Biventricular pacing preserves left ventricular performance in patients with high-grade atrio-ventricular block: a randomized comparison with DDD(R) pacing in 50 consecutive patients


Department of Cardiology, Aarhus University Hospital, Skejby, Brendstrupgaardsvej 100, DK-8200 Aarhus N, Denmark

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Aims We aimed to investigate whether biventricular (BiV) pacing minimizes left ventricular (LV) dyssynchrony and preserves LV ejection fraction (LVEF) as compared with standard dual-chamber DDD(R) pacing in consecutive patients with high-grade atrio-ventricular (AV) block.

Methods and results Fifty patients were randomized to DDD(R) pacing or BiV pacing. LVEF was measured using three-dimensional echocardiography. Tissue-Doppler imaging was used to quantify LV dyssynchrony in terms of number of segments with delayed longitudinal contraction (DLC). LVEF was not different between groups after 12 months (P = 0.18). In the DDD(R) group LVEF decreased significantly from 59.7(57.4–61.4)% at baseline to 57.2(52.1–60.6)% at 12 months of follow-up (P = 0.03), whereas LVEF remained unchanged in the BiV group [58.9(47.1–61.7)% at baseline vs. 60.1(55.2–63.3)% after 12 months (P = 0.15)]. Dyssynchrony was more prominent in the DDD(R) group than in the BiV group at baseline (2.2 ± 2.2 vs. 1.4 ± 1.3 segments with DLC per patient, P = 0.10); and at 12 month follow-up (1.8 ± 1.9 vs. 0.8 ± 0.9 segments with DLC per patient, P = 0.02). NT-proBNP was unchanged in the DDD(R) group during follow-up (122 ± 178 pmol/L vs. 91 ± 166 pmol/L, NS) but decreased significantly in the BiV-group (from 198 ± 505 pmol/L to 86 ± 95 pmol/L after 12 months, P = 0.02).

Conclusion BiV pacing minimizes LV dyssynchrony, preserves LV function, and reduces NT-proBNP in contrast to DDD(R) pacing in patients with high-grade AV block.

KEYWORDS
Right ventricular pacing; BiV pacing; AV block; Heart failure; Three-dimensional echocardiography; Tissue-Doppler echocardiography

Background
Increasing evidence from randomized clinical trials shows that right ventricular (RV) pacing may lead to impairment of left ventricular (LV) systolic function and congestive heart failure (CHF) in patients with sick sinus syndrome. In patients with poor LV ejection fraction (LVEF), the detrimental impact of RV pacing seems even more obvious as indicated by the DAVID trial. Increasing percentages of RV pacing have been found associated with increasing incidence of CHF and atrial fibrillation. Long-term single-site RV pacing in patients with congenital heart block was shown to be associated with detrimental effects on LV performance. Furthermore, experimental studies have demonstrated that single-site RV pacing is associated with both functional and structural abnormalities in the LV myocardium, supposed to be caused by the asynchronous electrical activation of the paced ventricle.

To avoid inducing CHF in patients treated with pacemakers for sick sinus syndrome and in patients treated with implantable cardioverter defibrillators, new pacemaker software algorithms have been developed to minimize RV pacing. However, in patients with high-grade atrio-ventricular (AV) block, RV pacing is unavoidable. The percentage of time with ventricular pacing typically exceeds 90%. The treatment recommended for patients with high-grade AV block is atrio-ventricular synchronous pacing (DDD or VDD). In patients with CHF, poor LVEF, and left bundle branch block (LBBB), biventricular (BiV) pacing has been shown to improve LV function and reduce clinical heart failure. Furthermore, in patients with moderately depressed LVEF and atrial fibrillation, BiV pacing was found to preserve LVEF in contrast to single-site

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RV pacing after AV-nodal ablation. However, it is not known whether BiV pacing may protect against pacing-induced LV dysfunction and CHF in patients with high-grade AV block.

The aim of the present study was to investigate if BiV pacing may reduce LV dyssynchrony and preserve LV function as compared with rate adaptive dual chamber [DDD(R)] pacing in consecutive patients with AV block referred for their first pacemaker implantation.

Methods

Consecutive patients referred for their first pacemaker implantation during the period from September 2003 to June 2005 underwent screening for inclusion in the study (Figure 1). Fifty patients with permanent or paroxysmal high-grade AV block were included and randomized to either DDD(R) or BiV pacing.

The study was approved by the local ethical committee and followed the Helsinki declaration. The study was notified to the Good Clinical Practice unit at the Institute of Clinical Medicine, Aarhus University, Aarhus, Denmark and reported to www.clinicaltrials.gov. Patients volunteered for participation in the study and inclusion was done after obtaining informed consent.

Pacemaker implantation and pacemaker settings

All patients received a BIV pacemaker (Insync III 8042, Medtronic Inc., Minneapolis, MN, USA). All pacemaker leads were implanted transvenously, and both patient groups had active fixation leads implanted in the right atrial appendage and in the outflow tract of RV. Patients in the BiV group had a third LV lead implanted transvenously through the coronary sinus to a lateral or posterolateral branch of the coronary sinus tributary. In the DDD(R) group the third connection in the Insync III pacemaker was plugged. All pacemakers were programmed with a lower rate of 60 bpm., rate-adaptive AV delay, and a resting paced AV delay of 150 ms and a sensed AV delay of 120 ms. In the DDD(R) group the pacemakers were programmed to AV synchronous pacing of the RV. Sequential ventricular pacing was adjusted according to tissue-Doppler recordings in the BiV group.

Echocardiographic techniques

Echocardiography was performed using Vingmed Vivid Five, GE Medical, Horten, Norway with a multi-frequent transducer using 1.7 MHz and second harmonic mode. Two-, three-, and two-dimensional tissue-Doppler echocardiograms were recorded as digital loops for off-line analysis using EchoPAC version 6.4.2 and EchoPAC-3D version 1.0.1., GE Medical, Horten, Norway. All data were recorded and analysed by the same physician who was unaware of the pacing mode during the off-line analyses.

Three-dimensional echocardiography was performed during one breath hold at end-expiration using ECG-triggered coaxial rotation from the apical position with 30° interval between scanning planes. The resulting six different loops were analysed off-line by manually outlining the endocardial borders in end-diastole and end-systole. The EchoPAC-3D software calculated the LV systolic and diastolic volumes and LVEF. Of all three-dimensional recordings, 96% of cases were analysed with this method. In the remaining 4%, LVEF was measured by means of Simpson’s bi-plane method because of inadequate image quality of the three-dimensional recordings.

Tissue-Doppler recordings of the longitudinal velocity of the LV myocardium in the three standard apical views were used to analyse regional systolic and post-systolic motion towards the apex. Analysis was carried out in each of the 16 segments of the model of The American Society of Echocardiography. If present in a given segment, the peak velocity of post-systolic motion after aortic valve closure was recorded. Delayed longitudinal contraction (DLC)
was considered to be present if a segment with post-systolic motion of more than 1 cm/s exhibited negative strain rate (shortening).\textsuperscript{15,19} Thus, DLC was considered as a marker of LV dysynchrony. To avoid aliasing, the colour-coded area and the settings of the echocardiographic equipment were adjusted to obtain the highest possible frame rate (~130 frames/s).

The magnitude of the average longitudinal myocardial displacement towards the apex was obtained from tissue-tracking curves recorded in the three standard apical views in systole. A mean tissue-tracking score (TTS) from the 12 basal and middle segments was calculated.\textsuperscript{15}

The baseline echocardiographic assessment was performed within 12 h after pacemaker implantation. All echocardiographic measurements were done with the pacemaker programmed to 80 bpm.

In the BIV group the activation delay between the two ventricles (VV timing) was guided by means of tissue-Doppler techniques.\textsuperscript{15} Colour-coded tissue-Doppler recordings in the three standard apical views were obtained at five different VV intervals (RV 20 ms before LV, RV 12 ms before LV, simultaneous pacing of RV and LV, LV 12 ms before RV, and LV 20 ms before RV). The VV-timing interval exhibiting the least-extended dyssynchrony in contribution with the highest degree of systolic longitudinal displacement of the LV myocardium was considered to be the optimal setting in each individual patient and the pacemaker was programmed accordingly. This setting remained unchanged during follow-up. Tissue-Doppler-guided optimization of the VV-timing interval resulted in simultaneous stimulation of the ventricles in 17 patients, pre-activation of the RV-lead in four patients (12, 12, 12, and 20 ms before LV, respectively) and pre-activation of the LV-lead in another four patients (12, 20, 20, and 20 ms before RV, respectively).

Clinical and laboratory tests
At baseline and at follow-up visits, patients were examined by the same physician who was not blinded to pacing mode. Patients were classified according to New York Heart Association Functional Class (NYHA) and the pacemaker was tested. From the pacemaker telemetry the percentage of ventricular pacing was recorded. N-terminal pro brain natriuretic peptide (NT-ProBNP) was measured in blood samples collected after pacemaker insertion with the patient resting in the supine position for 30 min. Blood samples were centrifuged immediately after collection and frozen for later analysis. All blood samples were later defrosted and analysed together to minimize analysis variation using Elecsys 1010 (La Roche Ltd., Basel, Switzerland). A 6 min walk test was performed as the last test at every visit. The clinical and laboratory tests were repeated at the 12 month follow-up visit.

End points
The primary end point was LVEF measured by three-dimensional echocardiography at the 12 month follow-up. Secondary end points were the extension of LV dysynchrony assessed by tissue-Doppler imaging, diastolic filling patterns measured with pulsed-Doppler echocardiography, left atrial volumes, LV dimensions measured by M-mode echocardiography, plasma NT-proBNP, and 6 min walk test.

Statistical considerations
Power calculations were performed before including patients in the study. The risk of Type I error was set to 5% and the statistical power to 80%. On the basis of earlier studies the standard deviation of the LVEF measured by means of three-dimensional echocardiography was assumed to be 6%.\textsuperscript{16,17} With a minimal relevant difference of 5% (absolute percent) between LVEF in the DDD(R) and BIV groups, a total of 44 patients were needed for the study. With an expected dropout rate of 10%, the total number of patients included was decided to be 50. Statistical calculations were done using STATA 8.1 software (Stata Corporation, TX, USA).

All data were analysed according to the intention-to-treat principle. Paired analysis was used for comparison within groups and non-paired analysis for comparison between groups, all as two-sided tests. Student’s t-test was used for parametric data and χ² test, Wilcoxon or Mann–Whitney’s test for non-parametric data. Natural logarithm was used if appropriate for shaping data to the normal distribution. Normally distributed data were reported as mean ± SD, otherwise as median (first and third quartile). P values below 5% were considered statistically significant. No corrections were done for multiple testing.

Results
Patients were randomized to either DDD(R)- (n = 25) or BIV pacing (n = 25) (Figure 1). Implantation success in the study was 100%. Both groups exhibited 100% ventricular pacing (median) both at the 3- and the 12 month follow-up.

Baseline characteristics are shown in Table 1. No significant changes in cardiovascular medication were done during follow-up.

LV systolic function
No significant difference was observed in LVEF between the two treatment groups at baseline or at the 12 month follow-up (both NS). LVEF decreased in the DDD(R) group from 59.7(57.4–61.4)% at baseline to 57.2(52.1–60.6)% at the 12 month follow-up (P = 0.03). LVEF did not change significantly in the BIV group [58.9(47.1–61.7)% at baseline vs. 60.1(55.2–63.3)% at the 12 month follow-up (P = 0.15; Figure 2)]. Comparing changes in LVEF between baseline and 12 month follow-up, there was a highly significant difference between the DDD(R) [−3.5(−6.7–0.3)%] and the BIV groups [1.4(−2.5–−7.1)%], P = 0.007.

Nine patients had LVEF below 50% at baseline including seven patients in the BIV group and two patients in the DDD(R) group. In the subgroup of patients with LVEF above 50%, the LVEF similarly decreased in the DDD(R) group [59.8(58.6–62.2)% at baseline vs. 57.3(52.7–60.7)% at the 12 month follow-up; P = 0.04], and remained unchanged in the BIV group (60.3(57.7–62.3)% at baseline vs. 60.1(58.0–63.2)% at the 12 month follow-up, NS).

In the subgroup of patients with QRS < 120 ms before pacemaker implantation, LVEF decreased in the DDD(R) group (n = 19) from 59.7(56.7–60.9)% at baseline to 57.2(52.7–60.8)% at 12 months (P = 0.09) and was preserved in the BIV group (n = 13) from 58.8(55.0–61.6)% at baseline to 60.0(58.0–62.8)% (P = 0.31).

The LV diastolic volume remained unchanged in both groups during follow-up, whereas the LV systolic volume increased significantly in the DDD(R) group and was unchanged in the BIV group (Table 2). Chamber dimensions and wall thickness of the LV at baseline and the 12 month follow-up are also listed in Table 2.

Tissue-doppler imaging
Left ventricular systolic longitudinal displacement recorded by TTD did not differ statistically between treatment groups at baseline or at the 12 month follow-up. However, in the DDD(R) group the systolic TTS decreased significantly from 5.1 ± 2 mm at baseline to 4.3 ± 1 mm at the 12 month follow-up visit (P = 0.02). There was no change in the BIV group (4.7 ± 3 and 4.6 ± 2 mm, respectively; NS).
Analysis of segments with DLC in the 16 segments model at baseline and at 12 months of follow-up is shown in Figure 3.

At baseline the extent of dyssynchrony did not differ statistically between the DDD(R) group (2.2 ± 2.2 segments with DLC per patient) and the BIV group (1.4 ± 1.3 segments with DLC per patient; \( P = 0.10 \)). However, at the 12 month follow-up, patients in the DDD(R) group had significantly more segments with DLC than patients in the BIV group (1.8 ± 1.9 segments per patient vs. 0.8 ± 0.9 segments per patient, \( P = 0.02 \)).

**Six minute walk test**

Both groups showed significant improvement in the 6 min walk test. Walking distance increased from 458 ± 61 to 488 ± 91 m in the DDD(R) group (\( P = 0.004 \)) and from 432 ± 88 to 476 ± 106 m in the BIV group (\( P = 0.008 \)). There was no difference in improvement between groups and no difference between groups at baseline or at the 12 month follow-up (NS).

**NT-proBNP**

There was no difference between groups in NT-proBNP level at baseline or at 12 month follow-up (both NS). However, NT-proBNP remained unchanged in the DDD(R) group (baseline 122 ± 178 pmol/L, 12 month follow-up 91 ± 166 pmol/L, NS), whereas NT-proBNP decreased significantly in the BIV group from 198 ± 505 pmol/L at baseline to 86 ± 95 pmol/L at the 12 month follow-up (\( P = 0.02 \)).

**New York Heart Association classification**

There was no difference between groups in NYHA functional class (I/II/III/IV) at baseline or at 12 month follow-up (both NS). NYHA was unchanged in the DDD(R) group: (12/12/1/0) at baseline and (14/9/1/0) after 12 months, NS. A significant decrease in NYHA class was observed in the BIV-group from (12/9/3/1) at baseline to (19/4/1/0) at the 12 month follow-up, \( P < 0.001 \) (\( \chi^2 \) test).

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### Table 1 Baseline characteristics

<table>
<thead>
<tr>
<th></th>
<th>DDD(R) group n = 25</th>
<th>BIV group n = 25</th>
<th>( P ) value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, median quartiles</td>
<td>76 (67–81)</td>
<td>76 (71–81)</td>
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<td>Female patients, n (%)</td>
<td>8 (32%)</td>
<td>8 (32%)</td>
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<td>Body mass index, mean ± SD (kg/m²)</td>
<td>26 ± 6</td>
<td>25 ± 3</td>
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<tr>
<td>Mean blood pressure (mmHg)</td>
<td>155/83</td>
<td>146/79</td>
<td>0.12/0.24</td>
</tr>
<tr>
<td>Syncope, n (%)</td>
<td>11 (44%)</td>
<td>7 (28%)</td>
<td>0.24</td>
</tr>
<tr>
<td>Dizzy spells, n (%)</td>
<td>15 (60%)</td>
<td>18 (72%)</td>
<td>0.37</td>
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<tr>
<td>NYHA (I/II/III/IV), n</td>
<td>12/12/1/0</td>
<td>12/9/3/1</td>
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<tr>
<td>Intrinsic QRS-width (ms)</td>
<td>117 ± 33</td>
<td>143 ± 38</td>
<td>0.01</td>
</tr>
<tr>
<td>LBBB, n</td>
<td>1</td>
<td>3</td>
<td>0.29</td>
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<tr>
<td>Medical conditions</td>
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<td></td>
</tr>
<tr>
<td>Hypertensive/Ischaemic heart disease, n (%)</td>
<td>23 (92%)</td>
<td>24 (96%)</td>
<td>0.55</td>
</tr>
<tr>
<td>Heart valve disease, n (%)</td>
<td>3 (12%)</td>
<td>2 (8%)</td>
<td>0.64</td>
</tr>
<tr>
<td>Previous stroke, n (%)</td>
<td>0 (0%)</td>
<td>3 (12%)</td>
<td>0.07</td>
</tr>
<tr>
<td>Diabetes, n (%)</td>
<td>5 (20%)</td>
<td>3 (12%)</td>
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</tr>
<tr>
<td>Cardiovascular medication</td>
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<td></td>
</tr>
<tr>
<td>Beta blockers, n (%)</td>
<td>4 (16%)</td>
<td>4 (16%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Calcium channel blockers, n (%)</td>
<td>5 (20%)</td>
<td>1 (4%)</td>
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<tr>
<td>ACE inhibitors/ARBs, n (%)</td>
<td>15 (60%)</td>
<td>12 (48%)</td>
<td>0.40</td>
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<tr>
<td>Diuretics, n (%)</td>
<td>17 (68%)</td>
<td>12 (48%)</td>
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<tr>
<td>Aspirin, n (%)</td>
<td>13 (52%)</td>
<td>15 (60%)</td>
<td>0.57</td>
</tr>
</tbody>
</table>

LBBB, Left bundle branch block; ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker.

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**Figure 2**  
Left ventricular ejection fraction at baseline and at 12 months of follow-up in the two groups. Filled circles indicate median values with first and third quartiles.
QRS duration
At baseline before pacemaker implantation, patients in the BiV group had significantly wider QRS than patients in the DDD(R) group, 144 ± 38 and 117 ± 33 ms, \( P = 0.01 \) (Table1). That remained similar after excluding patients with permanent ventricular escape rhythm (143 ± 40 and 113 ± 29 ms, \( P = 0.01 \)). The QRS duration increased significantly in the DDD(R) group after pacemaker implantation to 155 ± 28 ms, \( P < 0.001 \) and decreased in the BiV-group to 137 ± 23 ms, NS. No further change was observed in either group during 12 months of follow-up.

Implantation procedure and complications
Surgery time was significantly shorter in the DDD(R) group than in the BiV group (34 ± 10 vs. 66 ± 21 min, \( P < 0.001 \)). The period of fluoroscopy was also shorter in the DDD(R) group than in the BiV group (4.8 ± 3 vs. 14.9 ± 8 min, \( P < 0.001 \)).

No pacemaker-related infection was observed during follow-up. A total of five patients underwent re-operation because of lead displacement. Atrial exit block occurred in one patient in the BiV group after 10 months. Two patients, one from either group, had dislodgement of the RV-lead 2–8 days after implantation. Dislodgements of the LV leads

| Table 2 Dimensions of the left atrium, left ventricle, and left ventricular ejection fraction |
|-----------------------------------------------|-----------------------------------------------|
| DDD(R) group \( n = 24 \)                      | BIV group \( n = 24 \)                         |
|                                              |                                              |
| Left atrial volume (mL) ± SD                  | Left atrial volume (mL) ± SD                  |
| 51 ± 16                                       | 59 ± 22                                       |
| 54 ± 13                                       | 61 ± 29                                       |
| Inter-ventricular septum (cm) ± SD            | Inter-ventricular septum (cm) ± SD            |
| 1.2 ± 0.4                                     | 1.2 ± 0.2                                     |
| 1.2 ± 0.3                                     | 1.2 ± 0.2                                     |
| LV posterior wall (cm) ± SD                   | LV posterior wall (cm) ± SD                   |
| 1.1 ± 0.3                                     | 1.1 ± 0.2                                     |
| LV diastolic dimension (cm) ± SD              | LV diastolic dimension (cm) ± SD              |
| 4.7 ± 0.6                                     | 4.9 ± 0.4*                                    |
| 4.9 ± 0.4*                                    | 5.3 ± 1.0                                     |
| LV systolic dimension (cm) ± SD               | LV systolic dimension (cm) ± SD               |
| 3.0 ± 0.7                                     | 3.2 ± 0.6                                     |
| 3.7 ± 1.0                                     | 3.7 ± 0.7                                     |
| LV diastolic volume (mL) ± SD                 | LV diastolic volume (mL) ± SD                 |
| 102 ± 23                                      | 117 ± 54                                      |
| 106 ± 20                                      | 120 ± 57                                      |
| LV systolic volume (mL) ± SD                  | LV systolic volume (mL) ± SD                  |
| 41 ± 11                                       | 58 ± 42                                       |
| 48 ± 16*                                      | 54 ± 42                                       |
| LVEF, median quartiles (%)                    | LVEF, median quartiles (%)                    |
| 59.7(57–61)                                   | 58.9(47–62)                                   |
| 57.2(52–61)*                                  | 60.1(55–63)                                   |

*\( P < 0.05 \) within group compared with baseline.

Figure 3 Bulls-eye plots demonstrating the segmental location of dyssynchrony. Numbers refer to the percent of patients with delayed longitudinal contraction (negative strain rate) in each individual segment.
occurred in two patients. One was diagnosed 5 days after implantation and the other at the 3 month follow-up. All re-operations were done without complications. Stimulation of the phrenic nerve was observed in three patients in the BiV group and all were managed by reducing the output on the LV channel.

Discussion

The main finding of the present study is that BiV pacing preserves LV function and minimizes LV dyssynchrony in contrast to DDD(R) pacing in consecutive patients with high-grade AV block. Implantation of BiV pacemakers in such patients seems feasible and associated with few complications.

LVEF did not differ at the end of follow-up. However, after 12 months of permanent RV pacing, LVEF measured by three-dimensional echocardiography and LV longitudinal systolic function measured by tissue-Doppler imaging both decreased while the diastolic LV-dimension increased. These findings confirm prior studies in patients with sick sinus syndrome where similar remodelling of the left ventricle after single-site RV pacing was revealed by M-mode echocardiography. In contrast, no changes in LV function or geometry was observed during BiV pacing in the present study, indicating that BiV pacing does not harm LV performance.

LB BBB, LV dyssynchrony, and low LVEF are associated with increased 1 year mortality in patients with CHF. The presence of myocardial dyssynchrony has been a target for cardiac resynchronization therapy, which was recently shown to reduce morbidity and mortality in patients with CHF and LB BBB. The present study using tissue-Doppler echocardiography demonstrated significantly more LV systolic dyssynchrony during 12 months of DDD(R) pacing as compared with BiV pacing. The segmental myocardial distribution of dyssynchrony seemed to be more regionally localized with preference to the septal and infero-posterior parts of the LV during DDD(R) pacing (Figure 3). In contrast, we found less dyssynchrony and a less obvious regional pattern of dyssynchrony during BiV pacing. The regional distribution of dyssynchrony during DDD(R) pacing in the present study most likely reflects single-site RV pacing as demonstrated in experimental animal studies. Apparently, BiV pacing seems to oppose the dyssynchrony induced by RV pacing.

Previous studies have demonstrated significant LV dyssynchrony and adverse LV remodelling during RV apical pacing. In acute studies RV outflow tract pacing has been associated with more beneficial LV haemodynamics than RV apical pacing. Compared with RV apical pacing, RV outflow tract pacing also seems to be associated with more beneficial LV haemodynamics during mid-term follow-up. However, RV outflow tract pacing as used in the present study still seemed to have an adverse impact on LV performance as compared with BiV pacing.

Analyses from the MOST trial showed both baseline and paced QRS duration to be independent predictors of hospitalization for heart failure. We observed a significant increase in QRS width during DDD(R) pacing but no change during BiV pacing. The change in QRS width in the DDD(R) group together with the observations of decreased LVEF, decreased longitudinal systolic function, and increased systolic volume may indicate a higher risk of later development of CHF as compared with BiV pacing. This is further supported by the findings of persistently elevated NT-proBNP level in the DDD(R) group in contrast to a significant decrease in NT-proBNP in the BiV group.

Overall, the complication rate observed in our BiV group of patients was acceptable (4/25, 16%) compared with patients who received BiV pacemakers in the CARE-HF (11%), MIRACLE (13%), and COMPANION-trials (9.9%). Implantation of BiV-pacing systems may be difficult in some patients and often time-consuming as indicated by surgery times of 162 and 164 min, respectively, in the MIRACLE and COMPANION trials. However, the present study demonstrated that successful implantation of BiV-pacing systems can be done with considerably shorter surgery time (in mean 66 min). We experienced no complicating haematomas or infections in the study. Right-sided lead dislodgements seemed to be more common in our study than expected in a general pacemaker population. A possible explanation may be the use of a new pace-lead with active fixation.

Pacing thresholds and R-wave amplitudes for LV leads have been found to be stable during long-term follow-up. Exit block of ventricular leads in patients with AV block is a serious event. Combined implantation of RV and LV leads may potentially reduce the rate of such events.

The present study documented beneficial effects as well as feasibility of BiV pacing in a relative small cohort of patients with AV block. However, there is no documentation so far that the use of BiV pacing in consecutive patients with AV block may improve clinical outcome as compared with conventional DDD(R) pacing. Therefore, it may seem premature to recommend BiV pacing generally to patients with AV block and normal LV function. The result of the present study supports the conduction of larger trials evaluating BiV pacing in subgroups of patients with AV block in whom BiV pacing from a theoretical point of view may seem superior to DDD(R) pacing, e.g. patients with pre-existing intra-ventricular dyssynchrony or moderately impaired LV function.

Study limitations

Because of various degrees of AV block and heart rates, we did not find echocardiography prior to pacemaker implantation relevant for later comparison. Randomization in the present study was therefore done regardless of the unknown pre-implant LVEF and regardless of the pre-implant intrinsic QRS duration. BiV pacing may increase LVEF in patients with CHF, low LVEF, and LB BBB even after few days. In the present study, only one patient in the DDD(R) group had LB BBB, whereas three patients in the BiV group had LB BBB (baseline LVEF values 37.5, 56.0, and 61.7%) in whom a potential benefit from BiV pacing might have occurred from the pre-implant stage to baseline. It is also well recognized that DDD(R) pacing acutely decreases LVEF. Therefore, we cannot rule out a statistically significant difference in pre-implant LVEF between groups. However, if LVEF in the DDD(R) group was superior to that of the BiV-group before pacemaker implantation, the adverse impact of DDD(R) pacing is strengthened by the stable LVEF after 1 year BiV pacing in comparison with the decreasing LVEF after 1 year of DDD(R) pacing.

Knowledge of the pacing mode during collection of data at follow-up visits might lead to bias. However, the 6 min walk
test showed no difference between groups during follow-up indicating no particular examiner bias. Furthermore, echocardiograms and plasma NTpro-BNP were analysed with no knowledge of the pacing mode and blinded to the point of time the images were recorded.

Conclusion

In patients with high-grade AV block, BiV pacing protects against LV dyssynchrony and dysfunction otherwise seen after conventional DDD(R) pacing. Implantation of BiV pacemakers in patients with high-grade AV block is feasible and safe, but cannot at present time be recommended for unselected patients because of lacking evidence of superiority with respect to morbidity and mortality.

Conflict of interest: none declared.

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Reference