Long-term follow-up of DDD and VDD pacing: a prospective non-randomized single-centre comparison of patients with symptomatic atrioventricular block

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Aims
This prospective non-randomized single-centre registry compared clinical outcome, pacing parameters, and long-term survival in patients receiving VDD or DDD pacemaker (PMs) for symptomatic atrioventricular (AV) block.

Methods and results
Single-lead VDD (n = 166) and DDD (n = 254) PMs were implanted in 420 successive patients with isolated AV block between January 2001 and December 2009. At the end of the follow-up period [median 25 (1–141) months], there was no difference in the incidence of atrial fibrillation [11.2% in the VDD group; 11.4% in the DDD group (P = 0.95)], myocardial infarction [31.1% in the VDD group; 25.2% in the DDD group (P = 0.20)], or dilated cardiomyopathy [9.9% in the VDD group; 8.9% in the DDD group (P = 0.74)]. At last follow-up, 65.9% of the VDD PMs and 89.3% of the DDD PMs were still programmed in their original mode with good atrial sensing. Due to permanent atrial fibrillation, 7.9% patients out of the VDD group had been switched to VVIR mode and 8.7% patients out of the DDD group to VVIR or DDIR mode. The P-wave amplitude was poor (sensed P-wave, 0.5 mV) in 19.1% of the VDD PM and 1.6% of the DDD PM (P, 0.001) and 7.1% of the VDD patients and 0.4% of the DDD patients had been switched to VVIR pacing mode due to P-wave undersensing and AV dissociation (P = 0.003). Symptomatic atrial undersensing requiring upgrading was similar in both groups. The overall survival, adjusted for age, was not significantly different in the VDD and the DDD group (log rank: 0.26). Moreover, Cox survival analysis excluded the pacing mode as a significant predictor of mortality [hazard ratio (HR) = 0.79, confidence interval (CI) (0.46–1.35), P = 0.39].

Conclusion
Comparing VDD and DDD pacing, a significantly larger number of VDD-paced patients developed poor atrial signal detection without clinical impact. However, atrial under sensing did not influence the incidence of atrial fibrillation, myocardial infarction, dilated cardiomyopathy, or mortality.

Keywords
VDD Pacemakers • DDD Pacemakers • Atrioventricular block • Atrial undersensing • Clinical follow-up

Introduction
Dual-chamber (DDD) pacemakers (PMs) are widely used to treat symptomatic patients with atrioventricular (AV) conduction defects. Indeed, clinical and haemodynamic advantages of maintaining AV synchronization during ventricular pacing are well documented.1–6

In current ACC/AHA/HRS guidelines, single lead VDD PMs are an alternative to DDD PMs in patients with AV conduction block and normal sinus node function.7 In this pacing mode, the use of a single-pass lead with far-field atrial sensing bipolar presents the advantages of reducing procedure time, complications,8 and cost,9 while maintaining the physiological benefits of AV synchrony.

Several retrospective studies on VDD pacing, demonstrating good clinical outcome with minimal atrial sensing problems, have confirmed that VDD pacing was an alternative to DDD pacing.10,11 However, other reports highlight the inability to stimulate the
atrium and the instability of the atrial sensing. Hence, the VDD pacing mode remains marginal in daily clinical practice.12,13

In order to clarify advantages and disadvantages of each pacing mode, we compared early and late complications, long-term clinical outcome and pacing parameters as well as long-term survival of our patient population suffering with symptomatic AV block who received VDD or DDD PMs.

Method

Study population

Between January 2001 and December 2009, 420 consecutive patients receiving VDD or DDD PMs as primary implantation for symptomatic AV conduction disorders were included in this prospective single-centre registry. Pacemaker implantation and patient follow-up took place in our centre. Assignment to VDD or DDD pacing was dependent on the choice of the physician. Patients under the age of 18 years, those with congenital heart disease, ejection fraction inferior to 35% (at echocardiography-Doppler or ventriculography), prior history of atrial fibrillation or sick sinus syndrome at the time of implantation were excluded. The absence of sinus node dysfunction was demonstrated, based on the patient’s medical file and history of supra-ventricular tachycardia, symptoms such as palpitation, and 12-lead resting electrocardiogram. Chronotropic insufficiency was excluded when patient were able to perform an exercise stress test. Patients lost during follow-up were censored at their last visit.

Pacemaker implantation technique and complications

Pacemakers were implanted under local anaesthesia following the same standardized technique, using the cephalic vein surgical approach. Pacing and sensing thresholds were determined at the time of implantation using standard programming system analysers. For both VDD and DDD PMs, steroid-eluting passive fixation leads were used. They were placed at the apex of the right ventricle under fluoroscopic guidance to achieve at least 5 mV R-wave detection and a stimulation threshold ≤1 V at 0.5 ms pulse duration.

For VDD leads, the distance from the ventricular tip to the atrial sensing bipole was chosen at the discretion of the implanting physician based on radiological information. Optimal localization for the atrial bipole was based on atrial sensing, using continuous P-wave measurement under fluoroscopy guidance.14,8 Achievement of a minimal atrial sensitivity of 1 mV both in inspiration and expiration was required.

For DDD PMs, atrial steroid eluting passive fixation leads were positioned under fluoroscopic control to achieve sensing values >1.5 mV and pacing threshold ≤1.0 V. Atrioventricular delays were programmed between 110 and 200 ms. All PMs had a rate-adaptive mode.

Early and late complications were recorded. A complication was defined as an event requiring either surgical revision—such as lead dislodgment, loss of sensing or exit block, cardiac perforation, pocket haematoma, infection, erosion—or an invasive procedure—such as a use of pleural catheter for pneumothorax or drainage of a haemothorax. Early complications were those that occurred within the first 3 months after implantation and late complications occurred thereafter.

Clinical follow-up and pacemaker control

Patients were followed up at 24 h and 2 months post-implantation and then every 6 months by a rythmologist. Visits included clinical examination, recording of a 12-lead ECG and PM interrogation. Atrial and ventricular pacing and sensing thresholds, AV sensing, and pacing relationship were collected. An atrial sensing threshold of <0.5 mV was considered poor. Patients with atrial undersensing were monitored after adaptation of the atrial sensitivity to ensure optimal AV synchrony.

Standard antero-posterior and lateral chest X-ray was performed at 24 h and 2 months post-implantation and when poor atrial sensing or AV dissociation was discovered on regular 6-monthly PM control.

Exercise stress test and 24 h Holter monitoring were also recorded if the patient’s clinical situation warranted it. The former was performed to show evidence of AV dissociation on exertion in patients experiencing exertional dyspnoea, the latter, to evaluate sinus node function and presence of arrhythmia in patients complaining of palpitations. The incidence of atrial arrhythmias was also assessed through analysis of the PM control. Only patient with permanent AV dissociation and/or PM syndrome were considered for upgrading of their PM. At least one transthoracic echocardiography was performed over the follow-up period. Left ventricular (LV) function and LV volume were measured.

Between 1 June 2009 and 31 December 2009, all patients were called back to undergo a final control visit which included a full medical examination, recording of a 12-lead ECG and PM interrogation and check, a standard antero-posterior and lateral chest X-ray, and a final transthoracic echocardiography. In the case of death or loss to follow-up, patients’ data were gathered from their last visit records.

Outcome events

Death and specified cardiovascular events were collected. Cardiovascular death was defined as sudden death, cardiogenic shock (whether from coronary heart disease or not), terminal heart failure, or fatal stroke. Myocardial infarction and dilated cardiomyopathy were also collected. If the follow-up visit was missed, outcome data were sought through a review of clinical records or through contact with the patient, his family, or the patient’s family doctor.

Statistical analysis

Statistical analysis was performed using the NCSS statistical software. Continuous variables were compared using a two-tailed Student’s t-test. Categorical variables were compared using the Fisher’s χ² test. Data are presented as mean with standard deviations. The level of significance was determined by a P value <0.05.

Overall survival functions were analysed using Kaplan–Meier curves and compared using the log rank statistics. All clinical variables were submitted to a univariate analysis. Variables which correlated to survival with a P value <0.10 were subsequently
proposed for inclusion into a Cox’s proportional-hazards model. In order to correct potential effect of age, groups were also compared after adjustment for this parameter.

Results

Patients population

A total of 420 patients were included in the study of whom 166 patients (98 men, mean age 77 ± 13 years) received a VDD PM and 254 (172 males, mean age 75 ± 15 years) received a DDD PM. Pacing indications were third-degree AV block in 277 patients (65.9%), second-degree AV block in 95 patients (22.6%), trifascicular AV block in 44 patients (10.5%), and other reasons in 4 patients (0.9%). The underlying disease was degenerative AV block (Lenegre-Lev disease) in 349 patients (83.1%), cardiac surgery in 15 years) received a VDD PM and 13 years) received a DDD PM. Patients’ demographic data (Table 1). At inclusion, there was no significant difference in the use of aspirin, angiotensin-converting-enzyme-inhibitor, angiotensin II-receptor antagonists, diuretic, nitrate or other vasodilator, beta-blocker, lipid-lowering agent in the two groups.

Table 1 Patients’ demographic data (n = number)

<table>
<thead>
<tr>
<th>Variables</th>
<th>VDD (n = 166)</th>
<th>DDD (n = 254)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline characteristics</td>
<td></td>
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<tr>
<td>Age at implant (years)</td>
<td>77 ± 13</td>
<td>75 ± 15</td>
<td>0.13</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>98 (59.0%)</td>
<td>172 (67.7%)</td>
<td>0.20</td>
</tr>
<tr>
<td>Body mass index</td>
<td>25 ± 4</td>
<td>26 ± 4</td>
<td>0.10</td>
</tr>
<tr>
<td>Cardiovascular risk factors</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>92 (55.4%)</td>
<td>140 (55.1%)</td>
<td>0.95</td>
</tr>
<tr>
<td>Diabetes, n (%)</td>
<td>45 (27.1%)</td>
<td>52 (21.7%)</td>
<td>0.11</td>
</tr>
<tr>
<td>Dyslipidaemia, n (%)</td>
<td>43 (25.9%)</td>
<td>94 (37.0%)</td>
<td>0.018</td>
</tr>
<tr>
<td>Family history of cardiovascular disease, n (%)</td>
<td>39 (23.5%)</td>
<td>40 (15.7%)</td>
<td>0.05</td>
</tr>
<tr>
<td>History of smoking, n (%)</td>
<td>30 (18.1%)</td>
<td>60 (23.6%)</td>
<td>0.18</td>
</tr>
<tr>
<td>Primary electrocardiographic indication for implantation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Complete atrioventricular block, n (%)</td>
<td>104 (62.7%)</td>
<td>173 (68.1%)</td>
<td>0.25</td>
</tr>
<tr>
<td>Second-degree atrioventricular block, n (%)</td>
<td>38 (22.9%)</td>
<td>57 (22.4%)</td>
<td>0.91</td>
</tr>
<tr>
<td>Trifascicular block, n (%)</td>
<td>21 (12.7%)</td>
<td>23 (9.1%)</td>
<td>0.24</td>
</tr>
<tr>
<td>Other, n (%)</td>
<td>3 (1.8%)</td>
<td>1 (0.4%)</td>
<td>0.14</td>
</tr>
<tr>
<td>Reasons for implantation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Idiopathic, n (%)</td>
<td>144 (86.8%)</td>
<td>205 (80.7%)</td>
<td>0.11</td>
</tr>
<tr>
<td>Aortic valve surgery, n (%)</td>
<td>12 (7.2%)</td>
<td>28 (11.0%)</td>
<td>0.27</td>
</tr>
<tr>
<td>Tricuspid valve surgery, n (%)</td>
<td>1 (0.6%)</td>
<td>2 (0.8%)</td>
<td>0.83</td>
</tr>
<tr>
<td>Other cardiac surgery, n (%)</td>
<td>1 (0.6%)</td>
<td>1 (0.4%)</td>
<td>0.76</td>
</tr>
<tr>
<td>Myocardial infarction, n (%)</td>
<td>2 (1.2%)</td>
<td>8 (3.2%)</td>
<td>0.20</td>
</tr>
<tr>
<td>Other, n (%)</td>
<td>6 (3.6%)</td>
<td>10 (3.9%)</td>
<td>0.86</td>
</tr>
</tbody>
</table>

Complications

The overall rate of complications was 7.9% (early complication: 4.8%). The total complication rate was 6.1% for VDD compared with 9.1% for the DDD group (P = 0.26).

Early complications

Early surgical re-interventions were required for atrial lead dislodgment (1.6% of DDD PM implantation), pocket bleeding (0.8% of DDD group and 0.6 of VDD group, P = 0.83), ventricular lead displacement (0.8% of DDD group and 0.6 of VDD group, P = 0.83), and ventricular myocardial perforation (0.8% of DDD group and 0.6 of VDD group, P = 0.83). Pneumothorax were more frequent after DDD PM implantation (2.0%) than after VDD implantation (1.2%) but the difference did not reach statistical significance (P = 0.55).

Late complications

Late surgical re-interventions were related to late ventricular lead dislodgment in 0.7% of all patient, symptomatic atrial undersensing in 1.8% of VDD implantations, and pocket or lead infection in 0.8% of DDD and 0% of VDD implantations, P = 0.25.

Clinical follow-up and pacemaker control

The median follow-up duration was 25 months (range: 1–119). The median follow-up duration was longer for the VDD group [median: 43 months (range: 1–119)] than for the DDD group [median: 26 months (range: 1–105)]. Five patients in the VDD group and eight patients in the DDD group were lost during the follow-up period. Among the 166 patients implanted with a VDD, 48 died during follow-up (30 from cardiovascular origin). In the DDD group, 30 deaths were recorded (12 from cardiovascular origin).

Clinical follow-up

Eighteen patients (11.2%) in the VDD group and 28 (11.4%) in the DDD group (P = NS) developed atrial fibrillation during the follow-up period. Atrioventricular dissociation due to poor atrial sensing was observed in 16 patients in the VDD group (on 12-lead resting ECG in 7 patients, during stress test in 9 patients). Only two of them required PM upgrading to DDD pacing. The incidence of myocardial infarction and dilated cardiomyopathy was not significantly different in the two groups (31.1 vs. 25.2% and 9.9 vs. 8.9% in the VDD and DDD groups, respectively, P = NS) (Table 2).
In the VDD group, when comparing patients with atrial signal detection <0.5 mV to those with atrial signal detection ≥0.5 mV, no statistically significant difference in mortality (P = 0.21) was found. In addition, multivariate analysis failed to highlight any clinical parameter [body mass index (BMI), relative risk (RR) = 1.00, P = 0.99], sex (RR = 1.55, P = 0.31), prior of myocardial infarction (RR = 0.94, P = 0.89), dilated cardiomyopathy of prior infarction (RR = 0.35, P = 0.34), age (RR = 0.99, P = 0.23]) as responsible for low atrial sensing. Finally, there was a trend for older patients to have lower atrial sensing but this correlation was not statistically significant (RR = 0.99, P = 0.23) in our registry.

**Pacemaker programming at the last follow-up control**

There was no difference in ventricular impedance, R-wave amplitude and ventricular stimulating threshold between the two groups. However, the detection of atrial signals (P-wave amplitude) was significantly higher in the DDD group (2.5 ± 1.8 mV) as compared with the VDD group (1.0 ± 0.8 mV) (P < 0.001).

At the last control, 65.9% of the VDD PMs and 89.3% of the DDD PMs were still programmed in their original mode with good atrial sensing (P < 0.001). Due to permanent atrial fibrillation, 7.9% patients out of the VDD group were switched to VVIR mode and 8.7% patients out of the DDD group to VVIR or DDIR mode (P = 0.17).

**Discussion**

Several retrospective studies on VDD pacing have been published. Clinical results were generally good and atrial sensing-related problems were minimal. Therefore, VDD mode appears to be a good alternative to DDD pacing, considering its advantages of a single lead, in terms of procedure time shortening, risk of mortality, and the need for a second thoracotomy.

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**Table 2 Pacing values, pacing mode, and clinical data at the last follow-up control**

<table>
<thead>
<tr>
<th>Pacing values</th>
<th>VDD (n = 166)</th>
<th>DDD (n = 254)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>P-wave amplitude (mV)</td>
<td>1.0 ± 0.8</td>
<td>2.5 ± 1.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>R-wave amplitude (mV)</td>
<td>11.0 ± 5.4</td>
<td>11.9 ± 5.6</td>
<td>0.24</td>
</tr>
<tr>
<td>Atrial impedance (Ω)</td>
<td>–</td>
<td>557.39 ± 226.7</td>
<td>–</td>
</tr>
<tr>
<td>Ventricular impedance (Ω)</td>
<td>562 ± 156.3</td>
<td>603 ± 216.2</td>
<td>0.074</td>
</tr>
<tr>
<td>Atrial stimulating threshold at 0.5 ms (V)</td>
<td>–</td>
<td>0.848 ± 0.66</td>
<td>–</td>
</tr>
<tr>
<td>Ventricular stimulating threshold at 0.5 ms (V)</td>
<td>0.680 ± 0.29</td>
<td>0.681 ± 0.38</td>
<td>0.98</td>
</tr>
<tr>
<td>Pacing mode</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VDD/DDD or others (%)</td>
<td>65.9%</td>
<td>89.3%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>VVI(R)/DDI(R) due to permanent atrial fibrillation (%)</td>
<td>7.9%</td>
<td>8.7%</td>
<td>0.17</td>
</tr>
<tr>
<td>VDD/DDD with atrial undersensing &lt;0.5 mV (%)</td>
<td>19.1%</td>
<td>1.6%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>VVI(R) due to atrial undersensing and AV dissociation (%)</td>
<td>7.1%</td>
<td>0.4%</td>
<td>0.003</td>
</tr>
<tr>
<td>Clinical data</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Myocardial infarction, n (%)</td>
<td>50 (31.1%)</td>
<td>62 (25.2%)</td>
<td>0.20</td>
</tr>
<tr>
<td>Dilated cardiomyopathy, n (%)</td>
<td>16 (9.9%)</td>
<td>22 (8.9%)</td>
<td>0.74</td>
</tr>
<tr>
<td>Cardiac valve surgery, n (%)</td>
<td>22 (13.7%)</td>
<td>44 (17.9%)</td>
<td>0.26</td>
</tr>
<tr>
<td>Incidence of atrial fibrillation, n (%)</td>
<td>18 (11.2%)</td>
<td>28 (11.4%)</td>
<td>0.95</td>
</tr>
</tbody>
</table>

Values are mean ± SD when appropriate.
complication, and cost reduction whereas maintaining the physiological benefits of AV synchronous pacing.

However, in spite of these encouraging results, in industrialized countries, VDD dual-chamber PM implantation is becoming scarcer compared with DDD pacing. This may be related to several countries, VDD dual-chamber PM implantation is becoming scarce logical benefits of AV synchronous pacing.

The present registry supports the current literature which tends to promote VDD pacing as a good alternative to DDD pacing. Indeed, the incidence of clinical events (myocardial infarction, dilated cardiomyopathy) was similar in the two groups, as was the incidence of atrial fibrillation, confirming that VDD pacing mode has no effect on the incidence of supra-ventricular tachycardia. Most importantly, the higher overall mortality detected in the VDD group was totally unrelated to the pacing mode. It was linked to the fact that a larger number of VDD PMs had been implanted at the beginning of the registry leading to an older population in the VDD group at the time of last follow-up control.

As opposed to what has been reported in the literature, the difference in early complication in the two groups did not reach statistical significance. This may be related to the fact that the surgical cephalic vein approach was preferred in all our cases, hence reducing the rate of pneumothorax. Moreover, operators individual experience influence both VDD and DDD PM implantation complication rate.

Although poor atrial signal detection was more frequent in the VDD group, symptomatic atrial undersensing requiring PM upgrading was not significantly higher compared with the DDD group. In the literature, many factors have been put forward to try and clarify atrial underdetection. First, atrial signal detection stability is strongly related to the right atrium size and the distance between the atrial sensing bipole and the ventricular extremity of the single lead. YIn et al. suggested that transthoracic echocardiography could be an interesting tool to help choosing the best-fitting single-pass VDD lead. The distance between the floating detection bipole and right atrial wall has also been studied but its role remains controversial. Secondly, an attractive haemodynamic explanation to intermittent atrial sensing failure has been provided by Carbone et al., using mitral Doppler flow analysis. A decrease in atrial volume at the opening of the AV valves, allowing the freely floating atrial lead to lie close to the right atrial wall, favours sensing of a small intracardiac electrogram and hence a better atrial signal detection. In their study, Higashi et al. showed the VDD leads implanted in ten dogs to be covered by thrombus up to 4 weeks after implantation. Macroscopic and histological examination suggested that an inflammatory process could foster the development of oedema, hypertrophy, and fibrosis of the atrial endocardium and could partly explain the variability of atrial signal detection. Finally, recent study showed that age, administration of non-dihydropyridine calcium channel blockers, and AF influence the incidence of inappropriate atrial sensing.

Atrial undersensing and AV dissociation are known to have some clinical consequences such as exercise intolerance and rhythmological consequences. Moreover, good atrial detection seems to be correlated with quality of life. In this registry, poor atrial detection (26.2% of our patients with VDD pacing) was more frequent than reported in the literature. However, it had little clinical implication as only three patients required PM upgrading. Moreover, 9.6% of VDD group presented with AV dissociation at rest and/or on exercise. Because of their advanced age and the few symptoms they experienced, conservative treatment was chosen. This decision was certainly based on the results of the study by Toff et al. which showed that single chamber ventricular pacing for high-grade AV block in elderly patients does not influence the rate of death from all causes compared with dual-chamber pacing.

Finally, in both groups, atrial undersensing was detected within 1 year after PM implantation. Atrial sensing threshold remained stable thereafter through the following PM controls as already mentioned in the literature.
Study limitation

Although the patients were prospectively included into this study, destination therapy was not randomized. Assignment to DDD or VDD pacing depending on the choice of the physician, selection of specific pulse generators and leads, and individual experience and skills may have influenced the results of our study.

Sinus node dysfunction was an exclusion criterion in our registry. However, full patient investigation, such as exercise stress test to exclude chronotropic insufficiency or long-term ECG Holter recording to exclude asymptomatic supra-ventricular tachycardia was not performed in all patients.

This study focused on long-term clinical outcome, pacing parameters, and long-term survival. Thus, the authors can neither comment on the quality of life in the two groups. However, these questions have been the subject of former trials.

Conclusion

In spite of the several advantages offered by VDD PMs, their main drawback is poor atrial signal detection. In this registry, a significant number of patients developed poor atrial signal detection without clinical impact. Moreover, atrial undersensing did not influence the incidence of atrial fibrillation, myocardial infarction, dilated cardiomyopathy, or mortality.

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References