Left atrial size predicts the onset of atrial fibrillation after major pulmonary resections†

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Abstract

OBJECTIVES: Atrial fibrillation (AF) is a frequent complication after pulmonary resections. Notwithstanding prevention and early treatment it may show a negative impact on the outcome. We assessed the role of echocardiographic variables to predict the onset of this complication.

METHODS: One-hundred and thirty-four patients were prospectively evaluated: 72 (53.7%) (Group I) underwent lobectomy or pneumonectomy; 62 (46.3%) receiving minor thoracic procedures were included in Group II. Previous AF was the only exclusion criteria. All patients preoperatively underwent bidimensional echocardiography. Demographics, type of resection, histology, staging, diagnosis of chronic obstructive pulmonary disease, induction chemotherapy, smoking history, magnesium levels, other cardiologic diseases, electrocardiographic and echocardiographic findings (atrial and ventricular diameters, left atrial area, left ventricular ejection fraction and diastolic dysfunction) were assessed.

RESULTS: Preoperative variables did not show any statistically significant difference between the groups. In 21 patients (15.7%) AF was observed 3.7 ± 1.8 days after surgery. All AF episodes occurred in Group I. Three patients (2.2%) with AF died during the postoperative course. The left atrial diameter and area were significantly enlarged in patients with AF ($P = 0.001$ and $P < 0.0002$); 18 AF episodes (86%) occurred in patients with atrial enlargement. At univariate analysis low postoperative magnesium levels, LV diastolic dysfunction, left atrial antero-posterior diameter >40 mm, left atrial area above 20 mm$^2$ and extended resections were statistically significant. At multivariate analysis only left atrial area enlargement was an independent predictive prognostic factor for postoperative AF.

CONCLUSIONS: Echocardiographic left atrial size evaluation may be useful to predict the onset of postoperative AF in patients undergoing lobectomy and pneumonectomy.

Keywords: Atrial fibrillation • Pulmonary resection • Echocardiography

INTRODUCTION

Atrial fibrillation (AF) is the most frequent cardiac complication after pulmonary resections, with an incidence ranging from multiple between 4 and 33% [1, 2]. It is characterized by the propagation of a chaotic impulse generated foci and is usually considered as a self-limited event; however, this complication often requires a longer hospital stay with higher costs [3]. In addition, thromboembolic and stroke events may complicate the postoperative course with dramatic consequences and increased perioperative mortality [4, 5]. Preoperative identification of high-risk patients and pharmacological prevention might help us to improve the outcome. Older age, previous history of cardiac disease and other associated disorders, parenchymal resections larger than segmentectomy, extended mediastinal lymph node dissection and administration of induction therapy have been reported to increase the risk of postoperative AF [6–8]. Recent reports showed that left ventricular (LV) diastolic dysfunction could be considered a predictive variable as well as the ratio between early transmural velocity and tissue Doppler mitral annular early diastolic velocity [9]. Previous studies demonstrated the relationship between atrial enlargement and occurrence of AF in patients undergoing coronary artery bypass graft and aortic or tricuspid valve surgery [10]. Based on these studies, we have assessed the role of echocardiography to identify patients at high risk of developing AF after pulmonary resections.

METHODS

One-hundred and fifty patient candidates to parenchymal resections were prospectively enrolled in this study; previous AF was
the only exclusion criteria. For this reason, 16 patients were excluded and 134 patients form the basis of our study (96 males and 38 females; mean age 68.6 ± 7.5 years). Seventy-two patients (53.7%) (Group I) underwent either lobectomy or pneumonectomy; 62 (46.3%) patients receiving minor resections were included in Group II. Preoperative work-up included chest X-ray, total body computed tomography, arterial blood gas analysis, pulmonary function tests, serum magnesium levels and electrocardiogram (EKG). The presence of chronic obstructive pulmonary disease, diabetes mellitus, systemic hypertension, previous cancers, previous cardiac disease, administration of cardiologic drugs, chemo-radiotherapy (induction therapy for lung cancer or adjuvant therapy for other cancers) and smoking history were recorded; type, side and extent of surgery, histology, postoperative magnesium levels, other complications and 90-days mortality were also assessed. All patients preoperatively underwent two-dimensional echocardiography; measurements were performed according to the American Society of Echocardiography guidelines [11]. From the parasternal long axis view, with M-mode analysis, left ventricular end-diastolic and end systolic diameter diameters, interventricular septum and posterior wall thickness and left atrium (LA) diameter were measured; atrial size was indexed for body surface. The LA maximal area was measured with B-mode analysis following the atrial border, the confluence of the pulmonary veins and LA appendage were excluded. Using the LV volumes calculated with the Teicholz formula from M-mode analysis it was possible to estimate the left ventricular ejection fraction (LVEF). The amount of tricuspid regurgitation was used to determine the systolic pulmonary artery pressure (sPAP). The degree of diastolic dysfunction was calculated as a ratio between the peak of early diastolic mitral flow velocity (E wave) and the peak of mitral flow velocity at atrial contraction (A wave).

Before the operation and during the postoperative course no specific AF prophylaxis was administered. During the postoperative course clinical examination of patients was performed twice a day until discharge; EKG is performed daily for the first few days or when required by the clinical examination. Postoperative intake/output balance was monitored in all our patients. Mild negative balance was maintained in all patients during the early postoperative course.

Continuous data and categorical variables were, respectively, reported as mean ± standard deviation and proportions. Univariate analysis was performed by the unpaired Student’s t test, Mann–Whitney U-test and Fisher’s exact test. Variables statistically significant at univariate analysis were considered for multivariate analysis. A linear regression analysis was used to identify variables predicting the onset of AF. A P value less than 0.05 was considered statistically significant. Statistical analysis was performed using SPSS version 17.0 (SPSS Inc., Chicago, IL).

RESULTS

Seventy-two patients (53.7%) underwent major procedures (Group I) including 46 lobectomies, 3 bilobectomies and 23 pneumonectomies; in 62 patients (46.3%) minor procedures (Group II) were performed (6 segmentectomies and 56 wedge resections). Demographics, clinical and functional data are reported in Table 1 and there were no statistically significant differences between the two groups. Lung cancer was the most frequent indication for surgery: 72 (100%) in Group I and 42 (67.7%) in Group II. Other indications were lung metastases in 11 cases and benign nodules in 9. In Group II, 14 resections (22.6%) were performed through videothoracoscopic or VATS; no VATS was performed in Group I. Eight patients required an extended resection in Group I (11.1%): three bronchial sleeves, three intracardiac pneumonectomies and two reconstructions of pulmonary artery. In all patients with lung cancer complete lymph node dissection was performed.

No intraoperative mortality was observed. In Group I 21 patients (29.8%) showed postoperative AF and none in Group II; the overall incidence was of 15.7%. The mean onset was 3.7 ± 1.8 days after surgery. All AF episodes required only pharmacological treatment and no patient underwent electrical cardioversion. Intravenous infusion of Verapamil (10 mg bolus followed by maintenance with 240 mg in 24 h) was administered as first line treatment; in case of failure (eight patients–38%), Amiodaron (5 mg/kg bolus followed by 20 mg/kg in 24 h) was infused. The conversion to sinus rhythm occurred after a mean of 1.6 days; 24 h after conversion the antiarrhythmic therapy was switched to oral. In 17 out of 21 patients (81%) medical therapy was stopped within one month and no further AF episodes were observed; in one patient it was stopped after 6 months. In the acute phase, the dose of subcutaneous low weight heparin was doubled in two cases (autopptic finding) and massive pulmonary embolism in one (clinical diagnosis); the latter patient died at home after two months and autopsy was not performed.

AF showed a statistically significant impact on hospitalization (8.3 ± 5.1 versus 5.8 ± 3.2 days; P = 0.01). At univariate analysis, the variables achieving statistical significance were: extended

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Group I: lobectomy and pneumonectomy; Group II: minor lung resections (wedge and segmentectomy). FEV1: forced expiratory volume in one second; CHT: induction chemotherapy; LAd: left atrium anteroposterior diameter; LAd/mm²: left atrium area; E/A: peak early diastolic mitral flow velocity to peak mitral flow velocity at atrial contraction; LVEF: left ventricular ejection fraction; Mg ++ pre: preoperative magnesium level; Mg ++ post: postoperative magnesium level.

*Other than atrial fibrillation.
probably a multifactorial mechanism should be considered. Several variables such as older age, male gender, previous history of cardiac disease, administration of induction chemotherapy and presence of other disorders have been advocated [12–15]; also extended resections and lymph node dissection, intraoperative blood transfusions, electrolyte imbalance and pulmonary complications have been reported to show an impact on the onset of this complication [16–18]. However, the clinical impact of each of these variables remains controversial.

Although several reports evaluated preoperative echocardiographic assessment cardiac chambers morphology to predict AF after cardiac operations, few studies focused on the noncardiac thoracic surgery population. We have previously reported on the usefulness of Doppler echocardiography to evaluate the right heart after major pulmonary resections [19]. Using tissue Doppler imaging in lung cancer patients undergoing surgery, Nojiri et al. [9] have demonstrated that postoperative AF may be associated with LV diastolic dysfunction, and in particular to the ratio between early transmitral velocity (E) and tissue Doppler mitral annular early diastolic velocity (Ee). They concluded that in patients with higher E/Ee ratio it could be possible to prevent AF by administering antiarrhythmic drugs during the perioperative course. After cardiac procedures an increased left atrial size may show an impact on the development of AF [10]; in fact, left atrial enlargement is closely related to an increased filling pressure and diastolic dysfunction; this variable acts as an index of severity and chronicity of LV diastolic dysfunction with a strong correlation between the progressive increase in atrial size and worsening of diastolic dysfunction. However, the exact mechanism of how this correlation leads to the development of AF is still unclear. A possible explanation could be that diastolic dysfunction may cause left atrial enlargement with stretching of the pulmonary veins take off, aberrant foci activation and consequent onset of AF [20]. This hypothesis is corroborated by autopic anatomical studies on human pulmonary veins in patients with and without AF: in fact, an extension of the atrial myocardium at the origin of the pulmonary veins was observed in 89% of the patients, with a higher rate in those with AF [21]. This finding could justify the higher incidence of AF after intrapericardial lung resections; it could also suggest us to section the pulmonary veins as far as possible from their origin when performing pulmonary resections to prevent stretching on the myocardial extensions at this level. Manipulation of the hilar structures during dissection should be reduced for the same reason [18], especially when atrial enlargement is diagnosed at preoperative echocardiographic evaluation.

The incidence of AF in our series (15%) is in line with other reports [1, 2, 7–9], although it was slightly higher in patients undergoing major lung resections (29.8%). However, comparison with the international literature might be difficult since even data reported from the general thoracic surgery database of the Society of Thoracic Surgeons might underestimate the incidence of this complication, as clearly stated by Onaitis et al. [22].

Eighteen patients (86%) with postoperative AF presented an enlargement of the left atrial area above 20 mm² and 14 (67%) had first degree diastolic dysfunction. On the basis of this observation, the increase of left atrial size seems useful to identify high risk patients. However, at multivariate analysis only an increased left atrial area reached statistical significance. Univariate analysis suggested that other factors may play a role, as the extension of parenchymal resection and electrolyte imbalance; unexpectedly, pneumonectomy showed only a trend

**DISCUSSION**

AF after lung resections is usually considered a self-limited event; however, the increased length of hospitalization and consequent costs, and the potentially dramatic consequences, require a careful approach. The causes are still unclear but
towards significance. Probably, this variable could play a more important role in larger series.

Further multicentre studies with larger cohorts of patients will be required in the future to confirm our data. However, the increased incidence of AF in patients with left atrial enlargement, should encourage us to prophylactically administer them anti-arrhythmic drugs when major lung resections are planned.

Conflicts of interest: none declared.

References

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