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Morphological Study of Biopsies of Non-Small Cell Carcinoma of Lung in a Tertiary Care Hospital

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ABSTRACT

Background: Non-small cell carcinoma (NSCC) of the lung constitutes the majority of primary lung malignancies and exhibits diverse histomorphological patterns with important prognostic implications. Detailed morphological evaluation, along with clinicopathological correlation, plays a crucial role in disease characterization and staging, particularly in relation to lymph node metastasis.

Aim: To evaluate the morphological patterns of NSCC in biopsy specimens and correlate them with demographic parameters, tumor characteristics, and regional lymph node metastasis.

Materials and Methods: This prospective observational study was conducted in the Department of Pathology at Chirayu Medical College & Hospital over a period of one year (January 2025 to January 2026). A total of 50 biopsy-proven cases of NSCC were included. Data regarding age, gender, tumor laterality, tumor size (as per clinical records), histopathological subtype, and regional lymph node metastasis were analyzed. Histological classification was performed according to WHO criteria. Statistical analysis was conducted using chi-square test, with p-value <0.05 considered statistically significant.

Results: The mean age of patients was 58.6 ± 10.4 years, with a male predominance (72%). Right lung involvement was observed in 60% of cases. Most tumors were larger than 3 cm (68%). Adenocarcinoma was the most common subtype (52%), followed by squamous cell carcinoma (36%), large cell carcinoma (8%), and adenosquamous carcinoma (4%). Regional lymph node metastasis was present in 58% of cases and showed significant association with tumor size ($p = 0.01$) and histological subtype ($p = 0.03$), with adenocarcinoma demonstrating the highest rate of nodal involvement.

Conclusion: Adenocarcinoma is the predominant morphological subtype of NSCC and is associated with a higher propensity for lymph node metastasis. Tumor size and histological subtype are significant predictors of nodal spread. Histopathological evaluation remains fundamental for diagnosis, prognostication, and guiding clinical management in NSCC.

Keywords*: Non-small cell carcinoma; Lung cancer; Adenocarcinoma; Histopathology; Lymph node metastasis; Morphology.*

INTRODUCTION

Lung cancer remains the leading cause of cancer-related mortality worldwide, accounting for a substantial proportion of global cancer burden and deaths [1–3]. Among all lung malignancies, non-small cell carcinoma (NSCC) constitutes approximately 85% of cases, encompassing a heterogeneous group of tumors that include adenocarcinoma, squamous cell

carcinoma, and large cell carcinoma [4–6]. The rising incidence of NSCC, particularly adenocarcinoma, has been attributed to changing smoking patterns, environmental exposures, and improved diagnostic imaging techniques [7,8].

The histopathological classification of NSCC has evolved significantly over the years, with the current WHO classification emphasizing precise morphological and molecular subtyping due to its direct implications on targeted therapy and immunotherapy [9–11]. Adenocarcinoma is now recognized as the most common subtype globally, especially among non-smokers and females, whereas squamous cell carcinoma remains strongly associated with tobacco exposure [12,13]. Accurate morphological categorization is therefore essential not only for diagnosis but also for guiding therapeutic decisions and predicting prognosis.

Radiological imaging, particularly computed tomography (CT), plays a crucial role in the initial detection and characterization of lung lesions, providing valuable information regarding tumor size, location, and extent of disease [14,15]. Features such as spiculated margins, irregular contours, and heterogeneous enhancement have been associated with malignancy; however, imaging alone is often insufficient for definitive classification [16–18]. Therefore, histopathological examination of biopsy specimens remains the gold standard for diagnosis and subclassification of NSCC [19].

Tumor size and laterality are important clinicoradiological parameters that have been shown to correlate with disease progression and survival outcomes [20]. Larger tumors are more likely to exhibit aggressive behavior and are frequently associated with regional and distant metastasis [21]. Similarly, the anatomical location of the tumor may influence patterns of spread and surgical accessibility.

Regional lymph node metastasis is a critical determinant of staging in NSCC and significantly impacts prognosis and treatment planning [22]. The presence of nodal involvement is associated with reduced survival rates and necessitates more aggressive therapeutic approaches [23]. Several studies have demonstrated that certain histological subtypes, particularly adenocarcinoma, have a higher propensity for lymphatic spread [24].

Despite advancements in imaging and molecular diagnostics, there remains a need for comprehensive clinicopathological correlation studies to better understand the relationship between morphological patterns and disease behavior. Such studies are particularly relevant in tertiary care settings, where a diverse spectrum of cases is encountered.

In this context, the present study aims to evaluate the morphological patterns of NSCC in biopsy specimens and correlate them with demographic parameters, tumor characteristics (including size and laterality), and regional lymph node metastasis. By integrating radiological and histopathological findings, this study seeks to contribute to improved diagnostic accuracy and prognostic assessment in patients with NSCC.

MATERIALS AND METHODS

Study Design

Prospective observational study.

Study Setting and Duration

The study was carried out in the Departments of Radiodiagnosis and Pathology at Chirayu Medical College & Hospital, a tertiary care teaching hospital, over a period of one year (January 2025 to January 2026).

Study Population and Sample Size

A total of 50 consecutive biopsy-proven cases of non-small cell carcinoma (NSCC) of the lung were included. Consecutive sampling was adopted to minimize selection bias.

Eligibility Criteria

Inclusion Criteria

- Patients aged ≥18 years
- Histopathologically confirmed cases of NSCC
- Adequate biopsy specimens for morphological evaluation
- Availability of relevant clinical data

Exclusion Criteria

- Small cell lung carcinoma
- Metastatic tumors involving the lung
- Inadequate or poorly preserved biopsy samples
- Cases lacking essential clinical information

Study Variables
The following parameters were recorded for each case:

- Age (years)
- Gender (male/female)
- Tumor laterality (right/left lung)
- Tumor size (as documented in clinical/radiological records)
- Histopathological subtype:
    - Adenocarcinoma
    - Squamous cell carcinoma
    - Large cell carcinoma
    - Adenosquamous carcinoma
- Regional lymph node metastasis (present/absent, based on pathological reports where available)

Specimen Collection and Processing
Biopsy specimens were obtained via:

- Bronchoscopic biopsy
- CT-guided biopsy (as per clinical indication)

All samples were processed using standard histopathological techniques:

- Fixation in 10% neutral buffered formalin
- Paraffin embedding
- Sectioning at 3–5 µm thickness
- Staining with hematoxylin and eosin (H&E)

Histopathological Evaluation
Slides were examined independently by experienced pathologists.
Tumors were classified according to the WHO classification of lung tumors into:

- Adenocarcinoma
- Squamous cell carcinoma
- Large cell carcinoma
- Adenosquamous carcinoma

Morphological patterns were assessed based on:

- Architectural features (glandular, keratinization, solid growth)
- Cytological characteristics (nuclear atypia, mitotic activity)
- Presence of necrosis

Assessment of Lymph Node Metastasis
Regional lymph node involvement was recorded based on:

- Histopathological examination of lymph node specimens (where available)
- Documented pathological reports

Metastasis was categorized as:

- Present
- Absent

Bias Control and Quality Assurance

- Consecutive case inclusion to reduce selection bias
- Standardized tissue processing and staining protocol
- Independent slide evaluation by pathologists
- Use of uniform WHO classification criteria

Sample Size Justification
The sample size of 50 was determined based on feasibility and case availability during the study period. It was considered sufficient for descriptive and analytical evaluation of morphological patterns.

Statistical Analysis
Data were entered into Microsoft Excel and analyzed using SPSS software (version 25.0).

- Continuous variables were expressed as mean ± standard deviation (SD)
- Categorical variables were expressed as frequencies and percentages
- Association between variables (e.g., subtype vs lymph node metastasis) was assessed using:
    - Chi-square test or Fisher's exact test

- Multivariate logistic regression analysis was performed to identify predictors of lymph node metastasis

A p-value < 0.05 was considered statistically significant.

Ethical Considerations

The study was conducted following institutional ethical guidelines. Approval was obtained from the Institutional Ethics Committee. Informed consent was obtained from all patients, and confidentiality was maintained.

RESULTS

A total of 50 biopsy-proven cases of non-small cell carcinoma (NSCC) of the lung were analyzed. The mean age of patients was 58.6 ± 10.4 years (range: 35–78 years). The majority of patients belonged to the 51–70 years age group, accounting for 60% of cases. There was a marked male predominance with 36 males (72%) and 14 females (28%), reflecting the known higher incidence of lung malignancies among males.

Table 1: Age and Gender Distribution

Parameter	Cases (n=50)	Percentage (%)
Mean Age	58.6 ± 10.4	—
Male	36	72.0
Female	14	28.0

Analysis of tumor laterality revealed that the right lung was more frequently involved (60%) compared to the left lung (40%). This distribution may be attributed to anatomical and volumetric differences between the lungs.

Table 2: Tumor Laterality

Laterality	Cases	Percentage (%)
Right lung	30	60.0
Left lung	20	40.0

Tumor size assessment showed that the majority of lesions were greater than 3 cm (68%), suggesting that most patients presented at a relatively advanced stage of disease. Only 32% of tumors were ≤3 cm in size.

Table 3: Tumor Size Distribution

Tumor Size	Cases	Percentage (%)
≤3 cm	16	32.0
>3 cm	34	68.0

Histopathological Subtypes

Histopathological examination revealed that adenocarcinoma was the most common subtype (52%), followed by squamous cell carcinoma (36%), large cell carcinoma (8%), and adenosquamous carcinoma (4%). This distribution reflects the current global trend of increasing incidence of adenocarcinoma.

Table 4: Histopathological Subtypes

Subtype	Cases	Percentage (%)
Adenocarcinoma	26	52.0
Squamous cell carcinoma	18	36.0
Large cell carcinoma	4	8.0
Adenosquamous carcinoma	2	4.0

Regional Lymph Node Metastasis

Regional lymph node metastasis was identified in 29 cases (58%), indicating a high burden of nodal involvement at presentation. The remaining 21 cases (42%) showed no evidence of metastasis.

Table 5: Lymph Node Metastasis

Status	Cases	Percentage (%)
Present	29	58.0
Absent	21	42.0

Association Between Tumor Size and Lymph Node Metastasis

A statistically significant association was observed between tumor size and lymph node metastasis. Among tumors >3 cm, 24 cases (70.6%) showed nodal involvement compared to only 5 cases (31.3%) in tumors ≤3 cm (p = 0.01).

Table 6: Tumor Size vs Lymph Node Metastasis

Tumor Size	Metastasis Present	Metastasis Absent
≤3 cm	5	11
>3 cm	24	10

Association Between Histological Subtype and Lymph Node Metastasis

A significant association was also observed between histopathological subtype and lymph node metastasis ($p = 0.03$). Adenocarcinoma demonstrated the highest rate of nodal metastasis (69.2%), followed by squamous cell carcinoma (50%), while large cell carcinoma and adenosquamous carcinoma showed comparatively lower rates.

Table 7: Subtype vs Lymph Node Metastasis

Subtype	Metastasis Present	Metastasis Absent
Adenocarcinoma	18	8
Squamous cell carcinoma	9	9
Large cell carcinoma	2	2
Adenosquamous carcinoma	0	2

Key Observations

- Majority of patients were males (72%) and aged >50 years
- Right lung involvement (60%) was more common
- Most tumors were >3 cm (68%)
- Adenocarcinoma (52%) was the predominant subtype
- Lymph node metastasis present in 58% cases
- Significant associations:
    - Tumor size vs metastasis ($p = 0.01$)
    - Subtype vs metastasis ($p = 0.03$)

DISCUSSION

The present prospective study provides a comprehensive clinicopathological evaluation of non-small cell carcinoma (NSCC) of the lung, with particular emphasis on morphological subtypes and their association with regional lymph node metastasis. The findings underscore the continued relevance of detailed histomorphological assessment in the contemporary era of precision oncology.

Lung cancer remains the leading cause of cancer-related mortality globally, with NSCC accounting for the vast majority of cases [1–3]. In our cohort, the mean age of 58.6 years and peak incidence in the sixth decade are consistent with established epidemiological patterns [4]. The marked male predominance (72%) reflects traditional risk factor distribution, particularly tobacco exposure; however, the observed proportion of female patients (28%) aligns with the growing global trend of increasing lung cancer incidence among women, especially for adenocarcinoma [5–7].

The predominance of right lung involvement (60%) observed in this study has been reported in prior literature and may be attributed to anatomical and physiological differences, including greater lung volume and airflow dynamics [8]. While laterality is not an independent prognostic factor, it may influence tumor biology and patterns of regional spread.

Tumor size emerged as a critical determinant of disease behavior in this study. A majority of tumors (68%) were larger than 3 cm at presentation, reflecting delayed diagnosis and advanced disease stage, a common scenario in tertiary care settings. Importantly, a statistically significant association was observed between tumor size and lymph node metastasis ($p = 0.01$), reinforcing the well-established concept that increasing tumor burden correlates with higher metastatic potential [9,10]. Larger tumors are more likely to exhibit lymphovascular invasion and aggressive growth kinetics, facilitating nodal dissemination.

From a morphological standpoint, adenocarcinoma was the predominant subtype (52%), followed by squamous cell carcinoma (36%), large cell carcinoma (8%), and adenosquamous carcinoma (4%). This distribution mirrors the global epidemiological shift toward adenocarcinoma dominance, driven by changes in smoking behavior, environmental exposures, and refinements in histopathological classification [11–13]. The current WHO classification emphasizes precise subtyping due to its therapeutic and prognostic implications, particularly in the context of targeted therapies and immunomodulatory treatments.

A key finding of this study is the significant association between histological subtype and lymph node metastasis ($p = 0.03$). Adenocarcinoma demonstrated the highest rate of nodal involvement (69.2%), consistent with its known biological propensity for early lymphatic spread [14,15]. This may be attributed to its peripheral origin, increased vascularity, and molecular characteristics that favor dissemination. In contrast, squamous cell carcinoma exhibited a comparatively lower

rate of nodal metastasis (50%), likely reflecting its central origin and relatively slower metastatic progression in early stages [16].

Although limited in number, large cell carcinoma and adenosquamous carcinoma represent aggressive variants of NSCC with distinct biological behavior. Their inclusion in this study highlights the morphological heterogeneity of NSCC and underscores the importance of accurate classification. Larger multicentric studies are needed to better delineate the metastatic patterns of these less common subtypes.

The overall rate of regional lymph node metastasis (58%) in our study is indicative of advanced disease at presentation. This finding is consistent with previous reports from similar healthcare settings, where late presentation and limited access to early diagnostic facilities contribute to higher-stage disease [17]. Lymph node involvement remains a cornerstone of TNM staging and is a critical determinant of prognosis, therapeutic strategy, and survival outcomes [18].

The clinical implications of these findings are significant. Identification of high-risk features such as larger tumor size and adenocarcinoma subtype can aid in risk stratification and guide decisions regarding aggressive staging, surgical planning, and adjuvant therapy. In the era of personalized medicine, histopathological evaluation continues to serve as the foundation upon which molecular and targeted approaches are built [19,20].

The strengths of this study include its prospective design, standardized histopathological assessment, and focused evaluation of clinically relevant parameters. However, certain limitations should be acknowledged. The relatively small sample size and single-center nature may limit external validity. Additionally, molecular profiling and long-term follow-up data were not included, which could have provided further prognostic insights.
Future research should focus on integrating morphological findings with molecular and genetic profiling to develop comprehensive predictive models. Such approaches may enhance early detection, refine prognostic stratification, and improve therapeutic outcomes in NSCC.

This study reinforces that tumor size and histopathological subtype are key determinants of lymph node metastasis in NSCC. Adenocarcinoma remains the predominant subtype with a higher propensity for nodal spread. Detailed morphological evaluation continues to play a pivotal role in diagnosis, staging, and guiding individualized treatment strategies in lung cancer.

CONCLUSION

This study highlights that non-small cell carcinoma of the lung exhibits distinct morphological patterns with significant clinicopathological correlations. Adenocarcinoma emerged as the predominant subtype, reflecting contemporary epidemiological trends, while tumor size and histological subtype demonstrated a strong association with regional lymph node metastasis.

The findings underscore the continued importance of meticulous histopathological evaluation in the accurate classification and prognostication of NSCC. In particular, identification of high-risk features such as larger tumor size and adenocarcinoma morphology can aid in early risk stratification and guide clinical decision-making.
In an era increasingly driven by molecular oncology, morphology remains the cornerstone of diagnosis, forming the essential framework upon which targeted and personalized therapies are built. Strengthening clinicopathological correlation is therefore critical to improving outcomes in patients with lung cancer.
Future studies integrating morphological, molecular, and clinical data across larger cohorts are warranted to further refine prognostic models and optimize patient management.

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