Review Article

A Comprehensive Review of Lung Cancer with Special Emphasis on Causes, Diagnosis, and Treatment: A Review

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ABSTRACT

One of the most prevalent malignant cancers in the majority of nations, lung cancer is the primary cause of cancer-related deaths globally. Patients with lung cancer continue to have inadequate survival rates despite ongoing advancements in diagnosis and treatment. Long-term smoking is still the most significant risk factor for the development of lung cancer, according to numerous epidemiological and experimental studies carried out as early as the 1970s. The authors of the study provide the most recent information on the molecular features, treatment, pathophysiology, and epidemiology of this malignancy. Lung cancer is the leading cause of cancer-related fatalities worldwide and one of the most common malignant malignancies in most countries. Despite continuous improvements in detection and therapy, lung cancer patients still have low survival rates. Numerous epidemiological and experimental investigations conducted as early as the 1970s have shown that long-term smoking is the most important risk factor for the development of lung cancer. The study's authors offer the most up-to-date details on the pathophysiology, epidemiology, therapy, and molecular characteristics of this cancer.

Keywords: Lung Cancer, Non-Small Cell Lung Cancer, Small-Cell Lung Cancer, Smoking, Chemotherapy.

INTRODUCTION

Lung cancer is a malignancy that begins in the lung tissue (bronchi, alveoli, etc.) and can spread (metastasize) to other organs.

There are two broad types:

Non-Small Cell Lung Cancer (NSCLC) — the more common form, accounting for roughly 85% of cases.

Small Cell Lung Cancer (SCLC) — less common but typically more aggressive.

Why the distinction matters: the subtype affects how the disease behaves, how fast it progresses, and what treatments can work. In the United States and around the world, lung cancer continues to be the leading cause of cancer-related fatalities for both men and women. Globally, the incidence of women is rising while that of men is gradually declining. Unquestionably, 85–90% of lung cancer patients develop bronchogenic carcinoma as a result of tobacco usage.

Additionally, there is proof that second hand smoke and environmental tobacco exposure can induce lung cancer in people who have never smoked. Lung cancer has been linked to other environmental exposures such pollution and indoor radon. Numerous occupational agents have been found to be either independent or contributory risk factors for bronchogenic cancer. Dietary and genetic variables have also been suggested as possible risk factors.

Lastly, research into biological indicators that may raise the risk of smoking-related carcinogenesis is becoming more popular due to developments in molecular biology. Knowledge of gene polymorphisms in lung tumours and their clinical usefulness is evolving. Over the past century, lung cancer has evolved from a rare and obscure disease to the most prevalent cancer worldwide and the leading cause of cancer-related deaths. The British writer Hasse was only able to locate 22 lung cancer cases that had ever been published in the late 1840s. [1]

History:

The term "lung cancer" was first used in clinical oncology around the start of the 20th century. Although lung tumour nomenclature has changed over time, understanding the causes of this disease entity was essential to medical history.

Based on many autopsy studies, Harting and Hesse verified in 1879 that miners were a group that was especially prone to the development of proliferative lesions in the lung tissue.

Since the 1930s, there has been a notable rise in the incidence and death of lung cancer due to smoking, which has made it feasible to determine that nicotine smoke is currently the most harmful risk factor.

Based on observations of several dozen lung cancer patients, Ochsner and DeBakey's research, which was reported at the time, supported the rise in lung cancer incidence seen in patients who smoked heavily throughout the first half of the 20th century [19–21]. Retrospective observations from the United States and Britain were released nearly simultaneously in 1950. They included scientific data and offered unified conclusions regarding the revolutionary significance of tobacco smoke exposure.[2]

Types of Lungs Cancer:

There are two main types of lung cancer: small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC). A third less common type of lung cancer is called carcinoid.

Small Cell Lung Cancer (SCLC):

There are two different types of small cell lung cancer: small cell carcinoma and mixed small cell/large cell cancer or combined small cell lung cancer. The types of small cell lung cancer are named for the kinds of cells found in the cancer and how the cells look when viewed under a microscope. Small cell lung cancer is almost always associated with cigarette smoking.

Non-Small Cell Lung Cancer (NSCLC):

Non-small cell lung cancer is more common. It makes up about 80 percent of lung cancer cases. This type of cancer usually grows and spreads to other parts of the body more slowly than small cell lung cancer does.

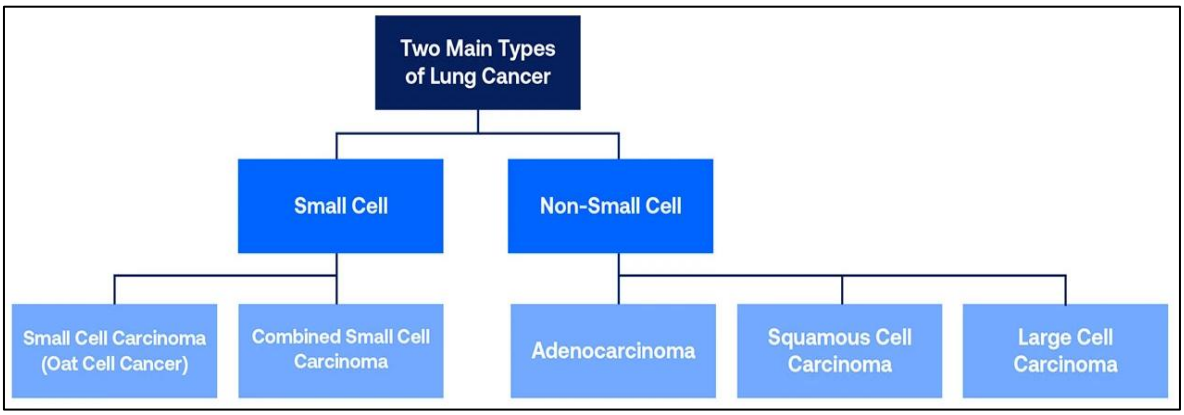

Figure 1: Classification of Lung Cancer[2]

There are three different types of NSCLC:

1. **Adenocarcinoma:** A form of NSCLC often found in an outer area of the lung. It develops in the cells of epithelial tissues, which line the cavities and surfaces of the body and form glands.
2. **Squamous cell carcinoma:** A form of NSCLC usually found in the centre of the lung next to an air tube (bronchus).
3. **Large cell carcinoma:** A form of NSCLC that can occur in any part of the lung and tends to grow and spread faster than adenocarcinoma or squamous cell carcinoma[3].

Epidemiology of Lung Cancer:

As of right now, lung cancer is the most often diagnosed malignant tumour and the leading cause of cancer-related death worldwide[24]. The most common type of cancer worldwide is lung cancer. Based on revised predictions from the International Agency for Research on Cancer (IARC), the following are global cancer statistics by world regions for 2022. Almost 20 million new cases of cancer were reported in 2022 and 9.7 million cancer deaths (including NMSCs).

One in five men and women are thought to have cancer at some point in their lives. Cancer claims the lives of about one in nine men and one in twelve women. In 2022, lung cancer was the most prevalent type of cancer. It affected 2.5 million new cases, or one in eight cancer cases worldwide (12.4% of all cancer cases). Breast cancer (11.6%), colorectal cancer (9.6%), prostate cancer (7.3%), and stomach cancer (4.9%) were the next most prevalent cancers among women. With an anticipated 1.8 million deaths (18.7%), lung cancer was also the most common cause of cancer-related mortality. Colorectal cancer (9.3%), liver cancer (7.8%), breast cancer in women (6.9%), and stomach cancer (6.8%) occupied the following positions. In terms of both cases and fatalities, lung cancer and breast cancer were the most prevalent cancers in men and women, respectively[4-8].

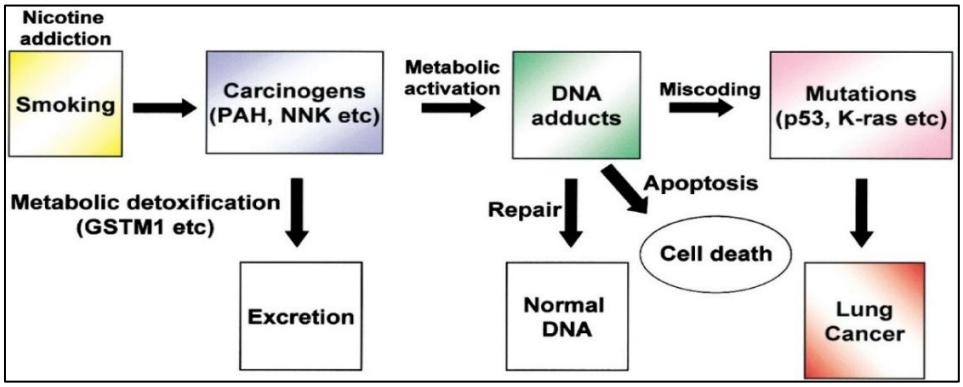

Figure 2: Nicotine addiction, tobacco smoke carcinogens, and the pathogenesis of lung carcinomas[9-12]

Pathogenesis of Lung Cancer: Lung cancer's molecular pathogenesis is a complex and diverse process. Numerous genetic variables and epigenetic modifications (such as point mutations, amplifications, insertions, deletions, and translocations) can lead to lung cancer. This is especially linked to the suppression of tumour suppressor pathways and the activation of a growth-promoting pathway. [9-12]

The accumulation of several genetic and epigenetic alterations in the cell nucleus over an extended period of time should be considered the biological underpinning of lung cancer. When a particular cell escapes the systems that control its division and placement, the cancer process begins. Its cell cycle is identical to that of normal cells, but it becomes insensitive to signals from other cells and does not subject to regulatory processes. Any neoplastic transformation is mostly caused by abnormalities in the expression of genes controlling the cell cycle. The initiation and progression of the neoplastic process is influenced by the following:

- Abnormalities in the regulation of the cell cycle;
- Mutations in proto-oncogenes and tumour suppressor genes;
- Disorders of the DNA repair process;
- Increased expression of growth factors and angiogenesis;
- Avoidance of apoptosis (mutations of anti- and pro-apoptotic genes);
- Increased telomerase activity;
- Tissue invasion and metastasis.

Another significant factor is the instability of the entire cell genome, which happens at the start of the carcinogenesis process. It is the outcome of numerous genetic anomalies building up over time. As a result, the DNA structure becomes weaker and more vulnerable to further mutations.

Mutations in tumour suppressor and proto-oncogene genes are associated with disorders of cell cycle regulation. The core of any cancer process is either increased proliferation or lack of proliferation inhibition, making the cell insensitive to inhibitory signals. TP53, RB, and p16 are the tumour suppressor genes that are most often mutated in lung cancer cells. One of the most significant factors in the pathophysiology of lung cancer is the disruption of its function.[13-15] A crucial component of the structure of all tissues, both healthy and diseased, is vascularization. In contrast to aberrant angiogenesis, which causes endothelial cells to divide hundreds of times more frequently and have a significantly longer survival period, this process is physiologically self-limiting. One of the primary and most potent pro-angiogenic agents is vascular endothelial growth factor (VEGF). For a tumour to continue growing, it requires its own vascular network if its diameter exceeds 3 mm. Therefore, the development of the tumour's capacity to form its own blood vessels is a crucial stage in the course of the cancer process. The majority of cancer cells, including lung cancer, contain VEGF mRNA. VEGFR is expressed more frequently in endothelial cells than VEGF. This implies that VEGF released by cancer cells may have a paracrine effect, activating endothelial cells through receptors on those cells.

Signs and Symptoms of Lung Cancer:

Lung cancer typically doesn't cause symptoms early on. Symptoms of lung cancer usually happen when the disease is advanced.

Signs and symptoms of lung cancer that happen in and around the lungs may include:

- A new cough that doesn't go away.
- Chest pain.
- Coughing up blood, even a small amount.
- Hoarseness.
- Shortness of breath.
- Wheezing.

Signs and symptoms that happen when lung cancer spreads to other parts of the body may include:

- Bone pain.
- Headache.
- Losing weight without trying.
- Loss of appetite.
- Swelling in the face or neck.

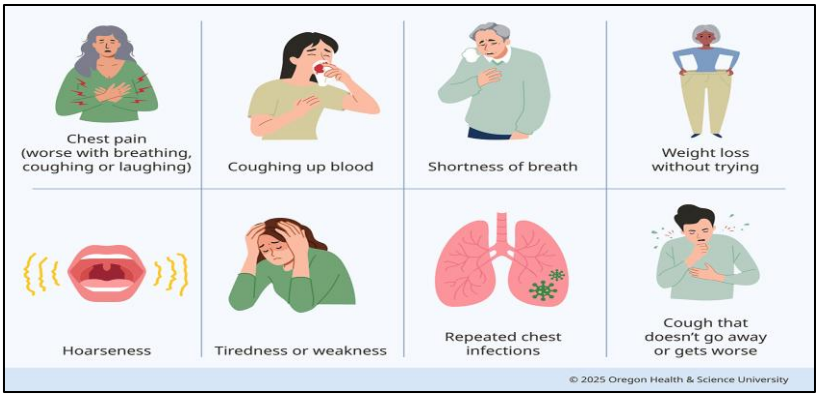

Figure 3: Signs and Symptoms of Lung Cancer [13]

Lung cancer risk factors:

Risk factors for lung cancer include:

- **Smoking:** Having a history of smoking increases risk. Smoking accounts for 80% to 90% of lung cancers.
- **Second hand smoke:** Being exposed to other people's smoking increases risk.
- **Environment:** Exposure to radon gas, which can build up in homes and other buildings, increases risk. So does exposure to other things in the environment, such as asbestos; air pollution, including diesel exhaust; and workplace chemicals.
- **Family history:** Having a close relative, such as a parent or sibling, with a history of lung cancer increases risk. The Knight offers expert genetic counselling to help you understand and manage your risk.
- **Age:** Being 65 or older increases risk.

Lung Cancer Stages: Doctors label cancer by stages. Stages show how much cancer is in your body, how far it has spread and how quickly it may grow.

Stages help doctors and patients understand how serious cancer is. Stages also help your Knight Cancer Institute team know how to best treat cancer.

What is cancer staging?

With lung cancer, stages show:

- The size of the main tumour
- Whether it has spread to lymph nodes
- Whether it has spread to other areas of the body, like the bones or liver

Tumour Sizes:

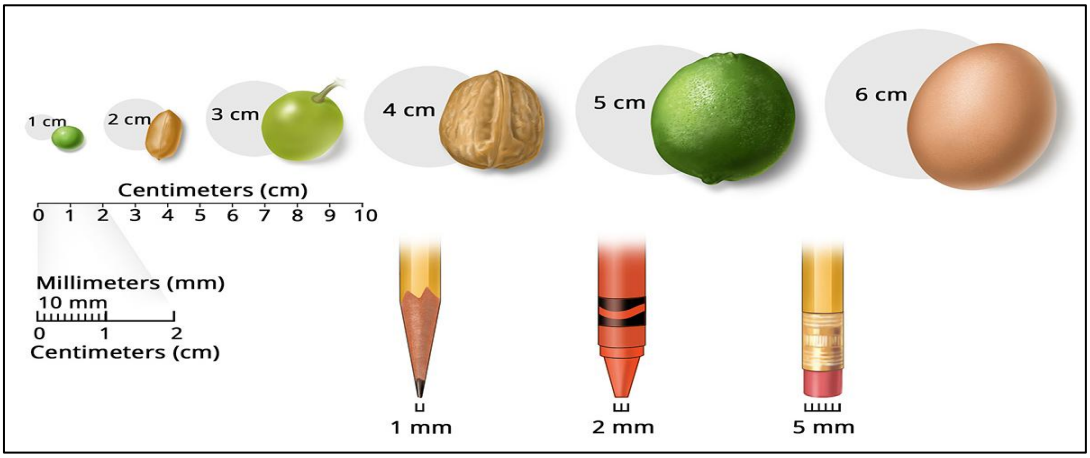

Figure 4: Different sizes of Tumour in Lung Cancer[14]

Stages of Non-Small Cell Lung Cancer (NSCLC):

- Stage 0 (Carcinoma in situ): An extremely early form of cancer that only affects the bronchus or upper lung lining and does not spread to deeper lung tissue.
- Stage I: A little tumour that only affects one lung and does not affect any lymph nodes.
- Stage II: The tumour is bigger or has migrated to neighbouring lung lymph nodes.
- Stage III: Locally progressed cancer that has migrated to adjacent chest lymph nodes or neighbouring structures (e.g., diaphragm, chest wall).
- Stage IV: Metastatic cancer that has migrated to distant organs such as the liver, brain, or bones, or to the other lung or surrounding fluid[15-16].

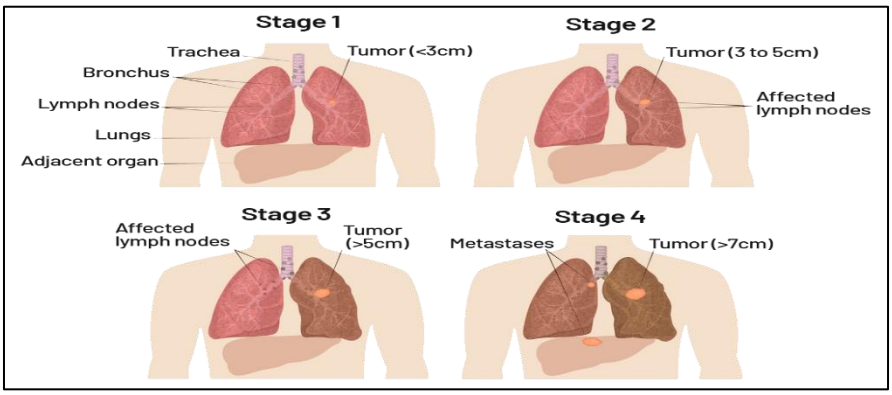

Figure 5: Stages of Lung Cancer[17]

Small Cell Lung Cancer (SCLC) Stages:

- **Limited Stage:** Confined to one lung and perhaps nearby lymph nodes in the chest.

Extensive Stage: Cancer has spread widely throughout the lung, to the other lung

Diagnosis and Treatment of Lung Cancer:

1. Diagnosis of Lung Cancer

Lung cancer is diagnosed using the following methods:

A) Medical History and Physical Examination:

- Doctor asks about symptoms like cough, chest pain, weight loss, smoking history, breathing difficulty.

B) Imaging Tests:

- Chest X-ray – detects abnormal mass in lungs.
- CT scan – gives detailed images of lungs.
- PET Scan – checks if cancer has spread.
- MRI – used especially for brain or spinal spread**.**

C) Sputum Cytology:

D) Biopsy (Most Important):

- Small tissue sample taken from lung and examined. Methods:
- Bronchoscopy
- Needle biopsy
- Surgical biopsy

E) Laboratory Tests: Blood tests to check general health.

F) Molecular Testing: Detects gene mutations like EGFR, ALK, ROS1 for targeted therapy.

2. Treatment of Lung Cancer:

Treatment depends on type, stage, age, and health of patient.

A) Surgery Used when cancer is localized. Types:

- Lobectomy (remove one lobe)
- Pneumonectomy (remove one lung)
- Segmentectomy (remove part of lung)

Figure 6: Affected Lung by the tumor[18]

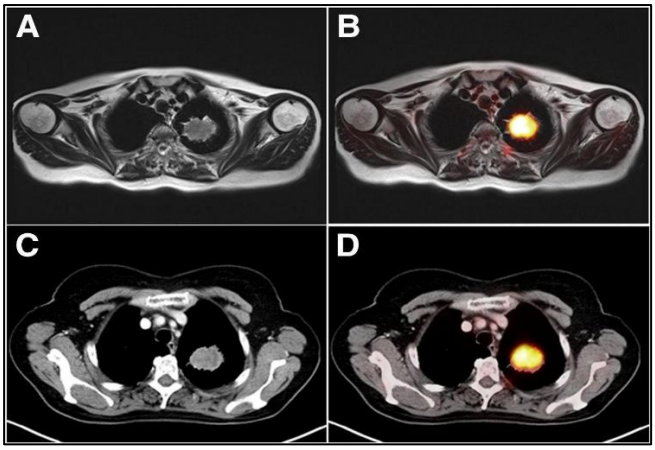

Figure 7: Examination of mucus under microscope to detect cancer cells[19]

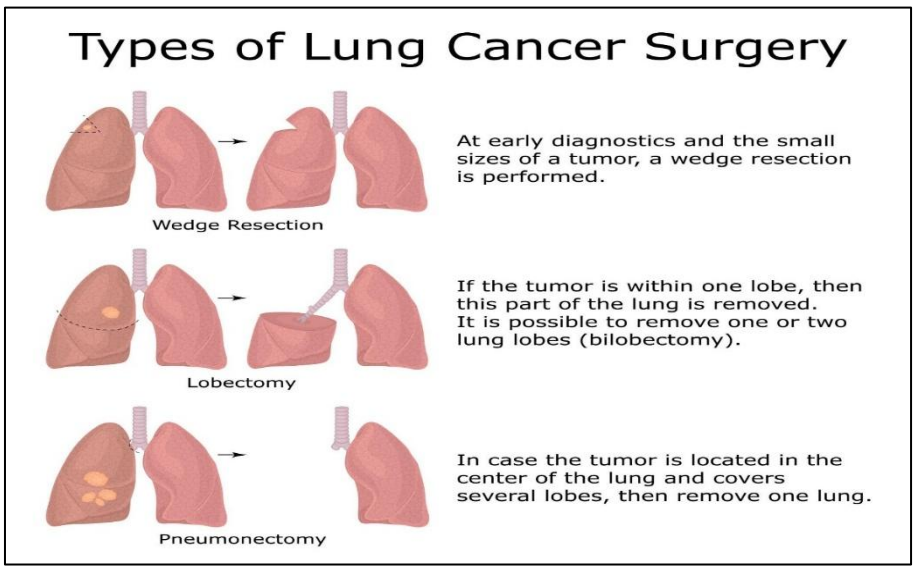

Figure 8: Types of Lungs Cancer[20]

B) Radiation Therapy: High-energy rays used to destroy cancer cells.

C) Chemotherapy: Anti-cancer drugs used to kill cancer cells.

D) Targeted Therapy: Drugs target specific mutations in cancer cells.

E) Immunotherapy: Boosts body immune system to fight cancer.

F) Palliative Care: Helps reduce pain and symptoms in advanced cancer.[21-25]

3.Prevention of Lung Cancer:

- Avoid smoking.
- Stop tobacco use.
- Avoid second-hand smoke.
- Reduce pollution exposure.
- Healthy diet.
- Regular exercise.
- Screening for high-risk smokers[22-29]

CONCLUSION

Lung cancer remains one of the most common and life-threatening cancers worldwide, with smoking being the major risk factor, along with environmental, occupational, and genetic influences. It is broadly classified into non-small cell lung cancer (NSCLC) and small cell lung cancer (SCLC), each differing in behaviour and treatment response. Early diagnosis through imaging techniques, biopsy, and molecular testing plays a vital role in improving patient outcomes. Advances in treatment such as surgery, chemotherapy, radiation therapy, targeted therapy, and immunotherapy have significantly improved disease management and survival rates. Preventive measures like avoiding smoking, reducing exposure to harmful substances, and regular screening in high-risk individuals are essential to lower incidence. Therefore, awareness, timely detection, and personalized treatment approaches are key to reducing the global burden of lung cancer.

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