

Abnormal heart rate variability and atrial fibrillation after aortic surgery

Variabilidade anormal da frequência cardíaca e fibrilação atrial após cirurgia aórtica

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DOI 10.5935/1678-9741.20140100

RBCCV 44205-1614

Abstract

Introduction: Complete denervation of transplanted heart exerts protective effect against postoperative atrial fibrillation; various degrees of autonomic denervation appear also after transection of ascending aorta during surgery for aortic aneurysm.

Objective: This study aimed to evaluate if the level of cardiac denervation obtained by resection of ascending aorta could exert any effect on postoperative atrial fibrillation incidence.

Methods: We retrospectively analysed the clinical records of 67 patients submitted to graft replacement of ascending aorta (group A) and 132 with aortic valve replacement (group B); all episodes of postoperative atrial fibrillation occurred during the 1-month follow-up have been reported. Heart Rate Variability parameters were obtained from a 24-h Holter recording; clinical, echocardiographic and treatment data were also evaluated.

Results: Overall, 45% of patients (group A 43%, group B 46%) presented at least one episode of postoperative atrial fibrillation. Older age (but not gender, abnormal glucose tolerance, ejection fraction, left atrial diameter) was correlated with incidence of postoperative atrial fibrillation. Only among a subgroup of patients with aortic transection and signs of greater autonomic derangement (heart rate variability parameters below the median and mean heart rate over the 75th percentile), possibly indicating more profound autonomic denervation, a lower incidence of postoperative atrial fibrillation was observed (22% vs. 54%).

Conclusion: Transection of ascending aorta for repair of an aortic aneurysm did not confer any significant protective effect from postoperative atrial fibrillation in comparison to patients with intact ascending aorta. It could be speculated that a limited and heterogeneous cardiac denervation was produced by the intervention, creating an electrophysiological substrate for the high incidence of postoperative atrial fibrillation observed.

Descriptors: Autonomic Nervous System. Atrial Fibrillation. Aortic Aneurysm. Heart Rate.

Resumo

Introdução: Denervação completa do coração transplantado exerce efeito protetor contra a fibrilação atrial no pós-operatório; vários graus de denervação autonômica aparecem também após a transecção da aorta ascendente durante a cirurgia de aneurisma da aorta.

Objetivo: Este estudo teve como objetivo avaliar se o nível de denervação cardíaca obtida por ressecção da aorta ascendente poderia exercer algum efeito sobre a incidência de fibrilação atrial no pós-operatório.

Métodos: Foram analisados retrospectivamente os prontuários de 67 pacientes submetidos a enxerto de substituição de aorta torácica (grupo A) e 132 com a substituição da valva aór-

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No financial support.
No conflict of interest.

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Article received on May 7nd, 2014
Article accepted on August 4nd, 2014

Abbreviations, acronyms & symbols	
AF	Atrial fibrillation
AGM	Abnormal glucose metabolism
CABG	Coronary artery by-pass grafting
CR	Cardiac rehabilitation
Hb	Haemoglobin
HR	Heart rate
HRV	Heart rate variability
LVEF	Left ventricle ejection fraction
POAF	Postoperative atrial fibrillation
SDANN	Standard deviation of the 5-min average of normal RR intervals
SDNN	Standard deviation of all normal RR intervals

tica (grupo B). Foram relatados todos os episódios de fibrilação atrial pós-operatória ocorridos durante 1 mês de seguimento. Parâmetros de variabilidade da frequência cardíaca foram obtidos a partir de 24 h de gravação do Holter; dados clínicos, ecocardiográficos e de tratamento também foram avaliados.

Resultados: No geral, 45% dos pacientes (grupo A 43%, grupo B 46%) apresentaram pelo menos um episódio de fi-

INTRODUCTION

Atrial fibrillation (AF) is the most common complication after cardiac surgery procedures; its incidence has been reported to range from 14 to 49% of cases after coronary artery by-pass grafting (CABG)^[1] as well as after aortic or mitral valve surgery^[2,3], with lower incidence after minimally invasive approach compared with median sternotomy surgery^[4].

Pre-existing electrophysiological vulnerability in the atria, injury from atrial ischemia and reperfusion, impairment of sino-atrial node function due to direct trauma to its nervous supply^[5], acute atrial stretch, metabolic derangements and pericarditis are all factors that could contribute to appearance of AF in the early postoperative period^[1].

Oscillations of cardiac autonomic tone play an important role in the modulation of normal cardiac electrophysiology^[6]; fluctuations of autonomic balance have been recognized to precede and accompany the development of perioperative AF (POAF) in patients undergoing cardiac and major thoracic surgery^[7,8].

In heart transplant recipients POAF is uncommon, unless in the setting of myocardial dysfunction or graft rejection; it has been supposed that in heart transplant patients a protective effect is produced by the complete cardiac autonomic denervation that derives from the intervention^[9-11]. It has been demonstrated, as well, that almost total cardiac denervation occurs also after transection of ascending aorta during the switch procedure for correction of transposition of the great vessels, and that a partial denervation occurs after grafting of

brilação atrial no pós-operatório. Idade mais avançada (mas não gênero, tolerância à glicose anormal, fração de ejeção, diâmetro do átrio esquerdo) foi correlacionada com a incidência de fibrilação atrial pós-operatória. Apenas em um subgrupo de pacientes com transecção aórtica e sinais de maior desarranjo autonômico (parâmetros de variabilidade da frequência cardíaca abaixo da mediana e a média de frequência cardíaca acima do percentil 75), indicando possivelmente denervação autonômica mais profunda, foi observada menor incidência de fibrilação atrial pós-operatória (22% vs. 54%).

Conclusão: Transecção da aorta ascendente para correção de um aneurisma da aorta não confere qualquer efeito protetor significativo de fibrilação atrial no pós-operatório em comparação com pacientes com aorta ascendente intacta. Pode-se especular que uma denervação cardíaca limitada e heterogênea foi produzida pela intervenção, criando um substrato eletrofisiológico para a elevada incidência de fibrilação atrial pós-operatória observada.

Descritores: Sistema Nervoso Autônomo. Fibrilação Atrial. Aneurisma Aórtico. Frequência Cardíaca.

ascending aorta/aortic arch for type A aortic aneurysm^[12-16]. If such partial denervation could exert a protective effect against POAF is not yet clear. To our best knowledge, no data are present in literature about the incidence of AF in the early post-operative period after transection of ascending aorta and its relations with the degree of HRV derangement occurring after the surgical procedure.

The aim of this study was to evaluate if the level of cardiac denervation obtained by removal of autonomic nerves and ganglia during substitution of ascending aorta for type A aneurism (evaluated by HRV parameters) could exert any effect on the incidence of AF in the postoperative period.

METHODS

We retrospectively reviewed the clinical records of all the patients consecutively transferred to our residential cardiac rehabilitation unit (CR) in the period January 2008 – August 2013 after graft replacement of ascending aorta and after aortic valve replacement. Exclusion criteria were: pre-existing AF, heart rhythm induced by pace-maker, coexisting cardiomyopathy, incomplete data.

For all patients, history of diabetes, haemoglobin (Hb) level and medications used were registered. To control different effects of various beta-blocker drugs on heart rate (HR), the dosages of beta-blockers were expressed as percentages of target dosage, based on data from clinical trials^[17]. During the third week after intervention, patients without history of diabetes underwent an oral glucose tolerance test, in order to identify subclinical abnormalities of glucose metabolism^[18].

On the day of transferral to CR, all patients were submitted to 24-h Holter recording; cardiac autonomic function was evaluated by time-domain heart rate variability (HRV) on this recording. For the purposes of this study, mean heart rate (mean-HR), standard deviation of all normal RR intervals (SDNN) and standard deviation of the 5-min average of normal RR intervals (SDANN) have been considered.

During the whole hospitalization in cardiac surgery and during at least the first five days of CR, all patients were maintained under continuous telemetry monitoring; all episodes of AF have been recorded.

Left ventricle ejection fraction (LVEF) was assessed by means of two-dimensional transthoracic echocardiogram (Simpson's method in patients with good quality echo windows; area-length method in the other cases); standard atrial dimensions and volume have been recorded, however, for this study, only antero-posterior left atrial diameter has been considered (absolute length and indexed by body surface area)^[19].

Statistical analysis

SPSS 15 Statistics Package for Social Sciences (SPSS Inc., Chicago, Illinois, USA) was used for the analysis. Descriptive statistics are expressed as mean \pm standard deviation for continuous variables; categorical variables are presented as absolute values with percentages.

Continuous variables have been evaluated by means of the Student t test for unpaired samples. Categorical variables were compared using the Pearson chi-square test (χ^2). Statistical significance was set at a probability value of 0.05.

Univariate analysis was performed to assess the association between occurrence of POAF (dependent variable) and demographic, clinical and HRV variables; all variables with a *P* value ≤ 0.2 in the univariate analysis were entered into a multivariate logistic regression model, in which variables were selected by step-wise, backward elimination; a *P* value < 0.05 was considered significant.

Statement

All participants were informed about the procedures they were undergoing. The usual diagnostic and follow-up routine for the CR had been applied; no special test or treatment was performed; no specific approval of the Provincial Ethics Committee was needed for the study.

RESULTS

Table 1 presents the clinical characteristics of the patients, while the main results are summarized in Table 2.

Table 1. Patients characteristics.

	Group A (n=67)	Group B (n=132)	<i>P</i>
Patients' characteristics			
Age, years	59.0 \pm 14.3	68.1 \pm 12.3	<0.001 (0.000)
Gender (male: n, %)	50 (75)	85 (64)	ns (0.144)
Days from intervention to CR	15.3 \pm 11.0	12.9 \pm 8.9	ns (0.101)
Duration of CR, days	14.4 \pm 4.3	15.4 \pm 3.6	ns (0.110)
Total observation period, days	29.8 \pm 11.1	28.3 \pm 9.5	ns (0.295)
Prevalence of Diabetes, n (%)	12 (18)	26 (20)	ns (0.762)
Prevalence of abnormal glucose metabolism, n (%)	18 (27)	54 (41)	ns (0.051)
Hb level, g/l	10.0 \pm 1.0	10.4 \pm 1.1	<0.02 (0.015)
Left Ventricular Ejection Fraction, %	59 \pm 7	57 \pm 8	ns (0.308)
Left atrial diameter, mm	41 \pm 6	43 \pm 7	ns (0.148)
Left atrial diameter-indexed, mm/m ²	22.2 \pm 3.4	23.5 \pm 4.2	<0.05 (0.038)
Simultaneous CABG, n of cases (%)	10 (15)	36 (27)	ns (0.051)
Previous coronary revascularization (CABG or PCI), n of cases (%)	2 (3)	8 (6)	<0.05 (0.034)
Simultaneous intervention on mitral valve, n (%)	3 (4)	11 (8)	ns (0.315)
Amiodarone treatment during Holter monitor test			
• n of cases (%)	17 (25)	31 (23)	ns (0.769)
• average dosage, mg	235 \pm 79	232 \pm 75	ns (0.895)
Metoprolol treatment during Holter monitor test			
• n of cases (%)	35 (52)	66 (50)	ns (0.765)
• % of target dosage	45 \pm 21	38 \pm 20	ns (0.112)

Group A=patients with grafting of ascending aorta/aortic arch; Group B=patients with aortic valve replacement without aortic repair; *P*=level of significance (between Groups A and B); CR=Cardiac Rehabilitation; Hb=haemoglobin; CABG=coronary artery by-pass graft; PCI=percutaneous coronary intervention

Table 2. Main results of the study.

	Group A (n=67)	Group B (n=132)	P
HRV parameters			
mean-HR, bpm	86.0±14.3	83.3±11.5	ns (0.157)
SDNN, ms	60.1±22.0	70.8±37.7	<0.05 (0.050)
SDANN, ms	53.6±19.6	63.0±32.7	<0.05 (0.048)
Incidence of Atrial Fibrillation			
- in whole groups, n (%)	29 (43)	61 (46)	Ns (0.695)
- in patients aged ≥68, n (%)	17 (77)	44 (55)	<i>P</i> <0.02
- in patients aged <68, n (%)	12 (27)	17 (33)	<i>P</i> <0.001
- in patients with mean-HR ≥93 bpm	5 (22)	11 (37)	ns
- in patients with mean-HR <93 bpm	24 (54)	50 (49)	<i>P</i> <0.01
- in patients with SDNN ≤75 th percentile	2 (12)	6 (23)	ns
- in patients with SDNN >75 th percentile	17 (43)	38 (43)	<i>P</i> <0.05

Group A=patients with grafting of ascending aorta/aortic arch; group B=patients with aortic valve replacement without aortic repair; P=level of significance (between Groups A and B); mean-HR=mean heart rate recorded at 24-h Holter; bpm=beats per minute; SDNN=standard deviation of all normal RR intervals during the whole 24-h Holter recording period; SDANN=standard deviation of the 5-min average of normal RR intervals during the whole 24-h Holter recording period; Ms=milliseconds

Among the total of 244 patients' records analysed, 45 cases had to be excluded because of the presence of exclusion criteria. A total of 199 patients were included in the present study: 67 of them belonged to Group A (50 men; age range 21-83 years) transferred to residential CR 15±11 days after surgery for graft replacement of ascending aorta; 132 patients formed the reference group (group B: 85 men; age range 29-88 years), admitted 13±9 days after aortic valve replacement without repair of ascending aorta.

Patients in group A were on average 9 years younger than those in group B; there was a slight, but not significant, prevalence of males in group A.

Diabetes prevalence was similar among the two groups, while abnormal glucose metabolism (AGM: diabetes + pre-diabetes) was slightly more frequent in patients of group B.

At the time of the study, the greatest majority of patients were anaemic, with evidence of lower Hb levels in patients of group A.

Echocardiographic LVEF showed mean values in the normal range in both groups. Left atrial antero-posterior diameter was similar among the two groups in absolute terms, however, its values resulted higher in group B when indexed by body surface area.

Although moderately higher in group B, the percentage of patients that had undergone also simultaneous CABG or intervention on the mitral valve did not reach statistically significant difference.

During the observation period, 45% of patients presented one or more episodes of AF, without statistical difference between the two groups.

Multivariate analysis of age (*P*<0.001), mean-HR (*P*<0.005) and min-HR (*P*<0.05) recorded by the 24 h Holter, history of previous CABG or PCI (*P*<0.02) and present treatment with amiodarone (*P*<0.001) were correlated with the appearance of POAF.

Patients who developed episodes of AF were older than those without episodes of AF (70.0±11.1 vs 61.0±14.3 years, *P*<0.001); patients older than the median age of 68 presented a significantly higher incidence of postoperative AF in comparison to younger cases (whole study population: 60% vs 30%, χ^2 17.95, *P*<0.001).

No difference was found as regards sex distribution of patients with or without episodes of AF (68% of males in both sets).

As regards comorbidities, hypertension was equally present among patients with (77%) or without (65%) episodes of AF (χ^2 3.14, *P*=0.076); the presence of AGM (31% in patients with AF vs 40% in patients without AF) did not correlate with the incidence of AF, both in the whole population of the study (χ^2 1.83, *P*=0.176) and in the separate analysis of groups A (χ^2 0.01, *P*=0.907) and B (χ^2 3.09, *P*=0.078).

The incidence of episodes of AF did not show correlation with the echocardiographic parameters analyzed. It was similar in patients with higher antero-posterior diameter of left atrium (diameter over the 75th percentile, >25.4 mm/m²) and in patients with smaller atria (whole population: χ^2 2.48, *P*=0.115; group A: χ^2 1.40, *P*=0.237; group B χ^2 1.07, *P*=0.300). No significant difference in LVEF was found between patients that presented one or more episodes of AF (AF-yes) and those without episodes of AF (AF-no), both in

group A and B (mean LVEF in group A: AF-yes 58.0±7.4, AF-no 59.2±6.6, $P=0.499$; mean LVEF in group B: AF-yes 56.3±6.7, AF-no 58.5±9.1, $P=0.127$).

The study of cardiac autonomic function (HRV from 24-h Holter recording) showed significantly more depressed values of SDNN and SDANN (mean values ≤ 60 ms) in patients of group A than in group B, being on average around 15% lower.

Only in a subgroup of patients of group A (transection and substitution of ascending aorta) that presented more compromised HRV parameters, the incidence of AF was significantly reduced: in cases with SDNN below the median (≤ 59.2 ms), the incidence of AF was 22%, while it was 48% in cases with SDNN greater than median ($\chi^2 4.31$, $P=0.038$). These results were confirmed also in cases with SDNN in the lowest quartile (SDNN ≤ 46.9 ms: incidence of AF 12%, vs 43% in patients with higher SDNN values, $\chi^2 5.07$, $P=0.024$). On the contrary, in the patients without transection of ascending aorta (group B) no difference in the incidence of AF was observed in relation to the degree of SDNN depression (for SDNN below vs over the median: 31% vs 45%, $\chi^2 2.19$, $P=0.139$; for SDNN lowest vs higher quartiles: 23% vs 43%, $\chi^2 3.42$, $P=0.064$).

Stratifying the whole group of patients into 4 sets according to quartiles of mean-HR recorded at 24-h Holter, a slightly greater percentage of cases from group A was in the highest quartile of mean-HR (≥ 93 bpm: group A 34%, group B 23%), but the difference was not statistically significant ($\chi^2 3.06$, $P=0.080$). Only those patients of group A with mean-HR in the highest quartile presented a significantly lower incidence of AF in comparison to the remaining patients with lower mean-HR (22% vs 54%; $\chi^2 6.62$, $P=0.01$); no difference in incidence of AF was noted in patients of group B stratified according to quartiles of mean-HR (in patients with mean-HR ≥ 93 bpm the incidence of AF was 37% versus 49% in the remaining patients, $\chi^2 1.42$, $P=0.233$).

In patients treated with beta-blockers, the average dosages were similar between the two groups at transferral from cardiac surgery to CR; during the rehabilitation period, beta-blockers have been progressively titrated, so that at the end of the observation phase the average dosages were significantly higher than the initial ones (group A 58±28% of target, $P=0.001$; group B 49±29% of target, $P=0.000$), without differences between the two groups ($P=0.089$). No correlation was found between beta-blocker treatment or individual dosage and incidence of AF, both for the whole group of patients ($\chi^2 1.52$, $P=0.218$) and for groups A ($\chi^2 0.18$, $P=0.674$) and B ($\chi^2 1.49$, $P=0.222$) separately considered. Due to episodes of AF occurred in the immediate postoperative period, one fourth of patients in both groups ($\chi^2 0.09$, $p=ns$) were under treatment with amiodarone, with similar dosages of the drug. Amiodarone treatment was strictly related to previous episodes of AF ($\chi^2 81.968$, $P<0.001$) even though not all cases

of AF had been put on amiodarone: out of the 90 patients that presented one or more episodes of AF, 42 (47%) were on amiodarone treatment at admission to CR and 12 more patients received amiodarone during the remaining hospitalization period. Of the 109 cases without episodes of AF during the observation time, only 6 (5%) were on prophylactic treatment with amiodarone at admission to CR. Among patients treated with amiodarone that presented AF, an equal percentage of cases had undergone transection of ascending aorta or aortic valve substitution ($\chi^2 0.000$, $P=1.000$).

DISCUSSION

In this study from a real world population, almost a patient every two presented one or more episodes of AF after an intervention of major cardiac surgery not primarily involving left atrium or mitral valve; such incidence of POAF is one of the most elevated reported in the literature for cardiac surgery cases^[1-3]. It must be said that our patients underwent a rather long clinical observation, they have been evaluated also by a 24-h Holter and submitted to prolonged telemetry monitoring, and all episodes of AF (including asymptomatic and self-limited episodes) have been recorded.

Comparing the whole group of patients that underwent graft substitution of ascending aorta (group A) with the group of patients in which ascending aorta was left intact (group B), no significant protective effect against POAF could be exerted by the resection of periaortic nerve terminations in the patients of group A. Knowing that fluctuations of activity of the cardiac autonomic nervous system precede the development of POAF in patients undergoing major cardiac or thoracic surgery^[7,8], it could be expected that altering the autonomic tone by surgical cardiac denervation could lead to reduction of the incidence of atrial arrhythmias in the postoperative period. This was not the case in our patients; indeed, conflicting results are reported in literature with techniques that aimed to alter cardiac autonomic control, by removing the epicardial anterior fat pad^[20-24] or all the nerves around the great vessels at the ventral surface of the base of the heart^[25-28]. Differently from these surgical techniques, aortic transection leads to complete removal of periaortic nerves and plexuses as well as of aortic mechanical stress receptors (while nerves and plexuses surrounding venae cavae and pulmonary artery are usually left in situ). A profound cardiac autonomic denervation is hence achieved^[12-15], and such level of denervation alters the sympatho-vagal balance in the heart and could exert major influence on atrial electrical properties and susceptibility to fibrillate^[29,30].

While in our patients of group A no reduction of POAF is apparent compared to group B, the situation is somehow different in a subgroup of them. A significantly lower incidence of AF (22% vs 54%) was observed in a minority of cases from the group of aortic transection, that seemingly

experienced a more advanced autonomic derangement after resection of ascending aorta: this is the subgroup of group A patients with more altered HRV parameters (SDNN below median; mean-HR over the 75th percentile). If the more depressed HRV parameters in this subgroup express a more extensive surgical denervation is unknown. In any manner, no significant reduction of incidence of AF (37% vs. 49%) was observed in the subgroup of patients from group B that also presented a similarly marked depression of HRV parameters. This observation could support the hypothesis that the possible protective factor against appearance of AF is not the level of postoperative depression of HRV parameters by itself (expression of the autonomic derangement usually present after cardiac surgery and attributable to a variety of mechanisms)^[31,32], but an advanced autonomic blockade obtained by extensive heart denervation (as after resection of ascending aorta). This situation somehow resembles the protective effect given by the marked denervation-dysautonomia that occurs after heart transplant. It must be in some way acknowledged that the small number of cases in the subgroups could leave the doubt that the results could simply be an effect of chance.

We must also remember that when cardiac autonomic nervous system is irregularly altered by surgical intervention, or only a partial or patchy cardiac autonomic denervation is achieved (as it could have been the case in some of our group A patients), no protection against episodes of postoperative AF can be expected; this consideration is based on studies that demonstrate no impact on incidence of postoperative AF from interventions (such as anterior fat pad removal) that produce only partial denervation of the heart and do not achieve the complete removal of nerve terminals observed in heart transplant. No protective effect against postoperative AF has been described also in patients after lung transplant, in which the sutures of donor's pulmonary veins to recipients left atrium lead only to incomplete heart denervation^[33]. Instead of being protective, an heterogeneous autonomic denervation in most cases could have contributed to the rather high incidence of AF in both groups of our patients, through a possible irregularity in the residual innervation of the atria.

As reported in previous studies^[2,34], older patients presented a greater incidence of postoperative AF; on the contrary, no significant correlation was found with presence of diabetes or impaired glucose metabolism, or with linear measures of atrial dimensions, or left ventricular ejection fraction.

Prophylactic administration of drugs such as amiodarone or beta-blockers have demonstrated to be effective at preventing the incidence of AF after cardiac surgery^[35,36], even though not all studies were able to demonstrate that commonly used preventive agents were associated with lower rates of AF in high-risk population^[37]. Our study was not aimed at verifying the effects of drugs on incidence of postoperative AF; amiodarone was administered after the first episode of postoperative AF; no correlation was found between

beta-blocker treatment or individual beta-blocker dosage and incidence of AF in any of the two groups.

Limitations of the study

This is a retrospective study; no details were available about the surgical technique used in specific patients, and in particular if anterior fat pad had been removed or injured during aortic valve substitution (group B); even though this was the case, patients of group B did not gain any advantage in terms of incidence of postoperative AF.

The total number of episodes of AF that occurred both in cardiac surgery and in cardiac rehabilitation has been recorded; the study did not collect data about duration of the single episodes. Although a part of patients was under treatment with amiodarone and/or beta-blockers during the study, they were equally distributed among the two groups; thus, treatment should not have influenced the results.

A limited number of cases was studied. Nevertheless, the number of patients that underwent transection of ascending aorta in our study (67 cases; 132 controls) is not dissimilar from that of subjects submitted to anterior fat pad removal or ventral cardiac denervation in other studies (Davis et al.^[20] 73 cases, 58 controls; Cummings et al.^[22] 29 cases, 26 controls; Alex et al.^[28] 70 cases, 70 controls; AFIST-III study^[23]: 88 cases, 92 controls; Breda et al.^[26] 25 cases, 25 controls); only in the study by Melo et al.^[25], a greater number of cases was recruited (207 cases, 219 controls).

HRV was not analyzed in our patients before surgery; it is already known that heart surgery leads to cardiac autonomic dysfunction, while the aim of this study was to compare influence of autonomic disturbances on POAF in two different types of heart surgery. The HRV analysis was performed on average 15 days after surgery; abnormalities of HRV persist during at least some weeks after cardiac surgery^[38], so that the time of HRV study in our patients should not have affected our findings. We were unable to perform frequency domain HRV analyses, that could have allowed a more specific determination of the variations of vagal tone and of the sympatho-vagal balance. In any manner, previous studies have determined that time-domain HRV indices measured over a 24-h period are well correlated with frequency domain indices in general population^[39] and in thoracic surgery patients^[8].

CONCLUSIONS

A high incidence of AF was observed in the postoperative period of patients submitted to surgery of the aortic valve and ascending aorta. Transection of ascending aorta for surgical repair of an aortic aneurysm did not confer a significant protective effect towards POAF in comparison to reference patients in which ascending aorta was left intact. A reduced incidence of POAF was observed only in a minority of cases with aortic transection, that presented a probably greater au-

tonomic denervation indicated by markedly depressed HRV parameters and elevated mean-HRV; in the remaining cases, it could be hypothesized that a likely heterogeneous cardiac denervation, secondary to limited or patchy nervous lesions, may have created the electrophysiological substrate for the observed high incidence of POAF.

Authors' roles & responsibilities	
LC	Analysis and/or interpretation of data, statistical analysis, final approval of the manuscript, conception and design of the study, carry out operations and/or experiments, manuscript writing or critical review of its content
NR	Analysis and/or interpretation of data, statistical analysis, final approval of the manuscript, carry out operations and/or experiments
ADO	Analysis and/or interpretation of data, final approval of the manuscript, carry out operations and/or experiments
TS	Final approval of the manuscript, carry out operations and/or experiments, manuscript writing or critical review of its content
CC	Analysis and/or interpretation of data, final approval of the manuscript, manuscript writing or critical review of its content
TB	Analysis and/or interpretation of data, final approval of the manuscript, carry out and/or experiments
GG	Final approval of the manuscript, carry out operations and/or experiments, manuscript writing or critical review of its content
FB	Final approval of the manuscript, conception and design of the study, implementation of operations and/or experiments, manuscript writing or critical review of its content

REFERENCES

- Steinberg JS. Postoperative atrial fibrillation: a billion-dollar problem. *J Am Coll Cardiol.* 2004;43(6):1001-3.
- Saxena A, Shi WY, Bappayya S, Dinh DT, Smith JA, Reid CM, et al. Postoperative atrial fibrillation after isolated aortic valve replacement: a cause for concern? *Ann Thorac Surg.* 2013;95(1):133-40.
- Bramer S, van Straten AH, Soliman Hamad MA, van den Broek KC, Maessen JG, Berreklouw E. New-onset postoperative atrial fibrillation predicts late mortality after mitral valve surgery. *Ann Thorac Surg.* 2011;92(6):2091-6.
- Mihos CG, Santana O, Lamas GA, Lamelas J. Incidence of postoperative atrial fibrillation in patients undergoing minimally invasive versus median sternotomy valve surgery. *J Thorac Cardiovasc Surg.* 2013;146(6):1436-41.
- Marin-Neto JA, Carneiro JJ, Maciel BC, Secches AL, Gallo L Jr, Terra-Filho J, et al. Impairment of baroreflex control of the sinoatrial node after cardiac operations with extracorporeal circulation in man. *J Thorac Cardiovasc Surg.* 1983;86(5):718-26.
- Kapa S, Venkatachalam KL, Asirvatham SJ. The autonomic nervous system in cardiac electrophysiology: an elegant interaction and emerging concepts. *Cardiol Rev* 2010;18(6):275-84.
- Dimmer C, Tavernier R, Gjorgov N, Van Nooten G, Clement DL, Jordaens L. Variations of autonomic tone preceding onset of atrial fibrillation after coronary artery bypass grafting. *Am J Cardiol.* 1998;82:22-5.
- Amar D, Zhang H, Miodownik S, Kadish AH. Competing autonomic mechanisms precede the onset of postoperative atrial fibrillation. *J Am Coll Cardiol.* 2003;42:1262-8.
- Cohn WE, Gregoric ID, Radovancevic B, Wolf RK, Frazier OH. Atrial fibrillation after cardiac transplantation: experience in 498 consecutive cases. *Ann Thorac Surg.* 2008;85(1):56-8.
- Dizon JM, Chen K, Bacchetta M, Argenziano M, Mancini D, Biviano A, et al. A comparison of atrial arrhythmias after heart or double-lung transplantation at a single center: insights into the mechanism of post-operative atrial fibrillation. *J Am Coll Cardiol.* 2009;54(22):2043-8.
- Noheria A, Patel SM, Mirzoyev S, Madhavan M, Friedman PA, Packer DL, et al. Decreased postoperative atrial fibrillation following cardiac transplantation: the significance of autonomic denervation. *Pacing Clin Electrophysiol.* 2013;36(6):741-7.
- Kondo C, Nakazawa M, Momma K, Kusakabe K. Sympathetic denervation and reinnervation after arterial switch operation for complete transposition. *Circulation.* 1998;97(24):2414-9.
- Ikegami H, Kobayashi H, Momose M, Maki M, Kusakabe K, Aomi S, et al. [Cardiac sympathetic denervation after aortic surgery in a patient with thoracic dissecting aneurysm: a case report]. *Kaku Igaku.* 1998;35(1):21-7.
- Momose M, Kobayashi H, Ikegami H, Nagamatsu H, Sakomura Y, Aomi S, et al. Total and partial cardiac sympathetic denervation after surgical repair of ascending aortic aneurysm. *J Nucl Med.* 2001;42(9):1346-50.
- Miyamoto S, Hadama T, Anai H, Sako H, Wada T, Iwata E et al. Denervation and reinnervation of the heart after aortic surgery, estimated by ¹²³I-metaiodobenzylguanidine scintigraphy. *Surg Today.* 2004;34(3):226-30.
- Hayashi G, Kurosaki K, Echigo S, Kado H, Fukushima N, Yokota M et al. Prevalence of arrhythmias and their risk factors mid- and long-term after the arterial switch operation. *Pediatr Cardiol.* 2006;27(6):689-94.
- Helfand M, Peterson K, Christensen V, Dana T, Thakurta S. Drug Class Review: Beta Adrenergic Blockers: Final Report Update 4 [Internet]. Portland (OR): Oregon Health & Science University; 2009 [Accessed Jan 23 2015]. Available from: <http://www.ncbi.nlm.nih.gov/books/NBK47170/>

18. American Diabetes Association. Standards of Medical Care in Diabetes-2009. *Diabetes Care*. 2009;32(Suppl 1): S13-S61.
19. Lang RM, Bierig M, Devereux RB, Flachskampf FA, Foster E, Pellikka PA et al; American Society of Echocardiography's Nomenclature and Standards Committee; Task Force on Chamber Quantification; American College of Cardiology Echocardiography Committee; American Heart Association; European Association of Echocardiography, European Society of Cardiology. Recommendations for chamber quantification. *Eur J Echocardiography*. 2006;7(2):79-108.
20. Davis Z. Retaining the aortic fat pad during cardiac surgery decreases postoperative atrial fibrillation. *Heart Surg Forum*. 2000;3(2):108-12.
21. Davis Z, Jacobs HK. Aortic fat pad destruction and postoperative atrial fibrillation. *Card Electrophysiol Rev* 2003; 7(2):185-8.
22. Cummings JE, Gill I, Akhrass R, Dery MA, 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.
23. White CM, Sander S, Coleman CI, Gallagher R, Takata H, Humphrey C, et al. Impact of epicardial anterior fat pad retention on postcardiothoracic surgery atrial fibrillation incidence: the AFIST-III Study. *J Am Coll Cardiol*. 2007;49(3):298-303.
24. Kazemi B, Ahmadzadeh A, Safaei N, Jodati A, Sohrabi B, Afrasiabi A. Influence of anterior periaortic fat pad excision on incidence of postoperative atrial fibrillation. *Eur J Cardiothorac Surg*. 2011;40(5):1191-6.
25. 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.
26. Breda JR, Breda AS, Freitas AC, Meneghini A, Tavares CM, Abreu LC, et al. Effect of ventral cardiac denervation in the incidence of atrial fibrillation after coronary artery bypass graft surgery. *Rev Bras Cir Cardiovasc*. 2008;23(2):204-8.
27. Omran AS, Karimi A, Ahmadi H, Yazdanifard P, Sheikh Fahtollahi M, Tazik M. Prophylactic ventral cardiac denervation: does it reduce incidence of atrial fibrillation after coronary artery bypass grafting? *J Thorac Cardiovasc Surg*. 2010;140(5):1036-9.
28. 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.
29. Chen P-S, Tan AY. Autonomic nerve activity and atrial fibrillation. *Heart Rhythm* 2007; 4(3 Suppl):S61-S64.
30. Kapa S, Venkatachalam KL, Asirvatham SJ. The autonomic nervous system in cardiac electrophysiology: an elegant interaction and emerging concepts. *Cardiol Rev*. 2010;18(6):275-84.
31. Soares PPS, Moreno AM, Cravo SLD, Nóbrega ACL. Coronary artery bypass surgery and longitudinal evaluation of the autonomic cardiovascular function. *Critical Care*. 2005;9:R124-R131.
32. Retzlaff B, Bauernschmitt R, Malberg H, Brockmann G, Uhl C, Lange R, et al. Depression of cardiovascular autonomic function is more pronounced after mitral valve surgery: evidence for direct trauma. *Philos Trans A Math Phys Eng Sci*. 2009;367(1892):1251-63.
33. Dizon JM, Chen K, Bacchetta M, Argenziano M, Mancini D, Biviano A, et al. A comparison of atrial arrhythmias after heart or double-lung transplantation at a single center: insights into the mechanism of post-operative atrial fibrillation. *J Am Coll Cardiol*. 2009;54(22):2043-8.
34. 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.
35. Arsenault KA, Yusuf AM, Crystal E, Healey JS, Morillo CA, Nair GM, et al. Interventions for preventing post-operative atrial fibrillation in patients undergoing heart surgery. *Cochrane Database Syst Rev*. 2013;1:CD003611.
36. Crystal E, Connolly SJ, Sleik K, Ginger TJ, Yusuf S. Interventions on prevention of postoperative atrial fibrillation in patients undergoing heart surgery: a meta-analysis. *Circulation*. 2002;106:75-80.
37. Piccini JP, Zhao Y, Steinberg BA, He X, Mathew JP, Fullerton DA, et al. Comparative effectiveness of pharmacotherapies for prevention of atrial fibrillation following coronary artery bypass surgery. *Am J Cardiol*. 2013;112(7):954-60.
38. Demirel S, Akkaya V, Oflaz H, Tükek T, Erk O. Heart rate variability after coronary artery bypass graft surgery: a prospective 3-year follow-up study. *Ann Noninvasive Electrocardiol*. 2002;7(3):247-50.
39. Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology. Heart rate variability. Standards of measurement, physiological interpretation, and clinical use. *Eur Heart J*. 1996;17(3):354-81.