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ORIGINAL ARTICLE

Minimizing right ventricular pacing in patients with sinus node disease and prolonged PQ interval: The impact on exercise capacity

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Abstract

Background: *Several clinical and experimental studies have shown that unnecessary right ventricular pacing in sinus node disease can be detrimental. Inter- and intra-ventricular asynchrony imposed by right ventricular pacing may cause reduction in contractility and relaxation of left ventricle, worsening mitral regurgitation, regional redistribution of myocardial perfusion and oxygen consumption, and asymmetrical hypertrophy of left ventricular wall. In some patients, sinus node disease coexists with impaired atrioventricular conduction. The optimal pacing mode in this population is not determined. Minimizing right ventricular pacing can preserve inter- and intra-ventricular synchrony. On the other hand, longer atrioventricular delay may cause atrioventricular asynchrony. The aim of this study was to prospectively assess the impact of minimizing right ventricular pacing in patients with DDD pacemaker implanted for sinus node disease and prolonged PQ interval on exercise capacity, cardiac function and quality of life.*

Methods: *The study enrolled 50 consecutive patients with prolonged PQ interval who were implanted with DDD pacemaker because of sinus node disease. Each patient was treated alternately with 2 pacing modes in random order for 4-month periods: conventional dual-chamber pacing and dual-chamber minimal ventricular pacing (prolonged atrioventricular delay). At the end of each phase the following tests were performed: cardiopulmonary exercise testing, echocardiographic evaluation and quality of life assessment (SF36).*

Results: *There was no significant relationship between pacing mode and cardiopulmonary parameters, echocardiographic parameters and quality of life.*

Conclusions: *Sequential atrioventricular pacing may be a reasonable choice for treating patients with sinus node disease and prolonged PQ interval.* (Cardiol J 2015; 22, 1: 75–79)

Key words: sick sinus syndrome, first degree atrioventricular block, pacing

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Introduction

Several clinical and experimental studies have shown that unnecessary right ventricular pacing (RVP) in sinus node disease (SND) can be detrimental. Inter- and intra-ventricular asynchrony imposed by RVP may cause reduction in contractility and relaxation of left ventricle (LV), worsening mitral regurgitation, regional redistribution of myocardial perfusion and oxygen consumption, and asymmetrical hypertrophy of the LV wall [1–7].

In 23–58% of patients with SND, atrioventricular (AV) conduction is also impaired. Two thirds of these patients have first degree AV block [8, 9]. Prolonged AV conduction may lead to diastolic mitral regurgitation and in some patients may decrease exercise capacity [10, 11].

The optimal pacing mode in patients with SND and concomitant first degree AV block is not determined. Minimizing RVP can preserve inter- and intra-ventricular synchrony. On the other hand, longer AV delay may cause AV asynchrony. The purpose of the present study was to assess the impact of minimizing RVP on exercise capacity, cardiac function and quality of life.

Methods

The study was approved by the Institutional Review Board of the Military Institute of Medicine (IRB followed the Helsinki recommendations, approval number 32/WIM/2008). All of the subjects provided informed consent.

We prospectively assessed patients that had had an implantation of DDD pacemaker in our hospital due to SND. The inclusion criteria were: (1) PQ interval ≥ 200 ms at baseline; (2) the percentage of RVP ≥ 90% during the 1st week after the procedure (with default AV delay). Patients were excluded if they had second or third degree AV block or severely impaired LV systolic function (LV ejection fraction [LVEF] ≤ 35%). Patients eligible for the study were included on the 7th day after implantation. The study had a crossover design. Every patient was observed for 2 consecutive periods lasting 3–5 months. In the 1st of the study periods standard AV delay was set. In the other, AV delay was prolonged to achieve minimized ventricular pacing. The order of these time periods was randomized. After the completion of the 1st period every subject was treated with the opposite AV delay settings for approximately the same time. At the end of each study period the following data was acquired: (1) percentage of ventricular and atrial pacing (extracted from the pacemaker storage); (2) exercise capacity assessed by cardiopulmonary exercise testing (CPET); (3) LV and left atrial dimensions and LVEF determined by echocardiography; (4) quality of life assessed by short form 36 questionnaire (SF36). A paired approach was adopted in the analysis of the data.

Pacemaker settings

The exact AV delay settings were individualized and dependent on a model of pacemaker, baseline PQ interval, and upper tracking rate. The maximal AV delay (for the lower rate) in the standard period was 180 ms, minimal: 170 ms (177 ms on average). In the minimized RVP period the numbers were 350 ms and 250 ms, respectively (301 ms on average). Automatic shortening of the AV delay was allowed during rate increases. The lower rate during the diurnal and nocturnal hours was set at 60 bpm and 50–55 bpm, respectively. The upper rate was set according to age and general condition of each patient. In the case of chronotropic incompetence, the rate response features were adopted. The above mentioned settings, except for the AV delays, were not changed during the whole study period.

Cardiopulmonary exercise testing

Symptom-limited CPET was performed on a cycle or treadmill ergometer with a protocol that was personalized with the aim of having each patient reach maximum exercise in 7–10 min. The protocol was the same for both study arms. Breath-by-breath measurements of gas exchange were obtained by a metabolic cart (ZAN 680; ZAN Messgerate GmbH; Germany). Minute ventilation (VE), oxygen uptake and carbon dioxide output (VCO_2) were averaged over 10 s. Peak oxygen uptake (VO_2) was expressed as the mean value of VO_2 during the last 30 s of the exercise test. Ventilatory anaerobic threshold (VAT) was detected by the V-slope method. VE/VCO_2 slope was calculated as a linear regression function using the data points from the whole exercise period. Peak oxygen pulse (O_2 pulse) was delineated as peak VO_2 divided by peak heart rate.

Echocardiography

All patients underwent comprehensive transthoracic echocardiography examination by system Vivid 7 GE. End-systolic and end-diastolic volumes, and ejection fraction were calculated by modified biplane Simpson's method.
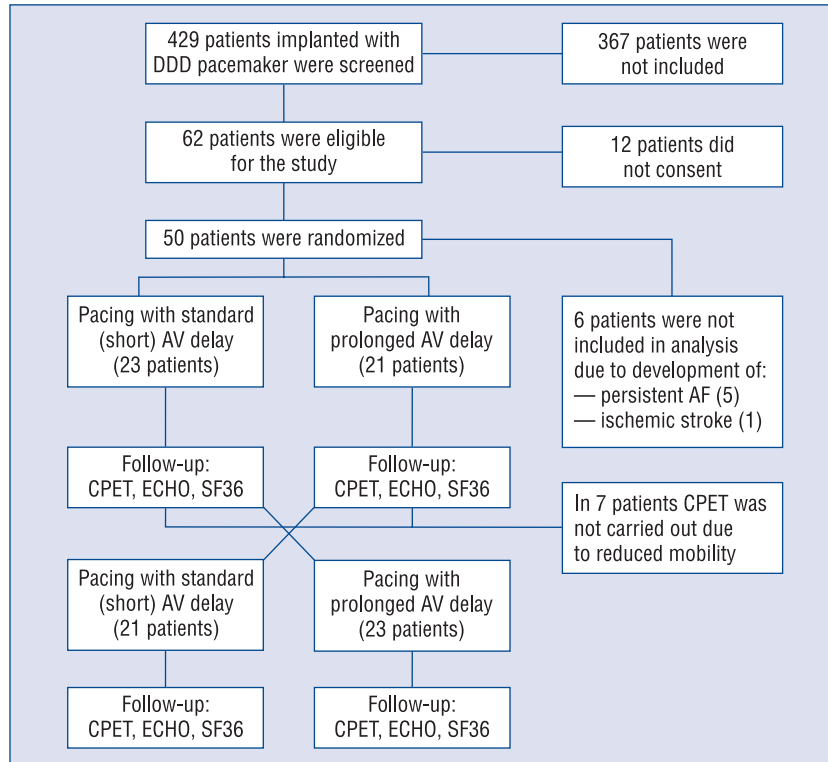
Figure 1. Flow diagram: screening, exclusion, randomization and follow-up of patients; AF — atrial fibrillation; CPET — cardiopulmonary exercise testing; ECHO — echocardiography; SF36 — short form 36 questionnaire.

Statistical analysis

Continuous data are expressed as mean ± ± standard deviation. A Student's paired t-test or Wilcoxon signed rank test in case of non-normally distributed data were used for repeated measures. For qualitative variables the Fisher's exact test was employed. Statistical differences with a p value < 0.05 were considered significant. All calculations were performed with statistical software (SAS 9.3; SAS Institute Inc.; Cary, NC, USA).

Results

From June 2008 to December 2011 we enrolled 50 patients on the study. The study flow diagram is presented in Figure 1. The demographic and clinical data for 44 patients used in the final analysis are summarized in Table 1.

The mean duration of pacing with standard AV delay and of minimized ventricular pacing was 124 ± 33 days and 121 ± 33 days, respectively (p = 0.81). During the minimized ventricular pacing period the percentage of RVP was reduced to a median of 16% in comparison to 98% during standard pacing (p < 0.0001). The QRS duration

Table 1. Baseline characteristics of the patients.

Age [years]	75 ± 7
Male gender	28 (64%)
History of paroxysmal AF	19 (43%)
Coronary artery disease	17 (39%)
Arterial hypertension	33 (75%)
PQ interval [ms]	234 ± 26
QRS duration [ms]	109 ± 18
LV ejection fraction [%]	60 ± 6
LV diastolic diameter [cm]	4.8 ± 0.5
RVOT position of ventricular lead	42 (96%)
Percentage of ventricular pacing during the first week after implantation [%]	97.2 ± 2.7
Medication:	
Beta-blocker	21 (48%)
ACE inhibitors	31 (71%)
ARB	7 (16%)
Antiarrhythmics (amiodarone, propafenone)	9 (21%)
Calcium-channel blockers	11 (25%)
Diuretics	21 (48%)

ACE — angiotensin-converting enzyme; ARB — angiotensin receptor blockers; AF — atrial fibrillation; LV — left ventricular; RVOT — right ventricle outflow tract

Table 2. Cardiopulmonary exercise testing and echocardiographic variables.

Variable	AV sequential pacing with standard AV delay	Minimized ventricular pacing	P
Peak oxygen consumption [mL/kg/min]	17.1 ± 5.9	16.6 ± 5.3	0.26†
Anaerobic threshold [mL/kg/min]	12.3 ± 5.0	12.3 ± 4.2	0.36*
VE/VCO$_2$ slope	29.2 ± 4.6	30.1 ± 8.1	0.69*
Left ventricular diastolic diameter [cm]	5.0 ± 0.6	5.0 ± 0.6	0.64†
Left atrium diameter [cm]	4.34 ± 0.47	4.21 ± 0.55	0.12†
Left ventricular ejection fraction [%]	59.3 ± 9.6	59.2 ± 12.1	0.99†

*Wilcoxon signed-rank test; †paired Student's t-test; AV — atrioventricular

Table 3. Quality of life.

Subscales of SF36 questionnaire	AV sequential pacing with standard AV delay	Minimized ventricular pacing	P
Physical functioning	63.5 ± 18.8	62.4 ± 22.5	0.48*
Physical role functioning	49.4 ± 26.7	45.9 ± 27.5	0.27†
Bodily pain	60.8 ± 24.0	61.9 ± 25.1	0.82*
General health perceptions	50.6 ± 13.2	47.3 ± 13.9	0.052*
Vitality	52.8 ± 18.3	49.6 ± 16.7	0.17*
Social role functioning	70.3 ± 24.0	64.8 ± 22.7	0.053*
Emotional role functioning	62.4 ± 27.5	61.2 ± 28.1	0.72*
Mental health	64.2 ± 18.4	63.6 ± 17.2	0.78†

*Wilcoxon signed-rank test; †paired Student's t-test; AV — atrioventricular

was also diminished: 113 ± 26 vs. 155 ± 20 ms, respectively (p < 0.0001). However, a quarter of patients still had more than 40% of RVP during minimized ventricular pacing. There were no significant differences between the study periods in percentage of atrial pacing (p = 0.38).

The peak oxygen uptake, ventilatory anaerobic threshold, VE/VCO$_2$ slope, LV diastolic diameter, left atrial diameter and LVEF did not differ according to the pacing mode (Table 2). When comparing the results of 8 subscales of the SF36 questionnaire, they did not reveal any significant differences between the study groups (Table 3).

Discussion

The present study compared minimized RVP with standard settings of AV delay in a selected group of patients with both SND and first degree AV block. The result was that no significant improvement in exercise capacity and quality of life was associated with a reduced percentage of RVP. These findings suggest that sequential AV pacing with standard AV settings may be a reasonable choice in this group of patients.

Several laboratory and clinical studies have shown that RVP may result in reduced LV systolic and diastolic function [6, 7, 12]. Due to ventricular desynchronization ventricular pacing may promote heart failure. The risk of developing heart failure grows with increasing cumulative percentage of RVP [13–15]. However, reducing ventricular pacing by extending AV delay may lead to AV desynchronization. Prolonged PQ interval or stimulus-R interval in atrial pacing may result in diastolic mitral regurgitation, and in consequence in heart failure [10, 11, 16]. Thus, the LV performance depends on both intra-ventricular and AV synchrony. Prolonged AV conduction in all patients included in the present study may explain why minimizing ventricular pacing had no impact on exercise capacity and cardiac function.

Similar observations were presented by Vardas et al. [17] in 15 patients with SND and normal AV conduction. They reported no difference in the anaerobic threshold according to the pacing mode: AAI or DDD with short AV delay [17]. The possible reason for this result may be that AV conduction during atrial pacing in patients with SND may paradoxically lengthen with increasing

pacing rate during exercise [18, 19]. This lack of physiological adaptation of the AV interval when exercising may be the result of the maladjustment of the adrenergic tone to the heart rate determined by the pacemaker [18].

In contrast to our findings, Wonisch et al. [20] reported improvement in CPET variables with pacing modes that minimize ventricular pacing in 17 patients with heart failure and cardioverter--defibrillator. The possible explanation of these results may lie in the fact that RVP in hearts that are impaired at the baseline leads to a greater extending of intra-ventricular desynchronization. The QRS duration (QRSd) and LV activation time due to RVP are increased when LVEF is less than 40% in comparison to hearts with preserved LV systolic function: QRSd 209 ms vs. 193 ms, respectively and LV activation time 186 ms vs. 129 ms, respectively [21]. In our study, however, the LV function was not impaired at baseline with mean LVEF of 60% and QRSd of 109 ms. This may be the reason we did not observe any deleterious effects of RVP.

Limitations of the study

There are several limitations of the present study. Small number of patients included, short follow-up period in each pacing mode, and residual ventricular pacing over 40% in a quarter of patients could have mitigated the possible benefit of minimized ventricular pacing.

Conclusions

The results of the present study support the view that sequential AV pacing in SND patients with prolonged PQ interval is a safe alternative regarding exercise capacity, cardiac function and quality of life. However, the study group was too small and the follow-up period too short to assess the impact of minimizing ventricular pacing on mortality and heart failure development.

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