How can the rate-adaptive atrioventricular delay be programmed in atrioventricular block pacing?

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Aims To optimize recommendations for programming of the rate-adaptive atrioventricular (AV) delay.

Methods and results Optimal AV delay (AVDopt) is the net effect of the pacemaker-related interatrial conduction time (IACT), duration of the left-atrial electromechanical action (LA-EAClong) and duration of left-ventricular latency (SV-EACshort). It can be calculated by AVDopt = IACT + LA-EAClong – SV-EACshort. We measured these three components in 20 DDD pacemaker patients (EF >45%) with the third degree AV block (AVB) at rest and submaximal ergometric exercise load of 71 ± 9 W which resulted in a 31.5 ± 9.9 bpm rate increase. Between exercise and rest, the components of and the final AVDopt showed no significant differences. Interatrial conduction time in VDD and DDD pacing varied by 2.3 ± 8.4 ms and 1.4 ± 8.8 ms, respectively, SV-EACshort changed by −2.6 ± 21.8 ms and AVDopt by −3.5 ± 33.3 ms and −4.3 ± 37.8 ms in VDD and DDD operation, respectively. The greatest variation was of LA-EAClong by −8.4 ± 32.7 ms. Linear regressions of the rate-dependent variations (Δf) in VDD operation yielded: ΔIACT(f) = 0.04Δf + 0.95 ms, ΔLA-EAClong = −0.59Δf + 10.1 ms, and ΔSV-EACshort = 0.14Δf − 7.2 ms which resulted in ΔAVDopt = −0.69Δf + 18.2 ms.

Conclusion A recommendation for programming of rate-adaptive AV delay in AV block patients cannot be given.

Keywords Rate-adaptive AV delay; DDD pacemaker; AV delay optimization

Introduction

Several invasive and non-invasive techniques enable determination of the individual optimal atrioventricular (AV) delay under resting conditions in DDD pacemaker patients.1–7 However, various authors have failed to prove an effect of AV delay programming in overall haemodynamics, for example, in the case of stroke volume.8

Most current pacemaker models also offer the possibility of programming a rate-adaptive AV delay. Various studies for DDD pacemaker patients with a third degree AVB have demonstrated that rate-adaptive AV delay, in comparison with fixed AV delay, can lead to an improvement in haemodynamics and exercise capacity.9–13

Few studies, however, have investigated the underlying causes of the benefits of rate-adaptive AV delay. According to a non-invasive study by Barbieri et al.,14 there was evidence that natural AV delay decreases with increasing heart rate. Furthermore, Daubert et al.,15 confirmed a shortening of AV delay under physiological conditions (4 ms/10 bpm) in an invasive study on healthy subjects.

Studies until now, however, have not disclosed which of the components of AV delay are responsible for their shortening in cases of exercise-related increasing heart rate. Ismer et al.16 demonstrated that pacemaker-related interatrial conduction time (IACT) remains constant between conditions of rest and submaximal ergometric exercise testing, both for VDD as well as for DDD pacing. The cause for the change in optimal AV delay under exercise conditions could be linked to other components of the AV delay. The aim of our study was to record separately, in DDD pacemaker patients, the components of the optimal AV delay during rate-increasing exercise, and consequently to derive recommendations for individual programming of rate-adaptive AV delay.

Methods

Inclusion criteria

Patients were included if they were able to perform exercise with at least a 20 bpm rate increase. All patients had been treated with a dual chamber pacemaker for complete AVB.
Exclusion criteria

Exclusion criteria were chronotropic incompetence, left ventricular ejection fraction (EF) <45%, heart failure in New York Heart Association (NYHA) Class II–IV, unstable angina pectoris, atrial fibrillation, and pacemaker malfunction. Furthermore, patients were excluded with any type of disorder of the oesophagus, because in such cases an oesophageal electrode could be harmful to the patient and, therefore, not possible to use.

Study equipment

We performed simultaneous recordings of transmitral flow, the left-atrial oesophageal electrogram, and the real-time sense-event markers as proposed by Ismer et al. and Melzer et al. This approach required the placement of a bipolar oesophageal electrode to provide a filtered left-atrial electrogram (LAE). Therefore, we applied a 5F oesophageal electrode (Osypka, Rheinfelden, Germany, TO2/5F) in the position of maximal left-atrial deflection and connected it to a filter amplifier (Fiab Rostockfilter, Vicchio-Firenze, Herten, Italy). The filtered oesophageal electrogram together with telemetric real-time pacemaker markers provided by the programmers analogue output were superimposed onto the display of transmitral flow velocity (TMF) from the Doppler-echo system (Sonolayer SSH-140A/Toshiba). To achieve this, the telemetric output of the programmer and the signal from the Rostockfilter were connected to the DC inputs of the echo device.

Components and calculation of the optimal AV delay

Ritter et al. and Ismer et al. define the optimal AV delay for any heart rate, based on diastolic optimization, as the net effect of the individual pacemaker-related IACT [IACT: MA – LA (right atrial sensed event marker – LA)] or SA – LA (right atrial pacing stimulus – LA)] and the left-atrial electromechanical action [LA-EAClong (LA – end of left atrial contribution to transmitral flow in a longer than physiological AV delay)] reduced by left-ventricular latency (SV-EACshort). The four determinants of the optimal AV delay were measured as follows using two screenshots (Figure 1).

Left-atrial electromechanical action (LA-EAClong) and pacemaker-related IACT in VDD pacing

To determine the LA-EAClong, we programmed a more than physiologically long AV delay (averaging 200 ms) in VDD pacing and measured the duration between the beginning of left-atrial deflection (LA) in the oesophageal electrogram and the end of undisturbed left-atrial contribution (EAClong) to transmitral flow (Figure 1, left).

In the same screenshot, pacemaker-related IACT in VDD pacing was measured between right-atrial sense-event marker (MA) and the beginning of left-atrial deflection (LA) in the oesophageal electrogram (IACT = MA – LA) (Figure 1, left).

Left-ventricular electromechanical latency period (SV-EACshort) and pacemaker-related IACT in DDD pacing

To determine left-ventricular electromechanical latency (SV-EACshort), we programmed a shorter than physiological AV delay (averaging 50 ms) during DDD pacing (Figure 1, right) (rate about 10 bpm above sinus rate) and measured the duration between ventricular pacing stimulus (SA) and the end of the truncated left-atrial contribution (EAC) to transmitral flow.

In the same screenshot, IACT in DDD pacing was measured between the right-atrial pacing stimulus (SA) and the beginning of the left-atrial deflection (LA) in the oesophageal electrogram (IACT = SA – LA) (Figure 1, right).

On the basis of these measurements, optimal AV delays were calculated for VDD (atrial-triggered, AVD_{optVDD}) and DDD (atrial paced, AVD_{optDDD}) modes using the formulæ:

\[
AVD_{optVDD} = MA - LA + LA-EAC_{long} - SV-EAC_{short}
\]

and

\[
AVD_{optDDD} = SA - LA + LA-EAC_{long} - SV-EAC_{short}
\]
Exercise testing

In order to enable echo measurements immediately after exercise, this study had to be performed in a supine position on a bicycle ergometer. We began with 25 W and increased the workload by 25 W every 2 min until the individually determined submaximal exercise level was reached. The patients were asked to aim for an intensity of exercise, which they could maintain steadily for 3 min, in order to have enough time during the exercise period to reprogramme the pacemaker from VDD to DDD mode. For this reason, the measurement of the components of the AV delay were taken under conditions of submaximal and not maximal exercise.

Statistical analysis

The data are expressed as mean ± SD. Individual differences between resting and exercise conditions were statistically analysed by Student’s t-test using SPSS 12.0 Base System and Professional Statistics for Windows™ (SPSS, Inc., San Rafael, CA, USA). A P value of <0.05 was considered statistically significant.

Results

Patients

Twenty patients were included in our study; 11 women and 9 men with a mean age of 62.7 ± 12 years. Table 1 shows the clinical characteristics of the patients. The mean interval between pacemaker implantation and inclusion in the study was 4.3 ± 2.8 years.

All of the patients had a pacemaker with the atrial lead in the right atrium and the ventricular lead in the apex of the right ventricle. The following types of pacemakers had been used: 13 Philos DR (Biotronik® Inc, Berlin, Germany); 3 Thera DR (Medtronic® Inc; Minneapolis, MN, USA); and 4 Kappa DR (Medtronic® Inc.).

Exercise test

All 20 patients fulfilled the criteria of the study protocol. Seventeen of them reached a subjective submaximal exercise level at 75 W, three of them at 50 W. Determinants of the AV delay could be measured in all cases.

Calculation of the optimal AV delay

By measuring, separately, the electrical (IACT) and electromechanical (LA-EAC_long and SV-EAC_short) delays, we succeeded in defining the optimal AV delays for VDD and DDD pacing for each patient for rest and submaximal exercise. Results are shown in Table 2.

Submaximal exercise load was between 50 and 75 W (71 ± 9 W) and resulted in significant rate increases (P < 0.0001) between 20 and 49 bpm, with a mean of 31.5 ± 9.9 bpm.

Comparing exercise with rest, pacemaker-related IACTs D f - LA in VDD mode, and D s - LA in DDD mode varied during exercise by 2.3 ± 8.4 ms (P = 0.244) and 1.4 ± 8.8 ms (P = 0.474), respectively. Left ventricular latency (SV-EAC_short) varied in similar order, by −2.6 ± 21.8 ms (P = 0.604). Most exercise-related changes concerned the left atrial electromechanical action (LA-EAC_long). This interval varied during exercise by −8.4 ± 32.7 ms, but was not statistically significant (P = 0.277).

As a consequence of these observations, compared with rest, (AVD optVDD = 92.1 ± 58.5 ms and AVD optDDD = 167.8 ± 60.0 ms), the mean values of the optimal AV delays during submaximal exercise conditions were slightly shorter (AVD optVDD = 88.6 ± 50.0 ms, P = 0.654 and AVD optDDD = 163.5 ± 54.5 ms, P = 0.625). The mean difference between individual exercise and resting AV delay was −3.5 ± 33.3 ms in VDD (P = 0.654) and −4.3 ± 37.8 ms in DDD (P = 0.625) mode, not statistically significant.

Slopes of the rate-responsive variations of the AV delay components were analysed by linear regression (Figures 2 and 3). The latter were not significant. It yielded the functions ΔD f - LA(f) = 0.04Δf + 9.95 ms, ΔD s - LA(f) = −0.16Δf + 6.6 ms in VDD operation, ΔLA-EAC_long = −0.59Δf + 10.1 ms and ΔSV-EAC_short = 0.14Δf − 7.2 ms which resulted into ΔAVD optVDD = −0.69Δf + 18.2 ms and ΔAVD optDDD AVDopt = −0.89Δf + 23.8 ms. The slopes of the mean rate-responsive variations of the IACTs and SV-EAC_short were 0.04 ms, −0.16, and 1.4 ms per 10 bpm rate increase, respectively (Figure 2). In contrast, the slope of LA-EAC_long

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Table 1: Clinical characteristics of the patients

| Clinical characteristics of the patients | Age (mean ± SD) 62.7 ± 12.1 | Gender (males/females) n/ % 9 (45%)/11 (55%) | Arterial hypertension (n/ %) 4 (20%) | Coronary artery disease (n/ %) 6 (30%) | Valvular disease (n/ %) 2 (10%) | Left-ventricular EF (mean ± SD) 55 ± 8.1% | Interval in years between pacemaker implantation and exercise testing (mean ± SD) 4.3 ± 2.8 years |

Table 2: Results of resting and submaximal exercise measurements

<table>
<thead>
<tr>
<th>n = 20</th>
<th>Rest</th>
<th>Exercise 71 ± 9 W</th>
<th>Difference exercise-rest</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate (bpm)</td>
<td>70.9 ± 11.7</td>
<td>102.4 ± 12.4</td>
<td>31.5 ± 9.9</td>
<td>P = 0.000</td>
</tr>
<tr>
<td>Mf - LA (ms)</td>
<td>23.0 ± 29.8</td>
<td>25.3 ± 33.0</td>
<td>2.3 ± 8.4</td>
<td>P = 0.244</td>
</tr>
<tr>
<td>Sf - LA (ms)</td>
<td>96.0 ± 24.9</td>
<td>100.1 ± 27.4</td>
<td>4.1 ± 8.8</td>
<td>P = 0.474</td>
</tr>
<tr>
<td>SF-EAC (ms)</td>
<td>192.4 ± 54.4</td>
<td>184.0 ± 55.5</td>
<td>−8.4 ± 32.7</td>
<td>P = 0.277</td>
</tr>
<tr>
<td>SV-EAC_short (ms)</td>
<td>123.3 ± 32.8</td>
<td>120.6 ± 34.2</td>
<td>−2.6 ± 21.8</td>
<td>P = 0.604</td>
</tr>
<tr>
<td>AVDoptVDD (ms)</td>
<td>92.1 ± 58.5</td>
<td>88.6 ± 50.0</td>
<td>−3.5 ± 33.3</td>
<td>P = 0.654</td>
</tr>
<tr>
<td>AVDoptDDD (ms)</td>
<td>167.8 ± 60.0</td>
<td>163.9 ± 54.5</td>
<td>−4.3 ± 37.8</td>
<td>P = 0.625</td>
</tr>
<tr>
<td>AVDoptDDD - AVDoptVDD (ms)</td>
<td>74.9 ± 30.9; P = 0.000</td>
<td>74.8 ± 35.7; P = 0.000</td>
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</table>
was $-5.9 \text{ ms per 10 bpm}$ and the resulting $\text{AVD}_{\text{optVDD}}$ are characterized by $-6.9 \text{ ms per 10 bpm}$ (Figure 3).

As expected, $S_{\text{A}} - LA$ and $M_{\text{A}} - LA$ ($P = 0.000$) as well as $\text{AVD}_{\text{optDDD}}$ and $\text{AVD}_{\text{optVDD}}$ varied significantly ($P = 0.000$) between resting and submaximal exercise conditions (Table 2).

Discussion

Modern DDD pacemakers are designed with rate-adaptive AV delay programming available. However, there is a lack of clear recommendations for effective programming of this parameter.19,20

Different studies have shown that pacemaker patients benefit from a rate-adaptive AV delay9–13 although this phenomenon has not been completely explained.

Therefore, we investigated the various components of the AV delay in AV block patients. Our results demonstrate the possibility to differentiate between the electrical and electromechanical components of the optimal AV delay not only during rest but also during submaximal exercise. Nevertheless, one disadvantage of the method that we used is the required placement of an oesophageal electrode.

On the basis of various statistically insignificant results in our study, we cannot definitively describe which role the various components of the AV delay ($\text{IACT}$, $\text{LA-EAC}_{\text{long}}$ and $\text{SV-EAC}_{\text{short}}$) play in the shortening of the optimal AV delay during exercise. Nevertheless, the resulting small slope of mean IACT variation vs. rate-increase confirms data previously published by Ismer et al.16 and Ausubel et al.21 demonstrating the IACT to be constant between rest and submaximal exercise. In contrast to this finding, Camous et al.22 have reported that the interatrial conduction intervals, in DDD mode, increase by $5.3 \pm 15.2 \text{ ms}$ with increasing heart rate, although this increase was entirely lacking.

![Figure 2](image2.png)

**Figure 2** Analysis of mean individual exercise-related rate-responsive variations ($\Delta f$) of the pacemaker-related IACT in VDD operation ($M_{\text{A}} - LA$) and left ventricular latency ($S_{\text{V}} - \text{EAC}_{\text{short}}$) by linear regression. Mean variations yielded small slopes of $0.4 \text{ ms per 10 bpm}$ for $M_{\text{A}} - LA$ and $1.4 \text{ ms per 10 bpm}$ rate increase for $S_{\text{V}} - \text{EAC}_{\text{short}}$.

![Figure 3](image3.png)

**Figure 3** Analysis of individual exercise-related rate-responsive variations ($\Delta f$) of the LA-EAC$_{\text{long}}$ and the resulting optimal AV delay ($\text{AVD}_{\text{opt}}$) in VDD pacing by linear regression. Slopes of LA-EAC$_{\text{long}}$ and the resulting $\text{AVD}_{\text{opt}}$ can be characterized by $-5.9$ and $-6.9 \text{ ms per 10 bpm}$ rate increase, respectively.
or only minimal in 43% of their patients. Furthermore, Wish et al.\textsuperscript{23} found that the optimal AV delay was related to the IACT.

Comparing the slopes of 0.4 and 1.4 ms for mean rate-related changes of IACT and S\textsubscript{EAC}\textsubscript{short} with those of −5.9 ms/10 bpm rate increase for the LA-EAC\textsubscript{long} and −6.9 ms/10 bpm for the resulting optimal AV delay in Figure 3, this study suggests, but cannot prove, our assumption that exercise-induced variations of the optimal AV delay could mainly reflect the variation of the LA-EAC\textsubscript{long} interval.

Duration of natural atrioventricular conduction interval was reported to decrease with exercise-increased heart rate.\textsuperscript{14,15} For an average heart rate increase of 78.7 ± 22.5 bpm, which is more than twice that of our cohort, Daubert et al.\textsuperscript{15} observed a physiological shortening of the AV conduction delay in 10 healthy subjects, with a decrease of mean 4 ± 2.1 ms every 10 bpm.

This shortening of the AV delay by 4 ± 2.1 ms every 10 bpm, as first described by Daubert et al.\textsuperscript{15} 20 years ago has only in part been adapted as standard programming for the rate-adaptive AV delay for DDD pacemakers. Table 3 shows the standard programming of the rate-adaptive AV delay of currently available pacemakers. These pacemakers were not used in our study.

In contrast to Daubert et al.\textsuperscript{15} the AV\textsubscript{Dopt} in our patient group did not vary significantly between rest and exercise in the conditions employed which in our case were submaximal. Therefore, the average exercise-related shortening of the AV delay of −6.9 ms per 10 bpm should be considered with reserve, although these results in principle support the findings of Daubert et al.\textsuperscript{15} Nevertheless, it is not possible to make a definitive recommendation for programming the rate-adaptive AV delay based on our findings.

There are various possible explanations for why our study resulted in statistically insignificant results. In comparison with the healthy subjects in the study by Daubert et al.\textsuperscript{15} the heart rate of our pacemaker patients increased to a much lesser degree (78.7 vs. 31.5 bpm). Furthermore, the resting and exercise AV\textsubscript{Dopt} revealed a much wider SD in our patients compared with those healthy subjects\textsuperscript{15} (20 compared with 50). In our study, a series of relatively less pronounced findings, which were not statistically significant, due to the low power, based on the Daubert et al.\textsuperscript{15} findings. This proved insufficient to establish statistically significant differences.

As a consequence of our study design and patient population, the findings of our study cannot be applied to patients with reduced left ventricular function with EFs of <0.45. Data on programming the rate-adaptive AV delay in such cases, as far as we are aware, is only known for cardiac resynchronization therapy. Scharf et al.\textsuperscript{24} optimized the AV delay in 36 patients with biventricular pacemakers/defibrillators on the basis of the velocity time integral determined from the echocardiogram. This resulted in a lengthening of the optimal AV delay under exercise conditions by 20 ms per 10 bpm.

In summary, our findings suggest that it would make sense to carry out a study such as ours with a study population of younger patients with AV block in order to achieve greater heart rate increases under exercise conditions, and thereby to increase the likelihood of establishing statistical significance of the findings. Furthermore, investigation of patients with EF < 0.35 is also needed in order to make recommendations for the programming of the rate-adaptive AV delay in these patients.

### Study limitations

In order to carry out the multiple-complex measurements under controlled exercise conditions, it was necessary to carry out this study under submaximal, instead of maximal, exercise conditions. Maximal exercise conditions with greater increases in heart rate would potentially result in significant results, where these measurements under submaximal exercise conditions did not. Because of these complex echocardiological measurements, it was necessary to perform the study with participants using a bicycle ergometer in a supine position. Our study did not include patients with an EF < 0.45, therefore our results cannot be applied to such patients.

### Conclusions

Our study of AV block patients with an average heart rate increase of 30 bpm under submaximal exercise conditions did not reveal significant differences in the components of the optimal AV delay (IACT, LA-EAC\textsubscript{long}, and S\textsubscript{EAC}\textsubscript{short}) under resting and exercise conditions. The electromechanical component LA-EAC\textsubscript{long} showed the largest average difference. As a result of the lack of statistical significance of these findings, we cannot definitively describe the role of the various components of the AV delay in the optimization of the rate-adaptive AV delay.

The total duration of the optimal AV delay additionally did not vary significantly between rest and exercise conditions in our study. Therefore, the average shortening of the optimal AV delay of −6.9 ms per 10 bpm in VDD mode has to be critically regarded. Although our findings are generally in accordance with the previous studies, a definitive recommendation for the programming of the rate-adaptive AV delay in AV block patients cannot be given based on these results.

### Table 3: Standard programming of rate-adaptive AV delay

<table>
<thead>
<tr>
<th>Pacemaker model</th>
<th>Standard programming of the rate-adaptive AV delay</th>
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<tbody>
<tr>
<td>Philos II DR/Biotronic</td>
<td>Between 50 and 150/min: −5 ms/10 bpm</td>
</tr>
<tr>
<td>EnPulse/Medtronic</td>
<td>Between 80 and 120/min: −10 ms/10 bpm</td>
</tr>
<tr>
<td>Insignia Ultra/Guidant</td>
<td>Steps of 2 ms between maximal and minimal AV delay</td>
</tr>
<tr>
<td>Identity DR/St Jude</td>
<td>Between 90 bpm and maximal sensor or tracking rate: either −10, −20, or −30 ms/10 bpm</td>
</tr>
<tr>
<td>Symphony/Sorin group</td>
<td>Between 60 and 120/min: −10 ms/10 bpm</td>
</tr>
</tbody>
</table>


References


