International Journal of Medical and Pharmaceutical Research

Online ISSN-2958-3683 | Print ISSN-2958-3675
Frequency: Bi-Monthly
Available online on: https://ijmpr.in/

Original Article

Comprehensive Diagnosis of Lung Tumors Using a Multimodal Pathological and Radiological Approach

Dr. Kondra Sreelekha[1], Dr. C. Srilekha[2], Dr. B. Kusumanjali[3], Dr. M. Neeraja[4]

[1] Post-Graduate-3rd Year, Department of Pathology, Viswabharathi Medical College, Kurnool, Andhra Pradesh.
[2] Assistant Professor, Department of Pathology, Viswabharathi Medical College, Kurnool, Andhra Pradesh.
[3] Assistant Professor, Department of Pathology, Viswabharathi Medical College, Kurnool, Andhra Pradesh.
[4] Professor & HOD, Department of Pathology, Viswabharathi Medical College, Kurnool, Andhra Pradesh.

Corresponding Author:

Dr. B. Kusumanjali
Assistant Professor, Department of Pathology, Viswabharathi Medical College, Kurnool, Andhra Pradesh.

Received: 10-11-2025
Accepted: 04-12-2025
Available online: 12-12-2025

ABSTRACT

Background: Lung cancer remains a leading cause of cancer-related mortality worldwide, largely due to late presentation and histological heterogeneity. Accurate diagnosis and precise tumor subtyping are essential for appropriate therapeutic planning and prognostic assessment. Integration of cytology, histopathology, radiology, and immunohistochemistry has emerged as an effective strategy to enhance diagnostic accuracy.

Objectives: To evaluate the effectiveness of a multimodal diagnostic approach integrating cytology, histopathology, radiology, and immunohistochemistry in the diagnosis and subtyping of lung malignancies.

Materials and Methods: This retrospective study included 50 cases of lung malignancies evaluated at a tertiary care centre. Cytological diagnosis was correlated with histopathological findings, radiological features, and immunohistochemical results wherever required. Tumor classification was performed according to standard histopathological criteria, and immunohistochemistry was used for poorly differentiated tumors and metastatic deposits.

Results: Cytology demonstrated high diagnostic accuracy in identifying major lung cancer categories, particularly non-small cell carcinoma and small cell carcinoma, with complete cytology–histopathology concordance in small cell carcinoma cases. Histopathology was essential for subtyping non-small cell carcinomas into adenocarcinoma and squamous cell carcinoma. Immunohistochemistry played a decisive role in classifying poorly differentiated tumors and confirming metastatic lesions. Adenocarcinoma was the most common subtype, followed by squamous cell carcinoma. Most cases occurred in the 51–60-year age group, with a male predominance. Radiological findings showed good correlation with histological subtypes.

Conclusion: A multimodal diagnostic approach significantly enhances the accuracy of lung tumor diagnosis and subtyping. Integration of cytology, histopathology, radiology, and immunohistochemistry is essential for precise classification and optimal clinical management of lung malignancies.

Keywords: *Lung cancer; Cytology; Histopathology; Radiology; Immunohistochemistry; Multimodal diagnosis.*

INTRODUCTION

Lung cancer is one of the most common malignancies worldwide and remains the leading cause of cancer-related mortality, accounting for a significant number of deaths each year. Despite advances in diagnostic techniques and therapeutic strategies, the overall prognosis of lung cancer continues to be poor, primarily due to late clinical presentation and the complex histological diversity of lung tumors. Accurate and early diagnosis, along with precise histological classification, is essential for appropriate treatment selection and improved patient outcomes.[1,2]

Histopathological examination of tissue biopsies has traditionally been regarded as the gold standard for the diagnosis of lung tumors. However, obtaining adequate tissue samples is often limited by tumor location, patient comorbidities, and procedural risks, particularly in advanced disease. In such circumstances, cytological techniques—including fine-needle aspiration cytology (FNAC), bronchial washings, brushings, and sputum cytology—serve as valuable, minimally invasive diagnostic tools. These methods allow early detection of malignancy and provide preliminary tumor characterization, especially in resource-limited settings.[3],[4]

Radiological imaging plays a crucial role in the initial detection, localization, and staging of lung lesions. Computed tomography (CT) of the chest offers detailed information regarding tumor size, margins, invasion of adjacent structures, and lymph node involvement, thereby guiding biopsy procedures and further diagnostic work-up. Nevertheless, radiological findings alone are insufficient for definitive tumor typing due to overlapping features between benign and malignant lesions and among different histological subtypes of lung cancer.[5],[6]

The introduction of immunohistochemistry (IHC) has significantly improved the diagnostic accuracy of lung tumors, particularly in poorly differentiated neoplasms and small biopsy or cytology specimens. IHC markers such as thyroid transcription factor-1 (TTF-1), Napsin A, p40, and cytokeratin panels enable reliable differentiation between adenocarcinoma, squamous cell carcinoma, small cell carcinoma, and metastatic tumors. This distinction is critical in the current era of personalized medicine, as therapeutic decisions and targeted treatments are closely linked to tumor subtype.[7–9]

Given the limitations of individual diagnostic modalities, an integrated multimodal approach combining cytology, histopathology, radiology, and immunohistochemistry provides a comprehensive and reliable framework for lung tumor diagnosis. Correlation of findings from multiple modalities enhances diagnostic confidence, reduces equivocal reporting, and facilitates accurate tumor classification. The present study aims to evaluate the effectiveness of this integrated diagnostic approach in the accurate diagnosis and subtyping of lung tumors in a tertiary care hospital setting.[10]

MATERIALS AND METHODS

Study Design and Setting

This retrospective observational study was conducted in a tertiary care teaching hospital. Medical records and pathology archives were reviewed over a period of three years, from **May 2022 to May 2025**, after obtaining approval from the institutional ethics committee.

Study Population and Data Collection

All cases that underwent cytological evaluation for lung lesions during the study period were identified from departmental records. Demographic details, including **age and gender**, along with **radiological findings**, were retrieved from hospital case files and radiology reports. Radiological assessment primarily included chest radiography and computed tomography findings, which were used to correlate with pathological diagnoses.

Cytological and Histopathological Evaluation

Cytological smears obtained through various sampling techniques were reviewed in all cases. Each cytological diagnosis was subsequently correlated with the corresponding **histopathological examination**, which served as the confirmatory diagnostic modality. Tumor classification and subtyping were performed in accordance with the **World Health Organization (WHO) Classification of Tumors of the Lung, 2021**.

Tissue Processing and Staining

Biopsy specimens were fixed in **10% neutral buffered formalin** and processed routinely. Following fixation, tissues were dehydrated, cleared, and embedded in paraffin wax. Sections of appropriate thickness were cut and stained with **hematoxylin and eosin (H&E)** for microscopic examination. The stained slides were independently reviewed to assess tumor morphology and architectural patterns.

Immunohistochemical Analysis

Immunohistochemistry was performed in selected cases where morphological features on cytology and histopathology were insufficient for definitive tumor typing. A panel of immunohistochemical markers, including **TTF-1, Napsin-A, p40, p63, synaptophysin, chromogranin, and CD56**, was employed based on the differential diagnosis. Appropriate positive and negative controls were used, and interpretation was carried out according to standard reporting criteria.

Inclusion Criteria

- All **neoplastic cytological smears** and **image-guided lung biopsies** diagnosed during the study period
- Both **primary lung tumors** and **metastatic lesions involving the lung**

Exclusion Criteria

- All **non-neoplastic** lung lesions
- **Benign** pulmonary lesions and inflammatory conditions

Data Analysis

The collected data were compiled and analyzed descriptively. Cytological findings were correlated with histopathological and immunohistochemical results to assess diagnostic concordance and tumor distribution.

RESULTS

Cytological evaluation demonstrated high diagnostic accuracy in identifying major lung cancer categories, particularly non-small cell and small cell carcinomas, with complete histopathological concordance in small cell carcinoma cases. However, cytology alone was insufficient for definitive subtyping in poorly differentiated tumors and metastatic deposits, where immunohistochemistry was essential to resolve diagnostic ambiguity and ensure accurate tumor classification as shown in Table 1.

Table 1: Correlation of Cytological Diagnosis with Final Histopathological and Immunohistochemical Diagnosis of Lung Malignancies

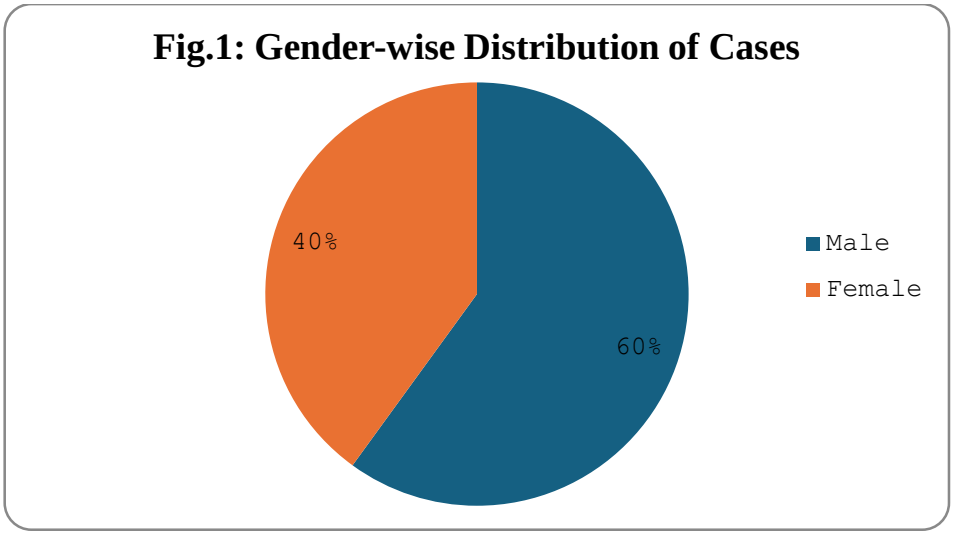
Cytological Diagnosis	No. of Cases (n)	Final Diagnosis	No. of Cases (n)	Confirmatory Modality
Non-small cell carcinoma	38	Adenocarcinoma	21	Histopathology
		Squamous cell carcinoma	17	Histopathology
Small cell carcinoma	3	Small cell carcinoma	3	Histopathology
Poorly differentiated carcinoma	3	Squamous cell carcinoma	2	Immunohistochemistry
		Adenocarcinoma	1	Immunohistochemistry
Metastatic deposits	6	Metastatic carcinoma	6	Immunohistochemistry

Most cases were observed in the **51–60 years** age group, followed by the **61–70 years** group, indicating a higher occurrence in middle-aged and elderly individuals. Fewer cases were seen at the extremes of age.

Table 2: Age-wise Distribution of Cases (n = 50)

Age Group (years)	Number of Cases (n)	Percentage (%)
30–40	5	10.0
41–50	9	18.0
51–60	18	36.0
61–70	10	20.0
71–80	6	12.0
81–90	2	4.0
Total	**50**	**100**

The gender-wise distribution shows a male predominance, with 30 cases (60%), while females accounted for 20 cases (40%) as shown in Fig.1



The chart illustrates the radiological distribution of lung malignancies, showing adenocarcinoma most commonly presenting as a peripheral lung mass with pleural effusion, followed by squamous cell carcinoma predominantly involving the central/hilar region. Small cell carcinoma appears less frequently and is associated with necrotic lung masses, while metastatic disease typically presents as multiple bilateral pulmonary nodules.

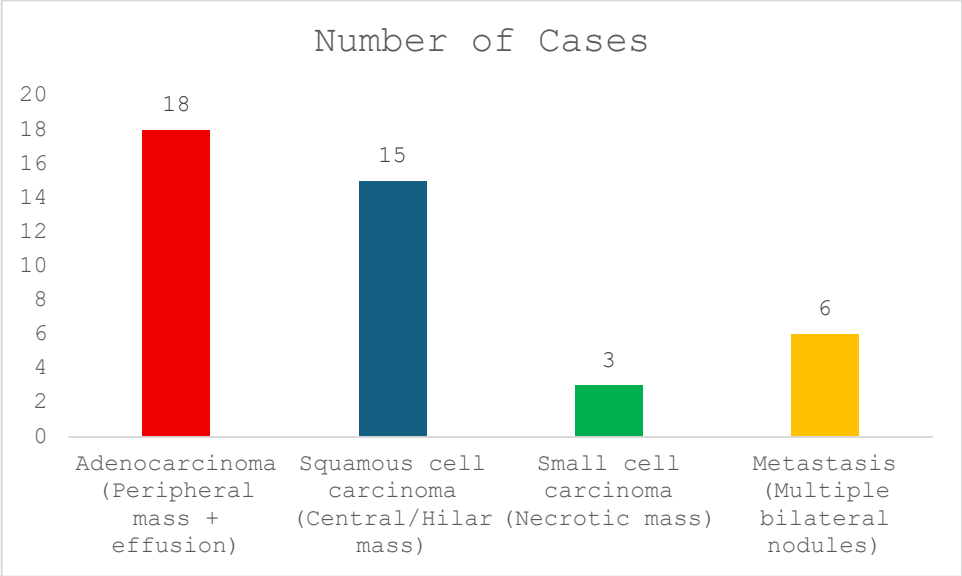
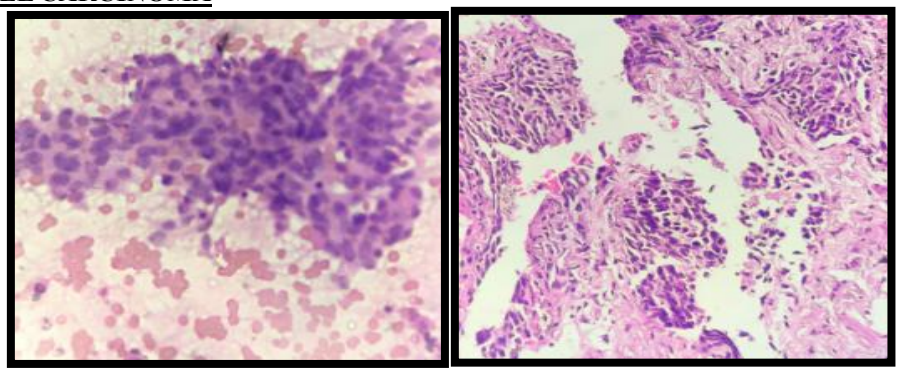


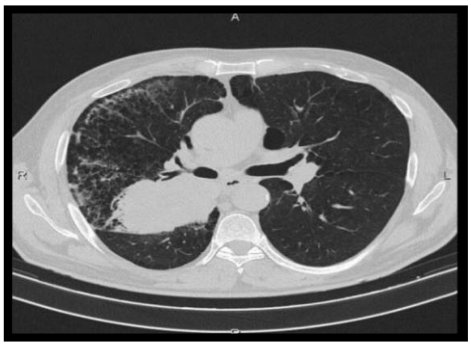
Fig.2: Number of Cases based on radiological findings

The figure demonstrates the cytological, histopathological, and radiological features of squamous cell carcinoma of the lung. Cytology shows polygonal malignant cells arranged in sheets in a necrotic background, while histopathology confirms squamous differentiation. The CT image reveals a centrally located/hilar lung mass, which is characteristic of squamous cell carcinoma.

SQUAMOUS CELL CARCINOMA



Cytology: **Histopathology:**

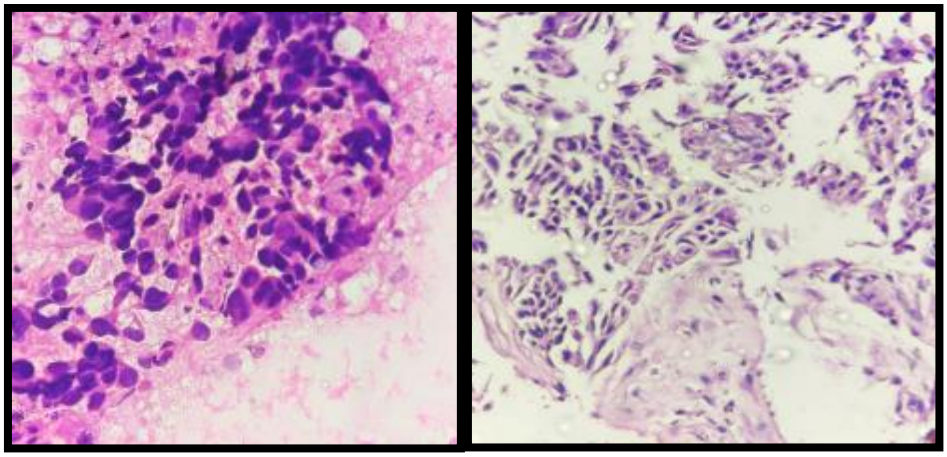


Radiology:

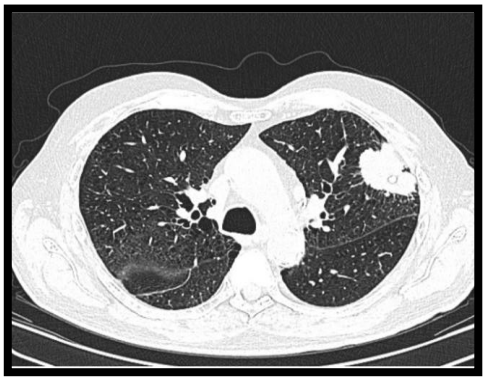
he figure depicts the **cytological, histopathological, and radiological features** of **lung adenocarcinoma**, Cytology shows **pleomorphic round to cuboidal malignant cells** with hyperchromatic nuclei, arranged in clusters, suggesting gland-

forming malignanc, histopathology confirms glandular differentiation, and radiology supports the characteristic **peripheral location of the tumor.**

ADENOCARCINOMA



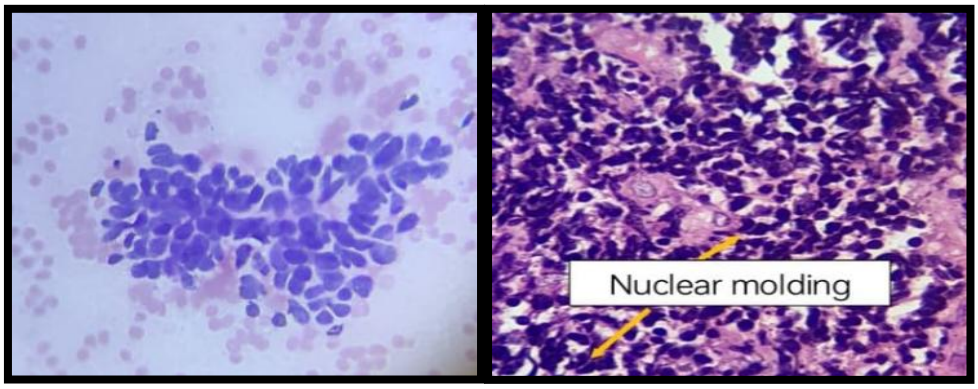
Cytology: **Histopathology:**



Radiology:

The figure demonstrates the **cytological, histopathological, and radiological features** characteristic of **small cell carcinoma of the lung**. Cytology shows **small, round to oval malignant cells** arranged in clusters with scant cytoplasm. Histopathology reveals sheets of tumor cells with **prominent nuclear molding**, where nuclei appear closely compressed against each other, confirming the diagnosis. Radiology demonstrates a **mass lesion in the hilar/central region**, a typical radiological presentation of small cell carcinoma

SMALL CELL CARCINOMA OF THE LUNG

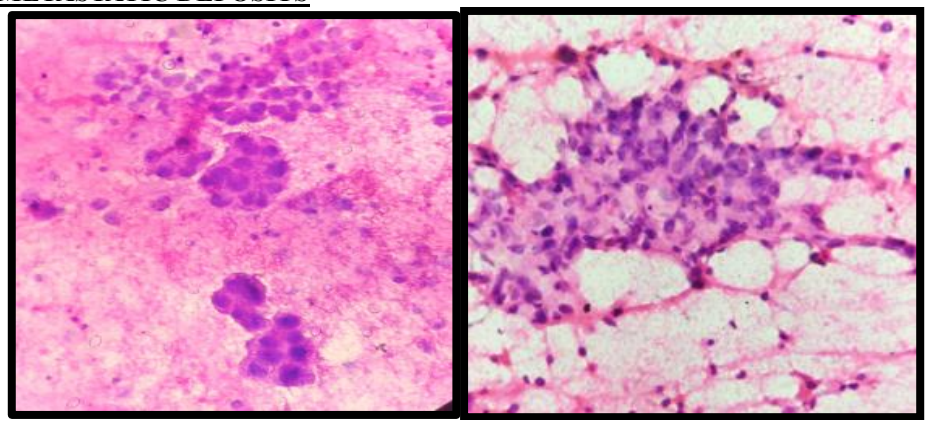


Cytology: **Histopathology:**

Radiology:

The figure highlights a strong cyto–histo–radiological correlation, where cytology and histopathology reflect the morphology of the primary tumors, and imaging confirms widespread bilateral pulmonary involvement, supporting the diagnosis of metastatic lung disease.

PULMONARY METASTATIC DEPOSITS



Cytology: **Histopathology:**

Radiology:

DISCUSSION

Accurate classification of lung malignancies is fundamental for appropriate therapeutic planning and prognostic assessment, as treatment strategies vary considerably across different histological subtypes. In the present study, cytological evaluation demonstrated high diagnostic accuracy in identifying the major categories of lung cancer, particularly non-small cell carcinoma (NSCC) and small cell carcinoma (SCC). Complete cytology–histopathology concordance observed in all cases of SCC can be attributed to the distinctive cytomorphological features of this tumor, such as small cell size, scant cytoplasm, nuclear molding, and finely granular chromatin, which allow confident diagnosis even on limited cytological material.[11]

Among cases diagnosed as NSCC on cytology, histopathological examination was essential for definitive subtyping into adenocarcinoma and squamous cell carcinoma. Although cytology reliably categorizes tumors into broad groups, architectural features such as gland formation and keratinization are better appreciated on tissue sections. Similar findings

have been reported in previous studies, emphasizing that histopathology remains the gold standard for accurate subtyping of NSCC.[12,13]

Cytology alone was insufficient for precise classification of poorly differentiated carcinomas and metastatic deposits in the present study. In these diagnostically challenging cases, immunohistochemistry (IHC) played a crucial role in resolving tumor lineage and confirming the site of origin. The use of appropriate IHC marker panels enabled reliable differentiation between primary lung malignancies and metastatic tumors, highlighting the indispensable role of IHC in modern lung cancer diagnostics, particularly when dealing with small biopsies and cytology specimens.[14,15]

The histological distribution in the present study revealed adenocarcinoma as the most common subtype, followed by squamous cell carcinoma, small cell carcinoma, and metastatic deposits. This pattern is consistent with several recent studies that have documented a shift toward adenocarcinoma predominance in lung cancer.[16,17] The proportion of squamous cell carcinoma observed in this study is comparable with other Indian studies, while the relatively lower frequency of small cell carcinoma may reflect regional variations in smoking habits and demographic characteristics.[18]

The age-wise distribution showed a peak incidence in the 51–60-year age group, followed by the 61–70-year group, indicating a higher burden of lung malignancies among middle-aged and elderly individuals. This observation correlates well with global epidemiological data and reflects cumulative exposure to risk factors such as tobacco smoking, occupational hazards, and environmental pollutants over time.[19]

A male predominance was noted in the present study, with males accounting for 60% of cases. This finding is consistent with published literature and is largely attributed to higher smoking prevalence and occupational exposure among men. However, recent trends suggest a gradual rise in lung cancer incidence among females, underscoring changing lifestyle and environmental risk factors.[20]

Radiological findings in the present study showed a strong correlation with histological subtypes. Adenocarcinoma most commonly presented as a peripheral lung mass, often associated with pleural effusion, consistent with its origin from distal airways. Squamous cell carcinoma predominantly involved the central or hilar region, reflecting its bronchogenic origin. Small cell carcinoma demonstrated centrally located masses with necrosis, highlighting its aggressive nature, while metastatic lung disease typically presented as multiple bilateral pulmonary nodules suggestive of hematogenous spread.[21,22]

Overall, the present study highlights the diagnostic value of a multimodal approach integrating cytology, histopathology, radiology, and immunohistochemistry. Such an integrated strategy enhances diagnostic accuracy, facilitates precise tumor classification, and plays a pivotal role in guiding optimal clinical management of lung malignancies.[23]

CONCLUSION

An integrated multimodal diagnostic approach incorporating cytology, histopathology, radiology, and immunohistochemistry significantly improves the accuracy of lung tumor diagnosis and subtyping. Cytology serves as a rapid and minimally invasive initial diagnostic tool, while histopathology and immunohistochemistry are crucial for definitive classification, particularly in poorly differentiated and metastatic lesions. The correlation of pathological findings with radiological features further enhances diagnostic confidence. Adoption of this comprehensive strategy facilitates precise tumor classification and supports optimal clinical management of lung malignancies.

REFERENCES

1. Sung H, Ferlay J, Siegel RL, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide. *CA Cancer J Clin*. 2021;71(3):209–249.
2. Torre LA, Bray F, Siegel RL, Ferlay J, Lortet-Tieulent J, Jemal A. Global cancer statistics, 2012. *CA Cancer J Clin*. 2015;65(2):87–108.
3. Rivera MP, Mehta AC, Wahidi MM. Establishing the diagnosis of lung cancer: diagnosis and management. *Chest*. 2013;143(5 Suppl):e142S–e165S.
4. Orell SR, Sterrett GF, Whitaker D. *Fine Needle Aspiration Cytology*. 5th ed. Philadelphia: Elsevier; 2012.
5. Webb WR, Müller NL, Naidich DP. *High-Resolution CT of the Lung*. 5th ed. Philadelphia: Wolters Kluwer; 2014.
6. Silvestri GA, Gonzalez AV, Jantz MA, et al. Methods for staging non-small cell lung cancer. *Chest*. 2013;143(5 Suppl):e211S–e250S.
7. Travis WD, Brambilla E, Nicholson AG, et al. The 2015 World Health Organization classification of lung tumors. *J Thorac Oncol*. 2015;10(9):1243–1260.
8. Pelosi G, Rossi G, Bianchi F, et al. Immunohistochemistry in lung cancer diagnosis. *Histopathology*. 2018;72(1):110–121.
9. Lindeman NI, Cagle PT, Aisner DL, et al. Updated molecular testing guideline for lung cancer. *Arch Pathol Lab Med*. 2018;142(3):321–346.
10. Rekhtman N. Multimodality approach to lung cancer diagnosis. *Mod Pathol*. 2017;30(S1):S1–S12

11. Travis WD, Brambilla E, Nicholson AG, et al. The 2015 World Health Organization classification of lung tumors. *J Thorac Oncol*. 2015;10(9):1243–1260.
12. Rekhtman N, Ang DC, Sima CS, et al. Immunohistochemical algorithm for differentiation of lung adenocarcinoma and squamous cell carcinoma. *Am J Surg Pathol*. 2011;35(4):557–570.
13. Thunnissen E, Allen TC, Adam J, et al. Immunohistochemistry of lung cancer. *J Thorac Oncol*. 2017;12(4):571–585.
14. Pelosi G, Rossi G, Bianchi F, et al. Immunohistochemistry in lung cancer diagnosis. *Histopathology*. 2018;72(1):110–125.
15. Lindeman NI, Cagle PT, Aisner DL, et al. Updated molecular testing guideline for lung cancer patients. *Arch Pathol Lab Med*. 2018;142(3):321–346.
16. Krishnamurthy A, Kumar S, Ramshankar V, et al. Lung cancer in India: A clinicopathological study. *J Cancer Res Ther*. 2014;10(4):855–859.
17. Sundaram V, Gokulakrishnan S, Suresh Babu MC. Histological spectrum of lung cancer in a tertiary care hospital. *Lung India*. 2017;34(3):254–258.
18. Malik PS, Sharma MC, Mohanti BK, et al. Clinico-pathological profile of lung cancer in North India. *Indian J Chest Dis Allied Sci*. 2013;55(2):89–93.
19. Alberg AJ, Brock MV, Samet JM. Epidemiology of lung cancer. *Chest*. 2013;143(5 Suppl):e1S–e29S.
20. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2020. *CA Cancer J Clin*. 2020;70(1):7–30.
21. Webb WR, Müller NL, Naidich DP. *High-Resolution CT of the Lung*. 5th ed. Philadelphia: Wolters Kluwer; 2014.
22. Hansell DM, Bankier AA, MacMahon H, et al. Fleischner Society glossary of thoracic imaging terms. *Radiology*. 2008;246(3):697–722.
23. Rekhtman N, Travis WD. Lung cancer diagnosis in the era of personalized medicine. *Mod Pathol*. 2016;29(Suppl 1):S1–S15.