

• EBUS 与肺癌 •

Application of Real Time Endobronchial Ultrasound-guided Transbronchial Needle Aspiration for Lung Cancer Staging

Ignasi GARCIA-OLIVÉ^{1,2}, José SANZ-SANTOS^{1,2}, Felipe ANDREO^{1,3}, Eduard MONSÓ^{1,3}

¹Respiratory Service, Hospital Universitari Germans Trias i Pujol, Badalona, Catalunya, Spain;

²Departament de Medicina. Universitat Autònoma de Barcelona;

³Ciber de Enfermedades Respiratorias-CibeRes, Bunyola, Spain

实时经支气管超声引导针吸活检 在肺癌分期中的应用

南娟 丁燕 翻译 刘谦 校对

天津医科大学总医院, 天津市肺癌研究所, 天津市肺癌转移与肿瘤微环境重点实验室

【摘要】线性经支气管超声引导针吸活检 (endobronchial ultrasound-guided transbronchial needle aspiration, EBUS-TBNA) 是新引进的技术, 它是实时超声下可视淋巴结的针吸活检。尽管有研究显示, 其为肺癌纵隔分期的有效方法, 但全世界多数机构并未应用该技术。本报道旨在分享我们应用EBUS-TBNA的经验, 并对相关文献做一简要概述。我们对有关该技术的已有文献进行综述, 并特别介绍了我们应用该技术方面的经验。EBUS-TBNA用以探查肺癌患者的转移性纵隔淋巴结和/或肺门淋巴结是有效且安全的。在其它病理状态下, 其亦为有效的诊断方法。

【关键词】EBUS; 线性经支气管超声引导针吸活检; 肺癌分期; 实时经支气管超声引导针吸活检

【中图分类号】R734.2 DOI: 10.3779/j.issn.1009-3419.2010.05.06

前言

经气管针吸活检 (transtracheal needle aspiration, TTNA) 和经支气管针吸活检 (transbronchial needle aspiration, TBNA) 应用于探查肺癌患者纵隔淋巴结转移已超过30年^[1-3]。许多研究报道, 该技术用于探查支气管癌患者纵隔转移的敏感性超过50%, 特异性接近100%^[4-8]。然而, 其敏感性有赖于淋巴结部位 (对气管隆突下淋巴结和右侧气管旁淋巴结的敏感性较高) 和淋巴结大小, 对直径大于20 mm的淋巴结尤为敏感^[9,11]。由于敏感性不稳定, 该技术未得到广泛应用, 仅30%操作呼吸内镜的肺科专家使用了

该技术^[12-13]。

在TTNA或TBNA之前, 应用径向支气管内超声 (endobronchial ultrasound, EBUS) 可见纵隔淋巴结和肺门淋巴结, 这使得该项技术的敏感性高达80%, 因为在穿刺前可见淋巴结部位的径向超声扫描图像^[14,15]。

随后, 线性EBUS的出现有助于在实时超声可视淋巴结下实施TTNA或TBNA, 这使得穿刺更为精准, 而且可以在影像学检查正常的纵隔中进行淋巴结取样^[16-18]。

最近, 有两篇综述评估了EBUS-TBNA在探查肺癌患者转移性纵隔淋巴结中的有效性和安全性^[19,20]。

方法

EBUS的可弯曲支气管镜安置有末梢弯曲的线性探头 (图1), 可产生超声图像, 并可对纵隔和支气管周围组织进行线性平行扫描。气管镜有一个工作通道, 适宜在直接超声可视下实施TBNA。推荐采用局

部利多卡因喷雾和静脉注射咪达唑仑实施局部麻醉和镇静^[21,22]。将气管镜置于气管或主支气管部位可探查纵隔淋巴结[气管隆突下淋巴结(图2)、主肺动脉窗淋巴结、右侧气管旁淋巴结(图3)和左侧气管旁淋巴结(图4)]和肺门淋巴结(图5)，并可测量其直径。在这一过程中，对于探查到的短轴直径超过3 mm的淋巴结，可以在直接超声可视下采用专门设计的21 G或22 G细胞学穿刺针进行取样^[18]，并实施快速的现场细胞学检查。首先对N3区域的所有可到达的淋巴结进行取样，随后为N2和N1区域的淋巴结，直至得到恶性肿瘤的阳性结果。所得组织用95%乙醇固定，苏木素-伊红染色，并根据其是取自含有淋巴细胞的正常淋巴结或取自含有肿瘤细胞群的转移性淋巴



Fig 1 Distal curved linear probe

Reprinted with permission from the copyright holder ©Tianjin Lung Cancer Institute and Blackwell Publishing Asia Pty. Ltd

图 1 末梢弯曲的线性探头

本图得到版权所有者©天津市肺癌研究所和Wiley-Blackwell复制许可



Fig 2 Endobronchial ultrasound of subcarinal node

Reprinted with permission from the copyright holder ©Tianjin Lung Cancer Institute and Blackwell Publishing Asia Pty. Ltd

图 2 支气管内超声所见气管隆突下淋巴结

本图得到版权所有者©天津市肺癌研究所和Wiley-Blackwell复制许可

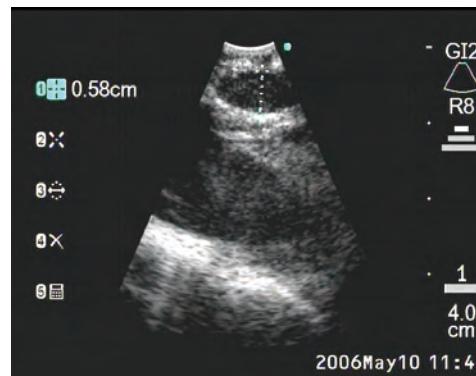


Fig 3 Endobronchial ultrasound of right paratracheal node

Reprinted with permission from the copyright holder ©Tianjin Lung Cancer Institute and Blackwell Publishing Asia Pty. Ltd

图 3 支气管内超声所见右侧气管旁淋巴结

本图得到版权所有者©天津市肺癌研究所和Wiley-Blackwell复制许可

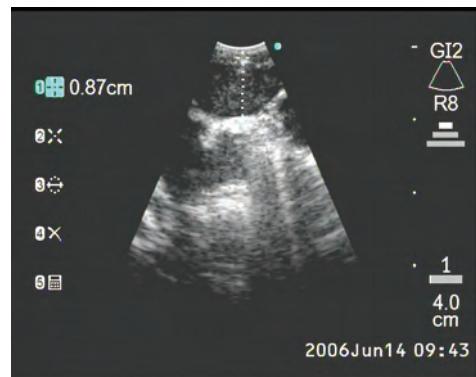


Fig 4 Endobronchial ultrasound of left paratracheal node

Reprinted with permission from the copyright holder ©Tianjin Lung Cancer Institute and Blackwell Publishing Asia Pty. Ltd

图 4 支气管内超声所见左侧气管旁淋巴结

本图得到版权所有者©天津市肺癌研究所和Wiley-Blackwell复制许可

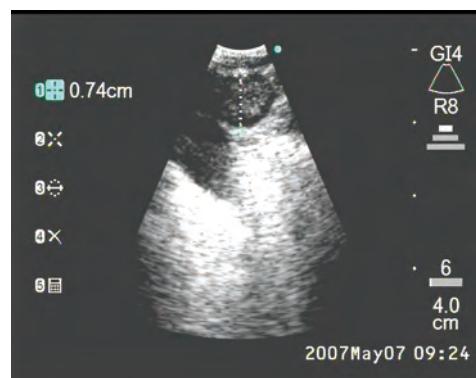


Fig 5 Endobronchial ultrasound of hilar node

Reprinted with permission from the copyright holder ©Tianjin Lung Cancer Institute and Blackwell Publishing Asia Pty. Ltd

图 5 支气管内超声所见肺门淋巴结

本图得到版权所有者©天津市肺癌研究所和Wiley-Blackwell复制许可

结以分类。吸取物中含有的组织太少将不能得到令人满意的结果，在这种情况下，我们可以重复操作，最多3次^[23]。

安全性

在本机构所研究的全部患者的操作过程中，以及随后的48 h内，均未出现操作相关的并发症。目前已有之前提及的综述的网络版^[19,20]。据其所述，可能的并发症有气胸^[24]、血氧不足^[25]、焦虑不安^[26]、咳嗽^[24,26]及穿刺部位出血^[27]。但是，这些并发症极为罕见。

EBUS在肺癌分期中的作用

自2003以来，许多关于肺癌分期的研究^[14-18,24,25,27-34]已经发表。在这些研究中，EBUS-TBNA均呈现出较高的敏感性和特异性。在其中部分研究中，研究者对EBUS-TBNA与CT-PET或CT等其它分期方法进行了比较，结果显示，与其它成像技术相比，EBUS-TBNA具有较高的敏感性和特异性^[30]。

EBUS-TBNA令人感兴趣的另一方面是，它可以从影像技术无法探查到的小于1 cm的淋巴结中取样^[16,18]。

EBUS-TBNA的主要局限是观察不到后面的淋巴结（5、7、8和9站）并从其中取样^[20,30]。在我们的操作过程中，在特定情形下，EBUS-TBNA可见并可从5站淋巴结中取样。

遗憾的是，未有证据显示纵隔淋巴结的超声图像特征可预测恶性，因此需对所有淋巴结进行取样，尤其是肿大和圆形的淋巴结^[18]，首先对N3区淋巴结取样，如果此处淋巴结未呈现恶性，则对N2区和N1区淋巴结取样。

我们采用该技术的体验良好。我们发现，在CT扫描呈现正常纵隔的大约30%的患者中，EBUS-TBNA检测肿大淋巴结的结果显示，25%的淋巴结为恶性^[18]。此外，我们之前的报道指出，超过1/2的患者无需行纵隔镜检查^[18]，这意味着由于无需住院，外科并发症和费用将减少。

EBUS可作为诊断方法

尽管大多数研究关注了EBUS在肺癌分期中的应用，但有些研究者认为EBUS-TBNA是诊断淋巴瘤^[35]、结节病^[36-38]、肺结核^[38]或肺癌的有效方法^[38,39]。

内镜超声和EBUS

据报道，内镜超声（endoscopic ultrasonography, EUS）与EBUS联用是创伤几乎最小的肺癌患者纵隔分期方法，可使某些患者避免进行纵隔镜检查^[28,33,40]。

总结

EBUS-TBNA用以探查肺癌患者甚至影像学检查纵隔正常的患者的转移性纵隔淋巴结和/或肺门淋巴结是有效且安全的。对于其它纵隔疾病，其亦为有效的诊断方法。EUS-TBNA与EBUS-TBNA联用几乎可以对整个纵隔进行取样。这将使纵隔镜检查的次数减少。

Conflict of Interest

I Garcia-Olivé, J Sanz-Santos, F Andreo and E Monsó do not have any financial or personal relationships with other people or organizations that could inappropriately influence their work in the present study.

Acknowledgments

Our work has been supported by funds from the CIBER de Enfermedades Respiratorias- CibeRes, Fondo de Investigación Sanitaria FIS 070170, Sociedad Española de Neumología y Cirugía Torácica (SEPAR), Societat Catalana de Pneumologia (SOCAP), Asociación Española de Endoscopia Respiratoria (AEER) and Redes Temáticas de Investigación Cooperativa en Cáncer RTICC RD06/0020/0056. Ciber de Enfermedades Respiratorias - CibeRes is an initiative of Instituto de Salud Carlos III.

参考文献

- Wang KP, Terry P, Marsh B. Bronchoscopic needle aspiration biopsy of paratracheal tumours. Am Rev Respir Dis, 1978, 118(1): 17-21.
- Wang KP, Terry P. Transbronchial needle aspiration in the diagnosis and staging of bronchogenic carcinoma. Am Rev Respir Dis, 1983, 127(3): 344-347.
- Wang KP, Brower R, Haponik EF, et al. Flexible transbronchial needle aspiration for staging of bronchogenic carcinoma. Chest, 1983, 84(5): 571-576.
- Shure D, Fedullo PF. The role of transcarinal needle aspiration in the staging of bronchogenic carcinoma. Chest, 1984, 86(5): 693-696.
- Schenk DA, Bower JH, Bryan CL, et al. Transbronchial needle aspiration staging of bronchogenic carcinoma. Am Rev Respir Dis, 1986, 134(1):

- 146-148.
- 6 Shenk DA, Chambers SL, Derdak S. Comparison of the Wang 19-gauge and 22-gauge needles in the mediastinal staging of lung cancer. *Am Rev Respir Dis*, 1993, 147(5): 1251-1258.
 - 7 Toloza EM, Harpold L, Detterbeck F, et al. Invasive staging of non-small cell lung cancer: a review of the current evidence. *Chest*, 2003, 123(1 Suppl):157S-166S.
 - 8 Sanz J, Saab M, Castellà E, et al. Rendimiento de la punción aspirativa transtraqueal y transbronquial para el diagnóstico anatomopatológico de la neoplasia broncopulmonar. *Rev Oncol*, 2004, 6(7): 439-442.
 - 9 Harrow EM, Abi-Saleh EV, Blum J, et al. The utility of transbronchial needle aspiration in the staging of bronchogenic carcinoma. *Am J Respir Crit Care Med*, 2000, 161(2 Pt 1): 601-607.
 - 10 Patelli M, Agli LL, Poletti V, et al. Role of fiberscopic transbronchial needle aspiration in the staging of N2 disease due to non-small cell lung cancer. *Ann Thorac Surg*, 2002, 73(2): 407-411.
 - 11 Fernández-Villar A, Iglesias F, Mosteiro M, et al. Factores predictores del resultado de la punción-aspiración transtraqueal de adenopatías mediastínicas neoplásicas. *Arch Bronconeumol*, 2005, 41(8): 434-438.
 - 12 Wang KP. Continued efforts to improve the sensitivity of transbronchial needle aspiration. *Chest*, 1998, 114(1): 4-5.
 - 13 Smyth CM, Stead RJ. Survey of flexible fiberoptic bronchoscopy in the United Kingdom. *Eur Respir J*, 2002, 19(3): 458-463.
 - 14 Herth FJ, Becher HD, Ernst A. Ultrasound-guided transbronchial needle aspiration: an experience in 242 patients. *Chest*, 2003, 123(2): 604-607.
 - 15 Herth FJ, Becher HD, Ernst A. Conventional vs endobronchial ultrasound-guided transbronchial needle aspiration: A randomized trial. *Chest*, 2004, 125(1): 322-325.
 - 16 Herth FJF, Ernst A, Eberhardt R, et al. Endobronchial ultrasound-guided transbronchial needle aspiration of lymph nodes in the radiologically normal mediastinum. *Eur Respir J*, 2006, 28(5): 910-914.
 - 17 Herth FJ, Eberhardt R, Krasnik M, et al. Endobronchial ultrasound-guided transbronchial needle aspiration of lymph nodes in the radiologically and PET normal mediastinum in patients with lung cancer. *Chest*, 2008, 133(4): 887-891.
 - 18 Garcia-Olivé I, Monsó E, Andreo F, et al. Sensitivity of linear endobronchial ultrasonography and guided transbronchial needle aspiration for the identification of nodal metastasis in lung cancer staging. *Ultrasound Med Biol*, 2009, 35(8): 1271-1277.
 - 19 Gu P, Zhao YZ, Jiang LY, et al. Endobronchial ultrasound-guided transbronchial needle aspiration for staging of lung cancer: a systematic review and meta-analysis. *Eur J Cancer*, 2009, 45(8): 1389-1396.
 - 20 Varela-Lema L, Fernández-Villar A, Ruano-Ravina A. Effectiveness and safety of endobronchial ultrasound-transbronchial needle aspiration: a systematic review. *Eur Respir J*, 2009, 33(5): 1156-1164.
 - 21 Reed AP. Preparation of the patient for awake flexible fiberoptic bronchoscopy. *Chest*, 1992, 101(1): 244-253.
 - 22 British Thoracic Society Guidelines on Diagnostic Flexible Bronchoscopy. *Thorax*, 2001, 56(suppl 1): 1-21.
 - 23 Baker JJ, Solanki PH, Schenk DA, et al. Transbronchial fine needle aspiration of the mediastinum. Importance of lymphocytes as an indicator of specimen adequacy. *Acta Cytol*, 1990, 34(4): 517-523.
 - 24 Bauwens O, Dusart M, Pierard P, et al. Endobronchial ultrasound and value of PET for prediction of pathological results of mediastinal hot spots in lung cancer patients. *Lung Cancer*, 2008, 61(3): 356-361.
 - 25 Lee HS, Lee GK, Kim MS, et al. Real-time endobronchial ultrasound guided transbronchial needle aspiration in mediastinal staging of non-small cell lung cancer: how many aspirations per target lymph node station? *Chest*, 2008, 134(2): 368-374.
 - 26 Plat G, Pierard P, Haller A, et al. Endobronchial ultrasound and positron emission tomography positive mediastinal lymph nodes. *Eur Respir J*, 2006, 27(2): 276-281.
 - 27 Yasufuku K, Chiyo M, Sekine Y, et al. Real-time endobronchial ultrasound-guided transbronchial needle aspiration of mediastinal and hilar lymph nodes. *Chest*, 2004, 126(1): 122-128.
 - 28 Vilman P, Krasnik M, Larssen SS, et al. Transesophageal endoscopic ultrasound-guides fine-needle aspiration (EUS-NNA) and endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TNA) biopsy: a combined approach in the evaluation of mediastinal lesions. *Endoscopy*, 2005, 37(9): 833-839.
 - 29 Yasufuku K, Chiyo M, Koh E, et al. Endobronchial ultrasound guided transbronchial needle aspiration for staging of lung cancer. *Lung Cancer*, 2005, 50(3): 347-354.
 - 30 Yasufuku K, Nakajima T, Motoori K, et al. Comparison of endobronchial ultrasound, positron emisión tomography and CT for lymph node staging of lung cancer. *Chest*, 2006, 130(3): 710-718.
 - 31 Herth FJ, Eberhardt R, Vilman P, et al. Real-time endobronchial ultrasound guided transbronchial needle aspiration for sampling mediastinal lymph nodes. *Thorax*, 2006, 61(9): 795-798.
 - 32 Ernst A, Ananthan D, Eberhardt R, et al. Diagnosis of mediastinal adenopathy-real-time endobronchial ultrasound guided needle aspiration versus mediastinoscopy. *J Thorac Oncol*, 2008, 3(6): 577-582.
 - 33 Wallace MB, Pascual JMS, Raimondo M, et al. Minimally invasive endoscopic staging of suspected lung cancer. *JAMA*, 2008, 299(5): 540-546.
 - 34 Vincent BD, El-Bayoumi E, Hoffman B, et al. Real-time endobronchial-guided transbronchial needle aspiration. *Ann Thorac Surg*, 2008, 85(1): 224-230.
 - 35 Kennedy MP, Jimenez CA, Bruzz JF, et al. Endobronchial ultrasound-guided transbronchial needle aspiration in the diagnosis of lymphoma. *Thorax*, 2008, 63(4): 360-365.
 - 36 Oki M, Saka H, Kitagawa C, et al. Real-time endobronchial ultrasound-guided transbronchial needle aspiration is useful for diagnosing sarcoidosis. *Respirology*, 2007, 12(6): 863-868.
 - 37 Nakajima T, Yasufuku K, Kurosu K, et al. The role of EBUS-TBNA for the diagnosis of sarcoidosis-comparisons with other bronchoscopic diagnostic modalities. *Respir Med*, 2009, 103(12): 1796-1800.
 - 38 Garcia-Olivé I, Valverde Forcada EX, Andreo García F, et al. Linear endobronchial ultrasound as the initial diagnostic tool in patients with indications of mediastinal disease. *Arch Bronconeumol*, 2009, 45(6): 266-270.
 - 39 Gilbert S, Wilson DO, Christie NA, et al. Endobronchial ultrasound as a diagnostic tool in patients with mediastinal lymphadenopathy. *Ann Thorac Surg*, 2009, 88(3): 896-900.
 - 40 Vilman P, Puri R. The complete "medical" mediastinoscopy (EUS-FNA+EBUS-TBNA). *Minerva Med*, 2007, 98(4): 331-338.

(本文编辑 周玲)