Atrial fibrillation and cardiac surgery: a never ending and always controversial history

Fibrilação atrial e cirurgia cardíaca: uma história sem fim e sempre controversa

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INTRODUCTION

According to Maisel et al. [1], the peak incidence of atrial fibrillation (AF) occurs on the second and third postoperative days. Loubani et al. [2] reported that 50% of the patients who developed AF in the postoperative period of cardiac surgery remained with the arrhythmia on the day of hospital discharge. The early postoperative course for most patients undergoing cardiac surgery is characterized by a typical pattern of pathophysiological derangements. During the first 24 hours, patients commonly are mildly hypothermic and fully anesthetized upon arrival in the ICU, requiring mechanical ventilation. Inotropic support may be required to terminate cardiopulmonary bypass and this is usually maintained for a few hours. Over the past few years, changes have occurred in the intraoperative and early postoperative management that influence how rapidly patients can recover from open-heart surgery. Atrial arrhythmias are common in the postoperative period of cardiothoracic surgery. They may occur in 11% to 40% of patients after myocardial revascularization surgery and in approximately 50% of those undergoing valvular surgery. The ventricular ectopy is noted less commonly and usually reflects some degree of myocardial injury.

Atrial fibrillation is the most frequent arrhythmia after cardiac surgery. It is commonly an auto-limiting condition, which rarely causes perioperative death, but can extend the length of hospital stay, increasing costs. Sometimes, it may be considered a cause of perioperative acute myocardial infarction and thromboembolic phenomena. The following risk factors are associated with AF in the postoperative period of cardiac surgery: left heart failure, systemic inflammatory response syndrome, septicemia or multiple organ failure, suspension of beta-blockers, chronic obstructive pulmonary disease, and the need for mechanical ventilatory support. Advanced age, however, is the risk factor most frequently associated with postoperative atrial fibrillation. In patients at higher risk, preventive measures should be considered [3,4].

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The aim of this text is to review the medical literature on new-onset arrhythmias after cardiac bypass surgery in adults, focusing on the most recent advances on this topic. Main attention is focused on possible predictors and prevention of postoperative AF. This text will try to present the multiple aspects of AF in the milieu of cardiac surgeries. After the final lecture we decided to include the subtitle "a never end and controversial history" based on its multiple aspects concerning mainly to etiology, physiopathology and prophylaxis.

PHYSIOPATHOLOGY

The mechanism of postoperative arrhythmias includes reentry, enhanced automacity and triggered activity. Transmural reentry is the most likely mechanism underlying ischemia reperfusion arrhythmias. Evidence suggests that both oxygen-derived free radicals and transient calcium overload play important pathologic roles in arrhythmogenesis after cardiac surgery. Though postoperative arrhythmias have been thought to be multifactorial, incomplete myocardial protection is a major cause. The vulnerability to reperfusion-induced arrhythmias is critically dependent on the duration of the preceding ischemia. Because myocardial ischemia may be an important factor in the genesis of arrhythmias, post-cardioplegic arrhythmias have been considered one of the variables comparing strategies for myocardial protection. It may be related to poor atrial preservation during surgery or to withdrawal of beta-blockers. Most centers initiate betablockers by the first postoperative morning. The concomitant administration of digoxin may lower the incidence of AF even further. Magnesium sulfate has been shown to reduce the incidence of AF as well as aid the conversion to sinus rhythm [5].

Knowledge about the risk factors for postoperative AF seems to have a fundamental importance in the elaboration of prophylactic and therapeutic measures for this arrhythmia. Age is the most cited risk factor in the literature, probably due to the higher content of atrial collagen in elderly patients. Other factors reported in the literature include chronic obstructive pulmonary disease, mitral valvular disease, use of inotropic agents, previous history of AF, and pericarditis. In the present study, age > 70 years proved to be a risk factor for AF [4].

The nonuse of beta-blockers during hospital stay was also strongly associated with postoperative AF in studies. In the literature, the suspension of beta-blockers is a very important factor for triggering postoperative arrhythmia. The comparison of the suspension of beta-blockers with their maintenance in the postoperative period caused a decrease in the incidence of AF, although a nn-significant

difference occurred, probably due to the small number of patients in the sample. In the multivariate analysis, the use of beta-blockers in the preoperative period proved to be a protective factor of postoperative AF. In regards to the etiology of the surgical disease, aortic valvular disease proved to be a factor associated with a great incidence of postoperative AF, reaching a value similar to that of mitral etiology. Factors associated with aortic valvular replacement that may explain this result are as follows: advanced age, left atrial enlargement, administration of inotropic agents, prolonged ventilatory support, postoperative acidosis, electrolyte imbalance and disorders in the atrioventricular and intraventricular conduction [6].

Another important factor is preoperative hypokalemia. Wahr et al.[7] reported that potassium levels <3.5 mmol/L were associated with a greater incidence of arrhythmias. The patients who developed postoperative AF had a greater fluid balance than those who did not develop it. A 1% additional risk of AF was observed for each milliliter accumulated above the mean fluid balance. In this case, arrhythmia may be triggered by atrial distension.

The durations of ischemia and extracorporeal circulation showed no significant differences in the patients who developed AF and those who maintained sinus rhythm. These data confirm those of previous studies, which compared the incidence of AF in patients who underwent conventional cardiac surgery and surgery without extracorporeal circulation, and could not identify the role played by extracorporeal circulation as a predisposing factor [8,9].

Left atrial enlargement has also been reported as a factor associated with postoperative AF. In a study using transesophageal echocardiography, left atrial enlargement did not predict that arrhythmia. In a case series, left atrial enlargement assessed through transthoracic echocardiography in the preoperative period showed no correlation with postoperative AF. The analysis of the P wave by use of 12-lead conventional electrocardiography showed no significant association between postoperative AF and left atrial enlargement [10].

Another not so mentioned possible mechanism was hypothesized by Hod et al.[11] who associated the early AF during evolving myocardial as a consequence of impaired left atrial perfusion. This impaired perfusion would be caused by proximal left circumflex artery occlusion. Concerning this hypothesis we studied 186 patients under coronary artery bypass grafting and reported an AF incidence of 6.04% (11 cases). In these eleven patients the left circumflex artery was involved in 81.20%, a percentage greater than ventricular fibrillation plus ventricular over-distention (63.4%) and the use of double stage cannulae for venous drainage (45.5%) (Figure 1) [12].

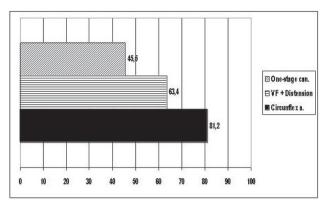


Fig. 1 - Atrial fibrillation risk factors in coronary artery bypass surgery patients (Adapted from Sgarbieri ¹²)

DIAGNOSIS

A typical ECG in AF shows a rapid irregular tachycardia in which recognizable P waves are absent. QRS complexes are generally normal, and the ventricular rate in patients with untreated AF generally ranges between 150 and 220 beats/min. However, in elderly patients, ventricular rates in untreated AF are typically slower. The ventricular rate may be accelerated in the presence of thyrotoxicosis, fever, catecholamines or catecholamine-like drugs, or conditions that enhance sympathetic tone. Although a cardinal feature of AF is irregularity of the RR interval, at the most rapid ventricular rate, this irregularity may be a somewhat simple noninvasive method for stratifying patients after myocardial infarction that may be at risk for ventricular tachycardia or sudden cardiac death [13].

Few reports have examined signal averaging of the P-wave. Several studies evaluated the utility of P-wave signal averaging in patients with history of paroxysmal AF and revealed that patients with paroxysmal AF had prolonged P-wave durations, atrial late potentials, and increased high-frequency components of the signal-averaged P-wave when compared with controls. One prior study addressed the issue of the prediction of AF after coronary artery bypass surgery with this method in patients before they underwent coronary artery bypass surgery to identify criteria that would be useful in predicting which patients are at increased risk for postoperative AF [10].

This kind of observations to evaluate atrial arrhythmias after cardiac surgeries is optimized by atriogram analysis. Usually in the trans-operative period, temporary epicardial electrodes are placed on the right atrium and in the right ventricle. These electrodes are useful for diagnosis and for therapy. The atrial electrode can be used to obtain the atrial

electric activity; both unipolar and bipolar. EKG and atriogram, permit a distinction between atrial and junction arrhythmias and of these with life risk ventricular arrhythmias. With the aid of two atrial electrodes it is possible to obtain bipolar atriograms connecting the electrodes in each derivation of the arms and the third EKG cable in the flank; recording in DI. The monitor usually comes with three electrodes to record the cardiac rhythm, and it can be used during the postoperative control. When the plan is to obtain the EKG by a normal twelve derivations apparatus, the two atrial leads are connected to the arms electrodes and the remaining positioned as normal. A bipolar atriogram should be used for reading DII or DIII. As an alternative, it is possible to connect one of the atrial leads to the precordial electrodes using the V1 derivation [14].

In the Division of Thoracic and Cardiovascular Surgery a master degree dissertation [15] used surface EKG epicardial leads to study the electric atrial activity in patients submitted to the surgical treatment of mitral valve disease by comparing two surgical approaches to the mitral valve: the classical left atrial subseptal incision and the Guiraudon incision. The standard positioning of the atrial electrodes is shown in Figure 2 and an atriogram example is presented in Figure 3.

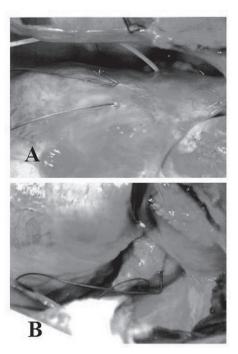


Fig. 2 - Atrial epimyocardial wires implanted for atriograms recorder A – Right atrium lead; B – Left appendage leads

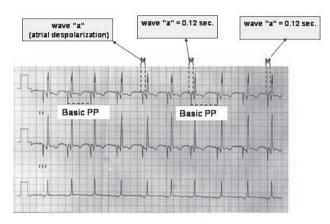


Fig. 3 - Left atrial electrogram recorded using epimyocardial leads, demonstrating the atrial repolarization "a" wave measure. Also, the spontaneous cycle time calculation (heart rate) through the basic PP interval is showed

PROPHYLAXIS

Kim et al. [16], comparing the length of hospital stay and costs in patients with and without AF after cardiac surgery, reported that the impact of this arrhythmia on the length of hospital stay was not very significant. However, an observational study of 3855 patients undergoing heart surgery reported significant differences in the mean length of hospital stay for patients with and without AF. In this study, the length of hospital stay in patients with AF was almost two times greater than that in patients who sustained sinus rhythm. Multivariate analysis showed a direct relationship between AF and the increase in the length of hospital stay. These data justify the great number of investigations about cardiac surgery AF prophylaxis.

Magnesium

Shiga et al. [17] performed a comprehensive meta-analysis in 2004 looking at the benefits of prophylactic magnesium in the prevention of AF post cardiac surgery. Seventeen randomized controlled trials were identified, comprising of 2069 patients. In the pooled magnesium groups the incidence of SVT was 23%, but in the control group it was 31% (P<0.002). In addition the incidence of ventricular tachycardia was also significantly lower, and the mean serum magnesium was significantly higher than those in the control groups. Magnesium reduced the incidence of AF by 29% across the 17 trials performed. In the cardiac surgical literature, prophylactic magnesium has been well established

in the prevention of AF with a reduction of up to 30% in the incidence of AF across 17 trials. However, there have been no studies looking at magnesium therapy in cardiac surgical patients going into AF. In the general medical literature we found 7 papers that looked at either addition of magnesium or magnesium alone in the therapy of AF. Four of these 7 papers demonstrated a significant benefit.

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Digoxin and beta-blockers

Recent studies suggest that prophylactic administration of agents typically used to slow atrioventricular nodal conduction may significantly reduce the incidence of postoperative AF. The most used therapies have been digoxin and beta-blockers. A metanalysis of 12 studies found no statistically significant benefit to the prophylactic use of digoxin; however, a significant benefit was associated with either beta-blockade (AF incidence reduced from 20.2% to 9.8%; p < 0.001) or combined therapy with beta-blockers and digoxin (from 29.4% to 2.2%; p < 0.001). Notably, many patients in these studies were taking beta-blocker therapy preoperatively; thus, the prophylactic benefit of postoperative beta-blockade in patients not taking betablockers preoperatively is unclear. Low-dose beta-blocker prophylaxis is generally well tolerated in the early postoperative period (after patients have been fully weaned from inotropic support), although initial dosing should be rather conservative for patients with poor systolic function, conduction abnormalities, or sinus bradycardia [20,21].

Sotalol and amiodarone

Recent interest has focused on two antiarrhythmic drugs, sotalol and amiodarone. Both drugs are class III antiarrhythmic agents with some betadrenergic blocking activity. When compared to placebo, both drugs were shown to be effective in reducing postoperative AF when administered prophylactically. The dosing regimens in many of these studies were complex, with therapy initiated either the day preceding surgery or hours to several days after surgery. Beta-blocker use in these trials was not well defined. Several of the studies required discontinuation of beta-blockers, while others required reducing the dose by 50%. Two recent metanalyses found no significant differences in

efficacy and safety between amiodarone and sotalol. However, the drugs have not been directly compared [20,21].

Although there is increasing evidence to support sotalol prophylaxis as a relatively safe and effective means to prevent AF after cardiac surgery, patients with poor left ventricular function (ejection fraction < 40%) are poorly represented in the available studies, furthermore, whereas low-dose postoperative oral sotalol appears to be more effective than traditional low-dose beta-blockade regimens (e.g., propranolol), this has not been clarified [20,21].

Low-dose amiodarone prophylaxis was recently examined in a prospective, randomized, placebo controlled trial of 124 cardiac surgical patients and included subjects with controlled congestive heart failure (New York Heart Association class 2.4 ± 0.9). 6 Patients received 600 mg/day of amiodarone for 7 days preoperatively and then 200 mg/day from the time of surgery until discharge from the hospital. The incidence of postoperative AF was reduced from 53% in the placebo arm to 25% among amiodarone-treated patients (p <0.003). A class III antiarrhythmic agent with beta-blocking activity, amiodarone appears to be well tolerated in patients with congestive heart failure, and no adverse hemodynamic side effects were seen with low-dose therapy in this cardiac surgical population [22].

It is clear, reviewing the literature, that two of most extensively studied drugs concerning AF prophylaxis are sotalol and amiodarone. While the overall incidence of AF was not significantly different, important differences between the 2 drugs were observed. In patients undergoing CABG only, the incidence of AF was similar (19% for amiodarone and 15% for sotalol). However, in patients undergoing more complex valvular surgery, the secondary analysis indicated that amiodarone was more effective in preventing AF than sotalol. Patients undergoing valvular surgery are at a higher risk of developing postoperative AF. Although a larger study of AF prophylaxis is needed in high-risk patients, it is suggested that the prophylactic use of oral sotalol should be reserved for low-risk patients (i.e., normal renal and cardiac function undergoing CABG only), with amiodarone used for the higher risk patients. If sotalol is more efficient in reducing the AF incidence than a Class III beta-blocker is completely unknown. Also, significant differences favorable to amiodarone concerning AF duration and number of episodes when compared with sotalol was observed [20,21].

As already mentioned, many of the previously reported studies with amiodarone and sotalol used complex dosing regimens with study drug initiated several days before surgery. Unfortunately, this practice is logistically impractical in many settings in which open-heart surgery is performed under acute or emergent conditions. The practice of administering drugs during the perioperative period is the most practical. Our practice includes the routine use of 50 mg of atenolol as a pre-anesthetic medication. The preference of using beta-blockers strongly appear in the medical literature [23]

Steroids

Because of the multifactorial etiology of postoperative atrial fibrillation and the well-known inflammatory response to CPB, steroids with the ability to inhibit inflammatory mediators, including interleukin (IL)-6, IL-8, tumor necrosis factor (TNF)-á, leukotriene B4, and tissue plasminogen activator, might have beneficial effects in decreasing postoperative atrial fibrillation after CABG. A randomized, double-blind, placebo-controlled trial was conducted by Prasongsukarn et al. [24] to determine the effect of steroids on the occurrence of atrial fibrillation after elective coronary artery bypass grafting. Eightyeight consecutive patients were prospectively entered in this study. No patient had documented or suspected arrhythmias before surgery. Forty-three patients received 1 g of methylprednisolone before surgery and 4 mg of dexamethasone every 6 hours for 1 day after surgery, and 43 patients received only a placebo. The primary end point was the overall occurrence of postoperative atrial fibrillation. Postoperative atrial fibrillation occurred in nine (21%) of the 43 patients in the steroid group, as compared with 22 (51%) of the 43 patients in the placebo group (P<003). Minor postoperative complications occurred in 15 steroid patients (35%) and in six patients (14%) receiving placebo (P < 0.01). Major complications occurred in four patients who received steroids (9%) and in two patients (5%) who received placebo (P < 0.68; for all complications P < 0.05). Prophylactic short-term steroid administration in patients undergoing coronary artery bypass grafting significantly reduced postoperative atrial fibrillation. In this study, there was no significant difference between the steroid group and the placebo group with regard to the length of hospital stay; however, the steroid group had more complications, which may contribute to prolonged hospitalization [24].

The use of steroids is, at least, controversial. The results of Prasongsukarn et al. [24] supported the recent report by Yared et al. [25] of a lower incidence of new-onset atrial fibrillation with the administration of dexamethasone 0.6 mg/kg after the induction of anesthesia. However, the study by Halvorsen et al. [26] showed that dexamethasone (8 mg in divided doses) was beneficial in reducing emetic symptoms and improving appetite after cardiac surgery but had no effect on the occurrence of postoperative atrial fibrillation [26].

Calcium-Channel Blockers

The non-dihydropyridine calcium-channel blockers verapamil and diltiazem, have several beneficial effects on the cardiovascular system. Because their cardiac effects are similar to those of beta-blockers, both drugs have been studied as alternatives to beta-blockers in the prevention of postoperative AF. Oral verapamil after CABG was ineffective in decreasing the incidence of postoperative AF or atrial flutter compared with controls. In contrast, perioperative infusions of diltiazem were associated with fewer cardiac complications after CABG. Two studies comparing 24-hour continuous infusions of diltiazem with nitroglycerin after operations demonstrated a lower incidence of postoperative AF in diltiazem-treated patients. These data suggest that diltiazem may have a role in the prevention of postoperative AF, whereas oral verapamil is ineffective. However, given the paucity of data compared with beta-blockers and given the mortality benefits of betablockers in surgical patients, prophylaxis of postoperative AF with diltiazem is best reserved for patients with contraindications to beta-blockers (e.g., severe bronchospastic airway disease). [8]

Pacing strategies

Crystal et al. [21] performed a meta-analysis in 2002 that looked at pharmacological and pacing strategies for the reduction of AF after Cardiac Surgery. They found that biatrial pacing significantly reduced the likelihood of AF. They also identified that right atrial and left atrial pacing reduced AF but that the results were not significant. In addition, the placing of the leads varied, and the pacing strategies from fixed rates to complex flexible algorithms were used. Debrunner et al. [27] in 2004 studied 80 patients undergoing valve surgery with or without CABG. Patients were randomized to biatrial pacing with an algorithm to keep pacing at 10 bpm over the intrinsic rhythm for three days. Control patients received right atrial pacing with pacing set at 80 bpm. They demonstrated a reduction in AF from 45% to 20% in the biatrial pacing group, although the administration of beta-blockers was not controlled in this study, and a large number of patients had beta-blockers withdrawn post-operatively.

Goette et al. [28] randomized 161 patients with a history of AF undergoing cardiopulmonary bypass. They randomized the patients into three groups, controls who had right atrial pacing, which was only used if clinically indicated, a right atrial pacing group with active pacing for five days and biatrial pacing with leads placed at Bachmann's Bundle and active pacing used for five days. They found no statistically significant results although 24

patients were withdrawn from the study for clinical reasons. Gerstenfeld et al. [29,30] published two studies in 1999 and 2001, studying biatrial pacing, right atrial pacing and controls in 61 patients, and later just comparing biatrial pacing with controls in 188 patients. In the smaller study, no significant differences were found although there were only 6–7 occurrences of AF in each group. In their second larger study, the incidence of AF in the control group was 35% but in the biatrial pacing group the incidence was only 19%. On further analysis this difference was attributable only to patients over 70 years of age.

In respect to pacing, AF and cardiac surgery, it is possible to read some papers all of which have at least controversial results. By reading these papers and the other aforementioned papers, the diversity in adopted methodologies is clear; data do not allow the establishment of atrial "pacing" as a prophylactic measure against the incidence of FA in cardiac surgery.

TREATMENT

As is well known, atrial contractile activity is responsible for 20% of the cardiac output. Heart failure is not uncommon in the postoperative period of heart surgeries, and the sinus rhythm recovery is, frequently, mandatory for hemodynamic stabilization. If the AF reversal is not possible, it is important to control the heart rate.

The postoperative treatment of AF follows conventional clinical protocols. Amiodarone impregnation is one of the most popular adopted therapeutic approaches. Particularly, in patients under coronary bypass surgery our tendency is to use beta-blockers, mainly the endovenous use of metoprolol or, sometimes, diluted atenolol by sublingual via. The use of beta-blockers and/or amiodarone even if it does not treat the AF, surely makes the control of the heart rate possible.

As anti-arrhythmic drugs have an negative inotropic effect, the use of electrical cardioversion should be considered. The electrical treatment, culturally, is not a routine in Brazilian cardiac surgery postoperative recovery units. Maybe, this fact should be reversed, as electrical cardioversion is safe and the most effective method to treat AF. In our already mentioned experience with patients under surgical myocardial revascularization AF was presented at around 1.66 ± 2.17 days in the postoperative period and 45.5% of the patients had more than one distinct episode of the arrhythmia. Treatment constituted of cardioversion in 25%, oral atenolol in 18.75% and digitalis associated with quinidine in 56.25% [12]. This experience is illustrated in Figure 4.

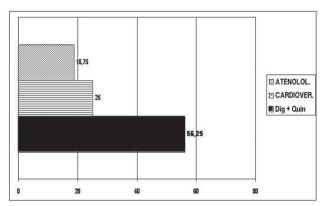


Fig. 4 - Atrial fibrillation treatment in coronary artery bypass surgery patients (Adapted from Sgarbieri 12)

A high-evidence issue in cardiac surgery was written according to a structured protocol. The question addressed was whether treatment with magnesium in addition to an anti-arrhythmic is beneficial to patients who have initiated with atrial fibrillation after cardiac surgery. Altogether 466 papers were identified using the following search, of which eight papers presented the best evidence to answer this clinical question. The author, journal, date and country of publication, patient group, relevant outcomes and weaknesses were tabulated. They concluded that while the literature on magnesium prophylaxis and non-cardiac surgical studies on magnesium therapy for atrial fibrillation suggest that magnesium may be of benefit, there are currently no studies in post-cardiac surgery atrial fibrillation to support the use of magnesium therapy for these patients [31].

CONCLUSION

Atrial fibrillation and coronary artery bypass surgery (CABG) and beta-blockers are protagonists of a never-ending story. Dr. Adam E. Saltman wrote a brilliant chapter of this story in a recent editorial published in The Journal of Thoracic and Cardiovascular Surgery [22]. In this editorial Dr. Saltman points out that despite the astonishing advances that have been made in cardiac surgery over the past 40 years, newonset AF remains its most common complication. Long thought a nuisance, it has now been clearly shown to increase length of stay, intensive care unit utilization, morbidity, and even long-term mortality. It occurs in anywhere from 15% to 40% of patients and little progress has been made in our understanding, prevention, or treatment of it. Also, Dr. Saltman discussed about the growing number of papers about the efficacy of amiodarone to treat AF in the milieu of CABG and concluded that until more convincing evidence emerges, the routine administration of beta-blockers remains the standard AF perioperative prophylaxis. Amiodarone should be reserved

for those patients in whom beta-blockade would be contraindicated or who poorly tolerate the drug, such as those with poor ventricular function, congestive heart failure, severe lung disease, thyroid disease, or allergies.

Srinivasan et al. [23] presented one result against all clinical and pharmacological proof: the incidence of atrial arrhythmia significantly increased in patients who had received preoperative beta-blockers. The authors pointed to study limitations, the most important being the retrospective, observational, and non-randomized natures, beside the capital limitation of the study that did not collect details of dosage and duration of treatment nor the type of beta-blocker used. These data have to be emphasized as a possible cause of the apparent paradoxical increase in atrial arrhythmias in the beta-blocker group of patients.

Another important data to explain this increased incidence is beta-blocker withdrawn. Anesthesiologists and the intensive care team have to be careful about this pharmacological phenomenon. Once adopting preoperative beta-blocker therapy, the beta-blockade must be continued through the perioperative period, including its use in the operating room and during the early postoperative period. Frequently when the patient presents with AF, the ICU team starts high doses of amiodarone, but small doses of injectable metoprolol recover the sinus rhythm. Also, we frequently use atenolol diluted in water sublingually. Atenolol is water-soluble and its use sublingually should avoid the first-pass liver metabolism.

Our experience with 186 patients permitted us to suggest that some of the previously mentioned factors may contribute to the genesis of arrhythmias, such as single or double stage cannulation for venous drainage, inadequate myocardial protection, over-distention and cardiac fibrillation and, mainly, the presence of proximal circumflex artery obstructions responsible for atrial ischemia before and during surgery [12]. After this study, we designed a prospective study, including, coronary artery disease and heart valve disease, prescribing 50 mg of atenolol for all our patients the night before surgery with favorable results (unpublished data). If the patient was taking beta-blockers we continued to prescribe them.

Fortunately, a variety of pharmacologic strategies are now available to prevent AF after cardiac surgery. At least, low-dose postoperative beta-drenergic blockade is valuable for patients who receive these medications preoperatively and may be beneficial in all patients. Moreover, emerging data suggest that prophylaxis with antiarrhythmic compounds can significantly decrease the incidence of AF, length of hospital stay, and cost. Future trials will be focused on evaluating the risks and benefits of the newer prophylactic therapies and defining which subpopulations benefit most from such therapies.

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