The Egyptian Cardiothoracic Surgeon

In Press

Original Article

The challenging spectrum of mediastinal lesions and their surgical approach: Insights from a single-center experience

Ahmed Abdelaziz, Nora Mamdouh, Ahmed Tarek, Akram Allam, Ahmed Saad

Department of Cardiothoracic Surgery, Faculty of Medicine, Alexandria University, Alexandria, Egypt

Abstract

Background: Mediastinal masses represent a wide variety of pathologies. It occurs in both adults and pediatrics, and many of them are discovered incidentally. The difficult anatomical access for these lesions and their relation to important anatomical structures make diagnosis and treatment a challenge. In this study, we aimed to highlight and describe different pathologies and surgical approaches to these lesions, and to shed light on these important, challenging surgeries and the related morbidity and mortality.

Methods: We retrospectively reviewed the medical records for patients with mediastinal masses under our service between August 2020 and August 2023. Data collected included: age, sex, indication of surgery, approach, role of surgery, definitive pathology, operative time, length of hospital stay, and complications.

Results: A Total of 61 cases were included, 39 females and 22 males, with mean age 31.4 years. The mean operative time was 127.4 minutes (127.4 ± 48.0); mean hospital stay was 3.64 days (3.64 ± 4.89). The complication rate was 21.3% and perioperative mortality was 4.9%.

Conclusion: The wide spectrum of mediastinal pathologies is a challenge every time in decision-making for thoracic surgeons. The choice of surgical approach should be tailored for each case. Open surgery is still the gold standard for large or invasive lesions. Yet minimally invasive video-assisted thoracoscopic and robotic surgery has recently proven safety and efficacy for biopsies and complete resection of mediastinal masses, in selected cases treated by an experienced team.

KEYWORDS

Mediastinum; Video-assisted thoracoscopic surgery; Mediastinal masses; Mediastinal tumors; Mediastinal cysts; Echocardiography

Introduction

Mediastinum is the part of the thorax between the two pleural sacs of the lungs which harbors vital structures such as the heart with the great vessels, airway, esophagus, lymphatic and nervous structures [1,2].

Mediastinal masses occur in both pediatrics and adults due to the large spectrum of pathologies, most of which are discovered incidentally. Diagnosis and treatment of these lesions are always challenging due to their peculiar anatomical location and their relation to important vital structures [3].

Mediastinal masses are grouped by dividing the mediastinum into 3 regions: the anterior mediastinum, the middle mediastinum, and the

Corresponding author: Ahmed Abdelaziz a.abdelaziz84@gmail.com

posterior mediastinum. The anterior compartment harbors most of the mediastinal malignancies (60% of all mediastinal malignancies), even though most mediastinal masses are benign (two thirds) [4].

Mediastinal masses are variable in their size, location and nature; therefore, it isn't acceptable to have the same strategy when dealing with these lesions. The first step in the diagnostic algorithm is analyzing clinical and radiological data to reach a preliminary diagnosis. In most cases, the histological examination of the lesion is crucial to validate the clinical diagnosis and can direct further treatment away from surgery.

Furthermore, it provides essential prognostic information for each patient. Obtaining tissue biopsy can be done by ultrasound or computed tomography-guided transthoracic core needle biopsy or by surgery with its different approaches. Selection of the best method depends on many factors including the patient's clinical condition, the size and location of the mediastinal mass, and the decision of the multidisciplinary team treating the patient.

Some lesions, as thymomas and teratomas, are directly resected without preoperative biopsy, because they have characteristic diagnostic radiological features. On the other hand, if lymphoma is suspected, it is crucial to obtain tissue biopsy immediately for appropriate treatment planning. Histopathological diagnosis usually requires sufficient tissue for proper examination and further immunohistochemistry staining, making surgery a better choice than non-surgical core needle biopsy or fine needle aspiration cytology. [2]

Despite the challenging anatomical location of mediastinal tumors, surgical resection continues to be the most effective way for diagnosis and treatment. A lot of factors affect the selection of the surgical approach, including the location and size of the lesion, preference of the surgeon, available surgical equipment, and the skills of the anesthesiology team. In addition to other associated clinical factors such as body physique, previous thoracic surgery, and extent of the disease. Although median sternotomy and thoracotomy were the traditional surgical approaches; both have few indications nowadays, compared to 15 years ago. Video-assisted thoracoscopic surgery and even robotic-assisted thoracoscopic surgery are now more popular, as they provide less post-operative pain, smaller scar and provide faster recovery [4-7].

Patients and Methods

We retrospectively reviewed the medical records for patients, between August 2020 and August 2023, who underwent surgical interventions for mediastinal masses at our thoracic surgery unit. The study protocol was approved by the Faculty of Medicine, Alexandria University Ethics Committee (serial no: 0305853, IRB no: 00012098). The study was conducted in accordance with the principles of the Declaration of Helsinki. Demographic data (age and sex), location of the mass, operative data (indication of surgery, surgical approach, and operative time), complications, duration of hospital stay, and the definitive pathology were collected.

A total of 61 patients were included in our study, 39 were females (63.9%) and 22 were males (36.1%). The mean age was 31.4 years; mean duration of hospital stay was 4.4 days, and mean operative time was 127 minutes.

Radiological diagnosis was done using a single or combination of imaging modalities, including chest x-ray, computed tomography, magnetic resonance imaging and positron emission tomography, as required for each case. Contrast enhanced computed tomography was our gold standard investigation requested for all our patients, while magnetic resonance imaging was reserved for neurogenic tumors in the posterior mediastinum and for further evaluation of thymic cysts.

Surgical approaches:

Video-assisted thoracoscopic surgery (VATS)

It was used for resection of small non-invasive thymomas (4cm or less) and for thymectomy for all cases of non-thymomatous myasthenia gravis. The conventional tri- port right sided approach was used, with CO2 insufflation, double lumen

endotracheal intubation and the patient in the semi-supine position. We prefer the right-sided approach as we believe that it provides a better working space. Benign cystic lesions were operated in a similar manner either right or left.

Seven patients of undiagnosed mediastinal adenopathy in our study were operated on by video-assisted thoracoscopy. With double lumen endotracheal intubation and the patient in lateral decubitus position, we used either uni-port (single 3-5cm incision in the 5th intercostal space) or tri-portal approach. The commonly dissected lymph nodes for biopsy were the right para-tracheal group (Figure 1) plus or minus the right para-esophageal or subcarinal group.

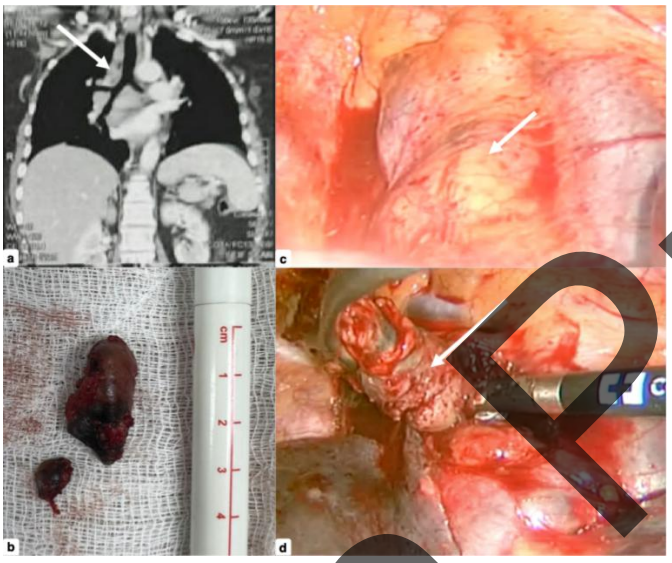

Figure 1: Right para-tracheal mediastinal lymphadenopathy, the arrow points to station 4R Lymph nodes. a: Computed tomography showing bulky amalgamated mediastinal lymph nodes; b: Two lymph nodes after excision, the largest measuring 3cm; c: Right-sided thoracoscopic view of bulky, bulging lymph nodes; d: Right-sided thoracoscopic view of 4R lymph nodes dissection

Median sternotomy

There was a consensus among surgeons at our institution to use this approach for patients with bulky thymomas, 5cm or more, with or without myasthenic symptoms, and for any invasive thymoma. This approach was also used for any patient with a sizable anterior mediastinal mass as teratoma or mediastinal goiter, with or without a cervical incision depending on the anatomy and nature of the thyroid lesion.

Posterolateral thoracotomy

The conventional posterolateral thoracotomy was utilized in 5 patients; two of them had huge mediastinal sarcoma almost occupying the entire hemithorax (Figure 2). Furthermore, this approach was used to resect a sizable Neuroblastoma of the posterior mediastinum, and for a sizable bronchogenic cyst in the middle mediastinum with anticipated adhesions close to the superior vena cava. Another patient operated through Posterolateral thoracotomy was diagnosed radiologically having a huge para-cardiac lipoma and after exploration a hernia of Morgagni was found and was treated successfully through this approach.

Figure 2: Computed tomography of the chest showing mediastinal sarcoma occupying the entire right hemithorax; the arrow points to the lesion

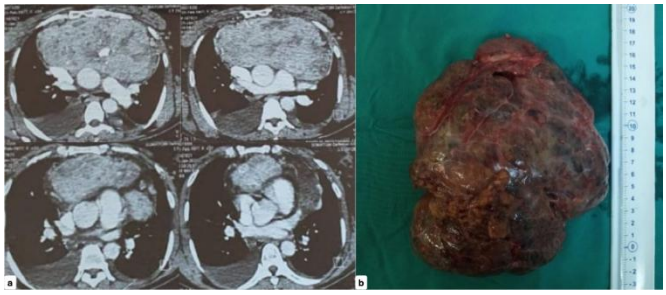

Figure 3: Huge isolated intra-thoracic goiter. a: Computed tomography showing the huge anterior mediastinal mass; b: Specimen after resection, pathology revealed multinodular benign goiter

Clamshell incision

Bilateral anterior thoracotomy with transverse sternotomy was used for resection of an extremely huge isolated intrathoracic goiter (Figure 3).

Right anterior mediastinotomy

A 3 cm parasternal incision in the right 2nd intercostal space was chosen for tissue biopsy from an anterior mediastinal mass close to the right anterior chest wall, after an inconclusive computed tomography-guided biopsy (Figure 4).

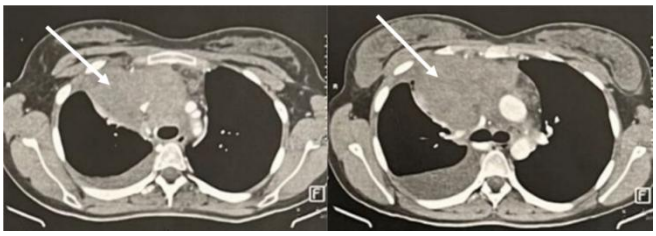

Figure 4: Computed tomography of an anterior mediastinal inflammatory myofibroblastic tumor, the arrow points to the tumor

Statistical analysis

Continuous variables were presented as mean (SD) or median (IQR), and categorical data were presented as numbers (%). Comparisons were made using t-test, Wilcoxon test, chi-squared, or Fisher's exact test, when appropriate. A two-tailed p-value of less than 0.05 was considered statistically significant. SPSS v.25 (IBM Corp-Chicago- IL- USA) was used for statistical analysis.

Results

Lesions were located in the anterior mediastinum in 36 patients (59%), the middle mediastinum in 21 patients (34.4%), and the posterior mediastinum in 2 patients (3.3%). The majority of lesions were located in the anterior mediastinum, with thymic hyperplasia and thymoma representing the most common pathologies in this compartment. In the middle mediastinum, sarcoidosis was the most commonly encountered pathology. Different pathologies and their location are collectively shown in Table 1.

The most commonly used surgical approach was (VATS), representing 55.7% of our cases (34 patients), followed by median sternotomy in 10 patients (16.4%). Other approaches included: mediastinoscopy in 9 patients (14.8%), posterolateral thoracotomy in 5 patients (8.2%), followed by less common other approaches. Table 2 summarizes all surgical approaches used for different pathologies.

Table 1: Anatomical distribution of mediastinal pathologies by location and pathology type

Location	Definitive pathology (surgical specimen)	Count (percentage)
Anterior	Thymic hyperplasia	18 (29.5%)
	Thymoma	10 (16.4%)
	Radiation induced granuloma	2 (3.3%)
	Multinodular goiter	2 (3.3%)
	Complex acquired thymic cyst	1 (1.6%)
	Inflammatory myofibroblastic tumor	1 (1.6%)
	Mature cystic teratoma	1 (1.6%)
	Parathyroid carcinoma	1 (1.6%)
Total anterior		36 (59%)
Anterior and middle	Multinodular goiter	1 (1.6%)
Entire Hemithorax	Mediastinal sarcoma	1 (1.6%)
Middle	Sarcoidosis	10 (16.4%)
	Mature cystic teratoma	3 (4.9%)
	Tuberculous granuloma	3 (4.9%)
	Hernia of Morgagni	1 (1.6%)
	Lymphoma	1 (1.6%)
	Bronchogenic cyst	1 (1.6%)
	Metastatic lung cancer	1 (1.6%)
	Metastatic breast cancer	1 (1.6%)
Total middle		21 (34.4%)
Posterior	Mediastinal sarcoma	1 (1.6%)
	Neuroblastoma	1 (1.6%)
Total posterior		2 (3.3%)
Grand Total		61 (100%)

The mean operative time was 127.4 minutes (127.4 ± 48.0); ranging from 45 to 300 minutes. Short operative times were recorded during diagnostic surgeries performed by mediastinoscopy, VATS and mediastinotomy, mainly in cases of undiagnosed mediastinal lymphadenopathies. Conversely, the longest operative times were observed during sternotomy for radical resection of tumors. In addition to, resection of complex rare pathologies like parathyroid carcinoma, mediastinal sarcoma and a complex acquired thymic cyst.

Our average length of hospital stay was 3.64 days (3.64 ± 4.89). Biopsies for undiagnosed mediastinal lymphadenopathy had the shortest hospital stays in our study, as mediastinoscopy

Table 2: Shows different pathologies encountered and our surgical approaches used

Approach	Definitive pathology	Count (percentage)
VATS	Thymic hyperplasia	17 (10.4%)
	Tuberculous granuloma	3 (4.9%)
	Sarcoidosis	3 (4.9%)
	Thymoma	3 (4.9%)
	Mature cystic teratoma	3 (4.9%)
	Radiation induced granuloma	2 (3.3%)
	Parathyroid carcinoma	1 (1.6%)
	Complex acquired thymic cyst	1 (1.6%)
	Lymphoma	1 (1.6%)
VATS total		**34 (55.7%)**
Median sternotomy	Thymoma	7 (11.5%)
	Multinodular goiter	1 (1.6%)
	Mature cystic teratoma	1 (1.6%)
	Thymic hyperplasia	1 (1.6%)
Median sternotomy total		**10 (16.4%)**
Mediastinoscopy	Sarcoidosis	7 (11.5%)
	Metastatic breast cancer	1 (1.6%)
	Metastatic lung cancer	1 (1.6%)
Mediastinoscopy total		**9 (14.8%)**
Posterolateral thoracotomy	Mediastinal sarcoma	2 (3.3%)
	Neuroblastoma	1 (1.6%)
	Bronchogenic cyst	1 (1.6%)
	Hernia of Morgagni	1 (1.6%)
Thoracotomy total		**5 (3%)**
Right anterior mediastinotomy	Inflammatory myofibroblastic tumor	1 (1.6%)
Median sternotomy and cervical incision	Multinodular goiter	1 (1.6%)
Clamshell incision	Multinodular goiter	1 (1.6%)
Grand total		**61 (100%)**

was performed as day case surgery, and VATS biopsies ranging from 1-2 days of hospital stay. The longest hospital stay in our study was 38 days after resection of a parathyroid carcinoma, and this was related to refractory chest infection.

The total complication rate was 21.3% (13 patients). Intra-operative bleeding represented the most common complication, occurred in 3 patients out of 61 patients (4.9%), and followed by post-thoracotomy neuralgia and phrenic nerve injury in 2 patients (3.3%) for each. All complications and their incidence are shown in Table 3.

Table 3: Different complications and their incidence in our study

Complication	Number of patients (%)
Bleeding	3 (4.9%)
Phrenic nerve Injury	2 (3.3%)
Post thoracotomy neuralgia	2 (3.3%)
Tracheal perforation	1 (1.6%)
Recurrent nerve injury	1 (1.6%)
Myasthenia crisis and respiratory failure	1 (1.6%)
Prolonged air leak	1 (1.6%)
Atelectasis	1 (1.6%)
Superficial wound infection	1 (1.6%)
Total	**13 (21.3%)**

Perioperative mortality occurred in 4.9% of our patients (3 patients). The role of surgery was diagnostic in 21 cases (34.4%), therapeutic in 22 cases (36.1%), and both diagnostic and therapeutic, for complete resection of undiagnosed lesions without preoperative diagnosis, in 18 cases (29.5%).

Comparing minimally invasive approaches as VATS and mediastinoscopy to open surgery it was shown that the mean operative time, mean length of hospital stay and mean duration of intercostal drainage was significantly greater in open surgery patients. In addition, regarding mortality, all our three patients died were recorded in the open surgery approach. Finally, regarding complications, results were similar in both VATS and open surgery patients while we reported a single complication during the mediastinoscopy approach (Table 4).

Discussion

The diversity of mediastinal pathologies in addition to the narrow anatomical compartments with limited working space render its surgery and

Table 4: Comparing Outcomes of VATS, mediastinoscopy and open surgery

	VATS (n = 34)	Mediastinoscopy (n = 9)	Open surgery (n = 18)	p
Mean operative time (minutes)	124.85 ± 40.87	77.78 ± 22.10	156.94 ± 49.32	<0.001*
Mean length of hospital stay (days)	2.24 ± 1.17	1.0 ± 0.0	6.69 ± 7.77	<0.001*
Mean duration of intercostal drain (days)	1.53 ± 0.96	1.0 ± 0.0	3.61 ± 4.42	<0.001*
Complications (number of cases)	6 (17.6%)	6 (66.7%)	1 (5.6%)	^{MC}p= 0.001*
Mortality (number of cases)	0 (0%)	3 (33.3%)	0 (0%)	0.003*

approach challenging for every thoracic surgeon [8], in literature most of mediastinal masses are benign with malignancy ranging 25-40% [9]. This corresponds to our cohort with the prevalence of benign pathologies more than malignant ones.

Our patients' mean age was 31.4 years, with female predominance conforming to the cohort published by Sapmaz et al [4].

The anterior mediastinum was the most common location for our surgeries seen in 59% of our patients, followed by the middle and finally the posterior mediastinum, these results coincide with the majority of medical articles published [4,9]. Thymic pathologies, either thymic hyperplasia or thymoma, where the most encountered in the anterior compartment of the mediastinum, the same finding was reported as by Sapmaz et al [4], Sarper et al [9] and Solaini et al [10] and Mouroux et al [11].

Most of our patients were asymptomatic and their diagnosis was made through accidental discovery by radiology or during workup for other non-mediastinal pathologies. For example, we diagnosed a patient with mediastinal lymphadenopathy while doing computed tomography for investigating her unexplained abdominal pain. Conversely, in symptomatic cases, commonly reported symptoms were dyspnea, chest pain and myasthenia gravis neurological symptoms.

Video-assisted thoracoscopic surgery (VATS) for a relatively large mediastinal tumor (5.0–10.0 cm) remains controversial. Traditional sternotomy or thoracotomy is still the standard surgery. However, it is more invasive due to its high surgical trauma and postoperative complications [12]. In recent years, minimally invasive surgical approaches, such as VATS, including a lateral intercostal approach and a Subxiphiod approach, have been applied treating mediastinal tumors and have gradually become the preferred surgical approach worldwide [13-15].

Our surgical approaches used varied. However, video-assisted thoracoscopic surgery was the most commonly utilized in more than half of our patients (55.7%), this was especially seen in the last two years during our practice, followed by sternotomy (16.4%) and posterolateral thoracotomy (6.6%). Our higher rate of video-assisted thoracoscopic surgery compared to other modalities coincides with the majority of the published articles in medical literature, especially over the last 10 years [16].

The long operative times encountered for some patients was related to extensive pleural adhesions either post-radiation or due to previous chronic infections, where the majority of the operative time was spent freeing up these adhesions.

Tuberculous lymphadenitis can be suspected whenever there are bulky lymph nodes (more than 2cm) with central hypodensity (caseous necrosis) and ring enhancement by contrast enhanced computed tomography. Yet in many cases lymph node biopsy is mandatory to confirm the diagnosis and exclude lymphoma, metastasis and other infections [17]. Our study included 3 cases of tuberculous granulomatous mediastinal lymphadenitis that were confirmed pathologically after doing VATS lymph node biopsy.

We reported a low incidence of complications (21%), the most common was intraoperative bleeding (4.9%). Our explanation is that some of our operated mediastinal pathologies are aggressive, vascular and huge. During resection of mediastinal sarcoma, for example, bleeding is

expected and is sometimes inevitable. Furthermore, we operated a significant number of thymectomies during our early experience where bleeding from tiny, short thymic veins was troublesome. Fortunately, in all cases it was managed by adequate compression or clipping.

Regarding mortality, the first patient died on the second day post-operative, due to anemic heart failure following emergency resection of a huge mediastinal mass, because unfortunately the amount of operative blood loss was not replaced adequately in the ICU, due to logistic problems during the COVID 19 era. The second patient died on day 7, due to myasthenic crisis following resection of thymoma. The last patient died on day 30, due to rapid tumor regrowth (mediastinal sarcoma) and respiratory failure.

VATS can be used safely for complete resection of mediastinal masses and cysts in selected patients, either for diagnostic or therapeutic purposes. This philosophy has been accepted and implemented in many hospitals all over the world in last 10 years including our hospital especially in the last 5 years. On the other hand, the rate of doing cervical mediastinoscopy and its diagnostic role has decreased compared to the past. Nowadays, many surgeons at our hospital prefer VATS for mediastinal lymph node excisional biopsy. This was a very common procedure done at our unit as we see many patients with undiagnosed mediastinal lymphadenopathy where Sarcoidosis, lymphoma and tuberculosis are popular causes. These diseases are characterized by bulky amalgamated lymph nodes with extensive fibrosis. Compared to mediastinoscopy, VATS offers better visualization, wider surgical field with more room for instruments and easier conversion to thoracotomy if needed. Furthermore, it allows exploring and dealing with any associated lung or pleural pathology and allows access to the inferior mediastinal nodes that are out of the reach of mediastinoscopy. It provides safe en bloc dissection of large amalgamated and adherent lymph nodes. Our target was to dissect and excise the whole node with an intact capsule, rather than incisional biopsies, to reach an accurate pathological diagnosis that depends on evaluation of the nodal architecture. This is consistent with many authors in literature, Rendina et al [18], Landreneau et al [19], Gossot et al [20], Solaini et al [10] and Mouroux et al [11].

With careful and multidisciplinary perioperative planning, minimally invasive surgery has shown to be safe and to provide at least similar outcomes when compared to open approaches in well selected cases. Although data is still limited, improved surgical techniques and available technology will pave the way to increased indications of minimally invasive surgery for mediastinal lesions [21].

Limitations

The limitations of our study include the retrospective nature and being a single center experience for a common topic in thoracic surgery during a period of 3 years only. However, it reflects the distribution and nature of part of the spectrum of mediastinal pathology in our country. In addition, it reflects the surgeons' preference and early experience. Especially that, more than 90 percent of the procedures were operated by only 2 young consultants.

Finally, nevertheless, surgery for mediastinal pathologies is a common thoracic surgery topic, the spectrum of Pathology and the experience of the managing team differs and hence articles written about this topic always carry what is new and interesting for others.

Conclusion

In conclusion, the choice of the surgical approach should be tailored for each case, putting in mind the wide variety of mediastinal pathologies and different presentations. Open surgery is still the gold standard for large or invasive lesions. Recently, minimally invasive approaches including video-assisted and robotic-assisted thoracoscopic surgeries have proven safety and efficacy for management of mediastinal lesions. Complete resections of mediastinal masses or cysts can be achieved through minimally invasive approaches, in selected cases and with experienced hands. Minimally invasive approaches are also very useful for biopsies from undiagnosed mediastinal lymphadenopathies.

This provides less pain, hospital stay and earlier post-operative recovery, which is beneficial especially in patients requiring post-operative adjuvant therapy.

Although surgery for mediastinal pathologies is a common thoracic surgery topic, the spectrum of pathology and the experience of the managing team differs and hence articles written about this topic always carries what is new and interesting for others. Finally, future research is needed from many hospitals over the world with different pathology map, experience and resources. The future data deduced will serve as a nucleus for developing guidelines and algorithms based on global consensus to help thoracic surgeons in making decisions while dealing with these challenging mediastinal lesions.

Funding: Self-funded
Conflict of interest: Authors declare no conflict of
Data availability: The relevant raw data can be obtained upon reasonable request by contacting the author.
Ethics approval: The study was conducted in accordance with the principles of good clinical practice and the Declaration of Helsinki. All patients provided written informed consent. The study protocol was approved by Alexandria Faculty of Medicine ethical committee (serial number: 0306982, IRB number: 00012098).

References

1. Stoddard N, Heil JR, Lowery DR. Anatomy, Thorax, Mediastinum. StatPearls. Treasure Island (FL): StatPearls Publishing; 2024 Jan. https://www.ncbi.nlm.nih.gov/books/NBK539819/
2. Ghigna MR, de Montpreville VT. Mediastinal tumours and pseudo-tumours: a comprehensive review with emphasis on multidisciplinary approach. European respiratory review. 2021;30:200309.
3. Ahuja J, Strange CD, Agrawal R, Erasmus LT, Truong MT. Approach to Imaging of Mediastinal Masses. Diagnostics. 2023;13 (20): 3171.
4. Sapmaz E, İnan MŞ, Işık H, Karataş O, Kavaklı K, Genç O. A retrospective analysis of surgical approach to the mediastinal lesions. Gulhane Med J. 2019; 61 (3): 118-22.
5. Mao Y, Lan Y, Cui F, et al. Comparison of different surgical approaches for anterior mediastinal tumor. Journal of Thoracic Disease. 2020; 12(10): 5430–9.
6. Pennathur A, Qureshi I, Schuchert MJ, et al. Comparison of surgical techniques for early-stage thymoma: Feasibility of minimally invasive thymectomy and comparison with open resection. The Journal of Thoracic and Cardiovascular Surgery. 2011;141(3):694–701.
7. Agatsuma H, Yoshida K, Yoshino I, et al. Video-Assisted Thoracic Surgery Thymectomy Versus Sternotomy Thymectomy in Patients With Thymoma. The Annals of Thoracic Surgery. 2017 ;104(3):1047–53.
8. Radkani P, Joshi D, Barot T, Williams R. Robotic video-assisted thoracoscopy: minimally invasive Approach for management of mediastinal tumors. J Robot Surg. 2018;12(1):75–9.
9. Sarper A, Gürkök S, Özuslu BA, Genç O, Balkanlı K. Primer mediastinal kitleler: 64 olgunun analizi. Türk Göğüs Kalp Damar Cerrahisi Derg. 2001;9(3):153–5.
10. Solaini L, Bagioni P, Campanini A, Poddie BD. Diagnostic role of videothoracoscopy in mediastinal diseases. Eur J Cardiothorac Surg. 1998 ;13(5):491-3.
11. Mouroux J, Maalouf J, Perrin C, et al. Current surgical methods for the etiological diagnosis of mediastinal adenopathies. J Chir. 1994;131(11):473-7.
12. Friedant AJ, Handorf EA, Su S, Scott WJ. Minimally invasive versus Open Thymectomy for Thymic malignancies: systematic review and Meta-analysis. J Thorac Oncol. 2016;11:30–8.
13. Ng CS, Wan IY, Yim AP. Video-assisted thoracic surgery thymectomy: the better approach. Ann Thorac Surg. 2010;89:S2135–41.
14. Batirel HF. Minimally invasive techniques in thymic surgery: a worldwide perspective. J Vis Surg. 2018;4:7.
15. Numanami H, Yano M, Yamaji M, et al. Thoracoscopic Thymectomy using a Subxiphoid Approach for Anterior Mediastinal tumors. Ann Thorac Cardio¬vasc Surg. 2018;24:65–72.

16. Weksler B, Tavares J, Newhook TE, Greenleaf CE, Diehl JT. Robot-assisted thymectomy is superior to transsternal thymectomy. Surg Endosc. 2012;26(1):261-6.
17. Venkateswaran R, Barron D, Brawn W, et al. A forgotten old disease: mediastinal tuberculous lymphadenitis in children. European Journal of Cardio-Thoracic Surgery. 2005 Mar;27(3):401–4.
18. Rendina EA, Venuta F, De Giacomo T, et al. Comparative merits of thoracoscopy, mediastinoscopy, and mediastinotomy for mediastinal biopsy. Ann Thorac Surg. 1994 Apr;57(4):992-5.
19. Landreneau RJ, Hazelrigg SR, Mack MJ, et al. Thoracoscopic mediastinal lymph node sampling: useful for mediastinal lymph node stations inaccessible by cervical mediastinoscopy. J Thorac Cardiovasc Surg. 1993; 106(3): 554-8.
20. Gossot D, Toledo L, Fritsch S, Celerier M. Mediastinoscopy vs thoracoscopy for mediastinal biopsy. Results of a prospective nonrandomized study. Chest. 1996 Nov;110(5):1328-31.
21. Rodriguez M, Milla L, Wee JO. The role of minimally invasive surgery in the management of giant mediastinal tumors: a narrative review. Mediastinum. 2022; 25;6:37.