Medical Research Archives

ESMED
European Society of Medicine

OPEN ACCESS

Published: June 30, 2022

Citation Shakya S, Sahni S, et al., 2022. Implications of the 8th TNM Classification on the Bronchoscopist, Medical Research Archives, [online] 10(6). https://doi.org/10.18103/mra.v10i6.2839

DOI
https://doi.org/10.18103/mra.v10i6.2839

ISSN: 2375-1924

RESEARCH ARTICLE

Implications of the 8th TNM Classification on the Bronchoscopist, a future perspective

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ABSTRACT

Primary lung malignancy remains the leading cause of cancer related deaths globally. A better understanding of the disease process with advancing diagnostic modalities has led to a change in the standard of care. Endobronchial ultrasound (EBUS) with transbronchial lymph node needle aspiration allows for mediastinal and hilar lymph node sampling for accurate staging and prognostication. In the latest 8th edition of the TNM classification, several changes were made including redefining T based on size, redefinition of metastasis (M) and changes were made to stage groupings. Nodal staging has remained the same as of the 7th edition of the TNM classifications. In this review, we are reemphasizing the importance of the extra step of nodal staging and its clinical significance. Furthermore, we highlight the necessity of more aggressive nodal staging using EBUS-TBNA in stage 1 lung cancer.

Keywords: Lung Cancer, EBUS-TBNA, TNM Classifications, Endobronchial Ultrasound

Lung cancer remains one of the most commonly diagnosed malignancies. It is the leading cause of cancer-related deaths worldwide in both men and women with an estimated 2.2 million new cases and 1.76 million deaths per year [1]. Over the past two decades, a better understanding of the disease process as well as new chemotherapeutics including targeted therapy has led to improved management leading to better outcomes. In addition, the standard of care in diagnosis and staging now includes endobronchial ultrasound with transbronchial lymph node needle aspiration (EBUS-TBNA). Once nodal sampling is performed, accurate staging leads to a variety of therapies based on the extent of mediastinal and hilar nodal involvement. Thus, it is crucial to appropriately stage lung cancer to assess possible curative therapeutic options.

Since the 1970s, TNM staging of lung cancer has been implemented to define disease extent which dictates management options and prognosis. TNM staging has undergone multiple revisions with the latest rendition, the 8th edition, being in use since 2018. The 8th edition has made several changes to previous TNM staging. Modifications were made to the primary tumor classification by redefining T based on size, redefinition of metastasis (M) and changes were made to the stage groupings [2]. The nodal staging remained the same as the 7th edition, but it highlighted the quantification of the number of nodes involved which played a significant role in further subdivision of stage groupings.

In the 7th edition of TNM classification for lung cancer the T descriptor was defined with main bronchus involvement that was two centimeters or more distal to the carina as T2 disease and tumor presence in the main bronchus less than 2 cm from the carina without invasion of the carina itself as T3 disease. In the 8th edition, involvement of the main bronchus, regardless of distance to the carina, did not seem to increase the risk after adjusting for tumor size both in pathologically and clinically staged tumors [2]. Based on these analyses, involvement of the main bronchus has been classified as T2 disease unless invasion of the main carina exists. This has led to the bronchoscopist no longer needing to define in detail the location of the tumor in the main bronchi.

Nodal staging outlines the tumor burden on the hilar and mediastinal lymph nodes which correlates with prognosis. Thus, a more precise subdivision of N1 into N1a (single station, ipsilateral hilum) and N1b (multiple stations); and N2 into N2a1 (single N2 station without N1 involvement), N2a2 (single N2 station with N1 involvement) and N2b (multiple N2 stations) were proposed. The 5-year survival rates of M0 patients after complete resection showed N1a, 59%; N1b, 50%; N2a1, 54%; N2a2, 43%; and N2b, 38% [2, 3]. This points to N1b and N2a1 having similar prognosis while N2a2 has significantly worse prognosis than N2a1. Additionally, treatment modality changes from surgical resection with curative intent in early-stage disease vs. chemoradiation in the advanced stage disease.

Mediastinal staging guidelines recommended noninvasive imaging with computed tomography (CT) alone or integrated with positron emission tomography (PET-CT) to determine clinical stage though noninvasive forms of mediastinal staging are not entirely reliable and a more invasive test is often recommended. Also, Fujiwara et al has recently developed a four point Canada Lymph Node Score (CLNS) to further determine the probability of nodal metastasis based on endobronchial ultrasonographic features. A lymph node with CLNS <2 has a low probability of 11.7% for malignancy [7]. In patients with triple-normal LN - cN0 disease, mediastinal lymph node sampling is not recommended if it is peripheral and less than 3 cm. However, postoperative pathological upstaging (pN2) has been documented in up to 5.6% to 35% of clinical N0 status [4,5,7]. This brings up an argument for mediastinal staging in those with the clinical N0/N1 stage. Several techniques, including

mediastinoscopy, surgery, open or video-assisted thoracoscopic surgery (VATS), EBUS guided transbronchial needle aspiration (TBNA), or endoscopic ultrasound (EUS)-guided fine needle aspiration (FNA) exist for an accurate preoperative mediastinal lymph node staging. EBUS-TBNA/EUS-FNA is currently the preferred modality as it is minimally invasive with high diagnostic yield. It has a sensitivity of 49% (95% CI, 41-57%) and NPV of 91% (range, 82% to 100%) for detection of occult N2/N3 disease and it must be performed in 14 patients to detect one additional case with mediastinal metastases. Additionally, EBUS-FNA improves sensitivity to 73% (95% CI, 57%-82%) and NNT to 7 for detecting N2/N3 disease[5].

For accurate staging, proper EBUS technique should be followed by sampling a minimum of three LN stations and examining five mediastinal stations. The N3 lymph node stations should be sampled first, followed by the N2 then N1 lymph node stations during the EBUS-TBNA procedure. With Rapid On-Site Evaluation (ROSE), if N3 node is positive, it is Stage IIIB and no further biopsy is required. However, if N3 nodes are negative, then N2 nodes need to be sampled. If the first N2 node is positive, then the needle should be changed to sample other N2 nodes to avoid false positive results on multiple N2 nodes as it will stage patients for N2b, which has worse prognosis [2,3]. If there are multiple N2 nodes that are positive, then no further N1 sampling is needed as the patient will be staged as N2b. However, if there is only one N2 node that is positive (N2a), then the N1 node should be sampled with a different fresh needle to differentiate between N2a2 and N2a1. If ROSE is unavailable, all N2 station lymph nodes should be sampled using different needles on each node.

The aforementioned are important observations suggested by Assallum and colleagues [6]. Although this deeper classification of the nodal staging has no impact on the therapeutic options of lung cancer so far, this should make a difference when the health care provider discusses the prognosis with his patient. Therefore, the clinical practice should continue to minimize misdiagnosis and focus on complete nodal assessment. Future staging and diagnostic guidelines should take into consideration the implications of staging and how it pertains to the clinical practice.

Conflict of Interest: None

Financial Disclosure: None

References

1. Sung, H., et al., *Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries*. CA Cancer J Clin, 2021. **71**(3): p. 209-249.
2. Lababede, O. and M.A. Meziane, *The Eighth Edition of TNM Staging of Lung Cancer: Reference Chart and Diagrams*. Oncologist, 2018. **23**(7): p. 844-848.
3. Lim, W., et al., *The 8(th) lung cancer TNM classification and clinical staging system: review of the changes and clinical implications*. Quant Imaging Med Surg, 2018. **8**(7): p. 709-718.
4. Sehgal, I.S., et al., *Role of EBUS TBNA in Staging of Lung Cancer: A Clinician's Perspective*. J Cytol, 2019. **36**(1): p. 61-64.
5. Leong, T.L., et al., *Preoperative Staging by EBUS in cN0/N1 Lung Cancer: Systematic Review and Meta-Analysis*. J Bronchology Interv Pulmonol, 2019. **26**(3): p. 155-165.
6. Assallum, H. and K. Harris, *The Impact of the Eighth TNM Classification for Lung Cancer on the Endobronchial Ultrasound Procedure*. J Thorac Oncol, 2018. **13**(7): p. E119-e120.
7. Hylton DA, Kidane B, Spicer J, Turner S, Churchill I, Sullivan K, Finley CJ, Shargall Y, Agzarian J, Seely AJE, Yasufuku K, Hanna WC; Canadian Association of Thoracic Surgery Research Group. *Endobronchial Ultrasound Staging of Operable Non-small Cell Lung Cancer: Do Triple-Normal Lymph Nodes Require Routine Biopsy?* Chest. 2021 Jun;159(6):2470-2476. doi: 10.1016/j.chest.2020.12.050. Epub 2021 Jan 9. PMID: 33434503.