Review Article

Surgical indications for mediastinal cysts—a narrative review

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Background and Objective: Whether and when surgical intervention is indicated for mediastinal cysts is a matter of some debate. While most mediastinal cysts are found incidentally, the anatomic location, clinical presentation, and symptoms, as well as the potential for malignancy, are important considerations that inform decisions related to whether to intervene surgically. The objective of this review is to summarize the current literature regarding the criteria for surgical excision of mediastinal cysts and provide a framework for the clinician and surgeon to arrive at a decision regarding the appropriateness of surgical intervention of mediastinal cysts.

Methods: A review of the published literature in the last 45 years (1977–2022) was conducted through PubMed, MeSh and Google Scholar. We included retrospective reviews, meta-analyses, and case studies published in the English language. A single author identified eligible studies, and those identified were reviewed by the team until consensus was met. Pediatric literature was excluded from this review.

Key Content and Findings: The current literature predominantly contains case studies, small retrospective studies, and meta-analyses describing mediastinal cysts. In the anterior mediastinum, multiloculated thymic cysts should be resected to rule out thymic malignancy. Intralesional fat, smooth borders, and a more midline location are features suggestive of a benign process, while asymmetric cystic wall thickening has been associated with malignancy. Both esophageal and bronchogenic cysts should be excised, taking into account the risk of complications (up to a 45% risk) of infection, rupture, or compression, as well as the rare risk of associated malignancy. Simple thymic and small pericardial cysts can be observed and followed with serial radiographic tools and should be resected if they increase in size, compress surrounding structures, or lead the patient to develop symptoms.

Conclusions: Since mediastinal cysts are rare and often asymptomatic, there are no formal guidelines outlining when surgical intervention should be undertaken. Based on our review of the literature, surgical intervention should be pursued if the patient's symptoms correlate with radiographic findings of a mediastinal cyst, there is compression of the surrounding structures, and concern of malignancy is present.

Keywords: Mediastinum; cysts; surgical indications

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Introduction

The diagnosis and indications for surgical resection versus drainage or observation of a mediastinal cyst are a matter of debate and clinical quandary. Many of these cysts are found incidentally, as part of radiographic evaluation of unrelated issues (1). On some occasions, the cysts are found in radiographic images from patients with symptoms such as cough, frequent infections, chest pain, dysphagia,

Table 1 The search strategy summary

Items	Specification
Date of search	5/1/2022–6/15/2022
Databases and other sources searched	PubMed, MeSh, Google Scholar
Search terms used	'thymic cysts', 'parathyroid cysts', 'mediastinal cysts', 'anterior mediastinal cyst', 'mid mediastinal cyst', 'pericardial cyst', 'posterior mediastinal cyst', 'esophageal duplication cyst', 'bronchogenic cyst', 'surgical indications for resection of mediastinal cyst'
Timeframe	1977–2022
Inclusion and exclusion criteria	Inclusion: prospective studies, retrospective studies, meta-analyses, case studies; exclusion: pediatric population, necrotic cysts, thoracic duct cysts
Selection process	A single author (PB) compiled a list of eligible studies. These were reviewed by the remainder of the team, until consensus was reached on the utility and quality of study

and odynophagia (2,3). However, the presence of those symptoms and the finding of a mediastinal cyst do not necessarily have a relevant correlation. The anatomic location of the cysts can narrow the differential diagnosis and the potential origin of the cyst. Relevant factors to consider include: whether the cyst is benign or malignant and whether there is the potential for malignant transformation over time. The radiographic appearance, location and anatomic relationship with the mediastinal structures, clinical presentation, including age, signs and symptoms or the lack thereof, and blood tests are all important variables when determining the need for surgical resection. The objective of this review is to summarize the current literature regarding the criteria for surgical resection of mediastinal cysts in order to help clinicians determine the best treatment for individual patients. We divided our discussion according to the anatomic location of the cyst—in the anterior, mid, or posterior mediastinum. We present the following article in accordance with the Narrative Review reporting checklist (available at https://med.amegroups.com/article/view/10.21037/med-22-27/rc).

Methods

Using a comprehensive approach, we conducted a narrative review to identify peer-reviewed and published studies focused on surgical indications for mediastinal cysts. We performed a limited search on PubMed and Google Scholar to identify articles on the topic (*Table 1*). The search was performed between 1 May, 2022 and 16 June, 2022. Search terms included 'thymic cysts', 'parathyroid cysts', 'mediastinal cysts', 'anterior mediastinal cyst', 'mid mediastinal cyst', 'pericardial cyst', 'posterior mediastinal cyst', 'esophageal duplication cyst', 'bronchogenic cyst', and 'surgical indications for resection of mediastinal cyst'. We reviewed studies published in the last 45 years (1977–2022) written in the English language. We included prospective studies, retrospective studies, and meta-analyses, and given the reduced amount of primary literature regarding mediastinal masses, we also included case studies in our analysis. A single author composed a list of eligible studies, which list was reviewed by the rest of the team until consensus was met. The less common cysts, including thoracic duct cysts, and lymph node necrosis, were not included in the review due to the lack of substantial literature related to indications for surgical resection.

Discussion

Anterior mediastinal cysts

The most common cystic masses in the anterior mediastinum are thymic cysts, cystic thymomas, and parathyroid cystic masses. Thymic cysts can be congenital or acquired and simple, uniloculated, or multiloculated. These lesions can be cervical or mediastinal in location and occasionally cervicomediastinal. Patients with thymic cysts do not usually present with symptoms. When present in the neck, thymic cysts can be palpated and an increase in size can be easily assessed by physical examination. Comparison with previous radiographic images to evaluate an increase in size of the mass, progressive thickening of the walls, development of septations, or nodularity is perhaps the most useful diagnostic tool to establish whether such cysts carry a malignancy.

For all types of anterior mediastinal masses, the presence of symptoms associated with the mass, such as chest pain, dyspnea, and cough, are indications for surgical resection. When the size or location of the cysts causes compression of neighboring structures, such as the great vessels, heart/pericardium, airway, esophagus, phrenic nerves, or lung, or when the patient develops symptoms, surgical resection should be considered. Under those circumstances, there is a higher level of concern for malignancy. In such cases, it is important to establish the extent of invasion to determine the cyst's resectability, the need for neoadjuvant therapy, and operative planning. The size criteria for resection of thymic cysts has not been established. Larger cysts have a higher probability of producing symptoms; however, when a cut off of 3 cm was used, the size alone did not directly correlate with the presence of symptoms or their final pathology (4). In their single-center institution retrospective review of 117 cases of benign thymic cysts, Wang *et al.* found that 76 were asymptomatic while 41 were symptomatic. When compared, average thymic cyst diameter did not vastly differ between symptomatic (36.85±22.50 mm) and asymptomatic patients (29.28±17.97 mm). In the same study, the majority of cysts found incidentally were smaller than 3 cm, and the patients were asymptomatic (4). Despite the limitations of a retrospective study, this study offers valuable information for thoracic surgeons related to the size of the cysts, the symptoms at the time of diagnosis, and relevance of both as criteria for resection. computed tomography (CT) scan and magnetic resonance imaging (MRI) images are not accurate when differentiating thymic cysts from thymic epithelial tumors to the extent that cysts are smaller than 3 cm, but the majority of surgically resected cysts smaller than 3 cm are benign (5). Thus, small cysts can be followed radiographically. If there is a radiographic atypical appearance suspicious for malignancy, resection is recommended regardless of the size of the cyst.

Congenital thymic cysts are frequently uniloculated simple cysts. These lesions are identified most often in children and young adults, particularly when the cysts are located entirely in the neck or cervicomediastinal region. These lesions are more frequently found in asymptomatic patients on cross sectional images obtained for reasons unrelated to the cysts. Simple cysts are most frequently oval shaped (50%), have a smooth contour (67%), are in the midline (61%) and outside the thymus (67%), do not have calcifications (89%) and have a CT scan attenuation of >20 HU (83%) (6-9). MRI is helpful in further characterizing cystic components when compared to CT scan (9). While it is generally accepted that cystic lesions in the anterior mediastinum show varying signal intensities on T1-weighted images and a higher signal intensity on T2-weighted images, there is often significant overlap (10). Although there are reports of thymic malignancies originating from simple cysts, it is debatable whether those lesions should be truly classified as simple cysts (11,12). Most simple cysts can be radiographically followed safely. In young patients with cysts of unclear etiology, MRI is the preferred method of radiographic follow up to avoid radiation associated with CT scans. However, simple cysts can increase in size and potentially compress neighboring structures secondary to the development of intra-cystic hemorrhage and, in rare cases, cause infections. In those circumstances, resection of the cyst is recommended.

The multiloculated cysts are generally acquired cysts related to infections and immune processes and can be associated with malignancies, particularly in patients with nodular sclerosing Hodgkin's lymphoma and seminomas (11,13-16). Paraneoplastic syndromes and autoimmune diseases, such as myasthenia gravis and Sjogren syndrome, also have been associated with thymic cysts (17). From the surgical standpoint, determining whether a thymic neoplasm is present, such as thymoma and thymic carcinoma, is the most important aspect of the diagnostic workup when a multiloculated cyst is discovered. Radiographically, the walls of multiloculated thymic cysts are thick with soft tissue attenuation inside the lesions and are always located in close relationship with the thymus (18). In addition, CT scan of the chest with IV contrast and contrast enhanced MRI are useful tools to define involvement of neighboring structures. Along those lines, on CT scans, a cystic thymoma appears nonhomogeneous with a single or multiple solid nodules present in the cyst wall (18). Contrast enhanced MRI can be helpful to differentiate thymic malignancies from thymic hyperplasia by identification of intralesional fat and a more midline location in the latter (18). Asymmetrical thickening of the wall can be an indication of an associated tumor(14). Percutaneous, image-guided biopsy or surgical biopsy should be considered to establish a definitive diagnosis when the radiographic appearance of the cyst is non-diagnostic. Of note, although there are reports of biopsy site seeding with a percutaneous biopsy of thymic malignancies, the rate of such events is very low and has only been described in case studies (19,20). If the radiographic appearance of the lesion is suspicious for cancer, a biopsy is not recommended, and if the lesion seems resectable in the CT scan or MRI, an R0 surgical excision is recommended.

Parathyroid cysts are sometimes associated with supernumerary parathyroid glands. Parathyroid glands are normally located in the neck; however, occasionally supernumerary glands or displaced glands can be found in the mediastinum, and although they can be located anywhere in the mediastinum, more frequently they are located in the anterior and mid mediastinum in the pre- and paratracheal compartments (21,22). When cysts develop in the mediastinal parathyroid glands, they are frequently uniloculated with thin walls. These cysts can grow with sizes reported anywhere from 0.5 cm to more than 12 cm (23). In about 15% of the cases, parathyroid cysts are located inside the thymic gland (21). These mediastinal parathyroid cysts can be associated with the cervical parathyroid glands or canalicular remnants, and vascular pedicles from the cyst to the gland can be identified. The parathyroid mediastinal cysts are frequently symptomatic, including: a palpable mass when the cysts have a cervicomediastinal location; dyspnea and dysphagia when the cysts compress the airway; and esophagus; and hoarseness when the cysts compress the recurrent laryngeal nerve. All these clinical presentations warrant a surgical resection and careful surgical planning including the potential need for reconstruction of the airway, esophagus, and vascular structures. Forty percent of the parathyroid cysts are functional and present with hypercalcemia or hyperparathyroidism. Any functional parathyroid cysts should be removed surgically, and intraoperative evaluation of appropriate decrease in the parathyroid hormone level should be confirmed. Persistent hypercalcemia in the setting of a negative neck exploration for hyperparathyroidism should prompt evaluation of a mediastinal lesion with CT scan and MRI. Single photon emission CT (SPECT), dual energy CT scan, as well as positron emission tomography (PET) CT scan and PET MRI have all been used to improve localization with a 96% sensitivity when more conventional imaging modalities have failed (24-27).

Despite being rare and accounting for only 0.1–2.6% of mediastinal cysts, hydatid cysts in the mediastinum should be considered in the differential diagnosis prior to resection (28,29). In a case series of 427 patients, 36% of identified hydatid cysts were located in the anterior mediastinum, while 45% and 18% were located in the posterior and middle mediastinum respectively (29). Hydatid cysts can be complicated or uncomplicated. CT scan and MRI are helpful in localizing the lesion; however uncomplicated mediastinal echinococcosis is radiographically indistinguishable from other mediastinal cysts (30). CT scan and MRI can both be helpful in characterizing a complicated hydatid cyst (contained rupture, complete rupture, or infection) (31). Surgical resection to mitigate the risk of rupture (47%) followed by albendazole for post-operative prophylaxis is recommended to reduce incidence or recurrence (31).

Middle mediastinal cysts

Approximately one third of mediastinal cysts are pericardial cysts. Most pericardial cysts are congenital and asymptomatic and are usually discovered incidentally in patients who are in their 40s or 50s. Transthoracic echocardiogram is often the first line test to detect pericardial cysts, and it usually shows a circumscribed, thin-walled echo-free space adjacent to the cardiac border without doppler flow. It is important to differentiate a cyst from a diverticulum—the latter, which can be identified by the presence of a defect in the pericardial lining. The most common locations of the pericardial cysts are the right and left cardio-phrenic recesses. Transthoracic echocardiograms obtained for reasons unrelated to the cysts frequently are the first to detect the pericardial cysts, but often further radiographic images are needed to better delineate the anatomy of the cyst. Chest CT or MRI are recommended if a pericardial cyst is suspected (32). Location along either cardio-phrenic angles is the most relevant indicator of a pericardial cyst (33). In a case series of 41 patients, when the lesions in question were found to be located significantly above the diaphragm, they were difficult to diagnose as pericardial cysts, and they were often mistaken as thymomas or pulmonary masses (33). MRI is particularly useful to delineate the cysts accurately, and a typical fluid signal intensity with high intensity on T-2 weighted sequences can confirm the cystic nature of the mass.

In a retrospective observational study from a single academic institution limited to 103 patients, the largest series to date, only 11 patients were symptomatic on initial presentation (34). Clinical manifestations of pericardial cysts vary depending on location and size and can include chest pain, dyspnea, or palpitations. More serious complications leading to hemodynamic compromise, tamponade, obstruction of right stem bronchus, or sudden death are rare (35). In this case series, only 7 of 11 symptomatic patients required intervention due to the severity of symptoms. Conversely, multiple case reports document the complete resolution of pericardial cysts with time. The mechanism of resolution of these cysts is unclear, but it is likely related to rupture or resorption. In the same case series, 29 asymptomatic patients were followed with serial

imaging for 13 months. A third of those patients showed a decrease in the size of the cyst whereas 17% demonstrated an increase in diameter of the cysts (35). In a different series of 29 asymptomatic patients, cyst diameter decreased by a mean of 25% in 34% of patients, increased by a mean of 13% in 17% of patients, and the remaining patients (49%) had no change (34). This study demonstrated that the size of the cysts or cysts growth did not correlate with the presence of symptoms, suggesting that in the absence of symptoms, serial radiographic follow up likely will not impact the therapeutic decision. The size of the cysts is highly variable and has been reported to vary from 2 to 28 cm. However, size criteria for resection have not been formally established. Currently, the presence of symptoms or compression of neighboring structures dictates the need for surgical resection in patients with pericardial cysts (36). In general, a surgical resection is recommended when these cysts are identified; however small cysts in asymptomatic patients can be safely followed with serial radiographic imaging because the criteria for surgical resection have not been established.

Bronchogenic cysts are best identified by CT scan and present as well-defined round masses with a density similar to water. On occasion, bronchogenic cysts can be mucoid in appearance and, thus, can be difficult to differentiate from a solid mass. Air-fluid levels may be seen when there is direct communication with the tracheobronchial tree (37). Due to their relationship with the respiratory tract and esophagus, bronchogenic cysts often are identified in patients with a cough, dyspnea, chest pain, odynophagia, and dysphagia related to the compression of the tracheobronchial tree or the esophagus. In addition, bronchogenic cysts can preset as an infected cyst. The infection can develop with or without communication with the aerodigestive tracts. When a communication is present, it is frequently due to perforation of the cyst into the aerodigestive tract. Multiple life-threatening complications related to compression of the cyst and intrathoracic cardiovascular structures, such as arrhythmias, coronary events, pulmonary artery hypoplasia, and superior vena cava syndrome, have been reported. There is a 45% reported risk of developing symptoms in the long term (38). Lastly, there are multiple case reports of malignancies arising from bronchogenic cysts (38). Therefore, surgical resection of all bronchogenic cysts should be strongly considered, even if incidentally found.

Posterior mediastinal cysts

The most common types of cysts in the posterior mediastinum are esophageal cysts (50–70%). Like patients with other mediastinal cysts, most patients with posterior mediastinal cysts are also asymptomatic, and their cysts are primarily discovered incidentally during other imaging studies. The diagnosis of esophageal cysts is difficult, but such diagnosis is key to the management of patients with such cysts, as it is crucial to differentiate esophageal cysts from malignant tumors. Malignant transformation of esophageal cysts has rarely been reported at approximately 1.8% in the largest retrospective case series of 107 patients to date (39,40). Esophageal duplication cysts most often involve the distal esophagus (41). Symptoms associated with these cysts are widely variable, highly dependent on size and location, and may include dysphagia, retrosternal chest pain, cough, respiratory distress, failure to thrive, and dyspnea. Additionally, initially asymptomatic cysts may, in rare instances, be complicated later by esophageal stenosis, respiratory system compression, rupture, or infection (41-46). There are no clear guidelines based on imaging characteristics or size to determine whether surgical treatment is warranted for asymptomatic lesions; however, the risk of ulceration, perforation, and malignancy should always be considered (41,47). Once the diagnosis of an esophageal cyst is made with a CT scan, barium swallow, MRI, or endoscopic ultrasound, a surgical resection should be considered.

Summary

Mediastinal cysts are heterogenous with variable clinical presentations and courses of disease depending on the type of cyst and their anatomic location. For multiloculated thymic, parathyroid cysts, bronchogenic cysts, and esophageal a surgical resection is recommended at the time of diagnosis. Simple thymic and small pericardial cysts can be observed and followed with serial radiographic tools. To the extent the cyst may be causing symptoms in a patient, or the cyst may become malignant or already exhibits malignant features, surgical resection is indicated. Mediastinal cysts are rare, and as such, most of the literature to date includes case series or case reports that have a low number of patient cases, which limits the general applicability of the reported findings and bases upon which to draw specific criteria for surgical resection. Even meta-analysis of the currently available data may not highlight more definitive conclusions. Therefore, continuing to report experiences and outcomes related to these uncommon diseases is highly encouraged.

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