ORIGINAL ARTICLE

POSTOPERATIVE ATRIAL FIBRILLATION - VIDEO-ASSISTED THORACOSCOPIC SURGERY VERSUS OPEN SURGERY

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Abstract

Objectives: *Compare the incidence of Postoperative atrial fibrillation (PAF) after anatomical lung resection for Non-Small-Cell Lung Cancer (NSCLC) following open surgery versus VATS.*

Methods: *Single center retrospective study of all consecutive patients diagnosed with NSCLC submitted to anatomical lung resection from 2015 to 2019 (N=564). Exclusion criteria: prior atrial fibrillation, previous lung surgery, concomitant procedures, pneumectomy, non-pulmonary resections, urgency surgery. Study population of 439 patients. Primary end-point: incidence of PAF.*

Univariable analysis was used to compare the baseline characteristics of the 2 groups. Inverse probability of treatment weighting (IPTW) multivariable logistic regression was used including 23 clinical variables to analyze the effect of the approach. The balance was assessed by standardized mean differences.

Results: *Thoracotomy was performed in 280 patients (63.8%) and 159 (36.2%) were submitted to VATS. Patients submitted to VATS were more likely to be females, had a lower prevalence of non-adenocarcinoma cancer, stage TNM III-IV, Diabetes Mellitus, respiratory disease, and chronic heart failure. They were submitted less often to neoadjuvant therapy, bilobectomy and they presented higher levels of diffusing capacity for carbon monoxide. After IPTW adjustment, all clinical covariates were well balanced.*

PAF occurred in 8.6% of the patients undergoing thoracotomy and 3,8% of the patients after VATS. After IPTW adjustment, VATS was not associated with a lower incidence of PAF (OR 0.40; CI95%:0.140-1.171; p=0.095).

Conclusion: *In this study, minimally invasive non–rib spreading VATS did not decrease the incidence of PAF when compared with standard thoracotomy regarding anatomical lung resection for NSCLC.*

Keywords: *diffusing capacity for carbon monoxide, non-small-cell lung cancer, postoperative atrial fibrillation, standard deviation, video-assisted thoracoscopic surgery*

INTRODUCTION

Postoperative atrial fibrillation (PAF) is one of the most common complications after noncardiac thoracic surgery, with reported rates between 4 and 37%. The incidence of PAF contributes to increased morbidity, such as increased risk of stroke, atrial thrombosis and systemic embolization, postoperative mortality and increases hospital stay and costs significantly[1-4].

There are some hypotheses for the etiology of PAF, as autonomic denervation or surgical stress induced by ribs spread, but the etiology of this condition remains unclear[1,2].

It is proved that video-assisted thoracoscopic surgery (VATS) has significantly less morbidity and a shorter hospital stay than open procedures[2-7]. Nevertheless, there are conflicting data regarding if VATS is related to incidence of PAF[1-7].

This study reviews the experience with anatomical lung resection for non-small-cell lung cancer (NSCLC) at a single center with the aim to compare the incidence of PAF following open surgery versus VATS.

MATERIALS AND METHODS

A retrospective research was conducted to identify all consecutive patients diagnosed with NSCLC submitted to anatomical lung resection at the Hospital Pulido Valente, between January 2015 and June 2019. The initial population included 564 patients. Patients with prior atrial fibrillation (26), previous lung surgery (29), concomitant procedures (10), pneumectomy (14), non-pulmonary resections (41), urgency surgery (5). were excluded. These exclusion criteria were selected a priori. Therefore, the study population consisted of 439 patients operated during a 5 year interval. We categorized patients into the following two groups according to the type of procedure: thoracotomy or VATS.

Table 1 **Operative data**

Procedure	Thoracotomy (n=280) n(%)	VATS (n=159) n(%)
Segmentectomy	11 (3.9)	4 (2.5)
Lobectomy	245 (87.5)	153 (96.2)
Bilobectomy	24 (8.6)	2 (1.3)

VATS: video-assisted thoracoscopic surgery

Operative technique

Operability was determined based on the existing guidelines for pulmonary resection. The operative data are listed in Table 1. Thoracotomy was performed in 280 (63.8%) patients. One hundred and fifty-nine patients (36.2%) were submitted to video-assisted thoracoscopic surgery (VATS). Patients converted from VATS to open surgery for any reason were assigned to thoracotomy group.

It was used an endoscopic stapler to divide the fused fissures/ intersegmental planes and to section the hilar structures. All patients were submitted to mediastinal lymph node dissection.

All patients received epidural analgesia or an intercostal nerve block for pain control.

Outcomes

Primary end-point was PAF defined by in-hospital electrocardiographically documented atrial fibrillation requiring initiation of pharmacological therapy.

Secondary end-point was the incidence of other postoperative complications, defined as a composite endpoint including at least one of the following in-hospital variables: primary respiratory failure atelectasis, respiratory infection, empyema, bleeding requiring surgery and reoperation.

Statistical Analysis

Categorical variables were expressed as absolute numbers and percentages and continuous variables were expressed as mean (standard deviation (SD)). Kolmogorov-Smirnov test was used to access the normal distribution.

Fisher's tests and t tests were used to compare the baseline characteristics of the 2 groups when data were dichotomous or distributed normally. The Wilcoxon signed-rank test was used for nonnormally distributed data.

We use inverse probability of treatment weighting (IPTW) multivariable logistic regression model to obtain unbiased estimates of average procedure effect on PAF 8. A total of 23 clinical variables were included in the model: age, gender, previous tumor, neoadjuvant treatment, Tumor, Node, Metastasis 8th edition (TNM) staging system III-IV, thoracotomy/VATS, bilobectomy, non-adenocarcinoma, hypertension, Diabetes Mellitus (DM), smoking (included ex-smokers), stroke, peripheral vascular disease, coronary artery disease, chronic heart failure, respiratory disease, gastrointestinal disease, anticoagulant therapy, diffusing capacity for carbon monoxide (DLCO%), serum hemoglobin, FEV1%, smoking index, use of beta-blockers. The balance between treatment groups after IPTW was assessed by standardized mean differences (SMD), with a difference of 10% or less considered ideal.

A probability value of $p<0.05$ was considered statistically significant. All analyses were performed using IBM SPSS Statistics for Windows, Version 23.0. (IBM Corp. Armonk, NY).

RESULTS

Patient Characteristics

Two hundred and eighty patients (63.8%) were submitted to thoracotomy and 159 patients (36.2%) were submitted to VATS. The demographic and clinical characteristics of these patients are summarized in Table 2. Briefly, patients submitted to VATS were more likely to be females ($p=0.004$), had a lower prevalence of non-adenocarcinoma ($p<0.001$) cancer, TNM stages III-IV ($p=0.001$) and no previous diagnosis of DM ($p=0.028$), chronic heart failure ($p=0.026$) or respiratory disease ($p=0,042$). They were submitted less

Table 2 **Patient demographics and comorbidities**

Demographics	Thoracotomy (n=280) n (%)	VATS (n=159) n (%)	*p*-value
Male sex	190 (67.9)	87 (54.7)	0.004
Mean age (years)	65.7	65.0	0.492
Non-adenocarcinoma	106 (37.9)	31 (19.5)	<0.001
TNM III-IV	67 (24.3)	18 (11.8)	0001
Neoadjuvancy	43 (15.4)	6 (3.8)	<0.001
Bilobectomy	24 (8.6)	2 (1.3)	0.001
DLCO% (mean)	78.7	84.5	0.001
FEV1% (mean)	89.2	91.5	0.222
Serum Hb g/dL (median)	13.4	13.7	0.188
Serum Creatinine mg/dL (mean)	0.93	0.86	0.261
Comorbidities			
Previous tumor	53 (18.9)	28 (17.6)	0.418
Arterial Hypertension	160 (57.1)	91 (57.2)	0.533
DM	48 (17.1)	16 (10.1)	0.028
Dyslipidemia	118 (42.1)	71 (44.7)	0.340
Smoker/ex-smoker	197 (70.4)	102 (64.2)	0.109
Mean smoking index (pack-year)	38.9	33.4	0.081
Stroke	22 (7.9)	6 (3.8)	0.066
Coronary artery disease	25 (8.9)	7 (4.4)	0.056
Chronic heart Failure	8 (2.9)	0 (0)	0.026
Peripheral vascular disease	12 (4.3)	5 (2.1)	0.376
Respiratory disease	90 (32.1)	38 (23.9)	0.042
Gastrointestinal disease	33 (11.8)	21 (13.2)	0.384
Anticoagulant therapy	2 (0.7)	1 (0.6)	0.702
Beta-blocker	41 (14.6)	24 (15.1)	0.501

DLCO%: diffusing capacity for carbon monoxide; DM: Diabetes Mellitus; FEV1%: forced expiratory volume in 1 s; Hb: Hemoglobin; TNM: Tumor, Node, Metastasis; VATS: video-assisted thoracoscopic surgery

often to neoadjuvant therapy (p<0.001), bilobectomy (p=0.001) and they presented higher levels of diffusing capacity for carbon monoxide (p=0.001). After IPTW adjustment, all clinical covariates were well balanced (Table 3).

PAF and outcomes

Globally, PAF occurred in 30 (6.8%) patients. Twenty-four patients (8.6%) submitted to thoracotomy and 6 (3,8%) patients after VATS presented PAF. After adjustment using the IPTW approach, VATS was not associated with a lower incidence of PAF (OR 0.40; CI95%:0.140-1.171; p=0.095).

There were no differences in other postoperative in-hospital complications, including primary respiratory failure atelectasis, respiratory infection, empyema, bleeding requiring surgery or reoperation (Table 4).

The mean length of stay was 8.7 (SD:6.8) days. The length of hospital stay was significantly greater for patients with AF compared with patients who did not have AF (p=0.001).

DISCUSSION

PAF remains one of the most frequent complications following pulmonary resection in lung-cancer patients, with described rates between 4 and 37%. The difference in incidence rates among the several studies can be explained by differences in PAF definitions, monitoring techniques, and prevention strategies[1-4]. The incidence of PAF in our study was 6.8%, encompassed in the referred range.

Several risk factors have been identified for the development of PAF. However, the type of surgical approach has been presented with conflicting data. It is widely known that VATS approach presents with significantly less morbidity after lung resection. For that reason, some studies suggest that incision-related effects may be responsible for the pathogenesis of PAF, defending VATS as a procedure with lower incidence of this complication. Ivanovic et al.[1] reported thoracotomy with a higher incidence of PAF in 3.6 folds compared to VATS; in the studies of Papiashvilli et al.[5] and Villamizar et al.[6], it was analysed only patients submitted to lobectomy/bilobectomy or lobectomy respectively and they identified a lower incidence of PAF on VATS approach. None of these researches were patient-matched.

Nevertheless, several studies with non-matched patients referred no difference between the two approaches[2,3]. Park et al.[4], with age and gender matched patients, reported equal frequency of AF after lobectomy regardless of the surgical approach[11]. From the analysis of the case-matched patients of European Society of Thoracic Surgeon database, Falcoz et al.[7] observed no difference in the incidence of PAF between the two groups. These referred studies support the concept that autonomic nerve system may play an important role in PAF - during the surgery, the autonomic nerves passing through pulmonary hilum are damaged, leading to unilateral denervation of cardium. This dissection is similar between VATS and thoracotomy, resulting in similar incidence of PAF[2]. Due to the retrospective nature of our research, we use inverse probability of treatment weighting to obtain unbiased estimates of average approach effects8. After the adjustment, VATS was not associated with a lower incidence of PAF.

In addition to increased morbidity and mortality, previous studies reported that PAF contributed to a longer hospitalization. In our study, PAF was also associated with prolonged length of stay.

This study has multiple limitations. It is based on the retrospective analysis of a population operated by different surgeons in a single center. The final decisions to select patients for surgery and the choice of surgical procedure may vary among surgeons.

Due to the low number of segmentectomies (N=15) and the fact that it is considered a less invasive procedure, they were considered with the lobectomies for statistical analysys. Only bilobectomies were analysed separately.

Table 2 **Standardized Differences in Baseline Variables Before and After Inverse Probability of Treatment Weighting**

Demographics	SMD Before IPTW (%)	SMD After IPTW (%)
Male sex	27	3
Age	6	9
Non-adenocarcinoma	32	4
TNM III-IV	32	7
Neoadjuvancy	32	8
Bilobectomy	32	8
DLCO%	32	9
FEV1%	12	8
Serum Hb	13	3
Serum Creatinine	11	7
Comorbidities		
Previous tumor	8	1
Arterial Hypertension	6	7
DM	21	2
Dyslipidemia	9	6
Smoker/ex-smoker	15	8
Smoking index	17	7
Stroke	18	1
Coronary artery disease	18	1
Chronic heart Failure	21	1
Peripheral vascular disease	9	8
Respiratory disease	20	1
Gastrointestinal disease	8	1
Anticoagulant therapy	4	1
Beta-blocker	6	9

DLCO%: diffusing capacity for carbon monoxide; DM: Diabetes Mellitus; FEV1%: forced expiratory volume in 1 s; Hb: Hemoglobin; TNM: Tumor, Node, Metastasis; VATS: video-assisted thoracoscopic surgery

Another limitation is the exclusion of other risk factors, such as electrolyte imbalance.

In summary, this study reports that minimally invasive non–rib spreading VATS did not decrease the incidence of PAF when compared with standard thoracotomy regarding anatomical lung resection for NSCLC, in our cohort of patients.

CONFLICT OF INTEREST

None declared

Table 4 **Operative data**

Morbidity	Thoracotomy (n=280) n(%)	VATS (n=159) n(%)	Adjusted OR (95% CI)	*p*-value
PAF	24 (8.6)	6 (3,8)	0.40 (0.140-1.171)	0.095
Primary respiratory failure	8 (2.9)	2 (1.3)	0.78 (0.160-3.776)	0.755
Respiratory infection	36 (12.9)	11 (6.9)	0.86 (0.330-2.249)	0.760
Empyema	6 (2.1)	2 (1.3)	0.46 (0.089-2.388)	0.357
Bleeding	9 (3.2)	4 (2.5)	0.73 (0.196-2.713)	0.637
Reoperation	13 (4.6)	5 (3.1)	0.57 (0.181-1.824	0.347
Total	74 (26.4)	21 (13.2)	0.59 (0.280-1.156)	0.119

PAF: postoperative atrial fibrillation; VATS: video-assisted thoracoscopic surgery

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