GENERAL

What Constitutes Lung Cancer? A Scientific Overview

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Lung cancer is caused mainly by the uncontrolled growth of cancer cells in the lung parenchyma or bronchial epithelium. Histologically, it may be divided into two groups, approximately:

Non-small cell lung carcinoma (NSCLC) accounts for approximately 85% of cases and encompasses subtypes such as adenocarcinoma, squamous cell carcinoma (SqCC), and large-cell carcinoma.

Approximately 15% of cases are SCLC, characterized by widespread metastasis and rapid growth.

Lung cancer caused more than 1.8 million deaths in 2020 and was the most common cause of death due to cancer worldwide. Lung cancer accounts for 5.9% of all cancers and 8.1% of cancer deaths in India.

Epidemiology and Burden in India

According to GLOBOCAN 2020 data, India recorded approximately 81,748 new lung cancer cases, ranking 4th in age-standardized incidence globally, while mortality was disproportionately high. Earlier GLOBOCAN 2018 figures aligned similarly, positioning lung cancer as India?s fourth most common malignancy (?67,800 cases) and third leading cause of cancer mortality (?63,500 deaths).

State-level analysis reveals substantial heterogeneity: Kerala and Mizoram record the highest incidence among males, while Mizoram and Manipur lead among females. Estimates suggest tobacco contributes to approximately 43% of lung cancer disability-adjusted life years (DALYs), with ambient air pollution accounting for an additional 43%.

Male predominance remains notable, with an observed male-to-female incidence ratio of ~4.5:1 in earlier reports, though the incidence in women and never-smokers has grown, particularly in adenocarcinoma subtypes.

What are the Associated Risk Factors?

? Approximately 85?90% of cases worldwide are caused by tobacco use.

? Passive smoking raises the risk for lung cancer by about 30%.

? Occupational exposures include asbestos, radon, silica, heavy metals, and industrial chemicals.

? Outdoor air pollution is another significant contributor in India.

? Prior Lung Disease, e.g., tuberculosis, chronic obstructive pulmonary disease, can obscure symptoms and delay diagnosis.

? Genetic and Molecular predispositions, such as EGFR mutations, ALK, ROS1 rearrangements, and PD-L1 expression, are all critical for precision treatment planning.

Evaluating Symptoms: Diagnostic Criteria and Approaches

Many individuals remain asymptomatic until the disease reaches its critical stage, making early detection challenging. However, in some patients, symptoms can be evaluated.

Clinical Presentation:

Symptoms are often non-specific: persistent cough, hemoptysis, dyspnea, chest pain, systemic features like weight loss and anorexia; up to ~94% of newly diagnosed NSCLC patients present at Stage IIIB/IV.

Diagnostic Pathway and Delays:

? Imaging: chest X-ray prompts CT for lesion characterization.

? Histological confirmation via bronchoscopy, image-guided biopsy, or surgical sampling.

? Molecular profiling mandatory in NSCLC: EGFR, ALK, ROS1, PD-L1 testing.

? The median time between a definite diagnosis and the initial phase of treatment is reported to be between 101 and 126 days after the onset of symptoms; this time is especially long for patients who have already had treatment for tuberculosis.

Clinical and Pathological Staging

- TNM staging remains foundational, with Stage I?II managed primarily by surgery ? adjuvant therapy.
- Stage III via multimodal approaches.
- Stage IV requiring systemic therapy.

Treatment Modalities in Lung Cancer

Managing lung cancer requires a combination of treatment options. Some of them are:

- Surgical Management: Resection (lobectomy/bilobectomy) with curative intent remains standard in early-stage NSCLC.
- Radiotherapy: Used adjuvantly or definitively (e.g., SBRT in medically inoperable cases).
- Chemotherapy: Platinum-doublet regimens remain standard in advanced disease, often combined with other agents (e.g., bevacizumab in non-squamous NSCLC).
- Targeted Therapy:

1. EGFR, ALK, and ROS1 tyrosine kinase inhibitors represent precision treatments with superior PFS in mutation-positive patients.
2. A global Phase III trial of EGFR-mutated advanced NSCLC showed that the combination of amivantamab + lazertinib extended median PFS to 23.7 months vs. 16.6 months with osimertinib.

- Immunotherapy: PD-1/PD-L1 checkpoint inhibitors (e.g., nivolumab, pembrolizumab) are increasingly used, either as monotherapy or combined with chemotherapy.

Outcomes & Survival Rates in Lung Cancer

Globally, 5-year survival rates average around 17?20% across all stages.

In India, advancements in diagnosis and therapy have increased median survival from 11 months to a 5-year survival of ~17.8% over the past decade. American data extrapolated locally estimate stage-specific survival as follows: Stage I?70?90%, Stage IV?3?8% . Additionally, Amerix Cancer Hospital reports an average 5-year survival rate of ~27%, influenced by stage distribution, age, comorbid status, and treatment access.

Despite improvements, stage III disease continues to pose a significant challenge; 5-year survival remains between 13?33%. Late-stage presentation (~83% in advanced stages) remains a key barrier.

National Initiatives and Infrastructure

- **National Cancer Control Programme (NCCP)**: Since 1975, with milestones including cancer registry expansion, tobacco control policies, and oncology training.
- **Cancer Registry System**: Regular data aggregation assists policy-making.
- **National Cancer Grid (NCG)**: Harmonizes care across 300+ institutes, setting standards for diagnosis, treatment, and stratified protocols.

- **Leading Centres**: Tata Memorial Centre, Chittaranjan National Cancer Institute, National Institute of Tuberculosis and Respiratory Diseases?all offer multidisciplinary, evidence-based lung cancer care.

Challenges and Gaps in Lung Cancer Management

- Late Diagnosis: Symptom overlap with tuberculosis leads to diagnostic delays averaging 3?4 months.
- Infrastructure Disparity: Urban?rural divide, with advanced diagnostics and oncology services largely urban-centric.
- Tobacco Prevalence: Persistent high rates?e.g., >50% male smokers in West Bengal?underscore cigarette cessation as a public health priority.
- Limited Molecular Testing: Coverage for EGFR, ALK, and PD-L1 testing remains inconsistent in non-metropolitan centres.
- Financial & Social Barriers: High out-of-pocket costs and lack of awareness impede access to curative treatment.

Future Directions in Lung Cancer Treatment and Research

- **Enhanced Screening**: The implementation of low-dose CT screening among high-risk populations could shift stage distribution and improve survival outcomes
- **AI Integration**: Emerging AI tools in imaging and prognosis may assist early detection and staging decisions
- **Precision Medicine Expansion**: Wider immunotherapy adoption, and ongoing integration of breakthroughs like EGFR/ALK inhibitors, as well as CAR-T cell trial outcomes, represent promising future improvements.
- **Tobacco Control and Public Education**: Targeted awareness strategies, particularly for adolescents, may curb incidence rates.
- **Decentralized Care**: Strengthening district-level oncology capacities via NCCP/NCG will reduce disparities.

Competing interests

The authors declare that they have no competing interests.

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