



The Journal of Multidisciplinary Research (TJMDR)

Content Available at www.saajournals.org

ISSN: 2583-0317



A REVIEW ON LUNG CANCER

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Received: 04 Jan 2025 Revised: 14 Jan 2025 Accepted: 08 Feb 2025

Abstract

Lung cancer is a kind of cancer that starts as a growth of cells in the lungs. The lungs are two spongy organs in the chest that control breathing. People who smoke have the greatest risk of lung cancer. The risk of lung cancer increases with the length of time and number of cigarettes smoked. Quitting smoking, even after smoking for many years, significantly lowers the chances of developing lung cancer. Lung cancer also can happen in people who have never smoked. Lung cancer is the prime cause of cancer death among both men and women according to WHO report 2.09 million cases globally. It is also the chief cause of cancer death among men and the second leading cause of cancer death among women worldwide. The lung cancer classified into two different types is small-cell lung cancers (SCLC) and non-small-cell lung cancers (NSCLC). This article focuses on modifiable risk factors, including tobacco smoking, occupational carcinogens, diet, and ionizing radiation. It also discusses briefly the molecular and genetic aspects of lung carcinogenesis. Lung cancer is the most frequent cancer type with high mortality and morbidity rate worldwide. Studies have chemotherapy. own that smoking, environmental factors including occupational exposure, radon exposure, air pollution, radiation, obesity, diet and hereditary susceptibility are related to developing risk of LC.

Keywords: Lung cancer; lifestyle; risk factors; aetiology, patophysiology.

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DOI: <https://doi.org/10.37022/tjmdr.v5i1.652>

Produced and Published by

South Asian Academic Publications

Introduction Cancer

Cancer is a disease in which some of the body's cells grow uncontrollably and spread to other parts of the body. cancer can start almost anywhere in the human body, which is made up of trillions of cells. Normally, human cells grow and multiply (through a process called cell division) to form new cells as the body needs them. When

cells grow old or become damaged, they die, and new cells take their place [1].

Lung Cancer

Lung cancer is a disease caused by uncontrolled cell division in lungs, usually in the air ways (bronchi or bronchioles) or small air sacs (alveoli). Cells divide make more copies of themselves as a part of their normal function. But sometimes they get changes (mutation) that cause them to keep making more of themselves when they shouldn't damage cells dividing uncontrollably create masses, or tumours, of tissue. That eventually keeps your organs from working properly [2].

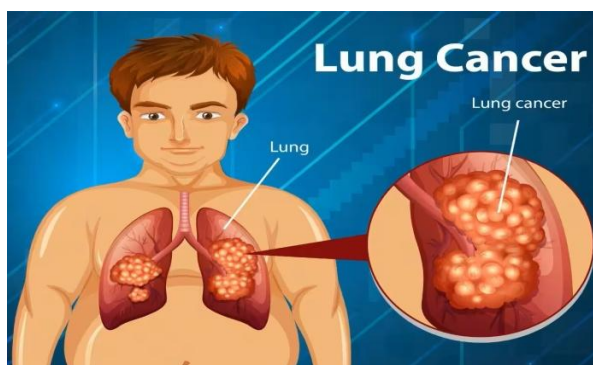


Figure-1: Diagrammatic representation of lung cancer Lung cancer is one of the most common Cancers we have, and many People die of this disease every year [2].

Lung cancer is the most important reason of cancer related deaths worldwide, as it is often asymptomatic at the onset of disease and generally discovered at advanced stages. LC is mainly divided into two large groups according to histological subtype as follows; small-cell lung carcinoma and non-small cell lung carcinoma (NSCLC). NSCLC comprises of 85% of all LC cases. Histological sub types of NSCLC include squamous cell carcinoma, large cell carcinoma, and adenocarcinoma. Among these subtypes, adenocarcinoma is the predominant subtype. LC screening via Low-dose Computed Tomography (LDCT) has been found to effective in decreasing mortality, hence the application of this practice is gradually increasing. One of the most important reasons of poor survival rate for LC is due in large part to the delayed diagnosis and advanced stage at the time of diagnosis. Providing an effective early diagnosis, itemized pathogenesis, and appropriate treatment and drug selection at the appropriate stage will be helpful in the optimal treatment of LC. Therefore, diagnosis of LC cancer at the earliest stage is highly vital, particularly in high-risk groups where the identification of new biomarkers is urgently needed [3].

Cancer is not just one disease, but a generic term used to encompass a group of more than two hundred diseases sharing common characteristics. Cancers (carcinomas) are characterized by their unregulated growth and spread of cells to other parts of the body Lung cancer is one of the most common cancers we have and a large number of people die of this disease every year. The disease is often discovered in a late stage, but also in earlier stages lung cancer patients have worse outcome than patients with other cancers. Even without spreading to other organs, during stage I, the survival rate of lung cancer is under 70%. In comparison, for example, breast cancer there is 95% survival in stage [4].

First location of spread in most of the lung cancer patients is lymph nodes. Pre operative assessment of spread to lymph nodes is important for consideration of further treatment. Lymph nodes will be removed during surgery to be analyzed using light microscopy for review. If there are areas of tumor cells in lymph nodes, the patient is offered additional chemotherapy. In most cases the spread

of cancer to lymph nodes remains unnoticed due to insensitivity of the clinical methods and the patients have low survival rate even after the diagnosis. More advanced and sensitive methods are needed to help this out. Lung Cancer, like all other cancers, results from an acquired abnormality in the body's basic unit of life, the cell. Normally, the body maintains a system of control mechanisms for cell growth, so that cells divide to produce new cells only when new cells are needed Disruption of this control system results in an uncontrolled division and proliferation of cells that eventually forms a mass known as a tumour. Although it can arise in any part of the lung; 90%-95% of the lung cancers arise from epithelial cells, bronchi and bronchioles Sometimes it may also arise from the other supporting tissues within the lungs like blood vessels⁵. Lung cancers arise through a multistep process involving many genetic and epigenetic changes that includes damage of many key cell-cycle genes [4].

Early detection: Promote screening programs for high-risk populations to identifying lung cancer at an early age.

2. Treatment advancement: Support research into new therapies, including targeted treatments and immunotherapy.

3. Smoking cessation: Implement programs to reduce smoking rates, as tobacco use is the leading cause of lung cancer.

4. Effective Treatment: Personalized treatment: Tailoring treatments (surgery, chemotherapy, radiation, immunotherapy) based on the genetic profile of the tumor.

5. Improving Prognosis and Survival Rates:

Extended survival rates: Research into treatments and therapies that can increase the life expectancy of patients.

Etiology

Smoking is the most common cause of lung cancer. It is estimated that 90% of lung cancer cases are attributable to smoking. The risk is highest in males who smoke. The risk is further compounded with exposure to other carcinogens, such as asbestos. There is no correlation between lung cancer and the number of packs smoked per year due to the complex interplay between smoking and environmental and genetic factors. The risk of lung cancer secondary to passive smoking increases by 20 to 30%. Other factors include radiation for non-lung cancer treatment, especially non-Hodgkins's lymphoma and breast cancer. Exposure to metals such as chromium, nickel, arsenic, and polycyclic aromatic hydrocarbons is also associated with lung cancer. Lung diseases like idiopathic pulmonary fibrosis increase the risk of lung cancer independent of smoking [5].

Pathophysiology

The patophysiology of lung cancer is very complex and incompletely understood. It is hypothesized that repeated exposure to carcinogens, such as cigarette smoke leads to dysplasia of lung epithelium. If the exposure continues, it leads to genetic mutations and affects protein synthesis.

This, in turn, disrupts the cell cycle and promotes carcinogenesis. The most common genetic mutations responsible for lung cancer development are MYC, BCL2, and p53 for small cell lung cancer (SCLC) and EGFR, KRAS, and p16 for non-small cell lung cancer [7].

Histopathological classification of lung cancers is based on cellular and molecular subtypes, which is an essential part of diagnosing and managing lung cancers. The 2021 World Health Organization (WHO) classification system of lung tumors divides the lung cancers as follows:

- Precursor glandular lesions
- Adenocarcinomas
- Adenosquamous carcinomas
- Squamous precursor lesions
- Squamous cell carcinomas
- Large cell carcinomas
- Sarcomatoid carcinomas
- Lung neuroendocrine neoplasms
- Salivary gland-type tumors
- Neuroendocrine tumors
- Neuroendocrine carcinomas
- And other epithelial tumors.

According to the WHO, identifying histologic features, measuring the depth of invasion, and mode of spread is of prognostic value. For example, they state that tumor spread through air spaces is associated with a higher recurrence rate after limited resections and should be reported on pathological evaluation. Also, the previously described clear cell, rhabdoid, and signet ring subtypes have been discontinued by the most recent WHO classification as they appear to be cytologic features that can occur in any adenocarcinomas. In the 2015 WHO classification system, poorly differentiated carcinomas were reclassified as squamous cell carcinomas if they had p40 expression; as adenocarcinomas with solid subtype if they had thyroid transcription factor 1 expression; and neuroendocrine carcinomas if they had chromogranin and synaptophysin positivity [7].

There are two types of lung cancer

1. Non-small cell lung cancer
2. Small cell lung cancer

1. Non Small Cell Lung Cancer

- Non-small cell lung cancers account for approximately 85% of all lung cancers and is the most common form of lung cancer in both men and women as well as smoke and non smokers.
- NACL is further types into three subtypes [8].

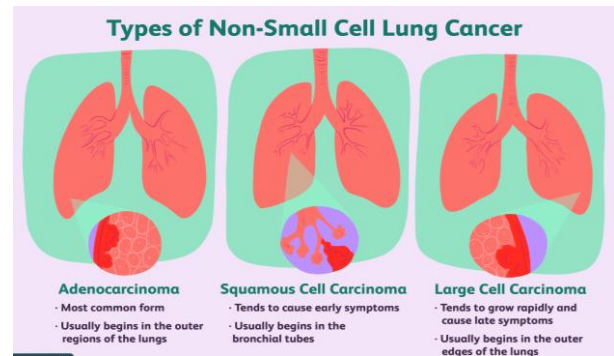


Fig-2: Types of non small cell lung cancer

Squamous Cell Carcinoma:

- Squamous cell carcinoma comprises 25-30% of all lung cancer cases. It arises from early versions of squamous cells in the airway epithelial cells in the bronchial tubes in the center of the lungs.
- This subtype of NSCLC is strongly correlated with cigarette smoking.
- This article discusses squamous cell carcinoma in the lungs and its symptoms and causes. It also presents information about diagnosis and treatment [8].

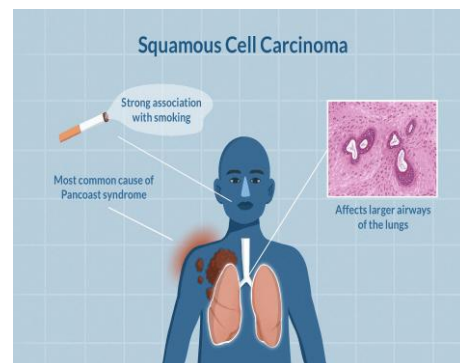


Fig-3: Diagrammatic representation of squamous cell carcinoma

Adenocarcinoma

- The most common type of lung cancer is adenocarcinoma.
- It comprises around 40% of all lung cancer.
- It tends to occur in the periphery of the Lung.
- Which might be due to the addition of filters in cigarettes preventing large particles from entering the lungs? this results in deeper inhalation of cigarette smoke, leading to peripheral lesions.

Stages of Cancer

In 'Stage zero' non-small cell lung cancer, abnormal cells are found only in the outer lining of the cells of the lungs. The cancer has not spread to the inner tissues of the lungs, the lymph nodes, or anywhere else in the body. stage zero non-small cell lung cancer is typically treated with surgery

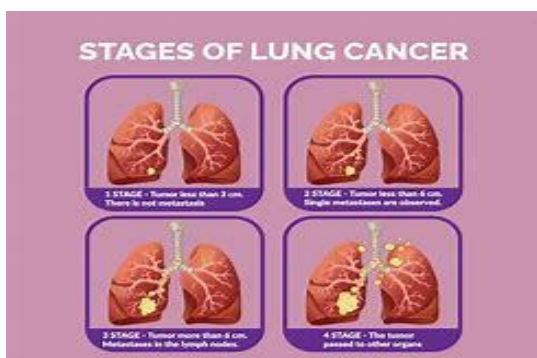


Fig-6: stages of lung cancer

Causes

- Lung cancer affect everyone, when lung cells mutate or alter, lung cancer can chip in. This mutation, which is a permanent alteration to a gene's DNA sequence can occur for a number of reasons.
- Lung cancer risk exists even if were exposed to these drugs longer periods.
- If have been exposed to any of the carcinogenic compounds, take advice of a doctor and take precautions to lessen risk and safeguard lungs.

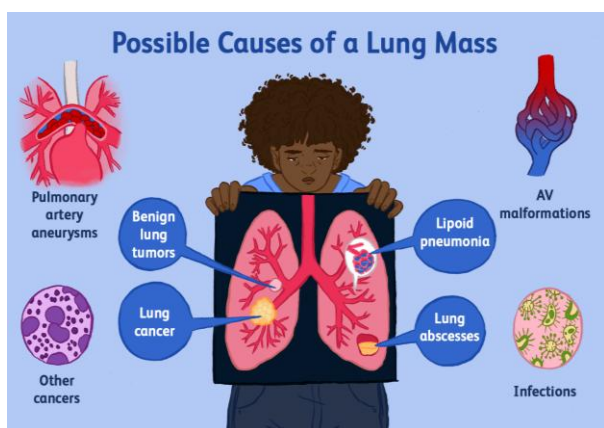


Fig-7: Diagrammatic representation of causes of lung cancer

Treatment

I. Chemotherapy:

- ✓ Approximately 40% of newly diagnosed lung cancer patients are stage4. The goal for treating these patients is to improve survival and reduce disease – related adverse events. For stage 4 NSCLC, cyto toxic combination chemotherapy is the first – line therapy, which might be influenced by histology age VS comorbidity, and performance status (PS).
- ✓ The American society of clinical oncology states that treatment for a patient with a PS of 0 or 1 is a regimen of a PLATINUM (cisplatin or carboplatin) plus paclitaxel, gemcitabine, docetaxel, vinorelbine, irinotecan, or pemetrexed.
- ✓ Therapy should also be stopped if the cancer grows or if after four treatment cycles, the disease is stable but the treatment is not shrinking the tumors [21].

II. SURGERY:

- ✓ Patients who have stage1,2, and 2A NSCLC typically have surgery to remove the tumour if the tumor is

found to be respectable and the patient is able to tolerate surgery.

- ✓ Surgeons may remove a lobe or section of the lung containing the tumor.
- ✓ A lobe cancer be removed via the scope through this small incision so that a larger incision does not have to be made[21].

III. Adjuvant:

- ✓ Some patients who have undergone a resection surgery may benefit from adjuvant therapy in reducing the risk of lung cancer relapse.
- ✓ Patients with stage 2A, 2B, and 3A NSCLC usually receive chemotherapy after surgery to kill any remaining cancer cells in order to prolong survival [21].

IV. Radio Therapy

- ✓ Radio therapy uses high – energy beams to damage DNA within cancer cells, thereby destroying them.
- ✓ Radiotherapy also can be part of “palliative care” to improve quality of life NSCLC patients who do not respond to surgery or chemotherapy [21].

V. Immuno Therapy

- ✓ Immunotherapy offered a revolutionary approach to combating lung cancer.
- ✓ Immunotherapy was safe and effective, and it presented a potential strategy for the treatment of lung cancer [21].

VI. Photothermal Therapy

- ✓ To address the limitations of PTT as a monotherapy, a series of combined therapies based on PTT have been extensively researched, which provided promising treatment strategies for lung cancer [21].

Drug Used to Treat Lung Cancer

TEPOTINIB: FDA Approval: February 15, 2024.

DRUG PROFILE:

Teptotinib is an oral tyrosine kinase inhibitor targeted against MET for the treatment of metastatic non-small cell lung cancer in patients exhibiting MET exon 14 skipping mutations [22].

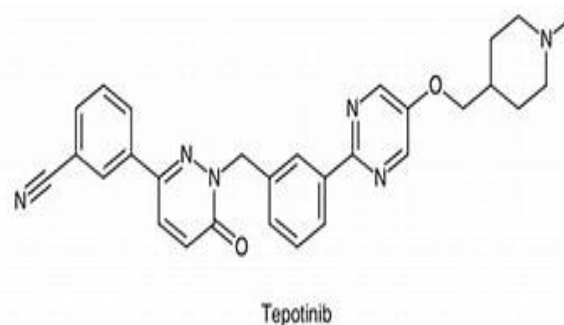
OTHER NAME: Teptotinib

BRAND NAME: Tepmetko

MOLECULAR WEIGHT: 492.583

CHEMICAL FORMULA: C₂₉H₂₈N₆O₂

STRUCTURE:



IUPAC NAME: 3-[1-[3-[5-[(1-methyl piperidin-4-yl) methoxy] pyrimidin-2-yl] phenyl] methyl]-6-oxo-1, 6-dihydropyridazin-3-yl] benzonitrile [22].

Dosage Forms

Tablet: 225 mg

Clinical Trials

Study#	Trial design	Dosage route of administration and duration	Study subject (n)	Median age (range)	Sex
Vision study (MS200 095-0022)	Sing le-arm, open-label phase-II trial	TEPMETK O 450 mg orally once daily, until progression of disease or unacceptable toxicity	N=146 (liquid biopsy, tumor biopsy, or both)	73 years (range 41to 94)	Female: N=70 (48%) Male :76 (52%)

Patients with epidermal growth factor receptor (EGFR) or anaplastic lymphoma kinase (ALK) activating alterations were excluded.

Identification of METex14 skipping alterations was prospectively determined using central laboratories employing either a polymerase chain reaction (PCR)-based or next-generation sequencing-based clinical trail assay using tissue (50%) and/or plasma (65%) samples.

Conclusion

While lung cancer remains a very challenging cancer to treat, new treatments that capitalize on advances in our understanding of cancer biology are providing both patients and physicians with a reason for cautious optimism. Because cancer is a highly varied disease, one of the primary treatment challenges is in selecting patients who are most likely to benefit from new therapies. Researchers are now focusing on identifying biological markers, such as genetic signatures, that could indicate which tumors are most vulnerable to angiogenesis inhibitors and other targeted agents. It is likely that a more personalized approach to treatment using biological markers and combinations of therapies will provide better results in the future.

Funding

No

Acknowledgement

Nil

Conflict of Interest

No conflict of interest.

Informed Consent

Not applicable.

Ethical Statement

Not applicable.

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