Postoperative outcome of patients undergoing lung resection presenting with new-onset atrial fibrillation managed by amiodarone or diltiazem

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Abstract

Objective: Atrial fibrillation (AF) is a common complication after thoracic surgery. The objective of the study was to prospectively evaluate the postoperative outcome of patients undergoing lung resection and presenting with new onset of AF. The postoperative course of AF was also evaluated in relation to either amiodarone or diltiazem employed as anti-arrhythmic agents. Methods: A prospective observational study during a 3-year period was designed to evaluate all patients presenting AF as a complication of anatomic lung resections. The absence of a history of heart rhythm disease was an inclusion criterion. Amiodarone was employed as the anti-arrhythmic drug during the first 18 months, and diltiazem in the second half of the study. Anti-arrhythmic drugs were started intravenously; when rhythm was restored or after 48 h of treatment, they were administered orally. AF duration, recurrences and the postoperative outcome of patients were recorded. Results: Thirty patients fulfilled inclusion criteria. No deaths occurred; median hospital stay was 10 days (range 6—37). AF presented as a solitary complication in 17 patients; in 10 patients it was associated with a respiratory complication and in the last three patients in one case each with pulmonary embolism, acute renal failure and chylothorax respectively. AF occurred on median post-operative day 2 (range: 1—9). Sinus rhythm restoration within the first 24 h was observed in 11 (70%) out of the 15 patients receiving diltiazem and in 10 (67%) out of the 15 receiving amiodarone. After 48 h, in 80% of patients in both groups cardioversion was achieved. AF recurrence occurred in 11 patients (37%). In 10 out of these 11 patients iterative intravenous treatment was attempted and in all a permanent cardioversion was achieved. Fisher’s exact test indicated AF recurrence as being significantly correlated to the presence of a respiratory complication (\( p = 0.02 \)). Conclusion: Postoperative outcome of patients undergoing lung surgery with new onset of AF resulted as being significantly complicated by AF recurrence in the case of an associated respiratory complication. The pharmacological strategies tested during this pilot study led to no differences in the postoperative course of AF.

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Keywords: Atrial fibrillation; Thoracic surgery; Anti-arrhythmic drugs

1. Introduction

The close correlation between thoracic surgical procedures and the onset of postoperative supra-ventricular arrhythmias was documented as early as the nineteen forties [1,2]. Atrial fibrillation (AF) accounts for most of such postoperative supra-ventricular arrhythmias and its occurrence has been reported to add health care costs and prolong hospital stay [3—6].

Immediate electrical cardioversion may be indicated in patients with new onset of AF and hemodynamic compromise; however, in most cases postoperative AF is clinically well tolerated and, after the assessment of arrhythmia precipitant factors, a pharmacological management is delivered to control cardiac rate and to restore sinus rhythm [7—9].

In the management of AF after cardio-thoracic surgery, amiodarone has been widely employed because of its intrinsic double capability to lower the heart rate and to control rhythm [8,10]; however, its use in general thoracic surgery has been questioned because of its potential acute lung damage effect [11,12]. Calcium channel antagonists and beta blockers are also considered as first line drugs in the management of postoperative AF because of their activity in heart rate control [13—16]; in the case of lung resection, calcium channel antagonists, and in particular diltiazem, are considered the first choice in order to avoid the bronchial spastic effect of beta blockers.
We decided to carry out a prospective observational study during a 3-year period to evaluate the outcome of patients undergoing pharmacological management of AF during the postoperative course of lung resection.

During this time, amiodarone and diltiazem were used in two successive periods, and we aimed at comparing them in terms of time needed to obtain rhythm restoration and rate of recurrence of AF after rhythm restoration. We also evaluated the impact of AF and of its treatment on the rest of the postoperative course after lung resection.

2. Materials and methods

2.1. Study population

All patients enlisted for anatomical lung resection during a 3-year study period (June 2002—June 2005) were considered eligible for the study. The absence of a history of heart rhythm disease was an inclusion criterion; those patients in treatment with calcium channel antagonists or beta-blockers but not for a heart rhythm disease were included in the study without discontinuation of drugs. Exclusion was planned for patients presenting with an intra-operative heart ischemic or rhythm complication and for patients who did not undergo an anatomical lung resection.

During the first eighteen months of the study, patients were assigned to be treated with amiodarone, which has in the past been the anti-arrhythmic agent routinely employed; during the second half of the study, all consecutive patients were assigned to be treated with diltiazem. Informed consent was obtained from all the patients. The research was conducted according to recommendations outlined in the Helsinki declaration.

2.2. Study design

During the study period, the medical history of all eligible patients was obtained, and they all underwent physical examination, routine blood test, spirometry, electrocardiograph and echo-cardiograph. Standard antibiotic surgical prophylaxis consisted of amoxicillin and clavulanic acid intravenous infusion at the time of anesthesia induction, repeated once after 12 h.

Postoperative analgesia was assured by a continuous infusion of ropivacain through a thoracic peridural catheter for the first three days postoperatively. Postoperative pulmonary embolism prophylaxis was assured by daily subcutaneous injection of low-molecular-weight heparin adapted to the patient’s weight.

Postoperative heart rhythm monitoring was assured during the first three postoperative days by continuous cardiac telemetry and then by four-times daily clinical examination. Long rhythm 12-lead electro-cardiographic strip was obtained in all suspected cases of arrhythmia. In the case of a characteristic tracing of AF, heart rate, arterial tension, arterial blood gas, serum electrolytes and cardiac enzymes were obtained before starting pharmacological treatment.

Pharmacological management of AF consisted of administration of the anti-arrhythmic drug by continuous venous infusion for a minimum period of 24 h; in the case of persistent AF on the new ECG tracing the treatment was renewed for the successive 24 h. On the first day of AF amiodarone was administered at a dose of 900 mg/24 h (600 mg over the first 3 h and 300 mg for the next 21 h) and diltiazem by continuous intravenous infusion at a dose of 150 mg in 24 h. In the case of persistent AF the drugs were renewed at the same doses, whereas in the case of sinus rhythm restoration amiodarone was switched to an oral dose of 200 mg/day and diltiazem to a dose of 120 mg/day. When AF duration was longer than 48 h, the two drugs were also switched to oral administration, and low-molecular-weight heparin doses were adjusted to a therapeutic threshold or anticoagulation therapy was set up. All patients had an external cardiologic visit planned 1 month after surgery.

2.3. Outcome assessment

Specific outcome included AF course evaluated by measuring the time, expressed in days, needed to achieve rhythm restoration and by recording the rate and duration of AF recurrence. Duration of hospital stay, as well as postoperative morbidity or mortality defined as those occurring within 30 days of surgical intervention, were also documented. Other postoperative complications included respiratory complications defined by the presence of complicated clinical sputum retention and/or pneumonia. Complicated clinical sputum retention was defined as the incapacity to clear bronchial secretions and the presence of hypoxemia or atelectasis or both, for whom a fiber optic bronchoscopy was required. In the case of a complicated sputum retention persisting for more than 24 h after bronchoscopy, a policy for cryco-thyroid mini-tracheostomy positioning was adopted. A diagnosis of pneumonia was made in the case of new and/or progressive pulmonary infiltrates on chest radiography plus two or more of the following criteria: fever (>38°C), leukocytosis (12 x 10^9/l), purulent sputum retention or isolation of pathogen in respiratory secretions.

Diagnosis of pulmonary embolism was sustained by an angiographic CT scan and by an ultrasound examination of the leg and pelvic deep venous system. Prolonged air leaks were defined as the need for a pleural drainage over a period of 7 days. Adverse effects due to anti-arrhythmic treatment were considered as being clinical events necessitating drug interruption.

2.4. Statistical analysis

Data are reported as median values with range. Categorical variables were compared using the chi-square test or Fisher’s exact test as appropriate. Continuous variables were compared using a parametric test (Student’s t-test). Data processing and analysis were performed using the statistical software SPSS 13.0. A p value less than 0.05 was considered significant.

3. Results

During the 3-year study period, 296 patients underwent anatomical lung resection at our institution. Thirty-five (12%) patients had a diagnosis of postoperative AF, 30 of


whom fulfilled the inclusion criteria and were included in the study protocol; the demographic data, preoperative clinical characteristics and operative records of these patients are listed in Table 1. Statistical analysis by Student’s t-test failed to show any difference between the two groups, treated respectively with amiodarone or diltiazem, regarding age, BMI, preoperative FEV1 or left ventricular ejection fraction.

3.1. Postoperative course

No postoperative death was recorded; median hospitalization time resulted as being 10 days (range 6—37). Major postoperative complications other than AF were seen in 13 patients and are listed in Table 2. In 10 patients, a respiratory complication occurred and a fiber optic bronchoscopy for aspiration and germ culture was always obtained at median postoperative day 3 (range 1—10 days). In four of these cases, because of clinical persistent sputum after 24 h a percutaneous cryo-thyroid mini-tracheostomy was positioned. Because of acute respiratory failure, another patient was admitted to the Intensive Care Unit (ICU) for ventilatory support by oro-tracheal intubation. Among patients with a respiratory complication, a final diagnosis of pneumonia was obtained in seven patients, with germ isolation in four cases. In four cases fiber optic bronchoscopy was performed prior to AF onset, in two cases on the same day as AF onset and in four others after AF diagnosis.

One patient had a diagnosis of pulmonary embolism and was admitted to ICU with a concomitant diagnosis of deep venous leg thrombosis. No cardiac ischemic complication was noted in any of the patients, and cardiac enzymes and serologic troponin level measured during the 48 h after AF onset resulted as being below a significant threshold in all patients. In the group treated with amiodarone, two cases of thrombus-phlebitis at the peripheral site of vein infusion.

3.2. AF course

Data on the course of AF in the total population and in the subgroup of patients treated either with amiodarone or diltiazem are shown in Table 3. The total group peak incidence of AF was on the second postoperative day, with a cumulative 80% of AF episodes occurring during the first three postoperative days. Median ventricular rate at AF onset was 95 beats/min (range: 76—150) and median systemic arterial support by oro-tracheal intubation. Among patients with a respiratory complication, a final diagnosis of pneumonia was obtained in seven patients, with germ isolation in four cases. In four cases fiber optic bronchoscopy was performed prior to AF onset, in two cases on the same day as AF onset and in four others after AF diagnosis.

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Table 1
Demographic and clinical data of study population

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>Amiodarone</th>
<th>Diltiazem</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td>n = 30</td>
<td>n = 15</td>
<td>n = 15</td>
</tr>
<tr>
<td>Age (years)</td>
<td>71 (58—78)</td>
<td>71 (58—78)</td>
<td>72 (58—78)</td>
</tr>
<tr>
<td>Sex (male/female)</td>
<td>23/7</td>
<td>10/5</td>
<td>13/2</td>
</tr>
<tr>
<td>Body mass index</td>
<td>26.4 (18.7—32.5)</td>
<td>25.8 (18.7—32.5)</td>
<td>26.9 (21.8—31.9)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>n = 12</td>
<td>n = 7</td>
<td>n = 5</td>
</tr>
<tr>
<td>Anti-arrhythmic drugs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Calcium channel blockers</td>
<td>n = 5</td>
<td>n = 2</td>
<td>n = 3</td>
</tr>
<tr>
<td>Beta blockers</td>
<td>n = 3</td>
<td>n = 2</td>
<td>n = 1</td>
</tr>
<tr>
<td>Ventricular ejection fraction (%)</td>
<td>55% (45—68)</td>
<td>55% (47—68)</td>
<td>57% (45—68)</td>
</tr>
<tr>
<td>Preoperative heart rate (beats/min)</td>
<td>79 (62—100)</td>
<td>80 (62—100)</td>
<td>79 (62—88)</td>
</tr>
<tr>
<td>COPD: FEV1/SDC &lt;0.7; FEV1 &lt;80%</td>
<td>n = 15</td>
<td>n = 6</td>
<td>n = 9</td>
</tr>
<tr>
<td>PaO2 (mmHg)</td>
<td>81 (63—105)</td>
<td>81 (65—96)</td>
<td>81 (63—105)</td>
</tr>
<tr>
<td>PaCO2 (mmHg)</td>
<td>40 (35—50)</td>
<td>40 (35—48)</td>
<td>41 (36—50)</td>
</tr>
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</table>

Table 2
Postoperative complications other than AF

<table>
<thead>
<tr>
<th>Major complications</th>
<th>Total</th>
<th>Amiodarone</th>
<th>Diltiazem</th>
</tr>
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<tbody>
<tr>
<td>Respiratory complication</td>
<td>10</td>
<td>4</td>
<td>6</td>
</tr>
<tr>
<td>Acute renal failure</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Pulmonary embolism</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Chylothorax</td>
<td>1</td>
<td>1</td>
<td>0</td>
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</table>

<table>
<thead>
<tr>
<th>Minor complications</th>
<th></th>
<th></th>
<th></th>
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</thead>
<tbody>
<tr>
<td>Prolonged air leaks</td>
<td>4</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Peripheral superficial venous thrombosis</td>
<td>2</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Blood transfusion</td>
<td>1</td>
<td>0</td>
<td>1</td>
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</table>

Table 3
Atrial fibrillation course

<table>
<thead>
<tr>
<th>Postoperative day of AF onset (median; range)</th>
<th>Total</th>
<th>Amiodarone</th>
<th>Diltiazem</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rhythm restoration within 24 h</td>
<td>n = 22</td>
<td>n = 10</td>
<td>n = 11</td>
</tr>
<tr>
<td>Rhythm restoration within 48 h</td>
<td>n = 24</td>
<td>n = 12</td>
<td>n = 12</td>
</tr>
<tr>
<td>AF recurrences</td>
<td>n = 11</td>
<td>n = 6</td>
<td>n = 5</td>
</tr>
</tbody>
</table>
pressure 137 mmHg (90–160). Median duration time of AF resulted as being one day; the number of patients with sinus rhythm restoration was 21 (70%) within 24 h and 24 (80%) within 48 h.

AF recurrence was seen in 11 patients (37%); the onset of AF recurrence was recorded on median day 2 (range 1–6) after cardioversion. In 10 out of these 11 patients, iterative intravenous treatment was attempted and permanent cardioversion achieved within 24 h.

Among seven of these patients a postoperative respiratory complication was recorded and, by Fisher’s exact test, AF recurrence resulted as being significantly correlated to the presence of a respiratory complication (p = 0.02).

4. Discussion

The incidence and course of AF in patients undergoing cardio-thoracic surgery has been widely explored in the past [4–8,17]; after major lung resection, however, respiratory complications are also frequently observed, and in this setting pneumonia was found in as high as 25% of cases in a recent report by Schussler and colleagues [18].

In our prospective study, evaluating patients presenting with AF during the post-operative course of anatomical lung resection, the postoperative temporal distribution of AF onset resulted as having, in accordance with previous reports, a peak incidence on the second postoperative day [19]. AF after thoracic surgery occurs in more than 50% of patients as a lone complication, or it can be associated with respiratory complications in as high as 25–30% of cases [20,21]. In our study, for data analysis, respiratory complications were identified in a group including those patients presenting with either complicated sputum retention or pneumonia and, in this setting, the observed incidence rate of such complications was 30%.

Pulmonary gas exchange disturbance and systemic inflammation are known to be among the possible post-operative precipitating factors of supra-ventricular arrhythmias. Rosselli and colleagues even found a temporal relationship between the onset of AF and the occurrence of a respiratory complication [20]. Although our study was not designed to investigate the risk factors implicated in AF onset, fiber optic bronchoscopy was performed to treat the ongoing respiratory complications on postoperative day three and, in this subgroup of patients, AF onset was also recorded on median postoperative day three; moreover, to strengthen the possible relationship between the two complications, we found that in patients in whom a postoperative respiratory complication occurred, a significantly higher recurrence rate of AF was encountered. Ultimately, these data on the difficulties to control sinus rhythm in the presence of a concomitant respiratory disease are in accordance with the well established rules on AF course in critically ill patients where the maintenance of sinus rhythm is almost completely ineffective [22]. At present, in the current literature there is no consensus supporting a strategy for the conversion of AF and the maintenance of sinus rhythm versus rate control and anticoagulation therapy in the management of postoperative AF [7]; however, as we included in the study only patients with no previous history of arrhythmia, we have considered the return to sinus rhythm before 48 h after AF onset as a crucial objective of the pharmacological management of such patients, in order to avoid anticoagulation therapy during the early postoperative period. In this light, both drugs tested in the study resulted as being effective both in controlling heart rate and in inducing the return to sinus rhythm, which was observed in 80% of both groups within 48 h.

Since in all patients with AF recurrence the first episode was successfully treated within 48 h of drug infusion, a new attempt to convert sinus rhythm was performed, except in one patient who, meanwhile, had been admitted to the Intensive Care Unit for acute respiratory insufficiency. In all of these cases, sinus rhythm was restored within 24 h, and no other episodes of AF were recorded during the first postoperative month. In this way we avoided anticoagulation therapy in the presence of AF recurrence.

In conclusion, although this is a single institutional cohort study with a small number of patients enrolled, we found that the postoperative outcome of patients with lung resection with a new onset of AF in the presence of a respiratory complication resulted as being complicated by a significantly higher risk of AF recurrence. The pharmacological strategies tested during this pilot study led to no differences in the postoperative course of AF.

References