

Risk Factors for Atrial Fibrillation After Thoracic Surgery

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OBJECTIVE: To determine the risk factors for atrial fibrillation after lung resection.

PATIENTS AND METHOD: Between January 2002 and December 2003, 149 patients underwent lung resection in our hospital. For all these patients, clinical, surgical, analytical, and oncological data were prospectively collected. The data were subjected to univariate analysis.

RESULTS: The mean (SD) age of the 127 men (85.2%) and 22 women (14.8%) who underwent lung resection was 61.8 (12.3) years (range, 17-79 years). Atrial fibrillation was documented in 17 patients (11.4%). Mortality at 30 days was 8.1%. The following risk factors for atrial fibrillation were identified: age 70 years or older ($P < .0004$), prior heart disease ($P < .005$), patients undergoing operations for lung cancer ($P < .04$), and type of resection—right bilobectomy ($P < .05$) and left pneumonectomy ($P < .03$). Hypertension, chronic obstructive pulmonary disease, and lung cancer stage were not risk factors. Likewise, systematic lymph node dissection and other forms of lung resection were not risk factors.

CONCLUSIONS: After lung resection, atrial fibrillation is a common complication that seems to be associated with old age, history of heart disease, operations for lung cancer, left pneumonectomy, and right bilobectomy. The identification of these risk factors may encourage prospective studies that assess the use of antiarrhythmic drugs to prevent atrial fibrillation during chest surgery.

Key words: Atrial fibrillation. Lung resection. Complications. Risk factors. Lung cancer.

Factores de riesgo en el desarrollo de fibrilación auricular tras cirugía torácica

OBJETIVO: Determinar los factores de riesgo en la fibrilación auricular (FA) tras la resección pulmonar.

PACIENTES Y MÉTODO: Entre enero de 2002 y diciembre de 2003 se realizaron en nuestro servicio 149 resecciones anatómicas pulmonares. Se recogieron prospectivamente las características clínicas, quirúrgicas, analíticas y oncológicas de todos los pacientes intervenidos. Se realizó un análisis univariante de todas las variables registradas.

RESULTADOS: La edad media (\pm desviación estándar) de los pacientes operados—127 varones (85,2%) y 22 mujeres (14,8%)— fue de $61,8 \pm 12,3$ años (rango: 17-79). Se detectaron 17 casos de FA (11,4%). La mortalidad a los 30 días fue del 8,1%. Se detectaron los siguientes factores de riesgo de presentar FA: edad ≥ 70 años ($p < 0,0004$), enfermedad cardíaca previa ($p < 0,005$), pacientes operados por carcinoma broncogénico ($p < 0,04$) y tipo de resección—bilobectomía derecha ($p < 0,05$) y neumonectomía izquierda ($p < 0,03$)—. No fueron factores de riesgo la hipertensión arterial, la enfermedad pulmonar obstructiva crónica, el estadio del carcinoma broncogénico, la disección mediastínica sistemática ni otro tipo distinto de resección pulmonar.

CONCLUSIONES: La aparición de FA después de la resección pulmonar anatómica es una complicación frecuente que parece asociarse en nuestra serie a edad avanzada, antecedentes de cardiopatía, intervención por carcinoma broncogénico, neumonectomía izquierda y bilobectomía derecha. La identificación de estos factores de riesgo puede ser de utilidad para iniciar estudios prospectivos encaminados a valorar el uso de fármacos antiarrítmicos para prevenir esta complicación.

Palabras clave: Fibrilación auricular. Resección pulmonar. Complicaciones. Factores de riesgo. Cáncer de pulmón.

Introduction

Atrial fibrillation is relatively common after any type of surgery and is associated with between 3.8% and 37% of operations involving thoracic organs (excluding

heart surgery).¹ The incidence of atrial fibrillation after lobectomies is between 10% and 20% and approaches 40% after pneumonectomies.²

Atrial fibrillation is associated with higher morbidity, greater risk of cerebrovascular accident, and longer hospital stay and, therefore, higher hospital costs, as well as with increased perioperative mortality and worse long-term survival.^{3,4}

A series of risk factors have been identified that are associated with presentation of atrial fibrillation after

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Manuscript received February 28, 2005. Accepted for publication May 3, 2005.

surgery. These are old age, prior heart disease, chronic obstructive pulmonary disease (COPD),⁵ a history of arrhythmias, and the type of surgery performed.^{1,3}

The aim of this study was to test the hypothesis that presentation of atrial fibrillation after anatomical lung resection significantly depends on preoperative comorbidity factors and to identify these factors and the excess risk.

Patients and Method

Between January 2002 and December 2003, 149 patients underwent lung resection in our hospital. For all these patients, clinical, surgical, analytical, and oncological data were prospectively collected. We excluded all nonanatomical lung resections and exploratory thoracotomies, as well as patients with atrial fibrillation diagnosed prior to surgery. All interventions were performed by classical thoracotomy. Lymph node dissection was not done systematically, that is, some patients underwent systematic dissection, whereas lymph node sampling was done in others. The type of lymph node dissection was left to the discretion of the treating surgeon. Lung function was assessed with the protocol of the Bronchogenic Carcinoma Cooperative Group of the Spanish Society for Pulmonology and Thoracic Surgery (GCCB-S).⁶ No patient received prophylaxis for atrial fibrillation.

Age, sex, lung function (absolute and percentage forced expiratory volume in 1 second [FEV₁], calculated postoperative FEV₁, and absolute and percentage forced vital capacity [FVC]), comorbidity (COPD, heart disease, diabetes mellitus, peripheral vascular disease), reason for resection (lung cancer and its pathological stage, lung metastasis, pulmonary neuroendocrine tumor, pulmonary aspergilloma, benign pathology), type of resection, type of lymph node dissection, prior chemotherapy, appearance of atrial fibrillation and when it presented, length of hospital stay, and mortality and causes of death at 30 days were all prospectively analyzed.

Prior heart disease was defined as a heart condition, including untreated arrhythmias, old myocardial infarction, rheumatic fever with valvular involvement, and heart failure from any cause, diagnosed at any time in life. Peripheral vascular disease was defined according to the criteria established in the GCCB-S protocol.⁶ COPD was defined as present when FEV₁ was less than 80% of the theoretical value and FEV₁/FVC was less than 70%. Chemotherapy was documented when it had been administered in the 3 months prior to surgery, whether as oncological treatment of distant metastasis or as induction therapy prior to lung cancer surgery.

Postoperative FEV₁ was calculated according to the formula described by Juhl and Frost.⁷

For the first 24 hours after surgery, all patients were kept in the resuscitation unit, where they underwent continuous electrocardiographic monitoring and measurement of oxygen saturation level by pulse oximetry. They were then transferred to the thoracic surgery unit, where pulse oximetry was monitored and an electrocardiogram was performed daily for the next few days. All cases of atrial fibrillation were confirmed electrocardiographically. All patients were attended by a physiotherapist and did breathing exercises with an incentive spirometer.

In all cases, atrial fibrillation was treated with digoxin and the antiarrhythmics amiodarone or propafenone, depending on the cardiac history of the patients.

Statistical Analysis

The data were analyzed with the SPSS program, version 11.5. Qualitative variables were compared with the χ^2 test or the Fisher exact test as appropriate. Quantitative variables were compared with the Student *t* test for independent variables. Excess risk was estimated with the Mantel-Haenszel test. The level of significance was set at a *P* value less than .05.

Results

The mean age (SD) of the 127 men (85.2%) and 22 women (14.8%) who underwent surgery was 61.8 (12.3) years (range, 17-79 years). Table 1 shows the most important clinical, oncological, and functional characteristics of these patients. The mean postoperative stay in hospital lasted 9.9 (5.9) days and the mortality rate was 8.1% (12 patients). Causes of death were pneumonia (4 patients), acute myocardial infarction (1 patient), bronchial fistula (3 patients), adult respiratory distress syndrome (3 patients), and pulmonary thromboembolism (1 patient).

Atrial fibrillation was documented after surgery in 17 patients (11.4%), and presented 2 to 3 days after surgery in 14 (82.3%) of these (Figure).

TABLE 1
Characteristics of the Patients Analyzed in Our Series*

Characteristics	
Age, years	61.86 (12.3)
Sex	
Male	127/149 (85.2%)
Female	22/149 (14.8%)
Lung function tests	
FEV ₁ , L	2.47 (0.8)
FEV ₁ %	83.4 (31.9)
PpoFEV ₁ , L	1.82 (0.67)
PpoFEV ₁ %	62.2 (26.8)
FVC, L	3.50 (0.93)
FVC%	105.6 (72.4)
Disease	
Lung cancer	123 (82.6%)
Metastasis	14 (9.4%)
Lung carcinoid tumor	5 (3.4%)
Localized aspergilloma	5 (3.4%)
Benign pathology	2 (1.3%)
Comorbidity	
Heart disease	22/149 (14.7%)
Hypertension	51/149 (34.1%)
COPD	87/149 (58.4%)
Diabetes mellitus	19/149 (12.7%)
Peripheral vascular disease	15/149 (9.3%)
Lung cancer stage	
IA	32 (26.1%)
IB	45 (36.5%)
IIA	6 (4.9%)
IIB	17 (13.8%)
IIIA	15 (12.2%)
IIIB	3 (2.4%)
IV	5 (4%)

*Data expressed as mean (SD) or number (%). FEV₁ indicates forced expiratory volume in 1 second; FVC, forced vital capacity; PpoFEV₁, estimated postoperative FEV₁; PpoFEV₁%, estimated postoperative FEV₁ expressed as a percentage; COPD, chronic obstructive pulmonary disease.

Return to sinus rhythm was achieved in 15 patients (88.2%). Only 2 of the patients who developed atrial fibrillation died, though the difference in mortality between patients with and without fibrillation was not statistically significant. The effects of the most important study variables and the results of the statistical comparisons are presented in Table 2. The type of surgery and the incidence of atrial fibrillation are shown in Table 3. The following risk factors for atrial fibrillation were identified: age 70 years or older ($P < .0004$), prior heart disease ($P < .005$), patients undergoing surgery for lung cancer ($P < .04$), and type of resection—right bilobectomy ($P < .05$) and left pneumonectomy ($P < .03$). Excess risk for the variables significantly associated with atrial fibrillation is shown in Table 4. Hypertension, COPD, lung cancer stage, and systematic lymph node dissection or other forms of

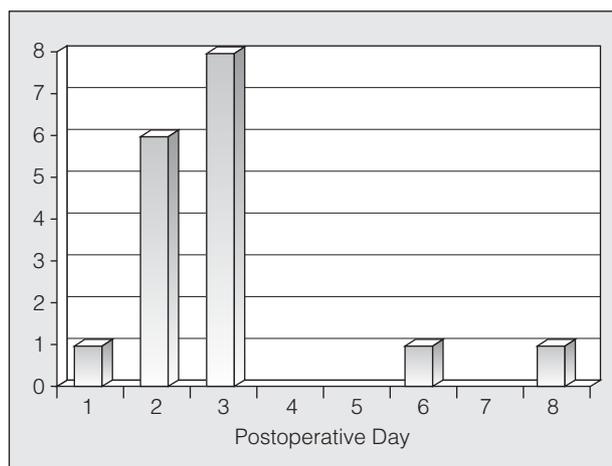


Figure. Presentation of atrial fibrillation (postoperative day).

TABLE 2
Statistical Analysis of the Series and Incidence of Postoperative Atrial Fibrillation*

Characteristics	No Atrial Fibrillation	Atrial Fibrillation	P^{\ddagger}
Type of resection			
Pneumonectomy	20 (83.4%)	4 (16.6%)	.373
Not pneumonectomy	112 (89.6%)	13 (10.4%)	
Upper lobectomy†	94 (86.2%)	15 (13.8%)	.136
Lower lobectomy	38 (95%)	2 (5%)	
Side of surgery			
Right	75 (89.3%)	9 (10.7%)	.766
Left	57 (87.7%)	8 (12.3%)	
Hypertension			
Yes	43 (86%)	7 (14%)	.372
No	89 (90.8%)	9 (9.2%)	
COPD			
Yes	77 (88.5%)	10 (11.5%)	.969
No	55 (88.7%)	7 (11.3%)	
Prior chemotherapy			
Yes	24 (96%)	1 (4%)	.201
No	108 (87.1%)	16 (12.9%)	
Age, years			
< 70	100 (93.5%)	7 (6.5%)	.0004
≥ 70	32 (76.2%)	10 (23.8%)	
Sex			
Male	112 (88.2%)	15 (11.8%)	.711
Female	20 (90.9%)	2 (9.1%)	
Oncological stage			
I-II	86 (86%)	14 (14%)	.951
III-IV	20 (87%)	3 (13.0%)	
Lung function tests			
FEV ₁	2.477 (803.0)	2.451 (531)	.904§
FEV ₁ %	83.5 (31.9)	85.7 (18)	.764§
PpoFEV ₁	1.825.7 (674.5)	1.783 (578)	.790§
PpoFEV ₁ %	62.2 (26.8)	62 (19)	.977§
Lymph node dissection			
No	118 (89.4%)	14 (10.6%)	.369
Yes	14 (82.4%)	3 (17.6%)	
Disease			
Lung cancer	106 (86.2%)	17 (13.8%)	.044
Other cancer	26 (100%)	0	
Heart disease			
Yes	15 (68.2%)	7 (31.8%)	.005
No	117 (92.2%)	10 (7.8%)	

*Data expressed as mean (SD) or number (%).

COPD indicates chronic obstructive pulmonary disease; FEV₁, forced expiratory volume in 1 second; PpoFEV₁, estimated postoperative FEV₁; PpoFEV₁%, estimated postoperative FEV₁, expressed as a percentage.

†The variable upper and lower lobectomy is related to manipulation of the superior or inferior pulmonary vein. Pneumonectomies and middle lobectomies which involved manipulation of the superior pulmonary vein were counted as upper lobectomies.

‡ χ^2 test or Fisher exact test.

§Student *t* test for independent variables.

TABLE 3
Analysis of Atrial Fibrillation and Type of Resection

Side	Type of Resection	N	Atrial Fibrillation	P*
Right	Pneumonectomy	9 (6%)	0	.54
	Upper lobectomy	40 (26.8%)	5 (12.5%)	.766
	Middle lobectomy	8 (5.4%)	1 (12.5%)	.96
	Lower lobectomy	19 (12.8%)	0	.246
	Bilobectomy	8 (5.4%)	2 (25%)	.005
	Total	84 (56.3%)	8 (9.5%)	
Left	Pneumonectomy	15 (10.1%)	4 (26.6%)	.037
	Upper lobectomy	29 (19.5%)	2 (6.9%)	.449
	Lower lobectomy	21 (14.1%)	2 (9.5%)	.838
	Total	65 (43.7%)	8 (12.3%)	

* χ^2 test or Fisher exact test.

TABLE 4
Predictive Analysis of Risk of Postoperative Atrial Fibrillation*

Variable	OR (95% CI)	P†
Age \geq 70 years	2.9 (2.3-3.3)	.001
Prior heart disease	1.8 (3.2-1.1)	.005
Lung cancer surgery	2.7 (3.6-1.2)	.044
Left pneumonectomy	1.2 (2.3-0.9)	.037
Right bilobectomy	1.7 (3.2-1.1)	.005

*OR indicates odds ratio; CI, confidence interval.

†Mantel-Haenszel test.

lung resection were not found to be risk factors for atrial fibrillation. Likewise, no other factors studied were associated with increased risk.

Discussion

Atrial fibrillation often occurs after thoracic surgery because other risk factors of multifactorial origin such as hypoxia, hypovolemia, sepsis, electrolyte imbalances, increased vagal activity, or increased cardiac preload are also present in addition to the operation itself and the associated manipulation.^{1,8} According to other studies, elderly patients, men, those with a prior history of heart disease, and those who undergo intraoperative transfusions are also at greater risk of suffering atrial fibrillation.³

Atrial fibrillation is a cause of morbidity because it increases the risk of cerebrovascular accident or peripheral embolism. It also increases the length of stay in hospital and in intensive care units.^{2,9}

The incidence in our series (11.4%) is similar to that reported for other series.^{3,8,10,11} The strongest risk factor, both in studies published in the literature and in our series, was age.⁹ It might be supposed that age could confound a possible relationship between the presence of atrial fibrillation and longer hospital stays and associated morbidity. Nevertheless, age is an important factor in view of the increasing mean age of the patients who undergo thoracic surgery. The risk of this arrhythmia has also been reported to be greater in male patients.^{2,3}

We did not find a significant relationship between estimated preoperative or postoperative FEV₁ values, regardless of whether expressed as absolute values or as percentages, and atrial fibrillation. However, a relationship between the severity of COPD and a higher risk of atrial fibrillation has been reported in the literature.⁵ Hypoxemia appears both in the preoperative and postoperative period, and so has also been associated with this arrhythmia.^{2,12} A number of studies have identified prior heart disease, in particular ischemic heart disease and congestive heart failure of varying causes, as a risk factor.¹³

The mechanism by which arrhythmias occur may be related to atrial stimulation in the sutured region of the sectioned pulmonary vein, a region that a number of prestigious studies have identified as a trigger zone. In fact, in up to 94% of cases, ectopic activity leading to atrial fibrillation originates in the pulmonary veins, in particular, in the superior pulmonary veins, and specifically 2 cm to 4 cm inside these veins.¹⁴ Some studies report a higher incidence in pneumonectomies^{15,16} and in these cases, the arrhythmias might be related to intrapericardial dissection of the superior pulmonary vein.¹² Other studies do not find any relationship between the type of pulmonary resection and this arrhythmia.¹⁷ In our series, this association was not significant, though our service is very reticent about performing right pneumonectomies in patients aged over 70 years. In addition, in our study, upper lobectomies were not more strongly associated with atrial fibrillation, even though such procedures involve more extensive manipulation of the superior pulmonary vein,³ where trigger zones might be expected more often for electrophysiological reasons.¹⁴ The large difference in the incidences of atrial fibrillation between anatomical and nonanatomical lung resections, which do not normally involve manipulation of periatrial or pericardial structures, could also be largely explained by this reasoning.¹²

To the best of our knowledge, no study has reported tumor stage as a determining factor,⁵ in contrast to the type of lung resection and lymph node dissection, which have been associated with atrial fibrillation. Systematic lymph node dissection also appears in the literature as a risk factor for the development of atrial fibrillation.¹² This could be related to lesion of vagal nerve branches, which are damaged on removing adipose-lymphoid tissue from mediastinal areas and areas around the lungs. Such procedures are nevertheless essential for reliable lung cancer staging.

The appearance of atrial fibrillation after surgery can lead to increased comorbidity. To avoid this risk, prophylaxis to prevent or reduce the chance of atrial fibrillation appearing has been considered. Such prophylactic agents include digoxin,¹⁸ β -blockers, amiodarone,^{19,20} and diltiazem.²¹ In high-risk patients,²¹ only amiodarone and diltiazem have been shown to provide effective prophylaxis against atrial fibrillation.²⁰ Amiodarone is considered the safest and most effective agent for treating atrial fibrillation.²² These studies

failed to reflect, however, a decrease in costs or length of stay in hospital with prophylaxis.

In conclusion, the appearance of atrial fibrillation after anatomical lung resection is a common complication that is associated with advanced age, history of heart disease, lung cancer operations, left pneumonectomy, and right bilobectomy. Identification of these risk factors could be useful for planning prospective studies that aim to assess the use of antiarrhythmic drugs to prevent atrial fibrillation.

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