

Research Article

Peri-Operative Factors that Predict Prolonged Air Leaks after Robotic-Assisted Thoracoscopic Pulmonary Lobectomy

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Abstract

Introduction: Prolonged Air Leaks (PAL) lasting more than 5 days after pulmonary resection lengthen chest tube duration and hospital length stays and may lead to further complications. We sought to identify perioperative factors associated with PAL in patients who underwent robotic-assisted pulmonary lobectomy.

Methods: We retrospectively analyzed all patients who underwent robotic-assisted pulmonary lobectomy from September 2010 to May 2014. Student's t-test, Chi-square test, Fisher's exact test, and Kruskal-Wallis median test were used, with $p \leq 0.05$ as significant.

Results: Of 232 study patients, 40 (17.2%) patients had PAL. Patients with PAL had significantly higher preoperative Forced Expiratory Volume in 1 second (FEV1), Total Lung Capacity (TLC), Functional Residual Capacity (FRC), and Residual Volume (RV), more intraoperative pleural adhesiolysis, and lower Body Mass Index (BMI), FEV1-to-Forced-Vital-Capacity (FVC) ratio, and prealbumin levels than non-PAL patients (all $p \leq 0.05$). Age, gender, preoperative weight, height, body surface area, albumin on postoperative day 1 or at discharge, preoperative FVC or diffusion capacity of the lung to carbon monoxide, skin-to-skin operative time, tumor size, and in-hospital mortality were similar between groups (all $p > 0.05$).

Conclusions: Higher preoperative TLC, FRC, and RV and lower FEV1 and FEV1/FVC ratio in PAL patients suggest that small airway obstruction and air trapping, in addition to lung parenchymal staple lines and pleural adhesiolysis that may provide surgical paths of air egress, contribute to PAL. Lower BMI and lower postoperative prealbumin levels in PAL patients suggest that nutritional deficits may hinder closure of surgical paths of air egress and contribute to PAL.

Keywords: Perioperative outcomes; Air leaks; Minimal invasive surgery; Robotic surgery; Lobectomy

Abbreviations

BMI: Body Mass Index; BSA: Body Surface Area; DLCO: Diffusing Capacity of the Lungs for Carbon Monoxide; FEV1: Forced Expiratory Volume in 1 Second; FRC: Functional Residual Capacity; FVC: Forced Vital Capacity; NSCLC: Non-Small Cell Lung Cancer; PAL: Prolonged Air Leak; RV: Residual Volume; RAVT: Robotic-assisted Video-Thoracoscopic; TLC: Total Lung Capacity; VATS: Video-Assisted Thoracoscopic

Introduction

The recuperation phase after any kind of surgical procedure is a dual

process that consists of tissue healing and functional rehabilitation. Respiratory complications after pulmonary resections can delay this process. Air leaks after pulmonary resections occur when air passes through the lung parenchymal staple lines or visceral pleural defects [1,2]. As part of the daily thoracic postoperative assessment, clinicians ask the patient to cough or perform maneuvers that increase the intra-thoracic pressure in order to evaluate the presence and degree of an air leak. If air bubbles are observed through the water seal chamber of the drainage system, an air leak is suspected. Persistence of vigor in bubbling following several maneuvers performed by the patient will likely indicate an active leak, while tapering vigor of bubbling may indicate only trapped air in the pleural space without an obvious visceral pleural defect.

Air leaks are commonly noticed immediately after pulmonary resections, with reported occurrences ranging from 28% to 60% following lung resections [1]. The majority of air leaks will resolve by Post-Operative Day (POD) #4 as the visceral pleura seals [3-5]. A Prolonged Air Leak (PAL) is an air leak that continues beyond the expected hospital Length of Stay (LOS) for the procedure and has been defined by The Society of Thoracic Surgeons (STS) database [1]. Most studies use a range of 5-7 days post-operatively as a cutoff for PAL, with larger recent studies suggesting the use of greater than 5 days post-operatively as the definition of PAL [1].

PAL has been reported as the most significant determinant of hospital LOS, more so than pain control, nausea, or vomiting

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[6,7]. Other presumed perioperative complications associated with PAL include atelectasis, pneumonia, empyema, pain, and higher hospital costs [6,8-10]. With PAL being associated with many postoperative complications, it becomes prudent to determine factors that contribute to their development. Some of those factors can be modified preoperatively or postoperatively as part of the recuperation, with the goal of decreasing the incidence of PAL.

The aim of this study is to determine the factors associated with the occurrence of PAL after Robotic-Assisted Video-Thoroscopic (R-VATS) pulmonary lobectomies and to compare these factors with published historical data for conventional Video-Assisted Thoracoscopic (VATS) surgery and traditional thoracotomy approaches.

Materials and Methods

We retrospectively analyzed prospectively collected data from patients who underwent R-VATS pulmonary lobectomy or bilobectomy at our institution by one surgeon from September 2010 through May 2014. Of these patients, we excluded those that converted to an open lobectomy via thoracotomy and any resections beyond the lobectomy or bilobectomy, such as wedge resections, segmentectomies, or pneumonectomies. This study was conducted in accordance with the amended Declaration of Helsinki as outcomes research for quality assurance as part of our departmental thoracic oncology clinical research database protocol. This database protocol was approved by our institution's Scientific Review Committee and our university's Institutional Review Board (IRB), which waived informed consent for this retrospective study, which is considered as review of existing data. Nevertheless, all patients gave informed consent for our standard surgical procedure, which consists of fiberoptic bronchoscopy, R-VATS lobectomy, or else R-VATS wedge resection followed by completion lobectomy, and then Mediastinal Lymph Node (LN) Dissection (MLND), with possible thoracotomy. Some patients also gave informed consent for any anticipated en bloc chest wall and/or vertebral resection, with possible reconstruction. Through our institutional surgical informed consent, patients gave permission to use surgery-related and tissue-related data for education and research purposes.

All our patients undergo fiberoptic bronchoscopy by the operating surgeon after the induction of general anesthesia. After placement of the dual-lumen endotracheal tube, the patient is then placed in either right or left lateral decubitus position, depending on which hemithorax the lesion is located. Our robotic-assisted lobectomy technique utilizes a three-port system, which includes a 4 cm camera port along the 6th Intercostal Space (ICS) at the anterior axillary line, which doubles as the assistant's access port, and two 1 cm instrument ports along the 3rd ICS at the anterior axillary line and along the 9th ICS at the posterior axillary line. This 3-port anterior approach is adapted from our 2-port approach for conventional VATS lobectomies, which uses a 1 cm camera port in the 8th or 9th ICS at the posterior axillary line and a 4 cm instrument port along the 5th or 6th ICS at the anterior axillary line and which allows use of the thoracoscope in either port. Since a 4 cm incision is ultimately required to deliver the resected lobe with the lung cancer from the thoracic cavity, we have not adopted a totally port-based approach. Our 3-port anterior approach differs from that of Park and colleagues only in the choice of ICS for the port incisions (e.g., the 3rd, 6th, and 9th ICS for our port incisions instead of the 4th, 7th, and 10th ICS for theirs) and the choice of the port which is shared by the assistant for access (e.g., our assistant sharing the 6th

ICS camera port incision instead of their assistant sharing the 4th ICS instrument port incision) [11]. Based on our three port incisions, the robotic patient cart is docked behind the patient and over the patient's ipsilateral shoulder, with alignment of the robotic patient cart's center post, the patient's scapular tip, and the camera port at the 6th ICS along the anterior axillary line.

From September 2010 through December 2011, our group used the da Vinci "S"[™] Robotic Surgical System (Intuitive Surgical Corp., Sunnyvale, CA, USA), with the "Si"[™] system being used from January 2012 onward. The lobectomy is performed with the pulmonary vein divided first, then the pulmonary artery branch (es) and bronchus, and then completion of the pulmonary fissures. While we have not needed to use the fourth arm of the robotic patient cart, we have created a fourth port, usually along the 9th ICS at the mid scapular line, on rare occasion to allow for another angle from which to apply the linear endostapler onto a difficult pulmonary artery branch, particularly when performing a left upper lobectomy.

After delivery of the lobectomy within an endopouch through the 6th ICS port incision, complete MLND is then performed. We prefer to have our assistant use a "sponge stick" to retract the lung and expose the mediastinal LN stations, rather than to use the fourth arm of the robotic patient cart, in order to simplify the robotic patient cart set-up and docking and to minimize risk of both internal and external collisions between the robotic patient cart arms. At the end of the procedure, a 32-French chest tube is introduced through the 9th ICS port incision and connected to drainage at -20 cm H₂O continuous suction. Any air leak was visualized through the water seal chamber of the chest drainage system (Ocean[™] Water Seal Chest Drain, Atrium Medical Corp. Merrimack, NH, USA). For this study, we defined PAL as evidence of active air passage through the water seal chamber at 7 days or more after surgery, as preceding studies have done [12,13].

Multiple pre-operative, intra-operative, and post-operative factors regarding these cases were analyzed. Descriptive analysis was used to characterize all study variables. Continuous variables were described with means, median when appropriate, and with standard error of the mean. Results are based on available data.

Patients with a missing variable were excluded at the moment of analyzing that specific variable. Categorical variables were described as proportions and percentages. To assess the difference in outcomes between patients with and without PAL, bivariate analyses were conducted on numerical variables through the student's t-test, while categorical variables were compared with the Chi-square test (Fisher's exact test used when expected frequency is fewer than 5). Independent-samples Kruskal-Wallis test was used to determine significant differences in variables that were described by medians. The SPSS v23.0 (IBM Corp., Armonk, NY, USA) software was used to conduct statistical analysis on this data, with $p \leq 0.05$ considered as significant.

Results

A total of 256 patients were identified under our criteria. Twenty-four of these cases resulted in an intra-operative conversion to open lobectomy via thoracotomy and were, therefore, excluded from this study, leaving a total of 232 patients for analysis. Of the 232 pulmonary lobectomy patients reviewed in our cohort, 40 of them (17.2%) had PAL at 7 days or more after surgery. Table 1 shows our overall cohort demographics. Mean age of our patient cohorts was 66.8 years, with females being the pre-dominant gender at 53.4%. Mean preoperative

percent of predicted Forced Expiratory Volume in 1 second (FEV1%) and mean percent of predicted diffusion constant of the lung for carbon monoxide (DLCO%) of our entire cohort were 87.7% and 75.2%, respectively. Mean diameter of the lesions excised was 3.1 cm, with upper lung resections being the most common at 66% of the resections (Table 2). Overall median skin-to-skin operative time was 173 min, and patients had a median hospital LOS of 5 days overall.

In Table 3, pre-operative factors associated with PAL occurrence include a lower mean Body Mass Index (BMI; 26 kg/m² vs. 28.3 kg/m²; p=0.025), lower mean post-operative pre-albumin level (11.6 mg/dL vs. 14.5 mg/dL; p=0.003), lower mean ratio of forced expiratory volume in 1 second to forced vital capacity (FEV1/FVC) (0.65 vs. 0.70; p=0.018), and higher mean percentage of predicted total lung capacity (TLC%; 108.6% vs. 98.3%; p=0.030), functional residual capacity (FRC%; 124.3% vs. 101.6%; p=0.016), and residual volume (RV%; 130.1% vs. 102.2%; p=0.022). Percent of predicted DLCO did not exhibit a significant difference between the two groups, (71.3% vs. 76.0%; p=0.22).

Also in Table 3, lysis of pleural adhesions demonstrated significant association with the occurrence of PAL, with 67.5% of PAL patients having had lysis of pleural adhesions compared to only 43.2% of non-PAL patients having had lysis of pleural adhesions (p=0.005). Location of resected lobe also demonstrated effect, with 82.5% of PAL patients having undergone upper lobe resections compared to 62.5% of non-PAL patients. While median skin-to-skin operative time was greater in the PAL group compared to non-PAL patients, the difference was not quite significant (194.5 min vs. 168.0 min; p=0.067).

There were no significant differences in other morbidity, including the occurrence of chyle leaks, hemothorax, or pneumonia. However, occurrence of PAL in patients did result in increased utilization of hospital resources as evidenced by increased median hospital LOS (10.5 days vs. 4.0 days, p<0.001). In-hospital mortality was increased, but not quite significantly, in patients experiencing versus those without PAL (5% vs. 0.5%; p=0.077).

Table 1: Patient demographics.

Variables (N=232)	Total
Age, yr*	66.8 ± 0.6 (29-86)
Gender Male	108/232 (46.6%)
Female	124/232 (53.4%)
Height, cm*	167.2 ± 0.6 (147.8-189.2)
Weight, kg*	77.5 ± 1.2 (34.7-161.6)
BSA, m ² *	1.89 ± 0.02 (1.25-2.86)
BMI, kg/m ² *	27.9 ± 0.4 (14.0-59.0)
Pre-Op FEV1%*	87.7 ± 1.4 (32-145)
Pre-Op FVC%*	96.5 ± 1.1 (60-138)
FEV1/FVC Ratio*	0.69 ± 0.01 (0.34-0.90)
(FEV1/FVC)%*	91.1 ± 1.0 (42.1-133.3)
Pre-Op TLC%*	100.1 ± 1.2 (60-138)
Pre-Op FRC%*	105.3 ± 2.2 (54-345)
Pre-Op RV%*	106.9 ± 3.0 (30-445)
Pre-Op DLCO%*	75.2 ± 1.3 (23.8-132.0)

*Mean ± S.E.M. (Range); BSA: Body Surface Area; BMI: Body Mass Index; Pre-Op: Pre-Operative; FEV1: Forced Expiratory Volume in 1 Second; FEV1%: FEV1 as percent of predicted; FVC: Forced Vital Capacity; FVC%: FVC as percent of predicted; TLC%: Total Lung Capacity as percent of predicted; FRC%: Functional Residual Capacity as percent of predicted; RV%: Residual Volume as percent of predicted; S.E.M: Standard Error of the Mean; DLCO%: Diffusion Capacity of the Lung for Carbon Monoxide as percent of predicted

Table 2: Perioperative outcomes.

Variables (N=232)	Total
Size of Tumor, cm*	3.1 ± 0.1 (0-9.7)
Upper Lobe Resection ^a	153/232 (66.0%)
Middle Lobe Resection ^b	17/232 (7.3%)
Lower Lobe Resection ^c	62/232 (26.7%)
Lysis of Pleural Adhesions	110/232 (47.4%)
Skin-to-Skin Operative Time, min**	173 (81-515)
Prealbumin on Post-Operative Day #1*	17.9 ± 0.3 (4.4-28.8)
Lowest Inpatient Postop Prealbumin*	14.0 ± 0.4 (3.0-28.8)
Last Inpatient Postop Prealbumin*	14.7 ± 0.4 (3.0-30.9)
Postop Hemothorax	5/227 (2.2%)
Postop Chyle Leak	4/232 (1.7%)
Postop Mucous Plugs Requiring Bronchoscopy	14/232 (6.0%)
Postop Pneumonia	20/232 (8.6%)
Chest Tube Duration, days**	4.0 (1-36)
Hospital Length of Stay (LOS), days**	5.0 (2-32)
In-Hospital Mortality	3/232 (1.3%)

*Mean ± S.E.M. (Range); **Median (Range); ^aUpper Lobe Resection includes right upper lobectomy, left upper lobectomy, or right upper/middle bilobectomy; ^bMiddle Lobe Resection includes right middle lobectomy only; ^cLower Lobe Resection includes Right Lower Lobectomy, left lower lobectomy, or right lower/middle bilobectomy; Postop: Postoperative; S.E.M: Standard Error of the Mean

Discussion

Prolonged Air Leak (PAL) has been documented with a prevalence of 13% in a cohort of over 600 consecutive pulmonary lobectomies [14]. Others have reported PAL in up to 26% of lung resections post-operatively [6,15]. However, these studies used differing standards for defining PAL. We used 7 days as the cut-off for PAL. Besides identifying the incidence of PAL, the aim of the study was to identify non-modifiable and modifiable factors related to this complication.

The results of our study show that robotic-assisted pulmonary resections continue to share similar risk factors for the development of PAL as conventional VATS, traditional thoracotomy, and even Lung Volume Reduction Surgery (LVRS) [16-18]. A commonly correlated peri-operative factor associated with PAL is a low FEV1/FVC ratio [16,18,19]. Lower FEV1/FVC ratio in PAL patients suggests that pre-existing obstructive lung disease predisposed patients to PAL. Possible reasoning as to why low FEV1/FVC ratios contribute to PAL occurrence might be that obstructive lung disease leads to air trapping due to small airway obstruction (Figure 1). Following resection, surgically created paths of egress may serve as an outlet of least resistance for this increased intrapulmonary air volume (Figure 1, right panel).

Our study also shows a lower FEV1% of predicted is correlated with the occurrence of PAL. The Global Initiative for Chronic Obstructive Lung Disease (GOLD) classification of airflow limitation in Chronic Obstructive Pulmonary Disease (COPD) is based on FEV1% of predicted value; therefore, patients with a higher GOLD classification are at greater risk for developing PAL in addition to increased mortality [20].

Other common risk factors include pleural adhesions, upper lobe resections, and a lower BMI [12,17,19]. Intra-operatively, aggressive or extensive lysis of pleural adhesions during surgery would be expected to be a risk for the development of PAL due to visceral pleural injuries and greater numbers of these paths of air egress. Upper lobe resections are correlated with PAL as they are thought to

Table 3: Significant factors contributing to prolonged air leaks.

Variables (N=232)	Patients with PAL (n=40)	Patients without PAL (n=192)	p-value
BMI, kg/m ² *	26.0 ± 0.8 (17.6-38.0)	28.3 ± 0.4 (14.0-59.0)	0.025
Pre-Op FEV1%*	80.3 ± 3.7 (32.0-145.0)	89.2 ± 1.4 (44.0-138.0)	0.015
FEV1/FVC Ratio*	0.65 ± 0.02 (.34-.86)	0.70 ± 0.01 (.37-.90)	0.018
(FEV1/FVC)%*	85.1 ± 2.8 (42.1-110.7)	92.2 ± 1.1 (49.6-133.3)	0.011
Pre-Op TLC%*	108.6 ± 4.4 (68.0-222.0)	98.3 ± 1.1 (60.0-146.0)	0.03
Pre-Op FRC%*	124.3 ± 8.7 (57.0-345.0)	101.6 ± 2.0 (54.0-220.0)	0.016
Pre-Op RV%*	130.1 ± 11.4 (55.0-445.0)	102.2 ± 2.6 (30.0-312.0)	0.022
Upper Lobe Resection ^a	33/40 (82.5%)	120/192 (62.5%)	0.029†
Lysis of Pleural Adhesions	27/40 (67.5%)	83/192 (43.2%)	0.005†
Lowest Prealbumin*	11.6 ± 0.7 (3.0-20.3)	14.5 ± 0.4 (3.0-28.8)	0.003
Chest Tube Duration, days **	12.5 (5-36)	3.0 (1-21)	<0.001°
Hospital LOS, days**	10.5 (6-23)	4.0 (2-32)	<0.001°

*Mean ± S.E.M. (Range); ** Median ± S.E.M. (Range); ^aUpper Lobe Resection includes Right Upper/Middle Bilobectomy; PAL: Prolonged Air Leak; BMI: Body Mass Index; Pre-Op: Pre-Operative; FEV: Forced Expiratory Volume in 1 second; FEV1%: FEV1 as percent of predicted; FVC: Forced Vital Capacity; FVC%: FVC as percent of predicted; TLC%: Total Lung Capacity as percent of predicted; FRC%: Functional Residual Capacity as percent of predicted; RV%: Residual Volume as percent of predicted; LOS: Length of Hospital Stay; S.E.M: Standard Error of the Mean; p-values: unpaired t-test was used for analysis, except when †Pearson Chi-Square test was used for two-way analysis or °Independent-Samples Kruskal-Wallis test.

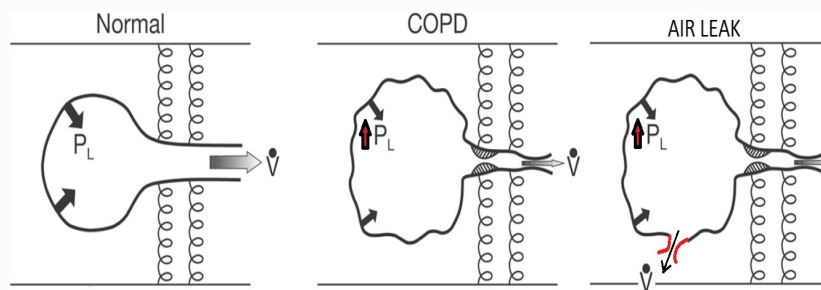


Figure 1: Illustrations of normal lung alveoli showing normal pressure of lung recoil, P_L , and normal egress of air, v (left panel) and of obstructive lung disease leading to air trapping due to small airway obstruction (middle panel), which leads to increased P_L and contributes to PAL through surgically created paths of egress, v (right panel). Adapted from Thomas et al. [22].

lead to large apical air spaces that decrease visceral-parietal pleural apposition and, thus, decrease pleural adherence to seal air leaks [15]. Lower mean BMI and lower mean post-operative prealbumin levels in PAL patients suggest that nutritional deficits may hinder closure of surgically created path(s) of air egress. Contrary to many studies, we did not find an association between PAL occurrence and infection [9].

Brunelli et al. [16] found that upper lobe resection occurred in 74.1% of PAL patients compared to 63.1% in patients without PAL ($p=0.04$), that pleural adhesions occurred in 50.6% vs. 30.1% of patients with and without PAL, respectively ($p=0.0002$), and that an FEV1/FVC ratio of 0.66 vs. 0.71 occurred in patients with and without PAL, respectively ($p<0.0001$). Similar to these results, the results of Singhal et al. [17], and those of the National Emphysema Treatment Trial (NETT) [18], we found upper lobe resection and pleural adhesions as predictive factors for PAL. However, these two studies found a reduced DLCO as predictive of PAL, while our DLCO% of predicted for PAL patients was only slightly, but not significantly, lower than for non-PAL patients (71.3% vs. 76% predicted; $p=0.22$), perhaps due to small group size in our study.

Our study also demonstrated that the increased median hospital LOS for patients who experienced PAL is consistent with evidence indicating that PAL results in greater hospital costs and LOS [21]. The incidence of any air leak complication has been associated with an increased hospital LOS by 2.5 days and an increase in hospital costs by \$6,000 [21].

Rivera et al. [13] developed an Index of Prolonged Air Leaks (IPAL) as a predictive model for PAL. Their scoring system associated greater occurrence of PAL with male gender, lower BMI, greater dyspnea score, presence of pleural adhesions, larger resections, and upper lobe resections. Our study overlaps their study by having analyzed the factors of gender, BMI, pleural adhesions, and location of resection. As with Rivera et al. [13] we found similar associations of PAL with lower BMI, pleural adhesions, and upper lobe resection. We also saw a greater number of males with PAL (55% vs. 44.8%, $p=0.22$), although this difference was not significant.

Conclusion

Higher preoperative TLC, FRC, and RV and lower FEV1 and FEV1/FVC ratio in PAL patients suggest that small airway obstruction and air trapping, in addition to lung parenchymal staple lines and pleural adhesiolysis that may provide surgical paths of air egress, contribute to PAL. Lower BMI and lower postoperative prealbumin levels in PAL patients suggest that nutritional deficits may hinder closure of surgical paths of air egress and contribute to PAL. By knowing these peri-operative factors most associated with PAL, surgeons could better optimize patients pre-operatively, such as by dietary protein supplementation, or appropriately counsel patients on post-surgical risks associated with pulmonary lobectomies. Modifications in intra-operative and post-operative management of at-risk patients, such as by dietary protein supplementation and preventing patients from straining due to constipation, could be made to prevent this costly complication.

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E.M.T., as guarantor of the content of this manuscript, had full access to all of the data in the study, and takes responsibility for integrity of the data and accuracy of the data analysis, including and especially any adverse effects. F.O.V., C.C.M., J.R.G., J.P.F., and E.M.T. contributed to surgical procedures and/or to perioperative patient care. R.A.P., F.O.V., E.P.N., and E.M.T. contributed to data collection, analysis, and interpretation. R.A.P., F.O.V., and E.M.T. contributed to study design and/or to writing of the manuscript.

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Conflict of Interest

E.M.T. and J.P.F. have had financial relationships with Intuitive Surgical Corporation in form of honoraria as robotic thoracic surgery proctors and observation sites. No other authors have any conflicts of interest or financial ties to disclose.

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