Complete Summary

GUIDELINE TITLE

Non-small cell lung cancer.

BIBLIOGRAPHIC SOURCE(S)

Dutch Lung Cancer Study Group. Non-small cell lung cancer. Utrecht, The Netherlands: Association of Comprehensive Cancer Centres (ACCC); 2004 Oct 15. 142 p. [526 references]

GUIDELINE STATUS

This is the current release of the guideline.

COMPLETE SUMMARY CONTENT

SCOPE
METHODOLOGY - including Rating Scheme and Cost Analysis
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SCOPE

DISEASE/CONDITION(S)

Non-small cell lung cancer (NSCLC)

GUIDELINE CATEGORY

Diagnosis
Evaluation
Management
Risk Assessment
Screening
Treatment

CLINICAL SPECIALTY

Family Practice
Internal Medicine
Nuclear Medicine
Nursing
Oncology
Pathology
Psychiatry
Psychology
Pulmonary Medicine
Radiation Oncology
Radiology
Thoracic Surgery

INTENDED USERS

Advanced Practice Nurses
Allied Health Personnel
Health Care Providers
Health Plans
Hospitals
Physician Assistants
Physicians
Psychologists/Non-physician Behavioral Health Clinicians
Social Workers

GUIDELINE OBJECTIVE(S)

Generally:

- To provide recommendations for the diagnosis treatment, follow-up, and types of support for patients with non-small cell lung cancer (NSCLC)
- To facilitate the best care for patients with NSCLC
- To offer an initial basis for developing transmural care or local protocols to promote guideline implementation

Specifically:

- To specify the role of positron emission scans in the staging of lung carcinoma
- To specify the role of induction chemotherapy for locally advanced lung carcinoma
- To specify the role of concomitant chemotherapy and radiotherapy for lung carcinoma
- To determine acceptable waiting times in diagnosis and treatment and assess the centralisation of certain healthcare services
- To more precisely define various surgical options

TARGET POPULATION

Adults with non-small cell lung cancer

INTERVENTIONS AND PRACTICES CONSIDERED

Diagnosis/Evaluation

1. Patient history
2. Physical examination
3. Imaging (chest x-ray, bronchoscopy, computed tomography [CT]-scan of chest and upper abdomen, fluorodeoxyglucose positron emission tomography (FDG-PET)
4. Laboratory evaluations
5. Cytology/histology (transthoracic lung puncture, aspiration of pleural effusion, mediastinoscopy and biopsy, endoscopic ultrasound [EUS] with fine needle aspiration [FNA])
6. Assessment of operability
    - Age
    - Cardiovascular status
    - Lung function (forced expiratory volumes in 1 second [FEV_1], diffusion capacity, maximum oxygen uptake)
    - Intraoperative assessment of type of resection and resectability
    - Intraoperative staging (intraoperative frozen section assessment, involvement of other organs/structures)
    - Surgical and pathological documentation
7. Diagnosis of metastases
    - PET scan or skeletal scintigraphy, CT or magnetic resonance imaging (MRI) of brain

Management/Treatment

1. Surgery
2. Postoperative radiotherapy for resectable non-small cell lung cancer (NSCLC)
3. Combination chemotherapy/radiotherapy for locally advanced NSCLC
4. Chemoradiotherapy and/or surgery for superior sulcus tumors
5. Chemotherapy/supportive care for Stage IIIB/IV NSCLC
6. Follow-up
7. Organization of care
    - Maximum acceptable waiting times
    - Treatment consultation and reporting
    - Referral (lung surgery center requirements)
8. Psychological care
    - Physical, psychological, and social functioning

MAJOR OUTCOMES CONSIDERED

- Relapse/recurrence rate
- Response to treatment
- Complications of treatment
- Disease-free and overall survival
- Quality of life
- Sensitivity and specificity of diagnostic assessments
- Correlation of waiting time to outcome

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Relevant articles were found by performing systematic searches in the Cochrane Library, Medline and Embase. Manual searches were also performed. Other guidelines for lung carcinoma were also consulted. For most chapters, searches covered the last 15 years, but in some cases earlier records were searched. The articles were selected based on the following criteria: (a) predominantly English or Dutch publications and (b) full articles whenever possible. The quality of the articles was evaluated by members of the study group using evidence-based guideline development (evidence-based richtlijnontwikkeling [EBRO]) evaluation forms. Articles of mediocre or poor quality were excluded. After this selection process, the remaining articles were used as the basis for the various conclusions stated in the guideline.

NUMBER OF SOURCE DOCUMENTS

- 11 articles on sleeve lobectomy
- 6 articles on pneumonectomy
- 8 articles on frozen section diagnosis
- 7 articles on mediastinal lymph node sampling or dissection
- 6 articles on pleural lavage cytology
- 12 articles on immunohistochemistry of lymph nodes
- 4 articles on the treatment of resectable non-small cell lung cancer (NSCLC)
- 5 articles on radiotherapy for locally advanced NSCLC
- 6 articles on neoadjuvant chemotherapy versus radiotherapy alone
- 8 articles on chemoradiotherapy versus radiotherapy alone
- 6 articles on waiting time and prognosis

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Levels of Evidence

For Articles Regarding Intervention	
A1	Systematic reviews covering at least some A2-level studies in which the results of the individual studies are consistent
A2	Randomised comparative clinical studies of good quality (double-blind,

	controlled), sufficient size and consistency
B	Randomised clinical trials of moderate quality or insufficient size, or other comparative studies (non-randomised, comparative cohort studies, patient-control studies)
C	Non-comparative studies
D	Expert opinion from, for example, working group members
For Articles Regarding Diagnosis	
A1	Studies on the effects of diagnosis on clinical outcomes in a prospectively followed, well-defined patient population with a predefined protocol based on the results of the study test, or decision theory studies on the effects of diagnosis on clinical outcomes based on the results of A2-level studies with sufficient consideration given to the interaction between diagnostic tests
A2	Studies that include a reference test with predefined criteria for the study test and the reference test and a good description of the test and the clinical population studied; a sufficiently large series of consecutive patients must be included, predefined cut-off values must be used and the results of the test and the gold standard must be evaluated independently. For situations in which multiple diagnostic tests are involved, there is in principle interaction and the analysis should take this into account by using, for example, logistical regression
B	Comparison with a reference test and description of the study test and population, but lacking the other characteristics of A-level studies
C	Non-comparative studies
D	Expert opinion from, for example, working group members

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

The selected articles were graded according to the level of evidence. Data derived from abstracts that were not (yet) published as full articles are mentioned, but did not have any decisive weight in the formulation of the conclusions and recommendations.

After the selection process, the remaining articles were used as the basis for the various conclusions stated in the guideline. The selected articles were then graded according to the level of evidence, in which the following classification was used. Data derived from abstracts that were not (yet) published as full articles are mentioned, but did not have any decisive weight in the formulation of the conclusions and recommendations.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Composition of the Working Group

A multidisciplinary study group was formed that consisted of representatives of all relevant specialties involved in the diagnosis and treatment of on-small cell lung cancer (NSCLC) (see "Assembling the Study Group" in the original guideline document). In creating the study group, consideration was given to the geographic distribution of the group members, the proportional representation of various concerned associations and authorities, as well as distribution among those with and without an academic background. In addition to the professional groups, a representative from the Netherlands Epidemiological Society (Vereniging voor Epidemiologie) was also present. Study group members acted independently with authorisation from their associations.

Formation of Basis Questions

In spring 2002, the Dutch Lung Cancer Study Group (Landelijke Werkgroep Longtumoren) conducted a survey to identify problem areas in the daily practice and organisation of care for patients with NSCLC. Through this process, a list of potential basis question was recorded. The list of questions was sent to a random sample of clinicians with the request to formulate their answers within their oncology boards. A total of 26 questionnaires were returned. A response was received from each region with a comprehensive cancer centre. Both academic and non-academic hospitals responded. Based on the results, the questions were prioritised and a definitive list of 24 basis questions was created. These questions focus on key problem areas in daily practice in the Netherlands. The basis questions (see appendix 1 of the original guideline document) form the foundation for the various chapters of the guideline. Therefore, the guideline is not intended to be comprehensive. Some additional instructional chapters have been included.

Methods of the Working Group

Given the scale of the task, the basis questions were divided into 14 clusters and a corresponding number of subgroups were formed with representatives from relevant disciplines. In addition, an editorial team that consisted of a chair, two vice-chairs, Centraal Begeleidingsorgaan voor de Intercollegiale toetsing (CBO) advisors and a project manager from the Vereniging voor Integrale Kanker Centra (VIKC) was responsible for the coordination and mutual agreement among the subgroups. The 14 subgroups worked over the period of approximately one year on draft text related to a certain part of the guidelines. Study group members wrote text individually or in subgroups that was discussed during meetings and agreed upon after incorporation of comments. The complete study group met seven times to intercorrelate the results of the subgroups. The text created by the subgroups was combined by the editorial team and standardised to create one document: the draft guideline.

Other Considerations

In addition to the scientific evidence, there are often other important aspects to consider in the development of a recommendation, including patient preferences,

the availability of special techniques or expertise, organisational factors, social consequences and costs. These factors are addressed in the section following the 'Conclusion' (see original guideline document). In this section, the conclusion that was based on the literature is placed in the context of daily practice and the advantages and disadvantages of the various protocol options are weighed. The final formulated recommendation is the result of the available evidence in combination with these considerations. The output of this procedure and the structuring of the guideline in this format are intended to enhance the transparency of the guideline. It allows for efficient discussion during the study group meetings and also increases the clarity for guideline users.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Level of Evidence for Conclusions	
1	At least one systematic review (A1) or two independently conducted A2-level studies
2	At least two independently conducted B-level studies
3	At least one A2-, B- or C-level study
4	Expert opinion from, for example, working group members

COST ANALYSIS

Published cost analyses were reviewed.

Screening

- Screening should not be difficult for the patient or produce many false-positive results by which extra costs, alarm and anxiety are created.
- Knowledge of the CT scan evidence before a bronchoscopy is cost-effective in patients with suspected lung cancer: the knowledge increases the diagnostic yield of invasive procedures and reduces the need for additional diagnostic testing.

Fluorodeoxyglucose-Positron Emission Tomography (FDG-PET)

Nearly all data regarding costs are derived from model studies based on decision theory analyses. Therefore it is possible to criticise the lack of sensitivity analyses regarding the usual factors (costs, efficacy). In one study, it appeared that the additional costs associated with PET were negated by the reduction in the number of days hospitalised and the number of operations.

Surgery

Sleeve resections were actually associated with a slightly higher local recurrence rate than pneumonectomy, but the long-term results were better. Moreover, the quality of life was better and sleeve resections were more cost-effective.

Chemotherapy versus Other

- For patients with stage IIIB/IV NSCLC and World Health Organization (WHO) performance status 0-1, the combination of best supportive care and chemotherapy as initial therapy improves 1-year survival and quality of life; this approach is viewed as cost-effective.
- For patients with stage IIIB/IV NSCLC and WHO performance status 0-1 with progression following platinum-containing chemotherapy, single-agent docetaxel plus best supportive care improves survival and quality of life; treatment is considered cost-effective.

Radiation Therapy

Multiple studies demonstrate that treatment with a fraction of 8 Gy is as cost-effective as treatment with multiple fractions for a total of 24 Gy (for example, 6 x 4 Gy).

Follow-up

Intensive follow-up for a longer time period to detect second primary lung tumours is not cost-effective, given the limited treatment options for these patients.

METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

The draft guideline was presented for discussion at a national guidelines meeting on 16 April 2004. For this meeting, all members of the relevant professional groups were invited personally or via an announcement in a medical journal. The comments from this meeting were incorporated in the definitive guideline.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Screening

Screening for lung cancer in smokers using semi-annual cytological sputum analysis and/or a chest x-ray is not indicated.

Diagnostic Procedures

Patient History, Physical Examination, and Chest X-Ray

For all patients with indications of lung carcinoma, a patient history should be taken, a physical examination should be conducted and a chest x-ray should be made.

Laboratory Tests

For all patients with suspected lung carcinoma, a limited laboratory evaluation should be performed, including at least haemoglobin, calcium, albumin, sodium, lactate dehydrogenase and alkaline phosphatase. A more comprehensive laboratory evaluation is performed to assess organ function prior to treatment.

Bronchoscopy

In principle, all patients with indications of lung cancer should undergo bronchoscopy. Bronchoscopy is recommended for patients with a peripheral tumour <2 cm for staging purposes, rather than to diagnose a lesion.

Chest Computed Tomography (CT)-Scan

All patients with suspected or confirmed non-small cell lung cancer (NSCLC) should be considered for a CT scan of the chest and upper abdomen, unless surgery, radiotherapy or chemotherapy is not being considered. Performing the CT scan before bronchoscopy is recommended.

Transthoracic Lung Puncture

For patients with a lung lesion suspected of malignancy, transthoracic lung puncture should be performed if the results could affect further management.

Pleural Effusion

Aspiration of pleural effusion should occur in patients without distant metastases. Puncturing should be repeated no more than twice if the result is negative.

If the cytological assessment of the pleural effusion is negative, supplemental thoracoscopy and possibly guided biopsy can be performed, provided that the outcome may affect further management.

Fluorodeoxyglucose Positron Emission Tomography (FDG-PET)

Patients with NSCLC who are deemed candidates for intentionally curative surgery should undergo FDG-PET scan after conventional evaluation for metastatic disease and before mediastinoscopy.

See also the recommendations for mediastinoscopy.

Mediastinoscopy

During cervical mediastinoscopy, sufficient biopsies should be taken from at least 4 of the 6 accessible lymph node stations, namely 2 ipsilateral stations, 1 contralateral station and node station 7.

Cervical mediastinoscopy should be performed in patients with (signs of) NSCLC in whom no extrathoracic metastases are found, and in whom CT and/or FDG-PET scans show evidence of lymph node involvement.

The imaging-based criteria that suggest (mediastinal) lymph node involvement are (a) at least one lymph node with a short-axis diameter >1 cm on the CT scan or (b) a focus of increased activity in the hilus or mediastinum on the FDG-PET scan.

In patients with a negative mediastinal FDG-PET scan, mediastinoscopy can be omitted provided that the following 4 criteria are met:

- There is clear uptake of FDG in the primary tumour
- There is no evidence of hilar metastases on the PET scan
- The tumour is not close to the mediastinum
- The short-axis diameters of the nodes visible on the CT scan are less than 1 cm

Endoscopic Ultrasound (EUS) with Needle Puncture

The value of EUS with fine-needle aspiration (FNA) lies mainly in detecting mediastinal lymph node metastases (particularly on the left side or in the lower mediastinum) and possibly in determining whether central tumours are unresectable (T4) (see the original guideline document for the tumor/node/metastasis [TNM] staging definitions).

Although the definitive role of EUS-FNA in lung carcinoma is under investigation, this procedure can be considered for:

- Analysis of PET-positive lesions that are suspected of N2 or N3 lymph node metastases
- Mediastinal restaging following chemotherapy
- Evidence of T4 mediastinum for central tumours on the left side

Treatment Criteria

Criteria for Medical (In)operability

Age

For patients aged 70 to 80 years, it appears that the increased surgical risk due to age is not a reason to withhold lung surgery. It is advised that these patients are evaluated for lung surgery in accordance with the recommendations listed below with extra attention given to comorbidity and general condition. Caution is warranted, however, when considering right-side pneumonectomy.

Resection should also be considered as a possible treatment modality for patients aged more than 80 years without relevant comorbidity and in good condition, provided that the doctor and patient find the surgical risk acceptable.

Cardiovascular Evaluation

Before surgery, cardiac disorders such as coronary disease, heart failure, valve disease and rhythm disorders should be detected through patient history, physical examination and ECG.

If lung surgery is planned for a patient with (signs of) heart disease, a cardiologist or an anaesthesiologist should assess the perioperative risk and advise on the perioperative protocol.

Lung Function

The surgical risk is not considered increased if the forced expiratory volume in one second (FEV_1) and the diffusion capacity (TLCO) are both >80% and there is no unforeseen exertional dyspnoea.

If these criteria are not met, it is advised to calculate the predicted postoperative lung function using the calculation method (perfusion scan with left-right proportion and, for lobectomy, supplemented with the segment method).

If the operability of the patient is questioned based on the lung function assessment and/or the patient history (unforeseen exertional dyspnoea), an exertion test that includes determination of the maximum oxygen uptake (VO_2max) is advisable.

Use of the flowchart in Figure 2.1 in the original guideline document is recommended for the evaluation of perioperative risk.

General

Before surgery, it should be determined what maximum degree of parenchymal resection is prudent.

For patients with an increased surgical risk, alternatives such as limited resection or chemotherapy and/or radiotherapy should be weighed against the increased risk of surgery in a multidisciplinary consultation.

Intraoperative Assessment of the Type of Resection and Resectability

For operable patients with NSCLC in whom tumour growth is limited to one lobe, lobectomy is the treatment of choice. Intentionally curative radiotherapy is a good alternative if the surgical risk is determined to be (too) high.

Patients in whom lung function is so limited that lobectomy is not possible may be considered for segment resection (preferred) or wedge excision if complete resection using this method is possible.

In principle, if the lung tumour has spread from one lobe to another, a lobectomy plus a wedge resection of the other lobe should be performed. For central tumours, bilobectomy or pneumonectomy may be an option.

If a conventional lobectomy is not possible due to tumour growth up to or past the level of the bronchial ostium, a sleeve lobectomy is advisable because complete

resection is possible with this technique even when lung function precludes pneumonectomy.

A sleeve resection of the pulmonary artery should be performed only if the patient cannot tolerate pneumonectomy due to lung function.

If there is tumour growth in the direction of the thoracic wall and it is questionable whether the tumour has spread through the parietal pleura, one should immediately opt for including the affected thoracic wall en bloc.

If during surgery it appears that the tumour has spread to the intrapericardially positioned portion of the pulmonary artery, it is often possible to conduct a pneumonectomy.

If during surgery it appears that the tumour has spread to or into the main carina, which precludes a conventional pneumonectomy, a sleeve lobectomy may be attempted. If this is not possible, it should be immediately ascertained whether a sleeve pneumonectomy can be performed on the right side. On the left side, a sleeve pneumonectomy can occur in 2 phases. Referral to a treatment centre is indicated.

If during surgery it appears that the tumour is growing into the vena cava superior, the adventitia of the aortic wall, the pericardium or the diaphragm, primary resection should not be ruled out *a priori*.

If during surgery it appears that the tumour is growing into the spinal column or into the left atrium substantially, it is seldom resectable.

If during surgery it appears that the tumour is growing into the pulmonary trunk or through the entire aortic wall or has led to pleuritis carcinomatosa, it is unresectable. This likely holds true also for spread to the oesophagus.

If during surgery it appears that there are more tumours present in one lobe, lobectomy is performed. If multiple tumours are present in different lobes (M1), primary resection is an option.

Requirements for Intraoperative Staging

If before surgery there is no known tissue diagnosis, intraoperative frozen section assessment of the tumour is recommended before proceeding to lung resection.

Intraoperative frozen section assessment is recommended if macroscopic findings of lymph nodes provide reason for it (indications of extranodal growth or bulky disease). This is applicable if the result of the assessment can influence the surgical procedure (lung resection and/or mediastinal lymph node dissection).

For central tumours, intraoperative frozen section assessment of the bronchial resection field is recommended, unless a positive result would have no influence on the surgical procedure. Regardless of the location of the tumour, all intrapulmonary and hilar lymph nodes (N1 node stations 10, 11 and 12) should be removed en bloc with the resected section if possible.

Regardless of the location of the tumour, all intrapulmonary and hilar lymph nodes (N1 node stations 10, 11 and 12) should be removed en bloc with the resected section if possible.

To determine the status of mediastinal lymph nodes (N2 stations), at least the lymph node stations to which the tumour preferably drains should be systematically sampled during surgery.

Specifically, this implies for tumours of the

- Right upper and middle lobe: node stations 2R, 4R and 7
- Right lower lobe: node stations 4R, 7, 8 and 9
- Left upper lobe: node stations 5, 6 and 7
- Left lower lobe: node stations 7, 8 and 9

Requirements for Surgical Documentation

Following an operation for NSCLC, the surgical documentation should contain:

- Surgical approach (thoracotomy, sternotomy, etc)
- Tumour location, size, extent and distance from the main carina
- Presence or absence of satellite lesions and metastases in other lobes
- Lymph node stations (extranodal growth) and surgical technique used to evaluate mediastinal lymph nodes
- Presence and characteristics of pleural effusion; pleural lavage (duration and method), if applicable
- Result of frozen section assessment, if performed
- Distance between the tumour and the resection field, particularly the bronchial resection field
- Radicality of the resection (R0, R1 or R2)
- Placement of clips to demarcate the resection field, if applicable
- Perioperative consultation with other specialists
- Complications, if applicable
- Conclusion: procedure performed and intraoperative staging

Requirements for Pathological Documentation

The pathology report should include at least all evidence that allows for indisputable conclusions regarding staging (pTNM stage) and the completeness of resection.

The recommendation for pathological reporting calls for the use of a checklist (see appendix 17 in the original guideline document).

Removed lymph nodes should be assessed using hematoxylin and eosin (HE) staining and immunohistochemical techniques.

Treatment

Resectable NSCLC

Postoperative radiotherapy is recommended if pathological assessment reveals involvement of the resection field. Postoperative radiotherapy should be considered for unexpected pN2 (possibly also pN3). The chance of improved local control should be weighed against the risk of radiotherapy-associated morbidity.

Postoperative radiotherapy is not indicated for pN0-1 nodes with R0 resection.

Locally Advanced NSCLC

Patients with locally advanced NSCLC (clinical stage III, based on cT4 and/or cN2-3) should be treated with combination therapy with curative intent. Exceptions include patients with World Health Organization (WHO) performance status 2, pleuritis carcinomatosa, extensive tumour invasion (requiring a radiotherapy field that would be too large with respect to lung function) or contralateral supraclavicular lymph node involvement.

Standard combination therapy consists of chemotherapy and radiotherapy. The value of surgery in this setting, particularly for stage IIIA N2 disease, has not yet been confirmed.

Radiotherapy is given at a biological equivalent of at least 60 Gy over 6 weeks.

At this time, chemotherapy is preferably given sequentially before radiotherapy. In accordance with the recommendations for advanced NSCLC, induction chemotherapy consists of 2 to 4 cycles of cis- or carboplatin in combination with a third generation cytostatic agent.

Chemotherapy can be given concomitantly with radiotherapy in selected patients provided that the associated increased risk of toxicity appears acceptable. For concomitant chemoradiotherapy, the chemotherapy regimen used is preferably one that has been used in published studies, such as cisplatin-containing chemotherapy in combination with vinca alkaloids, with or without mitomycin.

Superior Sulcus Tumors

For patients with locally advanced superior sulcus NSCLC and a WHO performance status 0-1, standard treatment consists of a multimodality approach using chemoradiotherapy and/or surgery. On the one hand, superior sulcus tumours can be considered the same as any other NSCLC. On the other hand, a more aggressive approach is justified, given the location and symptoms that are often difficult to treat if local control is not achieved.

For patients with a superior sulcus tumour that does not appear to be primarily resectable (stage cIII), sequential or concurrent chemoradiotherapy is advisable, in accordance with the recommendation for other NSCLC patients with stage III disease. If it is later determined that the tumour is in fact small enough to be resected, surgery can be considered for selected patients.

Treatment of patients with a superior sulcus tumour should occur in a specialised treatment centre.

Stage IIIB/IV

Chemotherapy Versus Supportive Care

For patients with stage IIIB/IV NSCLC and a WHO performance status 0-1, treatment should consist preferably of best supportive care and chemotherapy.

Choice of Chemotherapy

For patients with stage IIIB/IV NSCLC and WHO performance status 0-1, best supportive care and chemotherapy, consisting of cisplatin or carboplatin in combination with a third generation cytostatic agent, is preferred.

Age >70 Years

For patients aged more than 70 years with stage IIIB/IV NSCLC and WHO performance status 0-1, chemotherapy is preferred; comorbidity should be taken into account.

Number of Chemotherapy Cycles

For patients with stage IIIB/IV NSCLC and WHO performance status 0-1, 3 to 4 cycles of chemotherapy is preferred; fewer may be given in the event of disease progression or severe toxicity.

Second-Line Treatment

For patients with stage IIIB/IV NSCLC and WHO performance status 0-1 with progression following first-line chemotherapy, best supportive care is preferred; additionally, patients may be considered for second-line chemotherapy.

Follow-Up

Routine follow-up after treatment for patients with NSCLC should consist of patient history, physical examination and possibly chest x-ray.

More intensive follow-up (additional imaging, tumour marker assessment, bronchoscopy) should occur only in the context of a study protocol or in a training or academic setting.

The study group recommends the following with regard to the frequency of follow-up (alternating though different clinicians if desired):

- For the first year: every 3 months
- For the second year: every 6 months
- After the second year: annually for a minimum of 5 years

Diagnosis of Metastases

Patients with clinical stage III NSCLC must undergo skeletal scintigraphy (unless PET scan was performed and was negative) and CT or magnetic resonance imaging (MRI) of the brain to avoid unnecessary combination therapy.

Organisation of Care

Maximum Acceptable Waiting Time

The study group recommends the following maximum acceptable waiting times:

- General practitioner: 80% within 2 working days, maximal 3 working days
- Pulmonologist: 80% within 5 working days for evidence of a lung tumour or abnormal chest image
- Diagnosis (CT scan, bronchoscopy with pathological anatomy (PA), PET, mediastinoscopy): 80% with 3 weeks
- PA: the result of the PA test should be known within 1 week unless hindered by special processing
- Curative therapy: 80% within 2 weeks after the diagnosis is made
- Palliative therapy: 80% within 1 week

Eighty percent of patients should be through the diagnostic trajectory within 3 weeks. Within 5 weeks is acceptable if mediastinoscopy is conducted.

If indicated, 80% of patients should undergo surgery and/or (the preparation for) radiotherapy and/or start chemotherapy within 2 weeks after the completion of the diagnostic trajectory.

Treatment Consultation and Reporting

All new patients should be discussed during a multidisciplinary (lung) oncology review.

Referral

A lung surgery centre should meet the requirements set for academic institutions for lung surgery as described in the report of the Interdisciplinary Committee on Lung Surgery (Interdisciplinaire Commissie Longchirurgie).

A treatment centre should be consulted in the following situations:

- cT3 or cT4 disease
- Increased pulmonary of cardiac comorbidity
- Use of combined treatment modalities

As a minimum, a treatment centre should provide the support of pulmonologists, radiation oncologists, (thoracic) surgeons, clinical pathologists, radiologists and specialised nurses, in accordance with the requirements set by the relevant professional societies.

A treatment centre should have a minimum of two specialists in each discipline to ensure continuity.

A treatment centre should offer consultation to clinicians in other hospitals.

Psychosocial Care

Prevalence

Based on the prevalence of psychosocial problems in patients with lung cancer, the care providers involved should inquire about anxiety and depression in every patient with lung cancer.

Interventions

From the beginning and throughout all phases of diagnosis and treatment, medical specialists, general practitioners and/or (oncology) nurses should be educated to inquire about and treat physical symptoms because prompt medical and/or behavioural therapy for these symptoms may promote psychosocial functioning and quality of life.

From the beginning and throughout all phases of diagnosis and treatment, medical specialists, general practitioners and/or (oncology) nurses should inquire about psychosocial stress factors and psychological symptoms because prompt treatment may promote improved psychosocial functioning and quality of life.

An (oncology) nurse should be involved in the process of care because he or she is an integral link in the chain of treatment, care and early signalling of somatic and psychological symptoms.

Care providers should pay attention to psychosocial problems in family members and/or others close to the patient.

Organisation

General practitioners, medical specialists and (oncology) nurses should be aware that basic psychosocial care must be offered from the initial phases of diagnosis and treatment for NSCLC. This care consists of customised education, adequate handling and temporary admission if necessary.

Good psychosocial care requires the availability of adequate referral options to care providers who are trained to address the psychosocial needs of cancer patients, such as nursing specialists, social workers (associated with the hospital), psychologists, psychiatrists and/or specific patient programmes (discussion groups, relaxation groups, rehabilitation programmes, patient associations).

CLINICAL ALGORITHM(S)

The original guideline document contains clinical algorithms for:

- Recommended diagnostic tests and staging of patients with indications of lung cancer
- Determining perioperative risk before lung surgery by means of lung function assessment

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is not identified or graded for each recommendation.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

- Avoidance of unnecessary therapy for non-small cell lung cancer
- Improved outcomes
- Reduction in treatment related adverse events

POTENTIAL HARMS

- Adverse effects of treatment
- Complications of surgical and other procedures

CONTRAINDICATIONS

CONTRAINDICATIONS

- Transthoracic lung puncture is contraindicated in some patients, including those with pulmonary hypertension and increased bleeding tendency.
- Palliation other than chemotherapy (e.g., surgical intervention followed by radiotherapy) for bone metastases is contraindicated for life expectancy less than four weeks and a general condition so poor that an operation cannot be performed safely.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

Guidelines are not legal requirements, but rather scientifically founded and widely accepted views and recommendations to which healthcare providers would have to adhere to provide quality care. Given that guidelines are based on 'average patients', healthcare providers can deviate from the recommendations in the guideline as necessary in individual cases. Deviation from the guideline is in fact sometimes necessary if the patient's situation demands it. When there is deviation from the guideline, however, it must be rationalised, documented and, when necessary, discussed with the patient.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

During the various phases of development of the draft guideline, consideration was given whenever possible to the implementation of the guideline and the actual feasibility of the recommendations. The guideline will be distributed to all hospitals and oncology boards, scientific societies and Comprehensive Cancer Centres (Integrale Kanker Centra). A summary of the guideline will also be published in the *Dutch Journal of Medicine (Nederlands Tijdschrift voor Geneeskunde)* and attention will be given to the guideline in various specialty journals. In addition, the guideline will be reproduced on www.oncoline.nl. To stimulate the implementation and evaluation of this guideline, the study group will, as a next step, create an implementation plan and develop a list of indicators through which implementation can be measured. In general, indicators give healthcare providers the opportunity to assess whether they are providing the desired level of care. They can also be used to identify topics for improving the provision of care. The guideline will be tested by end-users in different regions and scientific societies, at which time on-site visits will also be organised.

IMPLEMENTATION TOOLS

Clinical Algorithm
Foreign Language Translations
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

End of Life Care
Living with Illness

IOM DOMAIN

Effectiveness
Patient-centeredness
Timeliness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Dutch Lung Cancer Study Group. Non-small cell lung cancer. Utrecht, The Netherlands: Association of Comprehensive Cancer Centres (ACCC); 2004 Oct 15. 142 p. [526 references]

ADAPTATION

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

DATE RELEASED

2004 Oct

GUIDELINE DEVELOPER(S)

Association of Comprehensive Cancer Centres - Disease Specific Society

SOURCE(S) OF FUNDING

Association of Comprehensive Cancer Centres

GUIDELINE COMMITTEE

Dutch Lung Cancer Study Group

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Chief Editors: Prof. dr. J.P. van Meerbeeck, pulmonologist, Universitair Ziekenhuis Gent, België , chair; Mw. prof. dr. C.C.E. Koning, radiation oncologist, Academisch Medisch Centrum, Amsterdam,vice-chair; Mw. dr. V.C.G. Tjan-Heijnen, medical oncologist, Radboud University Nijmegen Medical Centre, Nijmegen, vice-chair; Mw. drs. J. Wittenberg, epidemiologist, Kwaliteitsinstituut voor de Gezondheidszorg CBO,Utrecht, advisor (until October 2003); Mw. dr. C.J.E. Kaandorp, physician, Kwaliteitsinstituut voor de Gezondheidszorg CBO, Utrecht, advisor (as of October 2003); Dr. J.S. Burgers, general practitioner, Kwaliteitsinstituut voor de Gezondheidszorg CBO, Utrecht, senior advisor (as of October 2003); A.G. Boekema, medical officer, Vereniging van Integrale Kankercentra, Utrecht,project manager; Drs. V.K.Y. Ho, methodologist, Vereniging van Integrale Kankercentqra, Utrecht, policy advisor for national guidelines

Study Group Members: J.T. Annema, pulmonologist, Leids Universitair Medisch Centrum, Leiden; Dr. P. Baas, pulmonologist, Antoni van Leeuwenhoek Ziekenhuis, Amsterdam; Dr. M. den Bakker, clinical pathologist, Erasmus MC, Josephine Nefkens Instituut, Rotterdam; Mw. dr. P.F.A. Bakker, cardiothoracic surgeon, Universitair Medisch Centrum, Utrecht; Mw. J.S.A. Belderbos, radiation oncologist, Nederlands Kanker Instituut-Antoni van Leeuwenhoek Ziekenhuis, Amsterdam; Dr. B. Biesma, pulmonologist, Bosch Medicentrum, locatie Groot Ziekengasthuis, 'sHertogenbosch; Dr. E.C.M. Bollen, surgeon, Atrium Medisch Centrum, Heerlen; Dr. J. Bussink, radiation oncologist, Universitair Medisch Centrum St. Radboud, Nijmegen; H.E. Codrington, pulmonologist, Ziekenhuis Leyenburg, Den Haag; Mw. C.E. van Die, thoracic radiologist, Universitair Medisch Centrum St. Radboud, Nijmegen; Prof. dr. H.J.M. Groen, pulmonologist, Academisch Ziekenhuis Groningen, Groningen; Dr. J.M.W. van Haarst, pulmonologist, Ziekenhuis Hilversum, Hilversum; Dr. P.A. Helle, radiation oncologist, Medisch Spectrum Twente, Enschede A.G. Hensens, cardiopulmonary surgeon, Universitair Medisch Centrum St. Radboud, Nijmegen; Dr. F.M.J. Heijstraten, radiologist, Universitair Medisch Centrum St. Radboud, Nijmegen; Dr. O.S. Hoekstra, nuclear medicine physician, VU Medisch Centrum, Amsterdam; Dr. P.L. Jager, nuclear medicine physician, Academisch Ziekenhuis Groningen, Groningen; Mw. dr. M.L.G. Janssen-Heijnen, epidemiologist, Integraal

Kankercentrum Zuid, Eindhoven; Mw. dr. M.J.A. de Jonge, internist-oncologist, Erasmus MC, locatie Dani.l, Rotterdam; G.W.P.M. Kramer, radiation oncologist, Arnhems Radiotherapeutisch Instituut, Arnhem; Dr. H.B. Kwa, pulmonologist, Onze Lieve Vrouwe Gasthuis, Amsterdam; Dr. W.B. Lastdrager, surgeon, Gelre Ziekenhuizen, Apeldoorn; Dr. H.J. Mulder, surgeon, Medisch Spectrum Twente, Enschede; Prof. dr. E.M. Noordijk, radiation oncologist, Leids Universitair Medisch Centrum, Leiden; Dr. B.P. Ponsioen, general practitioner, Brielle; Dr. J.W.G. van Putten, pulmonologist, Martini Ziekenhuis, Groningen; Mw. A.M.C. Raat, general practitioner, Amersfoort; P.T.R. Rodrigus, radiation oncologist, Catharina-ziekenhuis, Eindhoven; Dr. W.J.G. Ros, social psychologist, Universitair Medisch Centrum Utrecht, Utrecht; Mw. J.P. Salomé, nurse practitioner, St. Franciscus Gasthuis, Rotterdam; N.J.J. Schl.sser, pulmonologist, Centraal Militair Hospitaal, Utrecht; Dr. J.H. Schouwink, pulmonologist, Medisch Spectrum Twente, Enschede; Mw. N.A.W.P. Schrama, oncology nurse, Ziekenhuis Bernhoven, Veghel; Dr. F.M.H.H. Schramel, pulmonologist, St. Antonius Ziekenhuis, Nieuwegein; Dr. E.F. Smit, pulmonologist, Martini Ziekenhuis, Groningen and VU Medisch Centrum, Amsterdam; A.H.M. van Straten, cardiothoracic surgeon, Catharina Ziekenhuis, Eindhoven; Dr. J.R.M. van der Sijp, surgeon, VU Medisch Centrum, Amsterdam; Dr. F.B.J.M. Thunnissen, pathologist, Nijmeegs Interkonfessioneel Ziekenhuis Canisius-Wilhelmina, Nijmegen; Mw. A.L.J. Uitterhoeve, radiation oncologist, Academisch Medisch Centrum, Amsterdam; E.F. Ullmann, pulmonologist, Rijnstate Ziekenhuis, Arnhem; Dr. G.P.M. ten Velde, pulmonologist, Academisch Ziekenhuis Maastricht, Maastricht; A.F.T.M. Verhagen, cardiothoracic surgeon, Universitair Medisch Centrum St. Radboud, Nijmegen; B.A. Verheij, general practitioner, Huizen; M.I.M. Versteegh, cardiothoracic surgeon, Leids Universitair Medisch Centrum, Leiden; Mw. M.S. Vos, psychiatrist, Ziekenhuis Bronovo, Den Haag; S.L. Wanders, radiation oncologist, MAASTRO Clinic, Heerlen; Dr. L.N.A. Willems, pulmonologist, Leids Universitair Medisch Centrum, Leiden

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

ENDORSER(S)

Lung Cancer Information Centre (Longkanker Informatiecentrum) - Disease Specific Society

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available in Available in English and Dutch from the Association of Comprehensive Cancer Centres Web site.

Print copies: Available from Association of Comprehensive Cancer Centres PO Box 19001, 3501 DA Utrecht, The Netherlands

AVAILABILITY OF COMPANION DOCUMENTS

A version of the guideline for Personal Digital Assistants (PDAs) is available from the Association of Comprehensive Cancer Centres Web site.

PATIENT RESOURCES

None available

NGC STATUS

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