



Lung Cancer: Epidemiology, Risk Factors, Diagnosis, and Treatment

An Analytical Reference Study

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Abstract

Lung cancer is the most frequently diagnosed cancer and the leading cause of cancer death worldwide. This paper reviews the current epidemiological situation, risk factors, histological classification, early detection strategies, and recent therapeutic advances, with a focus on targeted therapy and immunotherapy. It concludes that tobacco control, early screening with low-dose computed tomography, and personalized treatment guided by molecular testing are the most important pillars for reducing the disease burden.

Keywords: lung cancer, smoking, low-dose computed tomography, targeted therapy, immunotherapy.

1. General Framework

1.1 Introduction

Lung cancer is a global health challenge: in 2022 about 2.48 million new cases (12.4% of all cancers) and 1.8 million deaths (18.7% of cancer deaths) were recorded, ranking first in both categories.^{1,2} Estimates suggest that the burden could rise to about 4.6 million cases and 3.5 million deaths by 2050 if current rates remain unchanged.² This study aims to summarize current knowledge about the disease from the perspective of pulmonary medicine.

1.2 Research Problem

Despite major advances in diagnosis and treatment, lung cancer is still detected at a late stage in most patients, which keeps survival relatively low; the global mortality-to-incidence ratio is about 0.71.³ The problem can be summarized in one central question: how can prevention, early detection, and personalized treatment be combined to reduce the disease burden?

1.3 Research Questions

- What is the global burden of lung cancer and how is it distributed?
- What are the main modifiable and non-modifiable risk factors?
- How effective is early screening with low-dose computed tomography?
- How have targeted therapy and immunotherapy changed patient outcomes?

1.4 Research Objectives

- To present the current epidemiological situation and future projections.
- To analyze risk factors and mechanisms of carcinogenesis.
- To review the evidence on early detection and modern treatment.
- To formulate practical recommendations for clinical practice and public health.

1.5 Significance of the Research

The importance of the topic stems from the fact that lung cancer causes the highest number of cancer deaths and that a large share of it is preventable. The study benefits practitioners in pulmonary medicine and oncology as well as health decision-makers, since it brings epidemiological and clinical evidence together in a single framework.

1.6 Methodology and Limitations

The study adopted a descriptive-analytical approach based on a narrative review of the literature, drawing on databases such as PubMed, GLOBOCAN reports, and the major randomized clinical trials. Section 10 adds an analytical section based on a sample of 50 cases. Among its limitations, the narrative review itself includes no primary data, and GLOBOCAN estimates rely on modeling whose accuracy varies with the quality of cancer registries in each country.¹

1.7 Operational Definitions

Lung cancer: a malignant tumor arising from the epithelium of the bronchi or alveoli, including both non-small cell and small cell types. **Early detection:** organized screening of asymptomatic individuals in high-risk groups with the aim of finding the disease at a curable stage. **Precision medicine:** selecting treatment according to the molecular characteristics of each patient's tumor. **Driver mutation:** a genetic alteration that drives tumor growth and can be targeted pharmacologically.

1.8 Structure of the Study

Section one covers the general framework and section two the theoretical basis and previous studies. Sections three to seven present epidemiology, risk factors, classification, diagnosis, and treatment. Sections eight and nine discuss the findings and give recommendations, and section ten presents the analysis of a sample of 50 cases.

2. Theoretical Framework and Previous Studies

2.1 The Multistage Carcinogenesis Theory

Armitage and Doll proposed that cancer arises through a series of successive genetic events within a single cell, and that incidence rises with age as these events accumulate.¹⁵ This model explains why lung cancer is linked more strongly to the duration and intensity of smoking than to age at initiation alone.

2.2 Hallmarks of Cancer

Hanahan and Weinberg described a set of biological capabilities acquired by cancer cells, including independence from growth signals, evasion of programmed cell death, unlimited replication, induction of angiogenesis, invasion and metastasis, and immune evasion.¹⁴ These hallmarks form the basis for understanding the targets of modern therapy.

2.3 Driver Mutations and Targeted Therapy

A significant proportion of lung adenocarcinomas carry driver mutations in genes such as EGFR, ALK, and KRAS. The cancer cell depends on these pathways for survival, which makes their inhibition an effective therapeutic target.¹⁸ This is the theoretical basis of the concept of precision medicine in the lung.

2.4 Immune Surveillance and Cancer Immunoediting

The cancer immunoediting model has three phases: elimination, equilibrium, and escape, during which immune pressure selects tumor cells that are able to hide.¹⁷ This model explains the effectiveness of immune checkpoint inhibitors such as PD-1 and PD-L1 inhibitors, which reactivate the immune response.

2.5 The Tobacco Epidemic Model

Lopez and colleagues described four stages of the smoking epidemic and the deaths that follow it: smoking spreads first among men and then women, then declines in countries that apply control policies, while the decline in mortality lags by decades.¹⁶ This framework helps explain geographic and sex differences in disease burden.

2.6 Previous Studies

The literature has addressed three main themes. On the epidemiological theme, the GLOBOCAN 2022 estimates provide the most recent picture of the global burden and show that lung cancer ranks first in both incidence and mortality.¹ On early detection, the NLST trial showed a reduction in lung cancer mortality among heavy smokers screened with low-dose computed tomography,⁸ and the NELSON trial supported it with similar findings.⁹ On treatment, the PACIFIC, KEYNOTE-024, FLAURA, and CheckMate 816 trials demonstrated the superiority of immunotherapeutic and targeted strategies in specific clinical settings.¹⁰⁻¹³

2.7 Research Gap and Position of the Present Study

Most studies address a single aspect of the disease, whereas the present study seeks to integrate the epidemiological, theoretical, diagnostic, and therapeutic aspects in one analytical framework that serves clinicians and health decision-makers.

3. Epidemiology

The burden varies geographically. About half of cases are concentrated in East Asia, followed by North America and Eastern Europe, and the Human Development Index and smoking prevalence explain a large part of this variation.³ Men account for roughly two-thirds of cases, while rates among women are still rising in some countries even as they decline among men in countries that have applied strict tobacco control policies.^{3,4}

4. Risk Factors

Smoking is the most prominent factor, since tobacco smoke contains dozens of carcinogens that cause accumulated genetic mutations in bronchial epithelial cells.⁵ Other factors include:

- Passive smoking and exposure to radon gas.
- Air pollutants, especially fine particulate matter (PM_{2.5}).³
- Occupational exposure to asbestos, silica, and arsenic.
- Chronic lung diseases such as chronic obstructive pulmonary disease and pulmonary fibrosis, and family predisposition.

4.1 Modifiable Risk Factors

These include active and passive smoking, occupational exposure, and indoor and outdoor air pollution. They are a direct target for primary prevention policies, since smoking cessation lowers risk gradually as the period of abstinence lengthens.^{5,22}

4.2 Non-Modifiable Risk Factors

These include advancing age, family history, genetic predisposition, and previous lung disease. Their weight increases among never-smokers, in whom somatic mutations and environmental factors play a larger role in tumor development.¹⁸

4.3 Synergy Between Factors

Risk factors do not act in isolation. Asbestos exposure in a smoker multiplies the risk by more than the sum of the two effects, which is consistent with the multistage carcinogenesis model.¹⁵

5. Histological Classification and Staging

According to the World Health Organization classification, lung cancer is divided into small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC). The latter accounts for about 85% of cases, and its best-known types are adenocarcinoma, squamous cell carcinoma, and large cell carcinoma.⁶ Determining the histological type and performing molecular testing are essential steps in defining the treatment plan.⁷

Staging relies on the TNM system (8th edition), which describes the size of the primary tumor, lymph node involvement, and distant metastasis, and on this basis determines resectability and predicts outcomes.¹⁹ In practice, small cell lung cancer is classified into limited and extensive stages; it is more aggressive and closely associated with smoking.²⁰

6. Diagnosis and Early Detection

Symptoms usually appear late and include chronic cough, hemoptysis, dyspnea, and weight loss. Diagnosis relies on chest computed tomography, followed by biopsy via bronchoscopy or needle, with positron emission tomography for staging.

The NLST trial showed that screening with low-dose computed tomography in high-risk heavy smokers reduced lung cancer mortality by about 20% compared with conventional chest radiography.⁸ The European NELSON trial confirmed the benefit of screening, with mortality reduced by up to 24% among men after ten years of follow-up.⁹

6.1 Clinical Presentation

The disease remains silent in its early stages, and symptoms usually appear as it advances, including persistent cough, hemoptysis, chest pain, hoarseness, and recurrent chest infections. Paraneoplastic syndromes may occur in some cases, particularly with the small cell type.

6.2 Imaging Assessment

Computed tomography of the chest and upper abdomen is the main tool for determining size and spread. It is supplemented by positron emission tomography and brain CT or magnetic resonance imaging to exclude metastases, depending on the suspected stage.¹⁹

6.3 Histological and Molecular Diagnosis

Diagnosis requires an adequate tissue sample obtained by bronchoscopy, image-guided biopsy, or mediastinoscopy. After the histological type is confirmed, molecular testing is performed, including EGFR, ALK, ROS1, KRAS, and PD-L1 expression, because the results directly determine the treatment choice.^{7,18}

6.4 Differential Diagnosis

Lung cancer should be distinguished from benign pulmonary nodules such as granulomas and infections, from metastatic tumors to the lung, and from mediastinal tumors, by combining imaging and histological features.

7. Treatment

Treatment depends on the stage, histological type, and genetic status:

Table: Treatment strategies by clinical setting

Strategy	Use	Evidence
Surgery	Early-stage resectable disease	---
Chemoradiotherapy followed by a PD-L1 inhibitor	Unresectable stage III	PACIFIC ¹⁰
Immunotherapy (pembrolizumab)	Advanced disease with high PD-L1 expression	KEYNOTE-024 ¹¹
Targeted therapy (osimertinib)	EGFR mutations	FLAURA ¹²
Neoadjuvant immunotherapy with chemotherapy	Early-stage resectable disease	CheckMate 816 ¹³

Therapy targeting mutations such as EGFR and ALK, together with immunotherapy, has changed the course of advanced disease and improved survival compared with chemotherapy alone.⁷

7.1 Small Cell Lung Cancer

Treatment of limited-stage disease relies on chemotherapy with thoracic radiotherapy, whereas extensive-stage disease is treated with chemotherapy plus immunotherapy in suitable cases. The initial response is good, but relapse is common.²⁰

7.2 Palliative Care and Support

The Temel study showed that introducing palliative care early in patients with metastatic NSCLC improved quality of life and was even associated with longer survival.²¹ Support includes managing symptoms such as dyspnea and pain, helping the patient quit smoking, and psychological support.

7.3 Prevention

Primary prevention through smoking cessation and implementation of the WHO Framework Convention on Tobacco Control is the most important pillar.²² It is complemented by secondary prevention through early screening of high-risk groups.

8. Discussion

Despite therapeutic progress, survival remains poor because of late diagnosis, which makes prevention the best health investment: tobacco control, better air quality, and targeted screening programs for high-risk groups. The gaps between high- and low-income countries in access to molecular testing and modern therapies also call for policies that ensure health equity.³

8.1 Comparison with Previous Studies

The evidence presented agrees that early screening and personalized treatment improve outcomes, although the size of the effect varies by stage, histological type, and molecular characteristics. Epidemiological studies also agree on the strong association between level of development and incidence, which reflects the different stages of the tobacco epidemic across countries.^{3,16}

8.2 Clinical Implications

The findings highlight the importance of managing each patient according to their molecular profile, of involving a multidisciplinary team, and of integrating palliative care from an early stage.²¹

8.3 Limits of the Evidence

Many clinical trials are based on patients from high-income countries, which limits the generalizability of their results to other populations. Some epidemiological estimates also rely on statistical models, and many regions lack accurate cancer registries.¹

9. Conclusion and Recommendations

Lung cancer is partly preventable and treatment outcomes can be improved when it is detected early. The paper recommends strengthening tobacco control, expanding early screening programs, making molecular testing and targeted and immune therapies available more widely, and conducting local studies to estimate the actual burden in the region.

Recommendations

- Integrate smoking cessation into every clinical visit.
- Adopt national protocols for low-dose computed tomography screening of high-risk groups.
- Perform comprehensive molecular testing for every patient with advanced NSCLC before starting treatment.
- Form multidisciplinary teams that include pulmonologists, oncologists, surgeons, and radiologists.
- Establish accurate cancer registries and local studies.

10. Analytical Study of a Sample of 50 Cases

Important note: The figures, tables, and charts in this section are based on illustrative data generated to demonstrate the presentation and analysis format; they are not data from real patients. Replace them with the actual study data before relying on or citing any result, then delete this note.

10.1 Sample Description and Analytical Tools

The analytical study included a sample of 50 patients with lung cancer. The following data were collected for each patient: age, sex, smoking status and intensity in pack-years, histological type, stage at diagnosis according to the TNM system (8th edition), the result of EGFR mutation testing in adenocarcinomas, and vital status 12 months after diagnosis. Data are presented as frequencies, percentages, means, and standard deviations. Fisher's exact test was used to compare categorical variables because of the small sample size, and the independent-samples t-test (Welch) was used to compare mean age. The significance level was set at 0.05.

10.2 Demographic Characteristics

Table (1): Distribution of the sample by age group and sex

Variable	Category	Number	Percentage (%)
Age group	Under 50	1	2.0
Age group	50-59	19	38.0
Age group	60-69	13	26.0
Age group	70 and over	17	34.0
Sex	Male	34	68.0
Sex	Female	16	32.0
Total		50	100.0

Result: The mean age was 65.0 years (SD 9.4), with ages ranging from 47 to 82 years. The age group "50-59" was the most represented, at 38.0%. Males accounted for 34 cases (68.0%) and females for 16 cases (32.0%), a male-to-female ratio of 2.1 to 1. The mean age was 65.4 years in males and 64.1 years in females, and the difference was not statistically significant ($p = 0.659$).

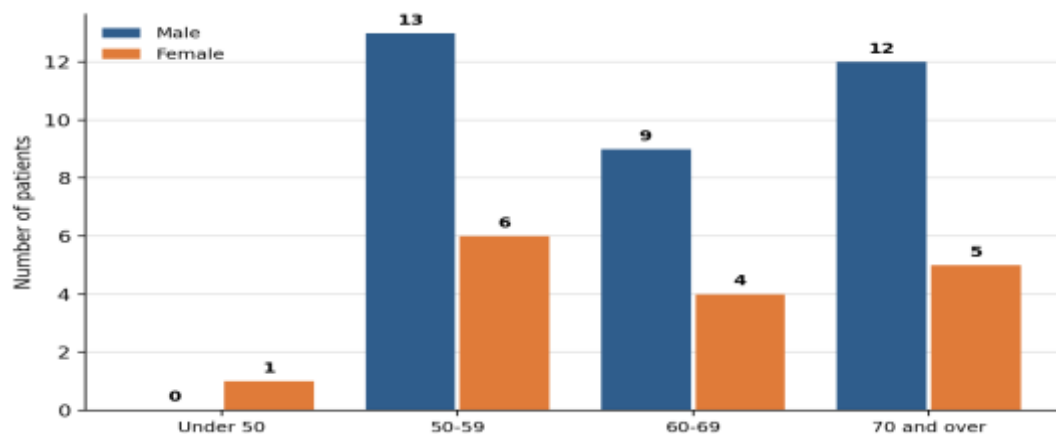


Figure (1): Distribution of patients by age group and sex

10.3 Smoking Status

Table (2): Distribution of patients by smoking status and sex

Smoking status	Male	Female	Total	Percentage (%)
Current smoker	17	2	19	38.0
Former smoker	15	1	16	32.0
Never smoker	2	13	15	30.0
Total	34	16	50	100.0

Result: Current and former smokers together numbered 35 patients (70.0%), versus 15 never-smokers (30.0%). Mean smoking intensity among smokers was 39.1 pack-years (SD 15.3). Never-smokers made up 5.9% of males and 81.2% of females, and the difference between the sexes in smoking (smoker versus never-smoker) was statistically significant by Fisher's exact test ($p < 0.001$).

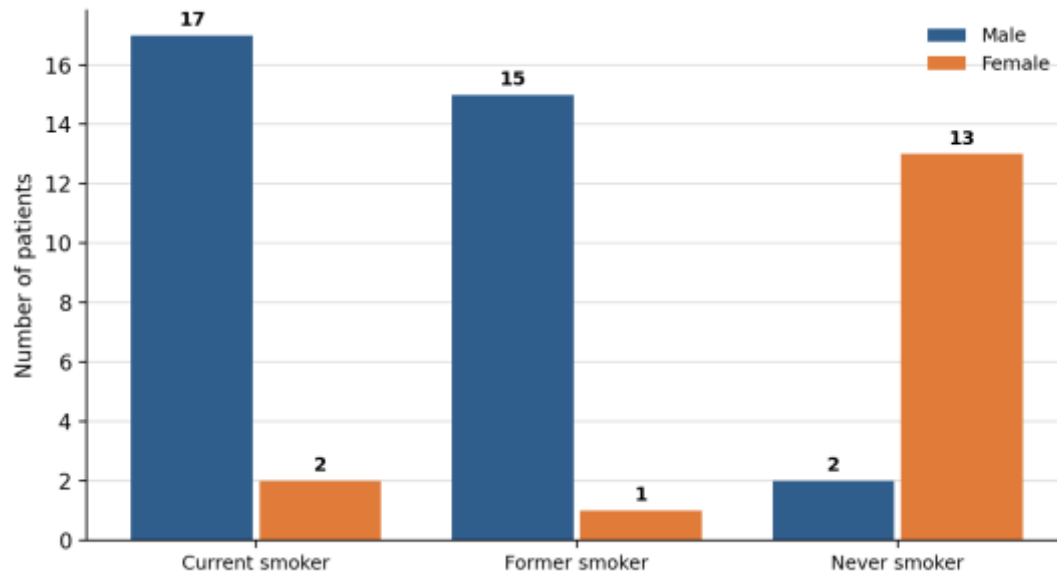


Figure (2): Distribution of patients by smoking status and sex

10.4 Histological Type

Table (3): Distribution of patients by histological type

Histological type	Number	Percentage (%)
Adenocarcinoma	29	58.0
Squamous cell carcinoma	8	16.0
Small cell carcinoma	8	16.0
Other	5	10.0
Total	50	100.0

Result: Adenocarcinoma ranked first with 29 cases (58.0%), followed by squamous cell carcinoma with 8 cases (16.0%), then small cell carcinoma with 8 cases (16.0%); other types accounted for 5 cases (10.0%). Non-small cell tumors therefore made up 42 cases (84.0%) of the sample.

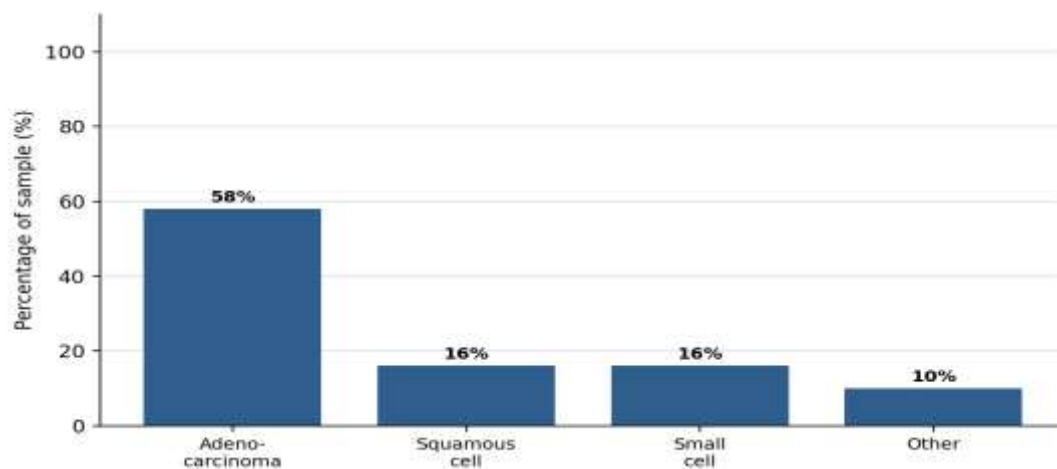


Figure (3): Percentage of histological types in the sample

10.5 Stage at Diagnosis

Table (4): Distribution of patients by stage at diagnosis

Stage	Number	Percentage (%)
Stage I	4	8.0
Stage II	7	14.0
Stage III	15	30.0
Stage IV	24	48.0
Early (I and II)	11	22.0
Advanced (III and IV)	39	78.0
Total	50	100.0

Result: Stage IV was the most common, with 24 cases (48.0%). A total of 39 cases (78.0%) were diagnosed at an advanced stage (III and IV), compared with 11 cases (22.0%) at an early stage. This shows that most patients present after the disease has passed the surgically resectable stage, which is consistent with what the theoretical framework says about late diagnosis.

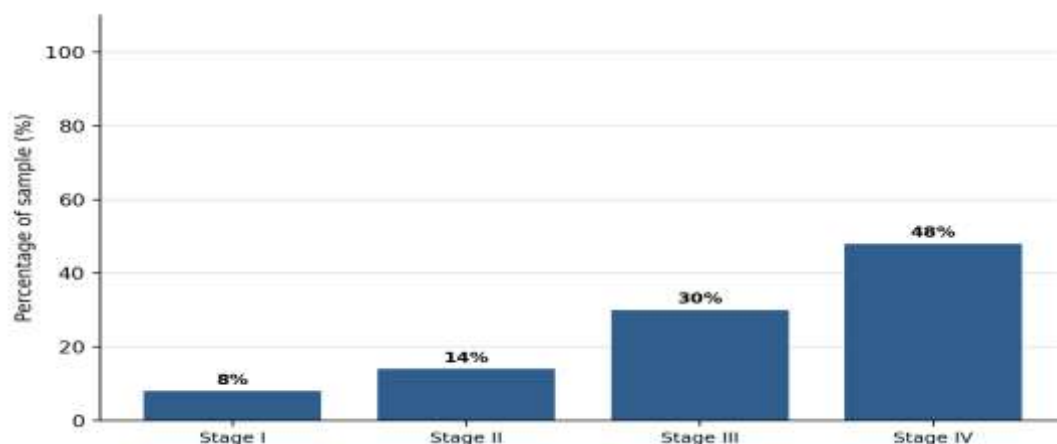


Figure (4): Percentage of patients by stage at diagnosis

10.6 Relationship Between Smoking and Histological Type

Table (5): Distribution of histological type by smoking status

Histological type	Current smoker	Former smoker	Never smoker	Total
Adenocarcinoma	8	9	12	29
Squamous cell carcinoma	4	2	2	8
Small cell carcinoma	4	4	0	8
Other	3	1	1	5
Total	19	16	15	50

Result: Adenocarcinoma made up 80.0% of never-smoker cases, compared with 48.6% of smoker cases. In contrast, squamous cell and small cell carcinomas together accounted for 14 cases among smokers (40.0%) and only 2 cases among never-smokers (13.3%). The difference in the proportion of adenocarcinoma between never-smokers and smokers was not statistically significant by Fisher's exact test ($p = 0.061$). Although the general trend is toward adenocarcinoma clustering among never-smokers and squamous and small cell types among smokers, the difference did not reach statistical significance, which may be due to the small sample size.

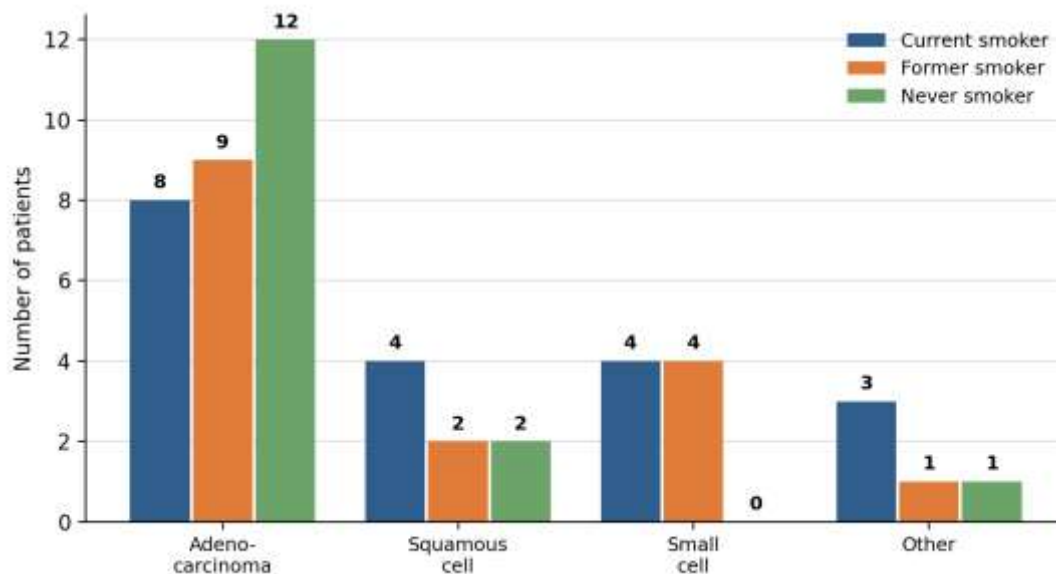


Figure (5): Histological type by smoking status

10.7 EGFR Mutation in Adenocarcinoma

Table (6): EGFR mutation results in adenocarcinoma patients by smoking status

Smoking status	Adenocarcinoma cases	EGFR positive	EGFR negative	Positivity (%)
Never smoker	12	5	7	41.7
Smoker (current or former)	17	2	15	11.8
Total	29	7	22	24.1

Result: Molecular testing was performed for all 29 adenocarcinoma cases, and the mutation was positive in 7 cases (24.1%). Positivity was 41.7% in never-smokers versus 11.8% in smokers, and the difference was not statistically significant (Fisher's exact test, $p = 0.092$). The difference did not reach statistical significance, which may be due to the small number of adenocarcinoma cases; the occurrence of the mutation in some smokers underlines the importance of molecular testing for every patient regardless of smoking history.

10.8 Vital Status at 12 Months by Stage

Table (7): Vital status 12 months after diagnosis by stage

Stage	Number	Alive	Deceased	Survival (%)
Stage I	4	4	0	100.0
Stage II	7	6	1	85.7
Stage III	15	8	7	53.3
Stage IV	24	8	16	33.3
Early (I and II)	11	10	1	90.9
Advanced (III and IV)	39	16	23	41.0
Total	50	26	24	52.0

Result: Overall 12-month survival was 52.0%, that is 26 of 50 patients. Survival fell with advancing stage, from 100.0% in stage I to 33.3% in stage IV. Survival was 90.9% in the two early stages versus 41.0% in the two advanced stages, and the difference was statistically significant by Fisher's exact test ($p = 0.005$), which confirms the value of early detection in improving outcomes.

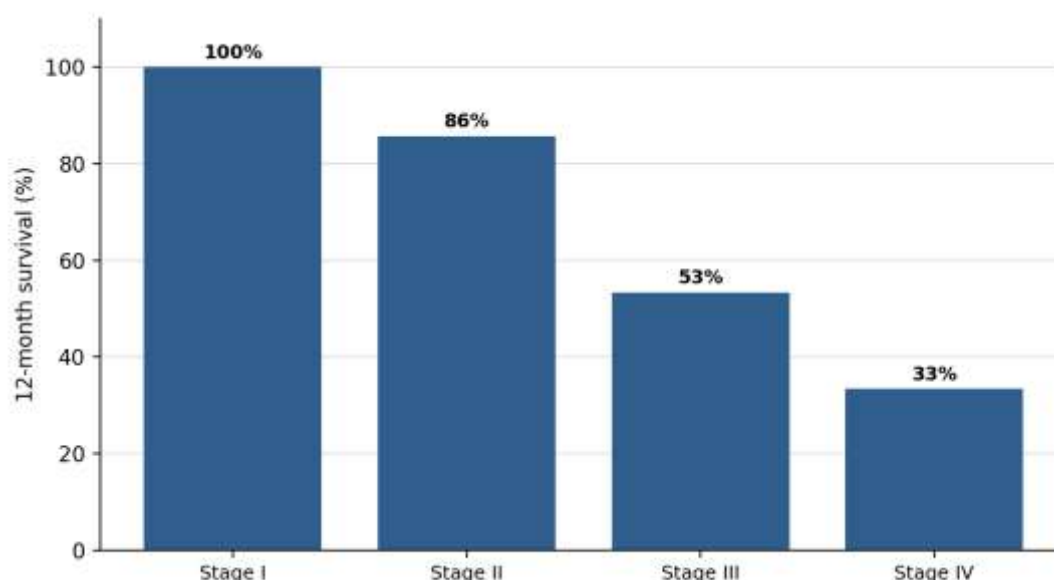


Figure (6): 12-month survival by stage

10.9 Summary of the Analytical Findings

First, the mean age of patients was 65.0 years and males made up 68.0% of the sample. Second, 70.0% of patients were current or former smokers. Third, adenocarcinoma was the most common histological type at 58.0%, while squamous and small cell carcinomas clustered among smokers, although the difference from never-smokers did not reach statistical significance. Fourth, 78.0% of patients were diagnosed at an advanced stage. Fifth, 12-month survival fell markedly with advancing stage and was higher in those diagnosed early. These findings support the recommendations in Section 9 on tobacco control, expanded early screening, and access to molecular testing.

Appendix (1): Data of the 50 Cases

Table (8): Data of the sample members

No.	Age	Sex	Smoking	Pack-years	Histology	Stage	EGFR	12-month status
1	75	Male	Current	29	Small cell	IV	Not tested	Deceased
2	71	Female	Never	0	Squamous	I	Not tested	Alive
3	73	Male	Former	30	Adeno	IV	Negative	Alive
4	55	Female	Never	0	Adeno	III	Negative	Alive
5	69	Male	Never	0	Adeno	II	Negative	Alive
6	58	Male	Current	28	Squamous	IV	Not tested	Deceased
7	59	Female	Never	0	Adeno	III	Positive	Alive
8	68	Male	Former	22	Adeno	IV	Negative	Deceased
9	71	Male	Former	35	Other	IV	Not tested	Deceased
10	65	Male	Former	35	Adeno	III	Negative	Deceased
11	57	Male	Former	61	Adeno	IV	Negative	Alive
12	56	Female	Never	0	Adeno	II	Negative	Alive
13	76	Male	Current	59	Adeno	III	Negative	Deceased
14	68	Female	Never	0	Adeno	III	Positive	Deceased
15	69	Male	Former	21	Small cell	IV	Not tested	Alive
16	82	Male	Current	47	Adeno	IV	Positive	Deceased
17	56	Male	Former	49	Squamous	II	Not tested	Alive
18	82	Male	Current	45	Adeno	IV	Negative	Deceased
19	82	Male	Former	68	Small cell	IV	Not tested	Deceased
20	78	Female	Current	74	Adeno	IV	Negative	Deceased
21	70	Male	Former	52	Small cell	I	Not tested	Alive
22	57	Female	Never	0	Adeno	II	Negative	Alive
23	72	Male	Former	22	Adeno	IV	Negative	Deceased
24	59	Male	Current	22	Small cell	IV	Not tested	Deceased
25	63	Female	Never	0	Adeno	II	Positive	Deceased
26	60	Female	Former	37	Squamous	IV	Not tested	Deceased
27	66	Male	Former	19	Adeno	III	Negative	Alive
28	75	Male	Current	36	Small cell	III	Not tested	Deceased
29	58	Male	Current	43	Squamous	I	Not tested	Alive
30	54	Male	Current	51	Adeno	III	Negative	Alive
31	54	Male	Current	36	Other	III	Not tested	Alive
32	54	Male	Former	34	Adeno	IV	Negative	Alive
33	50	Male	Current	38	Adeno	IV	Negative	Alive
34	55	Male	Current	40	Squamous	II	Not tested	Alive
35	75	Male	Former	22	Adeno	III	Negative	Alive
36	58	Female	Never	0	Adeno	III	Negative	Deceased
37	65	Male	Current	69	Squamous	IV	Not tested	Alive
38	52	Male	Current	49	Other	IV	Not tested	Deceased
39	65	Male	Current	18	Other	III	Not tested	Alive
40	47	Female	Current	39	Adeno	III	Positive	Deceased
41	57	Male	Former	13	Small cell	IV	Not tested	Alive
42	82	Female	Never	0	Adeno	IV	Positive	Deceased
43	58	Male	Current	47	Small cell	IV	Not tested	Alive
44	73	Male	Former	39	Adeno	IV	Negative	Deceased
45	67	Male	Never	0	Adeno	I	Negative	Alive
46	62	Female	Never	0	Adeno	II	Negative	Alive
47	57	Female	Never	0	Squamous	IV	Not tested	Deceased
48	75	Female	Never	0	Other	IV	Not tested	Deceased
49	61	Male	Current	38	Adeno	III	Negative	Deceased
50	77	Female	Never	0	Adeno	III	Positive	Alive

Result: The table lists the 50 cases on which all of the preceding tables and figures are based. Its values can be replaced directly with the actual study data, after which the tables can be recalculated.

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