Indian Journal of Thoracic and Cardiovascular Surgery
https://doi.org/10.1007/s12055-024-01798-3

REVIEW ARTICLE

Cardiovascular and airway consideration in pediatric thoracic anterior mediastinal mass

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Received: 29 December 2023 / Revised: 3 July 2024 / Accepted: 4 July 2024

Abstract
Mediastinal tumors are common neoplasms among the pediatric population. The symptoms may be due to the direct compression effects on the surrounding structures or "B" like symptoms of specific lymphomas or due to paraneoplastic syndrome. The cardiovascular and respiratory consequences of the compression effects along with the unique physiological nature of the pediatric airway place the anesthesiologist in a difficult situation and face a new situation called "can intubate-cannot ventilate." This clinical scenario is not rare, with physicians commonly being confronted with similar situations in patients with severe bronchospasm. This entity has not been incorporated in any of the difficult airway algorithms. But the mediastinal tumors differ from bronchospasm because they cause physical external compression of the airway. This review will bring the readers the common anterior mediastinal tumors in pediatrics, the physiological differences in the pediatric airway in relation to the compression effects of the mediastinal tumors, and the management aspects of the different surgical aspects of the tumor.

Keywords Mediastinal tumors · Can intubate-cannot ventilate · Pediatric airway

Introduction

A child is not a miniature adult. There are distinct anatomical, physical, and physiological differences between adults and children which may add to the disease burden in children. Most common intrathoracic masses in children are anterior mediastinal masses. The mediastinal masses are classified based on the location or vascularity or type of lesion or density [1, 2]. The inherent problems with the pediatric population like the presence of the narrowest subglottic region, low functional residual capacity (FRC), and low pulmonary reserve along with the extrinsic compressive effects of the mass on the trachea creating a low blood flow state predisposing to tracheomalacia pose an additional challenge in this age group.

Anatomy and classification of mediastinum

The mediastinum is divided into compartments to facilitate the diagnosis (identification and characterization) and treatment of various mediastinal diseases. The old classical model, Shield's model, and Felson's classification based on lateral chest radiographs divide the mediastinum into three compartments, namely the anterior mediastinum, the middle mediastinum, and the posterior mediastinum [3, 4]. International Thymic Malignancy Interest Group (ITMIG) (Table 1) has proposed a new way to classify the mediastinum into three compartments, namely the perivascular compartment (anterior), the visceral compartment (middle), and the paravertebral (posterior) compartment, based on the multidetector computerized tomography (CT) [5].

Among the mediastinal compartments, the anterior mediastinal masses need special attention as they may cause cardiovascular and respiratory compromise due to variable compressive effects on the airway and vascular system both in the preoperative and in the intraoperative period based on the size, location, and weight of the mass (manifested in supine position). The anterior mediastinal mass might be found incidentally without any symptoms. In symptomatic

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Published online: 21 August 2024

Table 1 International Thymic Malignancy Interest Group (ITMIG) classification of perivascular tumors (anterior mediastinal mass)

Perivascular tumors	Lesions
Thymic	Thymic cyst Thymic hyperplasia Thymolipoma
Vascular	Lymphatic malformation Venous malformation Infantile hemangioma Kaposiform hemangioendothelioma (KHE)
Germ cell tumors (GCT)	Teratoma Seminoma Non-seminomatous GCT
Lymphoma	Hodgkin's lymphoma Non-Hodgkin's lymphoma

children, the presentation is usually varied depending on the mass effects on the surrounding structures.

Anatomical considerations of pediatric airway

The pediatric airway differs from that of adult in many aspects. The head is relatively large with large occiput when compared to the body size. This predisposes to airway obstruction when the child is in supine position on a flat surface, effectively tackled by placing shoulder roll to orient the airway axis inline to overcome the obstruction. Laryngoscopy is difficult due to shorter neck and larger occiput in children. The large tongue, large "U"-shaped epiglottis short mandible, enlarged adenoids, and tonsils all contribute to difficult laryngoscopy and airway obstruction. The hypopharynx is shorter and narrower and less elliptical on cross section, making placement of supraglottic airway difficult. The higher position of the larynx and the antero-inferior to postero-superior position of the vocal cords make the placement of endotracheal tube difficult and often traumatic. The larynx and trachea are flexible cartilaginous structures which can cause dynamic obstruction during spontaneous negative pressure ventilation and more so in partial airway obstruction as encountered due to airway compression in anterior mediastinal masses. The funnel shape of the pediatric airway makes the subglottic part narrowest and so smaller size of the endotracheal tube should be selected to prevent trauma and to prevent airway edema encountered during airway manipulations [6, 7].

Physiological considerations of pediatric airway

The higher respiratory rate in the pediatric population helps to tide over the greater oxygen consumption and larger carbon dioxide production along with less functional reserve capacity. The pediatric population are prone to rapid desaturation due to the lower FRC and the relative greater oxygen consumption of 6 ml/kg/min whereas the oxygen consumption in adults is 3 ml/kg/min. The carbon dioxide production in children is 100–150 ml/kg/min compared to 60 ml/kg/min in adults and the same is reflected in the end-tidal CO2 (EtCO2) in apneic conditions [6].

The air flow dynamics which is governed by Poiseuille's law has a significant implication in the pediatric airway. As the resistance to flow is directly related to fourth power of radius, any edema of airway or subglottic stenosis, external compression, or congenital abnormalities of the airway lead to exaggeration of obstructive effects in an already compromised airway.

Anterior mediastinal masses in pediatrics

The thymus-related masses are usually solid lesions which may be mistaken for anterior mediastinal masses on imaging. Thymoma and thymic carcinoma are rare causes of anterior mediastinal tumors in the pediatric population [8]. But the most common pediatric anterior mediastinal mass is lymphoma which can be either a Hodgkin's lymphoma or a non-Hodgkin's lymphoma [9].

The vascular neoplasms that can be present as pediatric anterior mediastinal mass are lymphatic malformations (lymphangioma or cystic hygroma), venous malformations, infantile hemangiomas (most common), and Kaposiform hemangioendothelioma (KHE). The KHE needs special mention as these are locally aggressive infiltrative tumors with metastasis limited to local lymph nodes. They usually present with thrombocytopenia due to the tumoral consumption of the platelets called the "Kassabach-Merritt phenomenon" because these tumors have architectural pattern which causes turbulent flow and activated the platelets [10].

Presentation

Most of the children are asymptomatic and found incidentally. And those who have the symptoms depend upon the compression of airway or vascular structures that are present adjacent to the tumor. The respiratory symptoms range from cough, stridor, orthopnoea, and wheeze and the cardiovascular symptoms range from syncope, upper body edema (superior vena cava syndrome), to cardiovascular instability. Governed by Poiseuille's law, severe distress does not occur until very late in the disease process. A significant paradoxical reduction of blood pressure due to the positional change signifies right ventricle outflow tract (RVOT) obstruction. A Pemberton' sign might be demonstrated when both the upper limbs are raised above the head in the upright posture causing facial plethora with prominent cutaneous veins which signifies the presence of compression on the superior vena cava (SVC) and hence SVC syndrome [11]. It has to

be differentiated with the jugular vein distension without plethora in cases of pericardial effusion which may co-exist. When the compression is on any of the main bronchi or if there is pulmonary artery compression, then a gross ventilation perfusion mismatch can be seen presenting as decompensated cardiorespiratory circulations leading to hypoxia with symptoms like fatigue, headache, shortness of breath, and cyanosis in severe compression.

The symptoms are graded based on the tolerability to lie down as shown in Table 2.

Investigations

The chest radiograph is usually the first investigation for the incidental finding followed by the ultrasound, CT, or a magnetic resonance imaging (MRI) in which the characterization of the tumor should be made along with the clinical features and supporting laboratory examination.

CT-assisted risk stratification

Mediastinal mass ratio (MMR)

Defined as the ratio of the maximal width of the mediastinal mass to the maximum thoracic width in centimeters. It is further divided into three groups MMR small ≤ 0.30, medium 0.31–0.43, and large ≥ 0.44. The patients having MMR ≥ 0.44 are associated with respiratory symptoms at presentation and hence prone to complications during perioperative period [12].

Tracheal cross section area

The largest tracheal diameter (dc) at the thoracic inlet is noted which is marked as control along with the narrowest tracheal diameter (dn). The cross section area (CSA) is calculated using the formula CSA = π $(d/2)^2$. Hence, the compression caused by mediastinal tumor is expressed as percentage. CSAc = π $(dc/2)^2$, CSAn = π $(dn/2)^2$, % CSA = CSAn/ CSAc × 100.

Table 2 Grading of symptoms

Grades	Posture
Asymptomatic	Can lie supine without symptoms
Mild	Can lie supine with minimal cough or pressure symptoms
Moderate	Can lie supine for short periods but not indefinitely
Severe	Cannot tolerate supine position

When the bronchus is affected, it is considered significant if the cross section area is > 50% compressed comparing its entire length or comparing with the opposite bronchus [13].

MRI without contrast is used to differentiate the soft tissue and to demarcate their margins. As the mediastinal masses are present around the heart, its movement causes artifacts in both CT and MRI. The electrocardiogram (ECG)-gated CT and MRI produce clear images with almost no artifacts. The dynamic MRI where there would be cinematic display of the cardiac motion in relation to the mediastinal mass gives an idea regarding the tumor invasion and cardiac involvement.

The two-dimensional echocardiogram gives additional information regarding the cardiac involvement complimentary to that of CT and MRI. The fludeoxyglucose-18 (FDG) positron emission tomography (PET) scan can help in diagnosis, staging, and prognosis.

Dynamic airway examination by fiber optic bronchoscope (FOB) gives information about the extrinsic compression on the airway and gives an estimate regarding the positional changes and respiratory decompensation during anesthesia and surgery [14]. Also awake FOB under sevoflurane can give an idea about the least affected bronchi and can be helpful in planning of subsequent rescue procedures as chest wall tone is preserved preventing dynamic airway compression.

The pulmonary and coronary angiogram can be done for both diagnostic and therapeutic purposes. The information such as vasculature of the mediastinal mass, collaterals in case of caval compression [15], and feeding vessels can be useful for surgical planning as well as embolization to reduce the tumor burden and bleeding which may occur intraoperatively.

Spirometry gives an idea about the extrinsic compression of the airway with mixed restrictive and obstructive pattern with a mid-expiratory plateau (widening) with blunting of the expiratory limb of the flow volume loop. Spirometry does not have good correlation with the degree of airway obstruction. The upright and the supine spirometry must be done to know the extent of compression of the airway in the supine position due to gravitational dependance (weight of the mass) [16]. Peak expiratory flow rate (PEFR) < 50% also signifies that the institution of general anesthesia is associated with significant complications [17].

Role of preoperative tumor reduction strategies

The possibility of tumor reduction depends on the histological diagnosis. Apart from tumor reduction, it also helps in reducing the tumor infiltration to the surrounding structures and to increase the surgical exposure. The neo-adjuvant chemotherapy is useful in cases of primary

non-seminomatous germ cell tumors whereas neo-adjuvant chemotherapy and radiotherapy help to reduce the tumor burden of thymoma before surgery [18].

The use of preoperative steroid is surrounded by controversy. Steroids are advocated to reduce the airway edema and for reducing the edema in and around the tumor [19, 20]. Even though steroid reduces the edema and helps during tumor resection, it may affect the histological diagnosis, thereby leading to confusion in diagnosis. Hence, the biopsy is usually delayed up to 48 h of completion of the neo-adjuvant therapy with steroids [21]. The preoperative use of dexamethasone might trigger tumor lysis syndrome which may lead to renal failure especially in pediatric patients. Proper hydration may reduce the onset of tumor lysis syndrome [22].

Getting a histological diagnosis itself is difficult and challenging in anterior mediastinal tumors especially in children. Children will not cooperate under local anesthesia. Hence, even for biopsy, general anesthesia needs to be given with proper risk stratification.

Perioperative risk stratification and management (Figs. 1 and 2)

The normal effects of general anesthesia on respiration add to the compressive effects of the mediastinal mass. The FRC decreases as the diaphragm moves up, equilibrium between the chest wall expansion and the elastic recoil usually favors small lung volumes and there would be closure of the airways of the dependent lungs. Preoperative consideration of endobronchial balloon dilatation with stenting and caval stenting should be contemplated which are difficult in children.

The patients with anterior mediastinal mass may undergo different types of surgical approaches such as cervical mediastinoscopy, medial sternotomy, anterior mediastinoscopy, thoracotomy, thoracoscopy, cervical mediastinal exploration, and extra-thoracic lymph node biopsy.

The risk stratification of these patients is made depending on the presence of signs and symptoms and fulfilment of the diagnostic criteria. The categories that were considered previously were safe (both signs and investigative findings absent), unsafe (both are present), and uncertain (signs are present and the diagnostics are inconclusive). But this might no longer be valid as the uncertain category places the patient in a more risk zone, and hence, the uncertain category is considered equivalent to "unsafe" category (Table 3).

In case of large mediastinal mass or mediastinal mass causing SVC syndrome, there will be obstruction to the venous return from the upper limb; the choice of placement of the intravenous access must be to the lower limb with wide bore canula to ensure adequate hydration.

Regional anesthesia with spontaneous ventilation in the most comfortable position is ideal for diagnostic procedures but not always possible in pediatric patients. The fear of detachment from the parents, fear of new surroundings, and anxiety issues push the anesthesiologist to give general anesthesia in the pediatric population [23]. Avoidance of muscle relaxants would be ideal to preserve the

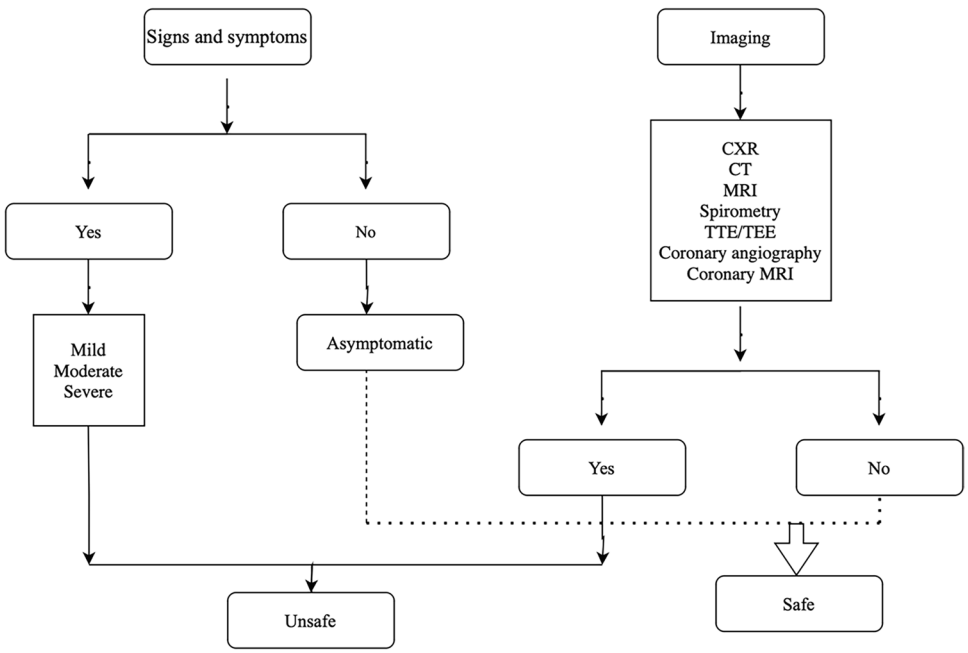

Fig. 1 Perioperative risk stratification

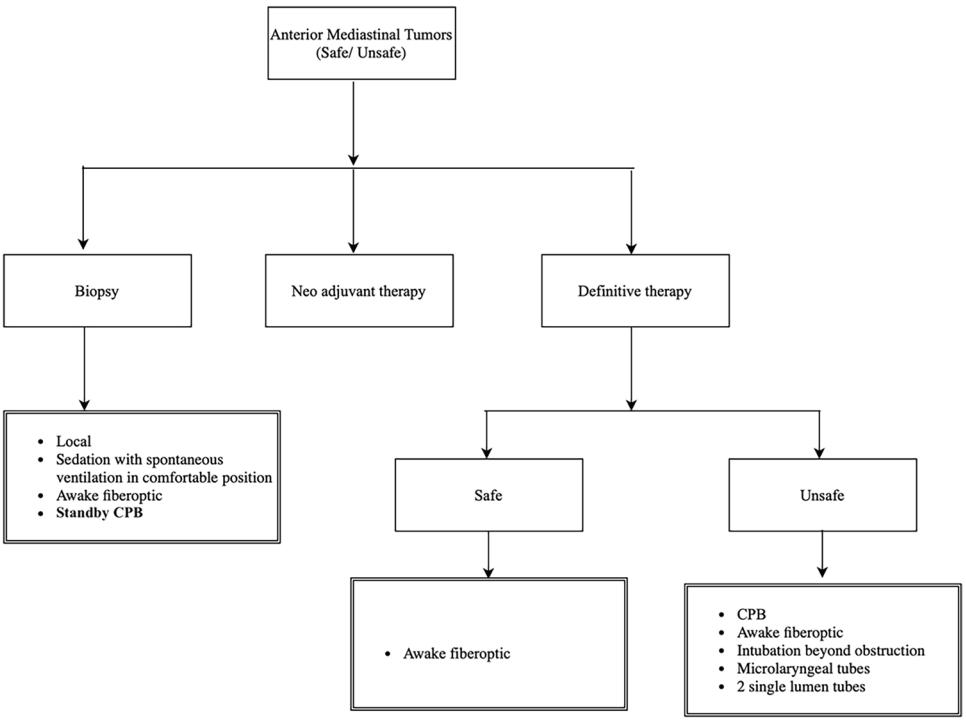

Fig. 2 Anterior mediastinal mass - airway management

Table 3 Risk stratification

Signs and symptoms	Investigations	Previous categories	Inference	Latest categories
No	No	Safe	Ventilation might be possible	Safe
Yes	Yes	Unsafe	Ventilation might not be possible	Unsafe
Yes	Uncertain	Uncertain	Consider as "unsafe"	

tone of the chest muscles, thereby preventing or decreasing the risk of airway and vascular compression. Therefore, inhalational sevoflurane with spontaneous ventilation would be an ideal choice. The use of inhalational agents is not without complications. The negative pressure created in spontaneous breathings may exaggerate the partial obstruction created by the mediastinal mass. It will be potentially dangerous and difficult to abort the semi-obstructed inhalation induction. A non-invasive continuous positive airway pressure (CPAP) can be considered to facilitate the pneumatic splinting of the compressed airway [24].

As the mediastinal mass is still in situ, the patient should be completely conscious without any residual sedation in the post operative period. Ultrasound-guided biopsy, CT-guided biopsy, and anterior mediastinoscopy under local anesthesia are other attractive alternatives.

Biopsy of anterior mediastinal mass comes with the challenge of keeping the mass in situ with concomitant loss of chest wall tone and regional edema surrounding the mass. So ideally resection biopsy should be done.

Perioperative considerations during surgery

The principle behind the successful perioperative management of anterior mediastinal mass is "noli pontes ignii consumere," i.e., "don't burn your bridges" [25].

The preferred intubation technique is awake fiberoptic intubation under local anesthesia which may not be possible in pediatrics. The use of long-acting muscle relaxants is contraindicated in mediastinal mass for intubation as they lead to loss of mechanisms of spontaneous ventilation and chest wall tone. Once the airway is secured, usage of long-acting non-depolarizing muscle relaxants is advised. Nitrous oxide when used for prolonged period can impair methionine synthase disturbs folate and vitamin B12 metabolism which ultimately leads to bone marrow suppression [26]. The preferred choices of gases for surgical procedures are air, oxygen, and inhalation agents like sevoflurane or desflurane.

The choice of endotracheal tube depends on the site of compression and type of surgery. Reinforced single long endo tracheal tube and micro laryngeal tubes can ensure airway patency acting like airway stents going beyond the

point of compression to ensure adequate ventilation in the presence of the mediastinal mass [27]. The current airway algorithms are silent regarding management of airway obstruction that occurs distally as they are predominantly based on laryngoscopic visualization. So, these come under a hypothetical category called "can intubate-cannot ventilate" [28]. Similar conditions prevail in situations such as severe bronchial asthma, blockade of the endotracheal tube due to distorted anatomy, herniation of the cuff over the tip of the tube, tracheal collapse due to invasive thyroid carcinoma, and spontaneous pneumothorax causing tension pneumothorax.

The double lumen tubes (DLT) are the choice in adults in cases of thoracotomy; their use is restricted to the age above 8 years of age. The smallest double lumen tube size available is 26 F. For inserting DLT, any 2 of the following three criteria should be met: (1) age — 8 years, weight — 30 kg, and a height of about 130 cm [29]. While using single lumen endotracheal tube care should be taken to intubate beyond the compression site by proper planning based on the imaging and using FOB. If one cannot negotiate further, either awakening the patient can be done or with the help of otolaryngologist a rigid bronchoscope can be placed. The use of heliox mixture, racemic epinephrine, and jet ventilation can buy some time before definitive management can be done [30, 31]. If any airway and hemodynamic compromise arises, the cardio thoracic surgeons should be on standby to do emergency sternotomy and lifting the mediastinal mass with silk sutures to relieve the compression of the airway and the great vessels [17].

The use of two single-lumen tubes is also documented in a resource-limited setting or where double-lumen tubes cannot be placed. One endotracheal tube is placed endobronchially and other tube is placed with in the trachea using the fiberoptic bronchoscope or traditional auscultatory methods [32]. But if the obstruction is beyond the trachea lower down, the possibility of inserting two reinforced single-lumen tubes is restricted in the pediatric population due to the smaller size of the airway [33]. In such condition, role of preoperative placement of endobronchial self expanding metallic stents under conscious sedation using fiberoptic bronchoscope is an option [34].

Role of extracorporeal circulation

It has been largely debated regarding institution of extracorporeal circulation, i.e., cardiopulmonary bypass in the event of severe airway and hemodynamic compromise. Even though the cardiopulmonary bypass (CPB) circuit is primed and kept ready, it will take a minimum of 15 min to get access to the canulation and establish proper oxygenation. If definitive airway and hemodynamic compromise is anticipated, proper planning with a team of anesthesiologists, cardiovascular surgeons, and perfusionists should be ready with primed CPB circuit and correct canulation sizes; vascular access can be achieved under local anesthesia with lignocaine and bupivacaine or under sedation with spontaneous ventilation using injection midazolam, fentanyl, propofol, dexmedetomidine, and inhalational agents like sevoflurane and finally general anesthesia [35].

The institution of extracorporeal membrane oxygenator (ECMO) is also being considered in patients anticipated to be developing airway and cardiovascular compromise [36].

Post operative care after surgical removal of the mediastinal mass

If the tracheal compression is > 50%, then there is higher prediction for postoperative complications. This is much more in the case of diagnostic procedures as the main pathology is still not removed which still causes the compression. The CPAP may be considered after diagnostic procedures. Some of the cases might be unresectable which holds grave prognosis and early death in the postoperative period [17].

Conclusion

Anterior mediastinal tumor is common in the pediatric population. As the airway and the cardiovascular system lie close to the tumor, the anesthesiologist will be facing a unique challenge "can intubate but cannot ventilate." Risk stratification of the tumor is based on signs and symptoms along with the positive and negative investigation. Once the patients are categorized as "safe" and "unsafe," the airway management depends on the type of planned procedure. The patient will accustom to a certain posture where the compressive signs and symptoms are minimal and is called "position of maximum airway patency" or "decubitus of choice." This information will be noted from the detailed history of the patient for the rescue of the airway in case of inadvertent compressive symptoms of the airway or the great vessels which may arise during the process of inducing the child for anesthesia or in the immediate post operative period which is the "the position of airway rescue." Different airway management strategies such as awake fiberoptic intubation, intubation beyond obstruction, and use of two-single lumen tubes can be used. Even though the use of CPB either in emergency or on elective basis is controversial, it is the final option if all the other methods fail. With proper coordination between the anesthesiologist team and the surgical team, the outcome of anterior mediastinal tumor is usually good. Further, the difficult airway societies should consider the

entity of "can intubate but cannot ventilate" and formulate guidelines accordingly.

Abbreviations FRC: Functional residual capacity; RVOT: Right ventricle outflow tract; CT: Computerized tomography; MRI: Magnetic resonance imaging; PEFR: Peak expiratory flow rate; ITMIG: International Thymic Malignancy Interest Group; GCT: Germ cell tumors; KHE: Kaposiform hemangioendothelioma; GLUT: Glucose transporter; SVC: Superior vena cava; MMR: Mediastinal mass ratio; CPAP: Continuous positive airway pressure; FDG: Flu deoxy glucose-18 (FDG); PET: Positron emission tomography; FOB: Fiber optic bronchoscope; DLT: Double-lumen tube

Author contribution Dr. Pavan Kumar Dammalapati has solely contributed to this review article.

Funding None.

Data availability Not applicable.

Code availability Not applicable.

Declarations

Ethics approval Not applicable.

Consent to participate Not applicable.

Consent for publication Not applicable.

Competing interests No.

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