

## Postoperative Atrial Fibrillation after Cardiac Surgery

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### Summary

Atrial fibrillation (AF) is an arrhythmia frequently seen in the postoperative period of cardiac surgery. In this context, it is associated with the presence of comorbidities, longer length of hospital stay, and higher costs related to surgery.

The mechanisms involved in the genesis of AF in the postoperative period of cardiac surgery (AFPO) are different from those causing paroxysmal AF. Knowledge of these mechanisms permits the use of efficient measures to reduce the incidence of this arrhythmia.

According to recommendations of the literature, treatment is efficient and safe, because the rates of reversion to sinus rhythm are high and complications are reduced, and it is not associated with a high frequency of side effects.

### Introduction

Postoperative atrial fibrillation (AF) is a frequent arrhythmia after cardiac surgery. Within this context, it is associated with the presence of comorbidities, longer hospital stays and higher surgery-related costs<sup>1-4</sup>.

### Epidemiology

This arrhythmia occurs more frequently within the first five days postoperatively, with a peak between 24 and 72 hours, and is infrequent after the first week<sup>5,6</sup>. In most cases it spontaneously converts into sinus rhythm and does not require pharmacological intervention<sup>6</sup>. Patients submitted to myocardial revascularization surgery (MRS) have a lower incidence of postoperative AF (from 30% to 40%), as compared with those submitted to valve surgery (60%)<sup>7</sup>. The use of extracorporeal circulation (ECC) is also associated with a higher incidence of AF, although some authors demonstrate that there is no difference in incidence relative to using or not using ECC<sup>8-10</sup>.

### Mechanisms

The mechanisms involved in the genesis of postoperative AF (POAF) are multifactorial, not very well defined and different from those found in paroxysmal AF. Atrial

### Key words

Atrial fibrillation; thoracic surgery; postoperative care; arrhythmia.

myocardium plays an important role in the physiopathogeny of POAF, since it is manipulable because of atriotomies used to enable ECC cannulations and to repair valvopathies. It is known that even after cardioplegia, the atriums still maintain residual electrical activity, which results in varied degrees of ischemia despite the adoption of myocardial protection measures<sup>11-13</sup>. Such incisions associated with atrial ischemia arising from the surgical procedure and from the underlying cardiopathy give rise to abnormalities in atrial conduction, in refractoriness and in the triggering of factors such as ectopic atrial beats<sup>14-16</sup>.

Inflammation also plays an important role in the physiopathogeny of POAF. It has been demonstrated that surgical manipulation of the myocardium, ECC and even isolated pericardiotomy may trigger different degrees of inflammatory response which manifests clinically in the form of leukocytosis, fever or arrhythmias<sup>17</sup>. This is biochemically marked by the elevation of inflammatory mediators such as interleukin-6, tumor necrosis factor- $\alpha$ , activation of the complement and of C-reactive protein<sup>18,19</sup>. The concentrations of these mediators begin to rise approximately six hours after the surgery, and peak in the second day postoperatively<sup>20</sup>. The inflammatory process eventually leads to abnormal anisotropic conduction which results in a decrease of the conduction speed and in heterogeneous impulse propagation, which facilitates the reentry and genesis of AF<sup>6</sup>.

More recently, there have been discussions about the predisposition to develop AF which is thought to be related to the passive electrical property of atrial myocardium, i.e. the cell-to-cell conduction property<sup>21,22</sup>. In human hearts, myocyte cell-to-cell conduction is formed by three types of connexins (connexins 40, 43 and 45). These connexins play a role in the propagation of the electrical stimulus during normal cardiac rhythm. However, in conditions where their biophysical properties are altered, such as after cardiac surgery, there are modifications in their expressions, thus resulting in differences in conduction speed between adjacent regions, thus predisposing the patient to the onset of AF<sup>23</sup>.

Alterations in the autonomous nervous system are also responsible for the onset of postoperative AF, especially after cardiac surgery, and its effects on the atriums are complex<sup>24</sup>. Some papers have described the changes in the relation between sympathetic and parasympathetic responses that can be observed immediately after cardiac surgery with ECC, which may indicate some susceptibility to the onset of arrhythmias<sup>25</sup>.

### Clinical implications

The presence of AF after cardiac surgery is related with the following factors: longer hospital stay, higher rate of

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readmission into intensive care units, long mechanical ventilation times, need for inotropic drugs or mechanical circulation support, and even reintubation<sup>26-28</sup>.

Its presence is significantly associated with postoperative complications such as hypoxia, hypovolemia, sepsis and electrolytic disorders<sup>29,30</sup>. It is also related to the following factors: higher incidence of gastrointestinal complications, kidney failure, cerebrovascular accident (CVA), heart failure (HF), need for antiarrhythmic drugs after hospital discharge and increase in mortality over a period that ranges from thirty days to six months after the surgery<sup>16,26,28,31</sup>.

## Predictors

The onset of AF after cardiac surgery is related to the presence of pre, intra and postoperative variables.

## Preoperative

Advanced age has been considered an independent predictor of postoperative AF after cardiac surgery<sup>32</sup>. Some papers have described that this arrhythmia affects more than 18% of the individuals above 60 years of age and approximately 50% of those above 80 after an MRS<sup>32,33</sup>. This association is due to the fact that these individuals present more comorbidities relating to age and have structural alterations in the atrial myocardium, such as distension and fibrosis that are secondary to alterations which are typical of aging<sup>34</sup>.

Arterial hypertension (AH) is also considered an important predictor, since it's associated with cardiac structural alterations such as fibrosis and dilation, and other AF-related comorbidities (for example, advanced age)<sup>34</sup>.

There is a stronger relation between male gender and the presence of POAF. This can be explained both by gender-related differences in ionic channels and by the effect of hormones on the autonomous tonus.

Another important predictor is a previous history of AF and heart failure.

## Intraoperative

Factors relating to the surgical procedure such as aortic cross-clamp time and use of ECC are related to the onset of POAF. The mechanisms suggested consist of atrial ischemia and the triggering of an inflammatory process<sup>33</sup>.

## Postoperative

Conditions associated with POAF are related to the presence of complications such as infections, prolonged mechanical ventilation, hemodynamic instability and use of vasoactive amines.

Other variables involved are advanced age, AF paroxysms prior to surgery, previous myocardial infarction, left ventricular dysfunction, AH, diabetes mellitus (DM), postoperative ischemia, discontinuation of beta-adrenergic drugs prior to surgery, duration of aortic cross-clamp, use of vasoactive amines and postoperative low cardiac output<sup>35,36</sup>.

## Prevention of postoperative AF

Although the risk factors for postoperative AF are known, no risk factor can be identified in a substantial number of patients. This justifies the importance of establishing prophylactic measures to reduce the incidence of this arrhythmia and consequently its clinical implications for patients undergoing cardiac surgery. The recommendations for the prevention and management of postoperative AF after cardiac surgery will be addressed below<sup>37,38</sup>.

## Use of betablocking agents

The administration of betablocking agents is the most effective measure in AF prophylaxis, and significantly reduces its incidence after cardiac surgery<sup>39-43</sup>. The use of betablockers is also related to a reduction in morbidity and mortality. In their series, Ferguson et al<sup>44</sup> observed a reduction of mortality from 3.4% to 2.8% in the patients who were given betablockers perioperatively.

The betablockers should be administered to all patients undergoing cardiac surgery as a first line therapy, unless there are contraindications. These agents should be administered in the morning on the day of the surgery and resumed in the first day postoperatively. If the patient was not using a betablocker, the drug should be administered preoperatively or after the surgery, respecting the contraindications<sup>37,38</sup>.

## Sotalol

Some studies have demonstrated the superiority of sotalol as compared with betablocker agents in the reduction of postoperative AF<sup>45-49</sup>. Cristal et al.<sup>41</sup> showed a significant difference of 12% in AF incidence with the administration of sotalol, as compared with 22% with betablockers. The administration of sotalol therefore can be an alternative to betablockers in POAF prevention<sup>37,38</sup>.

## Amiodarone

The administration of amiodarone is also related to the reduction AF incidence after cardiac surgery<sup>50-52</sup>. Thus, a reduction by 22.5% to 37% was reported for amiodarone, as compared with placebo in the prevention of AF<sup>41</sup>. Despite showing a reduction in POAF incidence, Butler et al.<sup>53</sup> reported the presence of bradiarrhythmias and pauses as complications of this therapy and limitations for its routine administration.

The prophylactic administration of amiodarone is therefore recommended for cases where the administration of betablockers is not possible. In those patients with a high risk of developing AF, the association of betablockers and amiodarone can be acceptable with a low incidence of complication. In these patients, attention should be given to the presence of bradiarrhythmias, and a temporary pacemaker should remain available in case it is needed<sup>37,38</sup>.

## Atrial stimulation

Artificial atrial stimulation reduces the incidence of POAF because of its suppressive effect on triggering events such as atrial

extrasystoles or the decrease of atrial refractoriness<sup>54,55</sup>.

Greenberg et al.<sup>54</sup> demonstrated a reduction in POAF incidence and hospital stay in patients who underwent left atrial stimulation or biatrial stimulation.

In a recent metanalysis, Burgess et al.<sup>56</sup> demonstrated that patients submitted to biatrial stimulation had 17.7% of POAF, whereas the control group had 35.3% of POAF incidence. Guidelines for the prevention of postoperative AF suggest that biatrial stimulation is a Grade of recommendation A – Level of evidence B<sup>38</sup>.

It is advisable that the stimulation be conducted with a rate between 80 and 90 bpm, for a period of 3 to 5 days, and can be increased if the basal heart rate of patients rises to values above 80 bpm<sup>37,38</sup>.

### Magnesium

Reduced magnesium serum levels are related to the presence of postoperative AF because such levels predispose to alterations in the action potential and repolarization of the myocyte cell membrane. This effect is due to the fact that magnesium is a co-factor of the sodium potassium ATPase enzyme that regulates the transmembrane gradient of sodium and potassium ions. In their metanalysis, Miller et al.<sup>57</sup> revealed a reduction in POAF incidence from 28% to 18%.

The prophylactic administration of magnesium is an effective strategy to minimize POAF incidence and should be considered for all patients undergoing cardiac surgery.

### Management of Postoperative AF

In the presence of hemodynamic instability, electrical cardioversion (ECV) is mandatory. In those cases where the ventricular response is high and appropriate control has not been achieved with antiarrhythmic medication, ECV can be performed following the same recommendations that are valid for nonsurgical cases<sup>58</sup>.

The role of potassium in POAF treatment has not yet been fully understood. The practice recommends that potassium serum levels be maintained between 4.5 and 5.5 mmol/l postoperatively<sup>38</sup>.

Unless contraindicated, betablockers (BB) are the

drugs of choice to control heart rate, especially when the ventricular function is preserved. Calcium channel blockers (CCB) are efficacious alternatives for this purpose, although they are related to hypotension. Digoxin is less effective than BB or CCB, particularly when there is an exacerbated adrenergic condition.

Many agents can be used to convert postoperative AF into sinus rhythm, such as amiodarone, procainamide, ibutilide and sotalol. Intravenous amiodarone has been preferred because of its good efficacy and because it is related to relatively few complications. An attack dose of 5 mg/kg in 30 minutes and a maintenance dose of 15 to 40 mg/h<sup>38,58</sup> is recommended.

The risk of CVA in patients undergoing cardiac surgery is well known, mostly in cases of MRS. Within this context, anticoagulation with heparin or oral anticoagulant is recommended when AF persists for more than 48 hours. The choice between heparin and oral anticoagulant should be personalized according to each patient and type of surgery<sup>58</sup>. If there are no contraindications, warfarin is preferable for high risk patients (age  $\geq$  65 years, heart failure, diabetes mellitus, AH, transitory ischemic accident or CVA); the values of the international normalized ratio (INR) should be maintained between 2 and 3. In these patients, even if there is reversal to sinus rhythm, warfarin should be continued for four weeks. A 325 mg dose of acetylsalicylic acid is an alternative for low risk patients.

A practical algorithm for prophylaxis and management of POAF in cardiac surgery is shown in figure 1.

### Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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There were no external funding sources for this study.

### Study Association

This study is not associated with any post-graduation program.

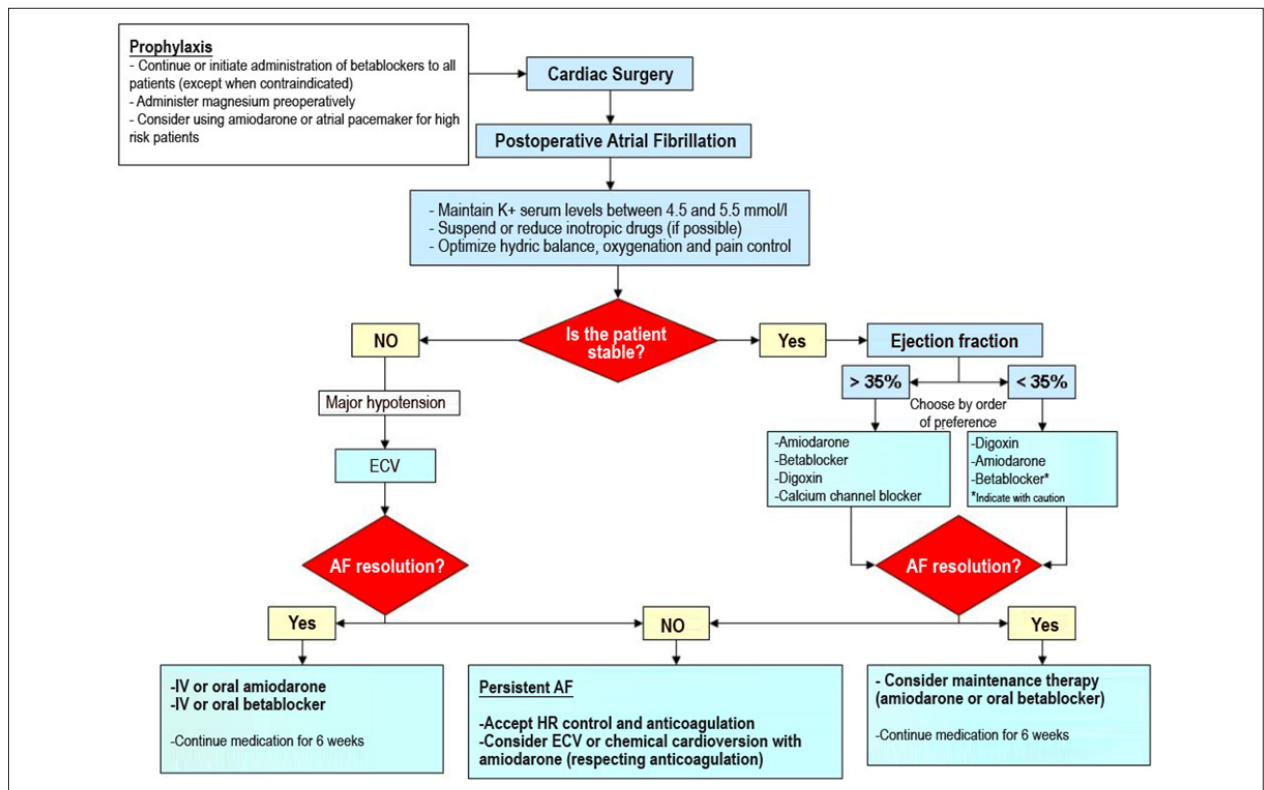


Figure 1 - Fluxogram for the prevention and management of af after cardiac surgery. (Adapted from dunning e cols.<sup>38</sup>).

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## Review Article

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