

Effect of temporary right atrial pacing in prevention of atrial fibrillation after coronary artery bypass graft surgery

Efeitos da estimulação temporária atrial direita na prevenção da fibrilação atrial no pós-operatório de revascularização do miocárdio com circulação extracorpórea

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Abstract

Objective: To evaluate the effects of temporary atrial pacing to prevent the atrial fibrillation following coronary artery bypass graft surgery and the risk factors to the occurrence of this arrhythmia.

Methods: We have studied 160 patients who, at the end of coronary artery bypass graft surgery, were submitted to epicardial electrode implantation in the right atrium lateral wall. They were randomized into two groups: non-pacing

(NP) group and right atrial (RA) pacing group. The cardiac rhythm was monitored over 72 hours following to the end of surgery and the variables studied were as follow: incidence of atrial fibrillation; the risk factors pre-, intra-, and postoperative for its occurrence, and postoperative events.

Results: There were 21 (13.1%) episodes of atrial fibrillation, 20 in the NP group and one in the RA group. The relative risk (RR) for the development of atrial fibrillation was 0.18 (95% CI; 0.05-0.60) for the RA group

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when compared to the NP group. The logistic regression identified that the study variables, such as younger age; use of beta-blockers in the preoperative, and the presence of right atrial pacing had been associated to a lower Odds ratios (ORs) for the occurrence of atrial fibrillation in the postoperative.

Conclusions: The temporary atrial pacing reduced the incidence of atrial fibrillation after the CABG surgery. Older age and a non-atrial pacing were the independent predictive factors of the occurrence of this arrhythmia.

Descriptors: Cardiac pacing, artificial. Atrial fibrillation. Myocardial revascularization. Postoperative complications. Extracorporeal circulation.

Resumo

Objetivo: Avaliar os efeitos da estimulação atrial direita temporária na prevenção da fibrilação atrial no pós-operatório de revascularização do miocárdio com circulação extracorpórea e identificar os fatores de risco para o aparecimento dessa arritmia.

Método: Estudamos 160 pacientes que, ao término da cirurgia de revascularização miocárdica, submeteram-se ao implante de eletrodos epicárdicos na parede lateral do átrio

direito e foram randomizados em grupos não-estimulado (NE) e grupo com estímulo atrial direito (AD). O ritmo cardíaco foi monitorizado durante as 72 horas seguintes ao término da operação e as variáveis estudadas foram: a incidência de fibrilação atrial, os fatores de risco pré, intra e pós-operatórios para o seu aparecimento e eventos pós-operatórios. Resultados: Foram detectados 21 (13,1%) episódios de fibrilação atrial, sendo 20 no grupo NE e um no grupo submetido à estimulação do átrio direito (AD). O risco relativo para o desenvolvimento de fibrilação atrial foi de 0,18 (IC 95%= 0,05-0,60) para o grupo AD quando comparado ao grupo NE. A regressão logística identificou que as variáveis idade mais jovem, uso de beta-bloqueador no pré-operatório e presença da estimulação atrial direita estiveram associadas a uma menor razão de chances (*odds ratio*) para o surgimento de fibrilação atrial no pós-operatório.

Conclusões: A estimulação atrial direita temporária reduziu a incidência de fibrilação atrial pós-operatória. A idade avançada e a não estimulação atrial foram fatores preditivos independentes para a ocorrência dessa arritmia.

Descritores: Estimulação cardíaca artificial. Fibrilação atrial. Revascularização miocárdica. Complicações pós-operatórias. Circulação extracorpórea.

INTRODUCTION

Atrial fibrillation (AF) has a frequency of occurrence ranging from 11% to 40% following coronary artery bypass grafting surgery [1]. It typically occurs between the first and the fifth day following surgery with frequency peak on the second day [2]. Although it is well tolerated in the majority of the patients [3], AF can result in hemodynamic instability, especially in those patients with left ventricular diastolic dysfunction because they present a reduced tolerance to the loss of atrial contraction [4]. Limiting the use of beta-blockers and amiodarone [5, 6], as a prophylactic pharmacological measurement of postoperative AF, have induced studies regarding prophylactic nonpharmacological measurements. Among them, the temporary cardiac pacing using epicardial electrodes in sites, such as right atrium, have demonstrated a reduction in the percentages of AF from 42% to 13% in its different pacing sites, with no differences between the types of stimuli [7].

Published studies, however did not allow establishing the actual value of the therapeutic approach, as well as the more effective types and modes of pacing yet [8-11].

The objective of the present study was to evaluate the efficacy of the atrial artificial electric pacing in preventing AF in the postoperative on-pump CABG and to identify the risk factors for the occurrence of this arrhythmia.

METHOD

The study population included 160 patients with coronary heart disease (CHD) requiring surgical treatment through on-pump CABG. Patients were excluded if they have associated cardiopathy, are currently using a pace-maker or requiring a pace-maker, and have a previous history of AF.

A 12-lead ECG was used to determine the preoperative cardiac rhythm and the following evaluations according to the study protocol. ECG was performed to detect mitral regurgitation with hemodynamic repercussion, which was a study protocol exclusion criterion.

Cardiac catheterism have identified coronary injuries (> 70%) in one to five arteries with a median of 3 vessels distributed as follows: anterior interventricular branch (AIVB) (87.9%); right coronary artery (RCA) (71.7%); left marginal artery (LMA) (51.2%); diagonal branch (DIAG) (42.5%); diagonalis branch (DD) (18.3%).

In this randomized clinical trial, we considered five clinical and electrocardiographic evaluation moments: moment zero, which corresponded to preoperative, immediate postoperative, 24, 48, and 72 hours following the procedure.

Following the removal of CPB and the patient's hemodynamic stabilization, temporary epicardial electrodes

were fixed in the right atrium lateral wall and in the right ventricle anterior wall, placed over the subxiphoid region with identification of the pacing sites.

At ICU admission, the patients were randomized through a list with a random assignment distribution comprising two groups: 1) NP Group comprising non-pacing patients (external pace-maker turned off); 2) RA Group comprising patients undergoing right atrial pacing (AAI pacing) over the first 72 postoperative hours (Figure 1).

Surgical Procedure

- Myocardial revascularization
- Implant of transient epicardial electrodes

Random Allocation

(immediate postoperative)

NP GROUP	Postoperative Assessment	RA GROUP
Non-pacing	Clinical evaluation	Righ atrium
	Electrocardiographic Assessment	pacing

Fig. 1 – Study flowchart

The assessment of pacing functions, atrial and ventricular electrodes' sensitivity/impedance was made through the measurements of pacing threshold, and P/R wave amplitude using a Biotronik Pacing System Analyzer ERA 20 (Biotronik Inc., Berlin, Germany) on right atrial/ventricular pacing.

The method of pacing used was the atrial demand inhibited pacing (AAI), with a programmed pacing frequency of 10 pulses per minute (ppm) over the patient's baseline frequency, not exceeding 120 ppm. An external dual-chamber pacemaker, model EDP 30, (Biotronik Inc, Berlin, Germany) was used. The artificial cardiac pacing was always performed by bipolar pacing with the electrodes connected to the pulse generator.

Following the 72-hour period, the pacing was turned off and the patients were followed-up until discharge from the hospital.

To record the cardiac rhythm in both groups, the patients underwent continuous cardiac monitoring, during ICU stay, and to daily records through a 12-lead ECG, during the hospital stay until discharge. To confirm the adequate functioning of the external pace-maker, daily reevaluations

of heart rate, pacing atrial thresholds, and sensitivity through measurement of P wave amplitude were performed.

Atrial or ventricular arrhythmias, when identified, were treated with antiarrhythmic drugs, such as amiodarone, 600-mg/d intravenous dose and/or 400-mg/d oral dose. In case of hemodynamic decompensation associated to arrhythmia, an electric cardioversion was performed.

In this respect, the use of anticoagulants in the patients who developed AF was avoided by the immediate diagnosis and sinus rhythm reversion. It must be emphasized, however, that in the failure of some cardioversion cases or recurrence of AF, it is mandatory the recommendation of this treatment regimen.

The risk factors were evaluated in three distinct periods:

1. Postoperative period: age, gender, history of SAH or SAH findings, DM, AMI, CHF, left ventricular end-diastolic diameter (LVEDD), left ventricle ejection fraction (LVEF), left ventricular end-diastolic pressure (LVEDP), and number of coronary vessels affected;
2. Intraoperative period: the duration of CPB and anoxic arrest, and the number of distal anastomoses and arterial grafts used for revascularization;
3. Postoperative period: volume of bleeding through mediastinal and/or pleural drainage, mechanical ventilation length of stay, and the length of stay in the ICU.

The AF finding until the end of the 72-hour observation period; the occurrence of AF in the overall admission period; the total postoperative length of hospital stay, were all considered as postoperative events.

The statistical method included the following analyses:

- 1) descriptive: applied to clinical, electrocardiographic, echocardiographic and cardiac catheterism;
- 2) univariate: estimated the variable differences between patients with AF and those who maintained sinus rhythm, using the following tests: chi-square test, likelihood ratio test, Student's *t* test, and Fisher's exact test, or the Wilconxon's rank sum; and
- 3) multivariate: correlated the pre- and intraoperative variable differences of the patients who have developed AF with those who have not, using the logistic regression model. Analyses were performed with the *Statistical Package for Social Sciences* software (SPSS version 10.0; SPSS, Chicago). A *p* <0.05 was considered statistically significant.

This study was conducted at Hospital São Joaquim da Real and Benemerita Associação Portuguesa de Beneficência de São Paulo, Brazil. The study was approved by the Research and Ethics Committee, and written informed consent was obtained from each patient. Patients were screened for inclusion and exclusion criteria between 2002 and 2004.

RESULTS

The surgical procedure for on-pump CABG was performed on the conventional way, i.e., through anterior median transsternal thoracotomy. The anticoagulation

protocol was performed with intravenous heparin sodium infusion with a dose of 4 mg/kg body-weight.

Following the CPB support with ascending aorta cannulation along the aortic arch and right atrium (RA) through a single cannula, the ascending aorta was clamped and myocardial protection was achieved with cold saline solution in the pericardial sac and an injection of antegrade sanguineous cardioplegia solution at 3°C, infused into the aortic root, with a dose of 10 mL/kg body-weight and repeated at every each 20 minutes. The patients were kept under mild hypothermia throughout the anoxic arrest.

The operative procedure was successfully performed in 160 pre-selected patients, equally distributed into two groups of 80 patients each.

The baseline characteristics were similar in both groups. There was not found significant differences between the studied pre- and intraoperative clinical variables (Table 1).

Table 1. Baseline characteristics and operative data of study patients

Characteristics	NP (n=80)	RA (n=80)	p
Age (Yrs)			
Mean ± Standard deviation	60.3±10.3	60.0±10.1	0.48
Range	36 - 83	42 - 83	
Male	60.0%	67.5%	0.20
SAH	80.0%	78.8%	0.97
DM	30.0%	45.0%	0.14
AMI	45.0%	48.8%	0.80
Smoking	52.5%	55.0%	0.89
Beta-blocker	28.8%	35.0%	0.67
LVEDP	14.9±6.4	13.8±3.5	0.39
> 2 treated arteries	23.7%	27.5%	0.08
Use of ITA (L/R)	76.3%	76.3%	0.41
Duration of CPB (min)	58.1±20.2	64.3±19.4	0.11
Anoxia duration (min)	44.7±18.0	49.9±17.6	0.15

AF = atrial fibrillation; NP = non-pacing group; RA = group submitted to right atrial pacing; SAH = Systemic arterial hypertension; DM = Diabetes Mellitus; AMI = Acute Myocardial Infarction; LVEDP = left ventricular end-diastolic pressure; ITA = internal thoracic artery; CPB = cardiopulmonary bypass

Five hospital deaths were observed, three directly related to the operative procedure. In the immediate postoperative three patients died; two deaths were caused by ventricular fibrillation, and one death caused by acute anemia due to aortic rupture. Two deaths were caused by pulmonary

complications on the 16th and 19th postoperative days, respectively. Of the total deaths, three occurred in the NP Group and two in the RA Group.

The artificial cardiac pacing was interrupted in three patients: in two patients the interruption was due to loss of command by increasing the pacing threshold; in one patient, the clinical staff decided by the interruption in the immediate postoperative period, after myocardial infarction.

During the study period, 21 (13.1%) episodes of AF were diagnosed, of which 20 in the NP group and 1 in the RA group. Relative risk for AF of 0.05 (95% CI; 0.0069 to 0.36) was identified in the RA group in comparison to the NP group (Table 2).

Throughout the length of hospital stay, 23 (14.4%) episodes of AF were detected, of which 20 in the NP group and three in the RA group (Table 2). The relative risk for developing AF was 0.18 (95% CI; 0.05 to 0.60) in the RA group, when compared with the NP group.

Table 2. Distribution of the atrial fibrillation events according to the two study groups.

Groups	AF 72 hours		total AF	
	n	%	n	%
NP	20	25.0	20	25.0
RA	1	1.25	3	3.75

AF = atrial fibrillation; NP = non-pacing group; RA = group submitted to right atrial pacing

Taking into consideration the first 72 postoperative hours, the mean time from the first episode of AF was 42.5±22.9 hours. The earliest episode occurred four hours after ICU admission. The majority of the episodes occurred between 24 to 48 hours after ICU admission.

Pharmacological intervention with amiodarone, 600 mg/d and/or 400 mg/d orally, was the treatment strategy used to interrupt the atrial fibrillation in 23 patients.

One patient required electrical cardioversion due to the persistence of AF, in spite of the instituted treatment. Once the treatment was achieved, there was a reversion to the sinus rhythm and all the patients have experienced the disappearance of all symptom. Recurrence of arrhythmia was not observed.

The comparison between the demographics of patients who developed AF with those who were in normal sinus rhythm within the first 72 hours, showed that younger age (p=0.0005) and the right atrial pacing (p=0.0001) have been associated with a lower incidence of postoperative AF (Table 3).

Table 3. Clinical and operative characteristics of the patients with AF in comparison to those patients in sinus rhythm during the first 72 hours postoperatively.

Variables	AF -72 hours		p
	Absent	Present	
Group			
NP	75.0%	25.0%	<0.001
RA	98.8%	1.2%	
Age	59.1±9.8	67.3±9.3	0.0005
Gender			
Male	86.3%	13.7%	0.76
Female	87.9%	12.1%	
SAH			
Absent	93.9%	6.1%	0.18
Present	85.0%	15.0%	
DM			
Absent	83.0%	17.0%	0.09
Present	93.3%	6.7%	
AMI			
Absent	87.1%	12.9%	0.94
Present	86.7%	13.3%	
Smoking			
Absent	85.1%	14.9%	0.54
Present	88.4%	11.6%	
Beta-blocker use			
Absent	83.5%	16.5%	0.08
Present	94.1%	5.9%	
LVEDP	14.1 ± 4.8	15.6 ± 6.9	0.19
Treated arteries (n°)			
1 – 2	84.0%	16.0%	0.10
3 – 4	95.1%	4.9%	
Use of ITA (L/R)			
Absent	86.8%	13.2%	0.99
Present	86.9%	13.1%	
Duration of CPB (min.)	62.0 ± 20.1	55.9 ± 17.5	0.19
Aoxia time (min.)	47.8 ± 18.3	43.3 ± 14.0	0.28

AF = atrial fibrillation; NP = non-pacing group; RA = group submitted to right atrial pacing; SAH = Systemic arterial hypertension; DM = Diabetes Mellitus; AMI = Acute Myocardial Infarction; LVEDP = left ventricular end-diastolic pressure; ITA = internal thoracic artery; CPB = cardiopulmonary bypass

Table 4. Clinical and operative characteristics of the patients with AF in comparison to those in sinus rhythm during the hospital stay.

Variables	total AF		p
	Absent	Present	
Group			
NP	75.0%	25.0%	<0.0001
RA	96.2%	3.8%	
Age	59.0±9.9	67.2±8.9	0.0003
Gender			
Male	86.3%	13.7%	0.82
Female	84.5%	15.5%	
SAH			
Absent	90.9%	9.1%	0.41
Present	84.3%	15.7%	
DM			
Absent	83.0%	17.0%	0.22
Present	90.0%	10.0%	
AMI			
Absent	84.7%	15.3%	0.72
Present	86.7%	13.3%	
Smoking			
Absent	83.8%	16.2%	0.54
Present	87.2%	12.8%	
Beta-blocker use			
Absent	82.6%	17.4%	0.11
Present	92.2%	7.8%	
LVEDP	14.2 ± 4.8	15.1 ± 6.7	0.42
Treated arteries (n°)			
1 – 2	83.2%	16.8%	0.13
3 – 4	92.7%	7.3%	
Use of ITA (L/R)			
Absent	84.2%	15.8%	0.77
Present	86.1%	13.9%	
Duration of CPB (min.)	62.1 ± 20.0	56.0 ± 18.5	0.19
Aoxia time (min.)	47.9 ± 18.2	43.2 ± 15.6	0.24

AF = atrial fibrillation; NP = non-pacing group; RA = group submitted to right atrial pacing; SAH = Systemic arterial hypertension; DM = Diabetes Mellitus; AMI = Acute Myocardial Infarction; LVEDP = left ventricular end-diastolic pressure; ITA = internal thoracic artery; CPB = cardiopulmonary bypass

The comparison between the demographics of patients who developed AF with those who were in normal sinus rhythm throughout the hospital length of stay, showed that younger age ($p=0.0003$) and the right atrial pacing ($p=0.0001$) have been associated with a lower incidence of postoperative AF (Table 4).

The analysis of the risk factors for the onset of AF, through the logistic regression, also have identified that the variables age and the presence of right atrial pacing (Figures 2 and 3) have been associated with a lower probability of occurrence (Odds Ratio) of the onset of this arrhythmia (Table 5).

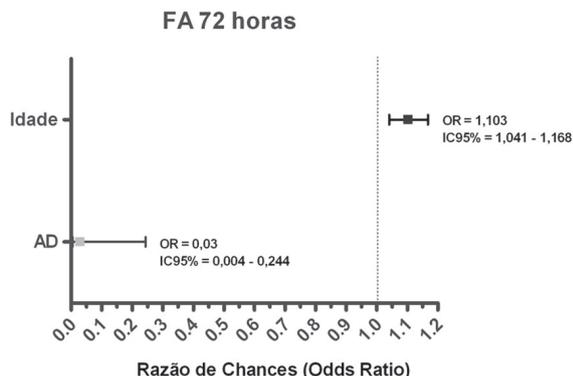


Fig. 2 – Risk factors and the Odds Ratio for occurrence of AF within 72 hours

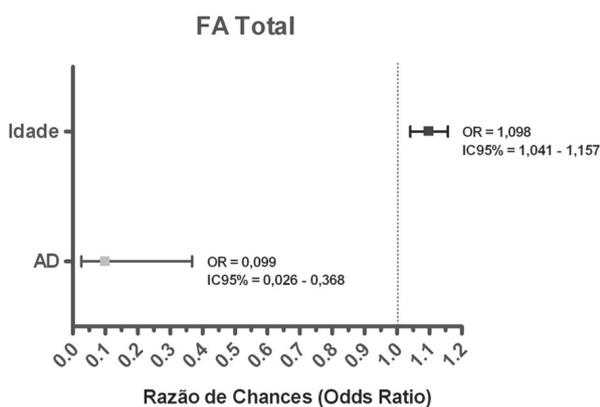


Fig. 3 - Risk factors and the Odds Ratio for occurrence of AF during hospital stay

Table 5. Risk factors and Odds Ratio (OD) for occurrence of postoperative AF.

Factors	AF 72 hours		total AF	
	Odds Ratio	95% CI	Odds Ratio	95% CI
RA	0.03	0.004-0.244	0.099	0.026-0.368
Age	1.103	1.041-1.168	1.098	1.041-1.157

AF = atrial fibrillation; RA = right atrial pacing; CI = 95% confidence interval; NS = not significant

The duration of the orotracheal intubation ranged from 2 to 28 hours [mean±SD] (8.9±3.6) and the postoperative hospital length of stay ranged from 1 to 37 days (7.5±3.8).

There was no correlation between the AF and the difference of orotracheal intubation or the ICU length of stay. However, the presence of AF had a significant association with the higher hospital length of stay (Table 6).

Table 6. Atrial fibrillation influence on postoperative outcome.

Variables	total AF		p
	Present	Absent	
OTI duration (hours)	9.8±3.1	8.7±3.6	0.02
ICU Stay (days)	1.9±1.7	1.7±2.6	0.16
Hospital length of stay (days)	9.5±6.3	7.3±3.1	0.007

AF = atrial fibrillation; OTI = orotracheal intubation; ICU = Intensive unit care

DISCUSSION

The importance of this study relies on the merit to demonstrate the significant benefit provided by the temporary atrial pacing to prevent atrial fibrillation in postoperative on-pump coronary artery bypass graft surgery.

The significant percentage of 25% of AF observed in the NP group is in accordance with the report by Hashimoto *et al.* [12] who analyzed data from 800 consecutive patients who underwent isolated coronary artery bypass and found a 23%-incidence of supraventricular arrhythmia, of which 61% corresponded to atrial fibrillation.

The understanding of the atrial fibrillation epidemiology has allowed identifying the risk factors associated to its occurrence. Older age, recognized as an independent risk factor for the onset of AF in the postoperative CABG, remained the most independent predictor for AF [12,13], in accordance with the present study that showed a mean age of 66.1±8.9 years. The elderly predisposition to develop AF is due to the “negative” atrial remodeling resulting from the increase of fibrous and adipose tissue and the degeneration of the atrioventricular bundle of the conduction system of the heart and sinoatrial node [14].

Concerning the analysis of the intraoperative potential risk factors, the present study did not show any significance as for the duration of CPB or anoxic arrest, myocardial protection, number of vessels compromised, or anastomoses performed.

It is important to stress that the exclusion of patients with valvar or conducting system heart diseases played a role in the lower incidence of AF, even in the NP group of 25%, when in comparison to the percentage of up to 60% reported in the literature [15].

Recent studies [16,17] have shown that variations in atrial temperature favor the increase of atrial refractivity dispersion, a primary substrate for the onset of AF, but it does not justify its onset in the late postoperative period, which has been attributable to the presence of structural atrial injuries intrinsic to the cardiopathies, such as the rheumatic and ischemic cardiopathies [18].

Amid the most severe consequences of AF are heart

failure and stroke [1,9-21]. Shin et al. [22], using direct measurements of the hemodynamic variables and the coronary artery bypass graft flow, observed a decline in the cardiac index when the AF was induced intraoperatively. The most important outcome, however, was the dramatic decrease of blood flow through arterial and venous grafts in consequence of the loss of atrial contraction and the diastolic shortening by means of an increase of an increase of the ventricular response.

In the present study there has been a case of stroke not related to the patients who developed AF, which resulted in the death of the patient.

An increase in length of hospital stay has also been observed as an outcome of AF onset in the postoperative period. Lima *et al.* [23] reported a mean length of ICU stay and a mean length of hospital stay of 36 hours and 4.8 days, respectively, higher than those observed in the patients who did not develop the arrhythmia. In the present study, it was also observed an increase in the length of hospital stay following the onset of AF of 9.5 ± 6.3 days for those who developed AF and 7.3 ± 3.1 days for those who did not.

The immediate diagnosis and the success of reverting to the sinus rhythm avoided the use of anticoagulants in patients who developed AF. It must be emphasized, however, that in the cases of therapy failure or the recurrence of AF, it is mandatory the introduction of this treatment regimen [24], further prolonging the length of hospital stay.

The high incidence of postoperative AF and its complications justifies the use of specific strategies for its prevention. Pharmacological and non-pharmacological measures have been studied, among them, the prophylactic administration of beta-blockers [24-25] of unquestionable value that has been recommended in the practice guidelines for the management of patients with AF, and the use of amiodarone, but recommended for reversion of postoperative AF and in the underlying prophylaxis of this complication [26-28].

The temporary atrial pacing in the postoperative period to prevent AF has been used as both a non-pharmacological alternative and an adjuvant to the beta-blockers. Nevertheless, up to date, there is no consensus regarding its actual value or what the best pacing technique to be used.

Different electrophysiologic mechanisms may explain the effect of atrial pacing to the AF prevention: heart rate control prevents the arrhythmogenic consequences of bradycardia; the overdrive may prevent atrial premature beats, especially through suppression of automatic foci; multisite atrial pacing corrects the asynchrony and the nonuniform activation resulting from organic or functional conduction blocks, and may contribute to preventing the occurrence of macroreentry. Multisite atrial pacing may also increase the coupling interval of the premature beat in the

abnormal substrate. Finally, a number of studies suggest that any treatment that effectively prevents the AF participates in a remodeling process of the electrophysiologic substrate, which subsequently enhances the preventive effect of the original treatment.

Saksena *et al.* [30] showed the effectiveness of multisite right atrial pacing in patients with AF who were drug-refractory. On the other hand, in a study by Kurz *et al.* [31] initially designed to examine 200 patients under biatrial synchronous pacing (BSP) was prematurely stopped after patient 21 because of the proarrhythmic effect of BSP, which provoked AF in six patients.

The present study allowed safe atrial pacing in the great majority of the patients resulting in a 2.5%-loss of atrial command, which corresponds to two cases in the RA group. It is worthy mention that the choice of the right atrium lateral wall as pacing sites to fix the electrodes took into consideration the wide reproducibility of this technique due to the facility of access and the lower complication risk in attempting to obtain a good adherence to the method by the surgeons.

The number of patients enrolled, superior to the series considered in the literature, showed a reduction of 25% in the NP group to 1.25% in the RA group. The temporary artificial atrial non-pacing was identified as an independent risk factor for the occurrence of AF following on-pump CABG

Regarding the in-hospital mortality rate recorded in our study (3.75%), it was verified that it was compatible with the literature data (2.71%) for the age group from 60 to 64 years following on-pump CABG [31].

The results of the present study are in accordance with those of recent studies tending to a consensus confirming the preventive effect of atrial pacing contributes to AF prevention in the immediate postoperative period of on-pump CABG surgery, thus reducing the morbidity and the mortality, as well as the hospital length of stay.

CONCLUSIONS

The electrical right atrial pacing isolated was effective in preventing AF in postoperative period of on-pump CABG surgery. Older age and the absence of electrical pacing were the most significant independent predictive factor for the postoperative AF onset.

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