Physiological Rate Adaptation with an Elevated Basic Rate for Prevention of Paroxysmal Atrial Tachyarrhythmia

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Summary

Atrial overdrive pacing may suppress atrial extrasystoles and thus prevent the onset of atrial fibrillation (AF). However, after restoration of the sinus rhythm the atrium is the most vulnerable to reinitiation of AF. The aim of our study was to evaluate the efficacy of rate-adaptive pacing based on myocardial contractility (DDD-CLS), used in combination with an elevated basic rate, in diminishing AF in patients with bradytachycardia syndrome. Twenty-six patients with a mean age of 59 ± 10 years (57% male, 65% presenting with Chagas disease) were enrolled in a prospective study. Each patient was taking amiodarone (400 mg/day) during the study. Two months after implantation the patients were randomized to receive either DDD pacing at a basic rate of 60 bpm or DDD-CLS pacing with a basic rate set to 80 bpm. The Mode switching option was activated in all patients and pacemaker statistics were used to count the number of mode switch episodes. A 3-channel, 24-hour Holter ECG was obtained in all patients. The mode crossover was performed after 3 months. Holter ECG recordings revealed a significant reduction in the number of atrial extrasystoles ($p < 0.01$) and the number of ventricular complexes during AF ($p < 0.05$) in the DDD-CLS pacing with an elevated basic rate. The number of mode switch episodes recorded in the pacemaker memory over 3 months was also reduced during DDD-CLS pacing with an elevated basic rate ($p < 0.001$). In conclusion, myocardial contractility-based, rate-adaptive pacing with a basic rate of 80 bpm reduced the incidence of paroxysmal AF.

Key Words

Cardiac pacing, overdrive pacing, Closed Loop Stimulation (CLS), atrial fibrillation

Introduction

Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia in clinical practice and is linked to a significant increase of morbidity and mortality. Based on the Framingham study [1], the cumulative incidence of AF is 2% in the general population, and it increases with age. It is also responsible for more than 5% of all cardiovascular disease-related hospital admissions. Non-pharmacological treatment should be provided for patients who are resistant or intolerant to antiarrhythmic drugs. Recent clinical studies have suggested an increased benefit of dynamic overdrive pacing with special algorithms in preventing recurrent AF [2-5]. It has also been demonstrated that an elevated atrial pacing rate in the conventional DDD mode results in a higher percentage of atrial pacing and fewer AF episodes [6,7].

According to the Closed Loop Stimulation principle (CLS, Biotronik, Germany), rate-adaptive pacing preserves intrinsic circulatory regulation and integrates the pacemaker into the natural cardiovascular control loop, enabling the heart rate to be controlled by the autonomic nervous system [8,9]. Because neural messages play a significant role in the genesis of several cardiac arrhythmias, CLS may drive preventive thera-

pies in order to avoid or limit the effects of arrhythmic events [10]. The aim of our study was to investigate whether the use of a higher basic rate of 80 bpm in conjunction with CLS would decrease the number of AF events in patients with bradycardia-tachycardia syndrome compared to fixed rate DDD pacing at a basic rate of 60 bpm.

Materials and Methods

Study Population

After providing written informed consent, 26 patients were included in the study (mean age 59 ± 10, 15 male and 11 female). All patients suffered from bradycardia-tachycardia syndrome, 65% had Chagas disease, and 75% were classified as New York Heart Association (NYHA) functional class I or II. Each patient was taking amiodarone (400 mg/day) during the study. The indication for pacemaker implantation was bradycardia-tachycardia syndrome, mostly due to Chagas disease. All the patients experienced at least two episodes of paroxysmal AF in the last 3 months, or one episode per month, documented by symptoms, duration, and ECG. Patients presenting with unmanaged angina pectoris, unresolved problems with atrial sensing, chronic AF, malignant ventricular arrhythmias, and symptomatic chronotropic incompetence were excluded from the study. Antiarrhythmic pharmacological therapy was stable during the study.

Pacemaker

All patients were implanted with an Inos^{2+} CLS pacemaker (Biotronik) and a bipolar atrial lead. The CLS system determines the impedance variations generated by changes of the myocardium-to-blood ratio in the volume around the ventricular tip during systole. Its control algorithm automatically and continuously monitors the patient's physiological condition. By integrating the pacemaker into the cardiovascular regulatory system, which is controlled by the autonomic nervous system, the pacing rate is provided as needed [8,9].

24-hour Holter ECG

A 3-channel, 24-hour Holter ECG (Diagnostic Monitoring Systems, USA) was used to identify atrial extrasystoles, defined as P-waves occuring 25% closer than usual to the preceding T-wave, and AF events, defined as narrow QRS complexes with irregular RR intervals and without preeceding P-waves.

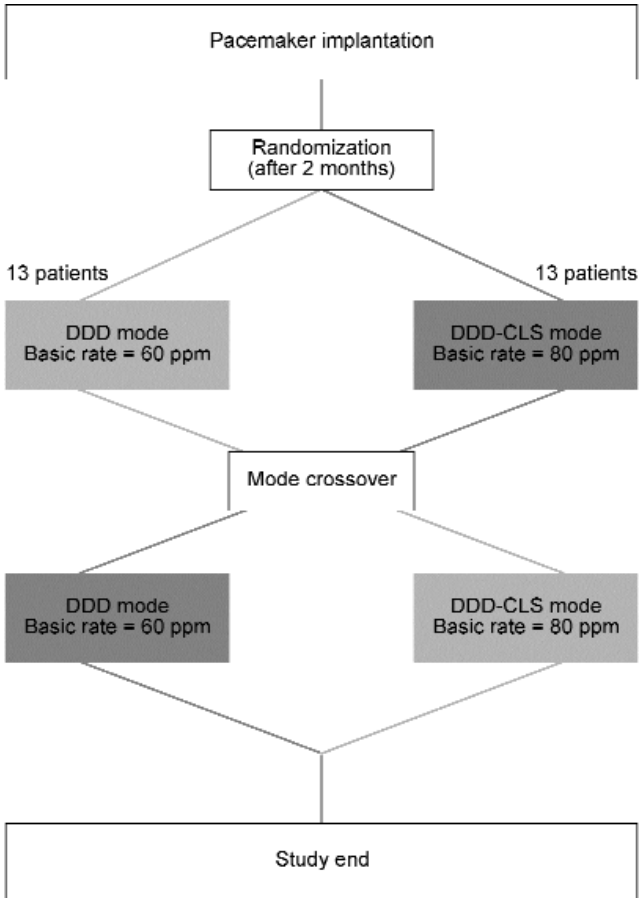

Figure 1. Flowchart of study sequence.

Study Design

This was a prospective, randomized, double-blind, crossover trial (Figure 3). The study protocol and consent form were approved by the local ethics review committee. Two months after implantation, we conducted a preliminary evaluation during which each patient's pacemaker was interrogated and all statistical functions were printed out. Sensibility, pacing threshold, and impedance tests were performed. All the parameters were adjusted according to each patient's requirements. After activation of the mode switch function, patients were randomized into two groups, consisting of 13 patients each:

- DDD mode, basic rate = 60 ppm
- DDD-CLS mode (rate-adaptive mode), basic rate = 80 ppm

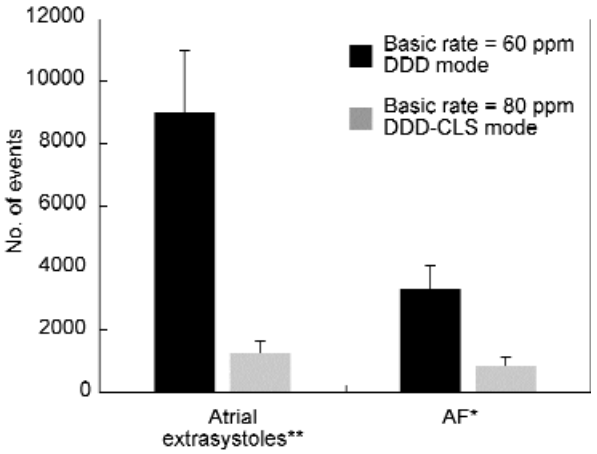

*Figure 2. Number of atrial extrasystoles and QRS-complexes identified as atrial fibrillation (AF) events. **p < 0.01, *p < 0.05.*

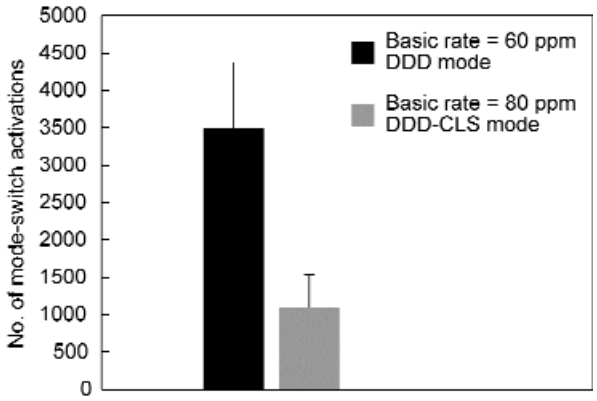

Figure 3. Number of mode switch episodes. p < 0.001.

The first evaluation was performed 3 months after the randomization to analyze the number of atrial extrasystoles and QRS-complexes identified as AF events from the 24-hour Holter ECG and counting the number of Mode Switch activations from the pacemaker statistics. The same procedure was performed 3 months after the crossover of pacing mode and basic rate. Desciptive data are shown as mean ± standard deviation.
Statistical analysis was performed using a paired t-test. A p-value < 0.05 was considered statistically significant.

Results

No differences in pacing and sensing thresholds were observed between the two groups during the course of the study. Analysis of the 24-hour Holter ECG in Figure 2 showed a decrease in the number of atrial extrasystoles by the factor of 7 ($p < 0.01$) and of AF events by the factor of 3.8 ($p < 0.05$) during CLS pacing at the 80 bpm basic rate. In Figure 3, there was a 3.3 times smaller number of mode switch activations in this mode ($p < 0.001$).

Discussion

The benefit of atrial pacing for preventing AF was first described in the studies of Rosenqvist [11], Langenfeld [12], Santini [13], and Hesselson [14], who demonstrated that patients with sinus node dysfunction paced in the AAI or DDD mode experienced significantly fewer AF episodes than those paced in the VVI mode. In agreement with these retrospective results, a prospective, randomized Danish Study was presented in 1997 [15], which compared the incidence of AF in AAI pacing to VVI pacing in 220 patients and proved clear benefits of AAI over VVI. Afterwards, the Canadian Trial on Physiologic Pacing (CTOPP) [16] analyzed the mortality and incidence of AF in 2,568 patients randomized into two groups: VVIR vs. DDDR. After 2 years of follow-up, the incidence of AF did not attain statistical significance. However, after 4 years of device therapy, the statistical difference was demonstrated, which became more pronounced with time. Thus, atrial pacing seems to prevent AF by eliminating bradycardia-induced dispersion of atrial repolarization that provides the substrate for AF and by overdrive suppression of supraventricular premature beats, which provide the trigger of AF.
In a prospective, randomized trial, de Vusser et al. [7] compared a group of patients with the basic rate (80 bpm) programmed above the intrinsic rate at rest (65 bpm) versus a group of patients with the basic rate of 70 bpm. In this study, the group with higher basic rate had a lower incidence of AF, implying the benefit of circadian overdrive pacing for the patient. Puglisi et al. [10] compared closed-loop pacing (CLS), dynamic overdrive pacing (DDD+) and accelerometer-driven pacing (DDDR) in patients with bradycardia-tachycardia syndrome. They observed a higher atrial pacing percentage with CLS and DDD+ as compared to the

DDDR group, with no differences between the first two groups. CLS also showed a better trend toward a lower incidence of AF.

Both studies are in agreement with our findings, which showed that overpacing with a basic rate of 80 bpm in conjunction with a sensor for rate-adaptive pacing based on the autonomic nervous system reduces the number of mode switch activations, atrial extrasystoles, and beats identified as AF events. Nevertheless, due to our study design, we cannot distinguish whether CLS, fixed-rate overdrive pacing, or the combination of both methods is the most effective therapy.

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