

The postpneumonectomy syndrome: clinical presentation and treatment[☆]

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Abstract

Background: Postpneumonectomy syndrome (PPS) is a rare complication after pneumonectomy. It consists of an excessive mediastinal shift resulting in compression and stretching of the tracheobronchial tree and the esophagus. The aim of this study was to give a comprehensive overview of diagnosis, variety of symptoms and evaluation of surgical treatment of PPS. **Methods:** We retrospectively reviewed the charts of all our patients with PPS since 1994 with respect to symptomatology, treatment and outcome. Our results were compared with case reports and case series in the literature. **Results:** Six women with a median age of 56.5 years (range 49–65) developed PPS after pneumonectomy for the treatment of lung cancer. Four presented with a right PPS and two with a left PPS, respectively. Symptoms consisted of shortness of breath in all patients and dysphagia as well as heartburn in two patients. Correction of PPS required re-exploration of the pneumonectomy space, reposition of the mediastinum followed by the insertion of single silicone prosthesis in five patients or fixation of the mediastinum with a xenopericardial graft in one patient. We could observe an improvement of the FEV₁/FVC ratio in all our patients and the clinical improvement of shortness of breath was better than we expected by changes of lung function. Four patients returned to their regular activities with a follow-up of four years. We found 73 cases of PPS in the literature, on the right side in 50 patients (68%) and on the left side in 23 patients (32%). Fifty-nine patients (81%) were treated surgically. Symptoms can be suspicious for cardiogenic origin and vary from heartburn to recurrent syncope. **Conclusion:** PPS is rare and not predictable. It can occur after right or left pneumonectomy. Symptoms are manifold and result from a shift, leading to compression and stretching of the two conduits located within the mediastinum, the tracheobronchial tree and the esophagus and consists of shortness of breath, stridor and heartburn. Diagnosis must be made by exclusion. Implantation of prosthesis is the most commonly used and effective treatment.

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1. Introduction

The term postpneumonectomy syndrome (PPS) was introduced by Wassermann et al. in 1979 [1]. We found only 73 cases of PPS in adults by an extensive search in the English literature from 1979 to 2007 [1–21]. The first report of tracheobronchial compression after a pneumonectomy was of a 6-year-old boy in 1972 [5].

PPS is a rare complication after pneumonectomy, due to an excessive mediastinal shift resulting in an eventual impairment of structures located within the mediastinum. After right-sided pneumonectomy, the left main bronchus

may be stretched over the descending aorta and the lower lobe bronchus will be kinked over the descending aorta. The mechanism of functional impairment after left sided pneumonectomy is less clear, except in patients with a right aortic arch. PPS occurs more often in children than in adults [22]. Patients with PPS typically complain about progressive dyspnea on exertion and stridor, eventually followed by respiratory failure or tracheomalacia. Diagnosis is based on computed tomography (CT), bronchoscopy and pulmonary function tests (PFT). Other conditions such as pulmonary embolism, recurrences of lung cancer or progressive chronic obstructive pulmonary disease (COPD) have to be excluded. We compare the reports of PPS of the last 28 years and our own experience in six patients with PPS after pneumonectomy since 1994. We present additional anatomical features and discuss the pathophysiologic mechanisms and the challenge of diagnosis and therapy.

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Table 1
Clinical features and surgical therapy in patients with postpneumonectomy syndrome.

Patient nr.	Age/sex	Cancer type and stage	Year and site of pneumonectomy	Onset of symptoms in months after pneumonectomy	Symptoms	Therapy	Outcome and follow-up
1	49/f	Large cell carcinoma, Stage IIA	1986 Right lung	6	DYP, STR, ARD, DYS, HB, WL	Implantation of a 420 ml silicone prosthesis	Asymptomatic, 4 years
2	52/f	Adenocarcinoma, stage IIIB	2001 Right lung (after IC)	12	DYP, STR	Implantation of a 325 ml silicone prosthesis	Asymptomatic, 4 years
3	65/f	Bronchioalveolar carcinoma, stage IA	2002 Right lung	6	DYP, STR	Implantation of a 325 ml silicone prosthesis	Asymptomatic, 4 years
4	56/f	Squamous cell carcinoma, stage IIIA	2006 Right lung	10	DYP, STR	Pericardial mediastinal fixation with a vertebro-sternal pericardial patch	Removal of the patch 5 months later due to infection, 1 year
5	58/f	Large cell carcinoma, stage IIIB	2002 Left lung (after IC)	12	DYP, STR, DYS, HB	Implantation of a 305 ml silicone prosthesis	Asymptomatic, 4 years
6	57/f	Adenocarcinoma, stage IA	2004 Left lung	12	DYP, HOA	Implantation of a 325 ml silicone prosthesis	Recurrent bronchial infections, 2 years

DYP: dyspnea; STR: stridor; ARD: acute respiratory distress; DYS: dysphagia; HB: heartburn; WL: weight loss; HOA: hoarseness; IC: induction chemotherapy.

2. Methods

An electronic search of the Medline database was performed using different key words that covered selected topics of PPS. The search terms were identified in the title, abstract or medical subject heading. Publications about PPS in children and in languages other than English were excluded. We retrospectively reviewed the charts of all our patients with PPS since 1994 with respect to symptomatology, treatment and outcome.

3. Results

3.1. Patients

From 1994 to 2006 we observed and treated six patients for PPS. The clinical features, type of treatment and outcome are summarized in Table 1. All were women. Five patients were treated from 2001 to 2006. In the same period we performed 250 pneumonectomies. Therefore, the incidence of PPS was 2%.

The median age of these six patients at time of pneumonectomy was 56.5 years (range: 49–65 years). Two patients underwent a pneumonectomy for a stage IIA and IIIB bronchial carcinoma, respectively (one on the right and one on the left side). Two patients had a right side sleeve pneumonectomy for a stage IIIA and IIIB bronchial carcinoma, respectively. Two patients had to undergo a completion pneumonectomy for the treatment of a second primary bronchial carcinoma 18 months and 48 months after a lobectomy (one on the right and one the left side). Four patients developed a right and two a left PPS. All patients complained about increasing shortness of breath on exertion. One patient needed assisted invasive ventilation. She had lost 7 kg within 3 months due to dysphagia. Another patient complained about increasing heartburn. One patient with hoarseness was seen and transferred by an ear-nose-throat specialist with the diagnosis of left recurrent laryngeal nerve palsy one year after pneumonectomy. The median time to

onset of symptoms after pneumonectomy was 11 months and ranged between 6 and 12 months. The median time period between pneumonectomy and correction of PPS was 30 months (range: 10 months–8 years).

PPS was treated by repositioning the mediastinum and implantation of silicone prosthesis in four patients. In one patient the mediastinum was fixed after reposition with a pericardial patch running from the spine to the sternum. The implantation of prosthesis was not necessary. Unfortunately, an infection of the pericardial patch occurred and the patch had to be removed 5 months later. One patient was treated with an adjustable tissue expander. Since this expander developed a leakage four years later it was replaced by silicone prosthesis. None of the patients developed a postoperative complication and all were discharged after a median hospital-stay of seven days (range 6–20 days).

Pulmonary function tests were performed before and 3 months after correction of PPS and improved impressively in all patients with a right-sided PPS. However not surprisingly the pulmonary function test did not improve clearly in patients after left-sided PPS, despite a distinct clinical benefit after surgery (Table 2). Four of the patients became asymptomatic. One patient suffered from recurrent bronchial infections. She was unable to quit heavy smoking. The patient with the infected pericardial patch complained about mild shortness of breath during exercise. The CTscan showed no tracheobronchial compression in any patient with left-sided PPS.

3.2. Summary of cases reported in the literature

Seventy-three cases of PPS in adults have been reported in the English literature [1–21].

3.2.1. Demographics

At onset of symptoms, the median age of the patients was 41 years and ranged from 18 to 75 years. The median interval between pneumonectomy and onset of symptoms was 2 years (range 1 month–49 years). The ratio between men to women was 1 to 1.4.

Table 2
Spirometry before and 3 months after correction of postpneumonectomy syndrome.

PPS	Preoperative					Postoperative				
	FEV ₁	Predicted (%)	FVC	Predicted (%)	FEV ₁ /FVC	FEV ₁	Predicted (%)	FVC	Predicted (%)	FEV ₁ /FVC
Right	0.80	31	1.50	50	0.53	1.30	50	2.21	75	0.59
	1.11	38	2.06	61	0.54	1.52	53	2.70	76	0.56
	1.46	68	1.85	72	0.79	1.74	81	1.85	72	0.94
	1.30	48	2.26	71	0.58	2.30	82	3.42	104	0.67
Left	1.78	83	2.24	88	0.79	1.87	87	2.34	88	0.80
	1.47	64	2.34	86	0.63	1.32	49	1.91	70	0.69
Mean	1.32		2.04		0.64	1.68		2.41		0.71

3.2.2. Clinical findings

Adequate clinical data were reported in 58 patients (79%). All patients had undergone pneumonectomy. A right PPS had developed in 50 patients (68%) and a left PPS in 23 patients (32%), respectively. In 38 patients (52%) the underlying disease was a malignant tumor in the lung, three patients suffered from histoplasmosis, four patients had a trauma, and six patients underwent a pneumonectomy due to a hypoplastic lung. The remaining 22 patients had various diagnoses or the underlying disease has not been reported. Six of the 23 patients with left PPS had a right aortic arch.

3.2.3. Treatment and outcome

Fifty-nine patients (81%) were treated surgically. In four patients a tracheobronchial stent was inserted. An additional patient had a temporary stenting before surgical treatment. One patient had a sulfur hexafluoride injection into the pleural space. In two patients the treatment was not reported and seven patients were not treated for PPS.

The surgical treatment consisted of reposition of the mediastinum and implantation of fixed volume prostheses (one in 16 patients or more than one in 7 patients) or one or more expandable prostheses (28 patients). The prostheses were implanted either intra- or extrapleural. In one patient an anterior resection of the thoracic vertebral body was performed and seven patients underwent complex surgical reconstruction. The median volumes of the implants (if stated) were 945 ml (range: 200–1950 ml) and up to four implants have been used. In one patient the implantation of a prostheses failed and there was no comment about the outcome of this patient [3].

Adequate information about the follow-up period and outcome was given in 58 patients (79%). The median follow-up was 2 years (range 3 months–6 years). The authors defined the outcome with descriptive terms such as 'well' or 'symptom free' in 41 patients. Four patients died due to operation related complications within 30 days (one pulmonary embolism, one pneumonia, one respiratory failure and one pericardial tamponade, respectively). In 13 patients the cause of death was not related to the operation (metastatic disease in 8 patients, leiomyosarcoma of the stomach, alcohol intoxication, graft failure after lung transplantation, myocardial infarction, or sudden death of unknown reason). Macaré van Maurik et al. reported 19 patients treated by insertion of one to three expandable prostheses. Eight reoperations were necessary due to luxation (1), malposition (2), herniation (1) or leakage (4)

of the expanders respectively [3]. The clinical course was not reported or incomplete in 15 patients.

4. Discussion

We report six patients with a postpneumonectomy syndrome. In all the mediastinum was repositioned and stabilized; in five patients by implantation of a silicone prosthesis, and in one patient the mediastinum was fixed with a pericardial patch running from the spine to the sternum.

From 2001 to 2006 in our hospital 250 pneumonectomies have been performed. We diagnosed PPS in 2% of our patient population. We found one single publication on the incidence

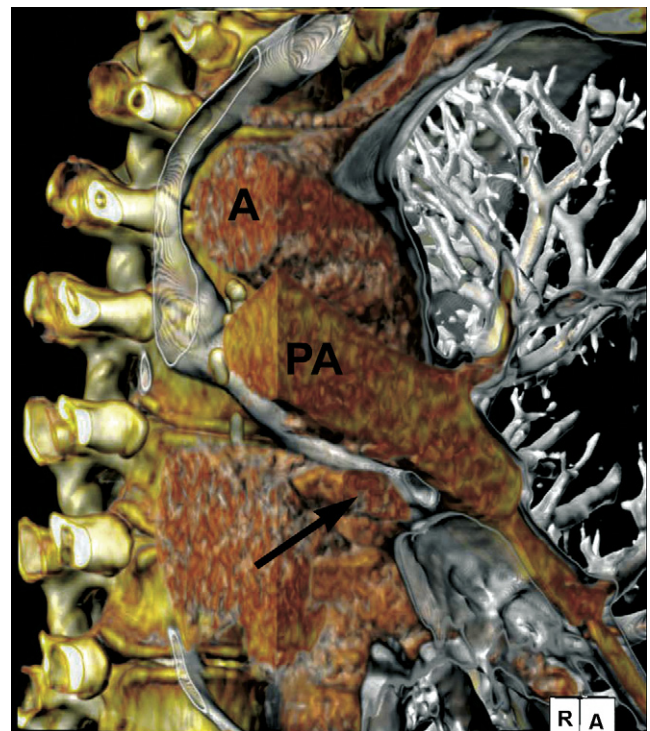


Fig. 1. 3D-reconstruction of CT scan of a patient (nr. 2) with right-sided PPS. The figure displays a slightly angled view from anterior of the patient's vertebrae, main vessel and respiratory tract. R/A indicates the right and anterior plane of the patient. She presented with dyspnea and stridor 1 year after right pneumonectomy. The arrow indicates compressed main bronchus of the left lower lobe between the aortic arch (A) and the left pulmonary artery (PA).

of this complication consisting of a case series from Jansen et al. who reported a single patient with PPS within a period of 18 years comprising 640 pneumonectomies (0.16%) [6]. The reason for our higher incidence of PPS remains unclear, but it is possibly due to under-recognition and under reporting of this complication by others.

4.1. Anatomy and pathophysiology

After pneumonectomy the mediastinum shifts to the site of the removed lung and the lung in the contralateral hemithorax becomes over-expanded. This results in a counter clockwise rotation (when interpreting standard axial CT slides) to the right of the heart and the tracheobronchial tree after right pneumonectomy. The left main stem bronchus becomes stretched and the lower lobe bronchus is kinked over the descending aorta which functions as a hypomochlion (Fig. 1). After left pneumonectomy, the mediastinum shifts to the left hemithorax, which results in a clockwise rotation of the heart and the right main stem bronchus becomes stretched over the anterior vertebral bodies [4,5]. However, the bronchus remains open as seen in CT scan. Not surprisingly the pulmonary function test does not show any major changes after repositioning of left-sided PPS. This is in contrast to right-sided PPS. As postulated by Grillo et al. in 1992 a right aortic arch is a precondition for the development of a left PPS [5], but two of our cases and several cases in the literature with left PPS were reported with a regular aortic arch [3,4,8,9,11,12,16,17,20].

4.2. Clinical presentation

Patients with PPS complain about a slow deterioration of their general condition and an insidious onset of increasing shortness of breath on exertion as well as a stridor that can be heard during inhalation and expiration [1–20].

Additional symptoms due to PPS may consist of heartburn and dysphagia and are due to displacement, and eventually compression of the esophagus [2,4,19]. We observed a palsy of the left laryngeal recurrent nerve in one of our patients, diagnosed one year after pneumonectomy, possibly due to the shift of the mediastinum to the left causing a prolonged traction of the nerve.

Clinical examination may misguide to a cardiovascular problem as the cause of increasing dyspnea. Casanova et al. described a 72-year-old patient with PPS camouflaged by the signs of a cardiogenic shock [23]. Gebitekin and Bayram reported a 21-year-old woman with recurrent syncope after pneumonectomy [20]. Another complication of PPS is tracheobronchiomalacia due to long-term pressure on the involved bronchus [4–6,16].

4.3. Further anatomic changes of the esophagus and the heart

Two patients (nr. 1 and 5) complained about heartburn and dysphagia. The CT scan of one patient (nr. 5) showed a left deviation and a dilatation of the esophagus (Fig. 2) and a dynamic swallowing study with gastrografin performed in the other patient (nr. 1) revealed a right posterolateral deviation

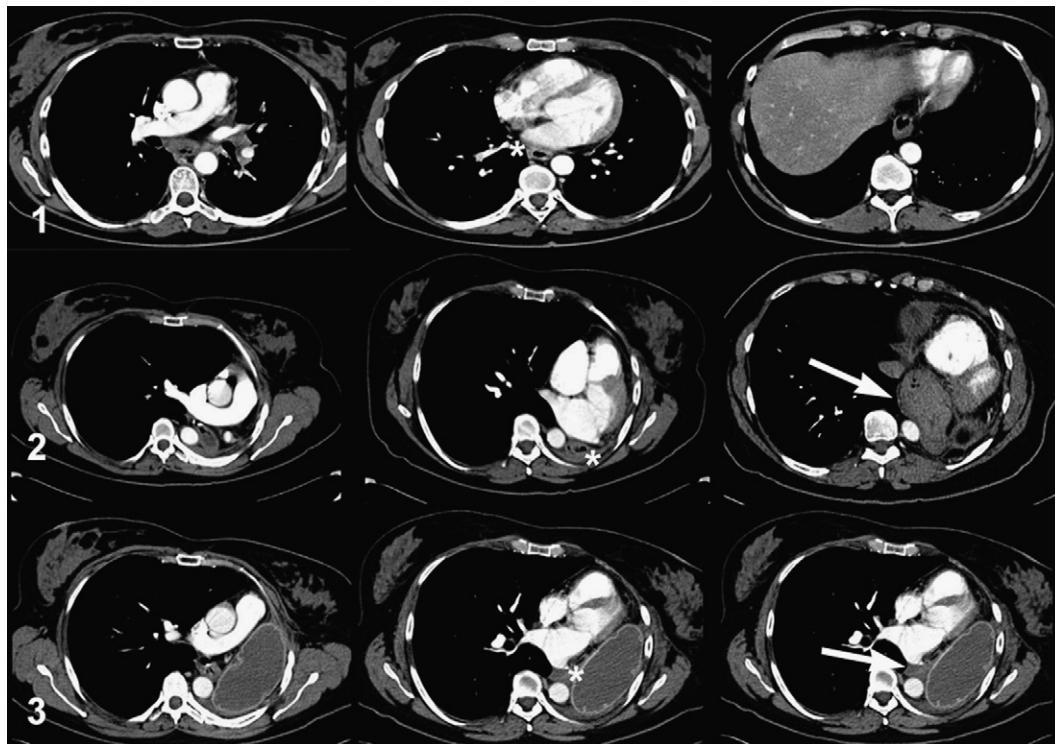


Fig. 2. CT scans of a patient (nr. 5) with left-sided PPS. She additionally complained about heartburn and dysphagia. CT scans before left pneumonectomy (lane 1), 1 year after pneumonectomy (lane 2) and after implantation of a silicone prosthesis (lane 3). The asterisk marks the esophagus on the middle sections. One year after pneumonectomy the esophagus is dilated, degenerating after implantation of the silicon prosthesis (arrow).

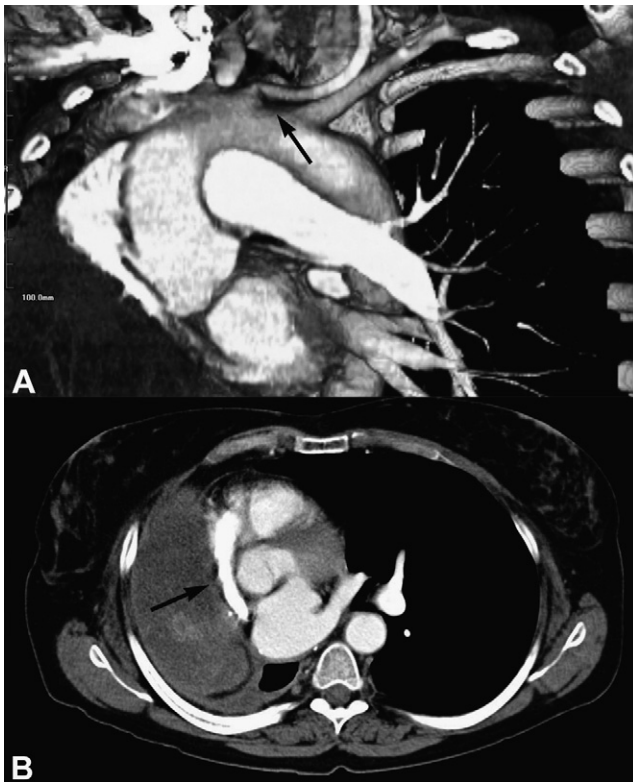


Fig. 3. Additional anatomical changes: 3D-reconstruction of the upper thoracic aperture shows kinking of the left common carotid artery (arrow) of a patient (nr. 2). (Incidental findings without clinical correlation) (A). Compression of the right atrium (arrow) in a patient (nr. 3) after right pneumonectomy (B).

of the dilated esophagus with a delayed passage. Endoscopy and 24 h pH monitoring were normal.

Additionally to the mediastinal shift, we found a kinking of the left common carotid artery in one patient (nr. 2) (Fig. 3A) and a compressed right atrium in another patient (nr. 3) (Fig. 3B). These two patients were asymptomatic in respect to these findings.

We assumed that an extensive mediastinal shift might intermittently impair venous return. Therefore we measured the pressure in the vena cava below and above the diaphragm and in the main pulmonary artery at rest in one of the patients (nr. 6) in different positions and found them within normal limits. Despite these findings it might be possible that an impaired venous blood return to the heart is relevant for symptoms if the patient is under exercise.

4.4. Diagnosis

Shortness of breath is not an unexpected symptom after pneumonectomy and is most commonly due to borderline preoperative lung function, recurrence of lung cancer, infection or pulmonary embolism. The diagnosis of PPS as the cause of dyspnea must be made by exclusion.

Chest radiographs reveal an extreme mediastinal shift to the side of pneumonectomy with a grossly hyperinflated remaining lung and a deviation of mediastinal structures.

Although an extensive shift of the mediastinum and heart was seen in two of our patients with left PPS as well, we could not find clear evidence of tracheobronchial compression in their chest CT scans. We excluded progression of underlying lung disease, pulmonary thromboembolism or pulmonary hypertension, recurrence of malignancy, congestive heart failure, exacerbation of COPD and particular anatomical features such as scoliosis, which may compromise the tracheobronchial tree [12,24]. Another condition, which has been observed several months after pneumonectomy is cardiac herniation [25].

Pulmonary function tests (PFT) show the typical changes after pneumonectomy. The forced vital capacity (FVC) may be higher than expected in patients after pneumonectomy, reflecting an overexpansion of the remaining lung (Table 2). Shamji et al. observed differences in the flow-volume loops in a patient with left PPS. There was a marked improvement of flow rates and FVC in the sitting as compared to the supine position before correction of PPS [11]. In all our patients with right-sided PPS FEV₁ increased after the operation. After the intervention the FEV₁ improved mildly in a patient with a left PPS and deteriorated in the other. An increase in the FEV₁/FVC ratio could be observed in all our patients and may reflect a decrease in the hyperinflation of the remaining lung. The improvement in shortness of breath, which was observed in our patients with right-sided PPS was more than expected by changes in lung function.

The chest CT may reveal a stretching and kinking of the left lower lobe bronchus over the descending aorta. In addition, esophageal deviation may be seen and compression of the right ventricle after right pneumonectomy may be a prominent finding.

If a CT scan does not show a narrowed bronchus, airway-compression may occur only under exertion, when forced respiration increases intra- to extrathoracic pressure differences, and PPS may be suspected anyway. Such findings may be appreciated on dynamic multi-slice CT scan or by bronchoscopy in a patient, who can perform breathing maneuvers during endoscopy. In mechanically ventilated patients documentation of airway compression may be elusive, since the positive airway pressure maintains open airways. The quality of echocardiography may be severely impaired due to the overexpansion of the remaining lung and the serofibrothorax.

4.5. Therapy

We found 73 reports of patients with a PPS in the English literature [1–21]. Most of the patients have been treated by either the implantation of prosthesis [1–7,9,11–14,16,20,21,24] or the insertion of tracheobronchial stents [9,10,12,15]. Recently, thoracoscopic reposition of the mediastinum in a 20-year-old woman has been described [21]. Additional surgical techniques such as aortic division and bypass, tracheobronchial reconstruction, pericardiography, pericardial flaps, pericardial fixation at the sternum, anterior resection of vertebral body or transposition of intercostal muscles has been described [5,7,11,12,14]. Other interventions like intrapleural injection of sulfur hexafluoride are anecdotic [8].

We performed a lateral thoracotomy and a lysis of scars and adhesions allowed the mediastinum and heart to return to a more central position. In all cases the pleura itself was not thickened. Prostheses were implanted intrapleurally and the necessary volume of the prosthesis was estimated intraoperatively. Thereby, the liberation of the compressed bronchus was more pivotal than a perfect central position of the mediastinum for the decision of prosthesis volume. After insertion of the prosthesis the central venous pressure should not increase. We did not perform any pericardial fixation or additional reconstructions. In contrary to most case reports [1–4,9,12,14] we used a single fix-volume prosthesis with a marked lower volume (median volume: 325 ml, range: 305–420 ml) to avoid an over-correction with compression of the remaining lung.

4.6. Conclusion

The PPS is a rare but sometimes life-threatening complication after pneumonectomy. Symptoms due to PPS may develop after a few months or many years after pneumonectomy and the occurrence of PPS is not predictable. A PPS is more often described after right pneumonectomy and in women. But there is no statistical difference in the published cases in respect to gender and side (chi-square test). And there seems to be no specific age distribution.

Patients present with a wide clinical spectrum, but the main complaints consist of increasing shortness of breath and dyspnea in combination with stridor. Additional symptoms like heartburn and dysphagia may be due to esophageal deviation secondary to the mediastinal shift. All these symptoms have to be differentiated from other cardiovascular or other pulmonary causes. The anatomic changes in PPS are strikingly dramatic and the involvement of additional structures apart from the tracheobronchial tree is not surprising. If a thoracic CT scan or bronchoscopy does not confirm a tracheobronchial compression, the diagnosis of a PPS must be made by exclusion. Tracheobronchial compression may occur only during increased physical activity. We postulate that the mechanism between left- and right-sided PPS is different. On right-sided PPS airway obstruction by kinking of the left lower lobe bronchus is the leading problem, but on the left-sided PPS the reason for symptoms is less clear.

Due to the rareness of the PPS recommendations for surgical therapy cannot be made based on controlled studies. Tracheobronchial stenting may be an option for high-risk patients. However, it is obvious that reposition of the mediastinum and fixation by implantation of a thoracic prosthesis is the treatment of choice, and most of the patients reported in literature underwent such a procedure. The role of other surgical procedures such as pericardial fixation or complex reconstructions remains unclear. A complete repositioning with more than one intrathoracic silicone prosthesis may not be necessary. The volume of the prosthesis may not fill the thoracic cavity completely and smaller volumes can be used. In conclusion, based on our experience, we suggest treating symptomatic patients by mediastinal repositioning with an intrathoracic prosthesis.

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