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Introduction
Lung cancer is the most common cause of cancer deaths worldwide. The number of death each year due to lung cancer is more than the total number of cancer deaths from breast, colon, and prostate cancer added together.
One of the most disturbing trends in lung cancer is the explosion in rates in countries of the developing world. In 1985, it was estimated that there were 921,000 lung cancer deaths worldwide, an increase of 17% from 1980\(^{(1)}\). The International Agency for Research on Cancer in France found that the rates of lung cancer in Africa in the early 1990s were similar to those in the United States in the 1930s, at about 5/100,000. By 1999, the rate of lung cancer in males of developing countries was 14/100,000 and on the rise, compared with a rate of 71/100,000 in developed countries, which continues to decline. These rates may actually be underestimates of the true rates of lung cancer, because many cases may go undiagnosed or under-reported in areas where health care is not readily available\(^{(1,2)}\).

In this review, the current practices for the diagnosis and staging of lung cancer will be discussed and broadly describes treatment strategy of this disease.

**Screening for lung cancer**

Clinical outcome for lung cancer is directly related to stage at the time of diagnosis, ranging from over 60% five year survival for stage I disease, to less than 5% for stage IV disease. In addition, within early lung cancers (stage I) there is a relationship between tumour size and survival\(^{(3)}\). While the potential for screening to detect early cancers may increase the overall cure rate and allow more limited surgical resection to achieve cure, an overall decrease in mortality and morbidity remains uncertain.

Imaging techniques and cytological analysis of sputum have been the focus of screening studies for lung cancer. However, systematic screening is not currently recommended by any major medical professional organization. The current position of the American Cancer Society and the U.S. Preventive Services Task Force is that there is no role for lung cancer screening, even in high-risk individuals\(^{(4)}\). This position is based on the results of five randomized, controlled trials that suggest that neither chest radiography nor sputum cytology satisfies the primary criterion of a beneficial screening test: reduction in lung cancer mortality\(^{(5,6)}\). There continues to be ongoing debate about the interpretation of these studies. One deficiency is that most of these studies did not include a “no screening” arm. Others have argued that the sample size of the studies was inadequate.

The Mayo Lung Project and the Czechoslovakian studies were powered to detect a 50% reduction in lung cancer mortality in the screened group and could have missed detecting a 20% to 30% reduction\(^{(4,7)}\). The lack of a clear result from chest X-ray screening and the refinement of CT scanning techniques have led to the evaluation of CT for lung cancer screening\(^{(8)}\). To date, results are only available from observational cohort studies\(^{(9,10)}\). Randomized trials are ongoing, but available baseline data offer no compelling evidence in favour or against the use of low-dose spiral computed tomography (LDCT) screening for lung cancer\(^{(11)}\).

**Presentation**

The symptoms of lung cancer are usually nonspecific, thereby delaying the diagnoses and leading to an advanced stage at the time of diagnosis. Cough is the commonest symptoms (75%) followed by chest pain in 25% to 50% of patients at the time of presentation\(^{(12,13)}\). The latter is usually related to involvement of the pleura, but can be related to extension into the mediastinum or chest wall. Dyspnea is frequently a complaint occurring in half of all new patients at presentation\(^{(11)}\). A partial list of the reasons for dyspnea related to lung cancer includes pulmonary embolism, superior vena cava syndrome, deconditioning, reactive airway disease, endobronchial obstruction with tumor, prior obstructive pneumonia, haemoptysis, hemorrhage, malignant pleural effusion, and extrinsic compression of the
airway by tumor.
Haemoptysis in a smoker should always raise
the suspicion of lung cancer. Weight loss, a
nonspecific symptom, in the right clinical
setting should raise the suspicion of both lung
cancer and metastatic disease. Weight loss
alone has been correlated with an advanced
presentation and poor outcome from lung
cancer.

Lung cancer staging
Correct staging of patients with lung cancer is
critical since it affects treatment options and
predicts survival. It is intuitive that early-stage
disease has a much better survival than late-
stage disease. The treatment options for lung
cancer have now evolved so that treatment for
patients in different stages is vastly different.
The staging of non small cell lung cancer
(NSCLC) using the tumor-node-metastasis
(TNM) classification underwent revision in
1997 and has recently undergone a major
revision. The new staging system is
remarkable in that it is based on over 100,000
cases of lung cancer from 23 institutions, 12
countries, and 3 continents. The data are
robust, internally validated, and externally
validated against the Surveillance
Epidemiology and End Results (SEER) cancer
registry.

Whereas the TNM staging system is applied
to NSCLC, a more simplified version is
employed for patients with small cell lung
cancer. In this classification, patients are
classified as having limited or extensive
disease. Limited disease (LD) is disease
limited to one hemithorax, although it can
include supraclavicular and mediastinal
lymphadenopathy. Extensive disease (ED) is
any disease outside of the hemithorax. The
implication in this classification is that LD is
treated with chemotherapy and radiotherapy
and ED is treated with chemotherapy alone.

Malignant pleural effusion can technically be
categorized as LD in the staging classification
for small cell lung cancer if the patient
otherwise meets criteria. However, for all
intents and purposes, patients with malignant
pleural effusions and small cell lung cancer
have the same characteristics as those with
ED, and the large cooperative group trials
have treated them as such.

Staging techniques
Chest radiography
The majority of lung cancers are detected
initially by plain chest radiograph. This
modality is readily available, inexpensive, and
provides a lot of information with minimal
radiation dose. However, it is insufficient for
staging and insensitive measure of mediastinal
lymph node involvement with cancer. Hence,
most patients undergo CT scan of the chest
unless they are so debilitated that no further
evaluation or treatment is planned.

Despite their limited utility in staging, chest
radiographs have an important role in the
assessment of a lung nodule or mass. Since
patients are more likely to have had a chest
radiograph than any other type of chest
imaging, comparing a current chest radiograph
to prior radiographs is often a good way to
determine whether a lung lesion is new,
enlarging, or stable. A new or enlarging lesion
is more likely to be malignant than a lesion
whose size and appearance have been stable
for years.

Computed Tomography of the chest (CT)
Most patients who present with possible lung
malignancy will require staging contrast CT
scanning of the chest and upper abdomen.
This investigation is helpful in defining the
size, location, and characteristics of the
primary mass (e.g., smooth-bordered,
speculated, calcified), the presence or absence
of lymphadenopathy and, the presence of
abnormalities in the liver and adrenal glands.
In addition, the bony structures of the thoracic
cavity can also be evaluated by chest CT.

A recent met-analysis assessing the
performance characteristics of CT scan for
staging the mediastinum including over 5000
evaluable patients in 35 studies. The
The median prevalence of mediastinal metastasis was 28% (range, 18 to 56%) and the pooled sensitivity and specificity of CT scanning for identifying mediastinal lymph node metastasis were 51% (95% confidence interval [CI], 47 to 54%) and 86% (95% CI, 84 to 88%), respectively. The corresponding positive and negative likelihood ratios were 3.4 and 0.6, respectively, suggesting that CT scanning has a limited ability either to rule in or exclude mediastinal metastasis. Based on the currently available data approximately 40% of all nodes that are deemed to be malignant by CT scan criteria are actually benign. In contrast, nearly 20% of all nodes that are deemed to be benign by the same criteria are actually malignant. This suggest that no node size that can reliably determine tumor stage and operability.

Nonetheless, CT scanning continues to play an important and necessary role in the evaluation of these patients. This conclusion is supported by the most recent American Thoracic Society/European Respiratory Society statement on the pretreatment evaluation of NSCLC and British Thoracic Society guidelines on the selection of patients with lung cancer for surgery, both of which recommend CT scanning for the evaluation of the mediastinum and guides the selection of nodes for biopsy by mediastinoscopy or needle aspiration.

CT can also be helpful in the evaluation of pleural effusion in patients with lung cancer and whether or not nodules or masses are present on the pleural surface.

Positron Emission Tomography (PET)

One of the most recent addition to the staging armamentarium for the evaluation of lung cancer is PET scan. With the image created by the biologic activity of neoplastic cells, PET is a metabolic imaging technique based on the function of a tissue rather than on its anatomy. Lung cancer cells demonstrate increased cellular uptake of glucose and a higher rate of glycolysis when compared with normal cells.

The radiolabeled glucose analogue [18F] fluoro-2-deoxy-d-glucose (FDG) undergoes the same cellular uptake as glucose but, after phosphorylation, is not further metabolized and becomes trapped in cells. Accumulation of the isotope can then be identified using a PET detector. In two well-performed studies that evaluated the use of PET in the preoperative setting for lung cancer, nearly 20% of patients were up or down staged by PET evaluation. Integrated PET/CT is a modality that combines PET and CT, thus providing both anatomic and metabolic information.

As with any test, false positive and false negative results occur with FDG-PET. False positive results are generally due to metabolically active infectious or inflammatory lesions, and can produce substantial FDG accumulation. Examples include rheumatoid nodules, active tuberculous and fungal granulomas. In regions where infections with tuberculosis or endemic fungi (e.g. histoplasmosis, coccidiodomycosis, blastomycosis) are common, FDG-PET may have a lower specificity. Additionally, brown adipose tissue in adults at the base of the neck, in the supraclavicular region, and in the superior mediastinum can exhibit strong uptake of FDG. Normal or hyperplastic thymic tissue can be glucose-avid, which can lead to high uptake of FDG in the anterior mediastinum.

Tumors with relatively low metabolic activities may fail to concentrate enough FDG to be detected, as has been reported with some broncho-alveolar carcinomas, well differentiated adenocarcinomas, and carcinoid tumors. Rare metastatic lesions from renal cell, prostatic, or testicular carcinomas that do not concentrate detectable amounts of FDG have also been noted. Small tumors (<7 mm in diameter) may not be detected because of the small amount of FDG uptake.
Magnetic Resonance Imaging (MRI)
The role of magnetic resonance imaging (MRI) in the diagnosis and staging of lung cancer is limited by poorer spatial resolution, as compared with that of CT and affected by cardiac and respiratory motion artifacts. The magnitude of these limitations has diminished with newer MRI scanners. MRI may be helpful in the diagnosis of brain and adrenal metastasis, and in the assessment of mediastinal or chest wall invasion, as well as spinal cord involvement.

MRI is superior to CT in assessing the pericardium, heart, and great vessels. Coronal images are useful in demonstrating the extent of tumor in the subcarinal region, aortopulmonary window, and superior vena cava.

MRI is also valuable in assessing neurological involvement in Pancoast tumours and the identification of tumour rather than osteoporotic collapse in wedge fractures of the spine in lung cancer patients. This imaging modality may be used instead of CT in patients who have had previous adverse reactions to iodinated contrast media and in patients with significant renal impairment, as it does not require the use of intravenous enhancement with iodinated contrast media.

Bone scanning
Bone scan is indicated in patients who have focal bone pain or elevated alkaline phosphatase that are suspicious for bone involvement.

Bone metastases can be identified with a technetium 99m MDP nuclear medicine scan. Such bone scans were once common, but they have been largely displaced by PET for two major reasons. First, PET detects bone metastases with similar sensitivity and better specificity than bone scans\(^{20-21}\). Second, PET has the added advantage of being able to identify metastases in the visceral organs.

Sputum cytology
Sputum cytology has long been used as screening or diagnostic modality for early detection of lung cancer. However, these methods have limitations in sensitivity, specificity or utility to some degree. In recent years, researchers all over the world have done lots of work on finding and identifying biomarkers for the early diagnosis of lung cancer. Three samples are commonly required giving a sensitivity and specificity of 66% and 99%, respectively\(^{29}\).

Central lesions are more likely to yield positive cytologic results than are peripheral lesions. Patients with haemoptysis with or without a mass on chest radiographs should have sputum cytology obtained.

Transthoracic Needle Aspiration (TTNA)
Transthoracic needle aspiration, usually under CT or fluoroscopic guidance, helps to establish a histological diagnosis and stage known or suspected cancer. The sensitivity and specificity of TTNA are 90% and 97%, respectively\(^{29-31}\). Generally, if a lesion is less than 3 cm in size and lateral to the midclavicular line, bronchoscopy would not be the diagnostic procedure of choice.

TTNA is an easy and relatively safe procedure but carries a risk of pneumothorax reported at 22% to 45%\(^{30,31}\). Risk factors shown to increase the incidence of pneumothorax include the presence of emphysema, a smaller lesion size, and a greater depth of needle penetration from the pleural surface to the edge of the lesion.

Fiberoptic bronchoscopy
Bronchoscopy has a crucial role in assessment and biopsy of endobronchial tumours and sampling of mediastinal lymph nodes through transbronchial needle aspiration (TBNA). About 50% of patients with advanced-stage lung cancer will present with central airways involvement either by bulky endobronchial disease, extension into the airways, or extrinsic compression of the airways by the tumor or by lymphadenopathy. These patients commonly present with shortness of breath, unilateral wheezing, haemoptysis, and cough. Endobronchial lesions can be visualized easily
The yield with three or more biopsies is nearly 100% for centrally located lesions\textsuperscript{(32)}. Data from 4507 patients in 35 studies revealed that central endobronchial biopsies provide the highest sensitivity (74%), followed by brushings (61%) and washings (47%). The combination of these techniques provides a diagnosis in 88% of cases\textsuperscript{(29)}.

**Endoscopic ultrasound (EUS)**

Due to its superior ability to sample the posterior mediastinum through the esophageal wall, Endoscopic ultrasound (EUS) is a modality that has significantly impacted lung cancer staging. Pooled analysis of more than 1000 patients with lung cancer and mediastinal adenopathy in whom EUS with fine-needle aspiration is performed showed a sensitivity and specificity of 84% and 99.5%, respectively\textsuperscript{(33)}. Additionally, EUS has been studied in patients with known lung cancer without apparent enlarged mediastinal lymph nodes on CT, and it has detected mediastinal involvement (stage III or IV disease) in up to 42% of cases\textsuperscript{(34)}.

Furthermore, using this modality it is possible to stage lung cancer from locations outside the mediastinum. Using EUS the left lobe of the liver, a substantial part of the right lobe of the liver, and the left adrenal gland can be identified and sampled in 97% of patients\textsuperscript{(35-36)}.

**Endobronchial Ultrasound (EBUS)**

Endobronchial ultrasound with fine-needle aspiration (EBUS-TBNA) is a new technique which enables diagnosis of lung tumors and the assessment of mediastinal and hilar lymph nodes. This is a minimally invasive procedure which can be performed during bronchoscopy session on an outpatient basis using local anesthesia and conscious sedation, has a high sensitivity and specificity (90% and 100%, respectively)\textsuperscript{(33)}. It can be used to sample the high mediastinal, paratracheal, and subcarinal lymph nodes as well as the hilar lymph nodes. With a high diagnostic yield, EBUS renders more invasive mediastinoscopy unnecessary. Complications are uncommon, especially when sampling is performed real-time which permits the sampling of lymph nodes that are smaller than 5 mm in short axis or near major blood vessels.

**Mediastinoscopy, anterior mediastinotomy and thoracoscopy**

Mediastinoscopy remains the gold standard for invasively staging the mediastinum in patients with known or suspected lung cancer. It allows direct inspection and biopsies of lymph nodes and masses in the superior mediastinum with a reported sensitivity of 78%, and specificity of 100%\textsuperscript{(33)}. This procedure provides large tissue samples for diagnosis from the paratracheal, and anterior subcarinal region and often performed prior to thoracotomy. An extended cervical mediastinoscopy can be carried out to reach aortopulmonary and para-aortic lymph nodes. As with any surgical procedure, mediastinoscopy has risks and limitations. It requires general anesthesia, with a morbidity of 2% and a mortality of 0.08%\textsuperscript{(33)}. Potential complications include pneumothorax, haemorrhage, recurrent laryngeal or phrenic nerve paralysis, injury to trachea, oesophagus or thoracic duct.

The decision to perform mediastinoscopy or mediastinotomy for lung cancer staging remains a variable one that depends on local resources and personal experience. Video-assisted thoracoscopic surgery, is a valuable tool for the evaluation of pleural and lung abnormalities.

**Treatment of lung cancer**

Treatment of non small cell lung cancer

The overall 5-year survival for patients diagnosed with lung cancer is a dismal 14%\textsuperscript{(37)}, and has not changed substantially since the 1980s. The survival curves vary by stage, with earlier-stage lung cancer patients enjoying a much better survival than do patients with late-stage disease. Lung cancer treatment is based on the disease stage and
patients’ performance status. To improve outcomes, there has been a shift towards multimodality therapy (surgery, chemotherapy, radiotherapy, and molecular targeted therapies). Hence a multidisciplinary approach becomes mandatory and has currently been incorporated in a number of national and international guidelines. In these settings patients are evaluated by the major disciplines involved in their care. This “tumor board” includes chest physicians, thoracic surgeons, radiologists, pathologists, oncologists, as well as nursing and palliative care. Adoption of this approach will usually ensure that patients receive optimal treatment and can be considered for enrollment in clinical trials.

In broad terms, early-stage lung cancer (Stage I) is treated with surgery alone. Stage II lung cancer is commonly treated with surgery followed by adjuvant chemotherapy. Locally advanced lung cancer (stage IIIA and B) is treated with a combination of chemotherapy and radiotherapy. Supportive care alone or with chemotherapy is usually indicated in the advanced and metastatic disease (Stage IV). However, there are important exceptions to these general rules. For example patients with Stages I, II or III NSCLC who have good performance status (WHO 0 or 1) and whose disease can be encompassed in a radiotherapy treatment volume without undue risk of normal tissue damage would be most suitable for radical radiotherapy.

Prognostic factors for lung cancer
Analysis of large databases evaluating more than 5,000 patients with inoperable tumor considered seventy-seven prognostic factors. The strongest predictors of survival are good performance score (Karnofsky scale), lower extent of disease (stage), age, and absence of weight loss. Some reports have shown female gender to be a predictor of better survival, but this varies between studies. Performance score and the presence or absences of symptoms are predictors of outcome even with resectable early-stage disease. Absence of smoking or smoking cessation has been associated with improved survival.

Moreover, there seems to be an inverse correlated with survival in the maximal standard uptake value of the primary tumor on PET scanning.

In more recent years, there have been numerous reports that various molecular markers are associated with outcome. Some of the best known markers include K-Ras, epithelial growth factor receptor (EGFR), p53, p16, and Bcl-2. However, in many instances, the results are conflicting about the prognostic significance of these individual molecular markers. In a meta-analysis, K-Ras mutations were associated with poorer survival, especially in adenocarcinoma where the hazard ratio was 1.59 (95% CI 1.26–2.02).

Molecular targeted therapy for lung cancer
Although chemotherapy has recently produced promising results as neoadjuvant and adjuvant strategies for early-stage patients, treatment outcomes for NSCLC patients must still be considered disappointing. Study and testing of several molecular targets for NSCLC treatment has recently been facilitated by advances in the knowledge of tumor biology and mechanisms of oncogenesis. Targeted therapies are designed to interfere with specific aberrant biological pathways involved in tumorigenesis.

To date, only a few of these new agents can offer hope of a substantial impact on the natural history of the disease, and negative results are more commonly reported than positive ones. Nevertheless, clinically meaningful advances have already been achieved. In chemotherapy-refractory advanced NSCLC patients, gefitinib (Iressa) and erlotinib (Tarceva), two epidermal growth factor receptor tyrosine kinase inhibitors (EGFR-TKIs), represent a further chance for tumor control and symptom palliation for a
subset of patients otherwise eligible only for supportive care\textsuperscript{(49,50)}. In chemotherapy-naive advanced NSCLC patients, the combination of the anti–vascular endothelial growth factor (anti-VEGF) monoclonal antibody bevacizumab (Avastin\textsuperscript{®}) with chemotherapy has been demonstrated to produce better survival outcomes than chemotherapy alone\textsuperscript{(51)}. In two large phase III trials named Iressa NSCLC Trial Assessing Combination Therapy (INTACT)-1 and INTACT-2, no survival benefit in favor of platinum-based polychemotherapy (cisplatin plus gemcitabine or carboplatin plus paclitaxel) plus gefitinib over chemotherapy alone was reported\textsuperscript{(52,53)}. As observed for the other EGFR-TKI gefitinib, the combination of erlotinib with platinum-based polychemotherapy (cisplatin plus gemcitabine or carboplatin plus paclitaxel) has been demonstrated to confer no survival advantage over chemotherapy alone in two large phase III randomized trials, named TALENT and TRIBUTE\textsuperscript{(54,55)}. Based on the promising results of a previous phase II randomized trial\textsuperscript{(56)}, a very recent randomized phase III trial compared the combination of bevacizumab with chemotherapy (carboplatin and paclitaxel) versus chemotherapy alone in the treatment of advanced non-squamous NSCLC\textsuperscript{(51)}. Patients with squamous histology were excluded because of the risk for grade 5 hemoptysis reported in previous studies. In more than 850 enrolled patients, a statistically significant advantage in median survival was reported in favor of the combination of bevacizumab plus chemotherapy (12.5 months vs. 10.2 months in the bevacizumab and chemotherapy-alone arms, respectively; \( p = .0075 \)). In addition, the response rate (27\% vs. 10\%; \( p < .0001 \)) and progression-free survival time (6.4 months vs. 4.5 months; \( p < 0.0001 \)) favored the bevacizumab arm.

Small Cell Lung Cancer (SCLC)

Small cell lung cancer (SCLC) is typically characterized by its rapid doubling time, high growth fraction, and the early development of widespread metastases. Usually it presents as a centrally located lung mass and can be associated with obstructive pneumonia. SCLC accounts for about 15\% to 20\% of all lung cancers. This cell type has the strongest association with cigarette smoking and is rarely observed in a never-smoker. It is the cell type most commonly associated with paraneoplastic syndromes such as the syndrome of inappropriate (excessive) antidiuretic hormone secretion (SIADH), ectopic corticotropin secretion, Lambert-Eaton myasthenic syndrome (LEMS), and sensory neuropathy.

This tumour rarely (5\%) present as a solitary pulmonary nodule/mass. It is generally staged according to the old Veterans Administration Staging System and classified as limited (LD) or extensive (ED) stage. LD-stage disease is confined to one hemithorax, the mediastinum, and the ipsilateral supraclavicular lymph nodes. It is a disease that can be safely encompassed within one radiation portal without irradiating too much normal lung. ED stage is any disease spread beyond these sites. Malignant pleural effusion or disease extending to the contralateral supraclavicular or hilar lymph nodes is generally considered to be ED.

Approximately one third of patients have LD at diagnosis. LD-SCLC has a response rate of 70\% to 80\% with standard chemotherapy and thoracic radiotherapy, and a complete clinical response of 50\% to 60\%. In a meta-analysis of trials with chemotherapy alone versus combined chemotherapy and thoracic radiotherapy, survival was significantly better with combined-modality therapy\textsuperscript{(57)}. Chemotherapy usually consists of a platinum-based regimen. The two most commonly used regiments are etoposide and cisplatin or etoposide and carboplatin. Chemotherapy beyond four to six cycles has not been shown
to prolong survival. Although considered highly responsive to chemotherapy and radiotherapy, SCLC usually relapses and becomes refractory to treatment within one to two years.

The median survival time for LD-SCLC is now 18 to 20 months when patients are treated with concurrent chemoradiotherapy, and 20% to 25% of patients will be alive at 5 years.\(^{58-60}\) By contrast, the median survival time for ED-SCLC is 8 to 9 months, with 10% of patients or fewer alive at 2 years.\(^{61,62}\) There are virtually no 5-year survivors with ED-SCLC. In the unusual case of SCLC that presents as a peripheral nodule, the treatment of choice is surgical resection followed by adjuvant chemotherapy and possibly sequential thoracic radiotherapy. Careful preoperative staging should be performed in these individuals to rule out metastatic disease. Pre-resection mediastinoscopy should also be performed. If there are mediastinal node metastases, then surgery should be abandoned, and the patient treated with concurrent chemoradiotherapy. Five-year survival for peripheral SCLC that is treated with surgery and adjuvant therapy is approximately 30% to 40%.

Prophylactic cranial irradiation (PCI) is an area of controversy. Despite no agreement on optimal dose and possible neuropsychological sequelae, most oncologists recommend PCI in patients who achieve a complete remission with initial treatment. The reasons being that if a patient with SCLC achieves a complete remission, and then there is a 50% chance of development of cranial metastasis within the next 2 years.

A meta-analysis of seven randomized trials of PCI versus no PCI for patients in complete remission reported an observed beneficial effect after PCI, with a 5.4% increase in absolute survival (20.7% vs. 15.3%) at 3 years.\(^{63}\)

When patients relapse after initial therapy, the median survival is 3 to 4 months. There are no cures with second-line therapy. If a patient has been off treatment for 6 months or greater, then it is reasonable to use the same agents that he or she received initially. If initial therapy did not include a platinum agent, then second-line therapy should be with a platinum-containing doublet.

**Palliative care**

Early integration of palliative care with standard oncologic care in patients with advanced lung cancer resulted improved survival by few weeks and a clinically meaningful improvements in quality of life and mood. Previous data have shown that a lower quality of life and depressed mood are associated with shorter survival among patients with metastatic cancer.\(^{64,65}\)

Early integration of palliative care for patients with advanced disease is a clinically meaningful and feasible care model that has effects on survival and quality of life.\(^{66,67}\) This care model offers great promise for alleviating distress for patients with advanced disease and carers, and address critical concerns regarding the use of health care services at the end of life.

**Key Messages**

Lung cancer is the leading cause of cancer-related death and clinical outcome is directly related to stage at the time of diagnosis.

Non-invasive diagnostic and staging techniques has recently expanded to include PET, MRI, EBUS, and EUS, reducing the need for invasive procedures.

There is no role for lung cancer screening. NSCLC Stage I is treated with surgery alone. Stage II lung cancer is commonly treated with surgery followed by adjuvant chemotherapy. Locally advanced lung cancer (Stages IIIA and B) is treated with a combination of chemotherapy and radiotherapy. Supportive care alone or with chemotherapy is usually indicated in Stage IV.

Promising novel targeted therapies designed to interfere with tumorigenesis, are currently been evaluated.
References


57. PORT meta-analysis trialists group: post operative radiotherapy in non–small cell lung cancer: systematic review and meta-analysis of individual patient data from nine
62. Roth BJ, Johnson DH, Einhorn LH, et al. Randomized study of cyclophosphamide, doxorubicin, and vincristine versus etoposide and cisplatin versus alternation of these two regimens in extensive small cell lung cancer: a phase III trial of the