Chronotropic response to exercise after pulmonary veins isolation or Cox-maze operation

Resposta cronotrópica ao exercício após isolamento das veias pulmonares ou cirurgia de Cox-maze

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Abstract

Objective: To evaluate the chronotropic response to exercise during immediate and late postoperative period after atrial fibrillation and mitral valve surgical treatment by different techniques.

Methods: Prospective controlled clinical study of 42 patients presenting chronic AF associated mitral valve disease, who underwent surgery by the techniques of pulmonary veins isolation (n=16), Modified Cox-maze procedure, without crioablation (n=13), both with isolated mitral valve repair (n=13). The preoperative clinical characteristics, surgical indications, kind and aetiology of valve lesion were similar between groups. The patients were outpatient followed-up and underwent series of ergometric tests.

Results: In the immediate postoperative period, chronotropic response was similar in the 3 groups with mean of 73.6 \pm 12.3% of maximal calculated heart rate. In the surgical pulmonary veins isolation group, there was an increment of heart rate, from 64.4 \pm 12.4% of maximal heart rate in the immediate postoperative period to 78.9 \pm 10.5% in the 12th month (*P*=0.012) of postoperative. In the Coxmaze group, heart rate varied, respectively, from 73.9 \pm 11.14% to 78.8 \pm 15.2% *P*=1.000) and in the control group (only mitral valve surgery), from 67.2 \pm 14.3% to 71.9 \pm 12.9% (*P*=0.889).

Conclusion: An attenuation of immediate postoperative chronotropic response to exercise was similar in the postoperative in the three different surgical techniques. There was a significant improvement in this response concerning to postoperative outcome in the pulmonary veins isolation group. These results suggest that simple surgical pulmonary veins isolation may be related to a better preservation of atrial chronotropism.

Descriptors: Atrial fibrillation. Cardiac surgical procedures. Mitral valve. Heart rate.

Resumo

Objetivo: Avaliar a resposta cronotrópica ao exercício nos períodos pós-operatório imediato e tardio, após tratamento cirúrgico de fibrilação atrial e valva mitral por técnicas distintas.

Métodos: Estudo clínico prospectivo controlado, com amostra de 42 pacientes, portadores de fibrilação atrial

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crônica associada à valvulopatia mitral, submetidos a cirurgia pela técnica de isolamento de veias pulmonares (n=16), pela técnica do labirinto (Cox-maze modificado, sem uso de crioblação) (n=13), ambas com correção de valvulopatia mitral, ou para correção de valvulopatia isolada (n=13). As características clínicas pré-operatórias, indicações para cirurgia tipo e etiologia da lesão valvar foram semelhantes entre os três grupos. Os pacientes foram acompanhados em ambulatório e submetidos a testes ergométricos seriados.

Resultados: A resposta cronotrópica no pós-operatório imediato foi semelhante nos grupos analisados, em média 73,6% \pm 12,3% da freqüência cardíaca máxima prevista. No grupo de isolamento das veias pulmonares, houve aumento de 64,4% \pm 12,4% da freqüência cardíaca máxima, no pósoperatório imediato, para 78,9% \pm 10,5% no 12° mês de pósoperatório (P=0,012). No grupo Cox-maze, a freqüência cardíaca máxima variou de 73,9% ± 11,14% para 78.8% ± 15,2% (P=1,000) e no grupo controle (apenas correção da valva mitral), de 67,2% ± 14,3% para 71,9% ± 12,9% (P=0,889).

Conclusão: A atenuação pós-operatória imediata da resposta cronotrópica ao exercício foi semelhante no pósoperatório das três diferentes técnicas cirúrgicas. Houve melhora significativa da mesma, na evolução pós-operatória, no grupo de isolamento das veias pulmonares. Estes resultados sugerem que o procedimento de simples isolamento cirúrgico das veias pulmonares pode estar relacionado à melhor preservação do cronotropismo atrial.

Descritores: Fibrilação atrial. Procedimentos cirúrgicos cardíacos. Valva mitral. Frequência cardíaca.

INTRODUCTION

The pathophyslology of atrial fibrillation has become more clearly understood only in recent years. Häissaguerre et al. [1] showed the existence of ectopic foci triggering episodes of paroxysmal atrial fibrillation inside the pulmonary veins. The authors also showed that ectopic foci from the pulmonary veins can restart atrial fibrillation after electrical cardioversion, and their ablation can prevent atrial fibrillation recurrence.

The Cox-Maze III surgery [2] is still the gold standard of treatment for atrial fibrillation; however, due to its technical complexity, this procedure is often not performed.

A systematic review was recently published [3], in which 3,832 patients who underwent Cox-maze III surgery with or without the use of energy sources were examined. It found similarities in the rates of conversion to sinus rhythm with the classical technique and the use of energy sources. The aforementioned review found lower postoperative heart rate in patients with permanent AF.

Some studies have been performed, aiming to create more simple and feasible surgical techniques. The Cox-Maze technique was described for sources of energy for ablation and other pulmonary veins isolation [4, 5], from which the surgical isolation without using energy sources for ablation has been chosen by our group, because the favorable results [6].

The heart rate and chronotropic response to exercise may be reduced or impaired after atrial fibrillation surgical correction. In extreme cases, the implant of atrial or AV pacemakers has been required [7-9].

In this series, we aimed to assess chronotropic response by comparing the patients' evolutions after 3 different surgical techniques: pulmonary vein isolation, the Maze procedure (a modified version of the Cox-Maze procedure), and, as the control group, the simple correction of mitral valve lesions without intervention in the atria.

METHODS

Samples and Experimentation

The study analyzed data from 42 patients who had undergone serial ergometric tests in the postoperative period from a larger group of 60 cases randomly selected from a randomized clinical study of patients referred for mitral valve surgical correction. All patients fulfilled all clinical and hemodynamic criteria for elective surgery. The criteria for inclusion in this study were: between 18 and 80 years of age and present permanent chronic atrial fibrillation documented in electrocardiograms for more than 6 months. Exclusion criteria: previous heart surgery (verified by presence of pericardial adhesions), pregnancy, or ejection fraction below 20%. We excluded 18 of the 60 patients who did not perform the initial series of ergometric tests required postoperatively for several reasons.

Thus, the sample was composed of 42 patients divided into three groups; namely:

1) Valve correction plus simplified technique for pulmonary vein isolation (PVI Group), n=16.

2) Valve correction plus Maze surgery using modified Coxmaze III technique without cryoablation (Cox Group), n=13.

3) Valve correction without associated procedure (control group), n=13.

All patients received follow-ups in the postoperative period in a specific outpatient clinic. They received regular consultations after surgery. There were assistant physicians in the cardiology outpatient clinic and in the emergency room of the RS Institute of Cardiology when necessary.

If, after surgery, the patient remained in atrial fibrillation, reversion through amiodarone therapy was performed, and, if ineffective, an electrical cardioversion with a shock of 200 Joules was also performed. A second shock of 300 Joules was performed if the first shock was not effective.

If, after being in sinus rhythm, the patient presents a return of atrial fibrillation, he or she was withdrawn from the study. We considered as valid only the postoperative period between the beginning of sinus rhythm and the patient's withdraw.

Ergometry was requested in consultations 2, 6, 12, 18 and 24 months after surgery, according to previous protocol and in order to examine chronotropic response in the early, intermediate, and late postoperative. It was performed only in patients who were in sinus rhythm.

The Bruce Treadmill Test was used to retrieve ergometry data.

After ergometry, the patients were classified by the chronotropic response as follows: appropriate chronotropic response during effort if reaching 85% of predicted for age; attenuated chronotropic response if reaching between 70% and 85% of predicted for age; and inadequate chronotropic response if below 70% of the predicted rates. All ergometries were performed in the Non-Invasive Methods Unit of the RS Institute of Cardiology, and the technicians involved were not accompanied by any of the other researchers from this study.

The significance level in the study was α =0.05 (P<0.05). The data were processed and analyzed with the aid of the following softwares: Microsoft Excel XP, Epi-Info version 6.0 and SPSS for Windows®, version 8.0.

Ethical standards

This study was submitted for analysis by the Research Ethics Committee of the Institute of Cardiology of RS, following the guidelines of the Research Unit/Board of Directors of IC/FUC from April 1999. We followed the ethical rules of Resolution 196/96 of the National Health Council of the Ministry of Health. The patients were included in the study only after signing a written informed consent.

RESULTS

The mean age of the 42 patients who underwent ergometry was 53.3 ± 10.7 years. Permanent atrial fibrillation was present for 6 to 132 months and was operated by the same surgical team. 33.3% of the patients (n=14) were males, with 5 men in the PVI Group (31.3%), 4 men in the Cox Group (30.8%) and 5 men in the control group (38.5%), (p = 0894).

There were a series of recommendations for surgeries. Mitral stenosis was recommended for 9 (56.3%) patients in the PVI Goup, 8 (61.5%) patients in the Cox Group and 3 (23.1%) patients in the control group. Mitral insufficiency was recommended for 4 (25%) patients in the PVI group, 4 (30.8%) patients in the Cox Group and 7 (44.2%) patients in the control group. Double lesion was recommended for 3

Statistical analysis

The categorical data were described in terms of frequencies and percentages. Quantitative variables were described by the mean \pm standard deviation and median and the interquartile range (25th and 75th percentiles). By performing the comparison between groups (considering the categorical data) the chi-square test and Fisher's exact test were used.

Quantitative data were analyzed using the technique of variance analysis for repeated measures, using the *post-hoc* (Duncan) test when necessary. In certain cases, analysis of variance (ANOVA) and also the Student's t-test were used for independent samples.

Table 1.	Preoperative	Clinical	Charact	eristics

	PVI	Cox	Control	Total	
Characteristics	n=16	n=13	n=13	n=42	Р
Age (in years)	53.12±8.65	51.16±8.83	$55.83{\pm}14.60$	53.35±10.69	0.574
Gender-%M	31.3 (n=5)	30.8 (n=4)	38.5 (n=5)	33.3 (n14)	0.894
Time of previous AF	24.00	24.00	13.00	18	
(in months)	(14.25-49.5)	(8-49.5)	(11-17)	(11-36)	0.116
LA (in cm)	5.35±0.79	5.30 ± 1.12	5.54 ± 0.75	5.39 ± 0.86	0.820
NYHA	2.87 ± 0.61	2.63 ± 0.80	3.00 ± 0.60	2.84 ± 0.67	0.698
Mitral lesion in %					0.262
Stenosis (in %)	56.3(n=9)	61.5(n=8)	23.1(n=3)	45.2(n=20)	
Insufficiency (in %)	25(n=4)	30.8(n=4)	44.2(n=7)	35.7(n=15)	
Double-lesion (in %)	18.7(n=3)	7.7(n=1)	32.7(n=3)	19.1(n=7)	
Surgery (in %)					
performed, %					0.698
Mitral prosthesis	31.3(n=5)	41.7(n=5)	46.2(n=6)	39(n=16)	
Mitral repair	68.8(n=11)	58.3(n=8)	53.8(n=7)	39(n=26)	

AF: atrial fibrillation; LA: left atrium; NYHA: functional class. Data were presented as mean \pm Standard deviation, rate (%) and median (p25-75). P= analysis of variance (ANOVA) for quantitative variables and chi-square for categorical variables

(18.7%) patients in the PVI group, 1 (7.7%) patient in the Cox Group, and 3 (32.7%) patients in the control group.

The variables of age, gender, time of previous atrial fibrillation, left atrium size, functional class, associated surgery and type of valve lesion were similar in the three groups (Table 1).

Ergometry

Postoperatively, the ergometric test was performed in patients who were in sinus rhythm. The results of chronotropic response tests for each group in the



Fig. 1 – Chronotropic response expressed in percentage of expected heart rate, by time, group; P=0.0012 for PVI group (IVP); the others NS (ANOVA)

postoperative period can be seen in Table 2 and Figure 1.

Left atrium

During the preoperative period, the left atrium size (in centimeters) in the PVI Group was 5.35 ± 0.79 , 5.30 ± 1.12 in the Cox Group, and 5.54 ± 0.75 in the control group (P= 0.820).

When comparatively analyzed, the left atrium size in the preoperative period $(5.39 \pm 0.86 \text{ cm})$ in the 2nd postoperative month showed a statistically significant difference, with P<0001 (Figure 2 and Table 3).



Fig. 2 – *Left atrium size (tamanho do atrio esquerdo) by time (tempo) and randomization group*

Table 2. Chronotropic Response by Group Expressed in Percentage of Maximum Heart Rate

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	PVI n=16	Cox n=13	Control n=13	Total n=42	
R Chrono	(% FC máx)	(% FC máx)	(% FC máx)	(% FC máx)	Р
2 nd mnth PO	64.4 ± 12.14	73.8 ±11.4	67.2±14.3	67.64±12.46	0.416
6 th mnth PO	69.6±9.9	77.3±15.6	73.3±9.4	73.6±12.2	0.408
12 th mnth PO	78.9±10.5	78.8±15.2	71.9±12.9	76.57±12.76	0.432
Р	0.012	1.000	0.889	0.003	-

R Chrono: chronotropic response. PO: Postoperative time Data are presented as mean \pm standard deviation

P= analysis of variance (ANOVA)

Table 3. Left Atrium Size by Group

	PVI	Cox	Control	Total	
LA (cm)	n=16(cm)	n=13(cm)	n=13(cm)	n=42 (cm)	Р
Preoperative	5.35±0.79	5.30±1.12	5.54±0.75	5.39±0.86	0.820
2 nd mnth PO	4.49 ± 0.49	4.92 ± 0.99	4.82 ± 0.82	4.72 ± 0.76	0.408
6 th mnth PO	4.49 ± 0.98	5.10 ± 0.96	4.64 ± 1.11	4.72 ± 0.76	0.366
12 th mnth PO	4.6 ± 0.8	5.07 ± 1.08	4.78 ± 0.89	4.81 ± 0.90	0.599
Р	0.001	0.053	0.001	0.002	-

LA: left atrium; PO: Postoperative time. Data are presented as mean \pm *standard deviation* P= *analysis of variance (ANOVA)*

DISCUSSION

The intervention into the atria - necessary for correcting atrial fibrillation - could impair the atrial contractility and the sinoatrial node function. These factors could reduce the clinical benefit of restoration of sinus rhythm after surgery for atrial fibrillation.

Pulmonary vein isoltaion by itself has been ineffective for treating chronic permanent AF. The addition of line block, which excludes the atrial posterior wall between the right and left veins (beyond the line of ablation or incision up to the mitral annulus) seems to be mandatory for restoring sinus rhythm [10]. In this series, the technique of surgical PVI included such lines of block, by cutting and suturing of the atrial wall. Thus, the block produced includes not only the pulmonary veins, but also the left atrial posterior wall. Recent electrophysiological studies used spectral mapping to identify areas of compact and fibrillar myocardium in the atrial wall [11], which hosted "AF-Nests." These cause arrhythmia. It is possible that the complete PIV technique may block many of these nests, contributing to better results.

The function of atrial transport has been studied in these cases. In a series that uses radio frequency in patients with a rheumatic mitral valve, rates of restoration of atrial contractility were noted in 90.3% of patients who were maintained in sinus rhythm [12].

In 1996, Cox et al. published results of eight and a half years of Maze surgeries, reporting that, out of 164 patients, 50 (30%) used a permanent pacemaker after surgery. Of these 50, 18% presented previous sinus dysfunction, and 12% had had pacemaker for transoperative AV block [13].

Sueda et al. developed a surgical technique for the treatment of chronic atrial fibrillation (AF) that involves mainly the LA posterior region in patients with mitral valve disease. In this study, at 6 postoperative months, 78% of patients had no AF, and 61% had recovered the left atrial contractility [4].

In their study, Imai et al. [14] reported that, after pulmonary vein isolation surgery, 5 (21%) patients needed a permanent pacemaker implant for atrial fibrillation.

Radiofrequency and cryothermia energy sources have been used to produce lines of block, further simplifying the PVI procedure, also known as "left Maze". The outcomes for restoring rhythm in these cases has been close to the classical Cox-maze procedure, especially if all lines of the left atrium are produced [15]. However, Reports of sinus node or sinoatrial dysfunction persist. In a recent study, Tuinenburg et al. [16] found that the reduction of variability of heart rate and vagal modulation of sinus node function occurred not only after Cox-maze surgery, but also after correction of mitral valve lesions.

Vasconcelos et al. (2004) reported results of a

randomized study with a control group of 15 patients (treated group) and 14 patients (control group), in which only one patient (in the treated group) developed significant postoperative sinus bradycardia, requiring the pacemaker implant [17].

In 2006, Canale et al. [18], reported that 5 of the 7 patients operated on for the associated treatment of atrial fibrillation (mini-Maze) and valvular disease, presented appropriate atrial contraction, but 1 out of 7 patients from their initial series presented sinus bradycardia, requiring a permanent pacemaker.

Sinus node dysfunction after Cox-Maze surgery was considered temporary [19], because studies on patients operated for chronic atrial fibrillation secondary to organic lesion demonstrated dysfunction in 12 of 15 cases at 3 postoperative months, with progressive improvement until the patient reached 12 postoperative months. The chronotropic response to exercise was reduced during the first 6 months and became normal at 12 months.

Advances in understanding the mechanisms involved in recovering of sinus function and chronotropic response were obtained by the same group of researchers above [9]. These researchers studied a series of 30 patients undergoing Cox-Maze surgery, compared to 15 heart transplant patients. The physiological effect of denervation was observed in both groups of patients in the immediate postoperative period, with no difference between Cox-Maze patients and transplant patients. Later, the effects of autonomous reinnervation were noted only in the Cox-Maze group. Inappropriate response to the exercise was evident until the third month in both groups, with progressive improvement at 6 and 12 months only in the Cox-Maze group. Left atrial function improved in parallel with the recovery of sinus function.

In this study 42 patients undergoing surgical treatment for atrial fibrillation were observed. These patients included a group operated on using the modified Cox-Maze III technique (without using of cryoablation), a group that underwent the pulmonary vein isolation (PVI) technique, and a third group in which the isolated mitral valve disease was treated. Out of these 42 patients, the use a permanent pacemaker was necessary in two patients. One belonged to the PVI Group, and the other was from the control group.

Limitations of the Study

No tests were performed preoperatively. Therefore, it is not possible to assess for sure whether the chronotropic impairment was due to the procedure or to the underlying disease. However, because the groups are similar to each other, improvement in chronotropism was observed in the long term in the PVI Group.

CONCLUSION

Chronotropic incompetence in exercise in the immediate postoperative period was similar in the three different surgical techniques assessed. There was significant improvement in chronotropic response to exercise in the late postoperative evolution in the PVI Group. These results suggest that the surgical procedure for simple pulmonary vein isolation can be related to better preservation of atrial chronotropism.

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