

## Original Article

# Pathophysiological mechanism of post-lobectomy air leaks

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**Background:** Air leak post-lobectomy continues to remain a significant clinical problem, with upper lobectomy associated with higher air leak rates. This paper investigated the pathophysiological role of pleural stress in the development of post-lobectomy air leak.

**Methods:** Preoperative characteristics and postoperative data from 367 consecutive video assisted thoracic surgery (VATS) lobectomy resections from one centre were collected prospectively between January 2014 and March 2017. Computer modelling of a lung model using finite element analysis (FEA) was used to calculate pleural stress in differing areas of the lung.

**Results:** Air leak following upper lobectomy was significantly higher than after middle or lower lobectomy (6.3% versus 2.5%,  $P=0.044$ ), resulting in a significant six-day increase in mean hospital stay,  $P=0.004$ . The computer simulation model of the lung showed that an apical bullet shape was subject to eightyfold higher stress than the base of the lung model.

**Conclusions:** After upper lobectomy, the bullet shape of the apex of the exposed lower lobe was associated with high pleural stress, and a reduction in mechanical support by the chest wall to the visceral pleura due to initial post-op lack of chest wall confluence. It is suggested that such higher stress in the lower lobe apex explains the higher parenchymal air leak post-upper lobectomy. The pleural stress model also accounts for the higher incidence of right-sided prolonged air leak post-resection.

**Keywords:** Pleural forces; biomechanics; lobectomy; air leak

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## Introduction

Postoperative air leaks are a common complication after lung resections. By conventional radiography, up to 40% of patients who undergo pulmonary resections will have a residual air space; three-quarters of these become spontaneously obliterated in the long term (1-3). The definition of prolonged air leak in the literature varies but is one that lasts more than either five or seven days (4,5).

Treatments available include the application of a blood

patch or pneumoperitoneum, and intrabronchial and flutter valves. Possible surgical procedures include glue application, buttressing of staple lines using pericardium strips, pleural tenting, muscle flaps and cavernostomy (6,7). Pleural tenting reduces the chance of a postoperative air leak and shortens the duration of chest drain duration, decreases hospital stay, and prevents apical residual air spaces and their complications (8). Use of pericardial buttressing strips and collagen sponge coated with the human coagulation factors fibrinogen and thrombin is associated with a reduction

in air leakage, earlier chest drain removal and decreased hospital stay (9). Improved surgical techniques and use of buttressing material have reduced but not abolished the risk of postoperative air leak (10). Postoperative air leaks are clinically important because they increase chest drain duration and hospital stay with an increased risk of space infection and higher hospital costs (11,12).

Upper lobectomy has been generally associated with a higher incidence of postoperative air leak (13,14), though not in all papers (15). Air leaks post-lobectomy have also been correlated with advanced age, low FEV1%, low BMI and the existence of pleural adhesions (15). Further, prolonged air leak may also be surgeon-dependent (3). Although it is understandable that poor quality lung as in emphysema is associated with an increased risk of postoperative air leak, it is not clear why different anatomical areas should suffer from the differing degrees of air leak when the lung parenchyma may appear macroscopically similar to a surgeon.

One answer to this question might be that different areas of the lung have differing levels of pleural stress, with pleural stress varying according to lung shape and location (16). As lung shape conforms closely to the form of the chest wall, differing chest wall shape may be associated with differing pleural stress extent. In a lung resection like a lobectomy, the remaining lung inflates into and conforms to the remaining space, taking up the shape of the resected lobe; this process occurs simultaneously with other physiological changes such as hyperinflation of the contralateral lung, mediastinal shifting, elevation of the ipsilateral diaphragm and ipsilateral crowding of the intercostal spaces (6).

Since it is impractical to directly measure pleural stress, an experimental finite element analysis (FEA) computer simulation was used. FEA modelling is an ideal method for calculating wall stress in pressure vessels with a complex shape. This method uses nodes in a mesh to model the original structure in three dimensions, reducing the complexity of the problem into a simpler solution with a finite number of mathematical calculations. Each node on the mesh has boundary conditions with the loads applied to it simulating the original loads.

Since the location of post-resection prolonged air leak remains contested (15), this paper aims to determine whether air leak following upper lobectomy was significantly higher than that following middle or lower lobectomy in a consecutive series of video assisted thoracic surgery (VATS) lobectomies from one centre. It also studies a model of pleural stress in the lung in order to correlate the

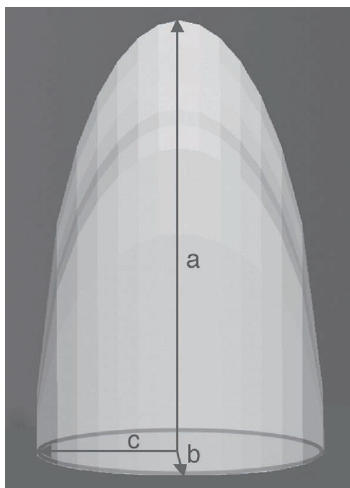
location of postoperative air leak with pleural stress, since visceral pleural stress levels have already been implicated in the pathophysiology of primary spontaneous pneumothorax (PSP) as capable of generating parenchymal air leak on their own (16).

## Method

### *Surgical patients*

Between January 2014 and March 2017, data was prospectively collected from 367 consecutive VATS lobectomy resections using a fissureless technique without use of sealants, buttressed staple line or pleural tents, operated in a single institution in Ravenna, Italy. The chest tube management in this series included the use of one drain when appropriate, with suction not routinely used, following an enhanced recovery after surgery (ERAS) fast track program (17). A persistent air leak was defined as one lasting more than five days following recent publications rather than seven days as previously, although the number of patients at five days was identical to that at seven days in our case series (4,18,19).

Every variable was compared between upper versus middle/lower lobectomy. The data collected included age, gender and presence of pre-operative pathologies such as myocardial infarction (MI), congestive heart failure, peripheral vascular disease, cerebrovascular disease, dementia, chronic obstructive pulmonary disease (COPD) defined following European Respiratory Society guidelines (20), connective tissue disease, peptic ulcer disease, diabetes mellitus, moderate to severe chronic kidney disease, hemiplegia, leukaemia, malignant lymphoma, solid tumour, liver disease, *acquired immune deficiency syndrome (AIDS)*. *Other data collected comprised the* Charlson comorbidity index, the Eastern Cooperative Oncology Group (ECOG) score of performance status, forced vital capacity (FVC), forced expiratory volume in 1 second (FEV<sub>1</sub>), FEV<sub>1</sub>/FVC ratio or Tiffeneau-Pinelli index, diffusion capacity adjusted by the alveolar volume (DLCO/VA), preoperative blood gas analyser pO<sub>2</sub>, pCO<sub>2</sub> and pH (partial pressure of oxygen, partial pressure of carbon dioxide, potential of hydrogen respectively), preoperative computerized tomography (CT) and positron emission tomography (PET) scan tumour sizing and staging and PET standardized uptake value (PET SUV). Further data collected included surgical technique (including operative time in minutes, lobe and side resected), pathological post-operative staging,



**Figure 1** Diagram of computational model used to calculate pleural stress. Dimensions: lung height  $a = 24$  cm, lung transverse radius  $b = 8$  cm and lung anteroposterior radius  $c = 6$  cm.

length of postoperative hospital stay and duration of total hospital stay. Electronic meters to quantify air leak were not available.

### FEA modelling

A finite element model of the lung was constructed with a first rib apical indentation. FEA is a method of solving complex structural analysis problems by simplifying the process through the use of a finite number of nodes that geometrically approximate the original shape.

The lung model created had height  $a$  of 24 cm, transverse radius  $b$  of 8 cm and anteroposterior radius  $c$  of 6 cm, see *Figure 1*, following methodology published by the authors (16,21). Meshing was performed using SOLID 187 element at a pressure of 40 kPa, with assumptions that the lung was elastic with a Poisson's ratio of 0.3. FEA of the model was performed using Ansys v11 (ANSYS, Inc., Philadelphia, PA, USA) finite element simulation package using linear modelling. The base of the model was constrained superiorly but allowed to inflate freely in the transverse and anteroposterior planes to mimic normal respiratory movements.

### Statistics

The Chi-square test was used to examine the association between categorical variables and the Barnard's test was

explicitly used to examine  $2 \times 2$  contingency tables using the facilities of R software (R Core team, Foundation for Statistical Computing, Vienna, Austria). Since some of the patients' characteristics had a continuous metric scale and satisfied the normality assumption, the Independent samples  $t$ -test was used; where the *Kolmogorov-Smirnov* test indicated that the data was non-parametric, the Mann Whitney test was used instead. A binary Logistic regression model was used to relate the presence/absence of prolonged air leaks with baseline and postoperative patient characteristics (predictors) using a forward stepwise procedure to develop a parsimonious model using the facilities of SPSS software (IBM Corp, Armonk, NY, USA). A 0.05 level of significance was adopted for all statistical tests and models.

## Results

### Surgical patients

The percentage of cases with air leak following upper lobectomy (6.3%) was significantly higher than the percentage of cases with air leak following middle or lower lobectomy (2.5%),  $P=0.044$  using Chi-square test and  $P=0.049$  using Barnard's test. Upper lobectomy was significantly more prevalent with a higher pre-operative MI rate ( $P=0.026$ ), longer skin-to-skin operative time ( $P=0.007$ ) and hospital stay ( $P=0.036$ ). Other pre- and postoperative characteristics did not reach statistical significance, as displayed in *Tables 1* and *2*. Similarly all parameters were compared between presence and absence of prolonged air leak and the results are shown in *Tables 3* and *4*. The mean duration of hospital stay and mean days from admission were both approximately six days longer in cases of prolonged air leaks compared to cases without a prolonged air leak ( $P<0.001$ ) with the mean duration of hospital stay and mean days from admission both approximately two days longer for upper lobectomy compared to middle or lower lobectomy ( $P=0.004$ ). There was also an expected increase in hospital stay ( $P<0.001$ ) and a medical history of leukemia ( $P=0.018$ , however numbers were very low). Interestingly there was a higher incidence of right-sided prolonged air leak (6.3%) versus the left-side (2.3%) but this did not reach statistical significance ( $P=0.112$ ). The parsimonious logistic regression model showed no significant predictors apart from prolonged hospital stay,  $P=0.027$ . None of the patients with prolonged air leak patients required further interventional therapy.

**Table 1** Comparison of baseline and postoperative patient characteristics (having a categorical scale) between upper lobectomy and middle/lower lobectomy using Chi-squared test and Barnard's exact test<sup>§</sup>

Parameter (% or ratio*)	Upper lobectomy, 207 patients	Middle/lower lobectomy, 160 patients	P value (Chi-squared test)
Gender male:female ratio	131:76	94:66	0.376
Myocardial infarction	11.6	5.0	0.026
Congestive heart failure	1.4	0.0	0.126
Peripheral vascular disease	13.5	8.8	0.154
Cerebrovascular disease	3.4	7.5	0.077
Dementia	1.0	0.6	0.719
COPD	28.0	27.5	0.912
Connective tissue disease	1.4	1.3	0.870
Peptic ulcer disease	2.9	2.5	0.816
Diabetes mellitus	11.6	13.1	0.658
Moderate-severe chronic kidney disease	2.9	1.3	0.284
Hemiplegia	0.0	0.0	1.000
Leukaemia	1.0	0.6	0.719
Malignant lymphoma	0.5	0.6	0.855
Solid tumour	4.3	3.1	0.552
Liver disease	2.4	3.1	0.679
Human immunodeficiency virus infection	0	0	1.000
CT scan: tumour stage			0.796
1A	54.1	57.5	
1B	23.7	19.4	
2A	18.4	17.5	
2B	2.9	4.4	
3	1.0	0.6	
CT scan: side R:L	117:90	91:69	0.946
CT scan: size (cm)			0.336
<2	61.4	66.3	
2-3	21.3	13.8	
3-5	14.5	15.6	
5-7	2.4	3.8	
>7	0.5	0	
CT: nodes	1.9	1.9	0.968
CT: metastasis	0	0	1.000
Operation: side right:left	134:73	102:58	0.845
Operation: lymph node dissection performed	99.5	97.5	0.098
Post-operative air leak (days*)	13	4	0.044, 0.049 <sup>§</sup>

COPD, chronic obstructive pulmonary disease; CT, computerized tomography.

**Table 2** Comparison of baseline and postoperative patient characteristics (having a continuous metric scale) of upper lobectomy versus middle or lower lobectomy using Mann Whitney test

Characteristics	Mean	Standard deviation	P value (Mann Whitney test)
Age (years)			0.627
Upper	67.97	10.059	
Middle/lower	67.46	9.549	
Charlson comorbidity index			0.330
Upper	4.26	1.630	
Middle/lower	4.08	1.791	
ECOG score			0.494
Upper	0.31	0.683	
Middle/lower	0.26	0.599	
FEV <sub>1</sub> value			0.756
Upper	2.40	0.591	
Middle/lower	2.38	0.608	
FEV <sub>1</sub> percentage			0.652
Upper	93.88	19.472	
Middle/lower	92.95	17.667	
FVC value			0.528
Upper	3.10	0.789	
Middle/lower	3.04	0.857	
FVC percentage			0.397 (Student's independent t-test)
Upper	96.96	19.379	
Middle/lower	98.84	21.129	
Tiffeneau-Pinelli index			0.325
Upper	78.66	11.841	
Middle/lower	80.07	14.421	
DLCO/VA ratio			0.694
Upper	81.12	20.436	
Middle/lower	82.17	21.906	
Pre-op pO <sub>2</sub>			0.266
Upper	83.57	13.484	
Middle/lower	85.45	12.207	

**Table 2** (continued)**Table 2** (continued)

Characteristics	Mean	Standard deviation	P value (Mann Whitney test)
Pre-op CO <sub>2</sub>			0.823
Upper	39.33	9.271	
Middle/lower	39.08	6.811	
Pre-op pH			0.259
Upper	7.39	0.249	
Middle/lower	7.42	0.039	
PET standard uptake value (SUV)			0.768
Upper	1.79	3.253	
Middle/lower	1.68	3.449	
Number of incisions apart from utility thoracotomy			0.053
Upper	1.99	0.574	
Middle/lower	1.86	0.687	
Number of trocars			0.209
Upper	1.49	0.565	
Middle/lower	1.41	0.576	
Operative time (skin to skin in minutes)			0.007
Upper	175.83	52.190	
Middle/lower	160.88	51.618	
Mean pathological staging			0.089
Upper	1.48	0.791	
Middle/lower	1.65	1.108	
Hospital stay after surgery (days)			0.036
Upper	8.07	9.540	
Middle/lower	6.41	3.376	
Duration of admission (days)			0.029
Upper	9.68	11.561	
Middle/lower	7.60	3.488	

ECOG, Eastern Cooperative Oncology Group; FEV<sub>1</sub>, forced expiratory volume in 1 second; FVC, forced vital capacity; DLCO/VA, diffusion capacity adjusted by the alveolar volume; pO<sub>2</sub>, pCO<sub>2</sub>, pH, preoperative blood gas analysis of partial pressure of oxygen, partial pressure of carbon dioxide and potential of hydrogen; PET SUV, positron emission tomography standardized uptake value.

**Table 3** Comparison of baseline and postoperative patient characteristics (having a categorical scale) between upper lobectomy and middle/lower lobectomy using Chi-squared test

Parameter	Prolonged air leak		P value (Chi square test)
	Yes	No	
Lobectomy			0.188
Upper	13	194	
Middle	0	25	
Lower	4	131	
Gender			0.421
Male	12	213	
Female	5	137	
Myocardial infarction			0.671
Yes	1	31	
No	16	319	
Congestive heart failure			0.702
Yes	0	3	
No	17	347	
Peripheral vascular disease			0.461
Yes	1	41	
No	16	309	
Cerebrovascular disease			0.209
Yes	2	17	
No	15	333	
Dementia			0.702
Yes	0	3	
No	17	347	
COPD			0.339
Yes	3	99	
No	14	251	
Connective tissue disease			0.620
Yes	0	5	
No	17	345	
Peptic ulcer disease			0.413
Yes	1	9	
No	16	341	

Table 3 (continued)

**Table 3** (continued)

Parameter	Prolonged air leak		P value (Chi square test)
	Yes	No	
Diabetes mellitus			0.412
Yes	1	44	
No	16	306	
Chronic kidney disease			0.529
Yes	0	8	
No	17	342	
Leukemia			0.018
Yes	1	2	
No	16	348	
Malignant lymphoma			0.755
Yes	0	2	
No	17	348	
Solid tumour			0.651
Yes	1	13	
No	16	336	
Liver disease			0.480
Yes	0	10	
No	17	340	
CT: tumour stage			0.564
1A	11	193	
1B	5	75	
2A	1	65	
2B	0	13	
3	0	3	
CT: tumour size (cm)			0.816
Less than 2	13	220	
2–3	2	64	
3–5	2	53	
5–7	0	11	
More than 7	0	1	
CT lung: side			0.502
Right	11	197	
Left	6	152	

Table 3 (continued)

Table 3 (continued)

Parameter	Prolonged air leak		P value (Chi square test)
	Yes	No	
Upper	14	212	
Middle	0	19	
Lower	3	118	
CT nodes			0.221
Yes	1	6	
No	16	343	
Middle	0	18	
Lower	3	99	
Prolonged air leak side			0.112
Right	14	222	
Left	3	128	
Lymph node dissection			0.620
Yes	17	345	
No	0	5	

COPD, chronic obstructive pulmonary disease; CT, computerized tomography.

### Computational analysis FEA model

Stresses develop within the pleura on inflation, with the magnitude of the stress varying at differing levels of inflation e.g., breathing and coughing. There was an approximate eighty-fold difference in relative stress between the highest and lowest pleural stress levels in this model on 40 kPa maximal coughing, see *Figure 2*, with pleural stress highest near the apex and at the furrows for the first rib of the upper lobe and lowest at the base of the lower lobe, with air leak expected to be more likely to occur in the higher areas of pleural stress within the lung.

### Discussion

The risk of a persistent air leak is associated with a low predicted postoperative forced expiratory volume in one second (FEV<sub>1</sub>), the presence of pleural adhesions, and an upper lobectomy or bilobectomy operation (22,23). Why is the presence of an air leak significant? It prolongs discharge from the hospital and increases the financial cost of the operation. Post resection residual pleural spaces also have

a worse prognosis with older age, air leak or infection (14). This paper explores biomechanical stress levels in the pleura to explain why the rate of post-lobectomy air leaks differs in the different lobes.

### Description of course of postoperative air space

A postoperative air space can be caused by the removal of a significant portion of the lung e.g. after bilobectomy resulting in reduced compliance and an inability to fill the residual space. It can also be due to leaks from the conducting zone e.g., broncho-pleural fistula, or the respiratory zone, like parenchymal leaks especially after extensive tissue dissection such as post-segmentectomy. Such spaces develop more commonly after upper lobectomy, at an apical location and on the right side especially in cases of lung cancer (14). A residual pleural space occurred in 40% after bilobectomy, 20% after lobectomy, and 5–10% after segmentectomy or wedge resection (2,13,23). Postoperative air spaces are in a dynamic state with approximately 20–40% of patient post-lobectomy having a residual air space; 75% of these become obliterated without intervention in the long term (8). Similarly, Solak reported an incidence at 40% on the first postoperative day decreasing to 10% at three months (4). The amount of air leak was related directly to the amount of suction applied and was least with a Heimlich valve (24).

### Use of chest drains

Simple chest drains have been superseded by more costly electronic meters that digitally quantify the amount of air passing through chest tubes and can also measure pleural pressure; they were not available for the series of patients in this paper. An air leak meter incorporated in some triple compartment chest drain systems may indicate the approximate degree of air leak from the chest cavity; however, interpretation may vary between skilled personnel (25). Also, such systems did not change the duration of chest drainage or length of hospitalisation in a randomised trial (26) but diminished inert observer variability (27). However, it permitted distinguishing an actual air leak from a pleural space effect (28) and prediction of the duration of air leak (29).

### Post-resection changes

Removing an upper lobe leaves a space near the apex that takes time to decrease in size. The reason for this is that the

**Table 4** Comparison of baseline and postoperative patient characteristics (having a continuous metric scale) of presence and absence of prolonged air leak >5 days using Mann Whitney test

Parameter	Prolonged air leak	Mean	Standard deviation	P value (Mann Whitney test)
Age at surgical procedure date	Yes	70.53	6.783	0.361
	No	67.61	9.941	
Scoring: age	Yes	3.53	0.800	0.383
	No	3.23	1.003	
Final score	Yes	4.29	1.611	0.875
	No	4.17	1.708	
ECOG score	Yes	0.18	0.393	0.554
	No	0.29	0.657	
FEV <sub>1</sub> value	Yes	2.24	0.550	0.539
	No	2.40	0.600	
FEV <sub>1</sub> percentage	Yes	95.28	21.813	0.683 (independent samples t-test)
	No	93.37	18.530	
FVC value	Yes	2.85	0.823	0.201
	No	3.09	0.819	
FVC percentage	Yes	98.96	20.548	0.949
	No	97.72	20.170	
Tiffenau-Pinelli index	Yes	80.15	14.935	0.461
	No	79.24	12.956	
DLCO/VA	Yes	78.25	23.921	0.508
	No	81.74	20.939	
pO <sub>2</sub>	Yes	85.10	13.295	0.942
	No	84.30	12.998	
pCO <sub>2</sub>	Yes	37.97	3.506	0.762
	No	39.28	8.488	
pH	Yes	7.39	0.056	0.338
	No	7.40	0.197	
PET SUV	Yes	2.00	4.472	0.624
	No	1.73	3.271	
	No	0.11	0.461	
Number of incisions apart from utility thoracotomy	Yes	2.00	0.354	0.711
	No	1.93	0.639	
Number of trocars	Yes	1.53	0.514	0.555
	No	1.45	0.573	

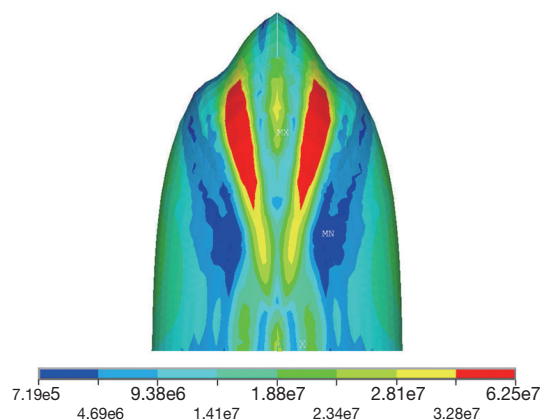
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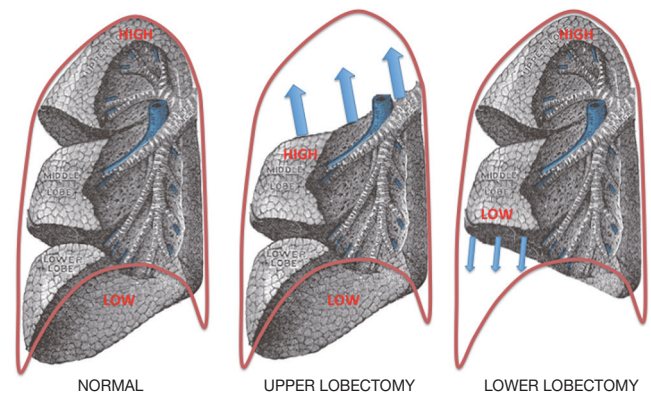
Parameter	Prolonged air leak	Mean	Standard deviation	P value (Mann Whitney test)
Operative time (skin to skin in minutes)	Yes	177.65	31.030	0.164
	No	168.91	53.214	
	No	1.56	0.951	
Grading	Yes	2.00	0.935	0.277
	No	1.84	0.805	
	No	1.84	0.805	
Hospital stay from surgery	Yes	13.47	4.611	<0.001
	No	7.05	7.533	
	No	7.05	7.533	
Days from admission	Yes	14.41	4.597	<0.001
	No	8.50	9.108	
	No	8.50	9.108	

ECOG, Eastern Cooperative Oncology Group; FEV1, forced expiratory volume in 1 second; FVC, forced vital capacity; DLCO/VA, diffusion capacity adjusted by the alveolar volume; pO<sub>2</sub>, pCO<sub>2</sub>, pH, preoperative blood gas analysis of partial pressure of oxygen, partial pressure of carbon dioxide and potential of hydrogen; PET SUV, positron emission tomography standardized uptake value.



**Figure 2** Pleural stress showing an eighty-fold variation in pleural stress that is maximal towards the apex and within the furrows produced by the first rib and lowest at the base. Scale is in Pascal (Pa), the SI derived unit of pressure and stress. MX, maximum, MN, minimum.

remaining lung's shape does not conform exactly to that of the rib cage and requires time before it can mould itself to match the chest wall. In an upper lobectomy, the exposed bullet shape of the apex of the lower lobe is expected to be subject to a much higher level of stress than the base of the lung extrapolating from our FEA model. In a lower/middle lobectomy, conformity between the remaining lung and chest wall is better, the apex remains in compliance with and supported by the chest wall, and this may decrease the chance of an upper air space, see *Figure 3*. After upper



**Figure 3** Diagram indicating the location of high and low pleural stress zones in the lung and how these are related to the degree of air leak post lobectomy. Diagram of lung adapted from (30).

lobectomy, the bullet shape of the apex of the exposed lower lobe will be associated with high pleural stress, and a reduction in mechanical support by the chest wall to the visceral pleura due to initial post-op lack of chest wall confluence. It is suggested that the presence of higher stress levels in the lower lobe apex explains the higher parenchymal air leak post-upper lobectomy, in contrast with lower lobectomy where there is no remaining unsupported lung with high pleural stress levels.

### *Lung as pressure vessel*

The lung when under internal pressure, for example

during coughing or deep expiration will result in the lung acting as a pressure vessel, with Laplace's Law describing how different areas of the visceral pleura are under different wall tension even though Pascal's principle states that pressure is transmitted equally throughout the lung. Such differing wall tension or pleural stress has been used to explain the pathophysiology of spontaneous pneumothorax, with the apical area of the lung suffering from intense stress that induces tissues near the apex to tear apart and the pleura usually supported by the chest wall and by adhesions to the chest wall, thus relieving pleural stresses (16).

Once the lung is separated from the chest wall as occurs post-lobectomy, several factors are at play. One is that the lung expands in shape post-upper lobectomy to conform to the apical part of the chest wall, with expansion known to generate higher pleural stress. Another is that the remaining lung post-upper lobectomy has a shape where the apex of the upper lobe resembles a high pleural stress state. Another is that pleural pressures post-op tend to return to normal slowly and, since the pleural pressure is more negative at the apex than at the pulmonary base, lung parenchyma becomes exposed to a greater distending pressure differential than at the base of the lung. Further, the apical pleura in the presence of an apical air space lacks the structural support that would be provided by the chest wall should the lung be fully confluent. Thus after surgery, pleural forces do not remain unchanged but may increase in the postoperative period. The factors listed above may therefore explain why air leaks may develop or increase in the early days after an operation as the lung expands and why the presence of a pleural space would be expected to be associated with a greater risk of postoperative air leak.

Air space problems are commonest after upper lobectomies compared to other lobar resections (13), further confirmed in our series of 367 patients,  $P=0.044$ . The pressure vessel hypothesis, initially used to explain the pathogenesis of spontaneous pneumothorax (16) and later the reactivation of pulmonary tuberculosis (19), would suggest that the remaining lung post-upper lobectomy would be subjected to more stress because of the bullet shape of the exposed lower lobe and would therefore be expected to be at a higher risk of air leak. Pleural tenting, by covering the apex of the lung, would be expected to reduce pleural pressures by supporting the visceral pleura at the high-risk neo-apical area of the remaining lung, thereby reducing the rate of post-op air leak.

### *Right versus left lung air leaks*

The value of predictions is that the scientific method is based on theoretical predictions that are logical consequences of scientific theories. The right lung being larger than the left would be expected to have higher stress on coughing or breathing as a pressure vessel. This would be predicted to result in a higher incidence of post-lobectomy prolonged air leak based on the hypothesis proposed here. Our data supports this prediction with a higher incidence of right-sided prolonged air leak (6.3%) versus the left-side (2.3%) but without reaching statistical significance (Chi-square  $P=0.112$ ). Therefore the lowest air leak frequency would be predicted for left lower lobectomy (left lung being smaller and lower lobe location both leading to less pleural stress); this is supported by a report that air leak occurred less frequently after left lower lobectomy ( $P<0.001$ ) (3).

### *Clinical correlates*

This hypothesis explains why post-lobectomy air leaks are reduced by using methods that buttress the apical part of the remaining lung to reduce pleural stress or that change the shape of the pleural cavity by obliterating it, for example by using a pleural tent or even by using minimally invasive osteoplastic collapse thoracoplasty (31). Buttressing reduces pleural stress by supporting the pleura; in effect by increasing the thickness of the parenchymal pleura thus decreasing stress. Examples of buttressing include placing subcutaneous fat pads with fibrin glue in combination with a few mattress sutures (32) and glue or collagen sponge application. Theoretically, an apically located collagen sponge that changes the shape of the apex of the pleural cavity would be expected to reduce the incidence of air leaks by decreasing apical stress.

### *Other factors*

Pleural stress has been associated with an anteroposterior flattened chest or low thoracic index (ratio of breadth to anteroposterior diameter of the chest) in both PSP and reactivation of tuberculosis (16,19). This pleural stress hypothesis would suggest that patients with a low thoracic index should be at a higher risk of postoperative air leak due to higher levels of pleural stress; this has yet to be confirmed or refuted. It may be argued that emphysema is known to affect

the upper lobe more commonly than the other lobes (33), so stapling an emphysematous upper lobe may result in prolonged air leak; however, this was not a factor in our series  $P=0.912$ .

## Conclusions

In this series of almost four hundred VATS lobectomies, air leak following upper lobectomy (6.3%) was significantly higher than that following middle or lower lobectomy (2.5%), resulting in a significant increase in a mean hospital stay of six days. A computer simulation FEA model of the lung indicates that the bullet-shaped apical region of the lung is prone to approximately eighty times higher stress than the lower part of the lung. This higher pleural stress manifests itself when there is a lack of lung-ribcage confluence and therefore support to the lung, as in the case of an apical air space as may occur after upper lobectomy when the highly stressed shape of the lower lobe apex is exposed in the initial post-op period. Such a mechanism may explain how why right-sided air leaks are commoner and why buttressing the apical portion of the remaining lung and changing the shape of the rib cage apex by use of a pleural tent decreases air leak. The pressure vessel hypothesis expounded here is consistent with known facts about post-lobectomy air leaks described above.

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## Footnote

*Conflicts of Interest:* The authors have no conflicts of interest to declare.

*Ethical Statement:* Ethics approval was obtained from the Institutional Review Board (No. 81/2014/O/Oss). The data was anonymously achieved according to the International Conference on Harmonization Guidelines for Good Clinical Practice. Informed consent for experimentation with human subjects was obtained from all individual participants included in the study. Privacy rights of the human subjects were always observed.

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