

Effect of ventral cardiac denervation in the incidence of atrial fibrillation after coronary artery bypass graft surgery

Efeito da denervação cardíaca ventral na incidência de fibrilação atrial após revascularização cirúrgica do miocárdio

João Roberto BRED¹, Ana Silvia Castaldi Ragnetti BRED², Andréa Cristina Oliveira FREITAS³, Adriano MENEGHINI⁴, Carlos Mendes TAVARES⁵, Luís Carlos de ABREU⁶, Neif MURAD⁶, Adilson Casemiro PIRES⁷

RBCCV 44205-975

Abstract

Objective: To evaluate the effect of ventral cardiac denervation on the incidence of atrial fibrillation after coronary artery bypass grafting.

Methods: Between September and November 2005, 50 patients from the same institution, without previous diagnosis of atrial arrhythmia, presenting with coronary heart disease with indication for coronary artery bypass grafting were enrolled in a prospective, randomized study. The exclusion criteria were: patients older than 75 years of age, previous history of atrial arrhythmia and associated heart surgeries. Denervation was performed before cardiopulmonary bypass by removing the adipose tissues around the superior vena cava, aorta and pulmonary artery. Patients submitted to denervation were compared with a control group regarding demographic, clinical and operative variables.

Results: There were no hospital mortalities. The additional time for denervation was 7.64 ± 2.33 minutes, and there were no associated complications. Postoperative atrial fibrillation occurred in two (8%) patients of the Control Group and in three (12%) patients who underwent ventral cardiac denervation. The risk of postoperative atrial fibrillation in patients undergoing ventral cardiac denervation was 22% higher than in the Control Group (confidence interval: 0.56-2.66); however, this result was not statistically significant ($p=0.64$).

Conclusion: Ventral cardiac denervation, despite being a fast and low-risk procedure, does not significantly reduce the incidence of atrial fibrillation after coronary artery bypass grafting.

Descriptors: Atrial fibrillation/prevention & control. Denervation. Coronary artery bypass grafting.

1. PhD. Collaborating professor
2. Specialist in Cardiology; Cardiologist
3. Cardiovascular surgeon
4. Master; Cardiologist
5. Master; Statistician
6. PhD student; Assistant professor
7. professor

Work carried out in the Cardiovascular Section of the ABC Foundation Medicine School, Santo André, Sao Paulo, Brazil

Correspondence address:

João Roberto Breda. Rua Antonio Bastos, 755 - Apto. 31 - Santo André, SP - Brazil - CEP: 09040-220. Tel.: (11) 4345-4011.

E-mail: jrbreda@hotmail.com.br

Article received on December 17th, 2007

Article accepted on May 21st, 2008

Resumo

Objetivo: Verificar o efeito da denervação cardíaca ventral na incidência de fibrilação atrial no pós-operatório de revascularização cirúrgica do miocárdio.

Métodos: Entre setembro e novembro de 2005, 50 pacientes consecutivos da mesma instituição foram alocados neste estudo prospectivo e randomizado. Foram selecionados pacientes portadores de insuficiência coronariana com indicação de revascularização cirúrgica do miocárdio, sem história ou diagnóstico prévio de arritmia atrial. Os critérios de exclusão foram: idade acima de 75 anos, história prévia de arritmia atrial e operações cardíacas associadas. A denervação era realizada antes do início da circulação extracorpórea pela remoção do tecido gorduroso ao redor da veia cava superior, aorta e artéria pulmonar. Os grupos foram comparados de acordo com as características clínicas, demográficas e variáveis operatórias.

Resultados: Não houve mortalidade hospitalar em ambos os grupos. O tempo médio adicional para realização da denervação foi de 7,64 + 2,33 minutos e não houve complicações associadas ao procedimento. Cinco pacientes apresentaram fibrilação atrial no pós-operatório, sendo dois (8%) no grupo controle e três (12%) no grupo denervação. O risco dos pacientes do grupo denervação apresentarem fibrilação atrial foi 22% maior do que no grupo controle (intervalo de confiança, 0,56-2,66), porém, este resultado não foi estatisticamente significativo (p=0,64).

Conclusões: A denervação cardíaca ventral, apesar de rápida execução e de baixo risco, não apresentou efeito na redução da incidência de fibrilação atrial no pós-operatório de revascularização cirúrgica do miocárdio.

Descritores: Fibrilação atrial/prevenção & controle. Denervação. Revascularização miocárdica.

INTRODUCTION

Atrial fibrillation (AF) is the most common sustained atrial tachyarrhythmia in clinical practice and presents with a high morbidity rate due to its hemodynamic involvement and the possibility of the occurrence of thromboembolic phenomena [1].

After coronary artery bypass grafting (CABG) the incidence of AF varies from 19 to 27% and is the most common morbidity after this surgery [2]. Thus, with the growing interest in understanding the physiopathologic basis responsible for the occurrence of this arrhythmia, operative techniques have been developed aiming at reducing its incidence [3].

Alterations in the autonomic nervous system after heart surgery have been presented as a possible factor responsible for the development of this phenomenon [4,5].

The aim of this work was to verify the effect of ventral cardiac denervation on the incidence of atrial fibrillation in the postoperative period of CABG.

METHODS

From September to November 2005, 50 consecutive patients, from the same institution, were enrolled in a prospective, randomized study. Patients with heart failure and indication for CABG but without prior diagnosis of atrial arrhythmia were selected.

Exclusion criteria were patient's age greater than 75 years old, previous history of atrial arrhythmia and the necessity of associated heart procedures other than CABG.

The patients were allocated to two equal groups of 25 patients: those submitted to ventral cardiac denervation and a control group for which denervation was not performed. The clinical and demographic characteristics of the two groups are described in Table 1.

All patients agreed to participate in the study by signing informed consent forms.

Table 1. Demographic and clinical characteristics of the patients

Variables	Control Group	Denervation Group	p-value
Gender (%)			
Female	36	48	0.39
Male	64	52	
Age (years)	59.4 ± 7.57	57.6 ± 13.9	0.564
Arterial hypertension (%)	68	88	0.083
Diabetes mellitus (%)	32	48	0.248
Left main coronary artery disease (%)	12	12	1.0
Three-vessel disease (%)	52	64	0.390
Two-vessel disease (%)	20	20	1.0
Single vessel disease (%)	16	4	0.157
Ventricular function (%)			
Good >50	80	80	1.0
Moderate [30-50]	16	16	1.0
Bad < 30	4	4	1.0
Pre-operative magnesium (mmol)	1.96 ± 0.27	1.92 ± 0.21	0.53
Beta-blocker (%)	92	92	1

Operative technique

The surgery began with hemodynamic monitoring with measurement of the mean arterial pressure, central venous pressure and urinary output, as well as respiratory monitoring by pulse oximetry.

After median sternotomy and exposure of the heart, ventral cardiac denervation was performed in patients of the denervation group, by removal of the nerves around the great vessels at the base of the heart, initiating the procedure on the right with the superior vena cava and finishing in the medial region with the pulmonary artery. Adipose tissue, surrounding these structures, was removed (Figure 1). The level of denervation was assessed by anatomopathological examinations of specimens obtained after denervation which were considered adequate fragments of adipose tissue when the thickness was greater than 0.50 centimeters.

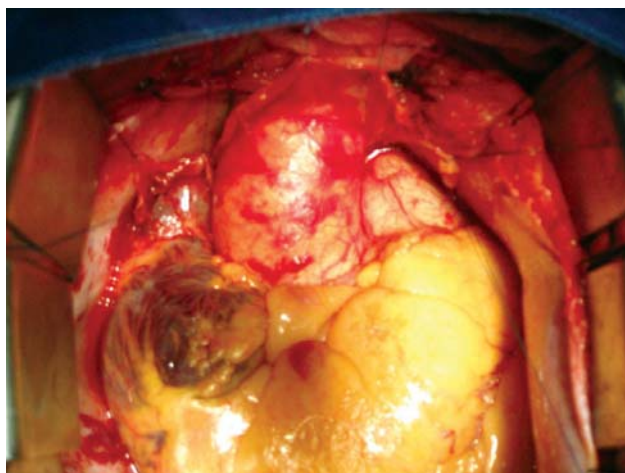


Fig. 1 - Ventral cardiac denervation with removal of the adipose tissue around the superior vena cava, ascending aorta and pulmonary artery

After ventral cardiac denervation, CABG was performed (with or without cardiopulmonary bypass) under light hypothermia using controlled hypoxia with intermediate aortic clamping as myocardial protection.

The groups were compared in respect to the operative data (Table 2).

All the patients were accompanied during the hospital evolution by a single member of the surgical team and the diagnosis of atrial fibrillation in the postoperative period was based on clinical signs and on an analysis of electrocardiograms performed daily for all patients.

Table 2. Operative data

Variables	Denervation Group	Control Group	p-value
CPB (%)			
without	4	12	
with	96	88	0.305
Number of grafts per patient	2.92 ± 0.81	2.48 ± 0.82	0.063
Anoxia time (minutes)	45.7 ± 13.8	44.0 ± 16.8	0.68
Perfusion time (minutes)	71.28 ± 19.4	64.48 ± 25.76	0.29
Denervation (minutes)	7.64 ± 2.33	-	-

Statistical analysis

The following statistical methods were utilized to analyze the results:

- Descriptive statistics utilizing measurements of location and spread;
- Test of normality by means of the normal probability plot with adjusted residuals to check the supposition of normality of the distribution of age in both groups;
- Heterocedasticity test to verify the supposition that there are no differences in the variances by means of the residual plot with adjustments;
- The Pearson chi-squared test, or Fisher Exact test when the former was not adequate, to study the association between success and failure in groups;
- The Student t-test to compare the means of the two groups;
- Relative risk to verify associations between variables.

RESULTS

There were no hospital deaths in either of the two groups of patients in this study.

The additional mean time to perform denervation was 7.64 ± 2.33 minutes with no complications associated to the procedure (Table 3).

There was no excessive bleeding in either of the two groups and the drainage volume over 24 hours was similar for both groups (Table 3).

Of the total of 50 patients, five presented with atrial fibrillation in the postoperative period; two (8%) cases in the Control Group and 3 (12%) in the denervation Group. The risk of patients in the Denervation Group presenting with atrial fibrillation was 22% higher than that of the Control Group (confidence interval: 0.56 – 2.55), however this result was not statistically significant (p-value = 0.64) – Table 3.

Table 3. Postoperative data

	Denervation Group	Control Group	p-value
Drain outflow (mL)	513 ± 251	520 ± 235	0.93
Postoperative magnesium (mmol)	1.92 ± 0.22	1.96 ± 0.27	0.53
AF (%)			
Yes	12	8	
No	88	92	0.64

All the patients were released from hospital in sinus rhythm and there was no great difference in the hospitalization time of patients from both groups (Control Group 7.28 ± 1.68 days and Denervation Group 7.44 ± 1.69 days), even for those who presented with AF.

DISCUSSION

The peak incidence of AF occurs on the second and third postoperative days in heart surgeries with 50% of the patients maintaining arrhythmia up to hospital release [6,7]. AF is the most common cardiac arrhythmia in the postoperative period of heart surgery and, although in most cases it presents as a self-limiting clinical condition, it may increase the hospitalization time and hospital costs [8].

The most frequent risk factor associated with postoperative AF is greater age; over 70-year-old patients are considered high risk for the occurrence of AF after heart surgery. Other factors such as gender, hypertension, duration of cardiopulmonary bypass, pre- and post-operative levels of magnesium and the use of amiodarone have been considered important in the occurrence of AF, even though the data about their real significance remain controversial [9,10].

The value of the prophylactic administration of magnesium to reduce the incidence of supraventricular arrhythmia after heart surgery was evaluated in a metanalysis of 2069 patients. This drug reduced the incidence of AF in 29% and of ventricular arrhythmia in 48% however, it did not reduce the time of hospitalization, the incidence of myocardial infarction or the mortality rate [11]. Another randomized study of 202 patients also concluded that the prophylactic administration of magnesium did not benefit patients sufficiently to recommend its routine utilization in heart surgeries [12].

The efficacy of the use of sotalol was compared to the administration of atenolol in the prevention of AF. A randomized study of 253 patients showed a reduction in the incidence of AF with both drugs (sotalol being more effective) however the pro-arrhythmogenic effect of these

drugs remains uncertain [13]. In another study, Wanderley et al. [14], comparing the use of low-dose propranolol and sotalol in the postoperative period of CABG and obtained an overall incidence of AF of 7.1% which was lower in the group taking sotalol but without significant statistical difference. Ventral cardiac denervation, described by Arnulff in 1936, was widely employed in the prevention of coronary artery spasms in the 1970s. Several works about the safety of the procedure were published although the post-operative rhythm was not mentioned [15].

The high incidence of AF after CABG justifies the search for a fast and safe procedure capable of preventing this arrhythmia [5].

On performing this operation, Melo et al. [16] concluded that ventral cardiac denervation is a low-risk procedure that significantly reduces the incidence of AF in the postoperative period of CABG. The role of denervation was analyzed in 207 patients in their study with a non-randomized control group being formed of 219 patients. The two groups presented with similar demographic characteristics. Post-operative AF occurred in 15 (7%) of the denervation cases and in 56 (27%) of the control group (p-value < 0.001). The authors cited the difficulty of diagnosis of arrhythmia as a limitation of the work as the event may be asymptomatic and none of the patients of the study were monitored by telemetry [16].

In contrast to this study, Cummings et al. [17] evaluated the influence of the nerves of the parasympathic nervous system present in the tissue removed during ventral cardiac denervation. A total of 55 patients were submitted to CABG after being randomized for denervation or not. After the surgery, by means of stimulation to prolong the length of the sinus cycle, it was observed that the patients submitted to ventral cardiac denervation did not obtain increases with stimulation. Thus, for the patients submitted to denervation, the incidence of AF was 37% against 7% for the control group. The authors suggested that the removal of adipose tissue during denervation increased the risk of AF in the postoperative period [17].

In our study, we noted a greater occurrence of AF in patients submitted to ventral cardiac denervation. Although the difference between the two groups was not statistically significant (p-value = 0.64), the risk was 22% higher for the occurrence of AF in the Denervation Group when compared to the Control Group (confidence interval: 0.56 – 2.66). The anatomopathological examination was utilized after the procedure to assess adipose tissue fragments with sizes greater than 0.50 centimeters being considered adequate [18]. In this study we did not identify predictive factors associated with the manifestation of AF in patients, who presented with this arrhythmia, of either group. This must be related to the homogeneity of the sample. Nevertheless, on interpreting the results, the small sample size and the

difficulty of diagnosing the paroxysmic events of arrhythmia, since telemetry was not utilized, must be taken into account.

Although the procedure proved to be simple, fast and without operative complications, a reduction in postoperative AF was not confirmed.

Hence, ventral cardiac denervation did not reduce the incidence of AF in the postoperative period of patients submitted to CABG. Additional prospective studies, with a larger number of patients and more accurate methods of diagnosis of AF are necessary to confirm the results obtained in this study.

REFERENCES

1. Gillinov AM, Blackstone EH, McCarthy PM. Atrial fibrillation: current surgical options and their assesment. *Ann Thorac Cardiovasc Surg.* 2002;74(6):2210-7.
2. Hogue CW Jr, Domitrovich PP, Stein PK, Despotis GD, Re L, Schuessler RB, et al. RR interval dynamics before atrial fibrillation in patients after coronary artery bypass graft surgery. *Circulation.* 1998;98(5):429-34.
3. Gillinov AM, McCarthy PM, Marrouche N, Natale A. Contemporary surgical treatment for atrial fibrillation. *Pacing Clin Eletrophysiol.* 2003;26(7 Pt 2):1641-4.
4. Kalman JM, Munuwar M, Howes LG, Louis WJ, Buxton BF, Gutteridge G, et al. Atrial fibrillation after coronary artery bypass grafting is associated with sympathetic activation. *Ann Thorac Surg.* 1995;60(6):1709-15.
5. Hogue C, Hyder M. Atrial fibrillation after cardiac operation: risks, mechanisms, and treatment. *Ann Thorac Surg.* 2000;69(1):300-6.
6. Maisel WH, Rawn JD, Stevenson WG. Atrial fibrillation after cardiac surgery. *Ann Intern Med.* 2001;135(12):1061-73.
7. Loubani M, Hickey MS, Spyt TJ, Galiñanes M. Residual atrial fibrillation and clinical consequences following postoperative supraventricular arrhythmias. *Int J Cardiol.* 2000;74(2-3):125-32.
8. Tineli RA, Rosa e Silva Jr. J, Luciano PM, Rodrigues AJ, Vicente WVA, Évora PRB. Fibrilação atrial e cirurgia cardíaca: uma história sem fim e sempre controversa. *Rev Bras Cir Cardiovasc.* 2005;20(3):323-31.
9. Svedjeholm R, Hakanson E. Predictors of atrial fibrillation in patients undergoing surgery for ischemic heart disease. *Scand Cardiovasc J.* 2000;34(5):516-21.
10. Amar D, Zhang H, Leung DH, Roistacher N, Kadish AH. Older age is the strongest predictor of postoperative atrial fibrillation. *Anesthesiology.* 2002;96(2):352-6.
11. Shiga T, Wajima Z, Inoue T, Ogawa R. Magnesium prophylaxis for arrhythmias after cardiac surgery: a meta-analysis of randomized controlled trials. *Am J Med.* 2004;117(5):325-33.
12. Hazelrigg SR, Boley TM, Cetindag IB, Moulton KP, Trammell GL, Polancic JE, et al. The efficacy of supplemental magnesium in reducing atrial fibrillation after coronary artery bypass grafting. *Ann Thorac Surg.* 2004;77(3):824-30.
13. Sanjuán R, Blasco M, Carbonell N, Jordá A, Núñez J, Martínez-León J, et al. Preoperative use of sotalol versus atenolol for atrial fibrillation after cardiac surgery. *Ann Thorac Surg.* 2004;77(3):838-43.
14. Wanderley JF, Lamprea D, Moraes CR, Moraes F, Tenório E, Gomes CA, et al. Profilaxia de fibrilação atrial no pós-operatório imediato de cirurgia coronária: comparação entre propranolol e sotalol utilizados em baixas doses. *Rev Bras Cir Cardiovasc.* 2001;16(4):350-3.
15. Arnulff G. De la section du plexes pré-aortique: justification et technique. *Presse Med.* 1939;94:1635-41.
16. Melo J, Voigt P, Sonmez B, Ferreira M, Abecasis M, Rebocho M, et al. Ventral cardiac denervation reduces the incidence of atrial fibrillation after coronary artery bypass grafting. *J Thorac Cardiovasc Surg.* 2004;127(2):511-6.
17. Cummings JE, Gill I, Akhrass R, Dery M, Biblo LA, Quan KJ. Preservation of the anterior fat pad paradoxically decreases the incidence of postoperative atrial fibrillation in humans. *J Am Coll Cardiol.* 2004;43(6):994-1000.
18. Alex J, Guvendik L. Evaluation of ventral cardiac denervation as a prophylaxis against atrial fibrillation after coronary artery bypass grafting. *Ann Thorac Surg.* 2005;79(2):517-20.