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EDITORIAL

Linear endoscopic ultrasound: Current uses and future perspectives in mediastinal examination

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Abstract

This editorial elaborates on the current and future applications of linear endoscopic ultrasound (EUS), a substantial diagnostic and therapeutic modality for various anatomical regions. The scope of endosonographic assessment is broad and, among other factors, allows for the evaluation of the mediastinal anatomy and related pathologies, such as mediastinal lymphadenopathy and the staging of central malignant lung lesions. Moreover, EUS assessment has proven more accurate in detecting small lesions missed by standard imaging examinations, such as computed tomography or magnetic resonance imaging. We focus on its current uses in the mediastinum, including lung and esophageal cancer staging, as well as evaluating mediastinal lymphadenopathy and submucosal lesions. The editorial also explores future perspectives of EUS in mediastinal examination, including ultrasound-guided therapies, artificial intelligence integration, advancements in mediastinal modalities, and improved diagnostic approaches for various mediastinal lesions.

Key Words: Linear endoscopic ultrasound; Mediastinal examination; Lung cancer; Computed tomography; Magnetic resonance imaging

Core Tip: Endoscopic ultrasound (EUS) enables accurate assessment of cancer depth and nodal involvement in lung and esophageal cancer. Linear EUS enhances diagnostic accuracy and streamlines assessment through artificial intelligence. EUS also provides, in image form, the submucosal lesion in the mediastinum. These are some of the current uses of mediastinal examination. Future perspectives of mediastinal examination are; use of artificial intelligence algorithms in diagnosing accurately, using of ultrasound-guided therapy and imaging modalities which enhance diagnostic precision of EUS in mediastinal examination.

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INTRODUCTION

The mediastinum is an anatomic region located between the lungs and contains various vascular structures, organs, and lymph nodes (LNs). Evaluating the mediastinum is crucial, particularly for assessing primary and secondary lesions, including pathological LNs. Endosonographic evaluation of the mediastinum seems to be very challenging. Therefore, we explored the current uses and potential future advancements of linear endoscopic ultrasound (EUS) in the field of mediastinal examination. The aim of this editorial was to shed light on the importance of this diagnostic tool, elucidate its current applications, and discuss potential future directions for improved patient care[1].

EUS is a powerful tool used in lesion diagnosis. EUS focuses on gastrointestinal tissues in different sonographic layers that align with histological tissues, enabling this tool to provide information on cancer stages and characterize various gastrointestinal lesions[2]. Currently, systems in which urinary catheters are accustomed to withdrawable needles for suction can be transferred from the end to the end of endoscopes, leading to lesions through the gastrointestinal tract. EUS guides the suctioning of the needle, ultimately allowing microscopic anatomical diagnosis of both metastatic and primary lesions. This permits accurate metastatic, primary tumor, and regional lymph node staging, in addition to other modalities, leaving out surgical exploration[2]. The initiation of curved linear-array echo endoscopy permits the real-time ultrasound direction of needles to target lesions[3].

EUS imaging has been highly important in pulmonary medication for more than ten years. This method includes endobronchial EUS-guided (EBUS), transcutaneous ultrasound (TUS), and EUS. The staging of mediastinal LNs affects the handling of patients with lung cancer[4]. The sampling of tissues is frequently performed for accurate staging of nodes. The current international guidelines for stages of lung cancer distinctly state that EBUS and EUS are the preferred tissue sampling methods for testing surgical stages. Acquired tissues of mediastinal LNs are frequently crucial for detecting cancerous diseases[4]. Computed tomography (CT), which involves the use of a transthoracic needle for suctioning, can be used to detect cancerous diseases. Nevertheless, this technique may lead to complications, such as bleeding and pneumothorax for lung tumors that are centrally located. Furthermore, such tumors are mostly inaccessible *via* a transthoracic approach[4]. EBUS fine-needle aspiration (FNA) has been proposed for detecting and sampling cancerous diseases[5].

For an accurate mediastinal nodal appraisal inclusive of tissue sampling, diverse approaches are available, including: Surgical procedures (*e.g.*, video-assisted thoracoscopy and mediastinoscopy), radiological methods [*e.g.*, CT, magnetic resonance imaging (MRI)], fluoroscopy, nuclear medicine techniques [*e.g.*, positron emission tomography (PET)] and endoscopic techniques (*e.g.*, bronchoscopy). Ultrasound imaging, such as conventional TUS of the pleural effusions and the ventrolateral thoracic wall, is highly important[6]. Transcutaneous mediastinal ultrasound can detect normal pathological LNs in the deep mediastinal region; hence, specialized knowledge is needed due to its lack of widespread use[7].

Issues within the gastrointestinal tract are among the main reasons for the use of EUS. EUS is compatible with categorizing esophageal cancer arising from the mucosa and extending to deeper layers.

MRI has been shown to make outstanding improvements to clinical management, decrease surgical intervention rates and reduce patient demand for follow-up. This technology has dramatically expanded in diagnosing and treating patients regarding issues in the mediastinal cavity. This expansion can be attributed to the exact matches of thoracic protocols and technological improvements[8]. MRI is widely considered a functional solution, mainly in ambiguous cases on CT. Imaging of diffusion-weighted vibrancy reflects the diversity of water. One advantage of diffusion-weighted and chemical shift chemical MRI over traditional MRI includes providing quantitative data without requiring contrast agent administration, which is helpful in tissue characterization. Chemical shift imaging helps contrast normal thymus and rebound hyperplasia from cancer tissue at diagnosis and after chemotherapy in oncologic patients. It can also differentiate between lymphoid hyperplasia and thymoma in autoimmune diseases such as myasthenia gravis. This is because chemical shift imaging can detect microscopic fat in tissue. Diffusion-weighted magnetic resonance provides diverse water in particles within the bounds of tissue. This technique is widely used as a cancer biological marker in the breast, heart, and rib cage for its ability to distinguish from noncancerous tissue, and for regulating healing[8].

CURRENT USES OF MEDIASTINAL EXAMINATION

Esophageal and lung cancer staging

Linear EUS enables precise evaluation of tumor depth and nodal involvement in esophageal cancer, assisting in planning the best course of treatment and enhancing patient success. Esophageal cancer is a severe illness that has a significant effect on health care systems worldwide. In the US, 1%-2% of the population has esophageal cancer, and up to 15% of patients who undergo endoscopy for gastroesophageal reflux disease are at risk. Despite a decline in esophageal squamous cell carcinoma incidence, the incidence of esophageal cancer is increasing in the United States, with an average of 20.6% *per* year. For esophageal cancer, numerous staging techniques, such as EUS, PET, chest CT, and MRI, have been used. Differentiating between the esophageal mucosa layers is impossible with CT or MRI[8]. In the last several decades, EUS has become a vital diagnostic and staging technique for esophageal cancer. It can provide fine-grained images of the layers of the esophagus wall and assess the extent of tumor invasion and metastasis to nearby LNs. When cross-sectional imaging is employed, EUS can provide essential data for effectively staging esophageal cancers. Appropriate staging directs the best course of treatment and offers prognostic information[9].

Chest CT scans provide important details about tumor size, lymph node involvement, and possible metastatic lesions. However, the sensitivity of chest CT alone for detecting mediastinal lymph node involvement is only 48%. Studies differ in their estimates, but it has been demonstrated that MRI is helpful for preoperative evaluation and that it is just as accurate in staging esophageal cancer as CT. MRI staging has a 40% accuracy rate with very low sensitivity and specificity. In 25%-35% of cases, problems from thoracoscopic tissue biopsy operations are possible when there is mediastinal lymph node involvement. PET is a noninvasive alternative to CT or MRI that has been demonstrated to be useful in identifying stage IV metastatic illness. However, its capacity to identify locoregional metastases is limited[9].

The prognosis for non-small cell lung cancer (NSCLC) is poor, with a survival rate ranging from 73% in the first stage to 25% in the second stage. Accurate staging is essential for patients with NSCLC to be assigned to surgical treatment, which is only curative in less severe cases. When individuals who may have lung cancer are treated, several diagnostic techniques are employed. Examples of these include procedures that enable pathologic diagnosis, such as mediastinoscopy, video-assisted thoracic surgery, thoracotomy, bronchoscopy, transthoracic needle aspiration lung biopsy, endosonography (EBUS-trans-bronchial needle aspiration /fine needle biopsy (FNB)/EUS-FNA and EUS-FNB), thoracocenteses, and medical thoracoscopy. While PET and CT are the mainstays, US and MRI may also be important in some situations[10]. NSCLC customarily metastasizes first to mediastinal LNs and the space where vessels and nerves pass from the bronchus to the lungs. For the staging of NSCLC, local tumor extension, lymph node metastasis, and metastasis (tumor node metastasis) standardization have evolved[11].

Mediastinal lymphadenopathies

Lymphadenopathy is characterized by irregularity in the density and size of the LNs. CT is used to evaluate lymphadenopathy, and its findings in the lymphadenopathy thorax are similar to those of diffuse soft-tissue attenuation through the mediastinum. These findings include obliteration of the mediastinal fat, loss of the typical oval shape, coalescence of adjacent and enlarged nodes, focal contour abnormalities, invasion of surrounding mediastinal fat, and hypo- or hyper density in the LNs[12]. Lymphadenopathy is frequently caused by infections, as well as neoplastic and inflammatory conditions. As a result, several factors should be considered when evaluating nodal illness to differentiate benign from malignant nodes. An inflammatory benign lymph node is usually echogenic and elongated (short/long axis is < 1/2), with a preserved central hyperechoic hilum. Conversely, malignant nodes have erratic boundaries and are usually echo poor and rounder than elongated with a lost hyperechoic hilum[12]. In terms of differential diagnosis, mediastinal lymphadenopathy is associated with malignant lesions and is benign. In most cases, benign lymphadenopathy is due to silicosis, histoplasmosis, anthracosis, tuberculosis, sarcoidosis or viral infection. Lung and esophageal cancers, along with a few original extra thoracic sites, such as the breast, renal cell carcinoma proximal to the stomach, head, and neck, are frequently linked to metastases to the mediastinum[13].

Some patients will have a presumptive diagnosis established in the “suggestive” or “diagnostic” branches of the algorithm that is not supported by test findings or the clinical history. Others may have unexplained lymphadenopathy following the first clinical examination. Before undergoing a biopsy, individuals with an encouraging clinical picture and unexplained localized lymphadenopathy should be observed for three to four weeks[14]. Patients with widespread lymphadenopathy or localized lymphadenopathy with a concerning clinical picture may require further diagnostic testing, which frequently involves a biopsy. FNA is sometimes considered an alternative to excisional biopsy. However, because of the small amount of tissue retrieved and the inability to evaluate the gland architecture, FNA frequently produces a large proportion of nondiagnostic findings. In addition, depending on the underlying condition, there may be a chance of sinus tract development[14].

Submucosal lesions

Approximately half of all benign neoplasms in the stomach and duodenum are submucosal mesenchymal lesions. Two major categories can be used to further categorize mesenchymal tumors. The first category is referred to as gastrointestinal stromal tumors, which are more significant and more common than the second group. They are specific to the gastrointestinal system and include epithelioid or spindle cells. In the past, many tumors in this category were mistakenly called leiomyosarcomas or leiomyomas[15]. The cancers that arise in physiologic soft tissue, such as lipomas, leiomyomas, glomus tumors, neurogenic tumors, hemangiomas, lymphangiomas, and other tumors, belong to the second group of mesenchymal tumors. This type of tumor is composed of mesenchymal cells that have undergone proper differentiation[15]

When assessing submucosal lesions, endoscopic submucosal-mucosal excision yields a diagnostic outcome that is noticeably greater than that of jumbo examination forceps when the bite-on-bite procedure is employed. Submucosal tumors are a diverse collection of histopathological lesions located beneath the mucosal lining of the gastrointestinal tract. Since many of these cancers lack distinctive EUS characteristics, obtaining tissue samples and pathologic confirmation is typically necessary for a conclusive diagnosis[16].

FUTURE PERSPECTIVE OF MEDIASTINAL EXAMINATION

Artificial intelligence integration

Artificial intelligence (AI) is a prediction method that uses arithmetical algorithms to learn from input data automatically and identify trends. Deep learning and artificial neural networks are potent machine-learning-based techniques that offer high-yield predictions and are increasingly being employed in the medical industry to assist with diagnosis[17]. Machine learning (ML), a learning technique that uses large amounts of input data to identify the complex patterns or features within, and is one way to construct AI. Three forms of ML exist. The first is supervised learning, in which the software learns by making corrections for discrepancies between the program's output and the correct data that corresponds to the input data. The second is reinforced learning, which involves assessing and rewarding the program's production rather than providing it with explicit correct data, allowing the computer to learn *via* modifications. The third includes supervised *vs* unsupervised learning, which have primarily been used for diagnostic imaging. When the distribution and similarity of the input are used to assume stationarity, the algorithm learns without the correct data[18].

The field of AI, encompassing ML, employs computer algorithms to learn from data, identify patterns, and make predictions. The ability of AI and ML to analyze vast and complex data structures and to generate prognostic models that personalize and improve diagnosis, prediction, monitoring, and treatment management, is a key factor driving the enthusiasm for these technologies. ML and AI are frequently promoted as solutions to prognosis challenges involving enormous datasets, numerous predictors, and various data sources and types[19]. However, there are worries that AI in clinical care is overhyped and contains methodological flaws, low transparency, and poor repeatability if not employed under suitable supervision, knowledge, or skill. Among the methodological issues are the frequently mentioned includes an incorrect emphasis on classification over prognosis. Another consists of overfitting, which occurs when many predictors or characteristics are included for the sample size. AI has been criticized for its a lack of thorough evaluation of predictive accuracy when applied to data other than the original data. Additional methodological flaws include a lack of a fair and impartial comparison with more basic modeling techniques, and a lack of limpidity in the AI and ML algorithms, which restricts independent assessment[19].

EUS-guided therapies

Another future perspective of mediastinal examination is endoscopic US-guided therapies, where EUS may target therapy, such as fiducial marker placement for radiation. Image-guided radiation therapy enables the exact administration of radiation treatment to afflicted tissue *via* real-time imaging, improving tumor control while sparing adjacent tissue. Using several radiation treatment beams to safely and efficiently target a specific spot, stereotactic body radiotherapy allows the delivery of high-dose radiation to a targeted area while limiting radiation where unessential[20]. EUS-guided fiducial placement is a promising therapeutic method since deep insertion of fiducials percutaneously by interventional radiology may be restricted by intervening structures, and operative installation by surgery is invasive. Targeting deep structures is made possible by EUS-guided fiducial implantation, which also minimizes invasiveness and lowers the risk of adverse events. Furthermore, placement may be performed under direct observation, and doppler imaging during EUS reduces the chance of vascular penetration. Additionally, the placement of EUS-guided fiducials facilitates the execution of additional procedures within the same session[20].

As a successful substitute for conventional surgical procedures, image-guided ablation is increasingly used to treat a wide range of benign and malignant disorders. This practice is increasingly recommended worldwide. Compared with surgery, percutaneous ablation has the benefit of reducing patient morbidity and the length of hospital stay and enables the treatment of individuals who are not surgical candidates[21]. While surgical resection is still the preferred treatment for primary and secondary hepatic tumors, several local ablative therapeutic techniques have been established as adequate substitutes for resection or as supplements to oncological care. Over the last twenty years, radiofrequency ablation (RFA) has become more integral in managing localized primary and secondary liver tumors. The treatment of small, circumscribed liver lesions was the initial indication and clinical application of RFA. The indications of RFA have progressively expanded to include more complex diseases, and its use in conjunction with other techniques, such as microwave ablation and transarterial chemoembolization, has an important role in the management of such lesions[22]. By applying a fast alternating radiofrequency current to probes inserted into tissue, RFA causes coagulation necrosis, which results in cell death[23].

EUS-guided drainage of mediastinal collections or abscesses

The occurrence of esophageal perforation and intrathoracic anastomotic dehiscence poses a significant risk of morbidity and mortality, with reported rates ranging from 10% to 35%. When dealing with intrathoracic esophageal transmural disruptions and leakage, a conservative approach is generally effective[24]. However, the development of a mediastinal abscess can lead to increased morbidity, mortality, and prolonged hospitalization. Wehrmann *et al*[25] conducted a study at a single center and demonstrated the feasibility and safety of using EUS-guided drainage for paraesophageal and mediastinal abscesses. Similarly, in a case report, Fritscher-Ravens *et al*[13] successfully detailed the use of EUS-guided drainage for a mediastinal abscess following percutaneous dilatational tracheotomy. Furthermore, Kahaleh *et al*[26] demonstrated the safety of EUS-guided retrocarinal collection drainage at the gastroesophageal anastomosis site post-Ivory-Lewis esophagectomy for severe esophageal strictures unresponsive to traditional endoscopic therapies. Overall, EUS-guided drainage for mediastinal abscesses has emerged as a secure and viable alternative to surgical intervention.

Enhanced imaging modalities

Ongoing research on linear EUS probes and imaging techniques is expected to enhance image resolution and depth penetration. These advancements would further increase the diagnostic precision of linear EUS in mediastinal examinations. To distinguish between malignant and benign pulmonary and/or nodal lesions, metabolic imaging of the thorax *via* PET, fluorodeoxyglucose, or in conjunction with CT depends on physiological characteristics such as glucose metabolism[27]. Techniques such as intraoperative X-ray fluoroscopy are used as rapid, dependable, and user-friendly navigation tools that display the location of a surgical instrument in the patient concerning bone landmarks. For example, these methods are still applied in spine and transsphenoidal surgery. Because ultrasonography can provide real-time images, it may also be used for immediate localization and navigation. Other instruments are required for localization and navigation when using tomographic procedures such as CT and MRI, unless the process is carried out inside the scanner. These instruments include navigation systems or traditional frame-based and frameless stereotaxy techniques. All tomographic modalities enable the assessment of the amount of resection and the definition of the location of an implant or other device in three-dimensional space[28,29].

CONCLUSION

Linear EUS has led to significant breakthroughs in mediastinal examination, transforming how clinicians approach diagnosis and management. The current uses of linear EUS in staging cancers, evaluating lymphadenopathies, and diagnosing submucosal lesions highlight its clinical significance. In the future, the integration of EUS-guided therapies, AI, and enhanced imaging modalities holds excellent promise for further advancements in linear EUS. Adopting these advancements will allow clinicians to offer more precise diagnoses and tailor treatment regimens, thereby improving patient outcomes.

FOOTNOTES

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