Minimal access surgery in children: Implementation of an innovating technique

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IPEG guideline for the surgical treatment of mediastinal masses in children

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Submitted
Abstract

Background
The role of the use of minimally invasive surgical (MIS) techniques is unclearly defined and evidence supporting this approach is limited.

Aim
To discuss the presentation, work-up, timing and surgical management of these masses in children, focusing on the following subjects:
1. Which masses are best approached with MIS to obtain tissue for diagnosis?
2. Which benign masses can be approached by thoracoscopic resection?
3. Which malignant masses can be approached by thoracoscopic resection?

Methods
To obtain data the search-strategy consisted of PubMed (Medline) and Embase search using keywords (MESH terms):
1. ((mediastinal mass) OR mediastinal tumor) AND pediatric AND diagnosis
2. ((mediastinal mass) OR mediastinal tumor) AND pediatric AND (benign AND thoracoscopy) and
3. ((mediastinal mass) OR mediastinal tumor) AND pediatric AND (malign AND thoracoscopy)

Results
1. Which masses are best approached with MIS to obtain tissue for diagnosis?
   There is level III evidence showing that MIS is safely applicable in the anterior, middle and posterior mediastinal compartment
2. Which benign masses can be approached for resection thoracoscopically?
   Compared with thoracotomy there is some level II evidence that MIS results in shortening of CTD and LOS.
3. Which malignant masses can be approached for resection thoracoscopically?
   There is level II evidence that in neurogenic tumors the non-dumb bell type can safely be operated in experienced hands by MIS. There is level II evidence that MIS compared with thoracotomy has a decreased CTD, LOS and decreased blood loss.

Conclusion
Minimal invasive diagnostic procedures concerning mediastinal lesions are safe and effective in any anatomical place. (Level III, Grade C recommendation).
Benign lesions can be resected by MIS safely. With MIS there is a decrease in length of stay, chest tube duration, blood loss and it is cosmetically superior over thoracotomy. (Level II, Grade C recommendation).
Thoracoscopic approach in malignant procedures is only recommended in neurogenic tumours. (Level II, Grade C recommendation).
IPEG guidelines for the surgical treatment of mediastinal masses in children

Preamble

Mediastinal masses are relatively rare but heterogenic in the paediatric population, with an extremely variable natural history. Most of them are malignant up to 61% \(^1\). Whether benign or malignant they require, mostly surgical, intervention for diagnosis or for definitive treatment.

The purpose of this document is to discuss the presentation, work-up, timing and surgical management of these masses in children, focusing on the following subjects.

1. Which masses are best approached with MIS to obtain tissue for diagnosis?
2. Which benign masses can be approached by thoracoscopic resection?
3. Which malignant masses can be approached by thoracoscopic resection?

Only in English published data from the last 15 years were collected.

The current recommendations are graded and linked to the evidence utilizing the definitions in Appendices 1 and 2.

Definition

Mediastinal masses can have their internal characteristics as they can be cystic, solid or mixed and can be benign or malignant. Knowledge of the anatomy helps in understanding the location and behaviour of these mediastinal masses. The boundaries of the...
mediastinum are the thoracic inlet, the diaphragm, the vertebral bodies and the sternum and are surrounded by the pleural sacs. Dividing the mediastinum in anterior, middle and posterior may help the understanding of mediastinal masses.

Disclaimer

Clinical practice guidelines are intended to indicate the best available approach to medical conditions as established by systematic review of available data and expert opinion. The approach suggested may not necessarily be the only acceptable approach given the complexity of the health care environment. These guidelines are intended to be flexible, as the physician must always choose the approach best suited to the individual patient and variables in existence at the moment of decision. These guidelines are applicable to all physicians who are appropriately credentialed and address the clinical situation in question, regardless of specialty. Guidelines are developed under the auspices of the International Pediatric Endosurgery Group Surgeons and its various committees, and approved by the Executive Committee. Each guideline is developed with a systematic approach and includes a review of the available literature and expert opinion when published data alone are insufficient to make recommendations. All guidelines undergo appropriate multidisciplinary review prior to publication and recommendations are considered valid at the time of publication. Because new developments in medical research and practice can change recommendations, all guidelines undergo scheduled, periodic review to reflect any changes. The systematic development process of clinical practice guidelines began in 2007 and will be applied to all revisions as they come up for scheduled review, as well as all new guidelines.

Diagnosis, non-surgical

History and physical examination

Besides fever, constitutional symptoms are frequent in older children with malignancies. Tracheal compression most commonly occurs with benign lesions. When serious compression is present a superior vena cava syndrome, wheezing, cough and stridor can occur. Depending on the side of the lesion nerve and vessel involvement can result in hoarseness, cyanosis and chest pain.

Paraneoplastic syndromes can occur in suspected malignancies. Opsoclonus-myoclonus is seen in neurogenic tumors.

Further a palpable lesion in the neck can be a sign of intrathoracal and/or mediastinal involvement or a sign of metastasis. In lesions of the posterior mediastinum spinal involvement can result in neurological symptoms as tendency to fall and imbalance whilst walking.
**Imaging**
Of mediastinal lesions 90% can be located by a PA and lateral chest radiograph. For exact localization, possible local invasion and consistency of the lesion CT is highly effective, also for detection of calcifications CT is better then MRI. But MRI may have some advantages over CT in defining tumors close to the spine as it more accurate in soft tissue detail as is important for involvement intraspinal. This also accounts for chest wall involvement. Also nuclear medicine has a role in the imaging of mediastinal lesions as the use of MIBG and PET can be performed when dealing with a suspected neuroblastoma.

**Laboratory**
Systemic disease linked to the mediastinal lesion should be identified eg bone marrow and tumor markers as AFP and HCG in teratomas. Also urine samples for catecholamines, like VMA and HVA in neuroblastomas, should be taken in case of suspected malignancies.

**Management**
After history taking and drawing laboratory tests, a diagram can be made to define the appropriate strategy based on the diagnostic images obtained. The characteristics of the lesion can be cystic, solid or mixed. With the help of understanding the anatomical location (figure 1) these diagrams can be used (figure 2,3). Mediastinal lesions can occur prenatally and are then often embryogenic remnants and usually, but not always, cystic.

When a solid or mixed solid/cystic lesion is present this is usually later in life and can be a benign or, in most cases, a malignant lesion. A lesion that normally occurs in the pleural cavity or in the lung itself, such as sequestration, can occur as well in the mediastinum.

<table>
<thead>
<tr>
<th>Tumors and Cysts by Location</th>
<th>Anterior</th>
<th>Middle</th>
<th>Posterior</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lymphoma</td>
<td>Enterogenous cyst</td>
<td>Neurogenic tumors</td>
<td></td>
</tr>
<tr>
<td>Germ cell tumor</td>
<td>Mesothelial cyst</td>
<td>Neurenteric cyst</td>
<td></td>
</tr>
<tr>
<td>Thymoma</td>
<td>Lymphoma</td>
<td>Lymphoma</td>
<td></td>
</tr>
<tr>
<td>Hemangioma</td>
<td>Thoracic duct cyst</td>
<td>Foregut duplications</td>
<td></td>
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<tr>
<td>Parathyroid adenoma</td>
<td>Granuloma</td>
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<tr>
<td>Thymic cyst</td>
<td>Hamartoma</td>
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<tr>
<td>Lipoma</td>
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<tr>
<td>Aberrant thyroid</td>
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<tr>
<td>Lymphangioma</td>
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</tbody>
</table>

**Figure 1.** Tumors and cysts by location in the mediastinum
**Figure 2.** Diagram for cystic mediastinal lesions

**Figure 3.** Diagram for solid and mixed type mediastinal lesions.
Antenatal and early postnatal diagnosis

Some solid lesions, such as teratomas with mediastinal involvement, are also diagnosed prenatally. Besides antenatal counseling of the parents one should keep in mind that neonatal airway compromise is the most serious complication after birth. A multidisciplinary approach is mandatory in these cases 4.

Cystic lesions

Antenatally diagnosed lesions are often, but not always, cystic. In older children some lesions are suitable for management with percutaneous administration of OK-432 (Picibanil) as in mediastinal lymphangiomas 12. Further in rare cases like Castleman-disease, a lymphoproliferative disorder of unknown etiology and well known for blood loss during surgery, preoperative embolization of the hypertrophic vessels of these tumors is an option 13.

Solid lesions

Biopsy is indicated in suspected lymphoma and nonseminomateous germ cell tumors. Studies show that VATS for mediastinal biopsy is safe 14 (Level III). During the above mentioned management, information regarding the nature of the tumor (benign or malignant) is required in order to apply the appropriate treatment. Various invasive approaches are possible like thoracotomy, sternotomy, parasternal mediastinotomy (Chamberlain procedure) and less invasive methods such as mediastinoscopy, image guided biopsy and thoracoscopy. This guideline will focus on the data in literature to apply criteria in the decision making of a thoracoscopic approach in the diagnostic approach, therapeutic approach in benign and in malignant lesions.

MIS as a diagnostic tool

“Which masses are best approached with MIS to obtain tissue for diagnosis?” To obtain data the following search-strategy was used. PubMed (Medline) and Embase search using keywords (MESH terms): ((mediastinal mass) OR mediastinal tumor) AND pediatric AND diagnosis

In general the need for biopsy is mandatory to evaluate the histological origin of a non-cystic mass as lymphomas, germ cell and neurogenic tumors. This can safely be done by a minimal invasive approach (IPEG 14), Level III. In some cases the need for a bronchoscopy is mandatory to evaluate bronchiotracheal compression and biopsy 15. Level III.

In the available literature Sandoval 16 describes the results from 9 biopsies with varying pathology (thymic hyperplasia, granuloma, Wilms tumor- a metastasis-, tuberculosis (TBC), mycobacterium avium and M.Hodgkin). No complications were mentioned. Level III.

Guvenc 17 states that in TBC thoracoscopic biopsy of the mediastinal lymph node for a definitive diagnosis is feasible even in the young age. Level III.
Moffat 18 presents 6 thoracoscopic biopsies in 4 lymphomas, 1 Ewing and 1 neuroblastoma. In one lymphoma with superior vena cava syndrome a bleeding occurred and was followed by thoracotomy. Level III.

Partrick 19 and Rothenberg published their experience in which they could easily biopsy 6 lymphomas and one malignant sarcoma. Level III.

Several papers mention also biopsies of varying origin as thymoma 20. Jaggers 21 state that thoracoscopic biopsies are a valuable tool mainly in the posterior but also in the anterior part of the mediastinum without any further data. Level III.

Esposito 9 in 1999 showed that the diagnostic accuracy of thoracoscopic biopsy of mediastinal masses is between 88 and 100%. Esposito 22 also published the experience of the Italian Society of Videosurgery in 2007 and stated that MIS undoubtedly provide more accurate information on tumor extension in the thorax. There were successful biopsies in 6 lymphomas, 4 thymic lesions, 1 rhabdomyosarcoma, 1 sarcoma and 1 germ cell tumor. Level III.

Waldhausen 23 published his series in which they successfully performed 7 mediastinal biopsies (100%) that showed 2 ganglioneuromas, 3 benign and 2 rhabdomyosarcomas. Level III.

Guye 24 shows in the French-Swiss study that in 48 malignant hemopathies, 12 primary and 36 secondary tumours, a successful in- or ex-cisional biopsy was performed. Level III.

The review of Gow 25 shows that MIS in mediastinal biopsy (8 to 25% of all the VATS in the available literature) is safe and useful to obtain a diagnosis. Level III.

**Short summery of the levels of evidence**

There is level III evidence showing that MIS is safely applicable in the anterior, middle and posterior mediastinal compartment.

**MIS as therapeutic tool for benign lesions**

“What benign masses can be approached by thoracoscopic resection?”

To obtain data the following search-strategy was used.

*PubMed (Medline) and Embase search using keywords (MESH terms): ((mediastinal mass OR mediastinal tumor) AND pediatric AND (benign AND thoracoscopy))*

Partrick 19 and Rothenberg showed in their publication that a foregut duplication is perfectly suited for a minimally invasive approach. They resected 12 duplications, and also 3 teratomas and 1 thymic lesion, all without complications. Level III.

Knudtson 26 in JSLS shared the idea that MIS in removal of bronchogenic cysts is a safe and effective method. Level III.

Hirose 27 published a successful resection of foregut duplications in 6 patients and stated that thoracoscopy has an excellent cosmetic outcome requiring little or no intravenous pain medication and therefore should be the standard of care for resection of these benign cysts. Level III.
Bratu 28 presented a study with 39 foregut duplications, 21 were removed by thoracotomy and 11 by MIS. The other 7 were operated by laparotomy or cervical. In comparison there was no difference regarding outcome between thoracotomy and MIS except that chest tube duration (CTD) and length of stay (LOS) were significantly shorter in the MIS group. Level II.

**Short summery of the levels of evidence**

Compared with thoracotomy there is some level II evidence that MIS results in shortening of CTD and LOS.

**MIS as therapeutic tool for malignant tumors**

“Which malignant masses can be approached by thoracoscopic resection?”

To obtain data the following search-strategy was used.

*PubMed (Medline) and Embase search using keywords (MESH terms): ((mediastinal mass) OR mediastinal tumor) AND pediatric AND (malign AND thoracoscopy))*

**Teratoma**

Martino4 published about teratomas in which they resect one case by thoracoscopy successfully. The tumor was cystic. They state that thoracoscopy is an accepted alternative for removal of some benign mediastinal masses as in mature teratoma.

**Thymus**

Thymic lesions are rare anterior mediastinal tumors (around 30 reported cases), Honda 29 described a single case of a cystic lesion that they could easily remove in toto by MIS. Pathology showed a cystic thymoma. They stated that if the tumor is easy to remove and the lesion is well circumscribed, VATS would be useful.

Rothstein 20 shows their experience with a case of thymoma in which they performed initially a MIS biopsy. They considered to perform a thoracoscopic resection but decided to do open surgery because of the risk of residual mass.

**Neurogenic tumors**

Interestingly is the paper from Iwanaka30 in which 38 laparoscopic and 10 thoracoscopic excisions and biopsies from solid tumors are discussed. Although the laparoscopic group favors the outcome in sense of length of stay, quicker postoperative feeding and start of postoperative chemotherapy this is not clearly shown for the thoracoscopic procedures. In one mediastinal teratoma there was a conversion to open surgery because of extension of the lesion adjacent to the large vessels. In another case a paravertebral dumb bell-type neuroblastoma which intruded the vertebral canal, was complicated by postoperative leakage of cerebrospinal fluid that needed a thoracotomy to solve the problem. They stated that in case of large or dumb-bell-type tumors the need to discuss the use of endosurgical procedures should be evaluated preoperatively. Further is mentioned that there are only a few pediatric cases that require advanced surgical procedures and thus make the learning-curve longer. Only in precise indications the advances of MIS can be clarified. Level II.
Chapter 1

The series of Fraga 31 is also small (n=5) and shows that neuroblastoma (NB), ganglioneuroblastoma (GNB) and ganglioneuroma (GN) can be treated with the same efficiency as the open procedures but with reduced length of stay and chest tube drainage although the tumors treated by MIS were smaller than the open ones. Level II.

Nio 32 presents also a small (n=6) number of NB, GNB and GN that could be resected safely with thoracoscopy. Level III.

Promising is the study by Lacreuse 33 in which 21 cases are presented, 9 neuroblastoma, 9 ganglioneuroblastoma and 3 ganglioneuroma, none of them were dumb-bell-type. All the procedures were done successfully by MIS except in 1 case with a huge mass because of dangerous dissection adjacent to the large vessels. Horner syndrome was temporarily seen in 4. Level III.

In a comparative retrospective study Petty 34 looked at 7 open versus 10 thoracoscopic cases of neurogenic tumors. The case mix was similar and the outcome was also similar concerning complications. Because improved cosmesis, the avoidance of a thoracotomy and significant reduced length of stay in the MIS group they favor the MIS procedure. Level II.

Also Malek 35 states that in a retrospective study of 26 open and 11 thoracoscopic procedures the MIS group has a favorable outcome as they have a decreased length of stay (LOS), reduced chest tube duration (CTD) and decreased blood loss. Level II.

In the French-Swiss multicenter study published by Guye 38 primary tumors were treated by MIS, 20 successfully resections (of which 2 thymic lesions and 17 neurogenic tumors) and 9 biopsies 24. In 9 cases a thoracotomy (conversion) was done because of size of the tumor. Two chylothoraces and one temporary Horner complicated the resection-group. Level III.

Short summary of the levels of evidence

There is level II evidence that in neurogenic tumors the non-dumb bell type can safely be operated in experienced hands by MIS. There is level II evidence that MIS compared with thoracotomy has a decreased CTD, LOS and decreased blood loss.

Additional aspects of MIS in mediastinal masses

Anaesthesiological remarks

It is important to mention that in some cases in anterior mediastinal lesions, i.e. giant lymphomas, a critical airway management should be performed 36,37. Serious signs and symptoms as well as imaging can play an important role in defining these risks 2. The rate of life-threatening airway complications can be 5.2% of all newly diagnosed mediastinal lesions and 55% in mediastinal M.Hodgkin disease. 38
Timing
In asymptomatic patients elective resection is advocated because of risk of infection and malignant transformation which can be postponed after the age of 6 to 12 months concerning anesthetic and surgical risk.

Surgical approach during MIS
The position varies in the literature. Some advocate lateral decubitus position as the best positioning for clear anatomical identification. Electrocautery, Ligasure, Harmonic scalpel and clips are used for vascular dissection. Depending on the size of the child 3, 5 or 10 mm trocarts were used.

Postoperative aspects
Studies comparing open and thoracoscopic resection are all retrospective in nature. In a study concerning 149 neuroblastomas located in the thorax its outcome favors MIS due to a significantly reduced length of stay and decreased preoperative blood loss. In a comparative study of 17 patients MIS revealed shorter length of stay.

Levels of evidence
1. Which masses are best approached with MIS to obtain tissue for diagnosis?
   There is level III showing that MIS is safely applicable in the anterior, middle and posterior mediastinal compartment.
2. Which benign masses can be approached for resection thoracoscopically?
   Compared with thoracotomy there is some level II evidence that MIS results in shortening of CTD and LOS.
3. Which malignant masses can be approached for resection thoracoscopically?
   There is level II evidence that in neurogenic tumors the non-dumb bell type can safely be operated in experienced hands by MIS. There is level II evidence that MIS compared with thoracotomy has a decreased CTD, LOS and decreased blood loss.

Recommendations
1. Diagnostic approaches
   A thoracoscopic biopsy for mediastinal masses can be performed in the anterior, middle or posterior compartment of the mediastinum.
   Grade C recommendation
2. Therapeutic approaches for benign lesions
   A thoracoscopic resection for benign lesions can be performed. It provides a significantly shorter chest tube duration, decreased length of stay and reduced blood loss.
   Grade C recommendation
3. Therapeutic approaches for malignant lesions
A thoracoscopic resection can be performed, depending on size and anatomical relationship with vessels in non-dumb-bell-type neurogenic tumors.

Grade C recommendation

Summary

Minimal invasive diagnostic procedures concerning mediastinal lesions are safe and effective in any anatomical place. (Level III, Grade C recommendation).

Benign lesions can be resected by MIS safely. With MIS there is a decrease in length of stay, chest tube duration, blood loss and it is cosmetically superior over thoracotomy. (Level II, Grade C recommendation).

Thoracoscopic approach in malignant procedures is only recommended in neurogenic tumours. (Level II, Grade C recommendation).
References


**APPENDIX 1: Levels of Evidence**

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<thead>
<tr>
<th>Level</th>
<th>Evidence</th>
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<tbody>
<tr>
<td>Level I</td>
<td>Evidence from properly conducted randomized, controlled trials</td>
</tr>
<tr>
<td>Level II</td>
<td>Evidence from controlled trials without randomization or Cohort or case-control studies or Multiple time series, dramatic uncontrolled experiments</td>
</tr>
<tr>
<td>Level III</td>
<td>Descriptive case series, opinions of expert panels</td>
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**APPENDIX 2: Scale Used for Recommendation Grading**

<table>
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<th>Grade</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade A</td>
<td>Based on high-level (level I or II), well-performed studies with uniform interpretation and conclusions by the expert panel</td>
</tr>
<tr>
<td>Grade B</td>
<td>Based on high-level, well-performed studies with varying interpretation and conclusions by the expert panel</td>
</tr>
<tr>
<td>Grade C</td>
<td>Based on lower level evidence (level II or less) with inconsistent findings and/or varying interpretations or conclusions by the expert panel</td>
</tr>
</tbody>
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