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Short Communication

Amiodarone prevention for atrial fibrillation relapse after surgical ablation

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Abstract

Background: Atrial fibrillation (AF) is the most common heart rhythm disorder. AF ablation based on endovascular or surgical techniques is a standard of care in everyday practice. Early recurrence of atrial arrhythmias is a significant problem after ablative procedures. Prophylactic use of antiarrhythmic drugs has become a possible solution.

Materials and methods: We performed a retrospective observational cohort study of 59 patients with heart disease requiring surgery under extracorporeal circulation (ECC) and have received radiofrequency ablation (RFA) for chronic or persistent AF with a successful conversion to sinus rhythm. Patients were divided into two groups: 36 were treated with amiodarone for three months postoperatively (treatment group), and 23 had no concomitant amiodarone therapy (control group). We compared the groups regarding freedom from recurrent atrial arrhythmia and the frequency of conduction disorders requiring permanent pacemaker implantation.

Results: No differences between the groups were found regarding demographic characteristics, risk profile, and heart diseases indicating cardiac surgery. During follow-up, a significantly higher proportion of patients with sinus rhythm in the group receiving amiodarone was found (80.56% vs. 52.17%; $p < 0.041$). No cases of premature discontinuation of amiodarone for side effects or noncompliance were registered in the treatment group.

Conclusion: Three months of amiodarone therapy post-surgical RFA of AF is an effective and safe strategy for relapse prevention.

Keywords

atrial fibrillation, surgical radiofrequency ablation, amiodarone, sinus rhythm

Introduction

Atrial fibrillation (AF) is the most common heart rhythm disorder (Go et al. 2014) and leads to many complications, thus increasing morbidity and mortality in patients left untreated. AF is a leading cause of heart failure and thrombosis in the left atrium, with subsequent peripheral embolism and stroke. AF ablation based on endovascular or surgical techniques is becoming more common in everyday practice (Calkins et al. 2018). These are procedures in which, through various devices delivering damaging energy, linear necrosis (so-called lesion or ablation lines) is created in a controlled manner in certain areas of the atrial walls, which serve as insulating barriers to the flow of electrical impulses. The purpose of the ablation procedure is to restore normal sinus rhythm by interrupting possible macro-reentrant circuits of circulatory excitation and isolating the area in the left atrium between the pulmonary veins, where the primary sources of pathological electrical activity responsible for starting AF are concentrated. In cardiac

surgery, such procedures are indicated mainly as additional supplements in patients with AF planned for surgical correction due to another underlying heart disease. In the surgical population, the prevalence is significantly skewed towards mitral valve disease because this pathology invokes the most significant degree of left atrial (LA) distension (Geidel et al. 2004). An AF prevalence of 30% is reported in mitral valve surgical patients and only 14% and 6% in patients undergoing aortic valve or isolated coronary surgery, respectively (Gammie et al. 2008). The main problem after performing RFA interventions is the early recurrence of AF (Cox 1991; Cox et al. 1991). Most of these early arrhythmias are transient and subside with proper medical treatment within the first post-procedure months, after the final completion of reparative processes (Cox et al. 1991). Recurrences after this period are associated with technical ablation leaks (Cox et al. 1991). In order to reduce these early relapses, prophylactic administration of antiarrhythmic drugs is an option (Calkins et al. 2018). Furthermore, this strategy is well-established after catheter ablation procedures but still controversial after surgical ablation.

Amiodarone (class III antiarrhythmic drug) is the most widely used medication in relapse cases. It is indicated for many types of supraventricular and ventricular arrhythmias. It is particularly appropriate for patients with compromised left ventricular function due to the minimal negative inotropic effect and low proarrhythmic effect. Side effects have been shown to increase after prolonged use (above six months), mainly related to the function of the thyroid gland. These facts are the main debate problem on the safety and efficacy of long-term drug therapy (Li et al. 2008; Lafuente-Lafuente et al. 2006). In order to clarify the impact of prophylactic use of amiodarone after surgical RFA, we performed a retrospective observational study of patients operated in our hospital. The study aimed to evaluate the effectiveness of three months of amiodarone intake on the AF recurrence rate following cardiac surgery with ECC combined with radiofrequency ablation (RFA).

Material and methods

We carried out a retrospective, observational study of data from 59 consecutive patients with heart disease requiring cardiac surgery under extracorporeal circulation (ECC) and receiving RFA for AF with a successful conversion to sinus rhythm. The preoperative duration of AF was documented by electrocardiography and ranged from 13 to 32 months (mean, 22±10 mo), therefore determined as chronic or persistent. The type of primary heart disease and the corresponding surgical procedures varied. The ablation procedures were performed with a bipolar radio-frequency clamp for making ablation lines using the lesion set described by Cox for the maze intervention (Cox 1991). Patients were divided into two groups: 36 were scheduled to receive amiodarone for three months postoperatively (treatment group), and 23 did not receive amiodarone (control group). All other medications remained as prescribed for patients following cardiac surgery, depending on their hemodynamics, and received postoperative beta-blockers as standard of care unless contraindicated. Intravenous amiodarone treatment was started immediately postoperatively and continued at 1200 mg/day for the first 48 hours, followed by 200 mg daily p.o. for three months. Postoperative AF or flutter episodes during follow-up were treated with external electrical cardioversion. A maximum of 3 applications per patient were allowed before discharge. If the patient experienced further relapses, the surgical ablation was considered unsuccessful. We compared the groups concerning freedom from recurrent atrial arrhythmia within the third postoperative month, establishing the proportion of those who maintained sinus rhythm, documented by a long electrocardiographic record from the follow-up examination. All analyses were conducted using SPSS, version 17.0. Continuous variables are presented as mean, standard deviation (± SD), and categorical variables as frequency (%). Analyses comparing patient characteristics and outcomes included the t-independent sampling test, the Mann-Whitney test for continuous variables, and $\chi 2$ analysis, or Fisher's exact test, for categorical variables. We compared the groups with respect to the absence of recurrent atrial arrhythmia, and procedure safety was further assessed by the frequency of conduction disorders requiring permanent pacemaker implantation within the third postoperative month.

Results

Comparing the preoperative patient characteristics (Table 1), there were no significant differences between groups regarding age, sex, left ventricle function, and the expected perioperative mortality calculated with the EuroSCORE-II. We also failed to establish differences between the groups in terms of proven in-literature predictors of surgical RFA failure, including the left atrium size ($p = 0.724$), mean preoperative duration of AF ($p = 0.553$); the proportion of long-standing persistent AF ($p = 0.280$); and the rate of patients with isolated mitral stenosis ($p = 0.368$).

Table 1. Patient characteristic.

Indicators	Control group n = 23	Treatment group n = 36	p
Age, years (mean ± SD)	60.4 ± 5.21	60.7 ±.4.69	0.876
Female, n (%)	6 (26%)	10 (28%)	0.941
EF, % (mean ± SD)	52.2 ± 12.4	51.1 ± 9.8	0.713
Arterial Hypertension, n (%)	20 (87%)	31 (86.1%)	0.687
Diabetes, n (%)	8 (34.7%)	13 (36.1%)	0.698
CKD, n (%)	2 (8.7%)	3 (8.3%)	0.255
Mean AF duration, months	21(16–32)	24(13–28)	0.553
Long-standing AF, n (%)	12 (52.2%)	20 (55.5%)	0.280
Mitral stenosis, n (%)	6 (26%)	11 (30.5%)	0.368
Mitral regurgitation, n (%)	5 (21.5%)	9 (25%)	0.661
Aortic stenosis, n (%)	4 (17.4%)	5 (13.9%)	0.781
Aortic regurgitation, n (%)	3 (13.6%)	4 (11.1%)	0.589
Coronary artery disease, n (%)	5 (21.5%)	7 (19.5%)	0.687
Left atrium size, mm (mean ± SD)	54 ± 8.9	56 ± 4.3	0.724
EuroSCORE II (mean ± SD)	2.38 ± 0.33	2.55 ± 0.23	0.232

SD – standard deviation; EF – ejection fraction; CKD – chronic kidney disease; AF – atrial fibrillation.

Both groups had similar surgical outcomes, presented in Table 2. According to our experience, surgical ablation of AF during cardiac surgery with ECC has a success rate of 100%, although 15.3% of the patients presented some supraventricular arrhythmia, four patients (6.8%) had paroxysmal episodes of AF, and five patients (8.5%) had paroxysmal atrial flutter. However, no difference was found regarding using electro-cardioversion during the early postoperative stay to control a single episode of supraventricular tachyarrhythmia ($p = 0.554$). Three patients in both groups had conduction disorders and received permanent pacemakers ($p = 0.656$).

Table 2. Postoperative characteristics.

Indicators	Control group n = 23	Treatment group n = 36	p
Mechanical ventilation > 24 hours, n (%)	1 (4.35%)	1 (2.78%)	0.822
Revisions for bleeding, n (%)	1 (4.35%)	2 (5.56%)	0.854
Acute renal failure, n (%)	1 (4.35%)	2 (5.56%)	0.554
Postoperative PM, n (%)	3 (13.04%)	3 (8.33%)	0.656
Hospital stay, days (mean ± SD)	6.8 ± 0.83	6.7 ± 0.68	0.899
Mortality, n	0	0	NS
Stroke/TIA, n	0	0	NS
Electrocardioversion, n (%)	3 (13.04%)	6 (16.67%)	0.762

PM – pacemaker; SD – standard deviation; TIA – transient ischemic attack.

No cases of premature discontinuation of amiodarone for side effects or noncompliance were registered in the treatment group. At the 3-rd month, we found a significantly higher proportion of patients with stable sinus rhythm in the group receiving amiodarone compared to the control group (29/36 (80.56%) vs. 12/23 (52.17%); $p < 0.041$) (Fig. 1) and no conduction disorders requiring PM implantation were registered.

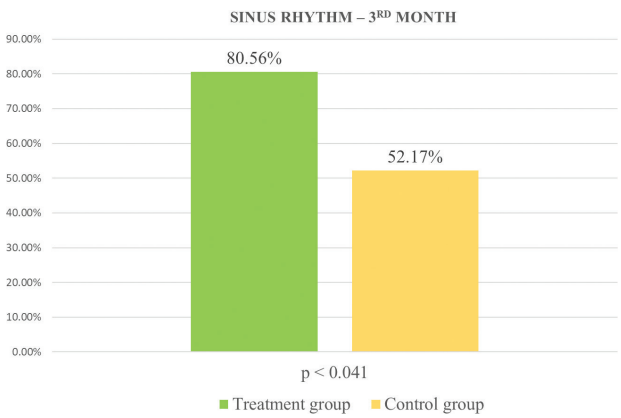

Figure 1. Patients with sinus rhythm three months after the operation.

Discussion

In this study, we concluded that prophylaxis with amiodarone after surgical RFA is safe and effective, and the result is comparable to the efficacy of this prophylaxis after catheter ablation (Calkins et al.,2018; Lafuente-Lafuente et al.,2006; Li et al.,2008; Roux et al.,2009). The European guidelines conclude that better AF prevention is afforded after catheter ablation with anti-arrhythmic therapy, representing reasonable practice (Roux et al. 2009; Calkins et al. 2018). There are no guidelines for specific anti-arrhythmic drug therapy following surgical ablation. There is significant heterogeneity between surgical ablation studies due to different definitions of AF recurrence, rhythm assessment protocols, and anti-arrhythmic therapy (Nashef et al. 2018). Amiodarone is the most widely used drug for better rhythm control after surgical ablation, although routine use is not universal. Combined application with beta-blocker is expected but not continuously routine. There is evidence of the likely benefits of statins, amiodarone, and several other drug regimens for preventing postoperative AF during routine cardiac surgery. To extrapolate this data to the surgical AF ablation population is reasonable, so more detailed, controlled trials are needed to define the precise short and long-term impact of drug therapy following surgical ablation procedures. It should be noted that the original operation developed in the late eighties of the 20th century by Dr. Cox (1991) aims not only to restore sinus rhythm but stop taking antiarrhythmics and anticoagulants. However, complete performance is often associated with an increased perioperative risk. As a result, in recent years, ablation techniques have been developed. The intervention is concentrated only in the left atrium and consists mainly of isolation of the pulmonary veins, posterior wall of the left atrium, and appendage resection. This minimization of the intervention volume reduces the success rate and increases the risk of early recurrence, making postoperative prophylaxis with amiodarone mandatory.

Several studies report a proportional relationship between the rates of early AF relapses (within the third month) and late (after the sixth month) recovery of persistent arrhythmia. However, the general opinion is that a single early arrhythmia recurrence in the first three post-procedure months or the so-called "stabilization period" or "blanking period" does not mean a particular failure of the ablation procedure. It is before settling on the final rhythm resulting from the ablation procedure. (Benussi et al. 2000) Moreover, given that the postoperative AF incidence in isolated myocardial revascularization is 25%–40% (Aranki et al. 1996), it is difficult to determine the percentage of patients with recurrence of postoperative atrial arrhythmias due to primary failure of the ablation technique. Nonetheless, these recurrences are associated with deteriorating quality of life due to increased morbidity, costs, rehospitalizations, and related adverse psychological effects (Roux et al. 2009; Lellouche et al. 2008; Maroto et al. 2011).

Limitations

The study has many limitations, the most important of which are retrospective patient registration, small total number of patients, and lack of a specific definition according to which the choice was made to continue prophylaxis with amiodarone in some patients or discontinuation in others. In general, in most patients operated on in the earlier years of the study period, amiodarone was discontinued immediately after discharge due to a lack of

data on the effectiveness of this prophylaxis in the literature. Another essential problem is the lack of longer-term follow-up for recurrent arrhythmias. Contributing to this is the fact that the use of devices, such as continuous telemetry or longer-term Holter monitoring, is not possible in the current conditions of the healthcare system, where funds for such devices are not provided. However, the tendency of recurrences to become more frequent without treatment and eventually to degenerate again into chronic AF gives us reason to say that many of these cases would be registered at the follow-up examination. Despite the mentioned limitations, the significant difference between the groups allows us to say that the results are representative, especially if they are considered in similar publications. However, in order to strongly recommend the use of prophylaxis with amiodarone after surgical RFA in all patients, larger and randomized trials will be needed.

Conclusion

Short-term prophylactic amiodarone treatment reduces early atrial arrhythmia recurrence after surgical RFA. The biggest concern with long-term treatment with amiodarone remains the manifestation of its side effects, especially regarding thyroid function. However, the course's relatively short period with careful patient monitoring is safe. Based on this study, we can recommend prophylaxis with amiodarone after surgical RFA for at least three months as an effective and safe strategy.

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