

## Review Article

## Open Access

Zhiguo Wang, Chunmeng Jiang\*

# Endoscopic ultrasound in the diagnosis of mediastinal diseases

DOI 10.1515/med-2015-0095

received October 18, 2015; accepted November 10, 2015

**Abstract:** EUS is a useful tool for diagnosis of mediastinal diseases. EUS-FNA plays an important role in staging of lung cancer and in tissue acquisition in patients with mediastinal masses. In this review, the following issues will be addressed: EUS-FNA and EBUS-TBNA, metastatic mediastinal lymph nodes diagnosed by EUS, EUS in assessment of mediastinal lymph node status for staging of lung cancer, mediastinal lymphoma diagnosed by EUS, sarcoidosis and tuberculosis diagnosed by EUS.

**Keywords:** EUS, mediastinal diseases

## 1 Endoscopic ultrasound in the diagnosis of mediastinal diseases

The evaluation of mediastinal masses poses a diagnostic challenge. This is because of their myriad of possible pathologic causes; their proximity to numerous vital structures, and the difficulty of access for biopsy [1]. Mediastinal lesions can be evaluated using non-invasive and invasive methods. In recent years, endoscopic ultrasound (EUS) and endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) has aided the diagnosis and staging of pulmonary malignancies and mediastinal disease [2-4].

EUS can accurately reveal middle and posterior mediastinal lesions surrounding the esophagus, and thus the operator must be familiar with mediastinal landmarks [5]. In contrast to first-line non-invasive methods such

as computed tomography (CT) and magnetic resonance imaging (MRI), EUS can demonstrate the anatomic relationship between lesions and normal mediastinal organs. EUS-FNA can be employed to obtain sampling for the pathologic diagnosis.

## 2 EUS-FNA and endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA)

EUS-FNA has become an important tool for evaluation of the mediastinum [6,7]. The main role of EUS-FNA in the thorax is in the diagnosis and staging of lung cancer and in tissue acquisition in patients with mediastinal masses or idiopathic lymphadenopathy [8-10].

A tissue diagnosis is frequently needed for assessment of mediastinal lesions, and has a significant impact on outcome and management [11,12]. EUS-FNA is a good choice for tissue sampling because of its high sensitivity and low morbidity [13]. In general, EUS-FNA can be used safely to biopsy subcarinal and posterior mediastinal masses even though it cannot reach the region anterior to the trachea or main bronchi [14]. EUS-FNA can also be an alternative for the diagnosis of lesions superior to the aortic arch [15]. Transthoracic mediastinal ultrasonography can be used to view and guide biopsy of upper and anterior mediastinal lesions *via* a suprasternal or parasternal approach [16].

In this context Lee et al. (2010) studied 125 consecutive patients with various mediastinal and pulmonary lesions, malignancy was confirmed in 62 (50%) of patients and excluded in 42 (34%) [17]. The sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of EUS-FNA in the diagnosis of mediastinal malignancies was 75%, 100%, 100%, 67%, and 83%, respectively. In a different study by Ardengh et al. (2011), EUS-FNA was undertaken in 51 patients with ages ranging from 26-87 years, and lesion diameters of; 1.1-9.8cm (mean, 3.9 cm) [18]. EUS-FNA was employed to diagnose 22 neoplasms, 5

\*Corresponding author: Chunmeng Jiang, The Second Hospital of Dalian Medical University, NO.467, Zhongshan Road, 116027 Dalian, Liaoning, China, Tel: 86-17709870655, E-mail: liuxiangcmu@163.com

Zhiguo Wang, The Second Hospital of Dalian Medical University, China

cases of tuberculosis, and two duplication cysts. Cytology was inconclusive or did not yield a specific diagnosis in five other cases.

Manucha et al. (2011) on the other hand evaluated 281 EUS-FNA aspirates from 269 patients and satisfactory aspirates were available in 259 cases [19]. In addition a cytologic diagnosis of granulomatous lymphadenitis was rendered in 206 cases. Zeppa et al. (2010) carried out FNA on 57 mediastinal lymph nodes, 8 mediastinal and 2 subdiaphragmatic masses [20]. Analyses of diagnostic categories compared with clinical and histologic controls showed a sensitivity of 96%, specificity of 89%, positive predictive value of 98% and efficiency of 95%.

Mediastinoscopy have shown to provide good access to the upper and anterior mediastinum, and can be used to acquire a large number of histologic samples [21]. Mediastinoscopy and EUS-FNA target different areas of the mediastinum, and can be considered to be complementary methods for mediastinal lesions. At times, thoracoscopy or thoracotomy is necessary to be carried out, especially for suspected false-negative cases of EUS-FNA.

EBUS-TBNA appears to be a minimally invasive method for the upper and anterior mediastinum (assessment areas are similar to those used for mediastinoscopy). Therefore, a combined approach of EUS-FNA and EBUS-TBNA could be a possible replacement for more invasive methods for evaluation of unclear mediastinal or hilar masses as well as for suspected hilar or mediastinal metastases [22,23]. An example of this is in a study conducted by Oki et al. (2015) who compared the tolerance, efficacy, and safety of EBUS-TBNA with EUS-FNA with an endobronchial endoscope for the primary pathologic diagnosis of lesions [24]. They found that EBUS-TBNA and EUS-FNA provided high accuracy with good tolerance, though the risk of infectious complications had to be monitored carefully.

EUS-FNA had the advantage of comparable tolerance with fewer doses of anesthetics and sedatives, a shorter procedure time, and fewer oxygen desaturations during the procedure compared with EBUS-TBNA.

EUS-FNA and EBUS-TBNA are accurate, minimally invasive procedures but are relatively expensive [25]. Sensitivity values have been reported to be 80-90% for EUS-FNA and 90-100% for EBUS-TBNA [26,27].

### 3 Diagnosis of metastatic mediastinal lymph nodes by EUS

Benign mediastinal lymph nodes are commonly encountered during EUS. Often they have a triangular or crescent shape, and an echogenic center may be visualized (which represents the hilum of the lymph node) [28]. On EUS, four imaging features are used as criteria for identification of malignant lymph nodes: diameter >1 cm; round shape; sharp border; homogeneous hypoechoic pattern [29]. Detection of metastatic mediastinal lymph nodes can affect cancer staging and further management.

EUS-FNA has been demonstrated to be able to assess suspected metastatic mediastinal lymph nodes from the following primary cancers: pulmonary neoplasm, digestive-tract neoplasm, breast, kidney, testicle, cervix, larynx, nasopharyngeal carcinoma, melanomas, pancreaticobiliary cancer, renal cell cancer, and anthracosilicotic spindle-cell pseudotumor [28, 30-34]. In malignant lymph nodes without a history of cancer, the results of cytologic examination in combination with clinical features and other diagnostic modalities can suggest the origin of the primary tumor [5,33].

### 4 EUS in assessment of mediastinal lymph nodes for staging of lung cancer

Caution is warranted if the unresectability of lung cancer is based solely on tumor invasion into mediastinal soft tissue and blood vessels upon EUS; analysis combined with other diagnostic modalities is warranted [35].

Regional mediastinal lymph nodes represent the most common metastatic site in lung cancer [23]. Accurate assessment of mediastinal lymph nodes affects the staging of lung cancer, the corresponding treatment plan, and the prognosis. Various noninvasive and invasive methods are available for this purpose.

One such methods is the contrast-enhanced CT of the chest and upper abdomen. This is recommended as an initial step for all patients with a suspected or confirmed diagnosis of lung cancer suitable for treatment [36-39]. CT has been used to define the probability of malignant involvement of mediastinal lymph nodes. Despite being the most common modality for imaging the mediastinum, CT cannot be used to reliably differentiate benign from malignant lesions in this anatomic region [40].

MRI provides valuable diagnostic information for assessment of the mediastinum because it provides excellent detail on soft tissue. Positron emission tomography (PET) has higher accuracy than CT for evaluation of involvement of mediastinal lymph nodes due to lung cancer. Lymph nodes with higher uptake of fluorodeoxyglucose than that of surrounding normal mediastinal structures are considered to be positive, but false-positives are seen in active infection and inflammation, where there is increased glycolysis [41]. Sarcoidosis, anthracosis, infections, and reactive lymph nodes lead to nodes that are positive on PET [42]. Therefore, PET is not a definitive test. Lymph-node sampling improves staging accuracy beyond the ability of PET [42]. However, non-invasive tests can identify nodes suspected to harbor cancer, but they do not provide a definitive tissue diagnosis [43].

Various invasive staging methods are available [44]. EBUS-TBNA (minimally invasive) has better access to anterior and superior mediastinal lymph nodes (lymph-node stations 2, 3, 4, 5, 7, 10 and 11), which are traditionally approached by mediastinoscopy [45, 46]. EUS-FNA (minimally invasive) has better access to posterior and inferior lymph nodes (lymph-node stations 4L, 5, 7, 8 and 9) [45]. A combination of EUS-FNA and EBUS-TBNA should allow investigation of most of the mediastinum, thereby reducing the need for the surgical staging of lung cancer [47]. However, if non-involvement of mediastinal lymph nodes is confirmed, then mediastinoscopy appears to be best suited to most situations [44]. Thus, selection of appropriate methods is dependent upon several considerations [43,44].

## 5 Mediastinal lymphoma diagnosed by EUS

The diagnosis of mediastinal lymphadenopathy can be difficult, especially if primary lesions are absent. Lymphoma is one of the main causes of mediastinal lymphadenopathy. On EUS, enlarged lymph nodes present as homogeneous, hypoechoic masses, and sometimes with internal anechoic necrotic areas, these enlarged lymph nodes may fuse together into a “clumped” form. EUS-FNA is a safe and accurate diagnostic procedure for lesions surrounding the gastrointestinal tract [48-53].

Stacchini et al.(2012) studied 56 patients using flow cytometry (FC) after EUS-FNA [51]. EUS-FNA-FC gave a diagnosis of lymphoma in 11 cases and of reactive lymphadenopathy in 20. The remaining patients were diagnosed

later by cytology and cell block sections: 13 carcinomas, 9 granulomatous lymphadenopathies, and 1 mediastinal extramedullary hematopoiesis were documented. Similarly in a study by Ribeiro et al. (2001), 38 consecutive patients with gastrointestinal lesions and/or enlarged lymph nodes identified on imaging that raised a suspicion of lymphoma underwent EUS-FNA of the lymph nodes or gut wall [52]. Twenty-three patients with lymphoma and 15 patients with benign disease or reactive lymphadenopathy were identified. The overall sensitivity, specificity, and accuracy of EUS-FNA cytology with flow cytometry/immunocytochemistry for the diagnosis of lymphoma was 74%, 93%, and 81%, respectively.

However, the diagnosis of lymphoma using EUS-FNA remains a diagnostic challenge due to the amount of material sampled [53]. Yasuda et al. (2006) evaluated the yield of endoscopic ultrasound-fine-needle aspiration biopsy (EUS-FNAB) using a large-gauge needle in patients with idiopathic mediastinal lymphadenopathy in relation to lymphoma subclassification [53]. Overall accuracy of EUS-FNAB for idiopathic lymphadenopathy was 98%, and lymphomas could be classified in accordance with World Health Organization classifications in 88% of cases. No serious complications were documented using EUS-FNAB.

## 6 Sarcoidosis and tuberculosis diagnosed by EUS

Sarcoidosis is known to resolve spontaneously in >70% of patients. Tuberculosis could be treated by anti-tuberculosis therapy. A pathologic study is often crucial for the diagnosis and therapeutic decision-making. Tuberculosis poses a challenge to healthcare professionals in its diagnosis and management. Esophageal tuberculosis is a form of extrapulmonary tuberculosis, which is rare [54].

Sarcoidosis is a chronic multisystem granulomatous disease and a common cause of bi-hilar lymphadenopathy in the Western world [55-57]. Ultrasound frequently reveals a typical pattern of isoechoic or hypoechoic lymph nodes, sometimes with prominent vessels and sometimes with a central hyperechoic strand within these nodes [30, 55, 56]. However, these EUS characteristics are not distinctive of sarcoidosis, and cannot be used to distinguish these lesions from tuberculosis or malignancy [55].

Mediastinal lymph nodes are frequently involved in these diseases, so EUS-FNA and EBUS-TBNA can aid the diagnosis [30]. Such differential diagnoses was investigated by Puri et al. (2012), who studied 48 patients with

a diagnosis of esophageal tuberculosis, of whom 32 had complete data (including follow-up data) [58]. The ubiquitous feature of esophageal tuberculosis was dysphagia. In all cases, lymph nodes were adjacent to the esophageal disease. Endoscopic biopsy and FNA of lymph nodes was suggestive of tuberculosis in 27/32 (84.35%) of cases, of which fine-needle aspiration cytology provided the diagnosis in 23/32 (72%) of cases.

Besides tuberculosis and sarcoidosis, necrosis or caseation in lymph nodes can also be seen in histoplasmosis and coccidioidomycosis [28].

## 7 Conclusions

Using EUS, distinction between a posterior mediastinal mass and lymph node can be difficult and multiple enlarged lymph nodes can fuse together as a mass [28]. EUS-FNA is a sensitive, accurate, fast, safe, and minimally invasive method that facilitates imaging and histologic diagnosis for paraesophageal mediastinal/pulmonary lesions [59-70]. Other conditions that can be detected by EUS-FNA include reactive lymph nodes, mediastinal abscess/mediastinitis, mediastinal cysts, neurogenic tumors, and thyroid neoplasms that invade the mediastinum [28].

**Conflict of interest statement:** Authors state no conflict of interest

## Reference

- [1] Devereaux BM, Leblanc JK, Yousif E, Kesler K, Brooks J, Mathur P, et al. Clinical utility of EUS-guided fine-needle aspiration of mediastinal masses in the absence of known pulmonary malignancy. *Gastrointest Endosc.* 2002 Sep;56(3):397-401
- [2] Barawi M, Gress F. EUS-guided fine-needle aspiration in the mediastinum. *Gastrointest Endosc* 2000;52(6 Suppl):12S-17S
- [3] Fuccio L, Larghil A. Endoscopic ultrasound-guided fine needle aspiration: How to obtain a core biopsy? *Endoscopic Ultrasound* 2014;3:71-81
- [4] Fujii LL, Levy MJ. Basic techniques in endoscopic ultrasound-guided fine needle aspiration for solid lesions: Adverse events and avoiding them. *Endoscopic Ultrasound* 2014;3:35-45
- [5] Fritscher-Ravens A, Sriram PV, Bobrowski C, Pforte A, Topalidis T, Krause C, et al. Mediastinal lymphadenopathy in patients with or without previous malignancy: EUS-FNA-based differential cytodiagnosis in 153 patients. *Am J Gastroenterol.* 2000 Sep;95(9):2278-2284
- [6] Savides TJ. EUS for mediastinal disease. *Gastrointest Endosc* 2009;69(2 Suppl):S97-99
- [7] Hebert-Magee S. Basic technique for solid lesions: Cytology, core, or both? *Endoscopic Ultrasound* 2014;3:28-34
- [8] Eloubeidi MA. Endoscopic ultrasound-guided fine-needle aspiration in the staging and diagnosis of patients with lung cancer. *Semin Thorac Cardiovasc Surg* 2007;19:206-211
- [9] Savides TJ, Behling CM. EUS for unexplained mediastinal lesions. *Endoscopy* 2006;38(Suppl 1):S73-6
- [10] Yasuda I, Tsurumi H, Omar S, et al. Endoscopic ultrasound-guided fineneedle aspiration biopsy for lymphadenopathy of unknown origin. *Endoscopy* 2006;38:919-924
- [11] Herth FJ, Rabe KF, Gasparini S, Annema JT, et al. Transbronchial and transoesophageal (ultrasound-guided) needle aspirations for the analysis of mediastinal lesions. *Eur Respir J.* 2006; 28: 1264-1275
- [12] Lachter J. Basic technique in endoscopic ultrasound-guided fine needle aspiration for solid lesions: What needle is the best? *Endoscopic Ultrasound* 2014;3:46-53
- [13] Vilmann P, Larsen SS. Larsen. Endoscopic ultrasound-guided biopsy in the chest: little to lose, much to gain. *Eur Respir J* 2005; 25: 400-401
- [14] Panelli F, Erickson RA, Prasad VM. Evaluation of mediastinal masses by endoscopic ultrasound and endoscopic ultrasound-guided fine needle aspiration. *Am J Gastroenterol.* 2001 Feb;96(2):401-408
- [15] Arluk GM, Coyle WJ. EUS and fine-needle aspiration in the evaluation of mediastinal masses superior to the aortic arch. *Gastrointest Endosc.* 2001 Jun;53(7):793-797
- [16] Koh DM, Burke S, Davies N, Padley SP. Transthoracic US of the chest: clinical uses and applications. *Radiographics.* 2002 Jan-Feb;22(1):e1
- [17] Lee YT, Lai LH, Sung JJ, Ko FW, Hui DS. Endoscopic ultrasonography-guided fine-needle aspiration in the management of mediastinal diseases: local experience of a novel investigation. *Hong Kong Med J.* 2010 Apr;16(2):121-125
- [18] Ardengh JC, Bammann RH, Giovani Md, Venco F, Parada AA. Endoscopic ultrasound-guided biopsies for mediastinal lesions and lymph node diagnosis and staging. *Clinics (Sao Paulo).* 2011;66(9):1579-1583
- [19] Manucha V, Kaur G, Verma K. Endoscopic ultrasound-guided fine needle aspiration (EUS-FNA) of mediastinal lymph nodes: experience from region with high prevalence of tuberculosis. *Diagn Cytopathol.* 2013 Dec;41(12):1019-22. doi: 10.1002/dc.21698. Epub 2011 Apr 28
- [20] Zeppa P, Barra E, Napolitano V, Cozzolino I, Troncone G, Picardi M, De Renzo A, Mainenti PP, Vetrani A, Palombini L. Impact of endoscopic ultrasound-guided fine needle aspiration (EUS-FNA) in lymph nodal and mediastinal lesions: a multicenter experience. *Diagn Cytopathol.* 2011 Oct;39(10):723-9. doi: 10.1002/dc.21450. Epub 2010 Oct 19
- [21] Serna DL, Aryan HE, Chang KJ, Brenner M, Tran LM, Chen JC. An early comparison between endoscopic ultrasound-guided fine-needle aspiration and mediastinoscopy for diagnosis of mediastinal malignancy. *Am Surg.* 1998 Oct;64(10):1014-1018
- [22] Vilmann P, Krasnik M, Larsen SS, Jacobsen GK, Clementsen P. Transesophageal endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) and endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) biopsy: a combined approach in the evaluation of mediastinal lesions. *Endoscopy.* 2005 Sep;37(9):833-839

- [23] Herth FJ. Mediastinal staging--the role of endobronchial and endo-oesophageal sonographic guided needle aspiration. *Lung Cancer*. 2004 Aug;45 Suppl 2:S63-67
- [24] Oki M, Saka H, Ando M, Tsuboi R, Nakahata M, Oka S, Kogure Y, Kitagawa C. Transbronchial vs transesophageal needle aspiration using an ultrasound bronchoscope for the diagnosis of mediastinal lesions: a randomized study. *Chest*. 2015 May;147(5):1259-66. doi: 10.1378/chest.14-1283
- [25] Herth FJ. Endobronchial ultrasound: First choice for the mediastinum. *Endoscopic ultrasound*. 2013;2(4):179-180
- [26] Herth FJ, Lunn W, Eberhardt R, Becker HD, Ernst A. Transbronchial versus transesophageal ultrasound-guided aspiration of enlarged mediastinal lymph nodes. *Am J Respir Crit Care Med* 2005;171:1164-1167
- [27] Vilmann P, Krasnik M, Larsen SS, Jacobsen GK, Clementsen P. Transesophageal endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) and endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) biopsy: A combined approach in the evaluation of mediastinal lesions. *Endoscopy* 2005;37:833-839
- [28] Savides TJ, Behling CM. EUS for unexplained mediastinal lesions. *Endoscopy*. 2006 Jun;38 Suppl 1:S73-76
- [29] Catalano MF, Nayar R, Gress F, Scheiman J, Wassef W, Rosenblatt ML, et al. EUS-guided fine needle aspiration in mediastinal lymphadenopathy of unknown etiology. *Gastrointest Endosc*. 2002 Jun;55(7):863-869
- [30] Annema JT, Rabe KF. State of the art lecture: EUS and EBUS in pulmonary medicine. *Endoscopy*. 2006 Jun;38 Suppl 1:S118-122
- [31] Ishikawa M, Kitayama J, Kaizaki S, Sako A, Nakao K, Sugawara M, et al. Diagnosis of nasopharyngeal carcinoma metastatic to mediastinal lymph nodes by endoscopic ultrasonography-guided fine-needle aspiration biopsy. *Acta Otolaryngol*. 2005 Sep;125(9):1014-1017
- [32] Agarwal B, Gogia S, Eloubeidi MA, Correa AM, Ho L, Collins BT. Malignant mediastinal lymphadenopathy detected by staging EUS in patients with pancreaticobiliary cancer. *Gastrointest Endosc*. 2005 Jun;61(7):849-853
- [33] Fritscher-Ravens A, Sriram PV, Topalidis T, Jaeckle S, Thonke F, Soehendra N. Endoscopic ultrasonography-guided fine-needle cytodiagnosis of mediastinal metastases from renal cell cancer. *Endoscopy*. 2000 Jul;32(7):531-535
- [34] Varghese LR, Stanley MW, Wakely PE Jr, Lucido ML, Mallery S, Bardales RH. A case report of anthracosilicotic spindle-cell pseudotumor of mediastinal lymph node: cytologic diagnosis by endoscopic ultrasound-guided fine-needle aspiration. *Diagn Cytopathol*. 2005 Oct;33(4):268-272
- [35] Varadarajulu S, Schmulewitz N, Wildi SM, Roberts S, Ravenel J, Reed CE, et al. Accuracy of EUS in staging of T4 lung cancer. *Gastrointest Endosc*. 2004 Mar;59(3):345-348
- [36] Detterbeck FC, Lewis SZ, Diekemper R, Addrizzo-Harris D, Alberts WM. Executive summary: Diagnosis and management of lung cancer, 3rd ed: American College of Chest physicians evidence-based clinical practice guidelines. *Chest*. 2013; 143 ( 5\_suppl ):7S-37S
- [37] Sanchez de Cos J, Hernandez JH, Lopez MF, Sanchez SP, Gratacos AR, Porta RR; Sociedad Espanola Neumologia y Cirugia Toracica. SEPAR guidelines for lung cancer staging. *Arch Bronconeumol*. 2011; 47 ( 9 ): 454-465
- [38] Vansteenkiste J, De Ruysscher D, Eberhardt WE, et al; ESMO Guidelines Working Group. Early and locally advanced non-smallcell lung cancer (NSCLC): ESMO clinical practice guidelines for diagnosis, treatment and follow-up. *Ann Oncol*. 2013; 24 ( suppl 6 ): vi89-vi98
- [39] National Institute for Health and Care Excellence Clinical Guideline. 2011. Lung cancer: the diagnosis and treatment of lung cancer. National Institute for Health and Care Excellence website. [http:// egap.evidence.nhs.uk/lung-cancer-cg121](http://egap.evidence.nhs.uk/lung-cancer-cg121). Accessed September 23, 2014
- [40] Tomiyama N, Honda O, Tsubamoto M, Inoue A, Sumikawa H, Kuriyama K, Kusumoto M, Johkoh T, Nakamura H (2009) Anterior mediastinal tumors: diagnostic accuracy of CT and MRI. *Eur J Radiol* 69:280-288
- [41] Murgu SD. Diagnosing and staging lung cancer involving the mediastinum. *Chest*. 2015 May;147(5):1401-12. doi: 10.1378/chest.14-1355
- [42] Silvestri GA, Gonzalez AV, Jantz AV, 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 ( 5\_suppl ): e211S-e250S.
- [43] Toloza EM, Harpole L, Detterbeck F, McCrory DC. Invasive staging of non-small cell lung cancer: a review of the current evidence. *Chest*. 2003 Jan;123(1 Suppl):157S-166S
- [44] Detterbeck FC, DeCamp MM Jr, Kohman LJ, Silvestri GA; American College of Chest Physicians. Lung cancer. Invasive staging: the guidelines. *Chest*, 2003, 123(1 Suppl):167S-175S
- [45] Rintoul RC, Skwarski KM, Murchison JT, Wallace WA, Walker WS, Penman ID. Endobronchial and endoscopic ultrasound-guided real-time fine-needle aspiration for mediastinal staging. *Eur Respir J* 2005; 25: 416-421
- [46] Kim ES, Bosquée L. The importance of accurate lymph node staging in early and locally advanced non-small cell lung cancer: an update on available techniques. *J Thorac Oncol*. 2007 Jun;2 Suppl 2:S59-67
- [47] Colella S, Vilmann P, Konge L, et al. Endoscopic ultrasound in the diagnosis and staging of lung cancer. *Endoscopic Ultrasound* 2014;3:205-212
- [48] Yasuda I, Tsurumi H, Omar S, Iwashita T, Kojima Y, Yamada T, et al. Endoscopic ultrasound-guided fine-needle aspiration biopsy for lymphadenopathy of unknown origin. *Endoscopy*. 2006 Sep;38(9):919-924
- [49] Ribeiro A, Vazquez-Sequeiros E, Wiersema LM, Wang KK, Clain JE, Wiersema MJ. EUS-guided fine-needle aspiration combined with flow cytometry and in the diagnosis of lymphoma. *Gastrointest Endosc*. 2001 Apr;53(4):485-491
- [50] Zimmer T, Patan M, Berdel WE, Dulce MC, Riecken EO. Value of endoscopic ultrasound examination of the mediastinum in Hodgkin's and non-Hodgkin's lymphomas. *Ultraschall Med*. 1997 Apr;18(2):67-71
- [51] Stacchini A, Carucci P, Pacchioni D, Accinelli G, Demurtas A, Aliberti S, Bosco M, Bruno M, Balbo Mussetto A, Rizzetto M, Bussolati G, De Angelis C. Diagnosis of deep-seated lymphomas by endoscopic ultrasound-guided fine needle aspiration combined with flow cytometry. *Cytopathology*. 2012 Feb;23(1):50-6. doi: 10.1111/j.1365-2303.2010.00842.x. Epub 2011 Jan 10
- [52] Ribeiro A, Vazquez-Sequeiros E, Wiersema LM, Wang KK, Clain JE, Wiersema MJ. EUS-guided fine-needle aspiration combined with flow cytometry and immunocytochemistry in the diagnosis of lymphoma. *Gastrointest Endosc*. 2001 Apr;53(4):485-491

- [53] Yasuda I, Tsurumi H, Omar S, Iwashita T, Kojima Y, Yamada T, Sawada M, Takami T, Moriwaki H, Soehendra N. Endoscopic ultrasound-guided fine-needle aspiration biopsy for lymphadenopathy of unknown origin. *Endoscopy*. 2006 Sep;38(9):919-924
- [54] Rana SS, Bhasin DK, Rao C, Srinivasan R, Singh K. Tuberculosis presenting as dysphagia: Clinical, endoscopic, radiological and endosonographic features. *Endoscopic ultrasound*. 2013;2(2):92-95
- [55] Fritscher-Ravens A, Sriram PV, Topalidis T, Hauber HP, Meyer A, Soehendra N, et al. Diagnosing sarcoidosis using endosonography-guided fine-needle aspiration *Chest*. 2000 Oct;118(4):928-935
- [56] Mishra G, Sahai AV, Penman ID, Williams DB, Judson MA, Lewin DN, et al. Endoscopic ultrasonography with fine-needle aspiration: an accurate and simple diagnostic modality for sarcoidosis. *Endoscopy*. 1999 Jun;31(5):377-382
- [57] Ozgul MA, Cetinkaya E, Kirkil G, et al. Lymph node characteristics of sarcoidosis with endobronchial ultrasound. *Endoscopic Ultrasound* 2014;3:232-237
- [58] Puri R, Khaliq A, Kumar M, Sud R, Vasdev N. Esophageal tuberculosis: role of endoscopic ultrasound in diagnosis. *Dis Esophagus*. 2012 Feb;25(2):102-106
- [59] Larsen SS, Krasnik M, Vilmann P, Jacobsen GK, Pedersen JJ, Faurshou P, et al. Endoscopic ultrasound-guided biopsy of suspected malignancy in the mediastinum has a major impact on the clinical decision process. *Ugeskr Laeger*. 2002 Jun 17;164(25):3341-3346
- [60] Kramer H, van Putten JW, Douma WR, Smidt AA, van Dullemen HM, Groen HJ. Technical description of endoscopic ultrasonography with fine-needle aspiration for the staging of lung cancer. *Respir Med*. 2005 Feb;99(2):179-185
- [61] Fujii LL, Levy MJ. Basic techniques in endoscopic ultrasound-guided fine needle aspiration for solid lesions: Adverse events and avoiding them. *Endoscopic Ultrasound* 2014;3:35-45
- [62] Okasha HH, Mansour M, Attia KA, et al. Role of high resolution ultrasound/endosonography and elastography in predicting lymph node malignancy. *Endoscopic Ultrasound* 2014;3:58-62
- [63] Sahai AV. Endoscopic ultrasound-guided fine-needle aspiration studies: Fanning the flames. *Endoscopic Ultrasound* 2014;3:68-70
- [64] Sahai AV. Endoscopic ultrasound-guided fine-needle aspiration: Getting to the point. *Endoscopic Ultrasound* 2014;3:1-2
- [65] Wani S. Basic techniques in endoscopic ultrasound-guided fine-needle aspiration: Role of a stylet and suction. *Endoscopic Ultrasound* 2014;3:17-21
- [66] Araujo J, Bories E, Caillol F, Pesenti C, Guiramand J, Poizat FF et al. Distant lymph node metastases in gastroesophageal junction adenocarcinoma: Impact of endoscopic ultrasound-guided fine-needle aspiration. *Endoscopic ultrasound*. 2013;2(3):148-152
- [67] Costache MI, Iordache S, Karstensen JG, Saftoiu A, Vilmann P. Endoscopic ultrasound-guided fine needle aspiration: From the past to the future. *Endoscopic ultrasound*. 2013;2(2):77-85
- [68] Ioncica AM, Bektas M, Suzuki R, Saftoiu A, Artifon EL, Bhutani MS. Role of EUS-FNA in recurrent lung cancer: Maximum results with minimum (minimally invasive) effort. *Endoscopic ultrasound*. 2013;2(2):102-104
- [69] Schuhmann M, Eberhardt R, Herth FJ. Endobronchial ultrasound for peripheral lesions: A review. *Endoscopic ultrasound*. 2013;2(1):3-6
- [70] Sharma SS, Jhajharia A, Maharshi S, Ram S, Shankar V, Katiar P. Mediastinal paraganglioma: Specific endoscopic ultrasound features. *Endoscopic ultrasound*. 2013;2(2):105-106