

Sinus node dysfunction associates with atrial high-rate episodes after DDD pacemaker implantation

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Abstract

Background Patients implanted with pacemakers frequently develop atrial fibrillation. Pacemaker-detected atrial high-rate episodes or AHREs, where one AHRE is defined as ≥ 160 beats/min lasting ≥ 5 minutes, may identify patients at increased risk for stroke and death. In this study, we sought to observe whether patients with sinus node dysfunction or atria-ventricular block are more likely to develop AHREs. **Methods:** A total of 103 patients (age 69.4 ± 13.5 years, 58% female) with DDD/DDDR pacemakers were enrolled for the study. These pacemakers were equipped with features that enabled the detection and storage of information such as the dates, durations and sequential episodes of AHRE. Patients were followed up for 2 years and the time of the first occurrence of AHRE was determined at follow-up visit. Other data such as age, gender, structural heart disease, concomitant non-cardiac diseases, the cumulative percentage of atrial pacing (Cum% AP) and ventricular pacing (Cum% VP) were also collected. **Results:** Atrial fibrillation developed frequently after the dual-chamber pacemaker implantation. AHRE occurred more often in patients with sinus node disease (SND) than those with atrioventricular block (AVB) (OR, 2.553; 95%CI, 1.122-5.814, $P=0.045$). **Conclusions:** AHRE developed frequently after dual-chamber pacemaker implantation. Patients with SND are more likely to develop AF compared to the patients with AVB.

Background

It is common for patients with implanted pacemakers to develop atrial fibrillation. It has been hypothesized that in patients with pacemaker implantation, pacemaker-detected AHRE lasting at least 5 minutes identify those that are more than twice as likely to die or have a stroke, and are nearly 6 times as likely to develop atrial fibrillation as compared to patients without AHRE^[1]. However, the clinical predictors for the patients who would develop atrial fibrillation (AF) still remain obscure. In this retrospective study, we evaluated whether SND rather than atrioventricular block (AVB) is a predictor of AHRE development in the patients with dual-chamber pacemaker implantation.

Methods

Study population

Eligible patients who had symptomatic bradycardia due to sinus-node disease or atrio-ventricular block met criteria for permanent pacemaker implantation. We observed 103 patients who had initially received a pacemaker implantation of a dual-chamber system (with or without sensor-modulated rate adaptation) at the Zhejiang Province People's Hospital. We enrolled the subjects between 30 July 2009 and 1 August 2014 and followed them for two years. The ventricular pacing leads of the pacemakers were placed at the right ventricular apex and the atrial pacing leads in the right atrium. The baseline demographic and clinical characteristics of the patients were recorded prior to taking pacemaker readings. The atrio-ventricular delay (AVD) was initially programmed to be 10-20% longer than either the interval measured from the atrial pacing spike to start of the conducted QRS complex or the PR interval when the sinus rate

was faster than the lowest rate in patients with SND. In patients with AVB, the AVD was initially programmed to 240ms and the atrio-ventricular interval after sensed atrial beats was set 30–40 ms shorter than the paced interval. The auto mode switch function was turned on. The percentage of atrial and ventricular pacing at each follow-up was calculated using the number of paced and sensed beats.

Study Outcome Event

The study outcome events measured were the time to first occurrence of AHRE lasting for at least 5 minutes after pacemaker implantation.

Patient follow-up

Patients were followed up for 1 month, 3 months, 6 months, 1 year and 2 years after DDD pacemaker implantation.

Definition

AHRE was defined as ≥ 160 beats/min lasting ≥ 5 minutes.

Statistical analysis

We measured cumulative event-free survival using the Kaplan-Meier method and compared unadjusted differences using the log-rank test. The percentage of ventricular pacing was also recorded and was used for Cox regression analysis. The continuous variables were expressed as mean \pm SD and the relative risks as hazard ratios with 95% confidence intervals. For all comparisons, $P < 0.05$ was considered statistically significant.

Results

Study population

The study population consisted of 103 patients - 60 women and 43 men - who received DDD pacemaker and were followed up for 24 months. Most of the patients were elderly and had a history of hypertension. The major indications of DDD pacemaker implantation were SND (seen in 70 patients) and AVB (seen in 33 patients). In addition, 18% of the patients had documented paroxysmal AF before enrollment. Other clinical characteristics, including medications, Cum% AP (atrial pacing) and Cum% VP (ventricular pacing) were also collected. Table 1 shows the baseline variables that served as the inclusion criteria in the prognostic models.

Table 1

AHRE after pacemaker implantation

Forty patients (39%) developed AHRE and SND was a more frequent predictor compared to AVB for the eventual development of AHRE, as showed in figure 1, **$P=0.004$** .

Figure 1

Pacing and AHRE

The Cum% AP and Cum% VP in the last follow up were recorded (table 2). There was a significant difference in Cum% VP values between the SND and AVB groups. However, after adjustment for age, gender, structural heart disease, concomitant non-cardiac diseases and the Cum% AP using cox regression, no association was seen between Cum% VP and AHREs ($P=0.185$).

Table 2

Discussion

In our study, we found that AHRE frequently developed in patients after DDD pacemaker implantation and SND was a major indication for the occurrence of AHRE.

Previous studies have reported that patients with SND are more likely to develop AF [2-4]. The most common cause of SND is the degeneration and fibrous replacement of the SA node, as often characterized pathologically, eventually reaching the atrium and resulting in atrial arrhythmia. Furthermore, a history of AF before pacemaker implantation was an independent predictor of AF occurrence after pacemaker implantation. This is consistent with observations in previous clinical trials.

We found no association between VP and AF which is in contrast to most published studies. A post hoc analysis of data from the Mode Selection Trial in Sinus-Node Dysfunction (MOST) indicated that VP increases AF [5]. Consistent with this finding, the SAVEPACE trial, which compared conventional dual-chamber pacing and dual-chamber minimal VP using pacemakers designed to promote atrioventricular conduction and preserve ventricular conduction, also concluded that VP increases AF [6]. In another post hoc analysis of data from DANPACE however, statistical modeling found no association between VP and AF which is in agreement with our study [7]. The programming of the pacemakers used in the different trials may explain the different results. In the MOST and SAVEPACE trials, the pacemakers were programmed with a short AVD (120-200ms) which resulted in a high Cum% VP. The mean Cum% VP was 90% in the MOST trial and 99% in the SAVEPACE trial. It is possible therefore that the short AVD used in the two trials had some impact on the occurrence of AF. It has been established that a short AVD may result in a premature closure of the mitral valve, thus compromising the atrial contribution to left ventricular filling and increasing the left atrial pressure that may trigger AF. Whether it is the atrioventricular synchrony or VP which plays the more important role in the deleterious effect still remains to be investigated. In our study, when we programmed a longer AV delay, we did not find any association between VP and AHRE.

This was an observational study and as a result, significant baseline patient characteristics and procedural differences were present before adjustment and residual confounding may have been present after adjustment; these limitations are expected in any observational study. Furthermore, the small sample size of our study may also have had some impact on the results. Therefore, an additional larger-scale prospective trial is needed to remove or minimize the confounders.

Limitations

The sample size of this study is small, and because it is a retrospective study, the results have certain limitations. Further prospective studies with larger samples are needed to further confirm the results.

Conclusions

AHRE occurs frequently in patients who have been implanted with the dual-chamber pacemaker. SND is the first indication of the association between pacemaker implantation and AHRE. However, when a longer AVD is programmed, VP is not associated with AHRE occurrence.

Abbreviations

AHREs: atrial high-rate episodes

Cum% AP: the cumulative percentage of atrial pacing

Cum% VP: the cumulative percentage of ventricular pacing

SND: sinus node disease

AVB: atrioventricular block

AF: atrial fibrillation

CAD: coronary artery disease,

CCB: calcium channel blocker

Declarations

Ethics approval and consent to participate

The study protocol was approved by the ethics committee of the Zhejiang Provincial People's Hospital. Because of the retrospective design of the study, the need to obtain informed consent from eligible patients was waived by the ethics committee.

Consent for publication

Not applicable. *Availability of data and materials*The datasets used or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

QX and HS designed the study. YM and HZ collected the data and analyzed the data. LW was in charge of Quality control the study and revision. The manuscript was approved by all above authors.

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Not applicable.

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Tables

Table 1. Baseline characteristics of study cohort

	Total	SND	AVB	P value
	N=103	N=70	N=33	
Age(years)	69.5±13.0	66.1±17.2	71.0±11.1	0.083
female	60(58.3%)	41(58.6%)	19(57.6%)	0.924
Diabetes mellitus	17(16%)	12(17%)	5(15%)	0.799
Hypertension	61(59%)	40(57%)	21(64%)	0.531
CAD	31(30%)	22(31%)	9(27%)	0.668
Cardiomyopathy	2(32%)	1(1.4%)	1(3%)	0.583
AF history	18(18%)	14(20%)	4(12%)	0.326
Drugs after pacemaker				
Beta-blocker	36(35%)	25(36%)	11(35%)	0.774
ACEI/ARB	44(43%)	29(42%)	15(46%)	0.744
CCB	41(40%)	29(42%)	12(36%)	0.585
statin	24(25%)	19(28%)	5(15%)	0.168
Other AAD	7(7%)	6(9%)	1(3%)	0.484

CAD coronary artery disease, AF atrial fibrillation, SND sinus node disease, AVB atrial-ventricular block, CCB calcium channel blocker

Table 2. Comparison of Cum%AP and Cum%VP between two groups

	SND	AVB	P value
	N=70	N=33	
Cum%AP	58.5±28.4	23.76±28.1	0.001*
Cum%VP	19.0±23.7	83.4±30.7	0.000*

Figures

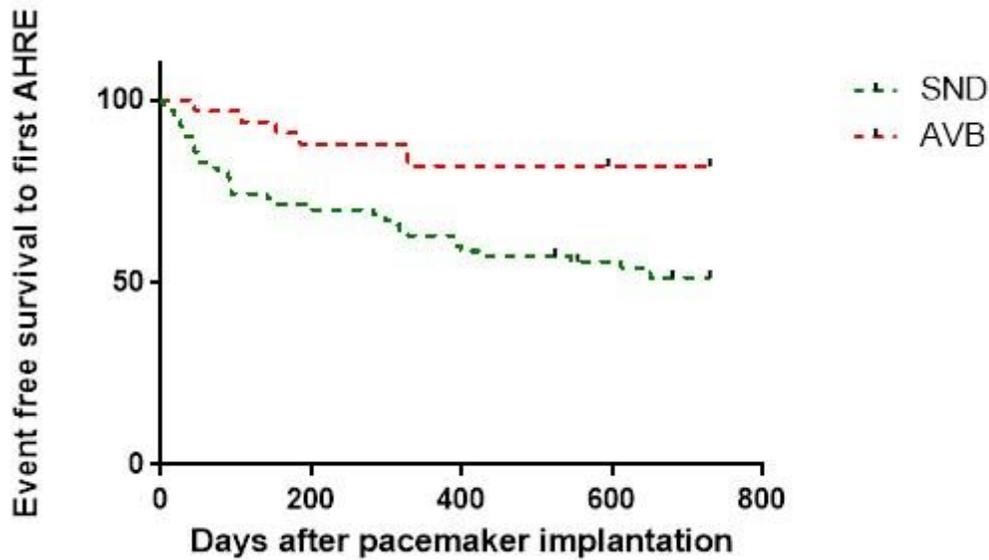


Figure 1

Event-free survival from AHRE based on the primary indication for pacing: sinus node disease (SND; n 70) or AV block (n 33). Patients with SND were more likely to experience AF. P=0.004 by log rank test.