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INTERVENTIONAL BRONCHOSCOPY

Intrabronchial Valves for Air Leaks After Lobectomy, Segmentectomy, and Lung Volume Reduction Surgery

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Abstract
Purpose Air leaks are common after lobectomy, segmentectomy, and lung volume reduction surgery (LVRS). This can increase post-operative morbidity, cost, and hospital length of stay. The management of post-pulmonary resection air leaks remains challenging. Minimally invasive effective interventions are necessary. The Spiration Valve System (SVS, Olympus/Spiration Inc., Redmond, WA, US) is approved by the FDA under humanitarian use exemption for management of prolonged air leaks.
Methods This is a prospective multicenter registry of 39 patients with air leaks after lobectomy, segmentectomy, and LVRS managed with an intention to use bronchoscopic SVS to resolve air leaks.
Results Bronchoscopic SVS placement was feasible in 82.1% of patients (32/39 patients) and 90 valves were placed with a median of 2 valves per patient (mean of 2.7 ± 1.5 valves, range of 1 to 7 valves). Positive response to SVS placement was documented in 76.9% of all patients (30/39 patients) and in 93.8% of patients when SVS placement was feasible (30/32 patients). Air leaks ultimately resolved when SVS placement was feasible in 87.5% of patients (28/32 patients), after a median of 2.5 days (mean ± SD of 8.9 ± 12.4 days). Considering all patients with an intention to treat analysis, bronchoscopic SVS procedure likely contributed to resolution of air leaks in 71.8% of patients (28/39 patients). The post-procedure median hospital stay was 4 days (mean 6.0 ± 6.1 days).
Conclusions This prospective registry adds to the growing body of literature supporting feasible and effective management of air leaks utilizing one-way valves.

Keywords Intrabronchial valve · Persistent air leak · Interventional pulmonary · Broncho-pleural fistula · Alveolar-pleural fistula

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Introduction

Air leaks are frequently encountered in clinical practice. Etiologies include trauma, iatrogenic leaks due to medical procedures (transthoracic needle biopsy, bronchoscopy, thoracentesis) or post-surgical pulmonary resections [1]. They can also develop after primary spontaneous pneumothorax, or due to secondary pneumothorax related to underlying lung disease such as emphysema, interstitial lung disease, cystic lung disease, malignancy, or necrotizing infections. Air can access the pleural space via direct communication with the central airways (broncho-pleura fistula) or with the alveolar spaces (alveolar-pleural fistula). Air leaks are relatively common after pulmonary resections and reported in up to 50% to 60% of patients in the immediate post-operative period [2]. They are even more likely to occur after lung volume reduction surgery (LVRS), being reported in up to 90% of patients [3].

Most air leaks resolve within the initial 5 to 7 days with conservative chest tube management. Prolonged air leaks (PAL), defined as those that last for more than 5 to 7 days, can lead to prolonged hospital stay, increased morbidity, higher healthcare costs and can contribute to patient mortality [4, 5]. There is considerable variability in the reported incidence of PAL which are reported in up to 5.6% to 26% of patients after pulmonary resections [5–15]. In the National Emphysema Treatment trial (NETT), 45% of patients undergoing LVRS had PAL, and more than 13% of patients had PAL 30 days after the surgery [3]. The type of resection (e.g. lobectomy versus segmentectomy), underlying lung disease (e.g. emphysema), pulmonary function, patient comorbidities, steroid use, and duration of mechanical ventilation are significant risk factors.

Management of PAL after pulmonary resections can be challenging and is generally affected by the patient's post-operative state and morbidity. Management options include surgical repair, pleurodesis, prolonged pleural drainage, Heimlich valve placement. Bronchoscopic management includes intrabronchial coils, glues, stents, or local silver nitrate which are reported with variable success rates [16–24].

One-way intrabronchial valves were initially designed for bronchoscopic lung volume reduction (BLVR) in patients with severe emphysema. Two different valve designs were recently approved by the FDA for BLVR in patients with severe heterogenous emphysema without significant collateral ventilation [25, 26]. The Spiration Valve System (SVS) (Olympus/Spiration Inc., Redmond, WA, US) is approved by the FDA in the United States under a humanitarian device exemption for treatment of post-surgical PAL after lobectomy, segmentectomy, or LVRS [8] (Fig. 1). Case reports and case series have reported variable success using one-way valves in the management of significant air leaks. These removable, one-way valves allow drainage of bronchial secretions and exhalation while simultaneously blocking inhalational airflow. This eliminates or significantly reduces airflow across the broncho-pleural or alveolar-pleural fistula with favorable effect on air leak [27–29].

Prior case series utilizing bronchoscopic one-way valves included patients with variable etiologies of air leaks, multiple comorbid conditions, wide range of underlying lung diseases, inconsistent definitions of response and outcomes; and reported a wide range of successful outcomes (complete or partial resolution of air leak after one-way valve procedures ranging from < 47 to > 90% depending on definitions) [30–41]. Efficacy appears to be related to underlying etiology and lung disease with most success reported in patients with post-pulmonary resection air leaks and least success in patients with secondary spontaneous pneumothorax.

Patients and Methods

This is a prospective registry of 39 patients with significant PAL at 11 different institutions in the United States enrolled from May 2012 until July 2015. All patients had significant air leaks after lobectomy, segmentectomy, or lung volume reduction surgery using the FDA-approved SVS indications. The registry was approved by the institutional review boards of participating centers. Thirty-five patients had PAL ≥ 5 days (35/39 patients). Four patients (4/39) had SVS procedures at the time of enrollment earlier than 5 days (one patient at day 2, one patient at day 3 and two patients at day 4 respectively). This was done due to the severity of air leaks and surgical teams concerns about clinical deterioration. Exclusion criteria included the presence of air leak only with cough or forced exhalation, presence of active asthma or pneumonia, inability to tolerate bronchoscopy, and inability to provide consent.

The SVS valves were implanted and removed using flexible bronchoscopy, either in the operating room or the bronchoscopy suite. The procedure of inserting and removing SVS valves was previously described [35]. Briefly, sequential balloon occlusions are performed to identify airway(s) contributing to the air leak. Sizing of the airways is done using a sizing balloon catheter. Placement is considered according to airway anatomy and the SVS valve is unsheathed through a catheter that is inserted within the working channel of the therapeutic bronchoscope. Removal of the SVS valve is accomplished using flexible bronchoscopy and forceps to grasp the removal rod of the valve and then to remove the valve with the bronchoscope and the biopsy forceps as one unit. The type of anesthesia used and duration of procedure for both implantation and removal were documented. If placement was not feasible, this was also documented.

Characteristics of air leaks were documented prior to and after bronchoscopic placement of SVS valves and were further classified according to severity as continuous, only during inspiration, only during expiration, or only during forced exhalation. We also reported time to subsequent valve removal whenever this was performed. Outcomes that were examined included positive responses to SVS placement, time to air leak resolution, and length of ICU and hospital stay. A positive response to valve placement was defined as complete air leak resolution immediately after the SVS procedure or improvement in air leak classification within 48 h after valve placement. A positive response was also considered when an air leak that initially required inpatient management due to leak size (requiring continuous suction or pneumothorax instability) improved after the bronchoscopic SVS procedure to a degree that allowed for outpatient management with a Heimlich valve. Adverse events requiring SVS removal were also documented. Statistical analysis was reported as percentages, means ± SD, medians and ranges, where appropriate. The analysis was done using OpenEpi (version 3.01).

Table 1 Demographics

	$N=39$ patients
Age (years old, mean ± SD)	62.6 ± 11.1
Gender—N (%)	
Male	29 (74.4%)
Female	10 (25.6%)
Lung disease—N (%)	
COPD/emphysema	26 (66.7%)
Lung mass	20 (51.3%)
Asthma	2 (5.1%)
Miscellaneous	7 (17.9%)
Smoking	
Past	28 (71.8%)
Current	9 (23.1%)
Never	2 (5.1%)
Surgery	
Lobectomy	30 (76.9%)
Segmentectomy	3 (7.7%)
LVRS	5 (12.8%)
Lobectomy + segmentectomy	1 (2.6%)
Other procedures for air leak ($N=11$)	
Additional chest tubes	7 (63.6%)
Muscle flaps	2 (18.2%)
Surgical repair	1 (9.1%)
Pericardial patch	1 (9.1%)

Results

The mean age of patients was 62.6 ± 11.1 years, and 74.4% were males. Most of the patients were current or former smokers (94.9%). The majority of patients (76.9%) were post lobectomy, 7.7% had segmentectomy, and 12.8% had LVRS (Table 1). Eleven patients (11/39) had other procedures to resolve air leaks prior to the SVS valve procedure, including placement of additional or repeat chest tubes (7 patients), muscle flap (2 patients), additional resection and repair with pericardial patch (1 patient), or parenchymal surgical repair (1 patient).

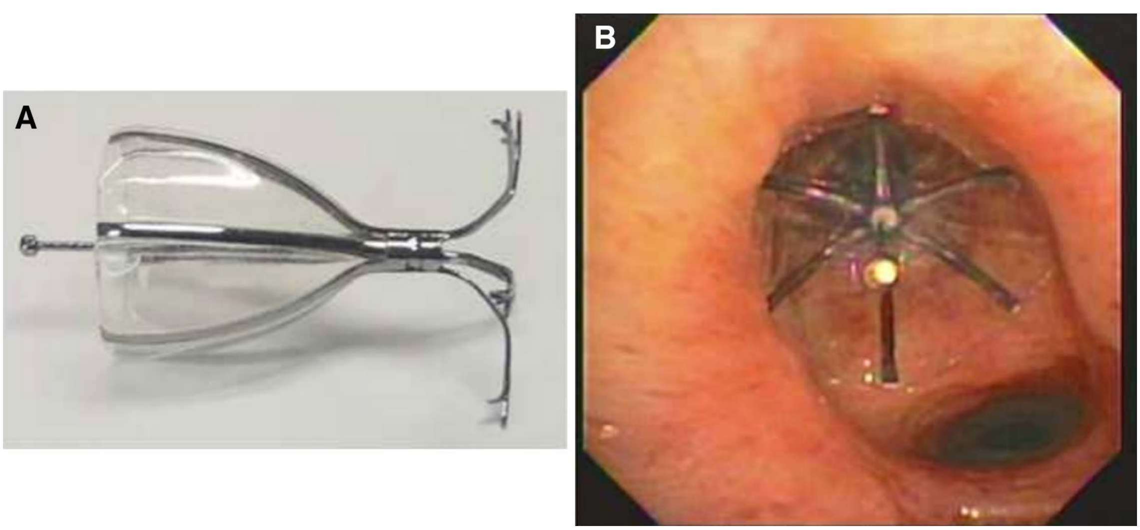

Fig. 1 The Spiration Valve System (SVS, Olympus/Spiration Inc. Redmond, WA, USA): **a** Intrabronchial valve. **b** Bronchoscopic image of the valve

Thirty-nine patients underwent bronchoscopy with an intention to perform SVS valve placement, with a median of 9.5 days after the original surgical resection (mean ± SD of 23.8 ± 38.8 days, one patient was excluded as the SVS procedure was done 1236 days after original surgical resection). Thirty-two patients (32/39 patients, 82.1%) had successful SVS procedures. A median of two valves were used per patient (mean ± SD of 2.7 ± 1.5 valves per patient, total of 90 valves used in 32 patients, range 1–7 valves per patient). The sizes of the valves used were 5 mm, 6 mm, and 7 mm valves. The larger 9 mm valve was not available during this prospective registry. The remaining 7 patients (17.9%) did not have valves placed due to difficult anatomy, inability to localize leak, finding of system leak at the time of the procedure, or spontaneous air leak resolution before any valves were placed.

When SVS placement procedure was feasible, 30/32 patients with valves placed (93.8%) had a positive response to the SVS procedure. When considering all patients, 76.9% of patients (30/39 patients) had positive response to the SVS procedure. The median post-procedure ICU stay was 0 days (mean ± SD of 0.7 ± 2.2 days, 32 patients, range 0–10 days), and the median post-procedure hospital stay was 4 days (mean ± SD of 6.0 ± 6.1 days, 32 patients, range 0–27 days). In patients with feasible SVS placement, complete resolution of air leak was documented in 87.5% of patients (28/32 patients) with a median time to air leak resolution of 2.5 days (mean ± SD of 8.9 ± 12.4 days, range 1–45 days). Four patients (12.5%) had persistent air leak through the documented follow-up period. Considering all patients in the registry with an intention to treat analysis, 71.8% (28/39 patients) are considered to have resolution of the air leak likely related to bronchoscopic SVS procedure.

Seventy-four valves (74/90 valves) were subsequently removed from 26 patients (27 removal procedures) by the end of the study, with 16 valves remaining in 6 patients. One patient required early valve removal procedure for documented atelectasis of the lingula causing dyspnea and hypoxia. All valve insertion procedures were done under monitored anesthesia care and general anesthesia. Half of the procedures were done in the operating room (51%) and the other half in a bronchoscopy suite (49%). The median bronchoscopy time for SVS insertion procedures was 48 min (mean ± SD of 53.2 ± 27.9 min). The median bronchoscopy time for SVS removal procedure was 21.5 min (mean ± SD of 31.1 ± 30.4 min). Table 2 summarizes the results.

Table 2 Results in 39 patients who underwent bronchoscopy with an intention to perform SVS placement procedure

	N (mean ± SD)	Median
Time to procedure (days)	38[a] (23.8 ± 38.8 days)	9.5
Number of valves per patient	32 (2.7 ± 1.5)	2
Post-procedure ICU stay (days)	32 (0.7 ± 2.2)	0
Post-procedure hospital stay (days)	32 (6.0 ± 6.1)	4
Procedure was feasible	32/39 patients (82.1%)	
Procedure was not feasible	7/39 patients (17.9%)	
Patients with positive response considering all patients in the registry	30/39 (76.9%)	
Patients with positive response when SVS procedure was feasible	30/32 (93.8%)	
Immediate air leak resolution	11 (34.4%)	
Improvement in air leak within 48 h	11 (34.4%)	
Improvement allowing outpatient management	8 (25.0%)	
Complete resolution of air leak at the end of study when SVS placement was feasible	28/32 (87.5%)	
Complete resolution of air leak considering all patients in the registry	28/39 (71.8%)	
Time to complete air leak resolution (days)	8.9 ± 12.4	2.5
Patients with SVS removed	26/32 (81.25%)	
Time to SVS removal (days)	51.9 ± 33.7	42.5
SVS insertion bronchoscopy time (mins)	53.2 ± 27.9	48
SVS removal bronchoscopy time (mins)	31.1 ± 30.4	21.5
Removal of SVS for adverse events (number of patients)		
Lobar atelectasis	1	

[a] $N = 39$ patients, who underwent all procedures regardless of successful SVS placement. One patient was excluded as there was a duration of 1236 days between initial surgery and SVS procedure

Comment

Currently, there are no clear recommendations for optimal treatment of post-surgical air leaks which are generally managed conservatively using a variety of techniques including prolonged tube thoracostomy drainage with or without continuous suction to promote pleural apposition, Heimlich valve placement, chemical pleurodesis, autologous blood patches, and other approaches while optimizing nutritional status and other comorbid conditions [16, 17, 36, 37]. Surgery is sometimes necessary to resolve air leaks if more conservative management fails. However, repeating surgery on patients with significant comorbidities after an initial thoracic resection could lead to further morbidity and mortality. To avoid re-operating on high-risk patients, various innovative minimally invasive techniques were developed including bronchoscopically placed coils, glues, stents, or application of local sclerosants such as silver nitrate [18–22]. The endobronchial Watanabe spigots were used with some efficacy to treat PAL, but usage has been limited due to complications such as migration, atelectasis, and pulmonary infections [23, 24].

The ability to treat persistent air leaks by bronchoscopy is dependent on the ability to localize the lobe(s), segment(s), and airways contributing to the air leak. The mechanism by which air leak improvement or resolution occurs is related to the one-way nature of the valve, limiting or completely eliminating airflow towards the broncho-pleural or alveolar-pleural fistula and area of injury distal to the valve, while simultaneously allowing air and secretions to drain out of the injured lung segment or lobe. This leads to redirection of airflow away from the injured lung segment which facilitates healing and ultimately closure of the underlying broncho-pleural or alveolar-pleural fistula with subsequent resolution of air leak. The SVS placement procedure was not possible in 17.9% of our patients due to various reasons including inability to localize air leaks and technical and anatomical considerations. This is similar to Gilbert et al. who reported that 21.4% of their post-pulmonary resection patients did not have valves placed [30]. This emphasizes the importance of patient selection.

The current literature reports variable outcomes after bronchoscopic one-way valve procedures ranging from complete resolution of air leaks to partial response, with inconsistent definitions [30–41]. Higher efficacy for resolution of air leaks with bronchoscopic one-way valve procedures was reported amongst post-surgical patients. This may be confounded by selection bias, as these patients are selected as good surgical candidates on the basis of adequate pulmonary function, are often not active smokers, and have elective surgeries with attempts to minimize risk factors for PAL. Gilbert et al. reported a subset of 22 patients (22/28 patients) with persistent air leaks after pulmonary resections that underwent successful one-way valve placement procedures with a mean time to air leak resolution of 10.5 days [30]. In a prospective study by Dooms et al., nine patients with persistent air leaks after thoracic resections had successful cessation of air leaks after management with one-way valves [35]. Fiorelli et al. reported that among a subset of 42 post-operative patients with air leaks, 35 underwent bronchoscopic valve procedures and had either moderate or complete resolution of PAL post-valve placement [41]. Bronchoscopic procedures including one-way valve procedures are often described as a salvage procedures to resolve persistent air leaks. Among our population, 11 patients (28.2%) had other procedures to resolve air leak prior to the SVS procedure. Management of persistent air leaks with one-way valves could have independent and additive effects to other procedures and time, modifying the course of air leaks. Our results are comparable to other reports in post-pulmonary resection patients.

Although this was a prospective, multicenter registry, it is limited with lack of generalizability of results due to small size and lack of comparison to standard treatment options like prolonged tube thoracostomy drainage, Heimlich valve, pleurodesis, and further surgical interventions. The lack of a control standard treatment arm and lack of randomization are significant limitations. The lack of objective quantification of the air leak is also a significant limitation. We used standard descriptive terms but not quantitative measures.

The results of our registry add to the growing body of literature supporting the use of one-way valves for management of post-pulmonary resection air leaks. The SVS bronchoscopic procedure is proving to be feasible, effective, and safe approach that can favorably affect the course of patients with post-pulmonary resection air leaks. This is especially true in high-risk patients with limited further thoracic surgical options. Randomized controlled trials comparing one-way valves to more conventional therapies remain necessary to better determine the role of this innovative bronchoscopic approach in the management of air leaks following pulmonary resections.

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Compliance with ethical standards

Conflict of interest Drs. M. Abu-Hijleh, K. Styrvoky, F. Woll and V. Anand report no conflicts of interest. Dr. L. Yarmus has received research, educational funding and consulting fees from Olympus Amer-

ica. Dr. M. S. Machuzak served as a consultant to Spiration/ Olympus America. Dr. D. A. Nader received research, educational and consulting fees from Olympus America. Dr. D. K. Hogarth served as a consultant to Spiration/ Olympus America. This ended in 2015. Dr. J. Toth has received research, educational and consulting fees from Olympus America. Dr. R. F. Casal served as an educational consultant Olympus America and had research grants from Siemens and Concordia. Dr. S. Hazelrigg reports no conflicts of interest. Dr. D. E. Wood has received research, educational and consulting fees from Olympus America.

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