DDD versus VVIR versus VVI mode in patients with indication to dual-chamber stimulation: a prospective, randomized, controlled, single-blind study

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Key words:
Pacemaker; Pacing; Quality of life.

Background. **The aim of this study was to compare VVI, VVIR and DDD modes in patients with indication to dual-chamber stimulation, depending on left ventricular function.**

Methods. **Two groups of patients were implanted with a DDD pacemaker: Group I with ejection fraction > 40% and Group II with ejection fraction < 40%. Patients with a history of atrial arrhythmia or retrograde conduction were excluded. At follow-up (1 month each) quality of life (QoL), patient preference and echo parameters were collected. At hospital discharge all patients were programmed in DDD for 1 month and then randomized to VVI or VVIR mode. At the end of the period in VVI or VVIR mode each patient underwent a control period in DDD and then was programmed in VVIR or VVI mode.**

Results. **Seventeen patients out of 23 preferred DDD mode and 6 did not perceive any subjective difference among DDD, VVI and VVIR modes (4/9 in Group I and 2/14 in Group II, p = 0.0017). QoL was significantly different between the two groups and at each follow-up showed the best values in DDD. The correlation between QoL and Tei index was 0.62 in Group I (p < 0.001) and 0.35 in Group II (p = 0.001). Neither ejection fraction nor fractional shortening showed any significant difference during the three phases of the study.**

Conclusions. **Most patients preferred the DDD mode. The Tei index showed a good correlation with QoL and both QoL and Tei index significantly improved with DDD mode as compared to VVI and VVIR.**

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Introduction

A properly timed atrial systole improves stroke volume through the Frank-Starling mechanism, by providing greater left ventricular end-diastolic fiber stretch. Consequently, end-systolic fiber shortening is also enhanced, without an increase in average pulmonary venous pressure[1]. A variety of invasive and noninvasive hemodynamic studies documented an improvement in cardiac output with dual-chamber sequential pacing compared with single-chamber ventricular pacing[2]. Nevertheless controversial data about the influence of pacing mode on cardiac performance and quality of life (QoL) were reported[3,4].

The long-term effect of pacing mode in patients with standard indication to dual-chamber stimulation has recently been investigated by large-scale trials[4-7] and the only evident and negative effect of VVI(R) pacing after 2-year stimulation, was a significantly higher incidence of atrial fibrillation and of pacemaker syndrome, as compared to DDD(R) mode.

The pacemaker syndrome caused by retrograde conduction was reported as a complication, which required the reprogramming of the system to dual-chamber pacing in 26 and 18.3% of cases respectively in the PASE[4] and MOST trials[5,8]. On the other hand the CTOPP trial[6] and Nielsen et al.[7] reported a crossover of 5 and 1.8% respectively. No evidence of impaired QoL was reported in one group of patients compared to the other.

The aim of this study was to compare VVI, VVIR and DDD modes in patients with standard indication to dual-chamber stimulation, by evaluating the patient's preference, QoL and echocardiographic parameters, depending on left ventricular function.

Methods

Two groups of consecutive patients were implanted with a DDD pacemaker (Ruby 3, Vitatron) equipped with VVI and also VVIR modes. Patients were divided into two groups according to their left ventricular function, as assessed by ejection fraction (EF) at enrollment: Group I with EF > 40% (control group) and Group II with EF < 40% (left ventricular dysfunction group). After pacemaker implantation in DDD mode, EF was assessed with an atrioventricular (AV) interval of 150 ms. In accordance with the standard procedure, all atrial leads were placed into the right atrial appendage and all ventricular leads were implanted in the right ventricular apex.

The study design is reported in figure 1. At each follow-up, QoL was assessed by means of the Minnesota Living with Heart Failure Questionnaire[9] and the following echo parameters were measured: EF; fractional shortening (FS); and Tei index (myocardial performance index-MPI)[10-12]. Patient preference was also collected at each follow-up.

At hospital discharge all patients were programmed in DDD mode (DDD_1) for 1 month and then randomized to VVI or VVIR mode. At the end of the period in VVI or VVIR mode each patient underwent a control period in DDD (DDD_2) and then was programmed in VVIR or VVI mode respectively to complete the assessment. Each phase lasted only 1 month to avoid any mechanical remodeling of the myocardium, and to minimize the differences caused by the natural progression of the associated diseases.

Patient population. Twenty-three patients (13 males, 10 females, mean age 71 ± 8 years) with sinus node dysfunction or advanced AV block and standard indication to DDD pacing entered the study. Patients with a left atrial diameter > 50 mm and/or a history of atrial arrhythmia were excluded from the study. Retrograde conduction was tested at implantation. Patients with retrograde conduction during ventricular pacing were excluded from the study. Table I shows the baseline characteristics of the two groups of patients, as regards indication for permanent stimulation and associated heart diseases. Nine patients (EF 57 ± 8%) were enrolled in Group I and 14 patients (EF 28 ± 4%) in Group II ($p < 0.0001$). FS was 34 ± 9% in Group I and 15 ± 3% in Group II ($p = 0.0003$). MPI was 0.46 ± 0.11 and 0.67 ± 0.08 in the two groups respectively ($p = 0.0014$). The analysis of the three MPI components, isovolumic contraction time, ejection time and isovolumic relaxation time, showed a statistically significant difference in the isovolumic contraction time (54 ± 11 vs 72 ± 16 ms in Group I vs II, $p = 0.033$) and ejection time (345 ± 51 vs 291 ± 39 ms, $p = 0.0135$), while the isovolumic relaxation time was similar (105 ± 14 vs 109 ± 11 ms, $p = 0.53$).

Age distribution was not statistically different in the two groups (70 ± 12 vs 72 ± 5 years in Group I vs II, $p = 0.613$).

Results

At the end of the study 17 patients preferred the DDD mode and 6 did not perceive any subjective difference among DDD, VVI and VVIR modes (4 in Group I and 2 in Group II, $p = 0.0017$). Patients who preferred the DDD mode confirmed this choice at the end of each period either in VVI or VVIR. The same happened for patients who did not perceive any difference. The 4 Group I patients who did not perceive any difference among the three pacing modalities, had sick sinus syndrome in 3 cases and 2:1 paroxysmal AV block in 1 case. Two of them had hypertension treated with the relative drug therapy. The 2 Group II patients who did not perceive any difference among the three pacing modalities, had sick sinus syndrome in 1 case

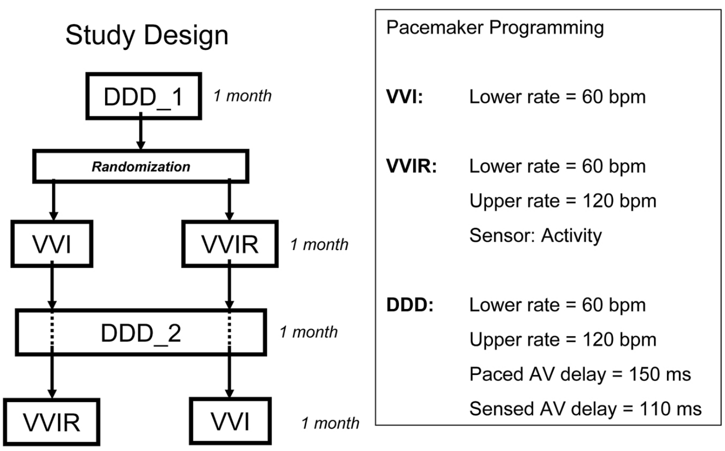

Figure 1. *Study design: each patient respected two baseline phases in DDD mode alternatively followed by VVI and VVIR modes in accordance with randomization. Pacemaker programming is also indicated for each pacing mode. AV = atrioventricular.*

Table I. Baseline characteristics of the patients with regard to the indication for permanent stimulation and associated heart diseases.

	Age (years)	Sex	Pacing indication	Cardiomyopathy
Group I	65	M	AVB 2:1	CAD
	72	M	SSS	Hypertension
	72	F	SSS	CAD
	82	M	3rd degree AVB	Hypertension
	44	F	3rd degree AVB	DCM
	61	M	AVB 2:1	Hypertension
	75	F	SSS	Hypertension
	77	M	SSS	CAD
	82	M	AVB 2:1	Hypertension
Group II	81	M	SSS	CAD
	68	F	SSS	CAD
	70	F	SSS	DCM
	69	M	AVB 2:1	CAD
	73	M	SSS	DCM
	75	M	3rd degree AVB	DCM
	73	F	SSS	DCM
	70	F	3rd degree AVB	DCM
	69	F	SSS	Hypertension
	74	M	SSS	Hypertension
	76	F	SSS	CAD
	69	F	3rd degree AVB	DCM
	82	M	SSS	CAD
	62	M	3rd degree AVB	Hypertension

AVB = atrioventricular block; CAD = coronary artery disease; DCM = dilated cardiomyopathy; SSS = sick sinus syndrome.

and third degree AV block in the other. The patient with AV block had a dilated hypokinetic cardiomyopathy treated with diuretics and digitalis, and the patient with sick sinus syndrome had a post-infarction ischemic cardiomyopathy. No patients preferred either VVI or VVIR mode.

At the end of the study all patients were programmed in DDD mode. AV delay was optimized by echocardiography in patients with permanent AV block and programmed with specific functions to promote spontaneous AV conduction in patients with sick sinus syndrome or paroxysmal AV block.

On average EF (Fig. 2) showed a variation of 6.8% between VVI(R) and DDD mode (p = NS), in patients with left ventricular dysfunction, and of 1.8% in the control group (p = NS). As for FS (Fig. 3) the mean variation was 10% between VVI(R) and DDD mode (p = NS) in patients with left ventricular dysfunction and 2.7% in the control group (p = NS). The mean variation of Tei index (Fig. 4) was 18% between VVI(R) and DDD mode ($p < 0.003$) in patients with left ventricular dysfunction and 22% in the control group ($p < 0.03$). QoL (Fig. 5) showed a significant difference between the two groups at each follow-up (p = 0.00004, p = 0.00075, p = 0.01279, and p = 0.01878 in DDD_1, DDD_2, VVIR, VVI, respectively, perfectly in accordance with the clinical status of the two groups).

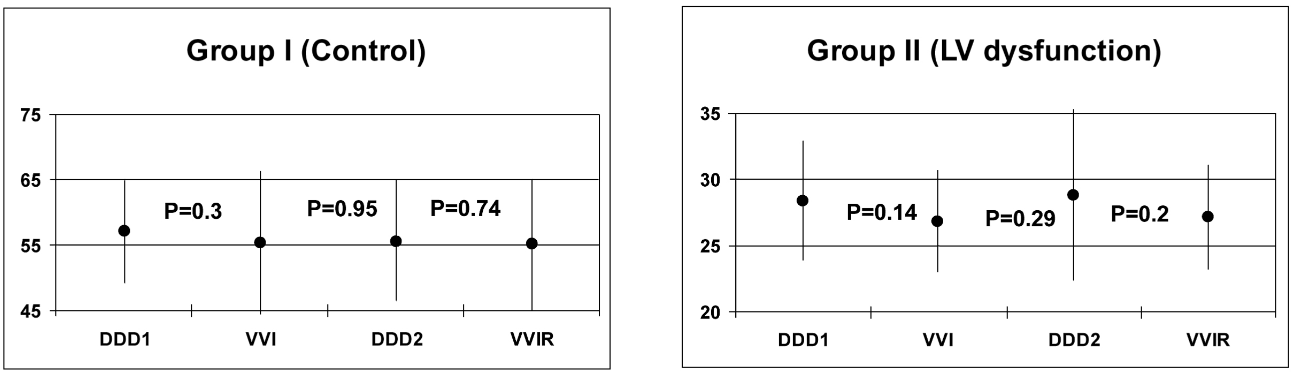

Figure 2. *In both groups of patients, ejection fraction did not show any statistically significant variation in the DDD, VVI and VVIR modes. LV = left ventricular.*

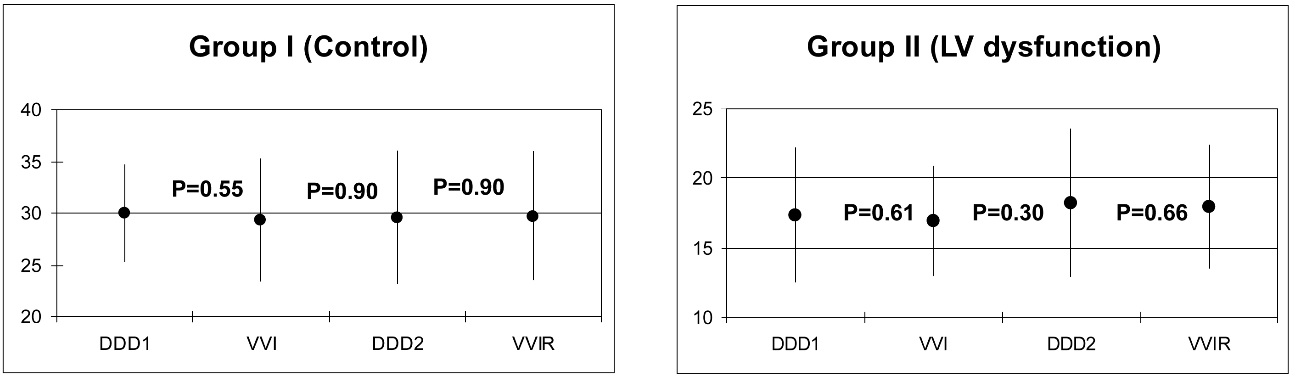

Figure 3. *In both groups of patients, fractional shortening did not show any statistically significant variation in the DDD, VVI and VVIR modes. LV = left ventricular.*

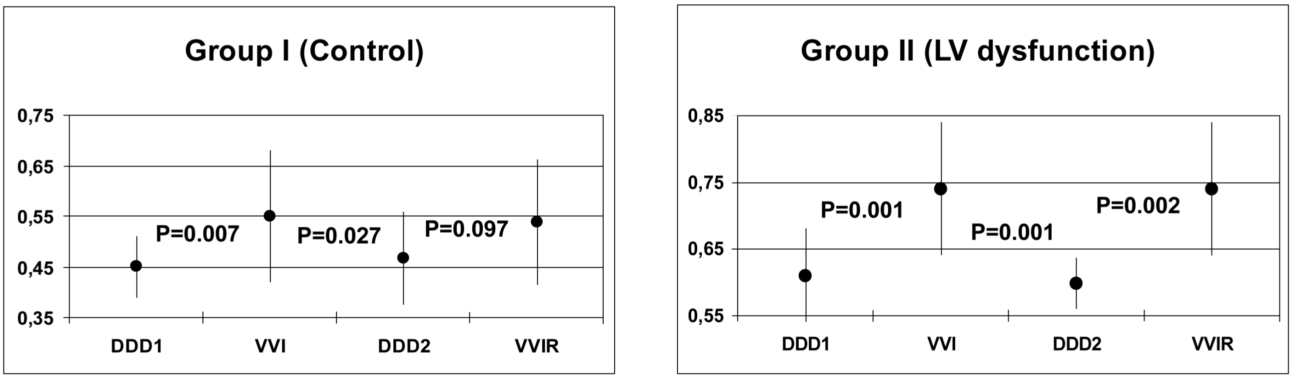

Figure 4. *Trend of Tei index: Tei index is significantly different in DDD, VVIR and VVI modes in Group II with left ventricular (LV) dysfunction. The trend is similar for patients of Group I with the exception of DDD2 vs VVIR (Student's t-test, paired, two-tailed).*

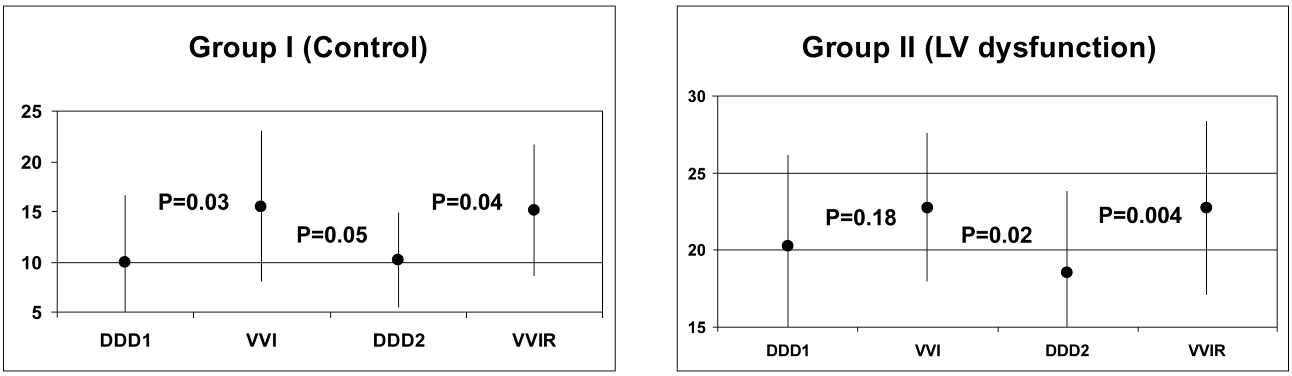

Figure 5. *Trend of quality of life assessed by the Minnesota Living with Heart Failure Questionnaire. Quality of life showed significant differences at each phase of the study, except in DDD1 vs VVI in Group II with left ventricular (LV) dysfunction (Student's t-test, paired, two-tailed).*

The correlation between QoL and MPI was 0.62 in Group I ($p < 0.001$) and 0.35 in Group II ($p = 0.001$). Neither EF nor FS showed any significant difference during the three phases of the study.

Ventricular pacing percentage was 100% in DDD mode in each patient (AV delay 150 ms) and ranged between 75 and 100% in VVI mode and between 85 and 100% in VVIR mode ($p < 0.02$ for VVI/VVIR vs DDD, and p = NS between VVI and VVIR).

Discussion

The intrapatient comparison of different pacing modes may allow pointing out the perception of therapy changes in each patient. Besides the short-term assessment of QoL and echocardiographic parameters may be independent of the progression of other associated diseases. The study compared DDD pacing mode with VVI and VVIR modes without optimizing the AV interval which was set at 150 ms for paced and 110 ms for sensed atrial events. In this condition even patients with sick sinus syndrome and preserved AV conduction were always paced in the ventricle. This was decided to compare VVI, VVIR and DDD modes, without spending additional time to tailor the more sophisticated modes like VVIR and DDD with respect to the simplest VVI mode. In this regard the results are even more important because we could expect a further improvement of the measured parameters when pacing therapy is tailored in each patient[13]. At least AV conduction could be preserved in patients with sick sinus syndrome, by programming the adequate AV interval or specific functions to minimize ventricular pacing, as we did at the end of the study in each patient.

The DDD mode is preferred by the majority of patients with indication to dual-chamber stimulation with respect to single-chamber pacing. Even rate response seems not enough to cover the gap between VVI and DDD modes, supporting the idea that AV synchrony has a higher impact than rate response in this patient population. This is also confirmed when retrograde conduction is excluded and DDD pacing is performed without the pacing site optimization and without programming the parameters, with the exception of sensing and pacing setting.

As reported in the literature, by exploring the long-term results of VVI pacing in this patient population, atrial fibrillation and pacemaker syndrome are relevant complications. Our study excluded patients with a history of atrial arrhythmias and patients with retrograde conduction to focus exclusively on the pacing mode and the relative patient's perception, QoL and cardiac performance. The related outcomes support the superiority of dual-chamber stimulation in this patient population, independently of left ventricular function. In this short-term evaluation, the impact of VVI(R) pacing, as assessed by Tei index, QoL and patient preference, is also evident. Actually there is no reason for VVI(R) stimulation in patients with sinus rhythm. At least single-chamber stimulation could be considered as AAI(R) pacing in patients with sick sinus syndrome and normal PR interval, even at the risk of late AV block occurrence in some patients[7]. Also in this case the patient should be properly selected to exclude the occurrence of atrial fibrillation episodes with bradycardia.

An important subanalysis of the CTOPP trial[14] clearly showed that many patients with sick sinus syndrome randomized to VVI pacing had a very low pacing percentage, meaning that they were in normal sinus rhythm and the pacemakers were inhibited for most of the time. As a matter of fact, the analysis of the patients really paced showed an evident superiority of DDD vs VVI mode, in contrast with the results of the overall patient population. However the CTOPP study evaluated the incidence of stroke, death, atrial fibrillation and hospitalization due to heart failure in the long run. On the other hand we wanted to point out the short-term effects of pacing mode in each patient through a crossover design. Besides, we evaluated the influence of pacing modes also in patients with left ventricular dysfunction. For this reason our study can be considered as complimentary to the previously published experience.

The chance of improving or at least preserving a good cardiac function and the chance of preventing or postponing atrial fibrillation development are of crucial importance for a good management of implanted patients[15,16]. On this basis, efforts should be made to understand which is the best pacing site for the right atrium, which one for the right ventricle and the best setting of programming options for each patient with a standard DDD pacemaker.

The correlation between QoL and Tei index might represent an opportunity for estimating the health perception of the patients, on the basis of measurable parameters of cardiac performance, but it should be further and deeply evaluated.

This study did not evaluate the exercise capacity of patients with a specific stress test in the different pacing modes, limiting the evaluation in their normal life.

In conclusion, the large majority of patients prefer DDD pacing mode, even when retrograde conduction is excluded. Among the assessed echo parameters MPI shows the best correlation with QoL in the overall patient population. Both QoL and MPI significantly improve with DDD pacing mode as compared to VVI(R), independently of the baseline left ventricular function.

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