

SPECTRUM OF BENIGN AND MALIGNANT MEDIASTINAL MASSES, DIAGNOSIS, INCIDENCE, AND MANAGEMENT IN THORACIC SURGERY

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Abstract

Objectives: The study aims to analyse the clinical spectrum of benign and malignant mediastinal masses, diagnosis, incidence of cases, and their management among patients with thoracic surgery.

Methodology: A prospective study was conducted from November 2022 to January 2024 at the Thoracic Surgery Department in Jinnah Postgraduate Medical Centre, Karachi. All patients aged 12 years and above who were vitally stable were included. All data were collected on a structured questionnaire, and the data were analysed using SPSS version 23.

Result: A total of 93 patients were included, with 58(62.4%) males. The mean age of patients was 40.49 ± 14.0 years. Malignant disease was present in 65(69.9%) patients, with squamous cell carcinoma of the oesophagus being the most common, 30(32.3%), followed by lymphoma, 21(22.6%). Benign masses were seen in 28(30.1%) cases, where thymoma was most frequent 9(10.75%). Radiological assessments, including computed tomography in 91 (97.8%) and MRI in 6(6.6%) patients, were conducted. The visceral compartment was the most common location in 44(47%) patients. The majority of masses were mixed density 91 (97.8%), and mediastinal lymphadenopathy was present in 71(76.3%) of both malignant and benign origin. Loco-regional disease was found in 28(30.1%). Pathological diagnoses were made in 76(81.7%). Treatment included medical management for 72(77.4%), surgery for 55(59%), and palliation for 133(14%).

Conclusion: Mediastinal masses comprise a heterogeneous group of lesions with a predominance of malignant pathology in this study. Squamous cell carcinoma of the oesophagus and lymphoma were the most common malignancies, while thymoma was the leading benign lesion. Multimodal management, combining medical, surgical, and palliative approaches, was essential for optimal outcomes. Early detection and individualized treatment remain key to improving prognosis in mediastinal mass patients.

INTRODUCTION

The diagnosis and management of mediastinal masses (MM) can be challenging, as diseases arising within the mediastinal compartment include various pathologies requiring a multidisciplinary approach.¹ A standardized strategy to evaluate mediastinal diseases is by the location of the mass within the mediastinal compartment.² Mediastinum is divided into three compartments according to the International Thymic

Malignancy Interest Group (ITMIG) classification: perivascular, visceral, and paravertebral, as shown in Figure 1.³ perivascular compartment (PC) consists of thymus, lymph nodes, and fat. The Visceral compartment (VC) includes the heart, great vessels, oesophagus, trachea, and mediastinal nodes, whereas paravertebral soft tissues and thoracic spine are in the paravertebral compartment (PVC).³

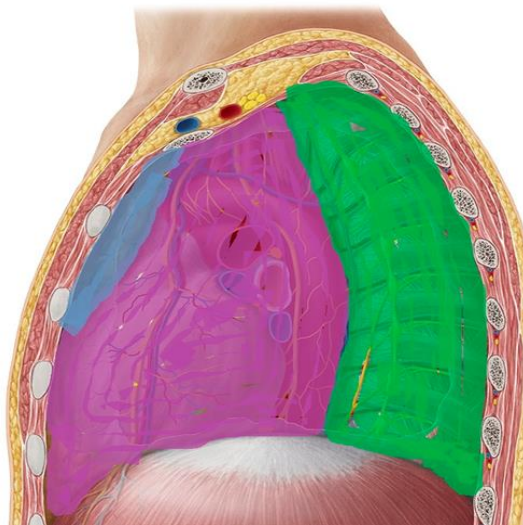


Figure 1: Prevascular compartment (blue colored), visceral compartment (purple colored), paravertebral compartment (green colored)

MM have a comprehensive histopathological spectrum, accounting for 3% of all thoracic masses, out of which 50% arise from the perivascular compartment.⁴ Thymoma, teratoma, thyroid masses, and lymphomas are most common in the PC and warrant great caution in diagnostic interventions due to proximity to critical organs.⁴ Visceral compartment pathologies include cysts, oesophageal tumours, lymphadenopathy and lymphoma, frequently present with compressive symptoms, whereas neurogenic neoplasms like Schwannoma and neurofibroma are benign nerve sheath tumours originating in the paravertebral compartment.⁵

Considering the heterogeneity of diseases in the mediastinum and their precise location, multi-dimensional imaging integrated with histological characterization is mandatory for optimum management.⁴ Chest radiography, computed tomography (CT), and magnetic resonance imaging (MRI) are the initial radiological modalities leading to

a differential diagnosis.⁶ Tumours inaccessible by minimal invasive radiological diagnostic techniques like CT or ultrasound-guided methods can be dealt with by mediastinoscopy and video-assisted thoracoscopy (VATS) for tissue diagnosis.^{7,8} Based on the histopathology and extent of disease, the treatment regimen may vary from chemotherapy, radiotherapy, to surgery, or a combination of all three.⁹

The rationale of this study is to describe the nature and characteristics of mediastinal masses presenting to a thoracic surgical unit. The last local literature regarding mediastinal lesions was by Amer et al. in the year 2017.¹⁰ Therefore, our study aims to define the MM, their incidence in our region, various methods for histopathological diagnosis and management carried out, and to endorse the local and international data.

METHODOLOGY

This prospective observational study was carried out in the Department of Thoracic Surgery at Jinnah Postgraduate Medical Centre, Karachi, between November 2022 and January 2024. Ethical approval was obtained from the Institutional Review Board (Letter No. F.2-81/2022-GENL/327/JPMC), and informed consent was secured from all participants. Patients aged 12 years or older with clinical and radiological findings indicative of mediastinal masses were enrolled, whereas Patients were excluded if clinically unstable, defined as severe respiratory distress requiring urgent airway management, abnormal haematological parameters, a Glasgow Coma Scale (GCS) score below 13, or clinical signs of shock.

All enrolled patients underwent a structured assessment, and data were collected through a questionnaire documenting demographic information, presenting complaints, and associated symptoms. Relevant laboratory and imaging investigations, including disease-specific biomarkers, chest X-ray, CT scan, and MRI, were performed, with additional details obtained from hospital records. Radiological findings were jointly reviewed with radiologists to enhance diagnostic accuracy. Final diagnoses were established based on combined histopathological and radiological evidence. Both medical and surgical treatment strategies were recorded according to the primary diagnosis. For tissue diagnosis, the choice of biopsy technique was determined by the location of the mass,

mediastinal structures involved, and accessibility, with preference for radiological approaches requiring minimal or no local anaesthesia. Surgical procedures were conducted according to established international standards and considered factors such as resectability (complete excision and absence of distant metastasis). When histopathological confirmation was essential to initiate medical treatment but a radiological biopsy was not feasible, an incisional biopsy was performed. Data analysis was conducted using SPSS Statistics version 22. Categorical variables were summarized as frequencies and percentages, while continuous variables were presented as mean $\pm$ standard deviation. The Chi-square test was applied, with a p-value ≤ 0.05 regarded as statistically significant.

RESULT

The study included 93 patients; out of the total, 58 (62.4%) were males and 35 (37.6%) females. Mean age was 40.49 ± 14.0 years (range: 14-68 years). Based on location 44(47%) masses were seen in the visceral compartment, followed by the perivascular 41 (44%) and paravertebral 8(9%) compartments. Dysphagia was the most common presenting symptom seen in 69(74.2%), followed by chest pain and shortness of breath (n=64; 68.8%, 47:50.5% respectively). Lactate dehydrogenase (LDH) was the commonest tumour marker observed in 21(22.6%) patients, followed by receptor antibodies in 18 (19.4%) cases. Table 1 summarizes the demographics, stratification of symptoms, and tumour markers.

Table 1: demographic characteristics and clinical features

Demographic details of patients		Frequency	P-Value
Gender	Male	58 (62.4%)	-
	Female	35 (37.6%)	
Location of mediastinal masses	Visceral compartment	44 (47%)	< 0.0001
	Prevascular compartment	41 (44%)	
	Paravertebral compartment	8 (9%)	
Clinical features	Dysphagia	69 (74.2%)	0.0012
	Chest pain	64 (68.8%)	0.0138
	Shortness of breath	47 (50.5%)	0.7689
	Weight loss	45 (48.4%)	0.8991
	Cough	38 (40.9%)	0.2618
	Orthopnoea	38 (40.9%)	0.2618

	neck swelling	31 (33.3%)	0.0157
	SVC syndrome	19 (20.4%)	< 0.0001
	Hoarseness	19 (20.4%)	< 0.0001
	Weakness of the limb	15 (16.1%)	< 0.0001
	Haemoptysis	5 (5.4%)	< 0.0001
Tumour markers	LDH	21 (22.6%)	0.0002*
	Receptor antibodies	18 (19.4%)	0.0005*
	AFP	5 (5.4%)	<0.0001*
	B-HCG	5 (5.4%)	<0.0001*

Chi-square and Fisher's exact tests were applied to assess the distribution of demographic, clinical, and tumour marker variables. *Significant findings included dysphagia ($p = 0.0012$), chest pain ($p = 0.0138$), and paravertebral mass location ($p < 0.0001$). Tumour markers such as LDH (lactate dehydrogenase), receptor antibodies, AFP (alpha-fetoprotein), and β -HCG (beta-human chorionogonadotropic) also showed statistically significant presence ($p < 0.001$).

Malignancy was reported in 65 (69.9%) patients out of which squamous cell carcinoma of the oesophagus (SCCE) was the most common aetiology ($n=30$; 32.3%), followed by lymphoma ($n=21$; 22.6%). Benign masses were noted in 28 (30.1%) patients, out of which thymic hyperplasia ($n=16$; 17.2%) was most frequent. Among all the oesophageal pathologies ($n=43$), SCCE was the most common, accounting for 69.7%. Classification of benign and malignant mediastinal masses is shown in Table 2.

Table 2: Classification of mediastinal masses

Reported Pathology of Patients	Frequency, n (%)
Malignant diseases N=65	
Squamous cell carcinoma of the oesophagus	30 (32.3%)
Lymphoma	21 (22.6%)
Adenocarcinoma of the oesophagus	9 (9.7%)
Synovial sarcoma	2 (2.2%)
Leiomyosarcoma of the oesophagus	1 (1.1%)
Small-cell lung carcinoma	1 (1.1%)
Metastatic lymphadenopathy	1 (1.1%)
Benign diseases N=28	
Thymoma	10 (10.75%)
Thymic hyperplasia	6 (6.45%)
Nerve sheath tumour	5 (5.4%)
Teratoma	2 (2.2%)
Leiomyoma of the oesophagus	2 (2.2%)
Cystic teratoma	1 (1.1%)
Hypolipemic	1 (1.1%)
Schwannoma of the oesophagus	1 (1.1%)

Chest radiograph and CT scan were carried out in the majority of patients. Additional radiological assessment, such as MRI, was done in 6 (6.5%)

patients with paravertebral compartment mass who had suspicion of spinal involvement. In relevance to the character of mass, a homogenous nature was

exhibited in 53 (57%) and a heterogeneous in 40 (43%). Mixed density (solid and soft) was seen in 91 (97.8%). Mediastinal lymphadenopathy was present

in 71 (76.3%), distant metastasis in 28 (30.1%), and chest wall involvement in 12 (12.9%) patients.

Table 3: Radiological assessment

Radiological assessment of the patients		Frequency	P-Value
Radiological assessment of patients	Chest x-ray	91 (97.8%)	0.99
	CT chest	91 (97.8%)	
	CT angiography	6 (6.5%)	
	Nerve conduction studies	6 (6.5%)	
	MRI	6 (6.5%)	
	Doppler ultrasound	2 (2.2%)	
Character of mass	Homogeneous	53 (57%)	0.19
	Heterogeneous	40 (43%)	
Density of mass	Mixed	91 (97.8%)	<0.001
	Soft tissue density	2 (2.2%)	
Lymphadenopathy	Mediastinal lymphadenopathy	71 (76.3%)	<0.001
	Cervical lymphadenopathy	31 (33.3%)	
Metastasis	Distant metastasis (visceral)	28 (30.1%)	0.02
	Chest wall involvement	12 (12.9%)	

Chi-square and Fisher's exact tests were applied to assess distribution patterns across radiological variables. Significant associations were observed for density of mass ($p < 0.001$), lymphadenopathy ($p < 0.001$), and metastatic spread ($p = 0.02$), indicating non-random distribution. Other variables showed no statistically significant variation ($p > 0.05$), suggesting uniform or selective diagnostic use.

In more than two-thirds of patients ($n=76$; 81.7%), pathological diagnosis was carried out through different methods defined in Table 4. Management

was planned according to the disease aetiology and extent, and comprised of medical treatment in 72 (77.4%), definitive surgery in 55 (59%), whereas palliation was given to 13 (14%) subjects. Definitive surgery was more frequently related to malignant masses ($p < 0.001$) and benign masses of the perivascular compartment ($p < 0.05$). The number of patients who received neo-adjuvant therapy followed by surgery, surgery and adjuvant therapy, only surgical management, and palliative followed my medical management are shown in Figure 2 below.

Table 4: Overview of diagnostic interventions and management

diagnostic interventions and management		Frequency	P Values
Biopsy $n=76$ (81.7%)	Upper gastrointestinal endoscopy	43 (46.2%)	0.000
	Radio-guided (trans-thoracic)	16 (17.2%)	
	Peripheral lymph node biopsy	13 (14%)	
	Chamberlain procedure	2 (2.2%)	
	Mediastinoscopy	1 (1.1%)	
	VATS	1 (1.1%)	
Complete excisional biopsy		17 (18.3)	1.0000
Medical treatment $n=72$ (77.4%)	Chemo-radiotherapy	52 (55.9%)	0.000
	Radiotherapy	10 (10.8%)	

	Immunotherapy	10 (10.8%)	
Definitive surgery n=55 (59%)	Thymectomy	17 (18.3%)	0.059
	McKeown esophagectomy	15 (16.1%)	
	Ivor Lewis esophagectomy	15 (16.1%)	
	Excision of mass	8 (8.6%)	
Palliative management	Feeding jejunostomy	13 (14%)	1.000

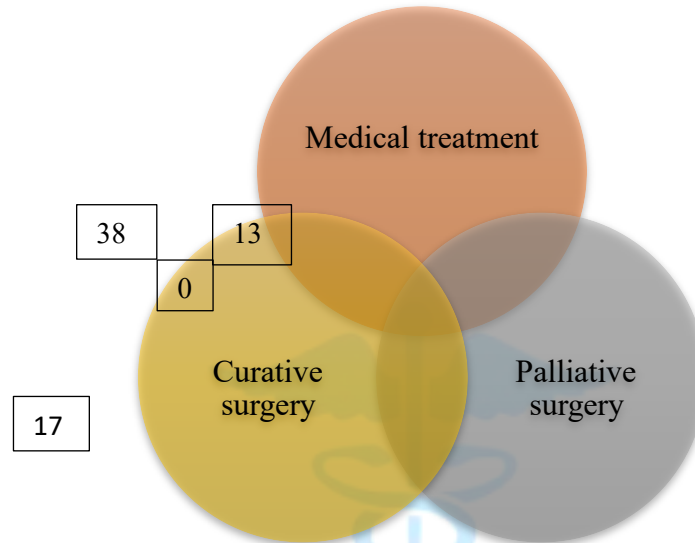


Figure 2: overlap in treatment

DISCUSSION

Prevalence of primary mediastinal masses is rare and ranges from 0.73% to 0.9% of all thoracic cancers.¹¹ It harbours a variety of malignant (67%) and benign masses (23%), with a similar incidence observed in our study: malignant (69.9%) and benign (30.1%).¹² A strategic multidisciplinary approach is essential for optimal management, which is based on radiological followed by histological evaluation that permits necessary medical and surgical interventions.¹³ According to an international study by Anja *et al*, most lesions were found in prevascular compartment (69.8%) followed by visceral compartment (13.5%) and paravertebral compartment (5.4%).¹¹ However, in our study VC tumours were seen in (n=44; 47.3%) followed by PVC (n=41; 44.1%) and paravertebral compartments (n=8; 8.6%) respectively. A meta-analysis by Morgan *et al*. reported an alarming rise in squamous cell carcinoma of the oesophagus, surpassing adenocarcinoma in East Asian countries, with an incidence rate of 6.3 per 100,000.¹⁴ These

findings align with the local literature reporting an overall incidence of 4.1 per 100,000 in Pakistan, with the province of Baluchistan having the greatest prevalence.¹⁵ Furthermore, Szolkowska M. *et al* reported lymphoma (25%) as the most diagnosed tumour group, followed by thymoma (13%) and thymic hyperplasia (7%) in the anterior mediastinum.¹⁶ Similarly, in our study, lymphoma accounted for 22.6%, thymoma for 10.75% and thymic hyperplasia for 7% of the masses. Mediastinal masses can manifest with symptoms resulting from the obstruction or compression of adjacent structures.¹⁷ In a review by Shahana *et al*, dyspnoea (18%) was reported as the most common local symptom, followed by dry cough (13.5%).¹⁸ In contrast, our study identified dysphagia (74.2%) as the most frequent symptom, followed by dyspnoea (50.5%), likely due to the greater prevalence of oesophageal pathologies presenting at our centre. MM with a rapidly growing nature can also manifest with life-threatening signs due to compression of the airway

and vessels.¹⁹ Mediastinal Lymphoma is often found to be responsible for these signs. Our study reported superior vena cava obstruction in 90.4% of lymphomas, which is higher than 16.1% seen by Pech-Alonso *et al.*¹⁹

Primary mediastinal lymphoma is a rare entity, and early pathological diagnosis and initiation of chemo-radiotherapy are the mainstay of treatment.²⁰ A total of 22 patients were reported during our study with mediastinal widening and lymphadenopathy featuring compressive symptoms without evidence of invasion. Peripheral lymph node biopsy was carried out in 13 patients, whereas the rest underwent radiologically guided biopsy. All of them were subsequently referred to oncology for further management, in line with the treatment plan outlined by other authors.²⁰

Thymomas are slow-growing thymic epithelial cell tumours seen in adults, showing indolent behaviour. Their histological types include thymomas, thymic carcinomas, and neuroendocrine thymic tumors.²¹ Thymomas can often be asymptomatic, may present with compression symptoms or neuromuscular effects associated with myasthenia gravis. CT scan is the preferred diagnostic and preoperative staging tool for thymomas.²¹ Surgical resection of thymic masses remains the primary treatment, although a multimodal approach, both medical and surgical, is beneficial for many patients. Median sternotomy approach offers superior visualization of the thymic tissue and has been the standard for thymectomy.²¹ Although median sternotomy has been the traditional approach, minimally invasive techniques, such as transcervical, video-assisted thoracoscopic surgery (VATS), and robotic video-assisted thoracoscopic surgery (RATS), have gained popularity in recent years.²¹

Our study involved 17 patients with thymic epithelial tumours, including 10 with thymoma, 6 with thymic hyperplasia, and one with thymolipoma. Additionally, 12 cases were associated with myasthenia gravis. All cases were considered resectable and underwent complete surgical resection through either median sternotomy or an anterior-lateral thoracotomy approach or VATS.

Mediastinal germ cell tumours (MGCTs) are the most common extragonadal germ cell tumors (GCTs) and typically occur in the prevascular compartment, with

a higher incidence in males.^{4,22} MGCTs are categorized into seminoma and nonseminomatous types. Seminomatous MGCTs consist of seminoma, while nonseminomatous MGCTs include pure yolk sac tumours, embryonal carcinoma, choriocarcinoma, teratomas (mature and immature).²² Treatment generally involves neoadjuvant chemotherapy followed by surgical resection of any remaining tumor, except in cases of benign teratomas, which only require surgical resection.²² In the context of this study, germ cell tumors were the second most common benign neoplasms found in the prevascular compartment. Management included pathological confirmation via mediastinoscopy in 2 cases (2.2%) followed by surgical resection through open thoracotomy in 1 case (1.1%). Malignant teratomas, however, require neoadjuvant chemotherapy.^{4,22}

Oesophageal cancer is 7th most common worldwide cancer that affects the quality of life of people. In our study, it was the most prevalent tumour of VC and 40 out of 43 were malignant oesophageal tumours with SCCE being most prevalent (69.7%). Various studies have explored that neo-adjuvant therapy approach helps in downsize of tumour, beneficial local control and improve rates of complete tumour resection commended with locally advanced oesophageal carcinoma stated by Shah *et al* in their article.²³ Neo-adjuvant chemo-radiotherapy was offered to all thoracic oesophageal carcinomas; squamous cell carcinoma 30 (32.3%) and adenocarcinoma in 9 (9.7%) patients, respectively. Out of 39 patients, 30 were deemed resectable with adequate margins achieved; the rest were managed palliatively. All patients with limited proximal mid-thoracic tumours had McKeown esophagectomy, whereas tumours involving the gastro-oesophageal junction and cardia had Ivor Lewis esophagectomy performed.²⁴ Concomitantly, 13 (14%) patients had tumours above the azygous vein and beyond resectable margins, and underwent oncological management as resection with clear margins is often not achievable.²³ Despite advances in diagnosis and treatment, patients present with an advanced and incurable stage. Palliative management is often decided by a multi-disciplinary team, including systemic therapies and enteral feeding for sustaining quality of life. Feeding jejunostomy was performed in patients who presented with late-stage

disease and were referred to an oncologist for further palliative management^{25,26}

The posterior mediastinum is a potential space located along the paravertebral sulci and is classically the most frequent location of neurogenic tumours. Neurofibromas and schwannomas, which are neurogenic tumours, typically originate from peripheral nerves.²⁷ Most reported paravertebral lesions are benign nerve sheath tumours, some of which extend into the spine, creating a dumbbell-shaped appearance. Schwannomas are the most frequently reported type of lesion in the paravertebral compartment. For tumours extending into the neural foramina, the recommended multidisciplinary approach is a posterior-lateral thoracotomy, performed in collaboration with a neurosurgical team^{17,28}

CONCLUSION

Mediastinal masses, though relatively uncommon, represent a diverse group of pathologies with significant diagnostic and therapeutic challenges. In this study, malignant lesions predominated, particularly squamous cell carcinoma of the oesophagus and lymphoma, highlighting the need for timely recognition and multidisciplinary management. Benign lesions such as thymomas, though less frequent, also require careful evaluation due to their potential for local invasion and recurrence. Radiological imaging, especially CT, played a crucial role in defining the extent and characteristics of disease, while histopathological confirmation remained the cornerstone of diagnosis. Surgical intervention, alongside medical and palliative therapies, formed the basis of individualized treatment strategies. Overall, early diagnosis through comprehensive imaging and pathology, coupled with appropriate surgical and oncologic management, is essential to improve outcomes in patients with mediastinal masses.

CONFLICT OF INTEREST

None

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None

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