Section: Miscellaneous

Original Research Article

THE RELATIONSHIP BETWEEN LUNG CANCER TUMOR PATHOLOGY AND RESPIRATORY FUNCTION CHANGES IN NEWLY DIAGNOSED PATIENTS: A PROSPECTIVE OBSERVATIONAL STUDY

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Received : 02/11/2023
Received in revised form : 25/12/2023
Accepted : 09/01/2024

Keywords:
Lung cancer, Tumor pathology, Pulmonary function, Respiratory impairment, Histopathological subtypes.

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DOI: 10.47009/jamp.2024.6.1.429

Source of Support: Nil,
Conflict of Interest: None declared

Int J Acad Med Pharm
2024; 6 (1); 2148-2153

Abstract

Background: Aim: This study aimed to investigate the relationship between lung cancer tumor pathology and respiratory function changes in newly diagnosed patients. **Materials and Methods:** A prospective observational study was conducted over 24 months, enrolling 120 newly diagnosed lung cancer patients. Inclusion criteria included histopathologically confirmed lung cancer and the ability to perform pulmonary function tests (PFTs). Baseline demographic, clinical, and tumor pathology data, including histological subtype, stage, and location, were collected. PFTs measured forced vital capacity (FVC), forced expiratory volume in one second (FEV_1), FEV_1/FVC ratio, and diffusion capacity for carbon monoxide (DLCO). Statistical analyses were performed to assess the impact of tumor pathology on respiratory function. **Results:** Among 120 patients, 66.67% were male, and 60% were current smokers. Adenocarcinoma was the most common subtype (50%), followed by squamous cell carcinoma (33.33%) and small-cell carcinoma (16.67%). Pulmonary function declined with advancing tumor stage, with FVC decreasing from 85.40 ± 7.20% in Stage I to 66.90 ± 7.40% in Stage IV ($p < 0.001$). Small-cell carcinoma patients had the lowest pulmonary function metrics (FVC: 68.40 ± 9.30%; DLCO: 65.10 ± 9.20%, $p < 0.05$). Central tumors caused greater impairment than peripheral tumors (FVC: 71.90 ± 8.20% vs. 76.40 ± 8.10%; $p = 0.009$). High-grade tumors were associated with the most severe respiratory function decline (FVC: 68.30 ± 8.40%, $p = 0.008$). **Conclusion:** Lung cancer pathology significantly impacts respiratory function, with advanced stages, central location, and aggressive histological subtypes linked to greater impairment. These findings emphasize the importance of early diagnosis and tailored management strategies to mitigate respiratory complications and improve patient outcomes.

INTRODUCTION

Lung cancer is one of the most prevalent and deadly malignancies worldwide, accounting for a significant proportion of cancer-related morbidity and mortality. Its clinical manifestations and impact extend beyond the oncological aspects, profoundly influencing pulmonary function. The dual burden of tumor pathology and respiratory impairment creates a unique challenge in the management of patients with newly diagnosed lung cancer. Understanding the relationship between tumor characteristics and respiratory function changes is crucial for tailoring treatment strategies and improving overall patient outcomes.[1] The respiratory system plays a critical role in oxygen delivery and carbon dioxide elimination, and its integrity is essential for sustaining life. However, lung cancer directly and indirectly compromises these functions. The presence of a tumor within the respiratory tract can mechanically obstruct airflow, impair gas exchange, and induce inflammatory changes. Additionally, systemic effects of cancer, including paraneoplastic syndromes, cachexia, and treatment-related complications, further exacerbate respiratory impairment. These changes are often multifaceted, involving anatomical, functional, and systemic pathways.[2] Tumor pathology is a major determinant of the degree and nature of respiratory function changes in lung cancer patients. Key pathological

ISSN (O): 2687-5365; ISSN (P): 2753-6556

features, such as tumor size, location, histological subtype, and stage, play significant roles in the extent of pulmonary compromise. Centrally located tumors, for instance, are more likely to obstruct major airways and cause profound airflow limitation, while peripheral tumors may lead to localized parenchymal destruction and pleural involvement. Similarly, histopathological subtypes such as small-cell lung cancer, known for its aggressive behavior, can result in rapid and severe declines in pulmonary function compared to less aggressive types such as adenocarcinoma.[3] The stage of the disease at diagnosis is another critical factor influencing respiratory function. Early-stage lung cancer may have minimal impact on pulmonary mechanics and gas exchange, whereas advanced stages are often associated with extensive tissue destruction, metastatic spread, and systemic inflammation, all of which contribute to significant respiratory impairment. The grading of tumors, reflecting their biological aggressiveness, also correlates with the extent of functional decline. High-grade tumors, due to their rapid proliferation and invasiveness, tend to cause more extensive structural and functional damage to the lungs.[4] In addition to tumor-specific factors, patient-specific variables such as age, smoking history, pre-existing respiratory conditions, and overall physical fitness further modulate the relationship between lung cancer and respiratory function. For instance, chronic obstructive pulmonary disease (COPD), which commonly coexists with lung cancer in long-term smokers, can exacerbate the impact of the tumor on respiratory function. Similarly, the cumulative effect of smoking on lung tissue may amplify the functional decline associated with the tumor.[5] The assessment of respiratory function in lung cancer patients involves a comprehensive evaluation of pulmonary mechanics and gas exchange efficiency. Pulmonary function tests (PFTs), including measurements of forced vital capacity (FVC), forced expiratory volume in one second (FEV_1), FEV_1/FVC ratio, and diffusion capacity for carbon monoxide (DLCO), provide quantitative insights into the extent of respiratory impairment. These parameters not only aid in evaluating the impact of the tumor but also guide therapeutic decisions, predict postoperative outcomes, and monitor treatment responses.[6] Despite advances in diagnostic and therapeutic modalities, the prognosis of lung cancer remains poor, with overall survival rates heavily dependent on the stage at diagnosis and the extent of functional reserve. Early recognition of tumor-induced respiratory changes is therefore critical for optimizing treatment strategies. Surgical resection, the cornerstone of therapy for early-stage lung cancer, requires careful preoperative assessment of respiratory function to minimize perioperative risks. In advanced stages, where curative options are limited, palliative measures aimed at relieving respiratory symptoms and improving quality of life take precedence.[7] The interplay between tumor pathology and respiratory function also has implications for emerging treatment modalities, such as immunotherapy and targeted therapies. These treatments, while offering promising outcomes in specific patient subsets, can cause pulmonary toxicities that further compromise respiratory function. Understanding the baseline pulmonary status and tumor characteristics is thus vital for mitigating these risks and maximizing therapeutic benefits.[8] Given the complexity and variability of lung cancer's impact on respiratory function, a nuanced understanding of the underlying mechanisms and contributing factors is essential. By systematically exploring the relationship between tumor pathology and pulmonary function changes, this study aims to provide insights into the pathophysiological interactions and their clinical implications. Such knowledge is crucial for developing personalized treatment approaches, optimizing functional outcomes, and ultimately improving the quality of care for lung cancer patients. Through a detailed analysis of newly diagnosed cases, this investigation seeks to bridge existing gaps in knowledge and contribute to the evolving understanding of lung cancer's multifaceted impact on respiratory health.[9]

MATERIALS AND METHODS

This prospective observational study was conducted to examine the relationship between lung cancer tumor pathology and respiratory function changes in newly diagnosed patients. The study was performed over a 24-month period in accordance with ethical standards, with all participants providing written informed consent. A total of 120 patients newly diagnosed with lung cancer were consecutively enrolled. The inclusion criteria were: (1) confirmed diagnosis of lung cancer via histopathology; (2) no prior treatment for lung cancer, including surgery, chemotherapy, or radiotherapy; (3) age $\geq$ 18 years; and (4) the ability to perform pulmonary function tests (PFTs). Exclusion criteria included significant comorbid pulmonary diseases such as severe chronic obstructive pulmonary disease (COPD) or interstitial lung disease, previous lung cancer treatment, or inability to provide informed consent.

Methodology

Baseline demographic and clinical data were collected, including age, gender, smoking history, tumor stage (based on the TNM classification), and histopathological subtype (e.g., adenocarcinoma, squamous cell carcinoma, or small-cell carcinoma).

Pulmonary Function Testing

Baseline respiratory function was assessed using standard pulmonary function tests (PFTs). The tests were performed by trained technicians according to the American Thoracic Society (ATS) guidelines. The following parameters were measured:

ISSN (O): 2687-5365; ISSN (P): 2753-6556

1. **Forced Vital Capacity (FVC):** to evaluate the maximal volume of air exhaled after full inspiration.
2. **Forced Expiratory Volume in 1 Second (FEV_1):** to assess airway obstruction.
3. **FEV_1/FVC Ratio:** to detect airflow limitation.
4. **Diffusion Capacity for Carbon Monoxide (DLCO):** to evaluate gas exchange efficiency.

Tumor Pathology Analysis

Tumor samples were obtained via bronchoscopy, transthoracic needle biopsy, or surgical resection, as clinically indicated. Histopathological classification followed international guidelines. Immunohistochemical markers, including TTF-1, p40, and Ki-67, were used to differentiate subtypes where necessary. Tumor grading and staging were determined according to the 8th edition of the TNM staging system.

The primary outcome was the association between lung cancer histopathology and baseline pulmonary function parameters. Secondary outcomes included subgroup analyses based on tumor location (central vs. peripheral), histological subtype, and stage.

Statistical Analysis

Continuous data were expressed as means ± standard deviations, while categorical data were summarized as frequencies and percentages. Comparisons of pulmonary function parameters across tumor subtypes were performed using analysis of variance (ANOVA) or the Kruskal-Wallis test, as appropriate. Multivariable regression models were employed to assess the relationship between tumor pathology and respiratory function changes, adjusting for confounding factors such as age, smoking history, and tumor stage. Statistical significance was defined as $p < 0.05$. Data analysis was performed using statistical software.

RESULTS

Table 1: Baseline Characteristics of the Study Population

The study included 120 patients, with 66.67% being male and 33.33% female. A statistically significant difference ($p = 0.045$) was observed in the gender distribution. Regarding smoking history, 60% of patients were current smokers, 26.67% were former smokers, and 13.33% had never smoked ($p = 0.032$). Tumor stages varied significantly among participants ($p < 0.001$), with the largest group in Stage III (33.33%) followed by Stages II and IV (25% each) and Stage I (16.67%). Adenocarcinoma was the most common histopathological subtype (50%), followed by squamous cell carcinoma (33.33%) and small-cell carcinoma (16.67%) with significant variation ($p = 0.002$).

Table 2: Pulmonary Function Test Parameters by Tumor Stage

Pulmonary function parameters showed a significant decline with increasing tumor stage. The mean FVC (% predicted) was highest in Stage I patients (85.40 ± 7.20) and progressively decreased to 66.90 ± 7.40 in Stage IV patients ($p < 0.001$). Similar trends were observed for FEV_1 (% predicted), which declined from 80.10 ± 8.10 in Stage I to 62.40 ± 7.90 in Stage IV ($p < 0.001$). The FEV_1/FVC ratio also decreased significantly across stages ($p = 0.034$), indicating worsening airflow limitation. DLCO (% predicted) demonstrated the steepest decline, from 82.30 ± 6.70 in Stage I to 62.50 ± 8.70 in Stage IV ($p < 0.001$), highlighting the impact of advancing cancer stage on gas exchange efficiency.

Table 3: Comparison of Pulmonary Function Parameters by Tumor Subtype

Pulmonary function parameters varied significantly by histopathological subtype. Patients with adenocarcinoma had the highest mean FVC (% predicted) at 74.80 ± 8.50, while those with small-cell carcinoma had the lowest at 68.40 ± 9.30 ($p = 0.014$). A similar pattern was observed for FEV_1 (% predicted), with adenocarcinoma patients showing higher values (71.20 ± 7.90) compared to small-cell carcinoma patients (64.20 ± 9.10) ($p = 0.010$). The FEV_1/FVC ratio and DLCO also followed this trend, suggesting that small-cell carcinoma has the most detrimental effect on pulmonary function.

Table 4: Tumor Location and Pulmonary Function

Tumor location significantly influenced pulmonary function parameters. Peripheral tumors were associated with better pulmonary function compared to central tumors. FVC (% predicted) was higher in patients with peripheral tumors (76.40 ± 8.10) than in those with central tumors (71.90 ± 8.20) ($p = 0.009$). FEV_1 (% predicted) and DLCO (% predicted) were also significantly higher in peripheral tumors, suggesting less impairment in respiratory function compared to central tumors. The FEV_1/FVC ratio was significantly better in peripheral tumors (0.79 ± 0.04 vs. 0.74 ± 0.05; $p = 0.008$).

Table 5: Multivariable Regression Analysis of Factors Affecting FEV_1

Age, smoking history, tumor stage, and histopathological subtype significantly impacted FEV_1. Age negatively influenced FEV_1 ($\beta = -0.32$, $p < 0.001$), as did smoking history ($\beta = -0.28$, $p = 0.002$). Tumor stage had the strongest negative association with FEV_1 ($\beta = -0.45$, $p < 0.001$), indicating a significant decline in pulmonary function with advancing cancer stage. Histopathological subtype also contributed to FEV_1 variability, with small-cell carcinoma being associated with worse outcomes ($\beta = -0.22$, $p = 0.005$).

Table 6: Respiratory Impairment by Tumor Grading

Tumor grading significantly affected pulmonary function. Patients with low-grade tumors exhibited the highest mean FVC (% predicted) (77.80 ± 7.50), FEV_1 (% predicted) (74.20 ± 7.30), and DLCO (% predicted) (74.10 ± 7.80). These values progressively decreased in intermediate- and high-

ISSN (O): 2687-5365; ISSN (P): 2753-6556

grade tumors (p-values: FVC = 0.008, FEV_1 = 0.011, DLCO = 0.009). This indicates that higher tumor grades are associated with greater impairment in lung function, reflecting more aggressive disease pathology.

Table 1: Baseline Characteristics of the Study Population

Characteristic	n	Percentage (%)	p-value
Gender			0.045
Male	80	66.67	
Female	40	33.33	
Smoking History			0.032
Current	72	60.00	
Former	32	26.67	
Never	16	13.33	
Tumor Stage			<0.001
Stage I	20	16.67	
Stage II	30	25.00	
Stage III	40	33.33	
Stage IV	30	25.00	
Histopathological Subtype			0.002
Adenocarcinoma	60	50.00	
Squamous Cell	40	33.33	
Small-Cell	20	16.67	

Table 2: Pulmonary Function Test Parameters by Tumor Stage

Parameter	Stage I (n=20)	Stage II (n=30)	Stage III (n=40)	Stage IV (n=30)	p-value
FVC (% Predicted)	85.40 ± 7.20	78.30 ± 6.50	72.10 ± 8.00	66.90 ± 7.40	<0.001
FEV_1 (% Predicted)	80.10 ± 8.10	72.90 ± 6.90	67.50 ± 7.30	62.40 ± 7.90	<0.001
FEV_1/FVC Ratio	0.81 ± 0.04	0.77 ± 0.05	0.74 ± 0.06	0.71 ± 0.07	0.034
DLCO (% Predicted)	82.30 ± 6.70	75.20 ± 7.10	69.80 ± 8.20	62.50 ± 8.70	<0.001

Table 3: Comparison of Pulmonary Function Parameters by Tumor Subtype

Parameter	Adenocarcinoma (n=60)	Squamous Cell (n=40)	Small-Cell (n=20)	p-value
FVC (% Predicted)	74.80 ± 8.50	72.30 ± 8.10	68.40 ± 9.30	0.014
FEV_1 (% Predicted)	71.20 ± 7.90	68.50 ± 8.30	64.20 ± 9.10	0.010
FEV_1/FVC Ratio	0.77 ± 0.05	0.75 ± 0.06	0.72 ± 0.07	0.027
DLCO (% Predicted)	70.80 ± 8.00	68.30 ± 8.50	65.10 ± 9.20	0.021

Table 4: Tumor Location and Pulmonary Function

Parameter	Central Tumor (n=70)	Peripheral Tumor (n=50)	p-value
FVC (% Predicted)	71.90 ± 8.20	76.40 ± 8.10	0.009
FEV_1 (% Predicted)	67.80 ± 8.40	73.10 ± 7.70	0.005
FEV_1/FVC Ratio	0.74 ± 0.05	0.79 ± 0.04	0.008
DLCO (% Predicted)	68.50 ± 7.60	72.30 ± 8.00	0.017

Table 5: Multivariable Regression Analysis of Factors Affecting FEV_1

Variable	β-Coefficient	95% CI	p-value
Age	-0.32	(-0.48, -0.16)	<0.001
Smoking History	-0.28	(-0.42, -0.14)	0.002
Tumor Stage (per unit)	-0.45	(-0.60, -0.30)	<0.001
Histopathological Subtype	-0.22	(-0.37, -0.07)	0.005

Table 6: Respiratory Impairment by Tumor Grading

Parameter	Low Grade (n=50)	Intermediate Grade (n=40)	High Grade (n=30)	p-value
FVC (% Predicted)	77.80 ± 7.50	72.40 ± 7.80	68.30 ± 8.40	0.008
FEV_1 (% Predicted)	74.20 ± 7.30	69.70 ± 8.10	65.40 ± 8.70	0.011
DLCO (% Predicted)	74.10 ± 7.80	69.80 ± 8.20	64.70 ± 8.50	0.009

DISCUSSION

This study provides valuable insights into the relationship between lung cancer tumor pathology and respiratory function, emphasizing the impact of tumor stage, histopathological subtype, and location on pulmonary function. The gender distribution in our study (66.67% male and 33.33% female) reflects the higher prevalence of smoking among men. Similarly, Bray et al. (2018) reported a male predominance (67%) among lung cancer patients, which was attributed to smoking habits and occupational exposures.[10] Our finding that 60% of patients were current smokers is consistent with Islami et al. (2017), who found that approximately 70% of lung cancer cases globally were attributable to smoking.[11] Their study also highlighted that current smokers had a relative risk (RR) of 13.6 for developing lung cancer compared to never-smokers.

ISSN (O): 2687-5365; ISSN (P): 2753-6556

This underscores the importance of smoking cessation in lung cancer prevention.

Our results demonstrated a progressive decline in pulmonary function with advancing tumor stage. FVC decreased from 85.40 ± 7.20% in Stage I to 66.90 ± 7.40% in Stage IV, while DLCO decreased from 82.30 ± 6.70% to 62.50 ± 8.70%. These findings are consistent with Boshier et al. (2018), who observed that FVC and DLCO values decreased by approximately 20% from early-stage (Stage I-II) to advanced-stage (Stage III-IV) lung cancer.[12] Similarly, Huang et al. (2019) found that Stage IV patients had a 30% reduction in DLCO compared to Stage I patients, attributed to increased tumor burden and parenchymal involvement. [13]

Adenocarcinoma was the most common subtype in our study (50%), with relatively preserved pulmonary function (FVC: 74.80 ± 8.50%; DLCO: 70.80 ± 8.00%). Patients with small-cell carcinoma exhibited the greatest impairment (FVC: 68.40 ± 9.30%; DLCO: 65.10 ± 9.20%). These results are similar to findings by Yang et al. (2020), who reported that small-cell carcinoma patients had a mean FVC of 67.50 ± 8.60% and DLCO of 63.00 ± 7.90%, significantly lower than adenocarcinoma patients (FVC: 75.20 ± 7.50%; DLCO: 71.80 ± 6.80%). [14] Small-cell carcinoma's aggressive nature and central airway involvement were identified as primary contributors to these disparities.

Central tumors were associated with worse pulmonary function in our study, with FVC and DLCO significantly lower in central tumors (FVC: 71.90 ± 8.20%; DLCO: 68.50 ± 7.60%) compared to peripheral tumors (FVC: 76.40 ± 8.10%; DLCO: 72.30 ± 8.00%). Travis WD et al. (2021) reported a similar trend, with central tumors causing a 15% greater reduction in DLCO compared to peripheral tumors due to airway obstruction and proximal tissue involvement. [15] Cheng et al. (2022) found that peripheral tumors were more likely to be resectable and detected at earlier stages, contributing to better respiratory outcomes. [16]

Our regression analysis identified tumor stage ($\beta = -0.45$, $p < 0.001$) as the most significant determinant of FEV_1, followed by smoking history ($\beta = -0.28$, $p = 0.002$) and histopathological subtype ($\beta = -0.22$, $p = 0.005$). These findings are consistent with Wang et al. (2019), who reported that each unit increase in tumor stage was associated with a 10% decrease in FEV_1. Additionally, their study found that smokers had a 15% lower FEV_1 than non-smokers, highlighting the compounded effects of smoking and tumor progression. [17]

High-grade tumors in our study were associated with the most severe decline in pulmonary function, with FVC decreasing to 68.30 ± 8.40% and DLCO to 64.70 ± 8.50%. Zhang et al. (2021) reported similar findings, noting that high-grade tumors were associated with a 20% reduction in FVC and a 25% reduction in DLCO compared to low-grade tumors.[18] These changes were attributed to increased tumor aggressiveness, tissue destruction, and systemic inflammatory effects.

CONCLUSION

This study highlights the significant relationship between lung cancer tumor pathology and respiratory function changes, emphasizing the impact of tumor stage, histological subtype, and location on pulmonary impairment. Advanced stages, central tumor locations, and aggressive subtypes such as small-cell carcinoma were associated with greater functional decline. These findings underscore the importance of early detection, comprehensive pulmonary assessment, and personalized management strategies to mitigate respiratory complications and improve outcomes in lung cancer patients.

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ISSN (O): 2687-5365; ISSN (P): 2753-6556