Complete Summary

GUIDELINE TITLE

Follow-up of non-small cell lung cancer.

BIBLIOGRAPHIC SOURCE(S)

Thomas WW Jr, Komaki RU, Gewanter RM, Gopal RS, Movas B, Rosenzweig KE, Weisenberger TH, Wolkov HB, Kaiser LR, Mauch PM, Schiller JH, Expert Panel on Radiation Oncology--Lung Work Group. Follow-up of non-small cell lung cancer. Reston (VA): American College of Radiology (ACR); 2005. 6 p. [23 references]

GUIDELINE STATUS

This is the current release of the guideline.

It updates a previously published version: Sause WT, Byhardt RW, Curran WJ Jr, Fuller D, Graham MV, Ko B, Komaki R, Weisenburger TH, Kaiser LR, Leibel SA, Brown RC. Follow-up of non-small cell lung cancer. American College of Radiology. ACR Appropriateness Criteria. Radiology. 2000 Jun;215 Suppl:1363-72.

The appropriateness criteria are reviewed annually and updated by the panels as needed, depending on introduction of new and highly significant scientific evidence.

COMPLETE SUMMARY CONTENT

SCOPE
METHODOLOGY - including Rating Scheme and Cost Analysis
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SCOPE

DISEASE/CONDITION(S)

Non-small cell lung cancer

GUIDELINE CATEGORY

Evaluation

CLINICAL SPECIALTY

Nuclear Medicine
Oncology
Pulmonary Medicine
Radiology

INTENDED USERS

Health Plans
Hospitals
Managed Care Organizations
Physicians
Utilization Management

GUIDELINE OBJECTIVE(S)

To evaluate the appropriateness of radiologic procedures for the follow-up of non-small cell lung cancer

TARGET POPULATION

Patients with non-small cell lung cancer

INTERVENTIONS AND PRACTICES CONSIDERED

1. Frequency of follow-up
2. Chest X-ray
3. Computed tomography (CT)
    - Single postoperative scan
    - Post treatment scan
4. Computed tomography of brain
5. Magnetic resonance imaging (MRI) of brain
6. 3-day pooled sputum cytologies
7. Nuclear medicine (NUC), bone scan
8. Positron emission tomography (PET)
9. Serum tumor markers (tissue polypeptide antigen [TPA], neuron-specific enolase [NSE])

MAJOR OUTCOMES CONSIDERED

Utility of radiologic examinations in the follow-up of patients with non-small cell lung cancer

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The guideline developer performed literature searches of peer-reviewed medical journals, and the major applicable articles were identified and collected.

NUMBER OF SOURCE DOCUMENTS

The total number of source documents identified as the result of the literature search is not known.

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Not Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not stated

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

One or two topic leaders within a panel assume the responsibility of developing an evidence table for each clinical condition, based on analysis of the current literature. These tables serve as a basis for developing a narrative specific to each clinical condition.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus (Delphi)

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Since data available from existing scientific studies are usually insufficient for meta-analysis, broad-based consensus techniques are needed for reaching agreement in the formulation of the appropriateness criteria. The American College of Radiology (ACR) Appropriateness Criteria panels use a modified Delphi technique to arrive at consensus. Serial surveys are conducted by distributing questionnaires to consolidate expert opinions within each panel. These questionnaires are distributed to the participants along with the evidence table and narrative as developed by the topic leader(s). Questionnaires are completed by the participants in their own professional setting without influence of the other members. Voting is conducted using a scoring system from 1 to 9, indicating the least to the most appropriate imaging examination or therapeutic procedure. The

survey results are collected, tabulated in anonymous fashion, and redistributed after each round. A maximum of three rounds is conducted and opinions are unified to the highest degree possible. Eighty percent agreement is considered a consensus. This modified Delphi technique enables individual, unbiased expression, is economical, easy to understand, and relatively simple to conduct.

If consensus cannot be reached by this Delphi technique, the panel is convened and group consensus techniques are utilized. The strengths and weaknesses of each test or procedure are discussed and consensus reached whenever possible. If "No consensus" appears in the rating column, reasons for this decision are added to the comment sections.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

An analysis in 563 patients with curative resection who were followed for 10 years with regular clinic visits and chest radiography found that only 3.8% of patients were able to undergo a second curative resection based on this program. The calculated cost per life-year gained was approximately $75,000. This cost was far above other large-scale surveillance programs in their country, and the intensity and duration of follow-up were reduced.

METHOD OF GUIDELINE VALIDATION

Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Criteria developed by the Expert Panels are reviewed by the American College of Radiology (ACR) Committee on Appropriateness Criteria.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

ACR Appropriateness Criteria®

Clinical Condition: Follow-up Non-Small Cell Lung Cancer

Variant 1: Middle aged patient, 3 months postoperative for stage II squamous cell cancer of lung, asymptomatic. Still smoking, KPS 90-100.

Radiologic Exam Procedure	Appropriateness Rating	Comments
Frequency of follow-up	8	

Radiologic Exam Procedure	Appropriateness Rating	Comments
Every 2-4 months for 2 years, then every 6 months until 5th year, then yearly for life		
X-ray, chest Every 6 months for 5 years, then yearly for life	8	
CT, chest Single postoperative scan, then yearly for life	8	The frequency of follow-up CT scans is controversial and may be impacted by many clinical factors. Chest CT may replace a routine chest x-ray.
CT, brain	2	
MRI, brain	2	
3-day pooled sputum cytologies	2	
NUC, bone scan	2	
PET	2	
Serum tumor markers (TPA, NSE)	2	
Appropriateness Criteria Scale **1 2 3 4 5 6 7 8 9** **1 = Least appropriate 9 = Most appropriate**		

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 2: Elderly patient, never smoked, postoperative 3 months neoadjuvant chemotherapy irradiation and surgery for stage IIIA adenocarcinoma of lung. No residual disease at surgery. KPS 80.

Radiologic Exam Procedure	Appropriateness Rating	Comments
Frequency of follow-up	8	

Radiologic Exam Procedure	Appropriateness Rating	Comments
Every 2-4 months for 2 years, then every 6 months until 5th year, then yearly for life		
X-ray, chest Every 6 months for 5 years, then yearly for life	8	
CT, chest Single postoperative scan, then yearly for life	8	The frequency of follow-up CT scans is controversial and may be impacted by many clinical factors. Chest CT may replace a routine chest x-ray.
CT, brain	2	
MRI, brain	2	
3-day pooled sputum cytologies	2	
NUC, bone scan	2	
PET	2	
Serum tumor markers (TPA, NSE)	2	
Appropriateness Criteria Scale **1 2 3 4 5 6 7 8 9** **1 = Least appropriate 9 = Most appropriate**		

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 3: Middle aged patient, heavy smoker, unresectable stage 3A adenocarcinoma. Treated with concurrent chemoradiotherapy to 66 Gy using conformal technique.

Radiologic Exam Procedure	Appropriateness Rating	Comments
Frequency of follow-up	8	

Radiologic Exam Procedure	Appropriateness Rating	Comments
Every 2-4 months for 2 years, then every 6 months until 5th year, then yearly for life		
X-ray, chest Every 6 months for 5 years, then yearly for life	8	
CT, chest Post treatment scan, then every 6 months for 5 years, then yearly for life	5	The frequency of follow-up CT scans is controversial and may be impacted by many clinical factors. Chest CT may replace a routine chest x-ray. The value of post-therapy screening should be discussed with the patient.
PET One after treatment only	4	This modality is currently under study and may be impacted by many clinical factors. The value of post-therapy screening should be discussed with the patient.
CT, brain	2	
MRI, brain	2	
3-day pooled sputum cytologies	2	
NUC, bone scan	2	
Serum tumor markers (TPA, NSE)	2	
Appropriateness Criteria Scale **1 2 3 4 5 6 7 8 9** **1 = Least appropriate 9 = Most appropriate**		

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

New technologies are being introduced into the follow-up of patients with non-small cell lung cancer (NSCLC) at a rapid pace. Very few of these have been examined in a scientifically justified and cost-effective manner. Nevertheless, their impact on day-to-day oncology practice is undeniable. This section examines the evidence supporting or refuting their integration into the current follow-up

recommendations. It is important to stress that many of these technologies are unquestionably valuable in assessing symptomatic patients with recurrence after initial treatment. The relevant question is whether and how they should be used in routine follow-up of the asymptomatic patient after primary curative treatment of NSCLC.

Rationale for Follow-up Recommendations

Despite the proliferation of treatment options including surgery, chemotherapy, post-operative chemotherapy, pre-operative chemoradiotherapy, and primary chemoradiotherapy, the patterns of failure remain relatively unchanged; many patients fail in the first 2 years post-therapy, long term survival percentages are often under 50%, salvage interventions are less efficacious than the initial therapy, and second primary cancers including metachronous lung cancers are common among long-term survivors. For example, one study reviewed a single institution experience of 743 resected patients for NSCLC and found only 43 with isolated locoregional recurrence. The median time to recurrence was 13.6 months and the most frequent site of recurrence was mediastinal nodes in 49% of recurrences. Only two were treated with re-resection. Median survival after diagnosis of recurrence was 10.5 months and median time to distant recurrence after locoregional recurrence was 8.4 months. For the purposes of this report, one can segment follow-up discussions into recommendations for postoperative patients and those with therapy for unresectable cancer.

One might expect the best outcomes among patients treated with surgery, such that incrementally more rigorous follow-up might be expected to enhance survival. The justification for this assumption is controversial. One study evaluated 130 patients divided retrospectively into routine versus symptomatic follow-up regimens after curative resection. Most patients' recurrences were diagnosed based on symptoms rather than routine tests. Survivals of patients with recurrent cancer were poor and unaffected by follow-up regimen. The authors questioned the value of routine follow-up imaging based on these data. Another study retrospectively evaluated 124 patients with resected NSCLC using physical examination and chest radiography every 3 months for 2 years and every 6 months for an additional 3 years. Annual chest CT scans were done. Only 14 patients with second malignant tumors could be treated surgically, and 9 of these were alive and without evidence of disease at a median of 20 months follow-up. The median size of resected tumors was 14 mm. The authors also concluded that locally recurrent lung cancers are infrequently resectable. Another study followed postoperative patients with physical examination and chest x-ray every 3 months, fiberoptic bronchoscopy and chest and abdominal CT scans every 6 months. Recurrence was found in 71% of patients and only 11% of these could have re-resection for curative intent. Recurrence was found in asymptomatic patients by a scheduled follow-up procedure in 26% of all recurrences. Three-year survival was 31% in these patients versus 13% for all patients. These authors used this data to justify an intensive follow-up schedule. A similar analysis in 563 patients with curative resection who were followed for 10 years with regular clinic visits and chest radiography found that only 3.8% of patients were able to undergo a second curative resection based on this program. The calculated cost per life-year gained was approximately $75,000. This cost was far above other large-scale surveillance programs in their country, and the intensity and duration of follow-up were reduced.

With respect to second primary lung cancers (SPLC) alone, one may identify highly selected subsets of patients who can benefit from aggressive follow-up. One study analyzed the records of the National Cancer Institute (NCI) Intergroup trial NCI#I91-0001 examining the effectiveness of isoretinoin A for chemoprevention of second primary tumors after complete resection of pathologic stage I NSCLC. All of these patients had rigorous follow-up designed to detect SPLCs. Among the 569 patients randomized to the placebo arm, second primary tumors of all kinds were found in 88 (15%) patients. Only 49 of these patients had SPLC (incidence of 1.99/100 patient-years). Despite semi-annual follow-up with chest radiographs, 12 (24%) patients had metastatic disease at the time of diagnosis and only 31 (63%) patients underwent surgery. Median survival was 4.1 years for those patients who had surgery and 1.4 years for those who did not and this difference was highly significant. On the whole, these data support regular clinical exams and chest radiographs for post-resection follow-up.

The value of chest spiral CT has been evaluated as a screening tool in high-risk smokers, but it has a high false positive rate and is not sensitive for detecting endobronchial disease or preinvasive disease. It is attractive to speculate that applying this technology to follow-up of resected lung cancer patients might identify recurrences earlier, resulting in more curative re-resections. There is no doubt this is being done to some extent in daily practice. No controlled trials on use of low-dose spiral CT in follow-up of lung cancer patients have been done. Smaller experiences confirm the usefulness of this modality in confirming recurrence when compared to chest radiography, but the impact on survival is unknown. For now, it may be reasonable to replace a follow-up chest radiograph with chest CT scans in high-risk patients after resection.

If the case for avoiding aggressive follow-up in resected patients is controversial, then it is surely less so in patients with unresectable NSCLC treated with chemotherapy, chemoradiotherapy, or other combined modality approaches. These patients tend to fail soon after therapy with symptomatic metastases, and most imaging is focused on restaging the patient for salvage therapy. Routine post-therapy imaging of asymptomatic patients outside of clinical trials cannot be recommended until more effective salvage regimens are developed.

New imaging technologies are being investigated, but no controlled clinical trials establish their use in routine follow-up. PET has been evaluated in follow-up of NSCLC primarily in unresected patients. It is felt to be less sensitive for evaluating metastatic or recurrent cancer than it is in initial staging. It is probably more accurate than CT in distinguishing tumor from fibrotic scar or pneumonitis in NSCLC patients. One study demonstrated a significantly improved survival in patients with a negative PET scan after first line treatment. The combination of PET/CT improves the diagnostic accuracy over that of either test alone. Other modalities such as 99mTC-tetrofosmin scintigraphy, Tc99m-sestamibi (Tc99m MIBI) and thallium-201 chloride single photon emission computed tomography (SPECT), and whole-body MRI have been investigated but have no proven clinical usefulness in routine follow-up.

Since the previous edition of the American College of Radiology guidelines, the American Society of Clinical Oncology has published guidelines for treatment of unresectable NSCLC. They recommended maintaining regular physical exams but did not advocate regular imaging in asymptomatic patients. They acknowledged

the investigational nature of low-dose spiral chest CT as a routine follow-up study. Many of the interventions described above, including fiberoptic bronchoscopy, sputum cytologies, tumor markers, and more established imaging studies, continue to have value in follow-up of symptomatic patients or in clinical trials. These recommendations acknowledge the disappointing efficacy of salvage regimens after first therapy despite early diagnosis of recurrence, as well as, their additional cost to the patient. Under the circumstances, similar recommendations from this report are justifiable.

Abbreviations

- CT, computed tomography
- KPS, Karnofsky performance score
- MRI, magnetic resonance imaging
- NSE, neuron specific enolase
- NUC, nuclear medicine
- PET, positron emission tomography
- TPA, tissue polypeptide antigen
- US, ultrasound

CLINICAL ALGORITHM(S)

Algorithms were not developed from criteria guidelines.

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The recommendations are based on analysis of the current literature and expert panel consensus.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Selection of appropriate radiologic imaging procedures for the follow-up of non-small cell lung cancer

POTENTIAL HARMS

Not stated

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

An American College of Radiology (ACR) Committee on Appropriateness Criteria and its expert panels have developed criteria for determining appropriate imaging examinations for diagnosis and treatment of specified medical condition(s). These

criteria are intended to guide radiologists, radiation oncologists, and referring physicians in making decisions regarding radiologic imaging and treatment. Generally, the complexity and severity of a patient's clinical condition should dictate the selection of appropriate imaging procedures or treatments. Only those exams generally used for evaluation of the patient's condition are ranked. Other imaging studies necessary to evaluate other co-existent diseases or other medical consequences of this condition are not considered in this document. The availability of equipment or personnel may influence the selection of appropriate imaging procedures or treatments. Imaging techniques classified as investigational by the U.S. Food and Drug Administration (FDA) have not been considered in developing these criteria; however, study of new equipment and applications should be encouraged. The ultimate decision regarding the appropriateness of any specific radiologic examination or treatment must be made by the referring physician and radiologist in light of all the circumstances presented in an individual examination.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

IMPLEMENTATION TOOLS

Personal Digital Assistant (PDA) Downloads

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Thomas WW Jr, Komaki RU, Gewanter RM, Gopal RS, Movas B, Rosenzweig KE, Weisenberger TH, Wolkov HB, Kaiser LR, Mauch PM, Schiller JH, Expert Panel on Radiation Oncology--Lung Work Group. Follow-up of non-small cell lung cancer. Reston (VA): American College of Radiology (ACR); 2005. 6 p. [23 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

1996 (revised 2005)

GUIDELINE DEVELOPER(S)

American College of Radiology - Medical Specialty Society

SOURCE(S) OF FUNDING

The American College of Radiology (ACR) provided the funding and the resources for these ACR Appropriateness Criteria®.

GUIDELINE COMMITTEE

Committee on Appropriateness Criteria, Expert Panel on Radiation Oncology--Lung Work Group

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Panel Members: William W. Thoms, Jr, MD; Ritsuko U. Komaki, MD; Richard M. Gewanter, MD; Ramesh S. Gopal, MD; Benjamin Movas, MD; Kenneth E. Rosenzweig, MD; Thomas H. Weisenburger, MD; Harvey B. Wolkov, MD; Larry R. Kaiser, MD; Peter M. Mauch, MD; Joan H. Schiller, MD

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

It updates a previously published version: Sause WT, Byhardt RW, Curran WJ Jr, Fuller D, Graham MV, Ko B, Komaki R, Weisenburger TH, Kaiser LR, Leibel SA, Brown RC. Follow-up of non-small cell lung cancer. American College of Radiology. ACR Appropriateness Criteria. Radiology. 2000 Jun;215 Suppl:1363-72.

The appropriateness criteria are reviewed annually and updated by the panels as needed, depending on introduction of new and highly significant scientific evidence.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the American College of Radiology (ACR) Web site.

ACR Appropriateness Criteria® *Anytime*, *Anywhere*™ (PDA application). Available from the ACR Web site.

Print copies: Available from the American College of Radiology, 1891 Preston White Drive, Reston, VA 20191. Telephone: (703) 648-8900.

AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- ACR Appropriateness Criteria®. Background and development. Reston (VA): American College of Radiology; 2 p. Electronic copies: Available in Portable Document Format (PDF) from the American College of Radiology (ACR) Web site.

PATIENT RESOURCES

None available

NGC STATUS

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