

INVASIVE MEDIASTINAL STAGING



Akif TURNA¹
 Burcu KILIÇ²
 İsmail SARBAY³

The lung cancer staging classification describes the anatomical extent of malignant pulmonary tumors in terms of three parameters: tumor (T), nodal status (N) and metastasis at pleural fluid, contralateral lung or distant organs(M)[1]. The treatment of non-small cell lung cancer (NSCLC) is determined by accurate definition of the stage[1]. Survival curves of the patients with non-small cell lung cancer at different stages show that, the patients with stage 1A to stage IIIA(T3N1) should be amenable to resectional surgery [2]. The patients with N2 or N3 disease should be referred to multimodality treatment [3,4,5]. Even for the patients who had chemoradiotherapy the surgical resection has been proven to be futile if there is recalcitrant N2 or N3 disease[6]. If there are no distant metastases, the status of the mediastinal lymph nodes is important. Although imaging studies can provide some guidance, in many situations invasive staging is necessary. In patients with extensive mediastinal infiltration, invasive staging is not needed [3,4] (Figure 1). Those patients should be referred to chemo/radiotherapy[3,4,5].

In patients with discrete node enlargement, staging by computerized tomography(CT) or positron emission tomography (PET) scanning is not sufficiently accurate (Table 1). The sensitivity of various techniques varies between 55-80% which is suboptimal. Although negative

predictive value of PET-CT is 91% as a result of a systematic review[4], positive predictive value is near a tossing a coin(i.e.58%)! For these reasons, one should not rely on CT or PET-CT in T2-T4 tumors[2-5]. Patients with peripheral T1 tumor (preferably non-adenocarcinoma histology) without mediastinal lymph node involvement on PET-CT, will be offered to resectional surgery without any invasive mediastinal staging modality since the false-negativity rate is below 5%(Figure 2)[4,5,8,9]. When PET scan is implemented, the rate of overlooked N2 disease is expected to be below 10% [8,9].

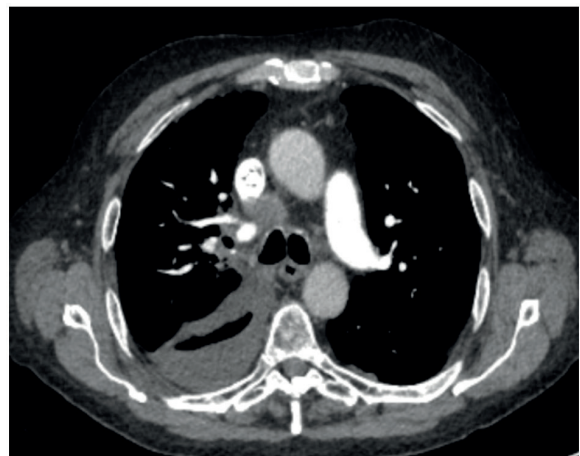


Figure 1. A patient with right upper lobe tumor adjacent with with right paratracheal lymph node. In these patients, there is no need for mediastinal lymph node biopsy provided that the tumor is diagnosed.

¹ Prof. Istanbul University-Cerrahpaşa, Cerrahpaşa School Of Medicine, Department of Thoracic Surgery. akif.turna@gmail.com

² Asst. Prof. Istanbul University-Cerrahpaşa, Cerrahpaşa School of Medicine, Department of Thoracic Surgery

³ MD, Istanbul University-Cerrahpaşa, Cerrahpaşa School of Medicine, Department of Thoracic Surgery

utilized for assessment of resectability of the tumor before resectional surgery[48]. A phase 2 trial concluded that mediastinal restaging after neoadjuvant chemo/radiotherapy done by videothoracoscopy is feasible and provided pathologic specimens of ipsilateral lymph nodes[49]. However, they also concluded that, restaging was limited by radiation to the lower paratracheal region.

CONCLUSION

Mediastinal staging should be performed in almost all NSCLC patients except the ones with peripheral cT1N0M0 squamous cell tumors[3]. Figure 13 shows mediastinal lymph nodes and staging procedures that can be used to take excisional or incisional biopsy of those lymph nodes. We recently were able to show that an appropriately accomplished pre-resection lymph node staging for the patients with NSCLC seems to be effective, helps to select best candidate who can benefit from surgery and provides higher survival following resection[50]. Every surgeon should select staging methods depended on radiologic and scintigraphic (PET-CT) evaluation of the par their ability, experience, patient's status, previous operations and morbidity, available instruments at the department.

REFERENCES

- Goldstraw P, Chansky K, Crowley J, Rami-Porta R, Asamura H, Eberhardt WE, et al. The IASLC Lung Cancer Staging Project: Proposals for Revision of the TNM Stage Groupings in the Forthcoming (Eighth) Edition of the TNM Classification for Lung Cancer. *J Thorac Oncol* 2016;11:39-51.
- Goldstraw P, Chansky K, Crowley J, Rami-Porta R, Asamura H, Eberhardt WE, et al. The IASLC Lung Cancer Staging Project: Proposals for Revision of the TNM Stage Groupings in the Forthcoming (Eighth) Edition of the TNM Classification for Lung Cancer. *J Thorac Oncol* 2016;11:39-51.
- De Leyn P, Doooms C, Kuzdzal J, Lardinois D, Passlick B, Rami-Porta R, et al. Revised ESTS guidelines for preoperative mediastinal lymph node staging for non-small-cell lung cancer. *Eur J Cardiothorac Surg* 2014;45:787-98.
- Silvestri GA, Gonzalez AV, Jantz MA, Margolis ML, Gould MK, Tanoue LT, et al. Methods for staging non-small cell lung cancer: Diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines. *Chest* 2013;143:211-50.
- NCCN Guidelines Insights: Non-Small Cell Lung Cancer, Version 2.2020 in: *Journal of the National Comprehensive Cancer Network Volume 18 Issue 1 (2020)*. https://www.nccn.org/professionals/physician_gls/PDF/nscl.pdf. Accessed January 12, 2020.
- Albain KS, Swann RS, Rusch VW, Turrisi AT, Shepherd FA, Smith C, et al. Radiotherapy plus chemotherapy with or without surgical resection for stage III non-small-cell lung cancer: a phase III randomised controlled trial. *Lancet* 2009;374:379-86.
- Melek H, Gunluoglu MZ, Demir A, Akin H, Olcmen A, Dincer SI. Role of positron emission tomography in mediastinal lymphatic staging of non-small cell lung cancer. *Eur J Cardiothorac Surg*. 2008;33(2):294-299.
- Verhagen AT, Bootsma GP, Tjan-Heijnen VCG, van der Wilt GJ, Cox AL, Brouwer MHJ, Corstens FHM, Oyen WJG. FDG-PET in staging lung cancer. How does it change the algorithm? *Lung cancer* 2004;44:175-81.
- De Langen AJ, Raijmakers P, Riphagen I, PaulMA, Hoekstra OS. The size of mediastinal lymph nodes and its relation with metastatic involvement: a meta-analysis. *Eur J Cardiothorac Surg* 2006;29:26-9.
- Rodríguez de Castro F, Rey A, Caminero J, et al. Trans-bronchial fine needle aspiration in clinical practice. *Cyto-pathology*. 1995;6(1):22-29.
- Vansteenkiste J, Lacquet LM, Demedts M, Deneffe G, Verbeken E. Transcarinal needle aspiration biopsy in the staging of lung cancer. *Eur Respir J*. 1994;7(2):265-268.
- Bernasconi M, Chhajed PN, Gambazzi F, et al. Combined transbronchial needle aspiration and positron emission tomography for mediastinal staging of NSCLC. *Eur Respir J*. 2006;27(5):889-894.
- Annema JT, van Meerbeeck JP, Rintoul RC, et al. Mediastinoscopy vs endosonography for mediastinal nodal staging of lung cancer: a randomized trial. *JAMA*. 2010;304(20):2245-2252.
- Decaluwé H, Doooms C, D'Journo XB, et al. Mediastinal staging by videomediastinoscopy in clinical N1 non-small cell lung cancer: a prospective multicentre study. *European Respiratory Journal*. 2017;50(6):1701493
- Yasufuku K, Pierre A, Darling G, et al. A prospective controlled trial of endobronchial ultrasound-guided transbronchial needle aspiration compared with mediastinoscopy for mediastinal lymph node staging of lung cancer. *J Thorac Cardiovasc Surg*. 2011;142(6):1393-1400
- Wallace MB, Pascual JM, Raimondo M, et al. Minimally invasive endoscopic staging of suspected lung cancer. *JAMA*. 2008;299(5):540-546.
- Doooms C, Tournoy KG, Schuurbijs O, et al. Endosonography for mediastinal nodal staging of clinical N1 non-small cell lung cancer: a prospective multicenter study. *Chest* 2014; 147: 209-215.
- Decaluwe H, Doooms C, D'Journo BD, Call S, Sanchez D, Haager B, Beelen R, Kara V, et al. Mediastinal staging by videomediastinoscopy in clinical N1 non-small cell lung cancer: a prospective multicentre study. *Eur Respir J* 2017; 50: 1701493

19. Czarnecka-Kujawa K, Yasufuku K. The role of endobronchial ultrasound versus mediastinoscopy for non-small cell lung cancer. *J Thorac Dis.* 2017 Mar;9(Suppl 2):S83-S97
20. Cetinkaya E, Seyhan EC, Ozgul A, et al. Efficacy of convex probe endobronchial ultrasound (CP-EBUS) assisted transbronchial needle aspiration for mediastinal staging in non-small cell lung cancer cases with mediastinal lymphadenopathy. *Ann Thorac Cardiovasc Surg.* 2011;17(3):236-242.
21. Harken DE, Black H, Clauss R, et al. A simple cervicomediastinal exploration for tissue diagnosis of intrathoracic disease; with comments on the recognition of inoperable carcinoma of the lung. *N Engl J Med* 1954;251:1041-1044.
22. Daniels AC. A method of biopsy useful in diagnosing certain intrathoracic diseases. *Dis Chest* 1949;16:360-366.
23. Carlens E. Mediastinoscopy: A method for inspection and tissue biopsy in the superior mediastinum. *Dis Chest* 1959;36:343-352.
24. Pearson FG, Nelems JM, Henderson RD, et al. The role of mediastinoscopy in the selection of treatment for bronchial carcinoma with involvement of superior mediastinal lymph nodes. *J Thorac Cardiovasc Surg* 1972;64(3):382-390.
25. Song WA, Zhou NK, Wang W, et al. Survival benefit of neoadjuvant chemotherapy in non-small cell lung cancer. An updated metaanalysis of 13 randomized control trials. *J Thorac Oncol* 2010;5:510-516.
26. Lerut T, De Leyn P. Mediastinoscopy. In Shields TW, Locicero J, Fein RH, Colson YL, Rocco G(eds). *General Thoracic Surgery*. Philadelphia: Lippincott Williams&Wilkins; 2019, pp.297-308.
27. Benouaich V, Marcheix B, Carfagna L, Brouchet L, Guitard J. Anatomical bases of left recurrent nerve lesions during mediastinoscopy. *Surg Radiol Anat.* 2009 Apr;31(4):295-9.
28. Deleyn P, Lerut T. Videomediastinoscopy. *Multimed Man Cardiothorac Surg.* 2005 Jan 1;2005(104):MMCTS.2004.000166.
29. Mouroux J, Venissac N, Alifano M. Combined video-assisted mediastinoscopy and video-assisted thoracoscopy in the management of lung cancer. *Ann Thorac Surg* 2001;72:1698-704.
30. Lardiniois D, Schallberger A, Betticher D, Ris HB. Postinduction video-mediastinoscopy is as accurate and safe as video-mediastinoscopy in patients without pretreatment for potentially operable non-small cell lung cancer. *Ann Thorac Surg* 2003;75:1102-6.
31. Martin-Ucar AE, Chetty GK, Vaughan R, Waller DA. A prospective audit evaluating the role of video-assisted cervical mediastinoscopy (VAM) as a training tool. *Eur J Cardiothorac Surg* 2004;26:393-5.
32. Sayar A, Citak N, Metin M, Turna A, Pekçolaklar A, Kök A, Urer N, Celikten A, Ulukol ZN, Gürses A. Comparison of video-assisted mediastinoscopy and video-assisted mediastinoscopic lymphadenectomy for lung cancer. *Gen Thorac Cardiovasc Surg.* 2011 Dec;59(12):793-8.
33. Hürtgen M, Friedel G, Tomes H, Fritz P. Radical video-assisted mediastinoscopic lymphadenectomy (VAMLA)-technique and first results. *Eur J Cardiothorac Surg* 2002;21:348-51
34. Call S, Obiols C, Rami-Porta R, et al. Video-assisted mediastinoscopic lymphadenectomy for staging non-small cell lung cancer. *Ann Thorac Surg* 2016;101(4):1326-1333.
35. Turna A, Demirkaya A, Ozkul S, Oz B, Gürses A, Kaynak K. Video-assisted mediastinoscopic lymphadenectomy is associated with better survival than mediastinoscopy in patients with resected non-small cell lung cancer. *J Thorac Cardiovasc Surg* 2013;146:774-80.
36. Kara HV, Karaaltın AB, Ersen E, Alaskarov E, Kilic B, Turna A. Minimally invasive injection laryngoplasty in the management of unilateral vocal cord paralysis after video-assisted mediastinal lymph adenectomy. *Wideochir Inne Tech Maloinwazyjne.* 2018 Sep;13(3):388-393.
37. Stamatis G, Fechner S, Hillejan L, Hinterthaler M, Krbek T. Repeat mediastinoscopy as a restaging procedure. *Pneumologie* 2005;59:862-6.
38. De Leyn P, Stoobants S, Dewever W, Lerut T, Coosemans W, Decker G, Naftoux P, Van Raemdonck D, Mortelmans L, Nackaerts K, Vansteenkiste J. Prospective comparative study of integrated PET-CT with remediastinoscopy in the assessment of residual mediastinal disease after induction chemotherapy for mediastinoscopy proven stage IIIa-N2 non-small cell lung cancer. *J Clin Oncol* 2006;24:3333-9.
39. Kuzdzał J, Zielinski M, Papla B, Szlubowski A, Hauer L, Nabialek T, Sosnicki W, Pankowski J. Transcervical extended mediastinal lymphadenectomy the new operative technique and early results in lung cancer staging. *Eur J Cardiothorac Surg* 2005;27:384.
40. Zielinski M, Hauer L, Hauer J, Nabialek T, Szlubowski A, Pankowski J. Non-small-cell lung cancer restaging with transcervical extended mediastinal lymphadenectomy. *Eur J Cardiothorac Surg* 2010;37:776-780.
41. McNeill TM, Chamberlain JM. Diagnostic anterior mediastinotomy. *Ann Thorac Surg* 1966;2:532-9.
42. Nechala P, Graham AJ, McFadden SD, Grondin SC, Gelfand G. Retrospective analysis of the clinical performance of anterior mediastinotomy. *Ann Thorac Surg* 2006;82:2004-5.
43. Kirschner P. "Extended" mediastinoscopy. In: Jepsen O, Ruhbek-Sorensen H, eds. *Mediastinoscopy*. Odense: Odense University Press, 1971.
44. Ginsberg RJ, Rice TW, Goldberg M, Walters PF, Schomcker BJ. Extended cervical mediastinoscopy. A single procedure for bronchogenic carcinoma of the left upper lobe. *J Thorac Cardiovasc Surg* 1987;94:673-8.
45. Lopez L, Varela A, Freixinet J, et al. Extended cervical mediastinoscopy: prospective study of fifty cases. *Ann Thorac Surg* 1994;57:555-8.
46. Call S, Rami-Porta R, Serra-Mitjans M, Saumench R, Bidegain C, Iglesias M, Gonzalez-Pont G, Belda J. Extended cervical mediastinoscopy in the staging of bronchogenic carcinoma of the lung. *Eur J Cardiothorac Surg* 2008;34:1081-4.
47. Metin M, Sayar A, Turna A., Gürses A. Extended cervical mediastinoscopy in the diagnosis of anterior mediastinal masses. *Ann Thorac Surg.* 2002;73:250 - 252.

48. Jiménez Merchán R, Congregado Loscertales M, Gallardo Valera G, Triviño Ramírez A, Ayarra Jarne J, Loscertales J. Exploratory videothoracoscopy and videopericardioscopy in the definitive staging and assessment of resectability of lung cancer. *Arch Bronconeumol*. 2009 Sep;45(9):435-41.
49. Jaklitsch MT, Gu L, Demmy T, Harpole DH, D'Amico TA, McKenna RJ, Krasna MJ, Kohman LJ, Swanson SJ, DeCamp MM, Wang X, Barry S, Sugarbaker DJ; CALGB Thoracic Surgeons. Prospective phase II trial of pre-resection thoracoscopic mediastinal restaging after neoadjuvant therapy for IIIA (N2) non-small cell lung cancer: results of CALGB Protocol 39803. *J Thorac Cardiovasc Surg*. 2013 Jul;146(1):9-16.
50. Turna A, Melek H, Kara HV, Kılıç B, Erşen E, Kaynak K. Validity of the updated European Society of Thoracic Surgeons staging guideline in lung cancer patients. *J Thorac Cardiovasc Surg*. 2018 Feb;155(2):789-795.