CLINICAL CHALLENGES AND INNOVATIONS IN LUNG CANCER MANAGEMENT

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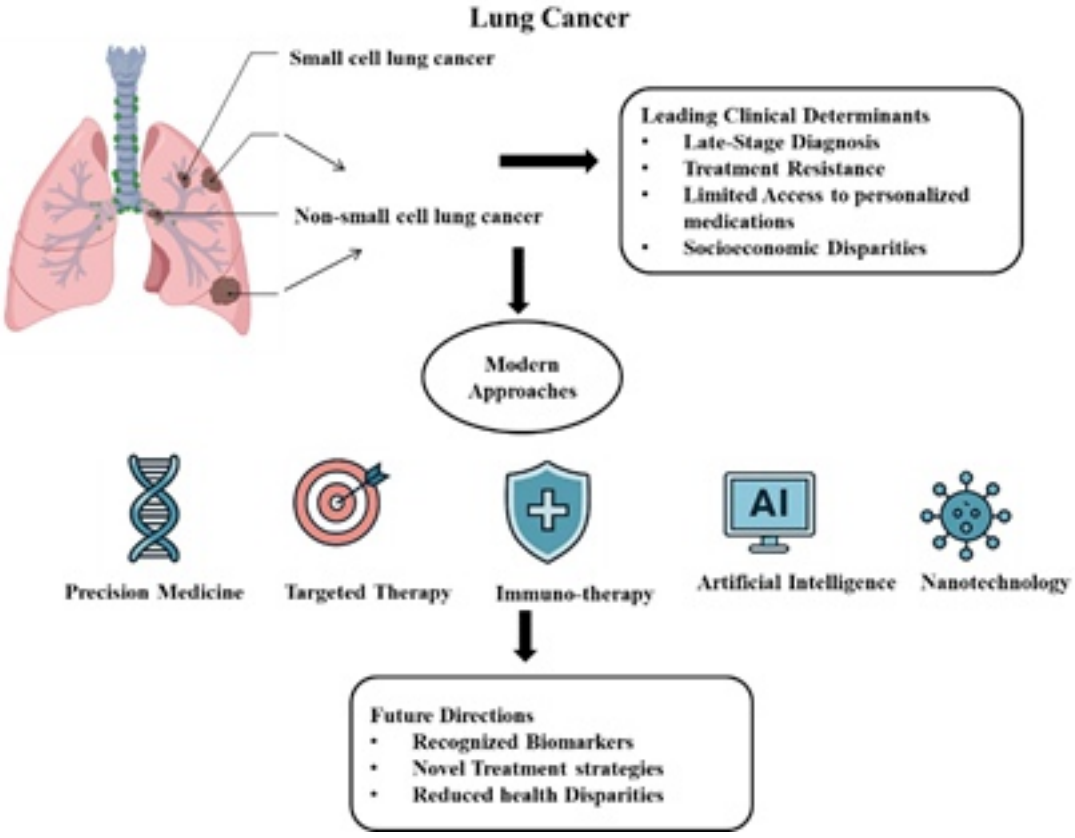
ABSTRACT

Lung cancer is the number one killer of the cancer court in the world today. Clinical challenges that surround the prognosis of lung cancer patients still challenge the strategies in therapy and diagnostic procedures though there have been improvements in the field of technology. Two most common histological subtypes, i.e., small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC) are central to these challenges. As such, the current synthesis has dealt with the leading clinical determinants of lung cancer outcomes: late-stage diagnosis, treatment resistance, limited access to personalized medications, and socioeconomic disparities. The current article also outlines modern approaches to therapy precision medicine, targeted therapy, immunotherapy, artificial intelligence (AI), and nanotechnology and transforming the healthcare industry. Future breakthroughs in management and testing are mentioned, with an emphasis on the recently recognized biomarkers and strategies of treatment that could enhance the survival of lung cancer patients. Finally, the ability to improve survival rates, optimality of treatment regimens, and the reduction of health disparities in lung cancer healthcare lies in the issue of systematically solving such clinical and technological challenges.

Key words:Lung Cancer, Non-Small Cell Lung Cancer (NSCLC), Treatment Resistance, Targeted Therapy, Immunotherapy



1. INTRODUCTION

Lung cancer has remained to be one of the greatest variety of significant human- health conditions by causing death of 18.0 % of all the worldwide cancer related death cases as well as cancer prevalence of 11.4 % worldwide. [1]. Lung cancer is the most prolific cause of death due to cancer in India and it is this cancer that is highly spreading both among the smokers and the non- smokers. [2]. A significant rise in the rate of rhinitis occurrence, especially in women and young groups, has been noted and this trend highlights the role of lifestyle and other environmentally oriented factors as the cause namely genetic predisposition, exposure to passive smoking, and air pollution [3]. Lung cancer, however, has continued to remain a disease with a poor prognosis because of late disease diagnosis as well as development of drug resistance despite massive advancements in the diagnostic methods and therapeutic regime [4]. The problem of early diagnosis is a major medical dilemma when it comes to the treatment of lung cancer. Weights lose, fatigue, chest pains, and constant coughs may be misconstrued

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One of the greatest barriers in oncology of today is the problem of therapeutic resistance. In non-small lung cancer (NSCLC), resistance to therapy is widespread and usually related to elaborate genetic transformation, especially an EGFR, ALK, and ROS1 [7] .Targeted treatment may be sensitive to select genomic changes present in early developmental stages of cancer, however it can change and become resistant as a cancer evolves over time through acquiring other mutations or tumor microenvironment changes. [8] . The diagnosis of small cell lung cancer (SCLC) has always remained aggressive, partly due to the high rates of refractoriness to radiation therapy and chemotherapy, two treatment modalities which are employed in the normal treatment schemes. Recurrence of SCLC has a strong tendency of swiftly appearing at the end of first line therapy hence the need to conduct studies in the mitigation of such innate resistance [9] .

The availability of state-of-the-art therapies has also been a significant impediment and this is especially so among low-and middle-income country dwellers. The methods of personalized medicine are promising but in the majority of the cases immunotherapy and targeted therapies are not available due to their price and accessibility [10]. The use of targeted therapy has produced respectable results in specific patient groups most notably in EGFR inhibitors like gefitinib and erlotinib and in ALK inhibitors like crizotinib and alectinib. In the said context, personalized medicine refers to the selective design of a medical approach with respect to the unique genetic constitution of a patient [11]. Classes of immunotherapeutic agents, which include immune checkpoint blockade (particularly in the form of pembrolizumab and nivolumab), have radically transformed the paradigm of lung-cancer therapy by providing long-lasting performance even at an advanced stage. However, the occurrence of treatment-related toxicities has been found to persist with prescription of the drug and development of resistance was also a major concern in the clinical perspective [12].

Artificial intelligence (AI) and molecular diagnostics are two new technologies, which are actively used nowadays to handle the obstacles in the health care sector. Specifically, such molecular diagnostic devices as next-generation sequencing (NGS) and others are used to identify genetic changes, thus helping to select effective therapy drugs [13]. The analysis of circulating tumor DNA (ctDNA) allows not only revealing tumors in an early stage but also provides opportunity to check on therapeutic response without applying invasive procedures. [14]. A combination of clinical records, genetic profiles, and medical images with the help of AI-based applications has come in handy to improve the accuracy of diagnosis and patient prognosis. Such systems also support streamlining of treatment processes through the improvement of therapeutic strategies on the fly and provision of personalized treatment [15].

Overall, lung cancer, being still a significant issue of public health, causes continuous treatment transformations through constant advances in fields of artificial intelligence (AI) and immunotherapy, targeted drugs, and personalized medicine [10] . To improve patient outcomes worldwide, however, it is imperative to address the obstacles to early detection, therapeutic resistance, and fair access to therapy. To fight the lung cancer epidemic, more research, better healthcare infrastructure, and international cooperation will be essential [16] .

2. EPIDEMIOLOGY AND RISK FACTORS

2.1 Global and Regional Incidence

Lung cancer continues to be the primary cause of cancer-related death worldwide, and its prevalence is rising in low- and middle-income nations [3]. Lung cancer incidence is predicted to increase further in nations like India, where smoking rates are still high, especially among men [17] . The rising incidence of lung cancer among never-smokers, particularly among women, points to the involvement of variables other than tobacco use, such as genetic predispositions and environmental contaminants[18].

According to the World Health Organization's (WHO) most recent figures, lung cancer kills more than 1.8 million people each year, with North America, Europe, and some regions of Asia having the greatest death rates.[19]. Curiously, although smoking rates are falling in high-income nations, the incidence of lung cancer is rising in places like China and India as a result of increased industrialization, air pollution, and tobacco use [17] .

2.2 Risk Factors

One of the most deadly and common malignancies in the world, lung cancer is mostly brought on by a combination of hereditary, occupational, and environmental factors. In as far as smoking has been viewed as the main etiological agent in lung cancer, the disease pathophysiology is quite complex and it is influenced by a complex interaction between lifestyle habits, environmental pollutants and genetic defects [20]. In order to develop effective both preventive and therapeutic measures it is necessary to outline main risk factors of lung cancer. In the current discussion there are four principal contributive factors that include tobacco smoking, hereditary mutations, exposure to environmental pollutants and familial predisdirection[21] .

Tobacco Smoke: The Leading Cause of Lung Cancer

According to prominent related epidemiological reports, tobacco smoke contributes to over 80 % of all the pulmonary-cancer-related deaths not only in the US, but also globally, and as such it remains the most important and well-defined predisposing factor in terms of lung cancer [22]. Smoked cigarette contains a variety of carcinogens including heavy metals, nitrosamines and polycyclic aromatic hydrocarbons (PAHs) that exposes the pulmonary system to a wide spectrum of carcinogenic agents. These compounds both have been known empirically to be associated with genetic changes that promote carcinogenesis. These agents also produce a sequence of mutations by damaging the cellular DNA of the lungs and leading to the eventual formation of morphologically aberrant lines of malignant cells [23] .

The two major lung cancer histological subtypes are the non-small cell lung cancer (NSCLC) and the small cell lung cancer (SCLC). Even though tobacco smoking is a known risk factor of both, its impact on the pathogenesis of SCLC is more relevant, as it is a particularly aggressive form of the disease [24]. [25].

Second-Hand Smoke Exposure

Second hand smoke (SHS) exposure is another well-established risk factor for lung cancer, in addition to active smoking. SHS is a combination of the mainstream smoke that the smoker exhales and the side-stream smoke that is released from the burning end of a cigarette [26]. Those who are not smokers, such as spouses, kids, and employees in places where smoking is permitted, are especially at risk from this exposure [27]. Even in people who have never smoked, long-term exposure to SHS has been demonstrated to dramatically raise the risk of lung cancer. According to research, nonsmokers who frequently come into contact with second hand smoke have a 20-30% higher risk of developing lung cancer than those who do not [28]. The risks of high rates of lung cancer occurrence and deaths are directly associated with long-term and constant smoking of cigarettes. There is some scientific way in which the relationship between the extent of smoking and incidence of cancer can be scaled in time: the lapse of time with continuity in smoking predisposes lung cancer menace to increase correspondingly. In addition to mere longevity, the processing of over two dozens of cigarettes daily presents the risk contributor significantly high to the smoker, whereas even a sporadic or a minimalized smoking has a cumulative effect of the smoker consuming so by increasing the likelihood of lung malignancy [29].

Occupational and Environmental Exposures

Lung cancer has a close association with environmental and occupational exposure, in epidemiological analysis, as well as cigarettes smoking. [30]. Occupational exposure to some of these harmful substances has been associated with the risk of lung cancer in the past [20]. An example scenario is Asbestos, a naturally deposited mineral that was traditionally used to form a favored insulation and construction commodity. Asbestos is regularly exposed to professionals in the construction, mining, ship building and manufacturing industries[31]. Aspiration of the asbestos fibers in the form of particles leads to the destruction of the lungs and an increasing risk of lung cancer, especially its mesothelioma line. Risk of development of lung cancer has also been reported to exist as a result of exposure to other carcinogens encountered at workplaces such as benzene, arsenic, cadmium and chromium [20].

Cancer of the lung is a major problem in the field of public-health, and radon, a colorless and odorless radioactive gas emitted because of the decomposition of uranium in rock and soil, may be viewed as a determinant environmental health factor. The fact that it can build to very dangerous levels in buildings makes exposure to radon especially relevant in places with poor ventilation of homes and buildings. [32]. Chronic radon exposure increases the risks of developing lung cancer, and especially so on smokers of cigarettes. Most of the epidemiological evidence shows that radon causes approximately 21,000 lung cancer deaths annually in the United States; it has also been described by the U.S. Environmental Protection Agency (EPA) as the second major cause of lung cancer in the U.S. after smoking [33].

Air Pollution: The Growing Environmental Threat

A strong correlation between high levels of ambient air pollution and lung cancer can be viewed in recent epidemiological studies. Of special interest is the contribution of fine particulate matter (PM2.5) i.e. particulate matter with diameter smaller than 2.5 mm that gains the entry to the lung alveolar bronchiolar interface [34]. Microscopic particulate matter is produced by a complex of human activities, the first of which is the burning of fossil fuels and other industrial process most popular and common was automobile exhaust emissions [35]. Chronic inflammation in the lung following exposure to PM 2.5 is linked to the increase of oxidative stress and DNA damage, which are both phenomena that favor the development of lung cancer [36].

Epidemiological data shows that urban areas with either high or moderate continuous measure air-pollution exposure, especially in the Asian and European cities, are also linked with an increased risk of lung cancer, especially, to non-smoking people. Namely, longitudinal studies reveal the genetic changes that resemble the alterations observed in the tobacco smokers that develops as chronic air pollution occurs, thus leading to the occurrence of the non-small cell lung cancer development [37]. Empirical studies that are currently available show that people exposed to the higher levels of ambient air-pollution concentrations living at the present time in those localities are at increased risk of developing lung cancer even

without smoking tobacco [38].

Genetic Mutations and Family History

Lung cancer is a multifactor pathology that is affected by environmental and lifestyle factors, on the one hand, and genetic changes, on the other hand, even when the person does not have a history of smoking tobacco or exposure to occupations linked to carcinogenic substances [39]. Even nonsmokers have been found to be at a higher risk of lung cancers due to certain genetic variants; this is especially the case of those belonging to the anaplastic lymphoma kinase (ALK), KRAS and the epidermal growth factor receptor (EGFR) genes. These observations are significant in affirmed that host genetics is involved in the development of the tumors regardless of external exposures [40]. The Epidermal growth factor receptor (EGFR) mutations are a very common driver mutation in lung cancer, specially in Asian communities, and are linked to positive clinical prognosis after receiving EGFR-specific inhibitor agents (e.g., Gefitinib, erlotinib). In a similar manner, the most important oncogenic action that drives the development of lung cancer is ALK rearrangements and patients with such chromosomal alterations can also follow treatment with crizotinib[41, 42].

Primary lung cancer is the major cause of reasons in cancer-related deaths in the world and the studies also point out that non- patients risk higher chances of cancer when subjected to a certain set of danger factors. A notable example is a family history of someone who has already had lung cancer, such as a parent, a sibling, or a child; a relationship that has been established many times in published works [43]. Familial risk refers to an inherited tendency to develop cancer which can be due to mutations within specific tumor-suppressor genes, to mutations within other high- to moderate-penetrance genetic changes that predispose to the development of neoplasia [44].

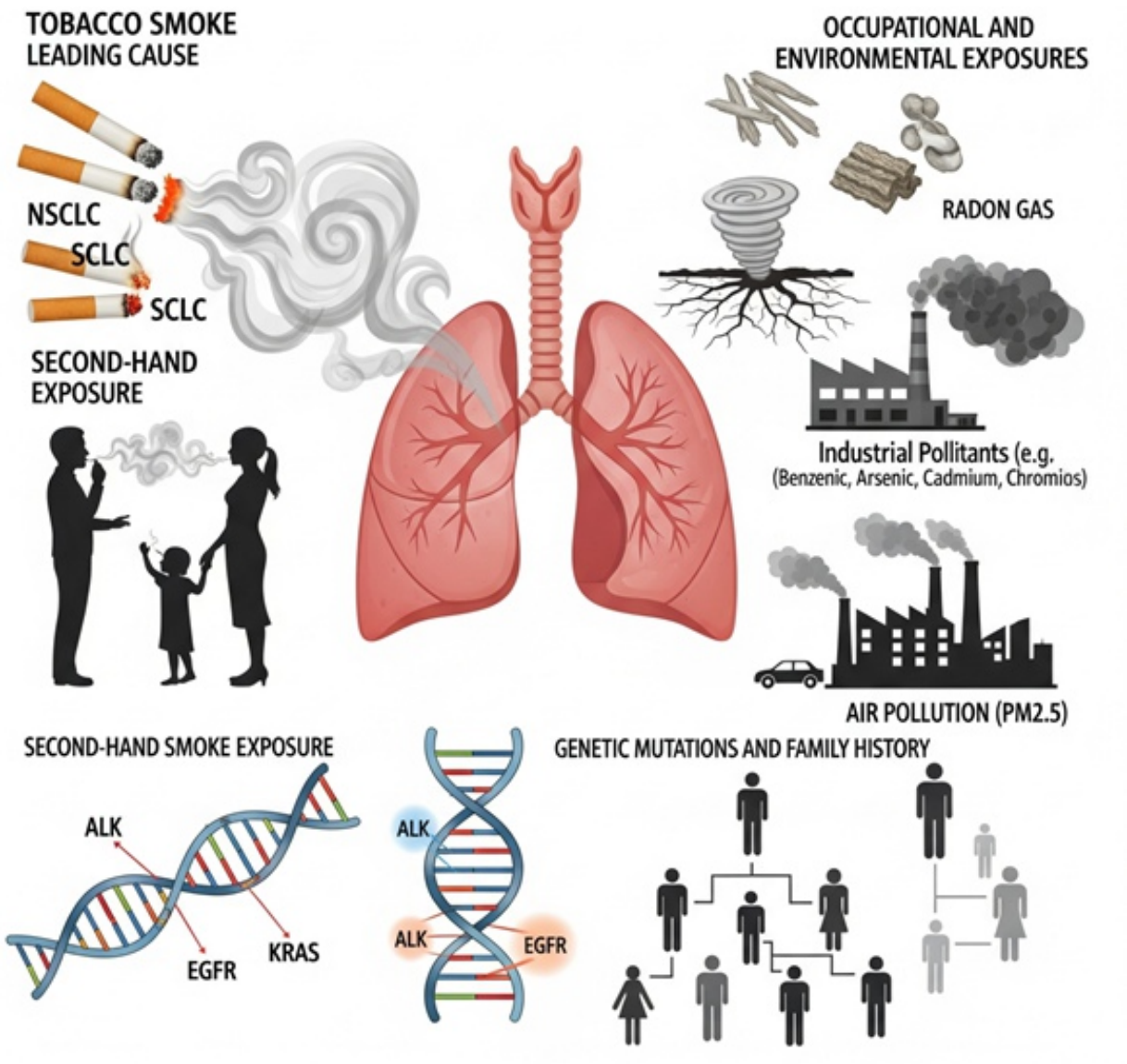

Figure 1: Major Risk Factors for Lung Cancer

This image comprehensively illustrates the key risk factors associated with the development of lung cancer. It highlights the profound impact of Tobacco Smoke (both active and Second-Hand Smoke Exposure), detailing its direct link to both NSCLC and SCLC. The illustration also features Occupational and Environmental Exposures, including substances like asbestos, radon gas, and various industrial pollutants (e.g., benzene, arsenic, chromium). Furthermore, it depicts the role of Air Pollution, specifically fine particulate matter (PM2.5), and emphasizes the significance of Genetic Mutations and Family History with examples of genes such as ALK, KRAS, and EGFR, and the concept of inherited predisposition.

3. CLASSIFICATION AND PATHOPHYSIOLOGY

3.1 Histological Classification

Lung cancer is an aggressive tumor whose development takes place in the lung tissue and is one of the most common oncological diseases diagnosed in different countries. There are two major histopathologic forms such as Non-Small Cell Lung Cancer (NSCLC) and Small Cell Lung Cancer (SCLC) differentiated by morphologic appearance (observable under an ordinary microscope) as well as their molecular makeup [45]. Small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC) have different clinical behavior, biology, response to treatment and prognosis. A review of these differences is discussed below [46].

1. Non-Small Cell Lung Cancer (NSCLC)

About 85% of all occurrences of lung cancer are NSCLC, making it the most prevalent kind. Based on the tumor's physical characteristics and cellular origin, it has three main kinds [47].

- **Adenocarcinoma:** The most common occurrence of any non-small-cell lung carcinoma (NSCLC) in non-smoking populations is adenocarcinoma. This subtype is mostly caused by peripheral lung and its leading characteristic is production of mucus and development of glandular differentiation [48]. The rate of growth of adenocarcinoma and its levels of detection at an early stage is generally slower or more probable, relative to that of other subtypes of NSCLC, and also relates with better prognosis. In addition, it is pre-disposed to characteristic changes in the genes code ALK, KRAS, and EGFR which, in turn, significantly speaks to therapeutic decision-making [49]. Etiology of adenocarcinoma has been awaiting its clarity in the past years, but it has improved a lot. Up to date, there is evidence that environmental exposures including passive smoking and air pollution are causes and factors that control the occurrence rate and distribution of adenocarcinoma in terms of histopathology. Specifically, such exposures seem to put a greater risk on adenocarcinoma among women and younger patients. At the same time, hereditary predispositions towards adenocarcinoma have already been proved, the mechanisms of which have not yet been fully identified [50].
- **Squamous Cell Carcinoma:** Squamous cell carcinoma (SCC) develops due to epithelial cells that line the airways, and it is usually related to the history of tobacco smoking. The most frequent conditions, where SCC is detected, involve the central areas of the lung, close to the bronchi.[51]. Occlusive symptoms including cough, hemoptysis (coughing up blood), and chest pain are frequently caused by these tumors because of their location. Squamous cell carcinoma is frequently detected later, after the illness has moved outside of the lung, and is typically more aggressive than adenocarcinoma[52]. However, compared to adenocarcinoma, squamous cell carcinoma might react more well to chemotherapy and radiation treatment, particularly when it is further advanced[53].
- **Large Cell Carcinoma:** Large, undifferentiated cells that lack the characteristics of squamous cell carcinoma or adenocarcinoma define this subtype. Any area of the lung might develop large cell carcinoma, which has a propensity to grow and spread swiftly [54]. Compared to adenocarcinoma and squamous cell carcinoma, large cell carcinoma is more difficult to treat and has a worse prognosis because of its aggressive nature; it is less responsive to targeted therapies, but it is typically treated with chemotherapy and occasionally radiation therapy[55].

2. Small Cell Lung Cancer (SCLC)

About 15% of all instances of lung cancer are small cell lung cancer (SCLC), a very aggressive and quickly spreading type of the disease[56]. Smoking is closely linked to SCLC, which is most frequently detected in heavy smokers. The aggressive behavior of SCLC is partly caused by the smaller and more rapidly growing and dividing cancer cells compared to those in NSCLC. Based on the degree of disease spread, SCLC is mainly divided into two subtypes: limited-stage SCLC and extensive-stage SCLC[57].

- **Limited-Stage SCLC:** In small-stage small-cell lung cancer (SCLC), there is a tendency towards confinement of the tumor to the primary lobe of a single lung, on the one hand, but the existence of metastatic disease in the regional lymph nodes cannot be described as a rare phenomenon. Standard treatment of this environment mainly consists of strong chemotherapy combined with radiation treatment. Some of them are very successful, but the recurrence is typical, which is often due to the development of acquired treatment resistance in a short period of time [58].
- **Extensive-Stage SCLC:** New data show that extensive-stage small-cell lung cancer (ES-SCLC) has advanced to include,

besides the lungs, brain, liver and skeletal involvement. The outlook of such a late presentation is not good and there are equally complicated treatment courses. Surgical intervention is not suitable because SCLC is most commonly diagnosed in an advanced stage, and its pathology is normally treated by immunotherapy and chemotherapy [59]. The high incidence of relapse even taking into consideration intensive regimens of treatment of the disease is explained by the emergence of the fast defense response to chemotherapy and other therapeutic compounds by small-cell lung carcinoma (SCLC). [60].

- The overall survival of small-cell lung cancer (SCLC) is considered poor since the disease is mostly asymptomatic up to its earlier stages and is commonly diagnosed when the disease is at its later stages usually metastatic cancer. Hematogenous metastases are frequent at presentation, most commonly in the liver, brain and bones. [61]. Small-cell lung cancer (SCLC) should not be subject to surgical excision due to the inclination of the diseases of spreading. Systemic treatment and especially chemotherapy, immune therapy as well as palliative therapy are therefore the most common treatment options of such malignant disease [59].

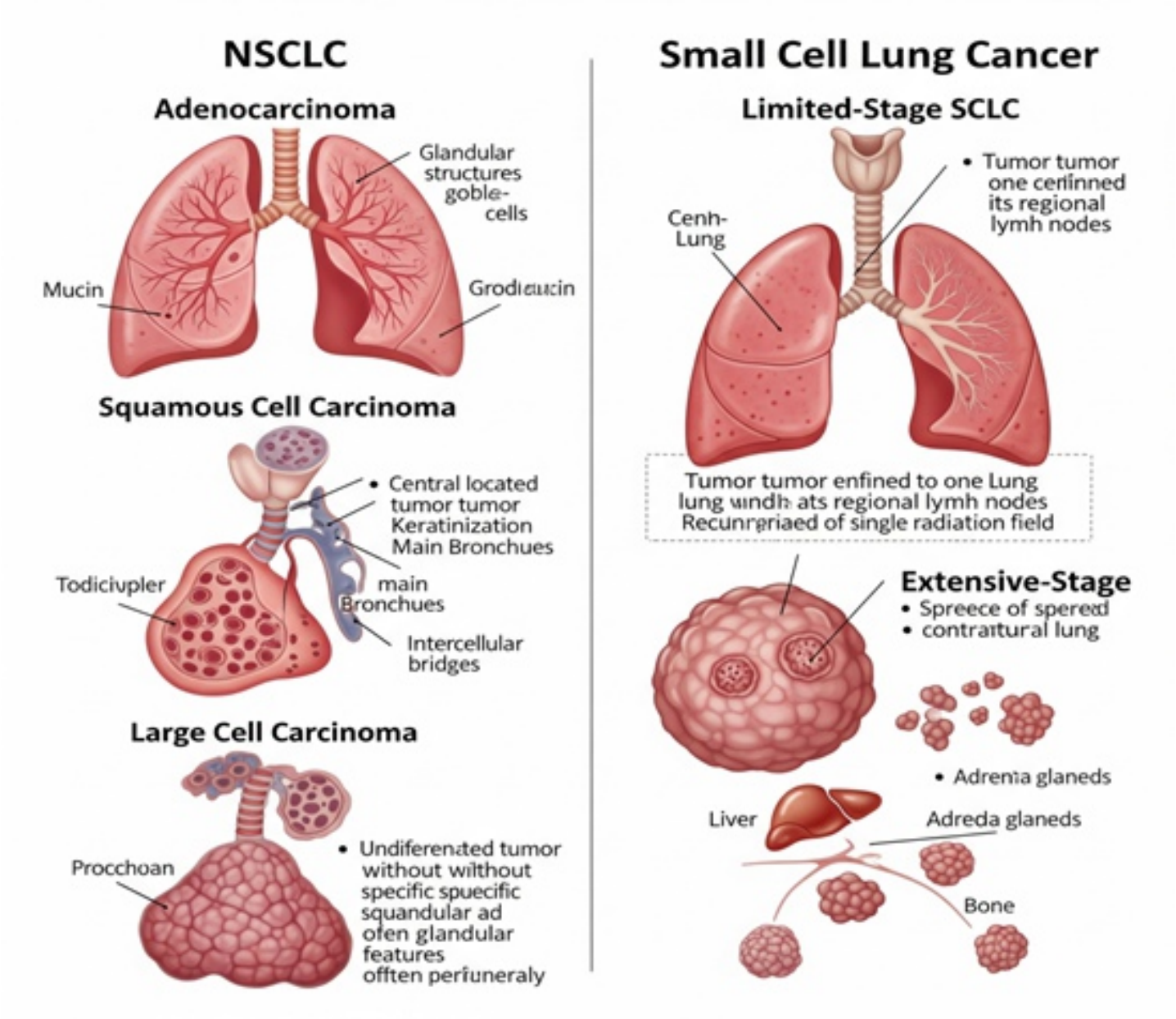

Figure 2:Types of Lung Cancer: NSCLC vs. SCLC

This image provides a comprehensive overview of the two primary forms of lung cancer: Non-Small Cell Lung Cancer (NSCLC) and Small Cell Lung Cancer (SCLC). It details the three main subtypes of NSCLC Adenocarcinoma, Squamous Cell Carcinoma, and Large Cell Carcinoma highlighting their distinct characteristics and common locations. Additionally, the image illustrates the two stages of SCLC, Limited-Stage SCLC and Extensive-Stage SCLC, showing the typical extent of disease spread for each.

3.2 Molecular Pathogenesis

The advanced genomics and its molecular structure are a constellation of mutations, the breaking of signaling cascades, and mutual feedback between the tumor microenvironment and lung cancer. All these alterations together stimulate tumor initiation, growth and metastatic spreading [62].We need to know what the molecular pathways of the disease are behind lung cancer, if we truly mean to go after it, we must address it as aggressively as we can. Here is a brief excursion to some of the principal processes that instigates and contributes to the dissemination of lung cancer [63].

1. Genetic Mutations

One of the most important drivers of lung cancer, especially in non-small cell lung cancer (NSCLC), is genetic mutations. These mutations often result in the activation of oncogenes or the inactivation of tumor suppressor genes, leading to uncontrolled cell proliferation. Key mutations include:[64]

- **EGFR (Epidermal Growth Factor Receptor):** Adenocarcinoma, a subtype of non-small cell lung cancer, frequently has EGFR mutations, which are linked to improved response to EGFR inhibitors like osimertinib and gefitinib. Because the EGFR signaling system is essential for controlling cell growth and survival, these mutations result in abnormal activation of the mechanism[65, 66].
- **ALK (Anaplastic Lymphoma Kinase):** Fusion proteins produced by ALK gene rearrangements promote tumor development in non-small cell lung cancer. EML4-ALK is one example of a fusion protein that activates several downstream signaling pathways to support cell survival and proliferation. Patients with ALK-positive malignancies have demonstrated significant therapeutic improvements from targeted therapy using ALK inhibitors, such as crizotinib[67].
- **KRAS (Kirsten Rat Sarcoma Viral Oncogene Homolog):** Lung cancer frequently has KRAS mutations, which are linked to resistance to some treatments, such as EGFR inhibitors. Tumor development and survival depend on downstream signaling pathways like the MAPK and PI3K/AKT pathways, which are constitutively activated by KRAS mutations[68].

2. Angiogenesis

The development of new blood vessels, or angiogenesis, is frequently triggered by tumors, which need a blood supply to continue growing. In order to ensure a sufficient supply of oxygen and nutrients to support tumor development and metastasis, lung tumors produce angiogenic factors, such as vascular endothelial growth factor (VEGF), which foster the creation of blood vessels[69, 70].

3. Immune Evasion

There are various mechanisms, which are used by the lung cancer cells in escaping identification through the immune system. Particular increase of immunological checkpoint proteins like PD-L1 is also noteworthy among them; the protein prevents the activity of the T-cells and paralyzes the adaptive immune system making it unable to recognize and destroy the tumor. Further, tumor cells secrete immunosuppressive factors, which remodel the microenvironment in a form that does not allow the development of a strong anti-cancer defense [71].

4. Tumor Heterogeneity

Tumor heterogeneity is genetic and phenotypic differences that are found within individual tumor and different places of metastasis [72]. The cancer cells are often heterogenous containing diverse subpopulations whose phenotype and genotypes are dissimilar. They can also display different susceptibility to chemotherapy or to targeted agents and this heterogeneity can precondition acquisition of resistance in the presence of multiple clones in a tumor. Thus, when multiple clones develop independently, the conventional eradication of the disease is hardly feasible and hence treatment failure occurs [73].

4. CLINICAL CHALLENGES IN LUNG CANCER MANAGEMENT

4.1 Late Diagnosis

Since lung cancer in the early stage often has no clinical manifestations, inability to diagnose the disease at an advanced stage is one of the greatest challenges to the disease management [74]. Later forms of lung cancer are often symptomatic, and one of the more indicative signs is a person coughing out blood, hemoptysis, and weight loss. These physical manifestations neither enhance the effectiveness of treatment nor overall survival but in addition, they worsen morbidity and death in the situations where large-scale screening is not held particularly in resource-poor facilities [75].

The main intervention, which is aimed at enabling early cancer detection, in the modern clinical practice is low-dose computed tomography (LDCT) screening of high risk patients mostly comprising of smokers. However, the test is limited by a high false

positive result and the need to recheck the result, which may be both expensive and consuming [76].

4.2 Resistance to Treatment

The responses toward immunotherapy, targeted therapy as well as chemotherapy presents a historical challenge in managing lung-cancer. Mechanisms that contribute to this are development of secondary mutations, highly heterogeneous tumors, and tumor adapts and evades detection by the immune system [77]. One of the secondary resistance mechanisms to EGFR inhibitors is the involvement of EGFR gene T790M mutation in the development of acquired resistance to non-small cell lung cancer (NSCLC) [78]. Like poorly differentiated neuroendocrine tumours, the small cell lung cancer (SCLC) tends to be intractable in the long-term due to its high rate of developing resistance towards first-line chemotherapeutic agents and radiations [79].

4.3 Limited Access to Personalized Medicine

Although there is a significant advancement in the formulation of precision-engineered therapeutics and immunotherapies, equitable access to these achievements is restricted, especially in low- and middle-income nations. Some of the challenges that impact the management of lung cancer in such environments are the astronomical pricing of pharmacologic products, intermittent access to molecular tests, and a lack of health-care infrastructure to implement their corresponding personalized treatment approaches [80].

Challenge	Key Issues	Examples / Notes	References
Late Diagnosis	- Early-stage lung cancer often asymptomatic- Diagnosis occurs at advanced stages	- Common symptoms in later stages: hemoptysis (coughing blood), weight loss- Leads to poor prognosis	[81]
	- Lack of large-scale screening in resource-poor settings	- Increases morbidity and mortality	[82]
	- LDCT is main screening tool for high-risk patients (e.g., smokers)	- Limited by high false-positive rate- Rechecking results is costly and time-consuming	[83]
Resistance to Treatment	- Resistance to immunotherapy, targeted therapy, and chemotherapy	- Causes: secondary mutations, tumor heterogeneity, immune evasion	[4]
	- EGFR T790M mutation contributes to resistance in NSCLC	- Common in acquired resistance to EGFR inhibitors	[84]
	- SCLC shows high resistance to chemotherapy and radiotherapy	- Often poorly differentiated, making long-term treatment difficult	[85]
Limited Access to Personalized Medicine	- Advanced therapies not equally accessible in low- and middle-income countries	- High drug costs, limited molecular diagnostics, poor healthcare infrastructure	[86]
	- Personalized medicine requires molecular testing and tailored treatment protocols	- Implementation challenges due to limited resources and access	[87]

Table 1 : clinical challenges in lung cancer management

5. INNOVATIONS IN LUNG CANCER MANAGEMENT

5.1 Targeted Therapy

It is cranking out cancer-cell growth that the medicines that the doctors now seek are going after and the lungs cancers are taking the hit. Consider non-small cell lung cancer with EGFR mutations: people that have been treated with EGFR inhibitors (gefitinib and erlotinib) now have much better prognosis. Alternatives Patients with ALK-positive malignancies receive treatment using ALK inhibitors think lorlatinib, alectinib, and crizotinib[88].

Historically, patients with the oncoming KRAS G12C mutation that caused few treatment options had gained a new hope with the emergence of selective KRAS G12C inhibitors, the first of which being sotorasib[89].

5.2 Immunotherapy

Immunotherapy and especially immune checkpoint inhibitors (ICIs) including atezolizumab, pembrolizumab, and nivolumab have proved to be a revolutionizing therapeutic modality in lung cancer. These agents activate the immune system by activating the PD-1/PD-L1 pathway, thus causing the immune system to develop the cognizance and destroy the malignant cells. The therapeutic effects prove to be not only immediate, but also lasting in some patients especially those with high PD-L1 expression [90, 91]. Investigators are also studying the chemotherapeutic agent combinations with immune-checkpoint inhibitors (ICIs); the findings of such clinical trials show that such regimens have presented better outcomes of overall and progression-free survival [92].

5.3 Liquid Biopsy and Molecular Diagnostics

With the advent of the liquid biopsy techniques, clinical professionals can see their way to monitor treatment response and identify mutations that indicate systems that are resistant to treatment in real-time [93]. The situation has recently changed because modern development of diagnostic technologies allows detecting genetic changes without invasive tissue biopsy, which is especially important in the case of oncology. Among them are exosome-based diagnostics and circulating tumor DNA (ctDNA) testing that have made a significant step forward [94].

5.4 Artificial Intelligence and Machine Learning

The application of machine learning (ML) and artificial intelligence (AI) to the detection and treatment of lung cancer has grown significantly. To increase diagnostic precision and find appropriate treatment options, AI algorithms are being utilized to evaluate pathology slides, genomic data, and medical imaging. AI is also being investigated to improve healthcare workflows, customize treatment plans, and forecast results [95].

5.5 Nanotechnology

By delivering chemotherapeutic agents directly to cancer cells, nanocarriers are increasing efficacy and reducing side effects. Nanotechnology has the potential to improve drug delivery, overcome obstacles to drug absorption, and reduce systemic toxicity [96].

6. MULTIDISCIPLINARY CARE MODELS

A multidisciplinary strategy involving oncologists, radiologists, pulmonologists, thoracic surgeons, pathologists, and palliative care specialists is necessary for the treatment of lung cancer. Treatment efficiency and survival rates have been demonstrated to increase with the use of a tumor board method, in which specialists from several disciplines work together to decide on the best course of action for each patient [97].

7. CLINICAL TRIALS AND ONGOING RESEARCH

Clinical trials and ongoing research are what propel the continued evolution of lung cancer management. Many recent trials focus on the utilization of novel immunotherapeutic drugs, combination treatments, and new molecular targets [98]. The clinical standard of care will probably change in the upcoming years as a result of new information from pivotal studies like Checkmate 227 and KEYNOTE-189 [99].

8. CHALLENGES IN LOW-RESOURCE SETTINGS

Lung cancer management in low- and middle-income nations is complicated by issues such delayed treatment initiation, restricted access to diagnostic testing, and a shortage of qualified healthcare professionals [100]. Improving early screening programs, expanding access to the newest medicines, and upgrading healthcare infrastructure are all necessary to address these discrepancies [101].

9. FUTURE PERSPECTIVES

With the combination of next-generation immunotherapies, tailored medicines, and AI-powered clinical decision support

tools, the treatment of lung cancer has a bright future. Targeted treatments Applications of precision oncology, a potential game-changer in lung cancer therapy, can make a big difference in this cancer. Using the deep molecular profiling approaches that consist of integrated technologies, including liquid biopsy and next-generation sequencing (NGS), clinicians can determine new biomarkers that facilitate tumor development and the manifestation of drug resistance. These discoveries open possibility to develop specifically-optimized treatment that will target peculiarities of every tumor. This means of stratification has the potential to minimize ineffective chemo bulkiness as well as the detrimental effects of toxicity and maximize endurance by using drugs most appropriate with a single patient tumor characteristics.All these modalities possess the potential of overcoming the short-comings of the current immunotherapeutic agents, especially when used together with conventional chemotherapy. Meanwhile, the future use of artificial intelligence-driven platforms in the management of cancer can potentially disrupt clinical decision-making by establishing better prognostication, support accurate treatment choice, and precision in monitoring treatment response. So, the lung cancer treatment landscape should change significantly over the next few years, not only under the influence of the development of molecular profiling practices but also because of the continued improvement of medication administration and personalized clinical management.

10. CONCLUSION

Even though lung cancer is a significant health challenge in the global community, newer developments have enabled us to know more about its biology and reinforced the success rate of treatment. Improvement in immunotherapy, precise medicine, and the use of new diagnostic techniques may significantly increase the survival rate and quality of life of many other people. The problems of the inability to treat diseases, late diagnosis, and barriers to care should also be addressed in order to guarantee that such discoveries will benefit all groups of people. It is the persistence of the war with lung cancer that will rely on the constant research and collaboration with other countries in the world.

Confllict of Interest

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