

## Reduction of Tachycardia Episodes in Patients with Chronic Atrial Fibrillation by Right Ventricular Pacing

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### Summary

*The ventricular rhythm during atrial fibrillation (AF) is usually irregular and random and may provoke dizziness, discomfort, and palpitations in many patients. It has previously been shown that continuous ventricular pacing in patients with AF has a stabilizing effect on the irregular ventricular rate during AF. It is generally accepted that control of heart rate (pharmacological and non-pharmacological) in AF require values below 90 beats/min. The purpose of this study was to assess the reduction of rapid ventricular rates (AF tachy) in patients with VVI pacing at 80 beats/min. In addition, the usefulness of the pacemaker's heart-rate histogram in controlling ventricular rate in these patients during 7 days follow up was estimated. A group of 45 patients with chronic AF and permanent VVI pacing was studied. Our results revealed that ventricular pacing at 80 beats/min and 80 beats/min with night program reduce AF tachy episodes by eliminating the majority (over 50 %) of heart rates above 88 beats/min. The mean ventricular rate significantly increased by 15 beats/min as a result of the VVI pacing at 80 beats/min and by 12 beats/min as a result of the VVI pacing at 80 beats/min with night program compared to the intra-individual AF control measurements (VVI40 beats/min). The percentage of paced events ranged from 40 % to 100 %, and was higher during both VVI 80 beats/min groups compared to the control measurements, but there were no statistical differences between them. We also found that, due to diagnostic pacemaker memory, it is possible to control the heart rate in AF patients during long-term follow-up.*

### Key Words

Atrial fibrillation, ventricular pacing, heart rate stabilization, pacemaker diagnostic memory function

### Introduction

Atrial fibrillation (AF) has long been recognized as the most frequent arrhythmia, occurring in up to 1 % in general population [1,2]. It is associated with significant morbidity and mortality [3-6]. The ventricular rhythm during AF is usually irregular and random and may provoke dizziness, discomfort, and palpitations in many patients [7-9]. The negative influence of an irregular ventricular rhythm during AF on the hemodynamic parameters of the heart has been described in the literature [10,11]; however, it is still unknown whether it is the fast heart rate (HR) or the irregularity that causes tachycardiomyopathy [7,12]. Pharmacological therapy aimed at controlling ventricular rate in AF is often asso-

ciated with proarrhythmic side effects [13-15]. Patients with chronic AF and symptomatic bradycardia often receive ventricular pacemakers (VVI). However, after implantation, many of these patients continue to have symptoms of palpitations, which may be largely a result of ventricular rate variability and fast HR (tachy-AF). It has previously been shown that continuous ventricular pacing in patients with AF has a stabilizing effect on the irregular ventricular rate during AF [16-19]. These studies suggested that right ventricular pacing, by inducing retrograde concealed atrioventricular (AV) nodal conduction, could eliminate short RR-cycles during AF and may be used as a nonpharmacological means

Clinical characteristic	No. of patients
Myocardial infarction past history	4
Stenocardia CCS-class I/II	8
Stenocardia CCS-class III/IV	0
Valvular heart disease with heart failure NYHA-class III/IV	0
Hypertension	28
Drug therapy	No. of patients
Digoxin	22
$\beta$ -blocker	34
Ca <sup>2+</sup> channel blocker	12

Table 1. Clinical characteristic and drug therapy of 45 patients enrolled in the study. NYHA = New York Heart Association; CCS = Canadian Cardiac Society.

of controlling ventricular responses in AF [20]. The pacing rate had to be set above the mean ventricular rate to suppress all spontaneous ventricular activity [21]. Previous investigators have used a PC computer with special HR stabilization algorithms to study the effect of overdrive ventricular pacing on rate control in patients with AF either while at rest [18,22,23] or during exercise [24]. However, these studies have not investigated the efficacy of rate regularization during daily activity and over a long period of follow-up. It is also generally accepted that controlling the HR during AF requires values below 90 beats/min [25].

#### Aim of the Study

The purpose of this study was to assess the reduction of AF tachy episodes in patients with VVI 80 beats/min pacing during daily activity and the usefulness of the HR histogram in Actros S pacemakers (Biotronik, Germany) in controlling the ventricular rate in patients with AF.

## Materials and Methods

#### Patient Data

A group of 45 patients (24 male, 21 female; mean age  $72.5 \pm 6.6$  years) with permanent VVI pacing was studied. All patients were implanted with Actros S (VVI) pacemakers and a single passive-fixation endocardial lead (SX 60-BP, TIR 60-BP, or PX 60-BP, all from Biotronik). Prior to implantation, all patients presented

with complete or incomplete Morgagni-Adams-Stokes (MAS) attacks accompanied by documented episodes of HR pauses over 3 s in Holter monitoring or in standard ECG recording. The patient characteristics are shown in Table 1. Only the patients with chronic AF (AF from 6 months to 5 years, mean 1.8 years) and intact AV nodal conduction were included in this study. Patients with complete AV block or documented hyperthyroidism were excluded from the study. Antiarrhythmic medications remained unchanged during the whole course of this study. The ejection fraction ranged from 22 % to 81 %, mean  $60.8 \% \pm 15 \%$ .

#### Methods

In order to observe the patients over a long period, the Actros pacemaker memory data was used. Event counter, activity report and HR histogram of Actros S diagnostic memory function enabled to analyze the following data:

- percentages of paces events (Vp);
- mean and maximum HR; and
- percentages of sensed and paced events situated within certain HR ranges.

According to the Actros S heart-rate histogram, episodes with a ventricular rhythm over 88 beats/min were considered as AF tachy.

#### Study Procedure

The patients had undergone pacemaker implantations between 2 and 67 days (mean 23 days) prior to enrollment in the study. Observation was conducted during 21 days. For the first 7 days, the pacemaker was set in the VVI mode at 40 beats/min. The results for this mode were then considered to be the control AF-data. Then, for the next 7 days, the pacemaker was switched into 80 beats/min mode. Finally, during the last week, a pacing rate of 80 beats/min with an activated night program (NP = VVI 70 beats/min pacing from 10:00 pm to 06:00 am) was analyzed.

#### Data and Statistical Analysis

Mean and max HR, as well as pacing statistics, were calculated for each pacing mode (VVI 80 beats/min, VVI 80 beats/min NP) and compared to the control AF-group. Next, the effectiveness of VVI pacing at 80 beats/min and VVI paging at 80 beats/min with NP in reducing the AF tachy episodes, compared to control

	VVI 40 beats/min (control AF-group)	VVI 80 beats/min	P-value
Mean ventricular rate (beats/min)	66.5 ± 8.7	81.8 ± 3.4	< 0.01
Maximum ventricular rate (beats/min)	200.7 ± 28.3	205.9 ± 24.0	ns
Pacing events (%)	12.0 ± 14.9	85.8 ± 12.6	< 0.01

Table 2. Comparison of mean heart rate, maximum heart rate, and percentage share of ventricular pacing between VVI pacing at 40 beats/min (control AF-measurements) and VVI pacing at 80 beats/min during a 7-day follow-up. AF = atrial fibrillation; P-value from Wilcoxon's matched-pairs test; ns = not significant.

AF mode was calculated during a 7-day follow-up. Paired comparisons with Wilcoxon's matched-pairs test were used to compare the data.  $P < 0.05$  was considered as statistically significant.

## Results

### Pacing and Ventricular Rate Statistics

The statistics calculated from patients are shown in Tables 2 – 4. The mean ventricular rate significantly increased by 15 beats/min and 12 beats/min as a result of VVI pacing at 80 beats/min and VVI pacing at 80 beats/min with NP. Due to NP, the mean HR was significantly lower in the VVI 80 beats/min NP mode, than during VVI pacing at 80 beats/min for the whole day ( $P < 0.05$ ). There were no statistical differences in the maximum HR during higher ventricular pacing rates compared to a control AF-group. The percentage of paced events, ranging from 40 % to 100 %, was higher during VVI pacing at 80 beats/min and VVI pacing at 80 beats/min with NP than for the control AF-data, but there were no statistical differences between VVI 80/min and VVI 80/min NP.

### HR Histogram

The mean percentages of HR > 88 beats/min in certain rate ranges during control-AF, VVI 80 beats/min, and VVI 80 beats/min NP are shown in Tables 5 – 7. The significant reduction of HR in the majority of the HR ranges was found. The highest rates (> 161 beats/min) were not reduced during VVI 80 beats/min and VVI 80 beats/min NP pacing, but there were only 0.3 % of

	VVI 40 beats/min (control AF-group)	VVI 80 beats/min NP	P-value
Mean ventricular rate (beats/min)	66.5 ± 8.7	78.8 ± 2.9	< 0.01
Maximum ventricular rate (beats/min)	200.7 ± 28.3	205.0 ± 23.8	ns
Pacing events (%)	12.0 ± 14.9	84.0 ± 13.7	< 0.01

Table 3. Comparison of mean heart rate, maximum heart rate, and percentage share of ventricular pacing between VVI pacing at 40 beats/min (control AF-measurements) and VVI pacing at 80 beats/min with night program (NP = VVI pacing at 70 beats/min from 10:00 pm to 06:00 am) during 7-day follow-up. AF = atrial fibrillation; P-value from Wilcoxon's matched-pairs test; ns = not significant.

such rhythms. There were no statistical differences in the percent-ages of the HR in all ranges between pacing 80 beats/min and 80 beats/min NP.

### Reduction of the AF tachy episodes

Reduction of the HR above 88 beats/min episodes was obtained in every one patient during VVI 80 beats/min and VVI 80 beats/min NP comparing to the control AF-group. Figure 1 summarizes the results of the VVI 80 beats/min and VVI 80 beats/min NP in the reduction of the AF tachy episodes during the 7-day follow-up. NP, i.e., pacing 70 beats/min from 10:00 pm to 6:00 am, did not significantly increase the percent of AF tachy episodes compared to VVI 80 beats/min.

	VVI 80 beats/min	VVI 80 beats/min NP	P-value
Mean ventricular rate (beats/min)	81.8 ± 3.4	78.8 ± 2.9	< 0.01
Maximum ventricular rate (beats/min)	205.9 ± 24.0	205.0 ± 23.8	ns
Pacing events (%)	85.8 ± 12.6	84.0 ± 13.7	ns

Table 4. Comparison of mean heart rate, maximum heart rate, and percentage share of ventricular pacing between VVI at 80 beats/min and VVI at 80 beats/min with night program (NP = VVI pacing at 70 beats/min from 10:00 pm to 06:00 am) during 7-day follow-up. AF = atrial fibrillation; P-value from Wilcoxon's matched-pairs test; ns = not significant.

Heart rate range (beats/min)	VVI 40 beats/min V sense (%)	VVI 80 beats/min V sense (%)	P-value
88 – 96	7.3 ± 4.8	3.2 ± 2.5	< 0.01
97 – 107	5.2 ± 3.2	2.4 ± 2.2	< 0.01
108 – 120	3.5 ± 2.7	1.9 ± 2.3	< 0.01
121 – 137	2.5 ± 3.3	1.3 ± 1.7	< 0.01
138 – 160	1.6 ± 2.4	0.8 ± 2.0	< 0.05
161 – 192	0.3 ± 0.7	0.5 ± 1.9	0.7 (ns)
> 192	0	0	ns

Table 5. Mean percentage share of ventricular sensed events in certain heart rate ranges during VVI pacing at 40 beats/min (control AF-measurements) and VVI pacing at 80 beats/min during 7-days follow-up. AF = atrial fibrillation; P-value from Wilcoxon's matched-pairs test; ns = not significant.

## Discussion

This study demonstrates the feasibility and efficacy of right-ventricular pacing in stabilizing the ventricular rhythm in AF. Ventricular pacing at 80 beats/min and at 80 beats/min with night program reduce AF tachy episodes by eliminating the majority (over 50 %) of HR above 88 beats/min. Ventricular pacing at lower rates during the night still provides reduction of AF tachy episodes, significantly decreases the mean HR, and reduces the percentage of ventricular paced events as compared to VVI 80 beats/min. The achievement of rate regularity in the VVI mode at 80 beats/min and at 80 beats/min with NP was found to be effective during the 7-day follow-up. A high percentage of pacing (above 80 %) seems to be indispensable for significant reduction of AF tachy episodes during physical exercise. Our

study confirms that the rate of ventricular pacing should be between the mean and max HR.

However, fixed-rate pacing might not be expected to provide HR stabilization during various activities involving physical and mental stress. It is necessary to define when the pacing rate must increase and when it must decrease. The hypothesis that the rate adaptive pacemaker (VVIR) or even Close Loop Stimulation [26] for the appropriate response to various activities and conditions in patients with AF should be tested in future studies.

Due to diagnostic memory function in Actros S pacemaker controlling of HR in AF patients is possible during long term follow-up. For this reason, in our study pacemaker diagnostic memory function instead of 24-

Heart rate range (beats/min)	VVI 40 beats/min V sense (%)	VVI 80 beats/min NP V sense (%)	P-value
88 – 96	7.3 ± 4.8	3.2 ± 3.1	< 0.01
97 – 107	5.2 ± 3.2	2.5 ± 2.4	< 0.01
108 – 120	3.5 ± 2.7	1.7 ± 1.7	< 0.01
121 – 137	2.5 ± 3.3	1.6 ± 2.7	< 0.01
138 – 160	1.6 ± 2.4	0.7 ± 1.8	0.03
161 – 192	0.3 ± 0.7	0.2 ± 0.9	0.34 (ns)
> 192	0	0	ns

Table 6. Mean percentage share of ventricular sensed events in certain heart rate ranges during VVI pacing at 40 beats/min (control AF-measurements) and VVI pacing at 80 beats/min with with night program (NP = VVI pacing at 70 beats/min from 10:00 pm to 06:00 am) during 7-day follow-up. AF = atrial fibrillation; P-value from Wilcoxon's matched-pairs test; ns = not significant.

Heart rate range (beats/min)	VVI 80 beats/min V sense (%)	VVI 80 beats/min NP V sense (%)	P-value
88 – 96	3.2 ± 2.5	3.2 ± 3.1	0.95 (ns)
97 – 107	2.4 ± 2.2	2.5 ± 2.4	0.82 (ns)
108 – 120	1.9 ± 2.3	1.7 ± 1.7	0.33 (ns)
121 – 137	1.3 ± 1.7	1.6 ± 2.7	0.51 (ns)
138 – 160	0.8 ± 2.0	0.7 ± 1.8	0.03 (ns)
161 – 192	0.5 ± 1.9	0.2 ± 0.9	0.1 (ns)
> 192	0	0	ns

Table 7. Mean percentage share of ventricular sensed events in certain heart rate ranges in patients with VVI pacing at 80 beats/min and at 80 beats/min with NP (VVI pacing at 70 beats/min from 10:00 pm to 06:00 am) during 7-day follow-up. AF = atrial fibrillation; P-value from Wilcoxon's matched-pairs test; ns = not significant.

hour Holter monitoring system was used. Moreover, this system of monitoring enabled the estimation of HR stabilization in the daily activity of patients.

#### Comparison to Previous Studies

**Percentage share of ventricular pacing:** Wittkamp [21], who first described the methods of heart-rate stabilization by means of ventricular pacing used special aggressive algorithm that required 95 % ventricular pacing. The subsequent algorithms tested by Greenhut et al and Lau et al [22,24] showed that ventricular pacing was less aggressive ranging between 74 % and 85 % ventricular pacing. Algorithms with low percentage of ventricular paced events did not provide a reduction of AF tachy episodes in the long-term follow-up [27]. Our study confirmed, as shown by previous investigators [21,24], that rate regularization can be achieved using a pacing rate between the mean and max HR in AF patients. Furthermore, Wittkamp noted a high correlation between the percentage of paced events, the mean HR, and heart-rate stability during AF. This is why Vp retrieval from the Actros S memory function may be an indicator of rate stabilization in atrial fibrillation in long-term follow-up.

**Mean and max HR:** Ventricular pacing at 80 beats/min and at 80 beats/min NP significantly increase the mean HR as compared to the control AF-data. This result was confirmed in other investigations [21,24] in which different rate stabilization algorithms were used. The reason seems to be that the mean ventricular pacing rate is higher than the mean AF HR. The mechanism of rate control by ventricular pacing is

considered to be provoked by an induction of concealed VA-conduction that reduces the frequency of antegradely conducted impulses [20,28]. This is why the ventricular pacing at 80 beats/min, like other algorithms for rate stabilization, is not able to eliminate the minimum RR-intervals.

**Reduction of AF tachy episodes and clinical implication:** The effect that reducing the number of AF tachy episodes has on symptoms such as palpitations and shortness of breath are not known. Recent studies examined the effect of ventricular rate stabilization on

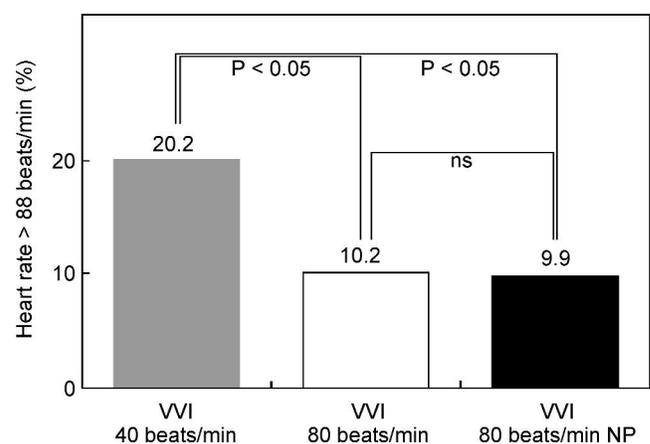


Figure 1. Percentage of cardiac events with intervals corresponding to heart rate above 88 beats/min during the 7-days follow-up in VVI 40 beats/min pacing (control AF-group), VVI 80 beats/min pacing and VVI 80 beats/min pacing with night program (NP = VVI 70 beats/min pacing from 10:00 pm to 06:00 am). P-value from Wilcoxon's matched-pairs test; ns = not significant.

hemodynamic parameters, demonstrating a trend toward improvement in cardiac output [29-33]. However, very little is to be found in the literature about the improvement in cardiac performance and/or survival as a result of HR control [34]. Some reports show the reversible effect of successful control of rapid HR on tachycardia-induced cardiomyopathy [35,36]. It is also well-known that rhythm irregularity and AF tachy rates affect cardiac contractility and are associated with cardiac output [31]. Pharmacological treatment is never able to suppress rhythm irregularity, and in this case, ventricular pacing may be very helpful. Moreover, pharmacological treatment is known to be connected with proarrhythmic side effects, which are sometimes life-threatening.

Our study revealed significant reduction of HR above 88 beats/min in patients with VVI 80 beats/min comparing to control AF patients. VVI 80 beats/min with NP still provides excellent results in decreasing AF tachy episodes. Although we do not use special algorithms for HR stabilization, our results in the reduction of HR above 88 beats/min are comparable those obtained when such algorithms and/or PC computer-based algorithms were used.

#### *Limitations of the Study*

A fixed rate of 80 beats/min might not be expected to provide the most appropriate pacing rate in all patients. The most appropriate pacing mode should be determined from the clinical status of the patient. For some patients, a fixed pacing rate of 80 beats/min may be too high. This is relevant, e.g., for patients with ischaemic heart disease. This type of pacing mode may aggravate angina pectoris. Assessing the most appropriate pacing rate for each patient requires further research into finding the best method of pacing in cases of AF.

#### **Conclusion**

- Right-ventricular pacing at 80 beats/min with NP significantly reduces AF tachy (> 88 beats/min) episodes in patients with chronic AF during daily activity in 7-days follow-up.
- The memory diagnostic function (event counter and HR histogram) may be useful in estimating HR stability (percentage share of ventricular pacing) and reducing AF tachy episodes during long-term follow-up.

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