

ORIGINAL ARTICLE

Clinical Presentation, Disease Characteristics, and Predictors of Advanced-Stage Disease Among Patients with Lung Cancer

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ABSTRACT

Background: Lung cancer is a leading cause of cancer-related morbidity and mortality and is often diagnosed at a late stage. This study aimed to characterize the clinical presentation, disease characteristics and identify independent predictors associated with advanced-stage lung cancer in primary lung cancer patients. **Methods:** This descriptive cross-sectional study was carried out for 6 months on 150 adult patients with primary lung. Information was gathered on demographic data, smoking habits, presenting symptoms, histology, tumor stage, metastatic status, and ECOG performance status via interviews, clinical examination, and medical record reviews. Stage III–IV disease was the outcome for multivariable logistic regression. Data were analyzed using SPSS version 26.0, descriptive statistics, association tests, and multivariable logistic regression; $p < 0.05$ was considered significant. **Results:** The mean age was 61.8 ± 10.9 years, and 102 (68.0%) were male. The most common histological type was NSCLC 117 (78.0%). Persistent cough 111 (74.0%), weight loss 71 (60.7%), dyspnea 88 (58.7%), fatigue 83 (55.3%), and chest pain 79 (52.7%) were common. Overall, 97 (64.7%) had stage III–IV disease and 58 (38.7%) had metastasis. Independent predictors were ECOG ≥ 2 (AOR=3.36; 95% CI: 1.63–6.94; $p=0.001$), current/former smoking (AOR=2.94; 95% CI: 1.39–6.23; $p=0.005$), SCLC (AOR=2.47; 95% CI: 1.08–5.64; $p=0.032$) weight loss (AOR=2.28; 95% CI: 1.15–4.50; $p=0.018$), and dyspnea (AOR=2.11; 95% CI: 1.05–4.22; $p=0.035$). **Conclusion:** Timely lung cancer diagnosis may be facilitated by early symptom recognition, risk-based referral, and comprehensive staging. These predictors require validation to assess their impact on early detection and treatment planning in future studies.

Keywords: Dyspnea; Lung Neoplasms; Neoplasm Metastasis; Neoplasm Staging; Smoking.

INTRODUCTION

Lung cancer is one of the most significant health problems globally and is the leading cause of cancer-related morbidity and mortality worldwide ¹. Lung cancer was responsible for about 2.5 million new cases and 1.8 million deaths in 2022, highlighting the significant public-health and clinical burden of lung cancer ². Poor outcomes are also affected by the continued prevalence of tobacco exposure as the most important modifiable risk factor, as well as aggressive tumor biology and delayed diagnosis ³. Lung cancer can be divided into two categories: non-small-cell lung cancer (NSCLC) and small-cell lung cancer (SCLC). NSCLC is the common form, while SCLC is associated with rapid dissemination, early dissemination, and frequently presents with a diffuse disease state ^{4,5}. Lung cancer may manifest in a variety of ways and can be influenced by a number of factors, including the location of the tumor, the histological type of the lung cancer, the stage of the disease, the nature of metastases, and smoking status ⁶.

The most common symptoms are persistent cough, dyspnea, chest pain, weight loss, fatigue, and hemoptysis ⁷. Based on population data, cough and dyspnea are present at diagnosis, and there is a significant number that have stage IV disease ⁸. There is a possibility for delayed presentation and diagnosis due to delayed recognition of warning signs, limited awareness, referral barriers, or limited access to diagnostic services ⁹. Lung cancer screening with low-dose computed tomography (LDCT) could save lives in high-risk populations that are most likely to benefit from screening, but the uptake of LDCT screening varies by region; and there are still patients who are diagnosed only after they have developed symptoms ¹⁰.

Furthermore, the clinical characteristics and factors influencing advanced disease may differ by health care setting and populations. To enhance clinical suspicion and referral patterns, it is therefore crucial to characterize presenting symptoms, histological patterns, stage, metastatic status and functional performance. The aim of the present study was to outline the clinical characteristics and presentation of patients with primary lung cancer and to determine independent predictors for advanced-stage disease.

METHODOLOGY

This descriptive cross-sectional study was carried out to assess clinical presentation and disease characteristics of patients with primary lung cancer. The study was conducted at a Tertiary care Hospital in Lahore in the Department of Pulmonology and Oncology for 6 months (August 2025- January 2026). The sample size was calculated using OpenEpi version 3.01 (released 2013, Atlanta, GA, USA) for a single population proportion with a 95% confidence level, 5% margin of error, and the expected prevalence as reported in previous literature. The minimum sample size was 150 patients, calculated using the formula $n = Z^2 P(1-P)/e^2$, where n represents the required sample size, Z is the standard normal deviate corresponding to the confidence level, P is the estimated prevalence, and e is the absolute precision ¹¹. So, 150 Patients with primary lung cancer (PLC) were recruited consecutively, who had been diagnosed by histological examination. The participants with newly diagnosed or even validated lung cancer were adult patients (≥18 years) histologically confirmed primary lung cancer, regardless of gender. Recurrent lung cancer after definitive treatment, secondary metastatic (extrapulmonary) lung cancer, and insufficient medical records or severe cognitive impairment that did not allow for reliable data collection were excluded.

Data collection was done by interview and patient's clinical examination and review of hospital medical records based on a structured, pretested data collection form. Demographic parameters were age, gender, smoking history, and pertinent medical history. Smoking history was divided into current smokers, former smokers, or never smokers. At diagnosis, clinical data about the symptoms were noted, such as persistent cough, dyspnea, chest pain, hemoptysis, loss of weight, tiredness, fever, hoarseness and digital clubbing. The Eastern Cooperative Oncology Group (ECOG) performance status scale was used to assess functional status.

Histopathological diagnosis was confirmed by bronchoscopic biopsy, computed tomography (CT)-guided biopsy or surgical biopsy as indicated by clinical findings. Histologically, it was classified according to the World Health Organization (WHO) classification as adenocarcinoma, squamous cell carcinoma and small cell lung cancer. Non-small-cell lung cancer (NSCLC) was defined as the combined category of adenocarcinoma and squamous cell carcinoma. T Tumor staging was done based on the American Joint Committee on Cancer (AJCC, 8th edition) Tumor-Node-Metastasis (TNM) staging system, and patients were categorized as Stage I to IV. Where clinically indicated, the diagnosis of distant metastasis was confirmed by radiological investigations such as contrast-enhanced CT, positron emission tomography (PET-CT), magnetic resonance imaging (MRI) or bone scintigraphy.

The Statistical Package for the Social Sciences (SPSS) version 26.0 was used to enter and analyze the data. The data were summarized as mean ± standard deviation for continuous variables and frequencies and percentages for categorical variables. The Chi-square test was used for associations between categorical variables and clinicopathological data and for associations between continuous variables and clinicopathological data, respectively. Statistically significant variables at univariate analysis were included in multivariable logistic regression to find independent predictors of presenting stage of the disease.

The odds ratio (OR) was computed and adjusted (AOR) with 95% confidence intervals (CIs). A two-tailed p-value <0.05 was deemed statistically significant. Followed by study approval, all participants gave informed consent to participate in the study. All the collected data were treated confidentially, anonymously, and only for research purposes according to the ethical principles of the Declaration of Helsinki ¹².

RESULTS

There were 150 patients with lung cancer in the study. The mean age of participants was 61.8 ± 10.9 years, with the largest proportion aged 60–69 years, 52 (34.7%), followed by 50–59 years 39 (26.0%), ≥70 years 35 (23.3%), and <50 years 24 (16.0%). 102 (68.0%) of the sample were males, 71 (47.3%) were current smokers, 43 (28.7%) were former smokers, and 36 (24.0%) were never smokers, as shown in **Table I**.

Table I: Baseline Demographic and Clinical Characteristics of the Study Participants (N=150)		
Variable	Frequency (n)	Percentage (%)
Age Group (years)		
<50	24	16.0
50–59	39	26.0
60–69	52	34.7
≥70	35	23.3
Gender		
Male	102	68.0
Female	48	32.0
Smoking Status		
Current smoker	71	47.3
Former smoker	43	28.7
Never smoker	36	24.0
Mean Age (years)	61.8 ± 10.9	

The most frequent histologies were adenocarcinoma 69 (46.0%), squamous cell carcinoma 48 (32.0%), and small cell lung cancer 33 (22.0%). Based on histopathological classification, adenocarcinoma and squamous cell carcinoma were categorized under non-small-cell lung cancer (NSCLC), while small-cell lung cancer was analyzed separately as SCLC according to WHO classification. The majority of patients had advanced disease (Stage III, 51(34.0%), and Stage IV, 46(30.7%)), and distant metastasis was seen in 58 (38.7%) of patients, as shown in **Table II**.

Table II: Histopathological and Disease Characteristics		
Variable	Frequency (n)	Percentage (%)
Histological Type		
Adenocarcinoma	69	46.0

Squamous cell carcinoma	48	32.0
Small cell lung cancer	33	22.0
Tumor Stage		
Stage I	18	12.0
Stage II	35	23.3
Stage III	51	34.0
Stage IV	46	30.7
Presence of Metastasis		
Yes	58	38.7
No	92	61.3

Table III shows that persistent cough was the most common presenting symptom (111 (74.0%)), followed by weight loss (91 (60.7%)), dyspnea (88 (58.7%)), fatigue (83 (55.3%)), chest pain (79 (52.7%)), and hemoptysis (56 (37.3%)). Other, less common, symptoms included fever (29 (19.3%)), digital clubbing (25 (16.7%)), and hoarseness (21 (14.0%)).

Table III: Clinical Presentation of Lung Cancer

Symptom	Frequency (n)	Percentage (%)
Persistent cough	111	74.0
Weight loss	91	60.7
Dyspnea	88	58.7
Chest pain	79	52.7
Hemoptysis	56	37.3
Fatigue	83	55.3
Fever	29	19.3
Hoarseness	21	14.0
Digital clubbing	25	16.7

Advanced-stage disease was significantly more frequent among current/former smokers (83 (85.6%) vs. 31 (58.5%); $p<0.001$), patients with weight loss (68 (70.1%) vs. 23 (43.4%); $p=0.002$), dyspnea (65 (67.0%) vs. 23 (43.4%); $p=0.006$), and ECOG performance status ≥ 2 (61 (62.9%) vs. 16 (30.2%); $p<0.001$). The frequency of metastatic disease in advanced-stage patients was 58 (59.8%), and in none of the early-stage patients ($p<0.001$), as shown in **Table IV**.

Table IV: Association Between Clinical Characteristics and Advanced Disease (Stage III–IV)

Variable	Early Stage (I–II) (n=53)	Advanced (n=97) Stage (III–IV)	p-value
Current/Formers smokers	31 (58.5%)	83 (85.6%)	<0.001
Weight loss	23 (43.4%)	68 (70.1%)	0.002
Dyspnea	23 (43.4%)	65 (67.0%)	0.006
ECOG ≥ 2	16 (30.2%)	61 (62.9%)	<0.001
Metastatic disease	0 (0.0%)	58 (59.8%)	<0.001

Table V shows that a lower frequency of persistent cough was seen in NSCLC than in SCLC (84 (71.8%) vs. 27 (81.8%)), but this difference was not statistically significant ($p=0.246$). SCLC was significantly associated with higher rates of hemoptysis (17 (51.5%) vs. 39 (33.3%)), weight loss (25 (75.8%) vs. 66 (56.4%)), Stage III–IV disease (27 (81.8%) vs. 70 (59.8%)), and metastasis (18 (54.5%) vs. 40 (34.2%)).

Table V: Association Between Histological Type and Clinical Presentation

Variable	NSCLC (n=117)	SCLC (n=33)	p-value
Persistent cough	84 (71.8%)	27 (81.8%)	0.246
Hemoptysis	39 (33.3%)	17 (51.5%)	0.048
Weight loss	66 (56.4%)	25 (75.8%)	0.041
Stage III–IV disease	70 (59.8%)	27 (81.8%)	0.021
Metastasis	40 (34.2%)	18 (54.5%)	0.034

ECOG performance status ≥ 2 was the strongest independent predictor of advanced-stage lung cancer (AOR=3.36; $p=0.001$), followed by current/former smoking (AOR=2.94; $p=0.005$), small cell lung cancer (AOR=2.47; $p=0.032$), weight loss (AOR=2.28; $p=0.018$), and dyspnea (AOR=2.11; $p=0.035$). Multivariable adjustment did not change the results for any of these factors, as shown in **Table VI**.

Table VI: Multivariable Logistic Regression Analysis of Factors Associated with Advanced Lung Cancer (Stage III–IV)

Variable	Adjusted OR	95% CI	p-value
Current/Formers smoking	2.94	1.39–6.23	0.005
Weight loss	2.28	1.15–4.50	0.018
Dyspnea	2.11	1.05–4.22	0.035
ECOG Performance Status ≥ 2	3.36	1.63–6.94	0.001
Small cell lung cancer	2.47	1.08–5.64	0.032

ECOG performance status ≥ 2 was the strongest independent predictor of advanced-stage lung cancer, followed by current/former smoking and small cell lung cancer **Figure 1**. Weight loss and dyspnea also remained significantly associated with advanced disease after multivariable adjustment.

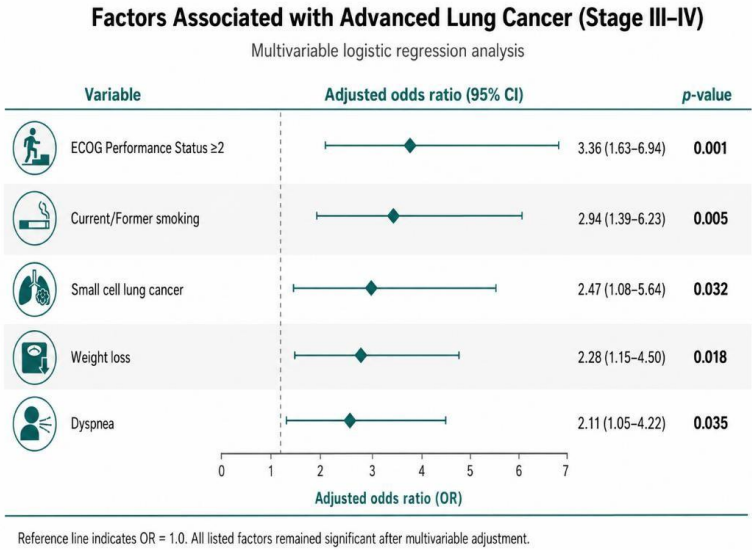


Figure 1: Adjusted odds ratios and 95% confidence intervals for factors independently associated with advanced-stage lung cancer

Overall, the findings demonstrate that lung cancer patients frequently present with advanced-stage disease and a substantial symptom burden. Clinical factors related to functional impairment, smoking exposure, tumor histology, and respiratory or constitutional symptoms were associated with advanced presentation. These findings highlight the importance of early recognition of high-risk clinical features and timely diagnostic evaluation to improve stage detection and management.

DISCUSSION

In the present study, the clinical and pathological profile of 150 lung cancer patients was examined, and most patients were diagnosed with advanced-stage disease ¹³. The mean age was 61.8, and the predominant histological type was adenocarcinoma, with the typical patient being an older male with a high number of tobacco pack-years. Similarly, a large prospective cohort study found a male majority and adenocarcinoma as the predominant histological type ¹⁴. The main complaints were persistent cough, weight loss, dyspnea, fatigue, and chest pain ¹⁵. Almost two-thirds of the patients were diagnosed with Stage III–IV disease, and over one-third had distant metastasis ¹⁶. A population-based observational study also found that 75.3% of patients were symptomatic at diagnosis and predicted poor survival ¹⁷.

Predominance of cough is clinically plausible because irritation of airways, endobronchial obstruction, and inflammation of the lungs can occur across different histological types ¹⁸. In this electronic-record research, cough, hemoptysis, weight loss, fatigue, and musculoskeletal pain appeared to be independently associated with advancing disease, with weight loss and dyspnea each doubling the odds, after adjusting for other factors ¹⁹. The role of constitutional and respiratory symptoms in relation to the extent of the disease and prognosis suggests that these are more prominent as the disease advances and may be confused with chronic respiratory and cardiovascular disorders unless it is noted by the clinician ²⁰. Current or past smoking was independently linked to an advanced stage of presentation (AOR=2.94) ²¹. Cough and breathlessness may be related to smoking and lead to delayed diagnosis, which is reflected in the male predominance and high prevalence of current or past smoking seen here and in lung cancer cohorts in history ²². However, no more than one fourth of the study participants were never smokers, and this should not preclude diagnostic evaluation in the presence of suspicious symptoms or imaging abnormalities ²³. The strongest independent predictor of advanced disease was ECOG performance status ≥ 2 ²⁴.

A higher frequency of hemoptysis, weight loss, advanced-stage disease, and metastasis was observed in small cell lung cancer compared to NSCLC; and small cell lung cancer was independently associated with advanced presentation (AOR=2.47), consistent with its aggressive biological behavior and tendency for early dissemination ²⁵. The presence of early metastatic involvement and the association of metastasis at the time of SCLC diagnosis with significantly decreased survival, as described here, further emphasizes the importance of early tissue diagnosis and thorough staging of suspected SCLC ^{26,27}. It also stresses the need to consider the combination of histology, ECOG, symptom burden, and metastatic status, and not individual components alone ²⁸.

The present study has some limitations such as a single-center cross-sectional design, 6-month study period, and moderate sample size that limit causal inference and generalizability. Center-to-center prospective studies in the future should include a symptom timeline, detailed tobacco exposure, molecular profile, and longitudinal outcomes. This research may help inform symptom-triggered referral and risk-based diagnostic pathways within the setting of locally validated prediction models and assess whether such pathways contribute to early-stage detection.

CONCLUSION

The study concluded that most of the patients were in an advanced stage of lung cancer, with the major symptoms being cough, weight loss, dyspnea, fatigue, and chest pain. Poor ECOG performance status, smoking history, small-cell histology, weight loss, and dyspnea were identified as independent predictors of advanced-stage disease. These results highlight the importance of prompt diagnosis, referral, and staging. These predictors warrant validation in future multi-center, prospective studies, and evaluation of the effectiveness of risk-based diagnostic pathways to enhance early detection, outcomes, and survival.

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