

التسريب الهوائي المديد بعد الاستئصال الرئوي عند مرضى سرطان الرئة غير صغير الخلايا

أ.د. نزار عباس*

د.تمام حسن*

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□ ملخص □

خلفية البحث: يعتبر تسريب الهواء المديد (PAL) من أهم أسباب الاختلاطات وزيادة فترة الاستشفاء بعد عمليات الاستئصال الرئوي. **هدف البحث:** يهدف هذا البحث إلى تحديد نسبة حدوث تسريب الهواء المديد وتأثيراته السريرية على المرضى الذين يخضعون لاستئصال رئوي من أجل سرطان الرئة البدئي، وإلى تحديد عوامل الخطورة السابقة للجراحة والتي قد تؤهب لحدوث PAL بعد الجراحة.

المرضى وطريقة الدراسة: تم إجراء دراسة مستقبلية لـ ١٦٧ مريض (٣٠ امرأة و ١٣٧ رجل) خضعوا لاستئصال رئوي من أجل سرطان رئة غير صغير الخلايا خلال الفترة الممتدة من بداية شهر كانون الثاني عام ٢٠١٧ ولغاية نهاية شهر آب للعام ٢٠٢٠ في شعبة جراحة الصدر في مستشفى الأسد الجامعي بدمشق. ولغرض الدراسة تم تعريف التسريب الهوائي الذي يستمر أكثر من ٥ أيام على أنه تسريب هواء مديد.

النتائج: تم تسجيل تسريب الهواء المديد عند ١١ مريض (٨.٧%). جميعهم كانوا ذكور مدخنين، مع معدل تدخين ٦٧ باكيت/سنة. المعدل الوسطي للعمر ٦٣ سنة. معظم مرضى PAL كان لديهم COPD (٨٢%) مقارنةً مع (٦٣%) عند مرضى بدون PAL. تقريباً نصف مرضى PAL تلقوا علاج كيميائي سابق للجراحة (٤٦%) مقارنةً مع (١٩%) فقط عند المرضى بدون PAL. حدث PAL عند مرضى سرطان الرئة اليمنى أكثر من الرئة اليسرى (٦٤% مقابل ٣٦% على الترتيب) وغالبيتهم كان لديهم سرطان شائك الخلايا (٧٣%) مقابل (٢٧%) سرطان غدي. معظم حالات PAL حدثت بعد استئصال الفص العلوي (٥٥%). معدل زمن العمل الجراحي في مرضى PAL كان أكبر من مرضى بدون PAL (٣.٤ ساعة مقابل ٢.٣ ساعة). كما سبب PAL زيادة في فترة الاستشفاء (وسطي ١٢.٣ يوم) مقارنةً مع (٥.٥ يوم) عند المرضى بدون PAL. كما ترافق PAL مع نسبة أعلى من إعادة القبول للمشفى (١٨%) مقابل (٦%) عند المرضى بدون PAL. **الخلاصة:** تبين أن نسبة حدوث هذا الاختلاط ٨.٧% عند المرضى الذين خضعوا لاستئصال رئوي من أجل سرطان رئة غير صغير الخلايا. وأهم العوامل المرتبطة بحدوثه هي التدخين وCOPD والمرضى الذين تلقوا علاجاً كيميائياً قبل الجراحة والذين يحتاجون استئصال فص علوي أيمن. ولذلك ننصح بالتركيز على هذه العوامل قبل الجراحة من أجل تخفيض نسبة حدوث هذا الاختلاط و تخفيض مدة البقاء في المستشفى بعد الجراحة ونسبة إعادة القبول.

الكلمات المفتاحية: التسريب الهوائي المديد، الاستئصال الرئوي، سرطان الرئة غير صغير الخلايا

*أ.د. نزار عباس. أستاذ الجراحة الصدرية في كلية الطب بجامعة دمشق

**د. تمام حسن. دراسات عليا دكتوراه جراحة صدرية في كلية الطب جامعة دمشق

Prolonged Air Leak Following lung resection in patients with non-small cell lung cancer

Prof. Nizar Abbas*
Dr. Tammam Hasan**

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□ABSTRACT □

Background: prolonged air leak (PAL) is one of the most common causes of complications and protracted hospital stay in patients who have received a pulmonary resection.

Objectives: The purpose of this study was to determine the incidence of PAL and its clinical implications in patients undergoing pulmonary resection for primary lung cancer and to identify those preoperative factors that may predispose to the development of PAL.

Materials and methods: This is a prospective study carried out at Alassad university hospital in Damascus. We included 167 patients (30 women and 137 men) who had underwent pulmonary resection for non-small cell lung cancer at our institution from January 2017 through August 2020. For the purpose of this study, an air leak lasting more than 5 days was termed prolonged air leak (PAL).

Results: we reported PAL in 11 patients (8.7%). All of them were male, all smokers, with an average smoking rate of 67 packets / year. The average age was 63 years. most PAL patients had COPD (82%) compared to (63%) for non-PAL patients. Almost half of PAL patients received pre-operative chemotherapy (46%), while it was (19%) of non-PAL patients. PAL occurred more in patients with right lung cancer than in left lung (64% versus 36%, respectively), and the majority had squamous cell carcinoma (73%) compared to adenocarcinoma (27%). The majority of PAL cases occurred after upper lobectomy (55%). In the PAL group, the average surgery time (3.4 hours) was greater than that of non-PAL patients (2.3 hours), and PAL caused a longer hospital stay after surgery (12.3 days on average) compared to (5.5 days on average) in non-PAL patients. Also, PAL cases were associated with a higher rate of re-admission to the hospital (18%) than non-PAL patients (6%). However, no patient needed reoperation to manage PAL.

Conclusion: This complication occurred in 8.7% of patient who underwent pulmonary resection for NSCLC. The most important risk factor is: smoking, COPD, neoadjuvant chemotherapy and upper lobectomy. So we recommend to pay more attention on these risk factors before surgery in order to decrease the incidence of this complication and length of stay and readmission to the hospital.

Key words: prolonged air leak, lung resection, non-small cell lung cancer.

*Professor of thoracic surgery. Faculty of medicine – Damascus University.

**PhD student in thoracic surgery. Faculty of medicine – Damascus University

Introduction:

One of the most common causes of complications and protracted hospital stay in patients who have received a pulmonary resection is prolonged air leak (PAL).

The incidence of postoperative air leaks depends on the timely distance to lung resection. Whilst an air leak is present in 28% to 60% immediately after completion of the surgery, it is reported in 26% to 48% of patients on postoperative day 1 (POD1), 22% to 24% on POD2 and still 8% on POD4 according to the literature.^{1,2,3,4,5}

PAL is defined as an air leak lasting beyond postoperative day 5, which is an average length of stay (LOS) after pulmonary lobectomy.

PAL can cause distress, anxiety, and pain, as well as other complications, and also increases the risk of other cardiopulmonary complications and empyema. Therefore, management of pulmonary air leakage is an important clinical issue for thoracic surgeons.^{6,7}

The purpose of this study was to determine the incidence of PAL and its clinical implications in patients undergoing pulmonary resection for primary lung cancer and to identify those preoperative factors that may predispose to the development of PAL.

Materials and methods:

This is a prospective study carried out at Alassad university hospital in Damascus. We included all patients who underwent pulmonary resection for a bronchopulmonary cancer.

One hundred sixty-seven patients (30 women and 137 men) underwent pulmonary resection for non-small cell lung cancer at our institution from January 2017 through August 2020 and were taken into consideration for the present study.

The same surgical team performed all the procedures through a posterolateral thoracotomy. The following operations were performed in order of frequency: right upper bilobectomy (n 26), left upper lobectomy (n 24), left lower lobectomy (n 23), right upper lobectomy (n 20), right lower lobectomy (n 18), lesser resections (n 7), right lower bilobectomy (n 6) and middle lobectomy (n 2). At the same period there were 34 pneumonectomy and 7 open & close procedures, which were not enrolled in this study.

After completion of the lobectomy, a mediastinal lymphadenectomy was performed in all patients. Moreover, after re-inflation of the lung, air leaks were pinpointed by squirting sterile water over the lung and sutured prior to chest closure. Buttressed staple lines or chemical sealants were never used in this series.

Chest tubes were removed when the quantity of the effusion was 100 to 200 mL in 24 h and when no evidence of air leak was present. This chest tube management was applied to all patients in this series, and it is the standard policy at our institution. The presence of an air leak was checked twice daily during the morning and evening rounds. Patients had an active program of physiotherapy including deep-breathing exercises. Chest radiographs were routinely performed every day and when clinically indicated (reduced breath sounds at auscultation, increased sputum production, fever and leukocytosis, reduced oxygen saturation, a suspicion of chest tube malfunctioning).

For the purpose of this study, an air leak lasting more than 5 days was termed prolonged air leak (PAL).

Results:

During the study period, a surgical intervention was performed on 167 patients with non-small cell lung cancer in our center. Most of them (82.6%) are males, and the average age is 59 years. Most of these patients were smokers (88%), with an average smoking rate of 52 baguettes / year.

Among these patients, 11 patients (8.7%) had prolonged air leakage (> 5 days). All of them were male, all smokers, with an average smoking rate of 67 packets / year. The average age of these patients was 63 years.

Lung functions were slightly lower in patients with prolonged air leak compared to non-PAL patients (average FEV1 1.91 versus 2.77, respectively, and the average FEV1 / FVC was 57.2% versus 73%, respectively). In terms of comorbidity, most PAL patients had COPD (82%) compared to (63%) for non-PAL patients, while diabetes and cardiovascular disease were similar in both groups. Almost half of PAL patients received pre-operative chemotherapy (46%), while it was (19%) of non-PAL patients.

In terms of surgical findings, PAL occurred more in patients with right lung cancer than in left lung (64% versus 36%, respectively), and the majority had squamous cell carcinoma (73%) compared to adenocarcinoma (27%). The majority of PAL cases occurred after upper lobectomy (55%), followed by bilobectomy (27%) and finally lower lobectomy (18%). Patients characteristics are summarized in table 1.

In the PAL group, the average surgery time (3.4 hours) was greater than that of non-PAL patients (2.3 hours), and PAL caused a longer hospital stay after surgery (12.3 days on average) compared to (5.5 days on average) in non-PAL patients. Also, PAL cases were associated with a higher rate of re-admission to the hospital (18%) than non-PAL patients (6%). All PAL patients were managed conservatively, no patient needed reoperation, whereas 4 patients in non-PAL group underwent reoperation for causes other than PAL. Post-surgery results are summarized in table 2.

When comparing PAL patients who received neoadjuvant chemotherapy with PAL patients who underwent surgery directly, we find that PAL occurred in 5 patients from the chemotherapy group (9.6%) and it occurred in 6 patients from the surgery alone group (5.2%). The chemotherapy patients were more elderly (67 versus 63 years) and the amount of smoking was more (77 compared to 57 baguettes / year). The average time of surgery in the chemotherapy group (3.7 hours) was more than in the surgery alone group (2.9 hours), and the length of stay was greater in the chemotherapy group (14 days versus 10.6 days). No difference was noticed between the two groups in terms of lung function before surgery, comorbidity, histological type of tumor, tumor stage, and in terms of the excised lobe.

Table (1): Comparison between PAL & non-PAL patents after lung resection in patients with non-small cell lung cancer

	PAL patients (n=11)	Non PAL patients (115)
Age (mean)	63	61
Sex		
Male	11 (100%)	95 (82.6%)
Female	-	20 (17.4%)
smoking		
Smoker	11 (100%)	101 (88%)
Non-smoker	-	14 (12%)
Pack/years	67	52
PFTs		
FEV1 (average)	1.91	2.77
FEV1/FVC (average)	57.2%	73%
Side		
Right	7 (64%)	88 (53%)
left	4 (36%)	79 (47%)
comorbidity		
DM	2 (18%)	16 (14%)
Cardiac disease	3 (27%)	31 (27%)
COPD	9 (82%)	72 (63%)
Neoadjuvant	5 (46%)	22 (19%)
Histology		
Scc	8 (73%)	66 (57%)
adeno	3 (27%)	41 (36%)
others	-	8 (7%)
Staging		
I	2 (18%)	18 (16%)
II	4 (36%)	25 (22%)
IIIa	3 (28%)	46 (40%)
IIIb	2 (18%)	25 (22%)
Resection type		
Upper lobectomy	6 (55%)	38 (33%)
Lower lobectomy	2 (18%)	39 (34%)
Bilobectomy	3 (27%)	29 (25%)
Lesser resection	-	9 (8%)

Table (2): Post-surgery results for PAL & non-PAL patents after lung resection in patients with non-small cell lung cancer

	PAL patients (n=11)	Non-PAL patients (115)
Length of surgery	3.4	2.3
Length of chest tube	12.2	5
Length of stay	12.3	5.5
Readmission	2 (18%)	7 (6%)
Reoperation	0 (0%)	4 (3.5%)

Discussion:

With increasing concern for quality of medical care, length of hospital stay, and cost of health care delivery, it has become the responsibility of the surgeon to control all factors that lead to a prolonged hospitalization.

A variety of studies have reported the incidence of PAL and several have developed tools to calculate risk in order to identify patients at high risk using preoperative variables (Table 3).

Table (3): comparison of several trials studying PAL after lung resection

Author	Year of study	Total cases	Procedure	PAL definition	PAL incidence (%)	Risk factors
Brunelli et al. ⁷	2010	685	Lobectomy	>5 days	13	Age >65, adhesion, FEV1
Rivera et al. ⁸	2011	24,113	Lung resection	>7 days	6.9	Male, BMI, dyspnea score, adhesion, surgical procedure, bulla resection, LVRS, upper lobe
Petrella et al. ⁹	2011	121	Lobectomy	>5 days	21.2	Male, right side, age, TLC, percentage emphysema on CT
Elsayed et al. ¹⁰	2012	1,911	Lung resection	>6 days	6.7	FEV1, upper lobectomy, different consultant practice
Liang et al. ¹¹	2013	380	Lung resection	>5 days	18	Radiologic emphysema, histopathologic emphysema, FEV1
Gilbert et al. ¹²	2016	225	Lung resection	>7 days	8	Male, smoking history, BMI ≤25, dyspnea score, %DLCO <80
Pompili et al. ¹³	2017	5,069	VATS lobectomy	>5 days	9.9	Male, FEV1
Zhao et al. ¹⁴	2017	1,051	VATS major lung resection	>5 days	10.6	Adhesion
Okada et al. ¹⁵	2017	146	Lobectomy	>5 days	16	Serum Alb ≤4.0 g/dL, air leakage on POD1
Attaar et al. ¹⁶	2017	2,317	Lung resection	>5 days	8.6	FEV1, smoking history, bilobectomy, high annual surgeon caseload, prior chest surgery, Zubrod score >2
Murakami et al. ¹⁷	2018	284	VATS lobectomy	≥7 days	5.3	Emphysema on CT
Our study	2021	126	Lung resection	>5 days	8.7	FEV1, smoking history, upper lobectomy, right side, neoadjuvant chemotherapy

FEV1, forced expiratory volume in 1 second; BMI, body mass index; LVRD, lung volume reduction surgery; TLC, total lung capacity; CT, computed tomography; DLCO, diffusing capacity for carbon monoxide; Alb, albumin; POD, postoperative day; PAL, prolonged air leak.

In ESTS database they recorded 9.8% incidence of PAL after lobectomy. The incidence in our study (8.7%) is comparable with these rates in other studies.

Some authors have concluded that PAL increases complication rates after routine pulmonary resection.^{18,19} Brunelli et al found an 8.2% to 10.4% rate of empyema in patients with air leak lasting more than 7 days versus a rate of only 0% to 1.1% in patients with lesser air leaks.¹⁸ However, they found no difference between the PAL patients and others for other cardiopulmonary complications. Varela et al found that air leak lasting at least five days was associated with greater pulmonary morbidity including atelectasis, pneumonia or empyema (relative risk:

2.78).¹⁹ Okereke et al found that any air leak was associated with more complications (30% vs 18%, p=0.07).²⁰

All studies of the association of LOS and/or costs with air leak after lung resection reported increased costs or LOS (or both) in patients with PAL.^{18,19,20,21,22} Varela et al found LOS to be increased by approximately 6 days at a total expense of more than €39,000.¹⁹ Brunelli et al found LOS to be increased by 7.9 days.¹⁸ Bardell and Petsikas found that PAL (defined as an air leak persisting for more than three days) increased LOS by four days and, of all factors studied, only PAL predicted increased LOS.²¹ Irshad et al found that the three most frequent complications delaying discharge beyond post-operative day 5 were PAL, pulmonary infection and atrial fibrillation.²²

Pulmonary lobectomies frequently require division across the lung parenchyma and, therefore, inherently create a potential source for parenchymal air leaks. In most instances, the air leak seals rapidly when the visceral pleura becomes adherent to the chest wall, and the chest tube is removed uneventfully. However, upper lobectomies often result in large apical air spaces with poor visceral-parietal pleural apposition, and thus, frequently predispose these patients to longer pulmonary air leaks.^{23,24}

Identifying patients with a higher risk of PAL pre-operatively may be useful in counselling patients for a higher risk of prolonged hospital stay. It may also alert the surgeon to handle the lung more meticulously during surgery, mainly avoiding excess dissection in the fissures and trying to ensure that the patient leaves theatre with a minimal amount of air leak.

The three most important pre-operative risk factors for PAL in our series were upper lobe resection, neoadjuvant chemotherapy and reduced FEV1. Brunelli et al, however, published a risk score for PAL that included only reduced FEV1 and three other different factors.¹⁹ The set of predictive variables and their scores were:

- age greater than 65 years, 1.0 point;
- presence of pleural adhesions, 1.0 point;
- FEV1 less than 80%, 1.5 points;
- body mass index less than 25.5 kg/m², 2.0 points.

Prevention of troublesome postoperative air leak following upper pulmonary lobectomy requires meticulous surgical dissection and attention to pneumastatic principles. A variety of surgical techniques and materials have been proposed in an attempt to lower the occurrence of parenchymal air leak. Thoracic surgeons experienced with lung reduction surgery for end-stage emphysema advocate application of a variety of staple reinforcement materials, including polydioxanone ribbon, expanded polytetrafluoroethylene sleeves, and bovine pericardial strips, to reduce PAL.²³ However, most lung cancer patients do not have the typical pulmonary pathologic changes found in end-stage emphysema, and thus, the routine use of such staple reinforcing techniques is neither cost effective nor justified.

Other surgical factors reported to be correlated with PAL include a lobectomy rather than a wedge resection or segmentectomy,²⁶ right-sided rather than left-sided resection,⁹ upper rather than lower or middle lobectomy,⁸ thoracotomy rather than video-assisted thoracoscopic surgery.²⁷ In addition, several studies have noted that detection of the presence of severe pleural adhesions is a relevant risk factor for PAL because of lung parenchyma injuries that occur during division of those adhesions,^{7,8} while factors related to the surgical technique employed are also important to prevent PAL during a pulmonary resection.

Conclusion

This complication occurred in 8.7% of patient who underwent pulmonary resection for NSCLC. The most important risk factor is: smoking, COPD, neoadjuvant chemotherapy and upper lobectomy. So we recommend to pay more attention on these risk factors before surgery in order to decrease the incidence of this complication and length of stay and readmission to the hospital.

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