

Usefulness of endosonography in pneumology

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Summary

The endosonography not only has applications in gastroenterology but in other areas as pneumology. The endosonography is useful to evaluate mediastinal areas like the aorto-pulmonary window, the subcarinal space and the para-aortic zone. With the ecobronchoscopy the para-tracheal spaces can be evaluated; therefore, with these two equipment the whole mediastinum can be evaluated and also a proper staging of the pulmonary cancer can be done, with no need of more invasive procedures as the mediastinoscopy.

Key words

Pulmonary cancer, endosonography, mediastinoscopy.

Mortality results from pulmonary cancer more often than any other cancer in the United States. Every year there are 170,000 cases and 154,000 deaths (1-4). Management strategies are based on histological type, either small cell carcinoma or large cell carcinoma, and on whether or not there has been a mediastinal invasion or the distance from the tumor. Determining the stage of the cancer, or staging, is fundamental not only for establishing a prognosis, but also for guiding therapeutic conduct. Staging requires multiple diagnostic tests for each patient, given that a study of a group of almost 3000 patients (5) showed that a correlation between clinical and pathological stage of the patient to be only 47%.

Usually the classification system of the American Joint Committee on Cancer (AJCC) is adopted for identification of stages. It can be summarized as follows: when the lesion does not invade the mediastinum it is classified as stage I or II which are candidates for surgical management. If the ipsilateral lymph nodes in the mediastinum have been compromised, the lesion is classified as stage IIIA, the management of which is induction therapy followed by surgical management. If the contra-lateral lymph nodes are compromised, or if there is a direct invasion of the medias-

tinum, it is classified as stage IIIB. Patients in this stage are referred for chemoradiotherapy. They have less than a 5% chance of surviving five years (7).

This classification shows the importance of detecting the number and location of the mediastinal adenopathies (Figure 1) associated with pulmonary cancer. One diagnostic method for staging is computed tomography (CAT scan or CT), but its utility for characterizing the size and location of adenopathies associated with a tumor have a sensitivity and specificity of only 70% (8). Positron emission tomography (PET) has an accuracy of 85% (9), but it has limitations. It gives a large number of false negatives for tumors with little metabolic activity and does not detect lymph nodes smaller than one cm. The performance of non-invasive methods coupled with the need for a pathological diagnosis have made the utilization of invasive methods necessary to insure appropriate staging before deciding upon the patient's treatment. Consequently, methods like bronchoscopy, cervical mediastinoscopy and previous mediastinoscopy have come into existence.

The bronchoscopy with transbronchial lung biopsy (TBBx) is very safe and well tolerated with a sensitivity of 60 to 70% (10), but it can only access lymph nodes loca-

ted in the subcarinal space or the hilum. It is incapable of reaching the aortopulmonary window or the posterior mediastinum.

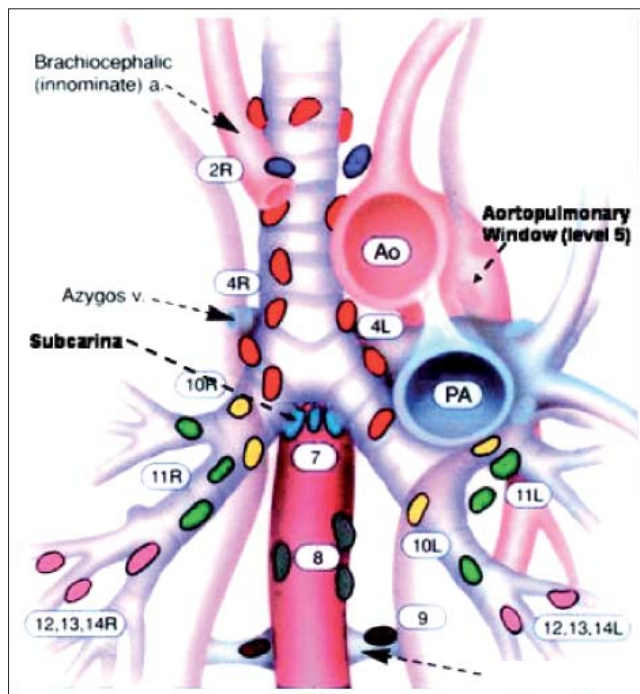


Figure 1. Places in which groups of lymphatic ganglia are found in searches for pulmonary cancer (Source: Reference 7).

Cervical mediastinoscopy is a surgical procedure that involves cutting a 2cm incision in the suprasternal notch, then dissecting this area. The mediastinoscope is advanced and used to perform the dissection of the pretracheal fascia to the carina which exposes all four paratracheal nodal stations (level 2R, 2L, 4R and 4L) and the subcarinal (level 7). These lymph nodes can be resected and studied thoroughly. The procedure requires general anesthesia and has risks of bleeding and laryngeal nerve damage (11).

Extended cervical mediastinoscopy is an extension of the previous procedure that allows biopsy of the aortopulmonary window (level 5) and the paraaortic region (level 6) (12). Thoracoscopy also allows evaluation of these stations (13).

Mediastinoscopy and thoracoscopy are very accurate diagnostic methods for staging but are expensive, invasive and require general anesthesia (14).

In staging pulmonary cancer endosonography acquires great importance since by placing a transducer in the mediastinum through the esophageal route we can assess groups of lymphatic ganglia that are not easily reached by other techniques. It permits us to evaluate potential compromise of the lymph nodes (Figure 2) in the subcarinal

space, the aortopulmonary window (station 5) and the posterior mediastinum (station 8). Endosonography not only identifies lymph nodes undetected by others techniques, but it can also be used to conduct a biopsy which can change the procedure of patient management (15).

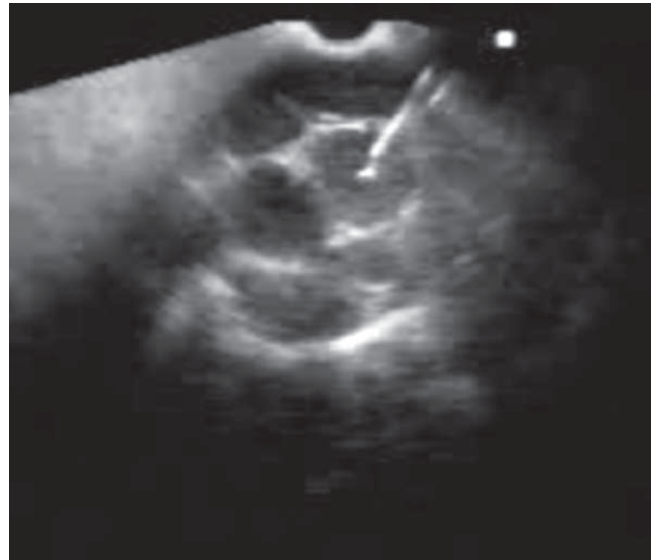


Figure 2. Patient with subcardinal adenopathies of unknown origin. On the right superior side of the picture the needle which was used to take the biopsy can be seen. This patient's pathology ruled out malignancy.

With a sensitivity of 90% and specificity of 100% for pulmonary cancer patients with adenopathies in the posterior mediastinum, the endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) is superior to a CAT scan for detecting malignancy (Figure 3) (16). In one of the biggest groups studied, EUS-FNA identified advanced mediastinal disease in 75 out of the 97 patients (77%) who had been previously identified as having pulmonary carcinoma and adenopathies by CAT scan. This avoided the need for other more invasive tests. Similarly EUS-FNA detected mediastinal invasion in 10 out of 24 patients without mediastinal adenopathy detected by CAT scans. This study reported a total sensitivity of 87% and a specificity of 100% for detecting mediastinal lymphatic nodes (17).

In a recent study (18) Wallace et. al. compared the diagnosis accuracy of the three methods: EUS-FNA, bronchoscopy with transbronchial biopsy (TBBx) and endobronchial ultrasound needle aspiration (EBUS-NA). The study sought to evaluate the sensitivity of the three methods used jointly or separately to detect metastasis to mediastinal lymphatic nodes in patients with pulmonary cancer. Pathological confirmation was used and patients were followed up at 6 or 12 months for comparisons. 138

patients met the inclusion criteria, 42 (30%) had malignant lymph nodes. The study showed that endobronchial US-guided fine needle aspiration, which detected 29 (69%) of the malignant lymph nodes, was more sensitive than TBBx, which detected 15 (36%) of the malignant lymph nodes ($p = 0.003$). The combination of EUS-FNA plus EBUS-NA had a higher sensitivity (93%) and a higher negative predictive value, NPV (97%), than either of the other methods used individually. This study suggests that EUS-FNA plus EBUS-NA can provide a complete assessment of the mediastinum in a minimally invasive way with very low morbidity and without the risks of mediastinoscopy.

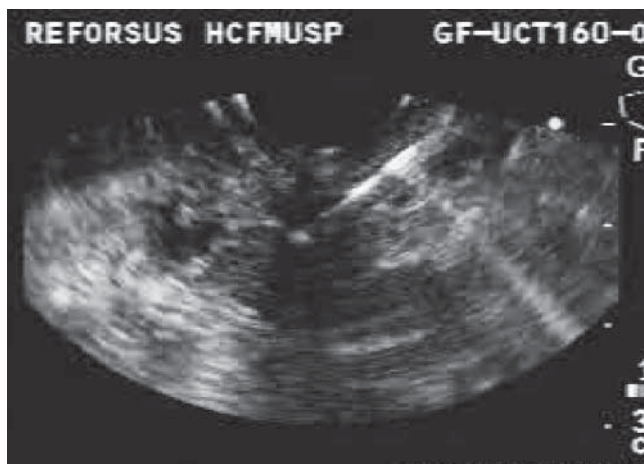


Figure 3. Patient with pulmonary cancer, we performed EUS-FNA of a subcarinal lymph node which tested positive for malignancy. Observe the lesion at the center of the image and the way the needle penetrates to the center to obtain the cell sample.

Mediastinoscopy is safe when handled by experts, but it has a 2% morbidity rate and a 0.08% mortality rate. It is also more expensive than EUS-FNA (19-21). Those who support mediastinoscopy do so based on its high NPV, particularly for patients with no mediastinal lymph nodes (19). In Wallace's study the NPV of the EUS-FNA plus EBUS-NA was 97% similar to the one reported for thoracoscopy with mediastinal dissection.

Few studies have made direct comparisons between mediastinoscopy and EUS-FNA. A study by Larsen et al. (22) compared these methods in patients with paratracheal or subcarinal lymph nodes. EUS-FNA was more precise than mediastinoscopy in subcarinal evaluation.

Multiple studies confirm that over the last 10 years endoscopic sonography has become a fundamental tool for staging lymph nodes in patients with pulmonary cancer. The EUS-FNA's PPV is over 99%, while its NPV is 81% (19). The reasons for false negatives seem to be lymph nodes inaccessible to the examination (23). Since endos-

copic sonography is performed through the esophagus, ecographic images can not penetrate the airways such as the front area of the trachea which is a blind spot for endoscopic sonography. Consequently, this exam is not the best choice for lymph nodes located at the back or for the subcarinal mediastinum.

EBUS-NA is performed with a fiber optic bronchoscope that penetrates through the trachea into the airway. This complements evaluation of the mediastinum since we can visualize the lymph nodes at the front mediastinum (24). Multiple studies suggest that the EBUS-NA is extremely precise for staging mediastinal lymph nodes (24-36). In patients with mediastinal lymph nodes the EBUS-NA has better precision than the TBBx (84% vs. 54%) (36).

It is important to clarify that, as is the case for many procedures, the utility of the EUS-FNA and the EBUS-NA varies widely among practitioners depending on each individual's experience, familiarity with mediastinal anatomy, the number of passes on each lymph node, the number of stations included, etc. All of these factors can be improved upon with training and an infrastructure that assures higher study quality. Another key factor which can improve results is close collaboration between pulmonologists, gastroenterologists, oncologists and chest surgeons.

MEDIASTINAL MASSES AND LESIONS

Endoscopic sonography allows us to determine if there are lesions or lymph nodes in the frontal mediastinum to the sides of the trachea or in the posterior mediastinum and to determine their relation to neighboring structures. It also shows their composition (solid, cyst, etc.) (37). All injuries located in these areas are accessible to the puncturing needle and samples can be obtained for histological diagnosis (Figures 4 and 5).

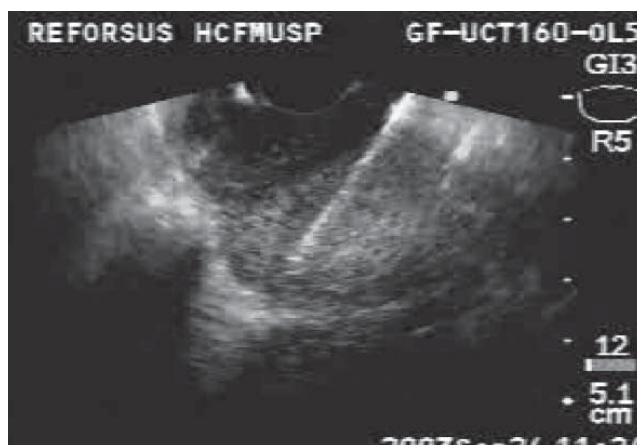


Figure 4. Patient with a frontal mediastinal mass. An EUS-FNA was performed and showed pulmonary cancer. The hyperechoic lineal image is the needle in the center of the lesion.

A recent study evaluated the utility of endoscopic sonography with fine needle aspiration in the evaluation of mediastinal masses (38). Of the 49 patients included endoscopic sonography diagnosed 22 cases (45%) with malignancies and 24 cases with benign masses. The diagnoses of 3 patients were inconclusive. The authors concluded that the endoscopic sonography is a minimally invasive technique that allows detection and biopsy of mediastinal masses with the advantage of being performed under sedation on a walk-in basis.

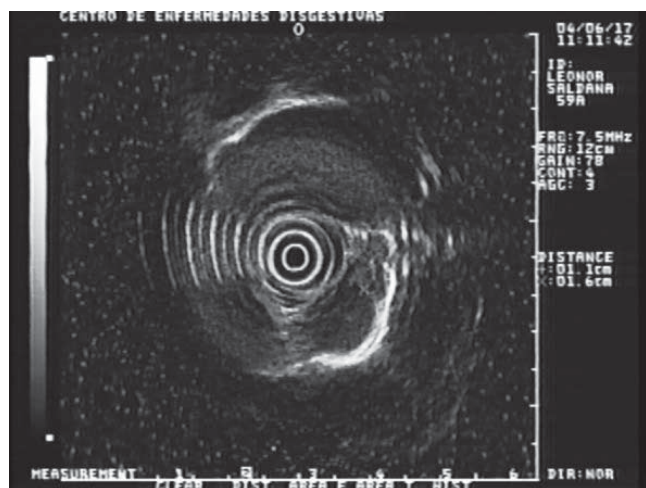


Figure 5. This radial endoscopic sonography shows metastasis in a female patient with breast cancer. The lesion is located between the left frontal auricula and the posterior descending aorta.

Multiple lesions, especially in the frontal mediastinum, can be diagnosed with endoscopic sonography. These include pulmonary cancer, extra-abdominal metastatic cancer, lymphomas, reactive lymph nodes, granulomatous diseases, sarcoidosis, histoplasmosis, tuberculosis, neurogenic tumor, and others. The precision rate of the EUS-FNA is approximately 97% (39).

DRAINAGE OF ABSCESSSES

Although until recently surgery was the traditional method for draining abscesses, practically any collection that is located around the gastrointestinal tract can be drained with the help of endoscopic sonography. There are reports of successful drainage of hepatic, mediastinal, pancreatic, perirectal and spleen abscesses. Images of abscesses can be clearly differentiated from normal structures. Various accessories can then be used to access and drain them. The process is complemented with antibiotics, thus avoiding surgical intervention in most cases. Mediastinitis and abscesses usually occur after chest surgery or esophageal perforation. Although patients generally have symptoms

of sepsis, a CT may or may not show a mediastinal collection. Fritscher –Ravens reported a series of 18 patients with mediastinitis on whom he performed EUS-FNA. The abscesses appeared as hypoechoic collections of 2-4cm that could be vacuumed, obtaining purulent material for study. No complications presented (40). Virginia's group (41) managed to obtain successful drainage of a mediastinal abscess followed by the placing of a stent. The Seedwald et. al. group (42) successfully drained subphrenic abscesses in two patients.

REFERENCES

1. Armengol JR, Benjamin S, Binmoeller K. Consensus Conference. Clinical applications of endoscopic ultrasonography in gastroenterology: state of the art 1993. *Endoscopy* 1993; 25: 358-66.
2. Rösch T, Classen M. Gastroenterologic endosonography. Textbook and Atlas. Thieme, Stuttgart, 1992.
3. American Society for Gastrointestinal Endoscopy. Role of endoscopic ultrasonography. *Gastrointest Endosc* 2007; 66: 425-35.
4. Jemal A, Thomas A, Murray T, Thun M. Cancer statistics, 2002. *CA Cancer J Clin* 2002; 52: 23-47.
5. López-Encuentra A, García Lujan. Comparison between clinical and pathologic staging in 2994 cases of lung cancer staging. *Ann Thorac Surg* 2005; 79: 974-9.
6. Mountain CF, Dresler CM. Regional lymph node classification for lung cancer staging. *Chest* 1997; 111: 1718-23.
7. McKenna RJ Jr, Libshitz HI, Mountain CE, McMurtrey MJ. Roentgenographic evaluation of mediastinal nodes for preoperative assessment in lung cancer. *Chest* 1985; 88: 206-10.
8. Bhutani MS, Hawes RH, Hoffman BJ. A comparison of the accuracy of echo features during endoscopic ultrasound (EUS) and EUS-guided fine-needle aspiration for diagnosis of malignant lymph node invasion. *Gastrointest Endosc* 1997; 45: 474-479.
9. Vansteenkiste JF, Mortelmans LA. FDG-PET in the locoregional lymph node staging of non-small cell lung cancer. A comprehensive review of the Leuven Lung Cancer Group experience. *Clin Pos Imaging* 1999; 2: 223-31.
10. Toloza EM, Harpole L, Detterbeck F, McCrory DC. Invasive staging of nonsmall cell lung cancer: a review of the current evidence. *Chest* 2003; 123(Suppl 1): 157S-66S.
11. Hammoud ZT, Anderson RC, Meyers BF. The current role of mediastinoscopy in the evaluation of thoracic disease. *Thorac Cardiovasc Surg* 1999; 118: 894-899.
12. Gdeedo A, Van Schil P, Corthouts B, et al. Prospective evaluation of computed tomography and mediastinoscopy in mediastinal lymph node. *Eur Respir J* 1997; 10: 1547-51.
13. De Leyn P, Schoonooghe P, Deneffe G. Surgery for non-small cell lung cancer with unsuspected metastasis to ipsilateral mediastinal or subcarinal nodes (N2 disease). *Eur J Cardiothorac Surg* 1996; 10: 649-654; discussion 654-655.
14. Harrow EM, Abi-Saleh W, Blum J, Harkin T, Gasparini S, Addrizzo-Harris DJ, et al. The utility of transbronchial nee-

- dle aspiration in the staging of bronchogenic carcinoma. *Am J Respir Crit Care Med* 2000; 161: 601-7.
15. Silvestri GA, Hoffman BJ, Bhutani MS, Hawes RH, Coppage L, Sanders-Cliette A. Endoscopic ultrasound with fine needle aspiration in the diagnosis and staging of lung cancer. *Ann Thorac Surg* 1996; 61: 1441-6.
 16. Aabakken L, Silvestri GA, Hawes R, Reed CE, Marsi V, Hoffman B. Cost-efficacy of endoscopic ultrasonography with fine-needle aspiration vs. mediastinotomy in patients with lung cancer and suspected mediastinal adenopathy. *Endoscopy* 1999; 31: 707-711.
 17. Gress FG, Savides TJ, Sandler A, Kesler K, Conces D, Cummings O, et al. Endoscopic ultrasonography, fine-needle aspiration biopsy guided by endoscopic ultrasonography, and computed tomography in the preoperative staging of nonsmall-cell lung cancer: a comparison study. *Ann Intern Med* 1997; 127: 604-12.
 18. Wallace M, Pascual J, Raimondo M. Minimally invasive endoscopic staging of suspected lung cancer. *JAMA* 2008; 299: 540-546.
 19. Detterbeck FC, Jantz MA, Wallace M, Vansteenkiste J, Silvestri GA. Invasive mediastinal staging of lung cancer: ACCP evidence-based clinical practice guidelines (2nd edition). *Chest* 2007; 132(suppl 3): 202S.
 20. Harewood GC, Wiersema MJ, Edell ES, Liebow M. Cost-minimization analysis of alternative diagnostic approaches in a modeled patient with non-small cell lung cancer and subcarinal lymphadenopathy. *Mayo Clin Proc* 2002; 77(2): 155-164.
 21. Aabakken L, Silvestri GA, Hawes R, Reed CE, Marsi V, Hoffman B. Cost-efficacy of endoscopic ultrasonography with fine-needle aspiration vs. mediastinotomy in patients with lung cancer and suspected mediastinal adenopathy. *Endoscopy* 1999; 31(9): 707-711.
 22. Larsen SS, Vilmann P, Krasnik M, et al. Endoscopic ultrasound guided biopsy versus mediastinoscopy for analysis of paratracheal and subcarinal lymph nodes in lung cancer staging [published online ahead of print December 13, 2005]. *Lung Cancer* 2005; 48(1): 85-92. doi:10.1016/j.lungcan.2004.10.002.
 23. Wallace MB, Ravenel J, Block MI. Endoscopic ultrasound in lung cancer patients with a normal mediastinum on computed tomography. *Ann Thorac Surg* 2004; 77(5): 1763-1768.
 24. 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(9): 833-839.
 25. Monse' E, Andreo F, Rosell A, Cuellar P, Castella E, Llatjos M. Usefulness of endobronchial ultrasonography with real-time needle aspiration for lung cancer staging [in Spanish]. *Med Clin (Barc)* 2007; 128 (13): 481-485.
 26. Yasufuku K, Nakajima T, Motoori K. Comparison of endobronchial ultrasound, positron emission tomography, and CT for lymph node staging of lung cancer. *Chest* 2006; 130(3): 710-718.
 27. Plat G, Pierard P, Haller A. Endobronchial ultrasound and positron emission tomography positive mediastinal lymph nodes. *Eur Respir J* 2006; 27(2): 276-281.
 28. Herth FJ, Rabe KF, Gasparini S, Annema JT. Transbronchial and transoesophageal (ultrasound-guided) needle aspirations for the analysis of mediastinal lesions. *Eur Respir J* 2006; 28(6): 1264-1275.
 29. Herth FJ, Ernst A, Eberhardt R, Vilmann P, Dienemann H, Krasnik M. Endobronchial ultrasound-guided transbronchial needle aspiration of lymph nodes in the radiologically normal mediastinum [published online ahead of print June 28, 2006]. *Eur Respir J* 2006; 28(5): 910-914.
 30. Herth FJ, Eberhardt R, Vilmann P, Krasnik M, Ernst A. Real-time endobronchial ultrasound guided transbronchial needle aspiration for sampling mediastinal lymph nodes [published online ahead of print May 31, 2006]. *Thorax* 2006; 61(9): 795-798.
 31. Yasufuku K, Chiyo M, Koh E. Endobronchial ultrasound guided transbronchial needle aspiration for staging of lung cancer [published online ahead of print September 19, 2005]. *Lung Cancer* 2005; 50(3): 347-54.
 32. 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(3): 416-421.
 33. Yasufuku K, Chiyo M, Sekine Y. Real-time endobronchial ultrasound-guided transbronchial needle aspiration of mediastinal and hilar lymph nodes. *Chest* 2004; 126(1): 122-128.
 34. Yasufuku K, Chhajed PN, Sekine Y. Endobronchial ultrasound using a new convex probe: a preliminary study on surgically resected specimens. *Oncol Rep* 2004; 11(2): 293-296.
 35. Rintoul RC, Skwarski KM, Murchison JT, Hill A, Walker WS, Penman ID. Endoscopic and endobronchial ultrasound real-time fine-needle aspiration for staging of the mediastinum in lung cancer. *Chest* 2004; 126(6): 2020-2022.
 36. Herth F, Becker HD, Ernst A. Conventional vs. endobronchial ultrasound-guided transbronchial needle aspiration: a randomized trial. *Chest* 2004; 125(1): 322-325.
 37. Binmoeller KF, Thul R, Rathod V. EUS-guided fine needle aspiration biopsy using a 18G needle. *Gastrointest Endosc* 1997; 45: AB168.
 38. Devereaux BM, Leblanc JK, Yousif E, Kesler K, Brooks J, Mathur P. Clinical utility of EUS-guided fine-needle aspiration of mediastinal masses in the absence of known pulmonary malignancy. *Gastrointest Endosc* 2002; 56: 397-401.
 39. Wierseman M I, Vasquez-Sequeiros. Evaluation of mediastinal lymphadenopathy with endoscopic US-guide fine needle aspiration. *Radiology* 2001; 219: 252-257.
 40. Fritscher-Ravens A. critical care transesophageal endosonography for diagnosis and management of posterior mediastinitis. *Crit Care Med* 2003; 31: 126-132.
 41. Kahaleh M, Yoshida C. EUS drainage of a mediastinal abscess. *Gastrointest Endosc* 2005; 60: 158-159.
 42. Seewald S, Brand B, Omar S, Yasuda I. EUS-guided drainage of subphrenic abscess. *Gastrointest Endosc* 2004; 59: 178-180.