Postpneumonectomy syndrome: Surgical management and long-term results

K. Robert Shen, MD, John C. Wain, MD, Cameron D. Wright, MD, Hermes C. Grillo, MD,* and Douglas J. Mathisen, MD

Objective: Postpneumonectomy syndrome is a rare syndrome of dynamic airway obstruction caused by extreme rotation and shift of the mediastinum after pneumonectomy, resulting in symptomatic central airway compression. We have treated this syndrome by mediastinal repositioning and placement of saline-filled prostheses into the pneumonectomy space. There is a paucity of outcome data for patients treated surgically, with only a single series of 11 patients previously reported. We analyzed our recent experience with treatment of this syndrome and report on the short and long-term outcomes and quality of life assessment of the largest series ever reported of patients treated by mediastinal repositioning.

Methods: Records were reviewed of all patients who underwent mediastinal repositioning for postpneumonectomy syndrome between January of 1992 and June of 2006. Long-term health-related quality of life was assessed by administration of the Saint George's Respiratory Questionnaire.

Results: There were 18 patients (15 women and 3 men) with a median age of 44 years (range 14–67 years). Thirteen patients had undergone right pneumonectomy, and 5 patients had undergone left pneumonectomy. None of the patients in whom postpneumonectomy syndrome developed after left pneumonectomy had a right-sided aortic arch. Five patients had undergone pneumonectomy in childhood (age < 13 years). The median interval between pneumonectomy and mediastinal repositioning was 7.5 years (range 1.1–54.8 years). The median follow-up was 32 months (range 4–143 months). The operative mortality was 5.6% (1/18). Complications occurred in 5 patients (27.8%): pneumonia in 3 patients and acute respiratory distress syndrome in 2 patients. The median hospitalization was 6 days (range 3–155 days). Some 77% (10/13) of patients reported significant improvement in their breathing and overall state of health after surgery; 15.4% of patients (2/13) were somewhat better, and 7.7% of patients (1/13) had no improvement. No patients' condition was worse after surgery. All patients who reported improvement in their symptoms after surgery remained symptomatically improved at the time of the quality of life assessment. Some 92.3% (12/13) were not at all or only slightly limited in their social activities because of breathing problems, and 84.6% (11/13) were not at all or only slightly limited in their ability to work as a result of their physical health.

Conclusion: Repositioning of the mediastinum with placement of prostheses for postpneumonectomy syndrome can be performed with low mortality and morbidity. Surgical repositioning provides immediate and lasting symptomatic relief to patients in whom postpneumonectomy syndrome develops.

From the General Thoracic Surgery Unit, Massachusetts General Hospital, Boston, Massachusetts.

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Address for reprints: Douglas J. Mathisen, MD, Chief, General Thoracic Surgery Unit, Hermes C. Grillo Professor of Thoracic Surgery, Massachusetts General Hospital, 55 Fruit Street, Blake 1570, Boston, MA 02114 (E-mail: dmathisen@partners.org).

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Abbreviations and Acronyms

COPD = chronic obstructive pulmonary disease
 FEV₁ = forced expiratory volume in 1 second
 FVC = forced vital capacity
 PEFR = peak expiratory flow rate
 QOL = quality of life
 SF-12 = short-form health survey [12 items]
 SGRQ = Saint George's Respiratory Questionnaire

Postpneumectomy syndrome is a rare condition that occurs in children or adults after a pneumonectomy. For reasons that remain poorly understood, in certain patients, the heart and mediastinum shift excessively toward the side of the pneumonectomy and the great vessels also rotate significantly. Herniation of the remaining lung with overdistension accompanies this shift and rotation. After either right or left pneumonectomy, the remaining distal trachea and/or main bronchus can become compressed against the vertebral column or aorta by the pulmonary artery. This results in severely symptomatic central airway compression and dynamic airway obstruction (Figure 1).

In 1992 we reported on our experience with the diagnosis and management of 11 adults with severe symptoms from postpneumectomy syndrome.¹ On the basis of lessons learned during this initial experience, we have surgically treated all subsequent patients with postpneumectomy syndrome with mediastinal repositioning and placement of breast prostheses into the pneumonectomy space to prevent recurrences. By restoring the normal anatomic relationships and allowing the compressed airway to return to its normal position and patency, mediastinal repositioning relieves the mechanical obstruction of the bronchial tree in those patients in whom malacia has not developed and also corrects overdistension of the herniated and hyperexpanded lung.

There remains a paucity of outcome data on patients with postpneumectomy syndrome treated surgically. Since our original report, only a collection of small case reports have been reported. The purpose of this study was to evaluate and analyze our recent experience with treatment of this syndrome and report on the short and long-term outcomes and quality of life (QOL) assessment of patients treated with mediastinal repositioning.

Materials and Methods

All patients who were evaluated and treated surgically for postpneumectomy syndrome at our institution between January of 1992 and June of 2006 were identified from a prospectively maintained surgical database. The institutional review board at Partners Healthcare and Massachusetts General Hospital approved this study, and all patients were contacted and agreed to participate in the QOL assessment. The medical records of these patients were reviewed for patient demographics, presenting signs and symptoms, surgical approach, date of surgery, interval between the pneumonectomy and

the development of postpneumectomy syndrome, preoperative and postoperative radiographic and pulmonary function studies, postoperative morbidity and mortality, length of hospitalization, and last follow-up visit or date of death. Because patients came from a wide geographic referral area, follow-up was necessarily carried out by patient questionnaire and with the cooperation of the referring physicians. Long-term QOL was assessed by a self-administered questionnaire on general QOL, the short-form health survey [12 items] (SF-12), and a health-related QOL questionnaire, the Saint George's Respiratory Questionnaire (SGRQ). The SF-12 is a comprehensive general QOL assessment tool based on the short-form health survey [36 items], which has been validated in more than 2000 publications to be useful in monitoring general and specific populations, comparing the burden of different diseases, and differentiating the health benefits produced by different treatments. The SGRQ is the most widely used disease-specific health status questionnaire used to measure health impairment in patients with chronic obstructive respiratory diseases, such as asthma and chronic obstructive pulmonary disease (COPD). It is a self-administered 51-item survey encompassing 3 components: symptoms, activity, and social or psychologic impacts. Scores range from 0 (best score) to 100 (worst score), and a change of 4 units has been shown to be clinically significant.

Results

Patient details are listed in Table 1. Eighteen patients were evaluated and treated surgically for postpneumectomy syndrome. Fifteen patients were female (83.3%), and 3 patients were male (16.7%). The syndrome developed after right pneumonectomy in 13 patients and after left pneumonectomy in 5 patients. None of the patients in whom the syndrome developed after left pneumonectomy had a right aortic arch. All patients had symptoms of progressive and incapacitating dyspnea that occurred with minimal effort and that occurred at rest in the most severely affected patients. Other presenting symptoms were audible stridor or wheezing (56%), recurrent infections (33%), cough (22%), gastroesophageal reflux (11%), hemoptysis (11%), chest pain (5%), and dysphagia (5.6%). The median age at the time of attempted correction was 44 years, with a range of 14 to 67 years. The median interval between the original pneumonectomy and the time of attempted correction was 7.5 years, with a range from 1.1 to 54.8 years. Five patients had undergone pneumonectomy in childhood (age < 13 years). Two patients had undergone prior operative procedures to reposition the mediastinum and required redo surgery. One patient had developed recurrent symptoms 4 years after her original repositioning operation, which had included placement of a breast prosthesis in the pneumonectomy space. Two subsequent attempts to reposition her mediastinum had failed to resolve her airway obstruction, and she had become ventilator dependent. In an attempt to liberate her from mechanical ventilation, she underwent aortic division with bypass from the ascending aorta to the descending aorta with a graft. She developed hemodynamic instability postoperatively and died of multisystem

TABLE 1. Patient details

Patient	Age at time of repositioning	Sex	Indication for pneumonectomy	Pneumonectomy side	Interval between original and corrective surgery (y)	Follow up interval (mo)	No. of implants	Volume of implants (mL)	Hospital length of stay (d)
1	41	F	Carcinoid	R	7.7	5.2	2	1000	155
2	46	M	Bronchiectasis	L	39.3	143	3	1205	6
3	46	F	Broncholithiasis	R	4.3	140.8	2	1000	11
4	26	F	Granular cell tumor	L	14.2	100	2	620	11
5	14	M	Bronchiectasis	R	1.2	97	3	1500	9
6	33	F	Infected cyst	R	33.5	31	4	1610	41
7	55	F	Lung cancer	L	8.1	60	3	780	6
8	28	F	Congenital hypoplasia	R	2.3	48	2	800	5
9	60	F	Lung abscess	R	54.8	51	2	300	3
10	31	F	Lung cancer	R	1.1	40	1	750	5
11	39	F	Congenital bronchial anomaly	R	1.1	32	2	1060	5
12	57	F	Lung cancer	R	1.2	12	2	810	5
13	60	F	Lung cancer	L	7.9	14	3	1050	66
14	49	F	Lung cancer	R	2.4	13	2	850	5
15	67	F	Broncholithiasis	L	18	13	2	575	5
16	20	F	Carcinoid	R	4.6	4	2	650	6
17	35	F	Trauma	R	7.3	8	1	225	31
18	65	M	Lung cancer	R	8.0	30	2	530	150

organ failure on postoperative day 2. The second patient was a 20-year-old woman who developed recurrent postpneumonectomy syndrome 1 year after her original mediastinal repositioning operation when one of her saline-filled breast implants spontaneously ruptured. She subsequently had Lucite balls placed into the pneumonectomy space, which did not relieve the symptoms (Figures E1 and E2). She was then referred to our institution, and at her third operation, we removed all of the Lucite balls and repositioned her mediastinum with saline-filled breast implants (Figures E3 and E4). She remains well and fully active 4 years after this procedure and recently gave birth to a child. The indication for pneumonectomy was neoplastic disease in 9 patients, chronic infection in 4 patients, congenital lung disease in 2 patients, broncholithiasis in 2 patients, and trauma in 1 patient.

Surgical Management

The mediastinum was repositioned in all 18 patients by reopening the side of the original pneumonectomy and lysing scar and adhesions sufficiently to allow the heart and mediastinal structures to be repositioned in a central position and the herniated lung to be reduced to the opposite side. An important technical point to emphasize is that the junction between the pneumonectomy stump and the main bronchus needs to be extensively dissected and liberated. That junction is often-times scarred to either the vertebral body or the posterior mediastinum, and complete liberation and lysis of the scar tissue there are essential. Otherwise, it is possible to reposition the mediastinal structures centrally, but if that tethering point has not been fully dissected, there will still be mechanical com-

pression of either the main or lobar bronchi, and the desired result will not be achieved. In 9 patients, the pericardium was also sutured to the fascia of the undersurface of the sternum with 2 vertical rows of 0 Prolene (Ethicon, Somerville, NJ) sutures. Care was taken not to produce tamponade by

Figure 1. Representative preoperative bronchoscopic appearance of the trachea and left main bronchus in postpneumonectomy syndrome after a right pneumonectomy.

excessively reducing the volume of the pericardial sac by reefing up too much pericardium. Careful monitoring of the patients' hemodynamics with a central venous line and arterial line was essential during this phase of the procedure.

The pneumonectomy space was filled with saline-filled breast prostheses in all 18 patients. The number and volume of prostheses were selected, which was sufficient to fill the pneumonectomy space returning the heart and mediastinum to a central position without compressing the heart and remaining lung. The volume necessary to reposition the mediastinum is determined by instilling a measured amount of saline into the pneumonectomy space. The median number of implants used was 2 (range 1–4). The median volume of prostheses placed was 805 mL (range 225–1610 mL). Intraoperative flexible bronchoscopy to assess the patency and stability of the airway was performed after repositioning the mediastinum and after prosthetic placement (Figure 2). It was also performed once the patients were placed supine after the completion of the operation. Pulse, blood pressure, and central venous pressure were carefully monitored during mediastinal repositioning and prosthetic placement, and once the patient was placed supine after the chest had been closed to detect tamponade physiology. An intraoperative chest radiograph was obtained in all patients to assess the mediastinal position and rule out any significant atelectasis. Sometimes after the thoracic incision is closed, the prosthetic volume instilled is too great, producing atelectasis and/or hemodynamic compromise. This was the case in 4 patients who had their partially closed incision reopened and the prosthetic volume reduced. Other than the first patient in the series who underwent aortic division, none of the subsequent 17 patients had any significant tracheobronchial malacia after repositioning, and none required placement of airway stents after surgery.

Our surgical management of this syndrome has evolved since our original report. Initially, 4 intercostal muscle bundles were dropped into the pneumonectomy space to lie against the pericardium. The anterior and posterior attachments were

preserved, and a strip of periosteum on the anterior surface of each rib was left to maintain bony integrity. This was done to provide a firm partition, which would solidify as the periosteum calcified, and prevent recurrence if the prosthesis needed to be removed later. This additional step is now thought to be unnecessary, and none of the patients in this series had intercostal muscles dropped into the chest. Attempting to affix the pericardium to the back of the sternum is also no longer thought to be necessary, and the last 9 patients in this series did not have this as part of their operative repair.

Hospital Course

There were no intraoperative deaths. One patient died after surgery, and the operative mortality for the series was 5.6% (1/18). The cause of death was multisystem organ failure after aortic division and bypass in a 45-year-old woman who developed recurrent postpneumonectomy syndrome 4 years after successful mediastinal repositioning with breast prostheses. The median hospitalization was 6 days (range 3–155 days). Complications occurred in 5 patients (27.8%). Pneumonia developed in 3 patients, and acute respiratory distress syndrome developed in 2 patients.

Long-term Outcomes

Follow-up was complete in all 17 operative survivors. The median follow-up was 32 months (range 4–143 months). One patient underwent reoperation to have his implants removed 1 year after placement because his dyspnea symptoms and pulmonary function studies had worsened after mediastinal repositioning with implants; it was thought that lobar compression developed as a result of the implants. His symptoms improved after removal of his implants.

Pulmonary Function Studies

Eleven patients had pulmonary function studies with spirometry performed before and after surgical correction (Table 2). The vital capacity decreased in all patients from a mean of 2.28 to 1.64 L ($P < .05$). The forced expiratory volume in

Figure 2. A, Preoperative bronchoscopy in a 39-year-old woman (patient 11) who developed postpneumonectomy syndrome after right pneumonectomy 1 year earlier. The left lower lobe bronchus (arrows) has been almost completely compressed. B, Postoperative bronchoscopy showing widely patent lobar orifices.

TABLE 2. Preoperative and postoperative spirometry

Patient No.	Preoperative testing								Postoperative testing							
	FEV ₁ % predicted		FVC % predicted		FEV ₁ /FVC % predicted		PEFR % predicted		FEV ₁ % predicted		FVC % predicted		FEV ₁ /FVC % predicted		PEFR % predicted	
2	2.02	54.0%	3.25	71.0%	0.62	75.6%	5.21	57.0%	1.39	38.0%	2.39	53.0%	0.58	64.0%	4.89	54%
3	1.65	60.0%	2.41	74.0%	0.68	85.0%	3.99	65.0%	1.61	59.0%	2.07	59.0%	0.78	99.0%	3.41	54%
4	1.15	43.0%	1.23	41.0%	0.93	104.0%	2.69	49.0%	1.06	38.0%	1.13	36.0%	0.93	106.0%	2.99	53.0%
5	1.65	48.0%	3.3	82.0%	0.50	57.0%	2.47	33.7%	1.45	42.0%	2.22	55.0%	0.65	75.0%	2.58	35.0%
6	1.06	33.0%	1.75	44.0%	0.60	74.0%	2.83	40.3%	0.74	21.0%	0.79	18.0%	0.94	113.0%	3.13	46.0%
8	1.7	52.0%	3.58	94.0%	0.48	55.0%	2.61	38.0%	1.40	41.0%	1.85	46.0%	0.76	89.0%	2.29	34.0%
9	1.17	55.0%	1.14	46.0%	0.88	121.0%	2.58	51.0%	0.43	21.0%	0.54	22.0%	0.80	97.0%	2.78	20.0%
13	1.08	47.0%	2.35	82.0%	0.46	58.0%	2.46	43.0%	0.97	43.0%	1.83	64.0%	0.53	66.0%	2.47	43.0%
16	0.78	23.0%	1.93	50.0%	0.41	47.0%	1.32	18.0%	0.88	27.0%	1.69	45.0%	0.52	48.0%	1.54	23%
17	1.17	38.0%	1.85	50.0%	0.63	76.0%	2.59	39%	0.98	32.0%	1.36	37.0%	0.72	86.0%	2.13	32.0%
18	1.18	30.0%	2.27	45.0%	0.52	68.0%	3.24	35%	1.34	34.0%	2.14	44.0%	0.63	79.0%	3.41	40%
Mean + SE	1.33 + 0.11		2.28 + 0.25		0.61 + 0.05		2.91 + 0.30		1.11* + 0.11		1.64* + 0.18		0.71* + 0.04		2.87 + 0.26	

FEV₁, Forced expiratory volume in 1 second (L); FVC, forced vital capacity (L); PEFR, peak expiratory flow rate (L/sec); SE, standard error. * $P < .05$ versus preoperative value.

1 second (FEV₁) decreased in 9 patients and improved in 2 patients. The mean decreased from 1.33 to 1.11 L ($P < .05$). The FEV₁/forced vital capacity (FVC) ratio improved in 8 patients, was unchanged in 1 patient, and decreased in 2 patients. The mean increased from 0.61 to 0.71 ($P < .05$). Peak expiratory flow rates (PEFRs) improved in 7 patients and decreased in 4 patients. Postoperative PEFR was not significantly different from preoperative values.

Health-related Quality of Life

Thirteen of the 17 operative survivors completed a general and disease-specific health-related QOL questionnaire. The median time between the mediastinal repositioning and the QOL assessment was 32 months (range 4–145 months). Ten patients (77%) reported significant improvement in their overall health and breathing after surgery (Table E1). Two patients (15%) reported somewhat better conditions, 1 patient (7.7%) reported no improvement, and no patients reported worse conditions compared with their preoperative status. All patients who reported improvement in their symptoms after surgery remained symptomatically improved at the time of the QOL assessment. Twelve patients (92.3%) were not at all or only slightly limited in their normal social activities because of physical or emotional problems related to their breathing problems. One patient was moderately limited, and none were severely limited. Eleven patients (84.6%) were not at all or only slightly limited in their ability to work or perform other strenuous activities as a result of their physical health. Two patients (15.4%) were limited in their ability to work or perform strenuous activity most of the time. In the month preceding the QOL assessment, 9 patients (69.2%) reported complete freedom from dyspnea symptoms or symptoms only a few days per month or only when there was a pulmonary infection. Two patients (15.4%) still had

persistent dyspnea symptoms several days per week, and 2 patients (15.4%) had dyspnea symptoms almost every day. Twelve patients (84.6%) described their lung/respiratory condition as causing no or few problems. One patient (7.7%) reported it as the most important problem affecting overall health. Scores from the SGRQ are shown in Table E2.

Discussion

For reasons that remain unknown, in a small subset of patients who undergo pneumonectomy, excessive mediastinal shift and rotation toward the empty hemithorax can occur. This mediastinal displacement results in airway obstruction that causes progressive and disabling symptoms. After right pneumonectomy, the mediastinum shifts to the right and posteriorly with counterclockwise rotation of the heart and great vessels, as seen on computed tomography scan. After left pneumonectomy, the mediastinum rotates clockwise. Mediastinal shift and rotation are accompanied by herniation and hyperinflation of the remaining lung. The trachea and mainstem bronchus are displaced toward the pneumonectomy space, and the main bronchus becomes compressed between the left pulmonary artery and vertebral column or descending aorta in the case of a right pneumonectomy, or between the right pulmonary artery and vertebral column or aorta in the case of a left pneumonectomy.

There have been many case reports in the literature describing postpneumonectomy syndrome in both children and adults. Although the incidence in adults is unknown, the syndrome is thought to be more likely to develop in infants and young children than in adults.²⁻⁴ In children, the incidence has been estimated to be 1 case per 640 pneumonectomies.⁴ Factors that have been proposed to explain the higher incidence in the younger age group include increased elasticity and compliance of the remaining lung

and mediastinal tissues and anatomic changes as a result of somatic growth. In our original report, only 2 of 11 patients had undergone pneumonectomy in childhood. In the present series, 5 of 18 patients had undergone pneumonectomy in childhood.

Postpneumonectomy syndrome seems to be more common after right pneumonectomy.⁵ Of the 29 patients we have treated at our institution, 20 developed the syndrome after right pneumonectomy and 9 developed the syndrome after left pneumonectomy. We do not have an explanation for this observation. Given the natural leftward position of the heart, it is possible that rightward mediastinal shift after right pneumonectomy produces more severe anatomic derangement and is therefore more likely to cause symptoms. Although we originally believed that the presence of a right aortic arch was a prerequisite for developing postpneumonectomy syndrome after left pneumonectomy, it has been shown that postpneumonectomy syndrome can occur with a left-sided aortic arch after left pneumonectomy.⁶⁻¹⁰ In contrast with our original report, none of the 5 patients who developed postpneumonectomy syndrome after left pneumonectomy had a right aortic arch.

A variety of methods to attempt surgical correction of postpneumonectomy syndrome have been reported. Most consist of single case reports. Division of the ligamentum arteriosum⁶, fixation of the aorta or pulmonary artery to the sternum,^{11,12} and placement of expandable metallic stents¹³ have been reported with varying results. Given the young age of many of these patients and the future possibility of stent migration, erosion into the pulmonary artery or aorta, and development of granulation tissue, long-term results with stenting confirming its safety and efficacy are needed before it can be recommended as primary treatment for this syndrome.

As our experience with this syndrome has grown, we believe that surgical correction is best achieved by restoration of the normal mediastinal position to allow the compressed airway to return to its normal position and patency. Several methods for repositioning the mediastinum have also been described. These include suture fixation of the pericardium to the back of the sternum,¹ surgical and chemical phrenectomy,⁵ and placement of prostheses to fill the empty hemithorax. Lucite plastic balls,¹² silastic implants,^{3,14,15} injection of sulfur hexafluoride into the pneumonectomy space,¹⁶ and saline-filled breast prostheses^{1,7,9,10} have been used prophylactically and therapeutically. Since our original report, we have treated all patients with postpneumonectomy syndrome with mediastinal repositioning and placement of saline-filled breast prostheses. This method of correction has also been widely adopted by other groups with success.^{7,9,10}

In our original report, 4 patients were found to have significant malacic changes in their airways in addition to shift and rotation of the mediastinum. Mediastinal repositioning and fixation by placement of prostheses are insufficient, and the

other procedures we have tried to address the malacic airway have not been successful. The only operative death in the current series was 1 patient who developed severe airway malacia and recurrent symptoms 4 years after mediastinal repositioning. Three subsequent attempts to reposition her mediastinum were unsuccessful, and she died of complications after an attempt to relieve her airway compression with aortic division and bypass. We did not encounter severely malacic airways in the 17 patients who underwent operation after this patient. We would recommend that patients who have malacic airways in addition to mediastinal shift undergo mediastinal repositioning and stenting of the airway with a completely covered stent. Kelly and colleagues¹⁷ reported successful management of such a patient using this strategy.

The benefit of repositioning the mediastinum is the result of relief of the compression of the bronchial tree and correction of the hyperinflation of the herniated lung. Pulmonary function studies in the 11 patients who had spirometry available before and after repositioning showed improvements in flow rates and a decrease in hyperinflation. All patients showed a decrease in FVC due to relief of hyperinflation. In most patients, the decrease in FVC was also greater in absolute amount than the decrease in FEV₁, resulting in an improvement in the FEV₁/FVC ratio. However, in contrast with the findings of our original report, which showed a consistent improvement in PEFR and an improvement in the FEV₁/FVC ratio in every patient, in this series, PEFR improved in 7 patients and decreased in 4 patients. The improvement in PEFR was not statistically significant. In the only other report in the literature that has reported on pulmonary function tests before and after mediastinal repositioning for postpneumonectomy syndrome, Valzi and colleagues⁹ reported a significant increase in the PEFR for all 5 patients in their series with a mean improvement of 44.2%. The FEV₁/FVC ratio in their patients improved in 3 patients, decreased in 1 patient, and was unchanged in 1 patient. The mean improvement was 13.2%. One possible explanation for the difference in PEFR findings is that perhaps there was less tracheal compression in the patients who did not have an improvement in PEFR after surgery. Hyperexpansion of the remaining lung may have been a more significant factor for these patients, and relief of dyspnea symptoms may have been due to a decrease in hyperinflation. In the 4 patients who had a decline in PEFR, the FEV₁/FVC ratio improved in 3. The 1 patient who showed decline in both the FEV₁/FVC ratio and PEFR also had worse symptoms after repositioning and underwent removal of his implants 1 year later. His symptoms improved somewhat after removal of the implants.

Studies in patients with COPD have demonstrated that evaluation of the effectiveness of treatments for COPD requires the assessment of both clinical and physiologic variables. In patients with obstructive lung disease with dyspnea as the primary symptom, spirometric parameters such as

FEV₁, FEV₁/FVC, and PEFR are well established in providing an objective measure of improvements in airflow after a therapeutic intervention. However, assessments of dyspnea, functional status, and overall health status are required to characterize response to treatment. The most widely used disease-specific health status questionnaire for patients with obstructive lung disease is the SGRQ. This standardized measure was designed to quantify the impact of disease of chronic airflow limitation on health and well-being.¹⁸ SGRQ scores have been shown to have good repeatability and correlate with a range of established measures of disease activity, such as spirometry, 6-minute walking distance, mortality, and the incidence of COPD exacerbations.^{18,19} The total mean SGRQ score of patients who underwent mediastinal repositioning and who completed the questionnaire was 25.9 ± 4.9 (Table E2). In a recent study evaluating the association between health-related QOL and disease severity using the Global Initiative for Chronic Obstructive Lung Disease guidelines, a total SGRQ score of 25 corresponded to a Global Initiative for Chronic Obstructive Lung Disease stage I, which was characteristic of patients with mild COPD.²⁰ An SGRQ total score of 25.9 also compares favorably to patients in the National Emphysema Treatment Trial. The baseline SGRQ total score was 52.5 ± 12.6 for patients in the surgical arm of the National Emphysema Treatment Trial and 53.6 ± 12.7 for patients randomized to medical therapy.²¹ The results of the QOL assessment suggest that the clinical symptomatic improvement in patients with postpneumectomy syndrome who undergo mediastinal repositioning is more significant than can be quantified by pulmonary function studies alone. Mediastinal repositioning provides significant improvement in relief of symptoms and enables patients to return to a high level of activity and good functional status. Moreover, these improvements in overall and disease-specific health-related QOL appear to be durable.

Conclusions

Although we still have no explanation from this study or other reports why extreme mediastinal displacement and rotation occur in a small subset of patients who undergo pneumectomy, once postpneumectomy syndrome is identified and becomes symptomatic, patients should undergo prompt surgical correction. Mediastinal repositioning and placement of saline-filled breast implants can be performed with low morbidity and mortality, and provide significant and durable symptomatic relief to patients with postpneumectomy syndrome.

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Discussion

Dr S. Murthy (Cleveland, Ohio). Dr Shen and colleagues have provided a retrospective descriptive review of their experience of the surgical management of a rare but devastating complication after pneumectomy. Although this a series of only 18 patients, it does represent the largest report of its kind. It is unfortunate that the follow-up of such a select group of patients is so incomplete, with only 13 of 17 patients who survived answering QOL questionnaires and 11 of 17 patients with full spirometric evaluation. Limited follow-up in the context of such a small study can drastically bias the interpretation of the results. To highlight this confound, the median length of stay for the 11 patients with spirometry was almost double that of the entire cohort at 11 days, and their mean length of stay was almost 40 days. Consequently, it is difficult for me to critically and meaningfully evaluate the findings. However, there are other aspects of the article

that are provocative and worthy of discussion, and I will direct my attention to these.

I am intrigued by the operation and am impressed that such an undertaking can be completed. Would you comment on the following technical issues. How do you size the implants, and how are cardiac hemodynamics measured intraoperatively and postoperatively to prevent cardiac tamponade, ventricular arrhythmia, or decreased venous return?

Dr Shen. The issue of how to size the implant is one that we believe is based in some ways on trial and error at the time of the operation. After the pneumonectomy space has been opened and all of the scar and adhesions have been mobilized to allow repositioning of the herniated lung back to the proper side and repositioning mediastinal structures, heart, and pericardium back to a central position, we typically have used a technique where a measured amount of saline is poured into the chest to be able to estimate the volume of this often complex space. On the basis of the measured volume of saline that is then removed from the chest, we then select a number of breast implant sizers, test-sizers, before committing to an actual implant. I think it also speaks to your second question on how to monitor these patients postoperatively. Once the approximate volume has been selected, a critical technical point is that extensive monitoring of hemodynamics in terms of pulse, blood pressure, and central venous pressure with central line monitoring is important to be on the lookout for tamponade physiology. In addition, we use flexible bronchoscopy extensively throughout the procedure once the mediastinal structures have been centrally located, as well as after test placement of the implants and after the chest has been closed. A final check once the patient has been turned supine is also done. It's worth noting that 4 of the 18 patients, after partial closure of the chest, developed tamponade physiology and had to have their partially closed incision reopened and the volume adjusted. We also make use of intraoperative radiography with a chest x-ray done at the end of the procedure, also looking for atelectasis and overcorrection. So I think the issue of how to correctly size the repositioning is intimately tied to the monitoring that's done in the procedure.

Dr Murthy. I have 2 other technical questions. Can you do this extrapleurally? It seems like that might be an easier approach, not having done one of these, but just thinking about it. Might tissue expanders be a more appropriate choice to fill the space? This is reported in the pediatric literature.

Dr Shen. The tasks that need to be achieved to successfully reposition the mediastinum are that the scar and adhesions holding the herniated lung, as well as the pericardium and other mediastinal structures, need to be lysed and divided to allow one to centrally reposition the mediastinum. Another important technical point to emphasize is that the junction between the pneumonectomy stump and the main bronchus needs to be extensively dissected and liberated. That junction is oftentimes scarred to either the vertebral body or the posterior mediastinum, and if you don't achieve liberation and complete lysis of that scar tissue there, you can still reposition the mediastinal structures centrally, but if that tethering point hasn't been fully dissected, you're still going to have mechanical compression of either the main or lobar bronchi and not achieve the desired result. Whether or not that can be done easier from an extrapleural approach, I don't think so. To accomplish all those things, I think it's necessary to open the pneumonectomy space.

As far as the issue of having adjustable tissue expanders, it has been described extensively in the pediatric literature. I think that for pediatric patients, to allow for further somatic growth, it is worthwhile to consider. In adult patients, it's really not necessary. Several other groups have reported the use of adjustable breast implants in adults and have not found the need to make adjustments after surgery.

Dr Murthy. I'll skip to the last point. Finally, what might be the mechanism for the apparent amelioration of this syndrome? Your spirometry data actually argue against that you have solved a functional airway obstruction. Other reports and my own common sense would suggest that there would be an improvement in spirometry measurements, especially FEV₁, if a suspected airway stenosis were to be relieved by your maneuvers. Perhaps it is the relief of some intracardiac shunt or right atrial compression that might lead to your improvement, and there is a syndrome, platypnea-orthodeoxia, that has been reported as a possible putative mechanism for this kind of problem.

Dr Shen. We believe that there are 2 important physiologic derangements that contribute to the overall syndrome. The first is obviously a mechanical compression of the main bronchus or lobar bronchus from the mediastinal shift, and so you get a functional and a dynamic compressive upper airway obstruction. The second component to the syndrome is due to the shift and herniation and overexpansion of the residual lung. In patients with symptoms of dyspnea and shortness of breath from this syndrome, I think it's a combination of these mechanisms, and each patient probably has a mix of the effects of the overexpansion and herniation of the lung, as well as the mechanical compression of the airway itself. We believe that the relief that patients get from surgical correction with mediastinal repositioning really comes from addressing both of those issues independently. They are independent and also connected. We did find in the spirometry data that the FVC decreased in every patient, reflecting correction of the hyperexpansion. The results with FEV₁ have not been consistent. In Dr Grillo's original report, 7 patients had preoperative and postoperative spirometry, 4 patients had improvement in the FEV₁, and 3 patients had decline. In this current series of patients, 9 decreased and 2 increased. I think the relief of dyspnea that patients get is probably a combination of the correction of the overexpansion of the herniated lung and relief of the mechanical obstruction on the airway. Depending on which component of that is more important for any given patient, that's probably ultimately what affects the end result of relief of symptoms.

Dr Murthy. That such a study could be done clearly demonstrates the expertise of you and your group.

Dr J. Deslauriers (*Quebec City, Quebec, Canada*). What do you think is the true incidence of this complication after pneumonectomy?

Dr Shen. I think it's extremely low. The only reported incidence I've seen is an estimate of 1 in 640 pneumonectomies in children, and obviously that's much lower in adults.

Dr Deslauriers. So it would be extremely rare.

Dr Shen. Extremely rare.

Dr Deslauriers. Perhaps 1 in 1,000 or something like that?

Dr Shen. At least, yes.

Dr Deslauriers. My second question has to do with the sometimes associated bronchomalacia. This problem was mentioned in

the first article written by Dr Grillo, and it relates to the destruction of bronchial cartilages that may occur over time. Do you still just put the intrapleural prosthesis, or do you do something else with the bronchus to stabilize it?

Dr Shen. You raise an important point in the management of this syndrome. It is difficult to determine which of these patients will continue to have malacic changes in the airway after repositioning. We typically do have these patients undergo awake bronchoscopy so they can do provocative maneuvers. Sometimes you're turning them on their side. We look specifically at the time of bronchoscopy to see if we can see the cartilaginous rings and dynamic change. Even with all of those maneuvers, we have not been able to determine with any high degree of accuracy preoperatively which patients will continue to have malacia after successful repositioning. In the original series of articles there were a number of things that tried to address the malacia, including tracheal resection of that segment with reconstruction. Our current recommendation would be that patients who have persistent malacic segments after repositioning undergo prompt tracheal stenting.

Dr Deslauriers. So you just do the described operation, hoping that the bronchus will be stabilized once the mediastinum is repositioned.

Dr Shen. Yes.

Dr Deslauriers. Do you perform a bronchoscopy while you're doing these procedures to see if the trachea has been repositioned in the midline?

Dr Shen. Yes, absolutely. It's one point I tried to stress with some of the questions that Dr Murthy asked. It is an important part of the technical conduct of the operation to be conducting flexible bronchoscopy at multiple time points during the operation: once the mediastinal structures have been repositioned into the central location to assess how you've relieved the compression on the airway, when the implants are placed, when you begin closing the chest, and then, finally, again looking with a bronchoscope when the patients are turned onto their back. In several of the cases in this series we found that the patients had been overcorrected and required reopening the incision and removing some of the volume from their implants.

Dr Deslauriers. Do these prostheses have a subcutaneous port where you can aspirate fluid out if required?

Dr Shen. Yes there are implants with subcutaneous ports available.

Dr Deslauriers. So you don't really need to reopen the chest.

Dr Shen. In 4 cases the chest had already been mostly closed, and according to the intraoperative chest x-ray or bronchoscopy, we found that they had actually been overcorrected, or they were fine when they were in the lateral decubitus position. Then when they were put supine again, they were overcorrected, and you needed to be able to at least access the implants to remove some volume. It would not be practical to routinely use the implants with subcutaneous ports, because multiple implants are being placed into the pneumonectomy space.

Dr Deslauriers. There were 3 patients in your series in whom the pneumonectomy had been done for chronic lung disease, presumably for tuberculosis, or destroyed lung. Because these patients usually already have their mediastinum shifted beforehand, why do you think they developed this syndrome?

Dr Shen. Why was the mediastinum not fixed in those patients?

Dr Deslauriers. Well, usually it's fixed, yes.

Dr Shen. The 3 patients who underwent operation for infectious reasons had airway obstruction or were developing chronic pulmonary infections. They were not necessarily patients who originally underwent pneumonectomy for infectious causes, and because they developed post-pneumonectomy syndrome I don't think their mediastinum was fixed before pneumonectomy.

Dr O. Adebo (Ibadan, Nigeria). I'm curious about the explanation that you gave for the pathology. Most of the pneumonectomies we do are for tuberculous destroyed lung, and at the end of the pneumonectomy, the patient's x-ray looks similar to that of patients with postpneumonectomy syndrome, and they have no symptoms. At the end of the pneumonectomy, the shift is as much, if not more, than what you showed from your x-rays, and I'm curious why those patients don't seem to develop any respiratory problem or symptoms despite the remarkable shift of the heart to the operated side, the pneumonectomized side, and we don't make any effort, of course, to reposition it because the lungs are invariably there already and the patient is well adjusted to it. So I'm wondering why the explanation you gave would be the one to undermine this syndrome.

Dr Shen. That's an interesting observation. I don't really have a good explanation for why you don't observe this syndrome in those patients who essentially have a destroyed lung. Have you ever seen this syndrome in patients who have undergone pneumonectomy?

One of the continuing unanswered questions with this syndrome is what are the predisposing factors, why is this such a rare syndrome, and are there factors that you could use to predict who is more likely to develop this syndrome. We don't really have any further insight into that. It seems to be that this is more prevalent in women and is more prevalent or more likely in patients who have undergone right pneumonectomy. If we were to look at the total, the 29 patients who were treated at Massachusetts General from 1979 to 2004, 22 of the 29 were women and 20 of the 29 patients had a right pneumonectomy. But as to the real question, why do some people get it and what are the predisposing factors, I think we still don't know.

Dr W. Klepetko (Vienna, Austria). I would like to come back to the importance of the hemodynamic component in the syndrome that was stressed before. We recently identified a series of 5 or 6 patients in our patient cohort who developed severe postpneumonectomy syndrome based on hemodynamic grounds either on the reopening of the foramen ovale or on the compression of the right atrium because of an unusually high elevation of the right diaphragm. These were all cases of right pneumonectomy. The leading symptom in those patients was always severe hypoxemia, which sometimes developed rapidly, and after the correction, either the closure of the intracardiac shunt or the repositioning of the diaphragm, the hypoxemia was overcome and blood gases were pretty much normalized.

What have you done to rule out such a hemodynamic component? Could you give us some data on your blood gases, which you did not show us. Were they impaired before the operation, and how did they behave after the operation?

Dr Shen. I don't have any data concerning preoperative and postoperative blood gases to be able to share with you. In many of the cases in this series that were evaluated, part of the preoperative

evaluation and determination that the patient had postpneumonectomy syndrome included echocardiography, and sometimes patients also have transesophageal echo studies in the operating room. We are looking specifically for alternative explanations for their symptoms.

Dr Klepetko. Have you seen in your large experience any patients with such a syndrome based on hemodynamic grounds only?

Dr Shen. No. There have been a couple of patients who continued to have similar symptoms after postpneumonectomy surgical repair with repositioning and were found to have some cardiac issues that were uncovered.

Dr T. Daniel (*Charlottesville, Va*). Congratulations, Dr Shen, on an interesting presentation of this rare condition. I don't know whether operating on 3 additional patients makes me an expert, but perhaps so. To suggest an answer to our colleague from Nigeria as to causation, we looked at some of our patients and the patients in Dr Grillo's first report, and there seems to be a narrow interval be-

tween the sternum and the anterior portion of the vertebral body that may show up in that difference in the sex incidence. Most women might have less of a barrel chest, and this may be a predisposing factor. Certainly for all the pneumonectomies done in the world, why such a small handful get it, we don't know, but that may be a predisposing cause.

To Dr Deslauriers' question as to why we don't use the adjustable port to modify these patients, 1 of 3 patients had a problem in the postoperative unit that required returning to the operating room and taking some fluid out. We used a breast prosthesis with an implantable port subcutaneously on the first patient and thought we got a good result, but 6 months after operation, she apparently had a stress fracture of the polyethylene catheter connecting the prosthesis to the extrathoracic position and had a, quote, "flat tire" and redeveloped the syndrome, and we reoperated on her with a successful result. So that's a factor you wouldn't think of.

Figure E1. Postpneumonectomy syndrome in a 20-year-old woman (patient 16) who underwent right pneumonectomy for carcinoid 4 years earlier. She developed postpneumonectomy syndrome within 1 year of pneumonectomy and had mediastinal repositioning with breast implants. Recurrent symptoms developed after one of the implants ruptured. The patient underwent reoperation with placement of Lucite balls. **A,** Chest roentgenogram shows heart and mediastinum displaced to the right with obliteration of the right pleural space. The lung is hyperexpanded and herniated, and numerous plombage balls can be seen. **B,** Lateral view demonstrates posterior displacement of mediastinal contents.

Figure E2. A, Computed tomography scan of the same patient shows shift of the mediastinum to the right and posteriorly with compression of the left mainstem bronchus between the pulmonary artery and the aorta. B, Despite the presence of numerous prostheses, the mediastinum is shifted into the pneumonectomy space.

Figure E3. At the time of the third corrective operation, numerous Lucite plumbage balls were removed from the pneumonectomy space and replaced with saline-filled breast implants.

Figure E4. Computed tomography scan after third corrective operation. Lung herniation has been corrected, and the mediastinum is in the central position with the left main bronchus to the left of the spine.

TABLE E1. Selected responses to Short Form-12 and St George's Respiratory Questionnaire: Total respondents = 13

1. **In general, would you say your health at present is:**
Excellent 7.7%
Very good 46.2%
Good 38.5%
Fair 7.7%
Poor 0%
2. **Compared with your condition before your operation, how would you rate your health in general now?**
Much better than before surgery 76.9%
Somewhat better 15.4%
About the same 7.7%
Somewhat worse 0%
Much worse 0%
3. **Compared with your condition before surgery, was your breathing better after operation?**
Much better 76.9%
Somewhat better 15.4%
About the same 7.7%
Somewhat worse 0%
Much worse 0%
4. **If your breathing was improved after your operation, has it remained so?**
Yes 100%
No 0%
5. **During the past 4 weeks, to what extent have your physical or emotional problems related to your breathing problems interfered with your normal social activities with family, friends, neighbors, or groups?**
Extremely 0%
Quite a bit 0%
Moderately 8.3%
Slightly 25%
Not at all 67%
6. **During the past 4 weeks, have you had to cut down on the amount of time you spend on work or other activities as a result of your physical health?**
All of the time 0%
Most of the time 15.4%
Some of the time 0%
A little of the time 23.1%
None of the time 61.5%
7. **During the past 4 weeks, have you accomplished less than you would like as a result of your physical health?**
All of the time 0%
Most of the time 23.1%
Some of the time 15.4%
A little of the time 7.7%
None of the time 53.9%
8. **During the past 4 weeks, have been limited in the kind of work or other activities as a result of your physical health?**
All of the time 0%
Most of the time 7.7%
Some of the time 23.1%
A little of the time 30.8%
None of the time 38.5%

TABLE E1. Continued

9. **During the past 4 weeks I have coughed**
Almost every day 7.7%
Several days per week 0%
A few days per month 30.8%
Only with lung/respiratory infections 30.8%
Not at all 30.8%
10. **During the past 4 weeks, I have brought up phlegm**
Almost every day 0%
Several days per week 7.7%
A few days per month 23.1%
Only with lung/respiratory infections 7.7%
Not at all 61.5%
11. **During the past 4 weeks, I have had shortness of breath**
Almost every day 15.4%
Several days per week 15.4%
A few days per month 23.1%
Only with lung/respiratory infections 23.1%
Not at all 23.1%
12. **During the past 4 weeks, I have had episodes of wheezing**
Almost every day 0%
Several days per week 0%
A few days per month 15.4%
Only with lung/respiratory infections 38.5%
Not at all 46.2%
13. **During the last 4 weeks how many severe or very unpleasant episodes of lung/respiratory problems have you had?**
More than 3 episodes 7.7%
3 episodes 7.7%
2 episodes 7.7%
1 episode 46.2%
No episodes 38.5%
14. **During the last 4 weeks, in an average week, how many good days (with few lung/respiratory problems) have you had?**
None 0%
1 or 2 0%
3 or 4 47.7%
nearly every day 84.6%
all 7.7%
15. **How would you describe your lung/respiratory condition?**
The most important problem I have 7.7%
Causes me a lot of problems 0%
Causes me a few problems 69.2%
Causes me no problems 15.4%
16. **Do you still have an audible wheeze?**
Yes 23.1%
No 76.9%
17. **Which of the following best describes how your breathing problem affects you**
It does not stop me from doing anything I would like to do 30.8%
It stops me from doing one or two things I would like to do 69.2%
It stops me from doing most of the things I would like to do 7.7%
It stops me from doing everything I would like to do 0%

TABLE E2. St George's Respiratory Questionnaire scores

Patient No.	Symptoms score	Activity score	Impacts score	Total score
2	53.98	35.79	29.34	35.87
3	16.33	0.00	4.20	5.00
5	47.26	29.70	18.88	27.72
7	34.90	49.13	16.57	30.50
9	36.60	31.72	5.85	19.59
10	9.63	35.79	6.53	16.66
11	11.56	0.00	0.00	2.07
13	33.43	73.83	25.53	42.75
14	53.96	86.59	64.94	70.05
15	33.28	23.72	12.36	19.82
16	59.35	23.72	21.20	28.86
17	37.48	29.63	25.39	28.94
18	8.92	18.81	4.56	10.00
Mean + SE				25.9 + 4.9

SE, Standard error.