ORIGINAL ARTICLE **THORACIC SURGERY**

UNIPORTAL VIDEO-ASSISTED THORACIC SURGERY ANATOMICAL RESECTIONS – DOES PREVIOUS TOBACCO EXPOSURE ADVERSELY INFLUENCE POST-OPERATIVE OUTCOMES?

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Abstract

A high percentage of patients presenting for lung surgery are either current or former smokers, which is typically associated with many anatomical and physiological pulmonary changes. The influence of tobacco on postoperative pulmonary complications remains controversial. The main goal of this study was to analyse the effects of smoking on the risk of post-operative complications and morbidity in patients submitted to lung resection surgery through uniportal VATS.

Peri-operative data on all cases of anatomical lung resection surgery through single-port VATS performed between December 2013 and July 2018 at three Portuguese institutions were collected and retrospectively reviewed Demographic data, diagnosis, pre-operative lung function tests, in-hospital length of stay (LOS) and intra and post-operative drainage levels were registered. Patients were divided in two groups according to tobacco exposure. Post-operative complications and morbidity were compared through statistical analysis

We performed 313 procedures, 303 of which were evaluated in regard to outcome. Mean age at time of surgery was of 62,85 years (SD=12,24). One hundred and sixty patients (52,81%) had a history of tobacco use, while 47,19% (n=143) had never smoked. Non-smokers had significantly better lung function than smokers ($p<0,05$). Smoking history showed a contribution to post-operative prolonged air leaks ($p=0,025$) morbidity ($p=0,05$), 2-day longer LOS ($\mu=5,36$ days vs. $\mu=7,53$ days; $p<0,05$), longer operative times and higher intra and post-operative drainage levels.

A history of smoking during a patient's life negatively impacts morbidity in patients submitted to uniportal VATS for anatomical lung resection, increasing early post-operative complications and prolonging in-hospital stays.

INTRODUCTION

Lung cancer is a leading cause of death worldwide. A high proportion of patients who suffer from lung cancer have a history of smoking, proven to contribute to a 12 to 20-fold increase in risk of lung malignancy.[1] Given the growing extent of life expectancy we see in current years, in face of technological and medical evolution, we can expect a concomitant increase in the diagnosis of all types of malignancies, including those involving the lung. Hence, pneumologists and thoracic surgeons are now faced with a new cluster of target population: those with life-long risk exposure.

The best conceivable treatment for early stage non-small cell cancer is surgery, whenever possible.[2] In face of our aging population, video-assisted minimally invasive approaches have risen and are now standard of care in most surgical centres for the treatment of lung cancer.[3] In our centre, Video-Assisted Thoracic Surgery (VATS) is performed through a single port, minimizing the aggressiveness to the thoracic cage and consequently minimizing post-operative pain.

Despite this trend for less traumatic surgical procedures, post-operative complications still occur, and many risk factors have been advocated in the literature as to contributing to their development.[4,5]

Most authors agree that smoking highly increases postoperative risks in all surgical procedures, hence, smoking cessation is recommended, especially in lung surgery. How duration of cessation impacts post-operative complications is still largely debatable, as some studies show

that short-term pre-operative cessation does impact outcome.[1,6] Most studies evaluate overall morbidity and mortality between smokers in comparison to non-smokers, not specifying the impact of tobacco abuse in the specific complications after thoracic surgery. With this in mind, the main goal of our study was to analyse the impact of smoking in the development of post-operative complications and overall morbidity in patients submitted to lung resection surgery performed through uniportal VATS.

MATERIALS AND METHODS

Study design

A retrospective study was conducted, including all patients submitted to anatomical lung resection surgery performed through uniportal VATS in three institutions located at the north of Portugal, within the period comprised between the 1st of December 2013 until the 31st of July 2018. The population was subsequently divided into two groups according to active smoking history: those with a history of smoking during their lifetime, regardless of active smoking at time of evaluation, were included in Group A, while those who had never smoked were included in Group B. Groups were compared according to pre-operative, intra-operative and post-operative variables in order to evaluate to what extent smoking impacts post-operative complications.

Collection of data

Data were collected through the patient's medical records and included in three clusters: patient-related data, including demographic variables such as age and gender; pre-operative data, regarding results of lung function testing (FEV1; FVC and DLCO) and diagnosis prior to surgery; surgery-related data, including laterality, choice of procedure, location and number of excised lymph nodes, operative time, the inadvertent need for conversion to thoracotomy and operative drainage counts; and post-operative data, including in-hospital length of stay (LOS), post-operative 24 hour drainage counts and post-operative complications. The post-operative complications evaluated in our study were, in particular: prolonged air leaks, defined as air leak lasting more than 7 days; atrial fibrillation development; fever; respiratory insufficiency leading to Acute Respiratory Distress Syndrome (ARDS); atelectasis; haemorrhage with the need for re-intervention and overall morbidity. Morbidity was defined as the development of two or more post-operative complications.

Patients were excluded from our study whenever data regarding post-operative complications was not attainable.

Statistical analysis was performed using SPSS Statistics software.

RESULTS

Population

A total of 313 procedures were performed during the study's timespan, in ten of which post-operative data was lacking, being excluded from out study's main goal evaluation. The male to female ration was approximately 1:1 and mean age at time of surgery was of 62,85 years of age (SD=11,17).

Patients were divided into two homogenous groups according to their smoking history: 160 (52,81%) patients were included in group A, the smoking group, while 143 (47,19%) were attributed to group B, the non-smoking group.

Regarding pre-operative evaluation, the attainment of all intended variables was not possible, although patients in group A showed lower means in all the evaluated variables (Table 1). Comparing between groups, this difference was statistically significant.

Table 1 **Pre-operative lung function tests results**

		FEV1 (%)	FVC (%)	DLCO (%)
Group A	Mean	104,80	116,63	93,16
	n	119	118	71
	SD	19,30	83,85	20,34
Group B	Mean	93,51	101,93	84,76
	n	139	136	86
	SD	20,01	16,92	17,57

The majority of patients (91,75%, n=278) were pre-operatively diagnosed with malignant lung disease, while the remaining 8,25% (n=25) were submitted to surgery for the treatment of benign lesions. There was a slightly higher percentage of patients being submitted to surgery on the right side (60,8%) while the remaining had left-sided procedures. These ranged from lesser resections such as segmentectomies to bilobectomies and pneumonectomies, all performed through a single 3-4cm intercostal port.

Regarding intra-operative data, the mean number of lymph nodes sample was similar in both groups (μ=6,93 in group A and μ=5,67 in Group B) and in both, two stations (hilar and mediastinal) were sampled. Mean operative times were longer in group A, *t= 104,50; SD=45,97*, comparing to group B, *t= 96,32; SD=50,55*, although this difference was not statistically significant (p=0,166).

Similarly, intra and post-operative drainage levels were about 10mL higher in group B, which was also insignificant both in clinical and statistical terms ($p>0,05$). In 18 procedures there was an intra-operative need for conversion to thoracotomy due to surgical difficulties, but no relation was found between this necessity and the patient's smoking status.

Complications and morbidity

Post-operative complications occurred in about 26,4% of patients submitted to thoracic surgery, although most had low severity and no long-term impact.

The incidence of discriminated post-operative complications in both groups is presented in table 2.

Table 2 **Incidence of post-operative complications among groups**

		Prolonged air leak	Fever	Respiratory insufficiency	Atrial Fibrillation	Atelectasis	Haemorrhage	Morbidity
Group A	n	40	4	4	5	2	3	52
	% (between groups)	25,00%	2,50%	2,50%	3,12%	1,25%	1,87%	32,50%
Group B	n	21	2	2	2	2	3	27
	% (between groups)	14,60%	1,40%	1,40%	1,40%	1,40%	2,10%	18,89%

Prolonged air leak occurred more frequently in patients with a history of smoking. Chi-square tests proved a statistical correlation between smoking and the development of prolonged air leaks ($p=0,025$). Accordingly, the remainder of post-operative complications, with the exception of atelectasis, had a slightly higher incidence in the smoking group, although in these cases, no statistical significance was reached.

Overall morbidity was also higher in group A, chi-square: $p=0,05$.

In-hospital length of stay was longer in the smoking group ($\mu=5,36$ days) when comparing to group B, (7,53 days) and this difference was considered significant after statistical analysis ($p<0,05$).

DISCUSSION

Despite current information on the potential damages of cigarette smoking, more than one billion people smoke tobacco products worldwide.[7] Smoking has damaging effects all throughout our organs and systems, contributing to premature death, chronic obstructive lung disease (COPD) development, cardiovascular disease and malignancy.[1,8,9] Being a proven carcinogen, tobacco contributes not only to the development of lung cancer, but also oral, laryngeal and oesophageal cancer, a finding possibly correlated to the connection between smoking and increased oxidative stress, along with its definitive impact on the lung parenchymal transcriptome.[7,10]

Tobacco products cause particle-related lung injury. CT scan analysis comparing the effects of tobacco in lung architecture performed by Soejima *et al* demonstrated that respiratory bronchiolitis, lung nodules and the development of upper lung field emphysema along with concomitant ground glass opacities suggesting fibrosis, are more prevalent in smokers than in non-smokers.[11] These preferential upper lobe changes are often expressed in lung function testing, through an accelerated decline in forced expiratory volume in 1 second (FEV1) values. Our study corroborated this association, with worse performance of smokers in pre-operative lung function tests due to chronic tobacco-induced emphysema, as previously shown in multiple studies.[1,5,12]

A high proportion of patients diagnosed with lung cancer are either current smokers or have a previous history of active tobacco exposure during their lifetimes. Surgical resection is widely considered the optimal therapy in the treatment of early stage non-small cell lung cancer (NSCLC).[3,5] With the development of video-assisted thoracic surgery, minimally invasive procedures are becoming the gold-standard for lung cancer treatment worldwide.[13] Since the end of 2013, our center began to perform uniportal VATS, which quickly became our preferred approach for all procedures in lung surgery. Although current literature on the theme is scarce, uniportal VATS has not shown inferiority when comparing to the multiportal variant. We believe, along with Louis *et al* and other authors, that, besides safe and feasible, a single port approach limits post-operative pain, a highly relevant factor in our patient's post-operative wellbeing and quality of life, especially in smokers, who have shown lower pain tolerance.[14-16]

VATS is historically associated with less post-operative complications than thoracotomy. Studies report a post-operative complication rate ranging from 3% in larger series to 30% in smaller series, such as ours.[5,17-19] In

our series, complication rate is in line with most studies with similar population size. It must be enhanced that a high number of studies contemplates solely potentially life--threatening complications, consequently lowering their post-operative complication rates.

Previous studies have investigated pre-operative risk factors influencing post-operative outcomes and complications after thoracotomy, although, few of them have done so in VATS.[5] Smoking has been advocated in most studies as a risk factor for post-operative complications and worse outcome, and smoking cessation is advisable in all cases, prior to surgery.[4,20,21] Despite this, consensus still lacks on the duration of time from smoking cessation to surgery. There are even, in fact, reports stating that current smoking can be correlated with lower mortality rates and that recent cessation could increase complication risk, although these findings might be biased, mainly due to the fact that current smokers are frequently younger than ex-smokers and hence, less prone to post-operative complications.[22,23] In their study, Nakagawa and his colleagues have proposed a 4-week minimum smoke-free period in order to diminish post-operative complications, while Mason's reports state that there is no minimum time for cessation, since any history of smoking seems to negatively impact outcome.[21,24] Bearing this in mind, we conducted our study in order to investigate whether smoking at any point during a patient's lifetime influences outcome after lung surgery, and have thus found that, in our population, a history of tobacco exposure constitutes a risk factor for specific post-operative complications and morbidity, regardless of duration from cessation.

Prolonged air leak, defined in our study as lasting over 7 days, is one of the most frequent complications after lung surgery. We have found that smoking significantly increases the risk for prolonged air leak, possibly due to tobacco-induced changes in lung architecture, with destruction of alveolar walls leading to pulmonary emphysema. The higher the rate of pulmonary emphysema, the higher the risk for prolonged air leaks, hence, a possible correlation between smoking duration and the risk for this complication may exist and can and should be a target for future investigation.[25]

Prolonged air leaks also contribute to longer in-hospital stays. In concordance, we have found that patients in our smoking group had approximately 2-day longer hospital stays than their abstinent counterparts, increasing infection risk, patient anxiety and hospital costs.

Procedure duration and intra and post-operative drainage levels do not seem to be influenced by smoking status. In light of our results, we can speculate that smoking increases post-operative pulmonary complications (with slightly higher, although non-significant) rates of pulmonary insufficiency and similar rates of lung atelectasis, but not cardiac complications, such as arrhythmia development. Although, given the size of our series, this cannot be confirmed.

Although in this series we have not evaluated the incidence of post-operative surgical site infection, smoking can also be a risk factor for its development, given its role in delaying wound closure, causing skin atrophy and reducing peripheral blood flow to infection-prone areas.[9]

Overall morbidity is affected by cigarette smoking in patients submitted to lung resection surgery even through minimally invasive approaches, such as uniportal VATS. Smoking cessation is advisable, although there is no clear desirable length for cessation duration, rather, population--based sensitization on the effects of tobacco must continue to be performed by Public Health ministries, so that overall exposure can be lessened.

Study limitations

This study has some limitations. First, because this was a small-sized retrospective study, it had low statistical power. Besides, the role of smoking in post-operative pain was not evaluated and could be of interest to evaluate its impact in prolonged length of stay in smokers. Besides, we could not compare outcomes between uniportal VATS and thoracotomy, since data from thoracotomy patients was not accessible.

CONCLUSIONS

Cigarette smoking at any time during a patient's life negatively impacts post-operative outcomes and morbidity in patients in need to be submitted to anatomical lung resection even through minimally invasive approaches such as uniportal VATS. More studies exploring the relationship between duration from smoking cessation and post-operative complications are needed.

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COMMENT

Cristina Rodrigues
Associated Editor for Thoracic Surgery

Smoking cessation: a matter of timely opportunity!

Tobacco exposure increases the risk of lung cancer and many other malignancies. So, smoking cessation is of paramount importance in public health.

A diagnosis of lung malignancy, as bad as it is, represents a major target for intervention in the enrolment in a smoking cessation program.

These programs are run by specialists, mostly pneumologists, but can be extended to primary care, through the family doctors. A multidisciplinary team evaluates and monitors the patients throughout the entire process.

Ideally, as referred by Rei *et al*[1], there should be a gap of at least 4 weeks between smoking cessation and lung surgery, but the need for lung cancer surgery is not usually compatible with a 30 day waiting period for a completion of a drug cessation program. The fact is that from the time of the first suspicion, to the operating table there is time for an early enrolment in such a program.

The benefits in improvement in lung function test, quality of life and decrease of post-operative complications are highly motivating and the opportunity should not be wasted.

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