

Endobronchial ultrasound: Echoing in the field of pediatrics

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ABSTRACT

Endobronchial ultrasound (EBUS) is a useful technique for the diagnosis and staging of the lung and mediastinal lesions, which is crucial for selecting treatment protocol. Under EBUS guidance, transbronchial needle aspiration (TBNA) is widely applied for obtaining specimens for histological, cytological, and molecular evaluation. Recently, the EBUS scope designed for adults has been used in large pediatric candidates. The presence of lung masses and mediastinal lymphadenopathy in the pediatric population presents a diagnostic challenge; however, EBUS is a promising tool for pediatricians to address these challenging issues. In some centers, the adult EBUS echobronchoscope is applied in transesophageal procedures for pediatric patients. EBUS-guided TBNA can also be used to perform minimally invasive interventional therapy, such as fiducial marker placement for assisting precision radiation, brachytherapy, and radiofrequency ablation therapy. With the development of EBUS equipment designed specifically for children, pediatric EBUS will play an increasingly important role.

Key words: Endobronchial ultrasound, endobronchial ultrasound-guided transbronchial needle aspiration, pediatric, transesophageal bronchoscopic ultrasound-guided fine-needle aspiration

INTRODUCTION

Endobronchial ultrasound (EBUS) is a technique used to diagnose diseases such as mediastinal lymph node staging of lung cancer and sarcoidosis.^[1] Under the guidance of EBUS, transbronchial needle aspiration (TBNA) is widely applied for obtaining tissue samples for pathology investigations, which is considered the gold standard for diagnosing lung and mediastinal lesions. This approach is

commonly used in adults. Due to the poor cooperation of children and the concerns of their parents, lymph node sampling is difficult. EBUS is a safe approach and demonstrates excellent sensitivity, specificity, and accuracy and has become a useful tool for pediatricians. This review describes the advances in pediatric EBUS in recent years and how to implement this technology correctly in future.

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THE HISTORY OF ENDOBRONCHIAL ULTRASOUND

The era of bronchoscopy began with Gustav Killian in 1876, who removed a pork bone from a farmer's airway by means of an esophagoscope.^[2] In 1989, groups in Germany began to research the application of micro-ultrasound probes in the airway for ultrasound detection. In the early 1990s, Ono *et al.* attempted to use a transbronchial ultrasonic probe with 7.5 Megahertz frequency to scan the airway.^[3] In 1990, the use of a radial probe with a balloon was first used to perform an intra-airway ultrasound examination.^[4] A convex-probe EBUS (CP-EBUS) was developed in 2004; this probe can be used to perform EBUS-guided TBNA (EBUS-TBNA).^[5] With the continuous improvement in technology and equipment, EBUS is now widely applied in adult clinical practice.

CLINICAL APPLICATION OF ENDOBRONCHIAL ULTRASOUND IN PEDIATRIC PATIENTS

Endobronchial ultrasound-guided transbronchial needle aspiration

Since the advent of EBUS-TBNA, it has expanded the scope of application of conventional bronchoscopes. However, few reports have mentioned its use in pediatric patients. Only four articles have described the use of EBUS-TBNA in pediatric patients, including a multicenter study and three case reports from the United States, India, and Australia. The multicenter study from the United States involved 21 patients.

In pediatric patients, EBUS-TBNA is mainly used to diagnose mediastinal lymphadenopathy. The multicenter study from the United States, 21 patients whose average age was 13.7 (± 4.1) years were used. All patients underwent EBUS-TBNA. Only eight (38%) patients underwent additional surgical procedures to obtain tissue for diagnosis. Thus, the use of this technology allowed 13 (62%) patients to avoid invasive surgical biopsy procedures. The authors concluded that EBUS-TBNA is feasible to use in pediatric patients.^[6]

Tuberculosis (TB) is a chronic infectious disease caused by *Mycobacterium tuberculosis*. Pediatric TB is an underappreciated global epidemic estimated to afflict around half a million children worldwide. Children are more susceptible to TB infection and

disease progression, including rapid dissemination into extrapulmonary infection sites.^[7] Diagnosis is mainly based on etiological examination. EBUS-TBNA is an effective means to obtain pathological tissue. Madan *et al.* reported a case in which diagnostic mediastinal lymph node sampling was successfully performed in 3-year-old children. These children had fever and dry cough for 3 months. Their general physical examination and examination of the respiratory system were unremarkable. Chest radiographs and computed tomography (CT) were suggestive of lymphoma. EBUS-TBNA was used to obtain tissue samples, and cytopathological examination was performed. This demonstrated granulomatous inflammation compatible with TB.^[8] Another study reported on two children who underwent EBUS-TBNA to obtain tissue samples and TB was diagnosed. One was a 9-year-old girl and the other one was a 10-year-old boy. Both of them had a fever, appetite, and had lost weight over a period of 2 months, and lymphoma was suspected firstly. EBUS-TBNA was used to obtain tissue samples, and the cytopathological examination confirmed TB.^[9] In the past, TB was difficult to diagnose in children, but with the development of pediatric EBUS, it will become easier to obtain an accurate diagnosis.

EBUS-TBNA can also be used in the diagnosis of sarcoidosis in children. Sarcoidosis is a multisystem granulomatous disorder with unknown etiology that rarely occurs in children and most frequently presents with bilateral hilar lymphadenopathy, pulmonary infiltration, and skin or ocular lesions.^[10] It often presents with characteristic clinical and radiological features, and thus, the clinical diagnosis is highly reliable. However, pathological confirmation demonstrating noncaseating epithelioid cell granulomas is essential to obtain a definitive diagnosis.^[11]

Wurzel *et al.*^[12] reported a previously well 13-year-old boy who was admitted to hospital with a 10-day history of progressive, ascending lower limb pain, weakness, and urinary hesitancy. A right-sided perihilar mass was incidentally identified on the spinal magnetic resonance imaging. A repeat chest X-ray obtained a month later showed no interval change in the size of the mass, which was presumed to be reactive lymphadenopathy. Three months later, the patient represented with a recurrence of leg pain, which was worse in the ankles and left knee. He also reported new paresthesia and hyperesthesia of the feet. He had weight loss of 4 kg. A contrast-enhanced CT study of

the thorax and abdomen was performed, which showed a lobulated mediastinal soft-tissue mass compatible with a conglomerate of lymph nodes in the right hilar, paratracheal, and subcarinal regions. Multiple subpleural nodules, measuring up to 7 mm in diameter, were also observed. Positron emission tomography (PET) using a fluorine-18 fluorodeoxyglucose tracer was, therefore, performed to identify metabolically active tissue sites. EBUS-TBNA was performed to obtain a histological diagnosis. A diagnosis of sarcoidosis was made based on multisystem involvement, the pattern of hilar and paratracheal lymphadenopathy on PET scan, the noncaseating granulomata seen on lymph node biopsy, and the absence of causal infective agents. They demonstrated the feasibility of EBUS-TBNA as a minimally invasive diagnostic tool for evaluating hilar lymphadenopathy in a child.

Other applications

In recent years, transesophageal bronchoscopic ultrasound-guided fine-needle aspiration (EUS-B-FNA) has garnered much attention. The esophagus is a hollow organ that lacks cartilaginous rings. Performing TBNA from the esophageal side is easier than performing EBUS-TBNA. EUS-B-FNA has been shown to be safe, and further diagnostic advances could be obtained by combining EUS-B-FNA with bronchoscopic procedures.^[13] The smaller size of the pediatric trachea limits the use of EBUS-TBNA. It has been considered that this difficulty can be circumvented by utilizing a transesophageal approach to the mediastinum (EUS-B-FNA) under moderate sedation, thereby expanding the benefits of using CP-EBUS in pediatric patients.^[8]

A multicenter study retrospectively analyzed 67 pediatric participants who underwent EBUS-TBNA or EUS-B-FNA. Except for two patients in whom no significant lymph node was detected on EBUS, an adequate sample was obtained in 60 (92.3%) participants, and a diagnostic sample was obtained in 37 (56.9%) participants. The sensitivity of EBUS-TBNA/EUS-B-FNA was 79.1%, and the diagnosis was changed in 28 (41.8%) participants. The authors of that study considered that EBUS-TBNA and EUS-B-FNA are safe and effective diagnostic methods for the evaluation of children with mediastinal lymphadenopathy.^[14]

However, EUS-B-FNA is also not without limitations. EUS-B-FNA can only access lymph node stations

4 L, 7, and 8, and there is a risk of esophageal perforation (0.02%) during intubation.^[15,16] Furthermore, the endoscopic visibility during EUS-B-FNA is limited due to the lack of air insufflation (which is required to ensure that the esophagus is splinted open) with the EBUS scope; hence, this procedure should be avoided in children with any structural abnormality of the esophagus.^[8]

In addition, a smaller caliber echobronchoscope can also be used in children. Sharma *et al.*^[17] performed a retrospective review to evaluate the indications, feasibility, safety, and impact of using the echobronchoscope for EUS (EB-EUS) in the pediatric patient population younger than 4 years. In their study of 10 children (six boys, four girls), aged from 2 months to 4 years, EB-EUS was performed by means of a linear echobronchoscope (EUB-1970 UK). All the procedures were completed successfully without any complication. The echoendoscope was successfully introduced into the stomach in all cases. The echobronchoscope was not advanced to the duodenum in four cases, including three cases with esophageal strictures and a 2-month-old child with a choledochal cyst. The average time for the procedure was 13.6 min. Their findings showed that EUS by echobronchoscopes is feasible and safe in young children.

PERFORMING PEDIATRIC ENDOBRONCHIAL ULTRASOUND

The first step of the procedure is anesthesia. The anesthesia used includes general anesthesia (GA), deep sedation, moderate sedation, and conscious sedation.^[18] To avoid a lack of cooperation or distress in children during EBUS, GA is usually used. Mittal *et al.*^[19] considered that it is important for anesthetists to monitor for hypoventilation during the procedure. End-tidal carbon dioxide (EtCO₂) monitoring is a useful tool in these cases. If EtCO₂ monitoring is unavailable, the removal of the EBUS bronchoscope between passes may help to prevent hypoventilation. Typically, during EBUS-TBNA performed under GA, an airway conduit is first placed, followed by EBUS bronchoscope insertion through the conduit. This may result in difficulty in airway access, as the epiglottis is longer, narrower, and posteriorly angled in children. It was proposed that EBUS bronchoscope-guided airway insertion (I-gel mounted over the EBUS bronchoscope) could solve this problem.

The next step is insertion through the oral cavity, in a similar manner as during bronchoscopy.^[20] The echobronchoscope was originally designed for adults. The lumens are essentially suitable for children over the age of 14 years, but it may not be possible to perform such examinations in younger children; for this reason, some doctors attempt EUS-B-FNA.

Kurimoto *et al.*^[21] devised a technique for endobronchial ultrasonography using a guide sheath (EBUS-GS) covering a miniature probe in 2004. This can also expand the range of applications of EBUS in pediatrics. EBUS-GS is a novel method used for collecting samples. In the EBUS-GS technique, a miniprobe covered with a guide sheath is introduced into the target bronchus through the working channel of the bronchoscope. The miniprobe with the guide sheath is gently moved backward or forward along the target bronchus until the lesion is detected. After an ultrasound image of the lesion is obtained, the miniprobe is withdrawn, leaving the guide sheath *in situ* as a working channel. Lesion samples can then be obtained through the guide sheath with a brush, biopsy forceps, or other devices.^[22] EBUS-GS can reduce the risk of bleeding and improve the safety of the operation and is worth using in pediatric EBUS.

ADVANTAGES AND DISADVANTAGES OF PEDIATRIC ENDOBRONCHIAL ULTRASOUND

Advantages

EBUS has widespread use in thoracic oncology and pulmonary medicine. EBUS-TBNA provides a higher diagnostic yield than conventional bronchoscopy in cases of lymphoma, lung cancer, sarcoidosis, and TB.^[23-29] It can reduce the number of punctures and improve the positivity rate. TBNA is performed under real-time monitoring of ultrasound images, which effectively avoids damage to the surrounding large blood vessels and improves the safety and accuracy. EBUS can clearly show the relationship between blood vessels, lymph nodes, and space-occupying lesions in the extranodal mediastinum. Children can easily inhale foreign objects, which cause asphyxia. EBUS provides an effective way for doctors to remove foreign bodies. This technology makes up for the lack of blur imaging of the tracheobronchial wall, tracheobronchial, and mediastinal structures by other methods.

Disadvantages

Although EBUS has many advantages, there are still some drawbacks. The specific structure of the bronchus in children poses some obstacles. The smaller size of pediatric trachea and their deeper position limit the use of EBUS. The incidence of device breakage is high and the cost for repair is high, etc.^[30,31] In addition, the use of EBUS is also contraindicated in patients with severely reduced lung function or respiratory failure, severely deteriorating cardiac function, massive hemoptysis, and general debilitating conditions. The diagnostic accuracy depends on many factors, such as the size of the needle, operator experience, and lymph node site. All of these factors can affect the results. Poor cooperation from the child and parental concern also influence the implementation of EBUS.

FUTURE OF PEDIATRIC ENDOBRONCHIAL ULTRASOUND

EBUS is frequently used in adults and is rarely reported in children. The presence of lung masses and mediastinal lymphadenopathy in the pediatric population requires pathological diagnosis. The conventional method for obtaining tissue is invasive surgery, such as mediastinoscopy. Using EBUS can markedly decrease the requirement for invasive surgical procedures. Contrast-enhanced EBUS and EBUS-elastography can be used to facilitate endosonographic staging by identifying the most suspicious lymph nodes and/or lymph node area of a particular mediastinal lymph node station for EBUS-TBNA.^[32,33] In addition to diagnosing diseases, EBUS-TBNA can also be used for treatment. This includes placement of fiducial markers for assisting precision radiation, radiofrequency ablation therapy, cryotherapy, brachytherapy, local drug therapy, photodynamic therapy, endotracheal stenting, balloon catheter dilatation, etc.^[34-36] These are widely used in adults and can be applied in pediatric EBUS in future.

Pediatric EBUS is a promising approach for examination of mediastinal diseases in children and should be performed by appropriately trained and experienced bronchoscopists. It is necessary to confirm the likely complications in pediatric EBUS and find solutions to them. This is necessary before EBUS can be widely applied in children. As EBUS is designed for adults, there is no clear statement about whether this technology can be used in pediatric patients. Due to the special nature of pediatric patients, a dedicated

echobronchoscope should be developed for use in children.

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Conflicts of interest

There are no conflicts of interest.

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