KESANS: International Journal of Health and Science
e-ISSN: 2808-7178, p-ISSN: 2808-7380
Web: http://kesans.rifainstitute.com/index.php/kesans/index

Overview of Lung Cancer

Ayu Indira Medika
General Practitioner, Indonesia
indirarara18@gmail.com

Article Information
Submitted: **27 November 2023**
Accepted: **01 December 2023**
Online Publish: **20 December 2023**

Abstract
The two main types of lung cancer are small cell carcinoma and non-small cell carcinoma. Lung cancer is a primary bronchogenic carcinoma. Patients who are diagnosed with lung cancer typically exhibit symptoms like hemoptysis, dyspnea, chronic cough, chest pain, or weight loss. Since the onset of symptoms typically indicates that a patient's stage has already progressed, screening with low-dose chest CT (LDCT) exams is advised for high-risk patients. Cytology and core biopsy specimens are the main sources of the diagnosis for these patients. Staging, histology, genetic, and immunotherapy biomarker tests form the basis of the treatment. The most often used pharmacological therapies include radiotherapy, adjuvant platinum-based chemotherapy, surgery, which might involve mediastinal lymph node dissection or lymph node sampling, as well as total removal of the tumor (typically stages I and II). Currently, meanwhile, immunotherapy is the most advanced form of treatment for NSCLC that is oncogenic driver negative.
Keywords: Immunotherapy; Air Pollution; Lung Cancer; Lung Malignancy; Cancer;

How to Cite **Ayu Indira Medika/Overview of Lung Cancer, Vol. 3, No. 3, 2023**
DOI https://doi.org/10.54543/kesans.v3i3.258
e-ISSN/p-ISSN **2808-7178 / 2808-7380**
Published by **Rifa'Isntitute**

Introduction

Lung cancer is the second most often diagnosed disease globally, accounting for 1.8 million fatalities and 2.2 million new cases expected for 2020. It is also the primary cause of cancer-related mortality. Lung cancer is the leading cause of cancer death in Indonesia, accounting for 12.6% of all cancer deaths. In 2018, lung cancer accounted for 8.6% of all cancer cases, trailing after breast, cervical, and colorectal cancer (Andarini *et al.*, 2023). Over 80% of lung cancer cases are caused by tobacco use, which also happens to be the world's greatest preventable cause of mortality (Thandra *et al.*, 2021). Nonetheless, outdoor air pollution was identified by the International Agency for Research on Cancer (IARC) in 2013 as a carcinogen that aggravates lung cancer (Kusumawardani, Indraswari and Komalasari, 2023). It is rare for lung cancer to exhibit obvious signs and symptoms in its early stages. Airway blockage or compression, tumor necrosis, and cavitation can all cause early symptoms like cough, hemoptysis, and dyspnea. The screening and diagnostic steps method should be clear and relevant given the high incidence of morbidity and death in lung cancer (Hana and Faizah, 2023).

Definition

The two main types of lung cancer, small cell, and non-small cell, are primary bronchogenic carcinomas. The information shown above is based on various histological examinations (Kim, Lee and Huang, 2022) (Xu *et al.*, 2021).

Epidemiology

Lung cancer mortality and incidence are increasing worldwide. In contrast with 2012 announced rates (1.8 million new cases and 1.6 million passings), GLOBOCAN assessed 2.09 million new cases (11.6% of absolute disease cases) and 1.76 million passings (18.4% of complete malignant growth passings) in 2018. This makes it the most common cancer and cause of cancer death in men and women combined, as well as the second most common cause of cancer-related death in women and the third most common type of cancer (Bade and Dela Cruz, 2020). Lung cancer accounted for 14.1% of all cancer cases in Indonesia in 2020, with 34,783 new cases reported, making it the most frequently diagnosed disease in men. According to data from the Republic of Indonesia's Ministry of Health, the prevalence of lung cancer is 9.89% in women and 16.77% in males (Kusumawardani, Indraswari and Komalasari, 2023).

Lung cancer was the highest incidence in the 50–70 age group, according to data analysis from the national referral hospital in Indonesia's 2008–2012 cancer registry (Asmara *et al.*, 2023). Significant differences have been seen in the incidence and demographic distribution of lung cancer between nations; these variations are influenced by factors such as economic development level and tobacco smoking rates. Even though cancer statistics in these countries are less reliable, it is anticipated that lung cancer incidence will rise in developing nations as a result of the recent rise in smoking prevalence in China, Indonesia, Eastern Europe, and the Northern and Southern parts of Africa (Bade and Dela Cruz, 2020).

Risk Factor

Age. Lung cancer affected both men and women on average at the age of 70. In the United States, Lung cancer is the leading cause of death for men and women over the age of 59 and 40. The shortening of telomeres, a decrease in NAD+ metabolite levels, and the loss of cells' capacity to both detect and repair DNA damage as well as act as a monitor for abnormal cells are all likely factors in biological ageing (Thandra *et al.*, 2021).

Gender. Men are more than twice as likely as women worldwide to get a lung cancer diagnosis and to pass away from the disease. The fact that men are more likely than women to smoke tobacco is the main cause of the gender gap. When it comes to NSCLC, women are more likely than men to have BRAF gene mutations and ALK gene rearrangements. Hormonal factors have also been proposed as a contributing factor. It has been observed that α oestrogen receptors (OR) are overexpressed in adenocarcinomas, and factors influencing oestrogen exposure, like menstrual cycle length, age at menarche and menopause, and parity, have varied degrees of correlation with lung cancer risk (Thandra *et al.*, 2021).

Family history. The gamble of cellular breakdown in the lungs is expanded by 1.7 times in those with a positive family history. Even after adjusting for prior smoking history, the risk increases by two to four times if the history is among first-degree relatives. The 5p15 locus, which contains the gene for telomerase reverse transcriptase (TERT), the 6p21 locus, which controls G-protein signaling, and the 15q25–26 loci, which have been linked to an expanded gamble of cellular breakdown in the lungs because of nicotine reliance, are among the chromosomal locales where varieties have been connected to an expanded heritable gamble of cellular breakdown in the lungs (Thandra *et al.*, 2021).

Etiopathogenesis

The carcinogens in tobacco smoke. Nicotine is the primary cause of tobacco addiction, while tar is the remaining total particle matter (PM) in cigarette smoke after water and nicotine have been eliminated. Tar exposure over time appears to be a significant contributor to the risk of lung cancer. Numerous substances, both organic and inorganic, such as benzene, vinyl chloride, arsenic, and chromium, as well as polycyclic aromatic hydrocarbons, aromatic amines, and N-nitrosamines, are found in mainstream smoke and have the potential to cause cancer. N-nitrosamines and polycyclic aromatic hydrocarbons must undergo metabolic activation to cause cancer. The tobacco-specific N-nitrosamines that arise from the nitridation of nicotine during tobacco processing and smoking are the agents of particular concern in lung cancer. 4-(methyltyramine)-1(3-pyridyl)-1-butanone appears to be the most significant N-nitrosamine specific to tobacco use that causes lung cancer. According to Bade and Dela Cruz (2020), the production of DNA adducts, their metabolites, and damage from free radicals are additional processes involved in the carcinogenesis of tobacco use (Bade and Dela Cruz, 2020).

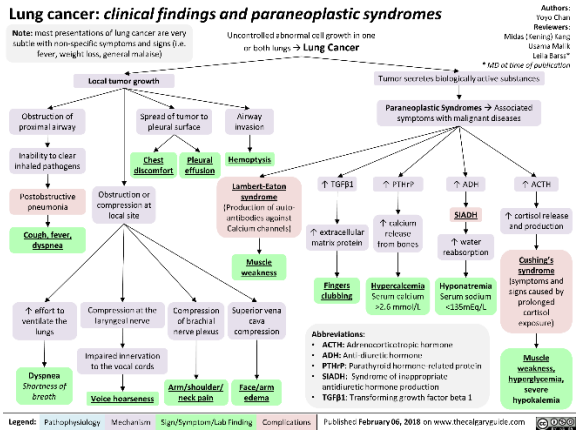

Figure 1. Pathogenesis of lung cancer.

E-cigarette vapor contains components such as formaldehyde, acetaldehyde, and reactive oxygen species in sufficient quantities to irritate the airways and epithelium of the lungs. According to Bade and Dela Cruz (2020), aerosols used in electronic nicotine delivery systems (ENDS) may include trace metals, nitrosamines, and polycyclic aromatic hydrocarbons, all of which have been linked to carcinogenesis (Bade and Dela Cruz, 2020).

Air Pollution. The highest quantities of smoke, Sulphur dioxide, and suspected particles have all been linked to air pollution, a major worldwide issue. It is commonly accepted that air pollution, specifically PM2.5, is a known cause of lung cancer. After smoking exposure, ambient air pollution outdoors is thought to be the second leading cause of lung cancer death worldwide; inside air contamination is believed to be the seventh driving reason (Berg *et al.*, 2023). O Cellular breakdown in the lungs risk has additionally been connected to openness to other inhalable synthetic compounds and outside surrounding air contamination (Turner *et al.*, 2020). We observe that the primary contributing factor in the case of squamous cell lung cancer appears to be the combined inhalation of SO2 and NO2 (Gawełko *et al.*, 2022).

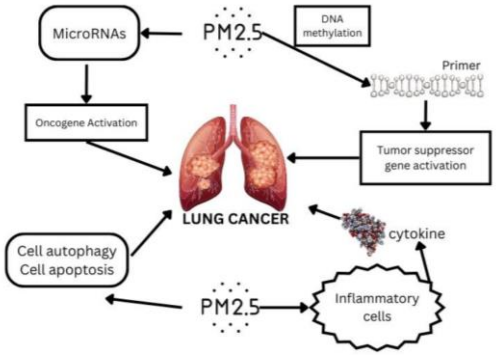

Figure 2. Air pollution and its role in the pathogenesis of lung cancer (Kusumawardani, Indraswari and Komalasari, 2023).

Through DNA methylation and microRNA dysregulation, PM2.5 causes tumor suppressor gene inactivation and oncogene activation in lung cancer. Modification of the tumor microenvironment is also observed in inflammatory cells triggered by PM2.5.

Changes in epithelial cell activity, oxidative stress, and antioxidant and inflammatory responses are brought on by PM2.5 exposure. Through increased expression of DUOX1 in bronchial epithelial cells and both NADPH and DUOX1 from alveolar and bronchial epithelial cells, PM2.5 exposure increases cell oxidative stress.

Furthermore, PM damages mitochondria, which hinders bronchial epithelial cells' ability to phosphorylate oxidatively. An inflammatory response can also be brought on by exposure to pollutants. NF-kβ is one inflammatory marker whose expression rises in response to exposure to fine particles. It is well known that the onset of acute inflammation is correlated with increased expression of chemokines, cytokines, and proteins (TNF, IL-1), as well as heme oxygenase-1 (HO-1), which is linked to angiogenesis and autophagy, in both in vitro and in vivo settings (Kusumawardani, Indraswari and Komalasari, 2023).

When the nucleotide sequence is changed during replication, DNA damage happens. Oncogene activation or inactivation of tumor suppressor genes may result from it. The mutations that have been linked to the pathophysiology of lung cancer are the result of a long-term accumulation of DNA damage. Constant irritation and pneumonic vascular endothelial brokenness can be exacerbated by switch record of p53, autophagy, and a huge height of vascular endothelial development factor (VEGF) brought about by openness to PM2.5.

Additionally, aberrant cell development, damage, and apoptosis can result from p53 mutations, all of which contribute to the pathophysiology of lung cancer. Cellular reactions to exposure to air pollution are known as epigenetic alterations, and they can take the form of altered histones, DNA methylation, or non-coding RNA. The guideline of post-transcriptional quality articulation, which incorporates separation, demise, and expansion, is worked with by miniature RNA (miRNA). MiRNAs like miR-21, miR-222, miR-155, miR-425, and miR-126-3p, which are important regulators, promoters, or inhibitors of angiogenesis and inflammation, are linked to exposure to air pollution and lung cancer (Kusumawardani, Indraswari and Komalasari, 2023).

Exposures at Work (Asbestos). Some people argue that asbestosis is a prerequisite for lung cancer linked to asbestos exposure. According to certain reports, asbestos can cause cancer even in the absence of asbestosis (Bade and Dela Cruz, 2020). According to Suraya et al. (2020), asbestos is the most prominent occupational carcinogen, responsible for between 55 and 85% of occurrences of occupational lung cancer (Suraya *et al.*, 2020).

Infections. Due to its detection in bronchial squamous cell lesions, Lung cancer has been linked to the human papillomavirus (HPV). It has been demonstrated that these HPV serotypes' E6 and E7 oncogenes immortalize highly susceptible to genetic damage human tracheal epithelial cells. A rare type of lung cancer called lymphoepithelioma-like carcinoma shows a high correlation with the Epstein-Barr virus. The inflammation caused by the proteins found in Chlamydia pneumoniae can result in cellular damage and damage to DNA, which can give cancer a selection advantage. Lung cancer etiology may be

influenced by inflammation and scarring associated with tuberculosis. HIV increases the risk of lung cancer through mechanisms that most likely involve immunomodulation, chronic inflammation, and other infections (Bade and Dela Cruz, 2020).

Diagnosis

Clinical Manifestation

It is rare for lung cancer to exhibit obvious signs and symptoms in its early stages. Patients will experience a range of symptoms associated with the main tumor, metastases, or paraneoplastic diseases as the disease progresses. According to Hana and Faizah (2023), tumor necrosis, cavitation, and airway blockage or compression may be the source of early symptoms like cough, hemoptysis, and shortness of breath. Patients who are diagnosed with lung cancer typically exhibit symptoms like hemoptysis, dyspnea, chronic cough, chest pain, or weight loss (Hana and Faizah, 2023). Regretfully, the appearance of symptoms typically indicates that a condition has progressed (Andarini *et al.*, 2023).

The lesion's location affects both the symptoms' presence and intensity. Individuals with peripherally situated cancers may not exhibit as many symptoms as those with central bronchial tumors. As lung cancer advances, distant metastases and intrathoracic dissemination are possible outcomes. Depending on the metastases and pattern of spread, the symptoms may change. From an advanced stage of lung cancer, the most common metastasis site is the bone, followed by the brain and liver.

There may be general symptoms including osteodynia, headache, anorexia, weakness, and inadvertent weight loss. The endocrine system is often linked to paraneoplastic syndrome in lung cancer cases. Hypercalcemia, ectopic Cushing syndrome, and the syndrome of inappropriate antidiuretic hormone secretion (SIADH) are endocrine paraneoplastic syndromes that can occur with lung cancer (Hana and Faizah, 2023).

Examining

The best method for reducing lung cancer mortality and helping to diagnose lung cancer at an early stage is low-dose chest (Lam *et al.*, 2023). It is highly advised to undergo LDCT every two years. Males over 45, those with a history of smoking or secondhand smoke exposure, exposure to chemicals at work or in the environment, and those with fibrosis lung disorders are considered high-risk persons.

More youthful individuals (north of 40) who have the previously mentioned gambles and a family or hereditary history of malignant growth ought to be firmly watched. The risk assessment is used to determine who is most likely to develop lung cancer. Age and tobacco use are two examples of weighted factors (Andarini *et al.*, 2023).

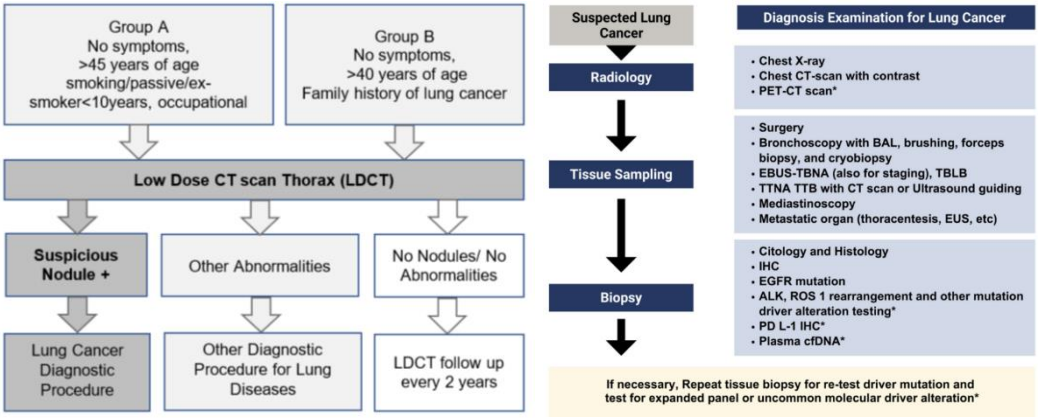

Figure 3. Sequential screening and diagnostic examinations for the diagnosis of lung cancer (Asmara *et al.*, 2023)(Andarini *et al.*, 2023).

A common definition of pulmonary nodules is rounded or irregular opacities that can be up to 3 cm in diameter and are either well or poorly defined. Finding non-calcified nodules, the majority of which are solid, that may raise suspicions for lung cancer is one of the goals of LDCT. If one or more lung nodes are discovered, more testing is required to determine if the nodule is the result of inflammation or cancer.

For additional treatment, a subsequent LDCT is completed 1 after 2 months. In contrast, if no lung nodules or other non-cancerous abnormalities (such as an aortic aneurysm, coronary artery calcification, or tumors/benign disease outside of the chest) are found after every 2-year control with LDCT, a follow-up for other respiratory diseases is recommended (Andarini *et al.*, 2023).

Further Analysis

After the identification of high-risk nodules, to confirm the diagnosis, determine the course of treatment, and forecast the patient's prognosis, additional testing may be required (Asmara *et al.*, 2023). CT filters are a more successful radiologic assessment for the location of cellular breakdown in the lungs, regardless of whether chest radiographs are the significant technique used to analyze thought cellular breakdown in the lungs. Since cellular breakdown in the lungs should not be visible on a chest X-beam, a CT check is oftentimes used to recognize and evaluate the sickness.

A good radiological modality to determine the location, size, and growth of a tumor in a close intrathoracic structure is a CT scan with contrast. For the assessment of lung cancer, PET/CT imaging is crucial. This method is thought to be the most effective for assessing treatment outcomes, identifying metastases, and defining cancer staging. As PET/CT can identify metabolic alterations in malignancy, it is more sensitive than chest X-rays and CT scans, two other imaging modalities. This ability will be valuable in recognizing disease before any apparent morphological modifications happen. Lung cancer evaluation does not typically involve MRI.

Due to the low organ density of the lung, this is the case. MRI, however, is more sensitive than CT and PET/CT at detecting tumor infiltration into the chest wall and

mediastinum. Additionally, it is more sensitive in detecting tumor metastases to the spine and brain (Hana and Faizah, 2023). Tumor metastases to the liver, kidney, lymph nodes, and other visceral organs can be assessed with ultrasonography. White light bronchoscopy (WLB) is the most common diagnostic procedure for making a definitive histological diagnosis of lung cancer (Nooreldeen and Bach, 2021).). Lung cancer can be directly localized with bronchoscopy, which can also be utilized to collect biopsy and cytology samples (Hana and Faizah, 2023).

Examination of Histopathology

The diagnosis of lung cancer in patients who appear in advanced stages and are incurable is mostly based on cytology and biopsy specimens (Nicholson *et al.*, 2022). Core biopsy is the recommended sample technique for initial lung cancer diagnosis. (Rajadurai *et al.*, 2020). Lung tissue biopsy samples must contain sufficient tissue material for histopathology methods to identify the subtype of lung cancer repeating the biopsy carries a higher risk of complications and delays the start of treatment (Nooreldeen and Bach, 2021).

Therefore, the first biopsy is essential for confirming an early diagnosis. Cancer of the lungs can be broken down into two types: based on how the histology looks under a microscope, small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC) (Hana and Faizah, 2023).

SCLC stands for Small Cell Lung Cancer

15% of cases of lung cancer are SCLC (Hana and Faizah, 2023). This is a peri-hilar mass, a central tumor emerging from the submucosa of the airway. As indicated by histological examinations, neuroendocrine cells of the basal bronchial epithelium are the wellspring of this specific kind of disease (Nooreldeen and Bach, 2021).

Under a microscope, SCLC is represented by cells that are round to fusiform, have little cytoplasm, and have nuclear chromatin that is finely granular. Often, extensive necrosis is discovered. This granular chromatin is a "salt and paper" characteristic of SCLC that can be observed in a cytologic material (Hana and Faizah, 2023).

This cancer is unique in that it can have limited or extensive stages and can spread to the liver, brain, and bone. The ipsilateral mediastinum, the ipsilateral mediastinal or supraclavicular lymph nodes, and a single radiation point are the only locations where the restricted SCLC stage can occur. As long as it is located on the same side of the cancer chest, the supraclavicular lymph nodes are classified as belonging to that type (Nooreldeen and Bach, 2021).

Non-Small Cell Lung Carcinoma (SCLC)

SCC is the most prevalent subtype of lung cancer, accounting for approximately 85% of cases of NSCLC (Hana and Faizah, 2023). This kind of cancer is classified by phases and histologically separated into squamous cell carcinoma, large-cell carcinoma, and adenocarcinoma.

The American Joint Committee on Cancer (AJCC) developed the staging terminology, which is known as the TNM staging system. The size of the primary tumor (T), the extent to which the tumor has spread to lymph nodes (N), and the presence of metastases (M) are all factors that are used in the TNM method to help determine the stage of cancer. Depending on the characteristics of the tumor, atelectasis or incomplete lung inflate may occur in a portion of the lung in the T2 category.

It was discovered that the tumor extended more than 2 centimeters from the carina into the major bronchus and the visceral pleura. This continues at the T3, where the entire lung becomes infected with atelectasis. Less than 2 cm from the carina, the tumor reaches the major bronchus and invades the diaphragm, chest wall, mediastinal pleura, and phrenic nerve.

Tumor invasion of the lung carina, vertebral bodies, and mediastinal organs occurs in stage T4, also known as the invasion stage. Regarding lymph node involvement, which is classified as N0 to N3, the involvement varies depending on the stage, ranging from no lymph nodes to ipsilateral to contralateral involvement. Only in the presence of M1, where malignant pleural effusion, bilateral lesions, and distant metastases are visible, is metastasis staged. Conversely, M0 denotes the lack of metastasis (Nooreldeen and Bach, 2021).

Biomolecular Examination

A molecular test of these genetic changes is typically the primary factor considered when deciding on a patient's course of treatment. Molecular testing can also provide precise information regarding cancer staging and prognosis prediction. There are several ways to test for certain genetic changes in lung cancer. In clinical practice, a molecular diagnostic establishes a patient's eligibility for a particular tyrosine kinase inhibitor (TKI) medication (Hana and Faizah, 2023).

Sub-atomic biomarkers could be useful in checking the movement of the disease and the reaction to treatment, as well as in the early and non-invasive diagnosis of lung cancer (Wadowska *et al.*, 2020). An epidermal growth factor receptor (EGFR) mutation is found in nearly 40% of NSCLC cases, and mutations in the anaplastic lymphoma kinase (ALK) gene are found in 13% of adenocarcinoma patients with wild-type EGFR (Rajadurai *et al.*, 2020).

ALK rearrangement and EGFR mutation play a major role in the pathophysiology of NSCLC. About 2–5% of NSCLC patients with brain metastases, which are often discovered at an advanced stage, have ALK rearrangement. According to the CAP/IASLC/AMP guidelines, atomic testing for EGFR transformation exons 18-21 and adjustments including ALK involving fluorescence in situ hybridization (FISH) ought to be performed on completely progressed stage lung adenocarcinomas. The prevalent EGFR TKI sensitizing mutation that results in TKI insensitivity should be detectable by an EGFR assay.

Regardless of clinical features, ROS1 testing was added to the recommendation in 2018 as a required biomolecular test for all patients with adenocarcinoma. ROS 1 (c-ros

oncogene 1) is typically present in young, non-smoking persons and is present in 1-2% of NSCLC patients. If standard EGFR, ALK, and ROS1 testing yield negative results, BRAF, MET, RET, and HER2 testing is not advised. On the other hand, Hana and Faizah (2023) state that KRAS should be done as part of wider testing panels, either at the beginning or if the results of EGFR, ALK, and ROS1 testing are negative. (Hana and Faizah, 2023).

Oversight

Operation

Treatment for lung cancer in stages I, II, and IIIA can involve surgery, which includes lobectomies, segmentectomies, sub lobar resections, pneumonectomy, and mastectomy.

While segmentectomy or sublobar resection are options for patients with cardiovascular comorbidities or reduced lung capacity, anatomical resection gives the highest chance of survival. Only difficult and high-risk cases should be treated with an open thoracotomy. Another technique is mastectomy with video-assisted thoracoscopic surgery, often known as thoracotomy, which is reserved for extremely specific stage IV cases due to its shorter hospital stay and lower death rate than open thoracotomy (Asmara *et al.*, 2023).

A combination of three treatments is typically offered to patients with stages I to II NSCLC: radiotherapy; adjuvant platinum-based chemotherapy; and surgery, which can involve mediastinal lymph node dissection or lymph node sampling, as well as complete resection of the tumor (usually stages I and II) (Kim, Lee and Huang, 2022).

Systemic Intervention

In Indonesia, chemotherapy is still the primary systemic treatment for both SCLC and NSCLC. It is applied at every stage of lung cancer. Chemotherapy based on platinum is widely accessible. Chemotherapy can be used as a postsurgical adjuvant therapy or as a neoadjuvant for lung cancer in its early stages. In order to provide palliative care or extend survival, the management strategy for lung cancer is multimodality, combining other modalities (radiation) with systemic treatment options (chemotherapy, immunotherapy, and targeted therapy) (Asmara *et al.*, 2023).

Nowadays, the most advanced form of treatment for oncogenic driver-negative NSCLC is immunotherapy. In advanced non-small cell lung cancer, immunotherapy still shows a significant overall survival benefit. In tumors with (high) positive PD-L1 expression, pembrolizumab or atezolizumab is better as a monotherapy than first-line chemotherapy (Alexander, Kim and Cheng, 2020).

Every three weeks for three to four cycles, doctors in clinical practice administer adjuvant platinum-based chemotherapy (platinum vinorelbine/pemetrexed [adenocarcinoma only]/taxanes/gemcitabine) to resected patients with stage IB, IIA, IIB, and IIIA NSCLC. The mainstay of care for unresectable stage III NSCLC cases is concurrent chemoradiotherapy, which involves chemotherapy followed by sequential

radiotherapy. According to the results of the PACIFIC clinical preliminary, durvalumab significantly expanded the movement free endurance of patients with stage III, hopeless non-little cell cellular breakdown in the lungs (NSCLC) who did not have their sickness progress after attendant chemoradiotherapy when contrasted with fake treatment.

Patients with advanced non-small cell lung cancer (NSCLC) who do not have targetable drivers may be given chemotherapy as a treatment option. Platinum-based chemotherapy, for example, cisplatin or carboplatin in blend with paclitaxel, docetaxel, gemcitabine, pemetrexed (for adenocarcinoma just), and vinorelbine, is prompted as the first-line chemotherapy routine. Original (gefitinib and erlotinib) and second-age (afatinib) EGFR tyrosine kinase inhibitors (TKI) are prompted for patients with cutting edge non-little cell cellular breakdown in the lungs (NSCLC) that have targetable drivers for NSCLC with EGFR change (Asmara *et al.*, 2023).

Many chemotherapeutic drugs exhibit effectiveness against small cell lung cancer (SCLC), both singly and in combination. However, etoposide-platinum has been shown to be the most effective initial line treatment (Saltos, Shafique and Chiappori, 2020). Treatment options for limited-stage SCLC typically consist of radiation, chemotherapy based on platinum (cisplatin/carboplatin with irinotecan and etoposide as the first option) and surgery (in very early stages that are amenable to surgery). Patients with extensive-stage SCLC may or may not receive chemotherapy that includes carboplatin, etoposide, or irinotecan in addition to palliative radiotherapy on primary and metastatic lesions (Asmara *et al*., 2023).

Radiotherapy

One essential lung cancer treatment option is radiation therapy. It can be used as definitive, neoadjuvant, adjuvant, or palliative therapy at any stage of NSCLC or SCLC with the goal of curing the disease. Another palliative treatment for superior vena cava syndrome is radiation therapy. Intensity-modulated radiation therapy is the fundamental radiation treatment method utilized for lung cancer patients in Indonesia.

It is advised to use more sophisticated technologies when they are available, such as dynamic breathing control, stereotactic body radiotherapy, four-layered registered tomography (CT), positron outflow tomography (CT), volumetric regulated circular segment treatment, and picture directed radiation treatment (Asmara *et al.*, 2023). Stereotactic ablative body radiation, or SABR, is the current standard of care for patients with peripherally located stage I–IIIA NSCLC that is either surgically refractory to surgery or medically inoperable. Thoracic radiotherapy for confined stage SCLC is a typical component of the executives; Radiotherapy with concurrent chemotherapy is the standard of care for most patients with stage III NSCLC. Radiation therapy should be administered earlier (Vinod and Hau, 2020).

Stereotactic radiotherapy or surgery combined with stereotactic radiotherapy is advised for patients with fewer than three brain metastases. Whole brain radiation is advised when there are more than three brain metastases, even if treatment would not enhance neurocognitive symptoms or overall survival (Kim, Lee and Huang, 2022).

Prognosis

An expected 1,761,000 passings from cellular breakdown in the lungs were accounted for in 2018, making up 18.4% of all disease related fatalities all around the world. As of 2010–2016, the US has a 20.5% 5-year survival rate for lung cancer, according to SEER (Thandra *et al.*, 2021).

Lung cancer's poor prognosis due to its advanced state most patients (>75%) have either a stage III or IV disease at diagnosis—is the primary threat to public health. Furthermore, Nooreldeen and Bach (2021) found a high correlation between the illness stage and the prognosis of patients with lung cancer (Nooreldeen and Bach, 2021). According to Thandra et al. (2021), the 5-year survival rate is 59.0% for patients with localized cancer at diagnosis (stages I–II), 31.7% for those with regional disease (stage III), and 5.8% for those with metastatic disease (stage IV) (Thandra *et al.*, 2021).

Only 26% of all patients with non–small cell lung cancer (NSCLC) is alive 5 years after diagnosis. Five years after diagnosis, just 26 percent of individuals with non-small cell lung cancer (NSCLC) are still living. When patients undergo historical cytotoxic chemotherapy regimens, the 5-year relative survival rate for metastatic illness is about 6%. With 5-year survival rates varying from 15% to 50%, depending on the biomarker, certain patients with metastatic non-small cell lung cancer (NSCLC) who are qualified for more recent targeted therapies or immunotherapies are, nevertheless, living longer (Ettinger *et al.*, 2021).

References

Alexander, M., Kim, S. Y. and Cheng, H. (2020) 'Update 2020: Management of Non-Small Cell Lung Cancer', *Lung*. Springer, pp. 897–907. doi: 10.1007/s00408-020-00407-5.

Andarini, S. *et al.* (2023) 'Indonesian Society of Respirology (ISR) Consensus Statement on Lung Cancer Screening and Early Detection in Indonesia', *Jurnal Respirologi Indonesia*. Perhimpunan Dokter Paru Indonesia, 43(2), pp. 144–150. doi: 10.36497/jri.v43i2.455.

Asmara, O. D. *et al.* (2023) 'Lung Cancer in Indonesia', *Journal of Thoracic Oncology*. Elsevier Inc., pp. 1134–1145. doi: 10.1016/j.jtho.2023.06.010.

Bade, B. C. and Dela Cruz, C. S. (2020) 'Lung Cancer 2020: Epidemiology, Etiology, and Prevention', *Clinics in Chest Medicine*. W.B. Saunders, pp. 1–24. doi: 10.1016/j.ccm.2019.10.001.

Berg, C. D. *et al.* (2023) 'Air Pollution and Lung Cancer: A Review by International Association for the Study of Lung Cancer Early Detection and Screening Committee', *Journal of Thoracic Oncology*. Elsevier Inc. doi: 10.1016/j.jtho.2023.05.024.

Ettinger, D. S. *et al.* (2021) 'Non-small cell lung cancer, Version 2.2021 featured updates to the NCCN guidelines', *JNCCN Journal of the National Comprehensive Cancer Network*. Harborside Press, pp. 254–266. doi: 10.6004/jnccn.2021.0013.

Gawełko, J. *et al.* (2022) 'Association between Air Pollution and Squamous Cell Lung Cancer in South-Eastern Poland', *International Journal of Environmental Research and Public Health*. MDPI, 19(18). doi: 10.3390/ijerph191811598.

Hana, J. and Faizah, N. N. (2023) 'Diagnostic Approach of Lung Cancer: A Literature Review', *Jurnal Respirasi*. Universitas Airlangga, 9(2), pp. 141–149. doi: 10.20473/jr.v9-i.2.2023.141-149.

Kim, J., Lee, H. and Huang, B. W. (2022) *Lung Cancer: Diagnosis, Treatment Principles, and Screening*. Available at: www.aafp.org/afpAmericanFamilyPhysician487.

Kusumawardani, I. A. J. D., Indraswari, P. G. and Komalasari, N. L. G. Y. (2023) 'Air Pollution and Lung Cancer.', *Journal of Respirology*, 9(2), pp. 150–158. doi: 10.20473/jr.v9-I.2.2023.150-158.

Lam, D. C. L. *et al.* (2023) 'Lung Cancer Screening in Asia: An Expert Consensus Report', *Journal of Thoracic Oncology*. Elsevier Inc. doi: 10.1016/j.jtho.2023.06.014.

Nicholson, A. G. *et al.* (2022) 'The 2021 WHO Classification of Lung Tumors: Impact of Advances Since 2015', *Journal of Thoracic Oncology*. Elsevier Inc., pp. 362–387. doi: 10.1016/j.jtho.2021.11.003.

Nooreldeen, R. and Bach, H. (2021) 'Current and future development in lung cancer diagnosis', *International Journal of Molecular Sciences*. MDPI AG. doi: 10.3390/ijms22168661.

Rajadurai, P. *et al.* (2020) 'Lung Cancer in Malaysia', *Journal of Thoracic Oncology*. Elsevier Inc, pp. 317–323. doi: 10.1016/j.jtho.2019.10.021.

Saltos, A., Shafique, M. and Chiappori, A. (2020) 'Update on the Biology, Management, and Treatment of Small Cell Lung Cancer (SCLC)', *Frontiers in Oncology*. Frontiers Media S.A. doi: 10.3389/fonc.2020.01074.

Suraya, A. *et al.* (2020) 'Asbestos-related lung cancer: A hospital-based case-control study in Indonesia', *International Journal of Environmental Research and Public Health*. MDPI AG, 17(2). doi: 10.3390/ijerph17020591.

Thandra, K. C. *et al.* (2021) 'Epidemiology of lung cancer', *Wspolczesna Onkologia*. Termedia Publishing House Ltd., pp. 45–52. doi: 10.5114/wo.2021.103829.

Turner, M. C. *et al.* (2020) 'Outdoor air pollution and cancer: An overview of the current evidence and public health recommendations', *CA: A Cancer Journal for Clinicians*. Wiley, 70(6), pp. 460–479. doi: 10.3322/caac.21632.

Vinod, S. K. and Hau, E. (2020) 'Radiotherapy treatment for lung cancer: Current status and future directions', *Respirology*. Blackwell Publishing, pp. 61–71. doi: 10.1111/resp.13870.

Wadowska, K. *et al.* (2020) 'Genetic markers in lung cancer diagnosis: A review', *International Journal of Molecular Sciences*. MDPI AG, pp. 1–24. doi: 10.3390/ijms21134569.

Xu, K. *et al.* (2021) 'Progress of exosomes in the diagnosis and treatment of lung cancer', *Biomedicine and Pharmacotherapy*. Elsevier Masson s.r.l. doi: 10.1016/j.biopha.2020.111111.