Long-Term Comparison of Single-Lead VDD Pacing with Dual-Lead DDD Pacing in Patients with AV Block

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Summary

Single-lead VDD pacemakers have proven to be a safe and reliable alternative to dual-lead DDD pacemakers in the treatment of atrioventricular block with normal sinus rhythm. This prospective, randomized, multicenter VDD vs. DDD study investigated the long-term safety and reliability of single-lead VDD therapy in comparison to dual-lead systems. Between November 1995 and June 1998, a total of 264 patients with high-degree atrioventricular block and normal sinus function were divided into three groups: group A with a dual-lead DDD pacemaker (90 patients), group B with a dual-lead VDD pacemaker (84 patients), and group C with a single-lead VDD pacemaker (90 patients). The patient characteristics collected before implantation showed a homogenous distribution between the three groups. The sex, age, weight, height, body mass index (BMI), right and left atrial diameter, and ejection fraction (number of patients with normal ejection fraction > 55% and mean ejection fraction < normal) parameters were comparable in all three groups. The indication also showed similar distributions in the symptom and etiology categories, as well as similar medication administration at study inclusion. Lead complications (oversensing, undersensing, dislocation) were similar in all study groups. There was no indication of sinus node dysfunction in need of pacing during the follow-up of group C (SL-VDD). SL-VDD pacing is thus shown to be a viable long-term alternative for the treatment of AV block with normal sinus node function.

Key Words

Dual-chamber-pacemaker, VDD system, single-lead, complications, long-term follow-up

Introduction

For patients with symptomatic, high-degree atrioventricular (AV) block and chronotropic competence, VDD therapy with one lead (single-lead VDD) has increasingly become an alternative to dual-lead DDD therapy [1-3]. Single-lead systems represent a reliable and safe therapy option for patients with normal sinus node function and AV conduction disturbances [4-7]. The question, then, is to what extent single-lead VDD therapy is an alternative to standard DDD therapy for these patients, especially over the long term. Single-lead systems have the advantage of a simplified implantation procedure, which allows shorter implantation and fluoroscopy times [8-10]. DDD systems, in turn, offer the possibility of atrial pacing in the presence of a deterioration of the sinus node function. On the other hand, previous studies found an incidence of

		Group A	Group B	Group C
General patient data	No. of patients	90	84	90
	Male sex	46 (51%)	46 (55%)	47 (52%)
	Age at implantation (years)	70 ± 10	68 ± 11	69 ± 15
	Weight (kg)	75 ± 11	75 ± 13	74 ± 12
	Height (cm)	168 ± 8	168 ± 9	167 ± 9
	Body mass index* (kg/m^2)	27 ± 3	26 ± 4	26 ± 3
	Right atrial diameter (mm)	36 ± 2	38 ± 7	38 ± 6
	Left atrial diameter (mm)	41 ± 6	42 ± 6	42 ± 6
	No. of patients with normal EF > 55%	74 (82%)	66 (79%)	73 (81%)
	EF from patients with EF < 55%	45 ± 7	45 ± 6	43 ± 8
ECG indication**	Unspecified	9 (10%)	4 (5%)	4 (4%)
	Atrioventricular block II	28 (31%)	31 (37%)	26 (29%)
	Atrioventricular block III	52 (58%)	47 (56%)	59 (66%)
	Bundle-brunch block	1 (1%)	2 (2%)	1 (1%)
Symptoms**	Unspecified	8 (9%)	2 (2%)	4 (4%)
	Syncope or presyncope	74 (82%)	77 (92%)	79 (88%)
	Other ***	8 (9%)	5 (6%)	7 (8%)
Etiology**	Unspecified or unknown	39 (43%)	34 (40%)	44 (49%)
	Ischaemic	47 (52%)	42 (50%)	43 (48%)
	Other ***	4 (4%)	8 (10%)	3 (3%)
Medication	ACE/AT2 inhibitor and antihypertensive	31 (34%)	31 (37%)	21 (23%)
	Nitrate	20 (22%)	21 (25%)	10 (11%)
	Diuretic	18 (20%)	11 (13%)	12 (13%)
	Calcium channel blocker	10 (11%)	11 (13%)	7 (8%)
	Cardiac glycosides	8 (9%)	6 (7%)	6 (7%)
	Beta blocker	8 (9%)	3 (4%)	3 (3%)
	Anticoagulant	1 (1%)	1 (1%)	1 (1%)
	Other medication	35 (39%)	32 (38%)	31 (34%)
	No medication/no information	37 (41%)	30 (36%)	47 (52%)

*Table 1. Patient characteristics in groups A, B, and C at the time of implantation. *A person whose body mass index (BMI) is between 25 and 29 is mildly to moderately overweight. **Codes from the European Pacemaker Registration Card, Version 7 (EPRC 7). This version of the registration card was adopted at the June 20, 1996 EWGCP meeting held in Nice, France. ***If no more than one patient per group appeared in one reporting group (as per EPRC 7), then this patient was classified under the "Other" reporting group. EF = ejection fraction.*

atrial arrhythmias between 4% and 10% for long-term DDD therapy [3,11]. The mechanisms that induce atrial arrhythmias remain a topic for research. It is possible that the mechanical and electrical excitement of the atrial myocardium is an important factor. In contrast, the mechanical stress of the atrial myocardium can be disregarded with a VDD lead, in contrast to a fixated atrial lead. Moreover, with VDD pacemakers the atrium is not paced even in the case of intermittent atrial bradycardias. Consequently, one can expect that VDD and DDD pacemaker systems have varying effects on the development of atrial arrhythmias.

	Group A		Group B		Group C	
No. of patients with sinus rhythm	81		82		83	
Sinus rhythm (valid no.)	73 ± 15 bpm	(36)	69 ± 13 bpm	(45)	70 ± 16 bpm	(54)
Basic rate (valid no.)	57 ± 7 bpm	(73)	57 ± 7 bpm	(76)	55 ± 7 bpm	(80)
Hysteresis (valid no.)	47 ± 5 bpm	(31)	49 ± 6 bpm	(39)	46 ± 4 bpm	(32)

Table 2. Sinus rhythm, basic rate, and hysteresis rate of all patients with normal sinus rhythm at the time of the "last follow-up visit".

In this prospective, randomized study, the long-term reliability of a VDD pacemaker system was compared to the reliability of a DDD system. Complications regarding the lead, the pacemaker, and the patients were documented in order to analyze the effect of the pacing system on the success of the therapy. Patients with AV block and normal sinus rhythm were randomized into three groups. Patients in the first group (A) received a dual-lead system (atrial and ventricular lead) with a DDD pacemaker programmed to DDD mode, which resulted in both mechanical as well as electrical atrial stress. In the second group (B) the patients received the same pacemaker lead system, the only difference being that the pacemaker was programmed to VDD, whereby the atrium was only subjected to mechanical stress. The patients in the third group (C) received a single-lead with a VDD pacemaker, which largely eliminated both mechanical and electrical atrial stress.

The first results of this study have already been published elsewhere [12]. As was expected for single-lead VDD systems, the simplified implantation procedure resulted in a significant reduction of the implantation time and fluoroscopy time of DDD systems in comparison to the implantation of two leads. Single-lead VDD pacing was equal to dual-lead systems regarding P-wave sensing and AV synchronicity over the long term of 4 years. In the context of this publication, the results of the following subanalyses are illustrated:

- Comparison of patient characteristics at the time of study inclusion to verify the homogeneity of the randomization.
- Comparison of the pacemaker programming and the complication rates (lead-specific) at the time of the "last follow-up visit" (see Materials and Methods).

It should be verified whether single-lead VDD therapy offers the same safety standard as dual-chamber therapy in terms of possible lead complications such as perforation, dislocation, over/undersensing, or repositioning over the long term of 4 years.

Materials and Methods

The Clinical Investigation on Long-Term VDD and DDD Therapy Study (VDD vs. DDD Study), started in 1995, was conducted as a prospective, randomized, multicenter study with 22 participating clinics from nine countries.

Patient Inclusion

Included were patients with an indication for the implantation of an antibradycardia pacemaker who require ventricular pacing. Patients had to exhibit an AV or intraventricular conduction disturbance and have normal sinus node function. The latter was verified by a preoperative recording of the sinus rate, whereby the average resting rate needed to be ≥ 80 bpm. Also included were patients with a resting sinus rate between 70 – 80 bpm, as long as an atropine test (1.0 mg) yielded a sinus rate increase of at least 25% to over 90 bpm. Additional tests were optional.

Not included in the study were patients with documented atrial tachycardias, atrial flutter, or atrial fibrillation. Other exclusion criteria were antiarrhythmic therapy of Class I, III, or IV, unstable angina pectoris, known severe heart disease, or other diseases with a limited life expectancy. All patients were educated about the contents, objective, and risks of the study and provided a written informed consent for study participation.

Study Design

The patients were divided into three patient groups according to a previously established randomization list:

- Group A ("DL-DDD"): dual-lead system and DDD pacemaker programmed to DDD mode;
- Group B ("DL-VDD"): dual-lead system and DDD pacemaker programmed to VDD mode;
- Group C: ("SL-VDD"): single-electrode lead and VDD pacemaker programmed to VDD mode.

Without clinical justification, the respective mode was not reprogrammed. For randomization, the assigned study group (A, B or C) of every patient was given in an envelope, which should be opened after the patient has been enrolled in the study.

According to the original study protocol, the patients in group B were to be reprogrammed to DDD mode during the 12-months follow-up. During an investigator meeting conducted in the first year of the study, an amendment was made to the protocol, according to which the patients of group B did not need to be reprogrammed, but rather were to remain in VDD mode even after the 12-months follow-up in order to retain the homogeneity of the groups. Because the amendment was not adhered to in the same manner by all the investigators, some patients in group B alternated programming modes between VDD and DDD. This decreased the number of patients in group B with continuous VDD programming over the entire duration of the study to such an extent that it was necessary to take group B out of the analysis of long-term data, especially regarding the incidence of atrial tachyarrhythmias.

The study's timeframe as stipulated by the protocol was 2 years and was increased from 2 to 4 years, as per the amendment. Intermittent analyses showed that the planned “time frame” of 4 years was too short for some of the investigated parameters in order to prove statistically significant differences between the groups. Therefore, between 2001 and 2002 current patient data (e.g., mode, complications) were interrogated during a "last follow-up visit" so that the follow-up “time frame” for some patients could be extended to up to 7 years after implantation.

Implants

Patients in groups A and B were implanted with Physios TC01, Actros D, and Dromos DR (R function inactive) pacemakers (all Biotronik). All suitable unipolar and bipolar atrial and ventricular leads with passive or active fixation were allowed. Mostly Biotronik leads were implanted, but leads of other manufacturers were used as well. Patients in group C were implanted with Dromos SL and Actros SLR (R function inactive) pacemakers and "single-lead" SL leads (all Biotronik).

Data Acquisition

In addition to the acquisition of the usual patient data (age, sex, etc.), an echocardiographic exam was also conducted before implantation. The diameters of the right and the left atrium and the left ventricular function were also determined. Also, the operation duration and the fluoroscopy time were documented during the implantation and added to the usual intraoperative measurements.

Regular study follow-ups were conducted every 6 months during the first 4 years after implantation. The atrial and ventricular thresholds, the impedance, and the amplitude of the filtered P-wave and R-wave were determined using a standard procedure. The minimum and maximum atrial amplitudes were also measured in supine position with the intracardiac electrogram. Any complications (patients, pacemakers, and leads) were documented. If atrial fibrillation was diagnosed by electrocardiographic diagnosis, the fibrillation was classified as paroxysmal (spontaneous conversion within 48 hours), persistent (lasting > 48 hours and re-quiring antiarrhythmic medication/cardioversion for conversion to sinus rhythm), or permanent (no conversion possible or intended). The event counters and trend monitors of the pacemaker were evaluated, especially as regards the question of whether the atrial rate was always above or below the programmed basic rate or the programmed upper tracking rate. In addition, AV synchronicity was determined. Changes to the pacemaker's parameter settings, especially of the pacing modes, were documented.

During the additional "last follow-up visit" conducted between 2001 and 2002, the following parameters were determined on the basis of the patient's files: date of the last regular follow-up, patient is alive or deceased (with date and cause of death), underlying rhythm (sinus rhythm or atrial fibrillation/flutter), pacing mode (if VVI: date of programming to VVI), lower rate, hysteresis rate. Also determined were the following complications or events that could possibly have occurred since implantation: atrial arrhythmias, sinus node dysfunction, pneumothorax, infection, perforation/penetration of device/lead, dislocation, oversensing, undersensing, threshold-related problems.

Results

Patient Characteristics at Implantation

The objective of the randomization was a homogenous distribution of the patients into groups A, B, and C. Table 1 shows the patient characteristics for the parameters determined during the inclusion phase. For the parameters determined in the category "patient data," only minimal differences were found in the average values/percentages in all three groups. The listed codes for pacemaker indication were also fairly equally distributed among the three groups. Slightly larger differences were found among patient medications, whereby the relative sequence of the cardiac medication classes was the same for all three groups: ACE/AT2 inhibitor and antihypertensive > nitrate > diuretic > calcium channel blocker > cardiac glycosides > beta blocker. For a quantitative comparison of the group values for the "pacemaker indication" and "medication" categories listed in Table 1, the differences in the number/percentage of patients without clear indication (e.g., "unspecified," "unknown," "no information") must be taken into account.

Lead Complications until the Last Follow-up Visit

The “time frames” between implantation and the respective "last follow-up visit" for the three groups were on average 3.2 ± 1.6 years (group A), 3.2 ± 1.6 years (group B) and 3.8 ± 1.5 years (group C). Table 2 shows the sinus rhythms, basic rate, and hysteresis rate of patients with normal sinus rhythm at the time of the "last follow-up visit." When comparing the three groups, similar values were determined, even though there were not always data from all patients (see valid N). The complications occurring in groups A, B, and C for leads up to the time of the "last follow-up visit" are listed in Table 3. The following complications occurred in all three groups in only limited cases (between 0 and 2 patients per group): pneumothorax, infection, perforation or penetration by the device, perforation or penetration by the lead, dislocation, and threshold-related problems (requiring atrial or ventricular repositioning). In the other complication categories of oversensing, undersensing, and threshold-related problems (requiring atrial or ventricular reprogramming), individual cases of slightly higher numbers were observed, with the percentage never being higher than 8% for any of the groups. The group comparison showed slightly higher values for group A during atrial oversensing (6%) and for group C during atrial undersensing (8%), as well as in the category "threshold requiring ventricular reprogramming" (6%). In total, the percentage of patients without complications was always over 90% for all complication categories.

Discussion

Single-lead VDD therapy for patients with symptomatic, high-degree AV block and chronotropic competence is the objective of a series of studies [8,9,13-16]. These studies range from retrospective studies to prospective, randomized, multicenter studies and papers that only test the respective single-lead VDD system to studies that compare VDD therapy with a single-lead and the established therapy form of DDD pacing with one atrial and one ventricular lead. In addition to the usual comparison between single-lead VDD therapy (group A) and dual-lead DDD therapy (group C), this was the first multicenter, prospective, randomized study to investigate a third patient group with dual-lead DDD pacemakers programmed to VDD (group B). This study design should allow the differentiation of purely mechanical stress of the atrial lead and electrical stress caused by the interaction between sensing and pacing for dual-lead systems. However, due to the problem described above regarding a large number of non-documented reprogrammings to DDD mode in group B that were not implemented according to protocol, only the program-independent complications could be compared.

The results for the general patient data (distribution between the sexes, average follow-up period, patient age) and for the parameters determined during the echocardiographic exam (ejection fraction, RA and LA diameter) show a homogenous distribution in groups A, B, and C, which validates the randomization list used here. There were also no differences regarding indications (symptom, ECG). The medication at the time of study inclusion also showed no significant differences and included the usual cardiac therapy. According to the study protocol, no further information was required regarding changes in medication during the follow-up, so that no data exists as regards antiarrhythmic therapy or the administration of oral anticoagulants.

The comparison of lead complications yielded a generally low complication rate in all three groups without significant differences. Atrial undersensing in group C

	Complication	Group A (n = 90)	Group B (n = 84)	Group C (n = 90)
Pneumotorax	Yes	1	0	0
	No	89 (99%)	84 (100%)	90 (100%)
Infection	Yes	0	0	0
	No	90 (100%)	84 (100%)	90 (100%)
Perforation/penetration of device	Yes	0	1 (1.2%)	0
	No	90 (100%)	83 (99%)	90 (100%)
Perforation/penetration of lead	Atrium	0	1 (1%)	0
	Ventricle	1 (1%)	2 (2%)	0
	No	89 (99%)	82 (98%)	90 (100%)
Dislocation	Atrium	1 (1%)	0	0
	Ventricle	1 (1%)	0	1 (1%)
	No	88 (98%)	84 (100%)	89 (99%)
Oversensing	Atrium	5 (6%)	2 (2%)	3 (3%)
	Ventricle	7 (8%)	5 (6%)	6 (7%)
	No	81 (90%)	77 (92%)	81 (90%)
Undersensing	Atrium	4 (4%)	2 (2%)	7 (8%)
	Ventricle	2 (2%)	0	1 (1%)
	No	85 (94%)	82 (98%)	82 (91%)
Threshold	Atrium repositioning	0	1 (1%)	
	Atrium reprogramming	3 (3%)	4 (5%)	
	Ventricle repositioning	1 (1%)	1 (1%)	1 (1%)
	Ventricle reprogramming	0	1 (1%)	5 (6%)
	No	86 (96%)	79 (94%)	84 (93%)

Table 3. Complications with leads in groups A, B, and C at the time of the "last follow-up visit".

(SL-VDD) was 8%, which in no case necessitated a surgical revision with lead repositioning. Obviously, the problem of atrial undersensing could be resolved by reprogramming or it was not clinically relevant. The 6% atrial undersensing in group A (DDD) can be partially explained by the use of unipolar leads in some study centers.

All three study groups distinguish themselves through a high ventricular lead stability with a generally low dislocation rate. The reprogramming of the ventricular output in group C (VDD) that was necessary for 6% of the patients can be attributed to a slightly higher chronic threshold of the SL-VDD leads, which was evidently caused by greater mechanical stress.

Evaluation of the sinus node function with determination of the sinus rate during the "last follow-up" yielded a stable, normal rhythm in all groups without indication of a sinus node dysfunction. The stability of the sinus node rate is also emphasized by the fact that in group C (SL-VDD) there was never any necessity for atrial pacing – which warranted an upgrade to DDD.

Conclusion

In this study, single-lead VDD pacing has proven to be a safe and an equal alternative to dual-lead DDD pacing in pacemaker therapy of AV block with normal sinus node function. It has the advantage of shorter operation duration and fluoroscopy time. The incidence of lead complications was comparatively low in this study, and a sinus node dysfunction requiring pacing could not be documented over the course of the follow-up.

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