptomatic presentation than were identified through regularly scheduled surveillance visits to the surgical clinic. These investigators also found that the costs of identifying recurrences would be much lower using family physicians than using intensive surveillance through the surgical clinic. Reviews of this topic\(^6\),\(^6\) have endorsed the concept of less intense surveillance because “more intensive diagnostic testing has yet to demonstrate survival and quality of life benefits.”\(^6\)

The concept of less intensive surveillance has been challenged by the work of Westeel et al.\(^6\) They instituted a very intensive surveillance program in 192 patients following curative-intent surgical resection for NSCLC. Visits were scheduled every 3 months for 3 years, with medical history, physical examination, and chest radiographs at each visit. Bronchoscopy and CT scans were performed at 6-month intervals. From the fourth year postoperatively, visits with chest radiographs occurred at 6-month intervals, and CT scans and bronchoscopy were performed annually. At year 8, surveillance was reduced to a visit and a chest radiograph annually. Westeel et al.\(^6\) claimed good compliance with this surveillance regimen in a subset of the entire group. There were two remarkable findings in this study. Survival for the 36 patients with asymptomatic recurrences was significantly better than for the 100 patients with symptomatic recurrences. A subset of 10 patients was treated with curative-intent therapy after asymptomatic recurrences were recognized through either bronchoscopy (5 patients) or CT scanning (5 patients). In their economic analysis, they suggested that this very intensive surveillance regimen provided an acceptable cost per additional year of life gained.

Reconciling the conflicting findings from these various studies is difficult. The panel recognizes that periodic patient encounters following curative-intent therapy for lung cancer are essential and strongly feels that imaging studies of the chest should be included in these visits. A CT scan is accepted as being more sensitive for detecting pulmonary nodules than is a chest radiograph and has been shown to be more accurate for evaluating lung cancer response during chemotherapy.\(^6\) Small series\(^7\),\(^7\) have shown that a CT can detect changes that are consistent with cancer recurrence earlier than can a chest radiograph. CT scanning is also being widely studied as a method for the early detection of lung cancer (see article on screening for lung cancer in this supplement). Unfortunately, the performance characteristics of CT scanning (ie, sensitivity and specificity) for distinguishing nonspecific posttreatment changes related to surgery, radiation therapy, and/or chemotherapy from a recurrence, and/or metachronous lung cancer have not been defined. Consequently, the panel was evenly divided between recommending a chest radiograph or a CT scan as the imaging procedure of choice.

**Recommendation 2**

In lung cancer patients who have been treated with curative-intent therapy, surveillance with a medical history, physical examination, and imaging study (ie, either a chest radiograph or a chest CT scan) is recommended every 6 months for 2 years and then annually. Patients should be counseled on symptom recognition and should be advised to contact their physician if worrisome symptoms are recognized. Level of evidence, poor; benefit, moderate; grade of recommendation, C.

**Physician Factors Influencing Current Surveillance Methods**

Numerous reports have evaluated individual factors that might influence the surveillance methods used by thoracic surgeons. Many thoracic surgeons perform regular surveillance for detecting recurrences and/or metachronous lung cancers following curative-intent surgical therapy.\(^7\)\(^2\) The most commonly used methods were the history, physical examination, chest radiograph, CBC count, and serum chemistry measurement. Infrequently used surveillance methods were CT scanning, bronchoscopy, sputum cytology, bone scan, and head CT scan. There was wide variation in the frequency with which these methods were used. This wide variation
was probably due to the common belief that the clinical benefits of a surveillance program, particularly in terms of improving survival, had not been demonstrated. Interestingly, the age of the surgeon, the geographic region of the practice, and the stage of the original lung cancer did not seem to influence the surveillance methods used by individual thoracic surgeons.73–75 Motivating factors for continued surveillance seemed to be pleasing the patient, avoiding malpractice litigation, and potentially improving the patient’s quality of life.76 A more important issue, not specifically addressed in the surveys, was articulated as follows by Shields77: “The least desirable course of action (in regard to care of the lung cancer patient following curative-intent surgical therapy) is to pass the patient from one team member to another without continued surveillance by the primary responsible physician.”

Recommendation 3

Ideally, surveillance for the recognition of a recurrence of the original lung cancer and/or the development of a metachronous tumor should be coordinated through a multidisciplinary team approach. This team should develop a lifelong surveillance plan that is appropriate for the individual circumstances of each patient immediately following the initial curative-intent therapy. If possible, the physician who diagnosed the primary lung cancer and initiated the curative-intent therapy should remain as the health-care provider who is overseeing the surveillance process. Level of evidence, poor; benefit, moderate; grade of recommendation, C

Alternative Surveillance Techniques

There is considerable interest in developing noninvasive, easily performed, safe, and accurate techniques for detecting recurrences and/or metachronous tumors at the earliest possible time. An additional radiographic approach to early detection is positron emission tomography (PET) scanning. PET scanning appears to have improved performance characteristics compared to CT scanning for identifying malignant pulmonary nodules and mediastinal nodal involvement in confirmed cases of lung cancer.78,79 Preliminary studies with PET scanning also have suggested that this technique may prove valuable in detecting recurrences.80–83 A 1999 study84 compared PET scanning to CT scanning for detecting recurrences in a group of 58 patients following curative-intent therapy for NSCLC. Both PET scanning and CT scanning were initially performed 3 months after the completion of therapy and subsequently at 6-month intervals. PET scanning correctly identified 13 recurrences, but CT scanning identified only 9 recurrences. PET scanning and CT scanning each incorrectly suggested a recurrence in one patient. The impact of these imaging results on patient survival and quality of life was not described. Patz and colleagues85 found that patients with positive findings on PET scans 8 months after undergoing curative-intent therapy for NSCLC had significantly shorter survival times than did those with negative findings on PET scans.

Another approach to the early identification of recurrences of lung cancer is based on measuring serum levels of tumor markers. Ichinose11 has recommended using serum carcinoembryonic antigen levels as a marker of tumor recurrence. Another marker used for detecting tumor recurrence has been serum levels of cytokeratin-19 fragments.86 More recently, levels of pro-gastrin-releasing peptide have been suggested as a useful marker of tumor recurrence in patients with small cell lung cancer.87

Recommendation 4

In lung cancer patients following curative-intent therapy, the use of blood tests, PET scanning, sputum cytology, tumor markers, and fluorescence bronchoscopy is not currently recommended for surveillance. Level of evidence, poor; benefit, negative; grade of recommendation, D

SMOKING CESSATION

Smoking is common in patients with lung cancer. Gritz and colleagues88 studied smoking behavior in 840 adults with stage I NSCLC who had participated in clinical trials. At the time of diagnosis, 60% of the patients were smokers. By 2 years after diagnosis, 40% of the smokers had quit smoking. Smoking cessation at the time of diagnosis of lung cancer may
reduce the rate of development of metachronous tumors. Richardson et al\textsuperscript{80} found that the relative risk of developing a second lung cancer following curative-intent therapy for small cell lung cancer was lower for those who had stopped smoking. Tucker and coworkers\textsuperscript{81} found that continuing to smoke increased the risk of metachronous lung cancers in small cell lung cancer survivors.

Recommendation 5

Lung cancer patients who smoke should be strongly encouraged to stop smoking. Level of evidence, fair; benefit, moderate; grade of recommendation, B

Summary

Following curative-intent therapy for lung cancer, patients should be followed for 3 to 6 months by the appropriate specialist for potential complications. In addition to this follow-up, a recurrence of the original lung cancer and/or the development of a secondary primary lung cancer should be expected possibilities. Most recurrences of the original lung cancer will occur within 4 years of undergoing curative-intent therapy, but 10\% of recurrences may occur ≥ 5 years after surgery. Following curative-intent therapy for lung cancer, the lifelong risk of developing a second primary, or metachronous, lung cancer may be 1 to 2\% per patient per year. The risk of developing a metachronous lung cancer may be even higher when the original primary cancer was roentgenographically occult, central, or a small cell carcinoma.

Curative-intent therapy is less likely to be possible with locoregional recurrences of the original lung cancer than with metachronous tumors. Although survival is not as good with the treatment of metachronous tumors as for the original primary cancer, reasonable 5-year survival rates should be expected with surgical resection of metachronous lung cancers.

Benefits in terms of survival advantages or improvements in quality of life have not been demonstrated with intensive surveillance programs compared either with a symptom-based approach or with a less intensive regimen. In addition, the intensive surveillance programs seem to be more expensive. A clinically reasonable and cost-effective surveillance approach would include a medical history, a physical examination, and an imaging study (either a chest radiograph or a chest CT scan) every 6 months for 2 years and then annually. In addition, patients would be counseled on symptom recognition and should be advised to contact the appropriate physician on symptom recognition. Further studies are needed to determine whether very intensive surveillance programs might be warranted in selected subsets of lung cancer patients (eg, patients with roentgenographically occult primary lung cancers and patients surviving > 2 years with small cell lung cancer and a complete response to original therapy) who have a very high expected rate of developing a metachronous lung cancer.

Ideally, surveillance programs for the recognition of a recurrence of the original lung cancer and/or the development of a metachronous tumor following curative-intent therapy should be coordinated through a multidisciplinary team approach. This team should develop a lifelong surveillance plan that is appropriate for the individual circumstances of each patient immediately following the initial curative-intent therapy. If possible, the physician who diagnosed the primary lung cancer and initiated the curative-intent therapy should remain as the healthcare provider, overseeing the surveillance process. Patients either with a recurrence of their original cancer or with a new primary lung cancer that has been identified through the surveillance process should be reevaluated by the entire multidisciplinary team for potentially curative retreatment.

Although advanced imaging techniques, such as PET scanning, appear to be more sensitive than a chest radiograph for identifying recurrences and/or metachronous tumors, their value in improving either survival or quality of life following curative-intent therapy for NSCLC is as yet unproven. Incorporating PET scanning into a surveillance program should await the results of adequately designed and controlled prospective trials. Similarly, serum levels of various tumor markers and fluorescence bronchoscopy should be demonstrated to be sensitive and specific predictors of tumor recurrence in adequately designed and controlled prospective trials before being incorporated into surveillance programs.

Summary of Recommendations

1. In lung cancer patients who have been treated with curative-intent therapy, the follow-up for complications related to the curative-intent therapy should be managed by the appropriate specialist and should probably last 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. Level of evidence, poor; benefit, moderate; grade of recommendation, C
2. In lung cancer patients who have been treated...
with curative-intent therapy, surveillance with a medical history, physical examination, and imaging study (either chest radiograph or chest CT scan) is recommended every 6 months for 2 years and then annually. Patients should be counseled on symptom recognition and should be advised to contact their physician if worrisome symptoms are recognized. Level of evidence, poor; benefit, moderate; grade of recommendation, C

3. Ideally, surveillance for the recognition of a recurrence of the original lung cancer and/or the development of a metachronous tumor should be coordinated through a multidisciplinary team approach. This team should develop a lifelong surveillance plan appropriate for the individual circumstances of each patient immediately following initial curative-intent therapy. 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. Level of evidence, poor; benefit, moderate; grade of recommendation, C

4. In lung cancer patients following curative-intent therapy, the use of blood tests, PET scanning, sputum cytology, tumor markers, and fluorescence bronchoscopy is not currently recommended for surveillance. Level of evidence, poor; benefit, negative; grade of recommendation, D

5. Lung cancer patients who smoke should be strongly encouraged to stop smoking. Level of evidence, fair; benefit, moderate; grade of recommendation, B

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