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Pleuropericardial Cyst: A Review of the Literature

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Keywords

Review; Pleuropericardial Cyst Differential diagnosis Management Complications

Abstract

Background: Pleuropericardial cysts (PPCs), account for 5 - 10% of all mediastinal tumours, are rare lesions occurring in approximately 1 in 100000 persons and are usually congenital and rarely acquired. They are detected postmortem or incidentally on routine chest X-ray (CXR) and in most cases multi detector Computer Tomography is used to confirm the diagnosis. As benign course and clinical latency are characteristic features of such cysts and the occurrence of complications is rare, the majority of them can be left untreated.

Methods: The aim of the study is to review the literature regarding PPCs and create a table which summarises all the published cases in order to draw a conclusion about the epidemiology, as well as the diagnostic and therapeutic approach to PPCs exclusively. We reviewed retrospectively the clinical manifestation, diagnostic and therapeutic approach in 101 cases of PPCs since the 19th century

Results: Our statistical analysis led to the following results: mean age of initial detection: 48.7 ± 17.2 years, female:male ratio: about 3:2, presence of symptomatology: 37/101 cases, most common location: right cardiophrenic angle (RCPA), most common method of initial detection: CXR in 49/101 cases, mean maximal diameter: 8.3 ± 3 cm.

Conclusion: The management of a pleuropericardial cyst should be based on an algorithm in which the cyst's size, shape and compressibility along with clinical presentation and patient's fitness and preferences are be taken into consideration. When interventional is required, surgical resection by means of traditional open surgery or minimally invasive methods are considered to be the gold standard and along with percutaneous aspiration are the methods that have mostly been used.

Introduction

Pleuropericardial cysts, account for 5 - 10% of all mediastinal tumours, are rare lesions occurring in approximately 1 in 100000 persons and are usually congenital but exceptionally acquired. They are detected post-mortem or incidentally on routine chest X-ray and in most cases multi detector Computer Tomography is used to confirm the diagnosis. As benign course and clinical latency are characteristic features of such cysts and the occurrence of complications is rare, the majority of them can be left untreated.

Cystic lesions surrounding the heart have been reported since 1854¹. The first published pathoanatomic case series including four diverticula and one cyst was completed in 1903². Kienböck described the radiographic appearances of what may have been a pericardial coelomic cyst and later enriched this description by introducing the differential diagnosis of pleuropericardial cysts^{3,4}. Otto Pickhardt was the first to delineate the thoracoscopic appearance and later proceeded to the resection of a pericardial coelomic cyst in a

53-year-old woman⁵. Symptoms coexisting with such cysts were first described by Freedman and Simon, D'Abreu and Churchill and Mallory. Reviewing the literature, it was Adrian Lambert who was the first to propose a pathogenesis, noting the similar embryological origin of PPCs and diverticula from disconnected mesenchymal lacunae which normally fuse to develop the pericardial coelom. He also attempted for the first time to differentiate the thin-walled cysts of the mediastinum, all of which had previously been reported as "probably of lymphatic origin"⁶. Greenfield et al. introduced the term "Spring water cyst"⁷. By 1958, at least 120 cases of mesothelial cysts had been reported^{8,9}.

PPCs are cyst walls made up of a single layer of mesothelial cells and a loose stroma of fibrous tissue with collagen and elastic fibres. They usually contain clear, serous fluid and that is why they are also called 'spring water' cysts¹⁰. Finally, both the expression of epithelial membrane antigen and calretinin and the absence of an actin-positive subepithelial smooth muscle layer may be helpful in the diagnosis of a PPC¹¹.

The aim of this study was to review the literature and present a review article about PPCs including a table with all the data of: a) all the published cases reported as "pleuropericardial cysts" in the title and b) some of the published cases described as "pericardial cysts" in the title which are also called "pleuropericardial cysts" either in other review articles or even in the same article. According to our knowledge, this is the first organized attempt to review whole literature with focus in PPCs.

Finally, we analysed statistically the data associated with the age of initial detection, gender and cyst size and location, in order to draw a conclusion regarding the epidemiology of PPCs exclusively.

Methods

We aimed to review the literature regarding PPCs and create a table which summarises all the published cases in order to draw a conclusion about the epidemiology, as well as the diagnostic and therapeutic approach of PPCs exclusively.

We first searched the PubMed and Medline databases for any publications concerning PPCs. After this we searched for a systematic review reporting PPCs. No systematic reviews were found. We found only a review of treatment of four cases with video-thoracoscopy. We also found a review for benign cysts of the mediastinum. We then independently searched PubMed (until February 2018) using the following free text terms: "pleuropericardial cyst", "pleuropericardial cyst" AND "treatment" OR "symptoms" OR "location" OR "intervention" OR "surgery" OR "case". Then we searched for pericardial cysts also. We included case reports, abstracts, editorials and articles in all languages describing the location or symptoms or

treatment or intervention or surgery in patients with PPC. The database created from the electronic searches compiled in a reference manager program (Endnote X8) and all duplicated citations was eliminated. The following data were collected: (1) publication details such as title, authors, and other citation details, (2) patient data such as age, sex, symptoms (3) details of PPC (location, size, and approval), (4) data of intervention or surgery, (5) follow-up data. All in all, we reviewed 139 publications and found 101 cases of PPCs.

As described in "Discussion", plenty of terms have been used to describe a PPC. So, review references are mostly based on the terms "pericardial" and "pleuropericardial" and we decided to include the following in table 1:

- 1) All the published cases referred as "pleuropericardial cysts" in the title.
- 2) All the published cases referred as "pericardial cysts" in the title which are called "pleuropericardial cysts" either in other review articles or even in the same article but later on, in the text.

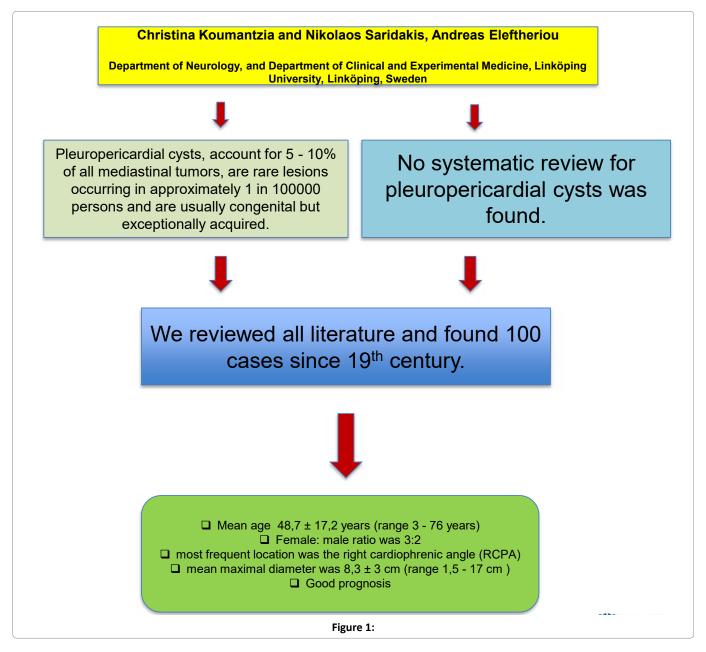
After having collected the data from all the cysts referred as PPCs (101 cases from 47 publications), we carried out an univariate statistical analysis regarding the following parameters: age of initial detection, gender, cyst size and location, method of initial detection as well as presence of symptomatology. Cases with non-mentioned data were excluded from the analysis.

Results

As far as the mean age of initial detection is concerned, our statistical analysis showed that this was approximately 48.7 ± 17.2 years, ranging from 3 to 76 years in 50 cases out of 101. Regarding gender, the female:male ratio was calculated to be about 3:2 (29:21) among 50 cases, while the most frequent location was the right cardiophrenic angle (RCPA) accounting for 39,6% followed by the left (LCPA) at 18,9% among 53 patients. CXR was the method used for initial detection in 49/101 cases. The percentage was probably higher, as the method for initial detection was not mentioned in 41 cases. Symptomatology was present in 37 cases out of 101. Finally, the mean maximal diameter was 8.3 ± 3 cm, varying between 1.5 and 17 cm in 42 out of 101 patients.

Discussion

Plenty of terms have been employed in the literature to characterise PPCs. Most have been used to define the localisation, the contents, the histology or the pathogenesis of such cysts. These terms are: pericardial coelomic cysts⁶, pericardial cysts, hydrocele of the mediastinum, simple cyst of the mediastinum, serosal cyst, spring- or clear- water cyst⁷, para-pericardial cyst, pleuropericardial cyst, pleural cyst and mesothelial mediastinal cyst.



PPCs are usually congenital in origin but other causes such as inflammation (rheumatic pericarditis, bacterial infection particularly tuberculosis, echinococcosis), trauma, post cardiac surgery and chronic haemodialysis 12-17 have been reported. Congenital PPCs usually originate from failure of fusion of one of the mesenchymal lacunae that form the pericardial sac, during embryogenesis after the third week of gestation^{6,18}. Another theory of the pathophysiology of such cysts explains the origin of PPCs by means of differential perseverance and graded constriction of ventral recess of the pericardial coelom. The ventral parietal recess is a diverticular structure where most of PPCs are located. Perseverance of this structure forms the diverticulum, constriction of the proximal part of which results in either a diverticulum with a narrow neck or a PPC in communication with the pericardial cavity, while

the complete closure of the proximal recess gives rise to a PPC¹. As far as inflammatory cysts are concerned, they develop as a result of loculated pericardial effusion¹².

PPCs account for 5-10% of mediastinal tumours and 11%² or 30%^{4,5} of mediastinal cysts. Prevalence is approximately 1 in 100000 persons⁸ and they constitute the second most common type of primary mediastinal cysts after bronchial ones^{19,20}. All ages may be affected, but PPCs are most frequently identified between the third and fifth decade of life, while they are rarely detected in childhood²¹⁻²⁴. More specifically, less than 20 cases in children have been reported in the literature²⁵. As far as gender is concerned, the female: male ratio varies among many studies and it has been described to be 1:1²², 8:4²⁶ and 2:3⁸. Finally, PPCs can be associated with other diseases such as Fanconi anaemia^{27,28}.

PPCs can occur in any compartment of the mediastinum²⁹, but are usually detected in the visceral mediastinum^{30,31} attached to the parietal pericardium. The most frequent site is the right cardiophrenic angle (51-75%), followed by the left $(28-38\%)^{19-21,32,33}$. Those PPCs occurring elsewhere other than the cardiophrenic angles (8% - 16%) are usually superior to the heart and right-sided³⁴. A frequent site is the right latero-tracheal region³⁵. In this case, the cyst originating from the upper recess of the pericardium extends posteriorly from the pericardial cavity around the ascending aorta^{36,37}. Other unusual sites that have also been reported include the other two mediastinal compartments, the vascular hila, the subcarinal area and the left heart border^{33,38-42}. Moreover, the PPCs that are detected in locations remote from the pericardium are believed to be pedunculated with a stalk that connects them with the pericardium^{43,44}. Almost 5% of PPCs are in communication with the pericardium through determinable tube-like structures⁴⁵. However, others studies indicate that they are always attached to the pericardium directly or by a pedicle^{10,19,20}, although a visible connection between the cyst and the pericardium is rarely detected^{46,47}. Finally, a PPC may occasionaly present as a mobile chest lesion, described by the term "wandering PPC"48 and in this case, it should be differentiated from solitary fibrous tumours of the pleura, which are the most common mobile chest masses49.

PPCs usually have a diameter of 2-15cm^{44,50-52} and weigh 100-200gr²⁵. However, there have been reported cases up to 28cm⁵³or even larger containing 1300ml of fluid³⁴ or measuring 25x37x5cm⁵⁴, while other were as large as a grapefruit⁵⁵.

The majority of PPCs are asymptomatic (50-75%) in adults and are found post-mortem or incidentally on routine CXR^{38,56}. However, two thirds of children diagnosed with a PPC develop symptomatology8.When they are symptomatic, in general due to increasing size and consequent compression or invasion on nearby organs, the symptoms are generally dominated by respiratory signs, such as dyspnoea, stridor, wheezing, chest discomfort including vague chest pain, heaviness, retrosternal pressure or substernal pain, persistent cough, sputum, haemoptysis, dysphagia and epigastric pain. Circulatory signs such as tachycardia, palpitations, fatigue, cyanosis and weakness may also be found^{8,19,31,44,47,50,57-61,62}. There can also appear signs of nervous compression presented as hoarseness due to unilateral vocal cord paralysis as a result of left recurrent laryngeal nerve compression⁶³, hemidiaphragm paralysis, hiccups, intercostal neuralgia, Horner Syndrome and Pancoast Tobias Syndrome⁶⁴. Finally, PPCs can atypically herniate through the chest wall and become palpable on clinical examination¹³.

The course of PPCs is usually benign as they are well-limited lesions with scant vascularisation. No cases

Table 1: Presentation of all data concerning 101 cysts referred as "pleuropericardial cysts" in the literature.

No of Ref- erence	Year	No of PPCs	Age (y) of initial detection	Sex	Symptoms Clinical presentation	Method for initial detection	Initial Suspicion	ст	MRI	Location	Size (cm)	Indication for further intervention	Follow up time
BIlal et al.	2017	17	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM
Naqvi et al.	2016	1	24	М	Exertional dyspnea (NYHA II), occasional cyanosis over the lips, loud P2 with 4/5 murmur in early and midpart of systole best heard in the auscultation position of pulmonary valve (pulmonary stenosis)	CXR	PPC	Large PPC with significant stenosis of main pulmonary artery + few subcentrimetric mediastinal lymph nodes	NP	LAM	NM	Symptomatic and complicated cyst	NM
Mouroux et al.	1996	13	Mean age: 49.9 (range 22-75)	4M 9F	-7/13: symptomatic -Chest pain pre- sented as the most common symptom in 5/7 patients due to cyst infection (1/5) or because of hernia- tion of the cyst (1/5)	13/13: CXR	NM	-11/13: 1-10 HU density -2/13: 38 and 52 HU density. -13/13: No con- trast uptake	Performed in 5/13 because of paravertebral position (2/5), abnormal density on CT (2/5) or herniation through the chest wall (1/5) but results are NM.	-5/13:RCPA -3/13:LCPA -2/13:R paratha- cheal space -2/13: Paraverte- bral medi- astinum -1/13:Ante- rior medi- astinum	Mean diameter: 7.5(±4) X 5(±2)	-7/13: Symptomatic cysts -3/13: Uncertain diagnosis -2/13: Compression on the SVC, although asymtpomatic -2/13: Practice of a potentially traumatic sport or professional activity	-Mean observation time via CXR: 57.7 mo, (range 4-125) -6/13: >72 mo follow up -No recur- rence along with absence of symptoms
Arghir et al.	2013	1	62	F	Progressive exer- tional dyspnea, night sweats, L chest pain, minor reccurent hemoptysis, tachycardia and hypertension	CXR	Heart disease (PPC after TTE)	Smooth ovoid thin-walled, sharply defined, homogenous mass(without tear drop config- uration)	NP	LCPA	10x11	Symptomatic cyst and uncertain diagnosis	1 mo AT via CXR: LVH, ascended left hemidia- phragm

					R basithoracic pain								
Elatiqi et al.	2015	1	52	F	for 6 months de- scribed as burning, impaired general status	CXR	NM	Well-limited, fluid density cystic lesion	NP	RCPA	NM	Symptomatic cyst and uncertain diagnosis	5 w AT via CT: tubercu- loid adenitis (+chest pain
Kang et al.	2010	1	49	М	Pain on the right hemithorax for 2 days, after physical exertion, worsened with movement and during inhalation	CXR	-Pul- monary embolism -PPC after CT	Well-defined, ovoid cyst filled by fat tissue and dense linear structures in its mid-anterior view ("whirl sign": torsion)	NP	RCPA	17x12,5	Symptomatic and complicated with torsion cyst	
Nitu et al.	2017	1	52	F	Chronic cough, night sweats, progressive exertional dyspnea, weight loss, pallor and diminished breath sounds on the L lower lung area.	CXR	Encysted pleurisy	Encysted pleural effusion	NP	LCPA	5x8	Initial size and possible compli- cations (but the patient refused surgery)	6 mo AD via CT: no growth of the remain- ing cyst
Bois- serie-Lac- roix et al.	1988	1	45	М	NM	CXR	Broncho- genic cyst or PPC	Rounded mass of water density	T1: intermedi- ate signal indensity, T2:increased signal indensity	R Latero-tra- cheal position	NM	RIsk of fissur- ation	NM
Sandeep Krishna Nalabothu et al.	2015	1	43	М	Exertional dyspnoea, pain in the R anterior chest	CXR	NM	Cystic mass	NP	RCPA	8x6	None	"regulargly" (NM)
Arthur et al.	1997	1	66	М	Intermittent chest discomfort unrelated to exertion for sev- eral mo, bilateral 2+ pitting pedal edema, hypertension, 3/4 systolic murmur and RBBB without RVH	TTE	NM	NP	Irregular mass of muscle density compressing the free wall of RV	Mass adjacent to the heart anteriorly	10x6	Symptomatic cyst and uncertain diagnosis	1 mo AT via TTE: no RV outflow trac- obstruction along with resolution of symptoms and clinical signs
Prachi et al.	2006	1	61	F	Asymptomatic	CXR	PPC	Well-defined, unilocular cystic mass adjacent to IVC and attached to the pericardi- um by a pedicle	NP	RCPA	NM	None	3 mo AD via CT: migration of PPC in the interval into the right ma jor fissure
Ochsner et al.	1966	11	NM specif- ically	NM spe- cifi- cally	10/11: Asymptomatic 1/11: Dyspnea and frequent episodes of substernal pain	CXR	NM	NP	NP	Symptom- atic cyst: RCPA Other cysts: NM	Symptom- atic cyst's diameter: 12 Other cysts' size: NM	1/11: Symptomatic cyst	-NM specif- ically -Generally: no recur- rence
Parienty et al.	1984	1	13	F	Asymptomatic	CXR	PPC	Homogeneous mass with low at- tenuation and no contrast uptake	NP	RCPA	NM	Growth of the cyst (observed after 12 y)	Lost to follow up for 12 y. 1 y AT (26 y old) via CXR: normal
Juneja et al.	2017	2	A,B: 65	A,B: F	A: Non productive cough, exertional dyspnea and R sided dull aching chest pain B: Persistent non productive cough for 1 y	A: TTE B: CXR	A: Encysted empyema B: D/D: 1.Cardio- megaly 2.L pleural effusion 3.L lower lobe mass	A,B:Fluid density lesions without significant con- trast uptake (B:large and well-defined)	A,B: NP	A: RCPA B: LCPA	A: 7x4x1,5 B: 10x3.4x5.5	A:NM (but the patient refused surgery) B: NM (but the surgery was deferred in view of the high risk)	A,B: NM
Swain et al.	2016	1	68	М	Hoarseness for 2 mo, L vocal cord paralysis (= L RLN paralysis)	Neck and thorax CT	Giant PPC	Giant, smooth ovoid mass with a thin, slightly high- er density wall and low density contents	NP	LAM (+ middle me- diastinum) extending downwards from the tho- racic inlet	NM	Symptomatic and complicated cyst	6 mo AT via NM method (completely asymptomat ic patient)

Mitu et al.	2017	1	71	F	Palpitations, vertigo, impaired general status, altered mental status, amnesia, hypotension, SR with extrasystoles	Abdomi- nal Ultra- sound	PPC	Oval, well defined, homogenous lesion without contrast uptake and signs of local aggresiveness	NP	Retrocar- diac in relation to IVC and esophagus	3x2.5	None	NM
Lozano et al.	2010	1	62	М	Asthenia, anorexia, itchy and dry cough, retrosternal pressure. Complicated with progressive dyspnea, orthopnea, oppressive chest pain (cardiac tamponate)	CXR	PPC	Thin-walled cyst, partial atelec- tasis	NP	LAM adjacent to the border of the heart and large vessels	12.1 × 10.1 ×14	Symptomatic and compli- cated cyst (hemodynamic instability)	NM
Adil et al.	2010	1	68	M	Dyspnea NYHA I associated with stridor (airway compression) and chest pain in the left upper thoracic wall for 3 mo	CXR	PPC	Large well-de- fined cystic mass, adjacent to the aortic arch, pulmonary trunk and L pulmonary artery and push- ing the L lung downwards	NP	LCPA extending superiorly to the apical pleural cavity and medially to the lung hilum	9x7x8	Symptomatic	1 mo AT via CXR: normal
El Ham- moumi et al.	2014	1	35	М	Moderate dyspnea for 4 months associ- ated with fever and mucous excretions	CXR	NM (opaci- ty of water density)	Pericardial effusion in a tick-walled cystic cavity	NP	Right para- tracheal region	NM	Symptomatic and complicated with cardiac tamponade cyst, uncertain diagnosis and pre- vention of further complicatons	1 mo and 8 mo via CT: complete recovery and no recur- rence
Bava et al.	1998	1	8	М	Chest pain, muffled cardiac tones, sinus tachycardia (110bpm), slight ST-segment eleva- tion in inferior and anterior leads	TTE	PPC	NP	Pedunculat- ed pericar- dial mass originating in the upper mediasti- num	LCPA	9x10	Uncertain diag- nosis and onset of signs of cardi- ac tamponade	4-year AT follow up via CXR and TTE: no recurrence
Yeste et al.	2017	1	51	М	Fever, arthralgia and weight loss	CXR	Infected PPC	Mass consistent with infected embryonic remnants	NP	LAM (+ middle mediasti- num)	9x7	Symptomatic and complicated with infection cyst, unusual anterior position	NM
Smahi et al.	2010	1	54	F	Exertional dyspnea and chest pain	CXR	PPC	Dumbbell shaped cystic mass surrounding the heart and great vessels	NP	Located bilateral in superio-an- terior and middle mediasti- num	-R portion: 14x9,5x15 -L portion: 8x4x12	Symptomatic and large-sized cyst	6 mo AT via (probably) CXR: No recurrence
Porti- llo-Carroz et al.	2006	1	55	F	Chest pain	CXR	PPC	Cystic lesion with no definable wall and no contrast uptake	NP	RCPA	Largest di- ameter: 6	None	NM mo AD ("regularly") via TTE: no significant findings
Beroukhim et al.	2011	1	5	M	NM	NM	NM	NM	Smooth- walled and well-defined cyst with heteroge- nous appear- ance, T1, T1 + fat sat, MDE: Iso/Hypo-in- tense FPP: Hy- pointense SSFP: Hyper- intense T2: strongly hyperintense	RCPA	Largest dimension: 6.3	NM	NM

Chaturvedi et al.	2017	1	3	F	Fever, Swelling all over the body (ana- sarca), pallor, tachy- pnea, tachycardia, firm hepatomegaly	CXR	Fulminant hepatic failure	Cyst missed. Only suggestive of a large pericar- dial abscess	NP	Arround the pericar- dium	NM	Persistent symptomatology	NM
Francese et al.	1991	1	41	М	NM (history of thy- roid papillary Ca)	Post-ther- apy radioio- dine TBS	Metastatic lymph node	Performed but the results are NM.	Abnormal retrosternal mass	L precordial region	3.5x5.5	Exclusion of metastasis	NM
Changping Jia et al.	2014	1	76	F	NM (history of thy- roid follicular Ca)	Post-ther- apy radioio- dine TBS	-NM initially (probably metastasis) -PPC after CT	Round, well-de- fined cyst-like soft tissue nodule	NP	RCPA	1x1.5	None	NM mo AD via CT and radioiodine TBS: no change
Hermens et al.	2001	3	A:35 B:43 C:71	A:M B,C: F	A: Chest pain for several years B: NM (probably nothing associated with the mass) C: Paroxysmal col- lapse, SVC syndrome	A,B,C: CXR	A:A cyst B:PPC C: Ret- rosternal goitre	A:Homogeneous content and water density B: Cystic forma- tion C: Large cystic formation with water density	A,B,C: NP	A: LCPA B: RCPA C: R para- tracheal position	Maximal diameter: A: 9.5 B: 9.8 C: 10	A,C: symptomat- ic cyst B: NM	A: 3 mo AT B: 48 mo AT C: 22 mo AT A,B,C: via CXR A,B,C: No recurrence
Mouroux et al.	2003	4	A: 37 B: 37 C: 51 D: 22	A: F B: F C: F D: H	A: Dyspnea B: Hypochondriac pain C: Fever D: Asymptomatic	A,B,C,D: NM	A,B,C,D: NM	A,B,C,D: NM	A,B,C,D: NM	A: RCPA B: RCPA C: LCPA D: LAM	A: 6x3 B: 15x6 C: 6x4 D: 5x5	A,B,C: symptom- atic cyst D: unusual location	NM
Lang-Laz- dunski et al.	2008	1	72	F	NM	NM	NM	NM	NM	NM (According to imaging: RCPA)	Diame- ter: 9	NM specifically	21 mo AT via NM method: no recurrence
Melfi et al.	2012	9	NM specifically	NM spe- cifi- cally	NM	NM specifically cally (In general CXR and CT was used as pre-operative evaluation)	NM specifically	NM	NM	NM specifically	-NM spe- cifically -Mean diameter of all included medi- astinal lesions: 3.1 Ranging from 1.6 to 4.2	NM	3 mo AT via CXR and 6 mo and 12 mo AT via CT: No recur- rence
Depart- ment of Veterans Affairs	2008	1	NM exactly	М	Asymptomatic (psychiatric patient)	NM	NM	NM	NM	NM	NM	NM (BUT the patient refused surgery)	NM
Mabille et al.	1980	1	NM	NM	Sudden onset of uni- lateral chest pain	CXR	PPC	NM	NP	NM	NM	Symptomatic cyst	NM
Khan Arfa	2005	1	NM	NM	NM	CXR	NM	Performed but results are NM	NP	NM (According to imaging: LAM + superior mediasti- num)	NM	NM	NM
Verslegers et al.	2012	2	NM	NM	NM	Breast MRI	NM	NM	T2: high sig- nal intensity	NM	NM	NM	NM
Halkic et al.	2002	1	67	М	Exertional dyspnea, dry cough and signs of left-sided pleural effusion	CXR	PPC	Extracardiac mass filled with fluid		Left peri- cardial	9x7	Symptomatic cyst	6 w AT via CXR: normal, asymptomat- ic patient
Ubeda et al.	2009	1	72	F	Increasing dyspnea for 2 mo, typical chest pain with effort, lower limb edema, jugular venous distension, pulmonary rales, 3cm hepatomegaly and atrial fibrillation	TTE	-Heart failure -PPC after CT	Giant PPC collapsing LV, RA and surrounding parencyma	NP	NM (ac- cording to CT images: dumbbell shaped sur- rounding the heart)	NM ("gi- ant")	Symptomatic cyst	NM

Pun et al.	2002	6	NM	NM	NM	NM	NM	NM	NM	NM	NM	NM (athough all resected)	NM
Traibi et al.	2012	3	NM specif- ically	NM	NM specifically	-NM spe- cifically -1/3 cases: CXR	NM	-NM specifically -1/3 cases: Cystic mass	NP	-NM specifically -1/3 cases: RCPA	NM specif- ically	-NM specifically -Uncertain diagnosis and symptomatic cyst generally	-NM specif- ically -3/3: No recurrence
Bacha et al.	2015	1	50	М	Chest pain for 2 years	СТ	NM	Cystic lesion	NP	Left supe- rio-posteri- or mediasti- num	Maximum diameter: 3,7	Uncertain diagnosis, atypical location and symptomatic cyst	3 y AT: as- ymptomatic patient
Eleftheriou et al.	2019	1	37	F	Dyspnea, Palpitations	CXR	Interme- diate pneu- monia	Cystic lesion (PPC) without pathologically enlarged lymph nodes and pleural effusion	NP	RCPA	5,5x5x 6cm	None	5y AD: as- ymptomatic patient

Table 2: All reported complications in the literature divided into 3 categories (complications due to compression, inflammatory and other complications).

References	Compression of adjacent structures	Inflammatory complications	Other complications
Koch et al., Shaver et al.	Cardiac compression		
Martins et al., Shaver et al., Lesniak-Sobelga et al.	Cardiac compression of right side of heart with deviation of septum		
Kruger et al.	Diastolic dysfunction, congestive heart failure, mitral valve prolapse		
Antonini-Canterin et al.	Pulmonary artery stenosis, ventricular outflow tract obstruction, cardiogenic shock		
Bandeira et al., Borges et al., El Hammoumi et al.	Cardiac tamponade		
King et al., Padder et al.	Cyst intra-pericardial rupture		
Elatiqi et al.	Spontaneous (because of quick expansion) or post-traumatic intra-cystic hemorrhage		
Kang et al., Bava et al.	Torsion of the cyst's intrapericardial pedicle		
Davis et al.	Lung compression and more specifically right main stem bronchus obstruction		
Forouzandeh et al., Luketich et al.	Atelectasis and obstructive pneumonia		
Blegrad et al.	Airway compression		
Blegrad et al., Kaul et al.	Obstructive syndromes include superior vena cava syndrome		
Arghir et al.	Azygos vein syndrome, thoracic duct syndrome and inferior vena cava compression		
Hoque et al., Yeste et al., Chopra et al., Mastroroberto et al.		Cyst infection or inflammation with or without erosion of the cyst into adjacent structures, such as the right ventricular wall or the superior vena cava	
Komodromos et al.		Sepsis, pericarditis	
Ilhan et al.			Pleural effusions, recurrent syncope
Vlay et al.			Atrial fibrillation
Fraser et al.			Mesothelioma
Fredman et al.			Sudden death

of malignant degeneration have been reported in the literature. However, cases of concomitant neoplasias and PPCs and even PPCs infiltrated by neoplasias in the context of tumor progression have been described⁶⁵. Self-resolution of a PPC probably due to rupture has also been reported in a few cases^{14,61,66-69}.

Complications

The mediastinum is a narrow non-extendable space. Consequently, every mediastinal mass, including PPCs, can compress adjacent organs and this can even occasionally lead to complications as well as life-threatening emergencies 9,14,37,58,64,70,71.

Diagnostic approach-Differential diagnosis

The diagnostic approach to PPCs is based on the clinical presentation and the results of imaging studies. However, the fact that PPCs may be clinically and radiologically similar to other mediastinal lesions makes the diagnosis challenging. The location and nature of mediastinal lesions are very important for the differential diagnosis. Differential diagnosis of PPCs is quite wide and includes not only lesions found in the middle mediastinum where PPCs are most commonly identified, but also lesions occurring in the other two mediastinal compartments 9,11,29,72-76.

A CXR can localise as well as identify PPCs by means of posterior-anterior and lateral views. However, a disadvantage of this method is the fact that it cannot provide much information about the morphology and the expanse of the lesion. Further imaging studies such as MDCT, MRI, ultrasonography, angiography and positron emission tomography (PET) scan are used in order to complement and corroborate the initial diagnosis or suspicion^{40,58,77}.

With CXR, PPCs are demonstrated as teardrop formations on the lateral views as the cysts tend to adjust to the medial aspect of the pulmonary fissure. Furthermore, this projection can depict the alteration in shape and the movable nature of fluid-filled PPCs, during respiration or postural changes^{41,51,64,78,79,80}. In postero-anterior projection, PPCs usually appear as rounded or oval opaque shadows with uniform density and well-defined borders and without calcification⁷⁷. PPCs can also take on different and unusual radiologic appearances, such as a dumbbell shape^{20,28,81}.

MDCT with or without contrast remains the gold standard for further investigation of a mediastinal mass¹⁴.

It estimates the size and nature of the mass, defines its position within the mediastinum and how it is related to the adjacent structures, providing valuable information about its morphology as well as its extent82,83. On a CT scan, the PPC is a thin-walled, well-marginated, oval homogeneous mass, usually unilocular, while multilocular cysts have also been reported⁸. Their attenuation is low (0-20HU), although sometimes it may be a little higher than water density (30-40 HU). This is probably because of a high protein and cells content due to bleeding or infection84. As they are commonly avascular²⁵, they are not enhanced with contrast agents^{46,85}. Other atypical CT findings include the presence of calcification, a sharp upper border^{25,44,86} and the presence of associated pericardial effusion. Moreover, MDCT can show stalks connecting PPCs to the pericardium, thus a certain diagnosis can be established even for PPCs in unusual locations^{48,87-93}. PPC torsion can also get depicted via a CT scan as a mass of soft tissue in which there is an internal intertwine with fat and soft tissue attenuation, called the "whirl sign" which was first described in intestinal volvulus^{28,94,95}.

Two-dimensional echocardiography was first used in order to detect a pericardial cyst⁹⁶. Transthoracic and in some cases transoesophageal echocardiography is a superior noninvasive method, which can accurately depict the PPC's position and distinguish it from other possible diagnoses (solid tumours, fat pads, coronary, ventricular or aortic aneurysms)^{14,20,96}. Ultrasonographically PPCs appear typically as homogeneous anechoic thin-walled masses^{29,67}. Transoesophageal echocardiography can be helpful especially for PPCs in unusual locations and in case of haemodynamic compromise in order to confirm a

Table 3: Differential diagnosis of PPCs including lesions that can be found in any mediastinal compartment, as particularly for large lesions it may be difficult to define their origin.

1. Congenital cysts of primitive foregut origin (bronchogenic cyst, enterogenic cyst and esophageal duplication cysts)	17. Lymphomas
2. Broncial cysts	18. Mesenchymal tumors (sarcomas ⁴⁴ , hemangiomas and lymphangiomas ¹³³)
3. Localised pericardial or pleural effusion ⁹	19. Right middle lobe pathology
4. Ventricular aneurysms or aneurysms of the ascending aorta	20. Morgagni hernia
5. Fluid-filled superior aortic recess ¹³⁴	21. Hiatus hernia
6. Prominent left atrial appendage	22. Diaphragmatic hump
7. Varicose pericardial vein ¹³⁵	23. Diaphragmatic tumors
8. Epicardial fat pad	24. Cystic degeneration of mediastinal tumors ¹³³
9. Lipoma	25. Metastatic and bronchogenic carcinoma ⁴⁴
10. Hydatid heart disease / Echinococcal cysts	26. Granulomatous lesions ⁴⁴
11. Thymic masses (thymic cyst, thymoma, thymolipoma, thymic lymphoma, thymic carcinoid)	27. Mediastinal abscesses ⁴⁴
12. Thyroid diseases (retrosternal goiter, thyroid adenoma)	28. Thoracic duct cysts ^{136,137}
13. Parathyroid cysts (very rarely)	29. Neurogenictumors (neurofibroma, cysticschwannoma)
14. Germ cell tumors (dermoid cyst, mature teratoma, malignant teratoma, seminoma)	30. Meningoceles ^{104,137}
15. Hattori's cyst / Mullerian cyst ¹³⁸	31. Mediastinal located pancreatic pseudocyst
16. Enlarged lymph nodes with cystic necrotic degeneration 133,139	
10. Emarged lymph flodes with cystic fleerotic degeneration	

suspected compression of the large vessels or the cardiac cavities^{97,98}. Finally, ultrasonography can set the diagnosis of PPCs prenatally beyond the 14th week of gestation⁹⁹.

MRI is similar to CT as far as the efficacy in detecting a tumour is concerned¹⁰⁰. MRI is a useful tool for both the initial diagnosis of a mediastinal mass and the posttherapeutic follow-up. It gives a better anatomical depiction of PPCs, including those in atypical locations and their relationships to adjacent structures, including blood vessels, without the use of contrast material²⁰. Thus, it is helpful in differentiating PPCs from vascular anomalies such as aortic aneurysms^{37,101,102}. MRI findings are diagnostic, showing a smooth-walled and well-defined structure with high signal intensity on T2-weighted images, low-to-intermediate signal intensity on T1weighted images and no enhancement after intravenous contrast administration^{85,93,103,104}. High signal intensity is rarely seen on T1-weighted images in the case of high protein content²⁰. Furthermore, MRI should be the method of choice with children and infants¹⁰⁴.

Arteriography provides help in defining whether the lesion in question is a part of a vascular structure ¹⁰⁵. In cases where diagnosis remains challenging, cyst puncture and sequent injection of a contrast material for diagnostic and therapeutic reasons has been used ¹⁰⁶. Finally, two incidentally detections of PPCs by means of I ¹³¹ total body scan due to the uptake of I ¹³¹ through the pericardial serosa have been reported ^{107,108}.

Therapeutic approach

The management of all mediastinal cysts can vary from conservative follow-up, percutaneous aspiration with or without ethanol, minocyclin or doxycyclin injection to surgical treatment by means of interventional thoracoscopy $or thoracotom y^{43,109,110,146}. PPCs are commonly asymptomatic\\$ and most of them can be left without treatment. So, in the case of an asymptomatic patient and undoubted radiological diagnosis of a PPC, conservative management with cautious follow-up by means of non-contrast-lowdose CT or ultrasound or MRI is advised^{38,70,98,111}. Although there are no specific guidelines concerning either the duration or the frequency of the follow-up and the information about safety is poor, it is widely suggested to take into consideration the patient's (new symptoms, complications) as well as the cyst's (size) stability in order to decide how to continue the management. The longest described follow-up lasted 25 years and eventually a 2.5L cyst was resected⁵². Treatment is indicated in the case of symptomatic, large-sized asymptomatic cysts, uncertain diagnosis and possibility of malignant potential, atypical location such as close to large vessels, high density on CT, or the presence of complications. Such treatment is required in order to prevent life-threatening emergencies such as

airway and/or haemodynamic impairment, or patient's concern^{23,32,40,41,112-114}. Thus, any anterior mediastinal lesion should be considered potentially malignant and should be surgically excised as soon as possible¹¹⁵.

Surgical excision of the cyst has been considered the gold standard of management especially in complicated cases with excellent outcomes 98,116. It is worthy noting that although cardiopulmonary bypass is not usually required for PPCs removal, it should be on standby, mainly in case of possible cardiac compression, erosion of the right ventricular free wall or if extensive cardiac manipulation is required⁴¹. Partial cyst resection is also recommended in the case of tight adhesions to the nearby structures¹¹⁶. Apart from traditional open surgery, resection of mediastinal masses including PPCs has been carried out successfully by VATS or VATS with mini-thoracotomy since 1992^{26,32,111,117-122}. These minimally invasive procedures reduce surgical trauma and postoperative pain compared to open surgery leading to a shorter period of recovery and hospitalisation^{123,124}. Furthermore, the Harmonic Scalpel which is an ultrasonically activated scissor, is recommended for performing VATS more quickly¹²⁵. However, VATS also has limitations especially for removing anterior and upper mediastinal lesions^{4,122,126-128} giving only a limited view of the area of interest. In addition, thoracoscopy should be an option for treatment only in the case of well-encapsulated and <6cm sized masses, although successful resections via VATS on larger ones have been reported^{52,111,126}. Robotic surgery using the da Vinci™ Robotic System is another minimally invasive therapeutic modality which has proved to be safe and useful, but its cost remains a strong limitation¹²⁹. Taking into consideration the above, smallto-moderate sized and typically located PPCs could be safely and successfully removed by these modern surgical procedures.

Percutaneous aspiration of the PPC contents by a thin needle puncture under ultrasound or CT guidance has been used for both diagnosis and therapy^{12,84,106,110}. However, complications such as vascular injury, pneumothorax, anaphylaxis, and infection have been referred and recurrence in about one third of patients has been recorded^{57,110,130-132}. Thus, percutaneous aspiration of such cysts must be performed only in case of comorbidities that contraindicate surgery, when there is a need for temporary decompression before the removal of a large symptomatic cyst^{9,12,133}, when there is a suspicion of a tubercular PPC in order to confirm the diagnosis preoperatively¹³ or when a patient refuses surgery.

To sum up, the management of PPCs is based on an algorithm. The cyst's size, shape and compressibility along with clinical presentation and the patient's fitness and preference should be taken into consideration so that the appropriate management can be chosen⁹.

Prognosis

The absence of symptomatology is an indicative sign of good prognosis¹⁴, while post-resection prognosis is excellent with low rates of morbidity and mortality^{87,98}. Only one case of recurrence after excision has been documented⁷⁸.

Limitations

After reviewing the literature and attempting to statistically analyse the data from table 1 we identified the following limitations:

- 1. Regarding the nomenclature and the classification of mesothelial cysts, plenty of terms have been used to describe a PPC. Thus, review references are mostly based on the terms "pericardial" and "pleuropericardial" and the inclusion criteria are mentioned in "Methods". That may have affected our results as some cysts which are referred to with a different term have been excluded.
- 2. We had to exclude many cases from the pool of PPCs as there were not specific data with regard to the examined parameters.
- 3. We chose to calculate the mean maximal diameter as an objective measurable feature of size. However, our result concerning this parameter may be biased and overestimated, given that our pool of cases of cysts with known size consisted mainly of symptomatic cysts (30 out of 42 patients) which are generally supposed to be larger.

Conclusion - Recommendations

PPCs are rare and usually clinically silent, but can occasionally cause life threatening complications. The majority of them are congenital due to developmental deficits and are most commonly found incidentally via routine radiography between the third and fifth decade of life. In this study, we found out that the mean age of initial detection is roughly 48.7 years, the mean maximal diameter is 8.3 cm and the female:male ratio is approximately 3:2, which is in line with the literature. The RCPA constitutes the most common location, according to our statistical analysis.

MDCT is recommended as the method of choice in all cases, while cardiac MRI can be useful when diagnosis is more challenging.

The management algorithm of PPCs can be divided into two main categories, based on whether there is symptomatology or not. The presence of symptoms depends on the cyst's size and eventual compression of the mass.

1. In the case of a small asymptomatic PPC that does not cause compression, follow-up with serial transthoracic echocardiography is recommended.

2. Apart from the symptomatic and/or complicated and/or large PPCs, surgery is also recommended in the case of an initially asymptomatic PPC which grows in size. This is in order to prevent complications and life-threatening emergencies. The patient's concern constitutes a relative indication for surgical management⁹.

Surgical resection by means of traditional open surgery or minimally invasive methods is considered to be the gold standard, and this along with percutaneous aspiration are the methods that have mostly been used. Percutaneous aspiration and ethanol sclerosis is recommended for large symptomatic PPCs while the patient is waiting for surgery.

List of abbreviations used

PPCs: Pleuropericardial cysts; CXR: Chest X-ray; MDCT: multi detector Computer Tomography; CT: Computed Tomography; MRI: Magnet Resonance Imaging; ER: Emergency Room; VATS: Video-assisted thoracoscopic surgery.

Authors' contributions

Andreas Eleftheriou, Nikolaos Saridakis and Christina Koumantzia were the major contributors in writing the manuscript.

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