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The effects of pacing mode on development of chronic AF in patients undergoing pacemaker implantation due to AV block : A retrospective study

Rustem Yilmaz[1], Filiz Akyildiz Akcay[2], Murat Yesil[2]

[1]Samsun Gazi Public Hospital, Department of Cardiology, Samsun, Turkey
[2]Izmir Katip Celebi University Atatürk Training and Research Hospital, Department of Cardiology, Izmir, Turkey

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Abstract

Permanent atrial fibrillation (AF) is the most prevalent arrhythmia among elderly patients. Permanent AF may cause thromboembolic events, heart failure, poor quality of life and recurrent hospitalizations. The effects of pacemaker mode on developing permanent AF have been investigated in several studies. In this study, we aimed to investigate the effects of physiological pacing (DDD) and non-physiological pacing (VVI) on the development of permanent AF in patients undergoing pacemaker implantation due to AV block who initially had a sinus rhythm and did not have significant coronary artery disease (CAD). We included 148 patients who underwent permanent cardiac pacemaker implantation (67 VVI and 81 DDD) due to AV block. All patients had P wave activity before pacemaker insertion, and none had significant CAD on coronary angiography. Trans thoracic echocardiography and a 12 lead ECG of each patient were performed. Of 148 patients who were included in the study, 81 had DDD pacemaker and 67 had VVI pacemaker. There were 72 women (48.6%) and 76 men (51.4%). The mean age was 67±7 years. Mean follow-up time was 5.7±1.8 years. Permanent AF developed in 16 (10.8%) patients. Age, gender, hypertension, diabetes mellitus, initial LA diameter, and LV ejection fraction were not statistically the difference between two groups. Pacemaker mode was the unique variable that reached statistical significance (p=0.003). Permanent AF developed in 13 (19.4%) patients and in 3 (3.7%) patients in VVI and DDD pacemaker groups, respectively (p=0.003). The comparison of initial and follow-up echocardiographic parameters such as change in LA diameters, LV ejection fractions, and LV end-systolic and end-diastolic diameters revealed that merely the change in LA diameters was statistically significant between the patients who developed permanent AF and who did not. In this study, we found that pacemaker mode significantly leads to the development of permanent AF. The risk of developing permanent AF was 7-8 times greater in the VVI group than that in the DDD group. Neither mode had effects on ventricular systolic functions. However, the mean left atrial diameter was significantly higher in the VVI group. According to these results, we suggest the insertion of a DDD pacemaker for the patient with P wave activity and AV block.

Keywords: DDD pacemaker, VVI pacemaker, Atrial fibrillation, pacemaker implementation

Introduction

Permanent pacemaker implantation has become one of the standard applications of modern medicine in the treatment of symptomatic brady-arrhythmias which are often irreversible. Today's technology has enabled the development of pacemakers that can give alerts in various modes according to the needs of the patient [1-2]. AV synchronous pacemakers that work closest to heart conduction physiology are used in appropriate patients.

Permanent atrial fibrillation (AF) is the most common supraventricular arrhythmia which increases with age. Permanent AF leads to thromboembolic events, heart failure, poor quality of life, and recurrent hospitalizations. The effect of pacemaker mode selection on the development of permanent AF has been investigated in many studies in patients requiring pacemaker insertion. In the UKPACE study, no significant difference was observed in the development of AF between DDD and VVI modes in Complete AV-block patients [3]. In a study by Andersen and co-workers, it was found that pacemaker mode selection was not effective in the development of permanent AF in patients with sick sinus syndrome [4].

In subsequent two large studies (CTOPP and MOST), unlike the previous ones, permanent AF was less common in patients with DDD pacemakers than in those with VVI pacemakers [5-6]. However, in these studies, patients with coronary artery disease (CAD) and older age were not excluded.

In this study, we investigated the effect of physiological (DDD) pacing and ventricular (VVI) pacing on the development of

***Corresponding Author:** Rustem Yilmaz, Clinic of Cardiology, Samsun Gazi Public Hospital, Samsun, Turkey, Email: drrustemyilmaz@hotmail.com

permanent AF in those patients who had AV complete block and initial P activity and did not have any severe coronary artery disease (> 50% stenotic lesion). However, in contrast to previous studies, we excluded older age patients and patients with CAD. Here, we found that the risk of permanent AF shows a considerable increase in patients with VVI pacemakers in comparison to patients with DDD pacemaker insertion.

Materials and Methods

A total of 148 patients, who had been diagnosed with Complete AV block and had a permanent pacemaker with initial P activity were included in the study. 67 patients were implanted with PVI (single chamber) pacemaker and 81 were implanted with DDD (double chamber) pacemaker. The type of pacemaker was decided according to the patient's comorbidity and the operator's preference. Patients between 45-75 years of age who did not have significant CAD on coronary angiography were included in the study. Those patients who had severe CAD, moderate to severe vascular diseases, and hyperthyroidism were excluded from the study. Ethics committee approval was obtained from Local Ethics Committee with protocol number 0446.

The patients were met in order to obtain the following information: (i) Age, gender, known arterial hypertension, diabetes mellitus, coronary artery disease, and history of thyrotoxicosis were questioned to extract demographic and clinical data. The systolic functions in the initial echocardiography, left atrium diameter, left ventricular systolic and diastolic diameters were evaluated after the insertion of the first permanent pacemaker. (ii) Patients were examined for a permanent pacemaker every six months. For the diagnosis of atrial fibrillation, 12-lead surface ECG recordings were obtained from all patients with a 12-channel electrocardiography device with a 25-mm / sec velocity and 10-mm / mV calibration. (iii) Two-dimensional, M-mode, and Doppler echocardiography was performed with General Electrics-Vivid 3 echocardiography device to exclude left ventricular ejection fractions (EF), left atrial diameter, left ventricular systolic and diastolic diameters, and valve pathology.

Statistical analysis

While evaluating the findings of the study, SPSS (Statistical Package for Social Sciences for Windows) 14.0 program was used for statistical analysis. The data were expressed as mean with standard deviation or frequency (percentage) for overall variables. Normality distribution was assessed using Shapiro Wilk test. Quantitative data were analysed by independent samples t test. The Pearson Chi-Square test was used for comparison between categorical variables. When performing statistical analysis, the p <0.05 value was considered statistically significant.

Results

Of the 148 patients included in the study, 81 were DDD, and 67 were VVI pacemaker patients. Initial characteristics and demographic information of the patients are given as follows.72 (48.6%) were female and 76 (51.4%) were males. 18 (12.2%) were under the age of 60 and 61 (41.2%) were between the ages of 60-70. 69 (46.6%) were between the ages of 70-75. The average age was 67±7. Hypertension and diabetes mellitus were present in 61 (41.2%) and 21 (14.2%) patients, respectively. The mean follow-up time was 5.7 ± 1.8 years (range: 1-9 years). Initial left atrium (LA) diameter was measured 3.6 ± 0.3cm, initial ejection fraction (EF) was determined as 61 ± 5%, baseline left ventricular systolic diameter (LVSD) was measured as 3.08 ± 0.4cm, baseline left ventricular diastolic diameter (LVDD) was measured as 4.68 ± 0.4cm.

The characteristics of the patients in the DDD (physiological pace) group are given in Table 1. In this group 41 (50.6%) were female with a mean age of 66 ± 7 years. Hypertension was seen in 34 (42%). DM was present in 12 (14.8%) with a mean follow-up time of 5.27 ± 2 years. Mean baseline LAD was measured as 3.6 ± 0.3 cm. However, LAD was measured 3.5-4.0 cm in 70% of patients. The mean baseline EF was determined as 61.6 ± 5% and the mean baseline LVSD was measured as 3.1 ± 0.4 cm. The mean baseline LVDD was measured as 4.7 ± 0.4 cm.

Of the patients in the VVI (ventricular pace) group (Table 1), 31 (46.3%) were women, with mean age 67.8 ± 6. 27 (40.3%) had hypertension, 9 (13.4%) had DM, and mean follow-up time was 6.21. ± 1.5 years. Mean baseline LAD was measured as 3.6 ± 0.3cm and LVSD was measured as 3.06 ± 0.4cm. Diastolic diameter was 4.66 ± 0.38cm. The baseline mean EF was determined as 60.21 ± 5.0%.

When the demographic and echocardiographic characteristics of patients in DDD (physiological pace) and VVI (ventricular pace) permanent pacemaker groups were compared, age, gender, hypertension, diabetes mellitus, baseline LAD, and baseline EF were statistically similar. However, the VVI group had significantly longer follow-up than DDD permanent pacemaker (P=0.001) (Table 1).

Table 1. Comparison of demographic and echocardiographic features of patients with DDD and VVI pacemaker

PM Mode		DDD n=81 (%)	I hVVI n=67 (%)	P
Gender	Female	41 (56.9)	31 (43.1)	0,623
	Male	40 (52.6)	36 (47.4)	
Age	<60	14 (77.8)	4 (22.2)	0.077
	60-70	29 (47.5)	32 (52.5)	
	70-75	38 (55.1)	31 (44.9)	
Hypertension	Yes	34 (55.7)	27 (44.3)	0.868
		47 (54)	40 (46)	
Diabetes Mellitus	Yes	12 (57.1)	9 (42,9)	1.000
	No	65 (54.3)	58 (45.7)	
Follow-up time (years)	1-3	11 (73.3)	4 (26.7)	0.001
	3-6	34 (73.9)	12 (26.1)	
	6-9	36 (41.4)	51 (58.6)	
Initial LAD (cm)	3.0-3.5	10 (52.6)	9 (47.4)	0.804
	3.5-4.0	39 (52.7)	35 (47.3)	
	4.0-4.5	7 (43.8)	9 (56.2)	
Initial EF (%)	<50	4 (50)	4 (50)	0.416
	50-60	9 (56.3)	7 (43.7)	
	>60	43 (50.6)	42 (49.4)	

Abbreviations: LAD: Left Atrium Diameter EF: Ejection Fraction

Effect of DDD (physiological) and VVI (ventricular) permanent pacemakers on permanent atrial fibrillation (AF) development in patients with initial P activity

Permanent AF developed in 16 (10.8%) of 148 patients included in the study. 13 (19.4%) of the patients who developed permanent AF were in VVI, and 3 (3.7%) were in the DDD pacemaker patient group.9 (56.3%) of the patients who developed AF were female, 7 (43.8) were male and 1 (6.3%) was under the age of 60. 8 (50%) of the patients were between the ages of 60-70, 7 (43.8) were between 70-75 years old with an average age 67.9 ± 5 years old. 6 (37.5%) had hypertension and 3 (18.8%) had diabetes mellitus. The mean follow-up time was 5.9 ± 1.9 years, the mean baseline LA diameter was measured as 3.7 ± 0.22 cm, and the mean baseline LVEF was determined as 60.9 ± 3.9% (Table 2).

Table 2. Comparison of the clinical and echocardiographic characteristics of patients with (+) and without (-) AF

Basal features		AF patients (+) (n=16) (n) (%)	Non-AF patients (-) (n=132) (n) (%)	P value
PM mode	DDD	3 (3.7)	78 (96.3)	0.003
	VVI	13 (19.4)	54 (80.6)	
Gender	Female	9 (12.5)	63 (87.5)	0.601
	Male	7 (9.2)	69 (90.8)	
Age	<60	1 (5.6)	17 (94.4)	0.643
	60-70	8 (13.1)	53 (86.9)	
	70-75	7 (10.1)	62 (89.9)	
Hypertension	Yes	6 (10.8)	55 (90.2)	0.795
	No	10 (11.5)	77 (88.5)	
Diabetes mellitus	Yes	3 (14.3)	18 (85.7)	0.702
	No	13 (10.2)	114 (89.8)	
Follow-up time (Years)	1-3	2 (13.3)	13 (86.7)	0.527
	3-6	3 (6.5)	43 (93.5)	
	6-9	11 (12.6)	76 (87.4)	
Initial LAD (cm)	3.0-3.5	1 (5.3)	18 (94.7)	0.191
	3.5-4.0	14 (18.9)	60 (81.1)	
	4.0-4.5	1 (6.3)	15 (93.8)	
Initial EF (%)	<50	0 (0)	8 (100)	0.430
	50-60	4 (25)	12 (75)	
	60-70	12 (14.1)	73 (85.3)	

Follow-up of the Complete AV-block patients after insertion of pacemaker showed that there was no significant difference in terms of age, gender, hypertension, and presence of diabetes mellitus, follow-up times, initial LAD, and LVEF between patients who developed atrial fibrillation (+) and who did not (-) (Table 2). However, regardless of risk factors, only 3 (3.7%) patients developed permanent AF in the entire DDD (physiological pace) pacemaker group, while this number was 13 (19.4%) in the VVI (ventricular pace) group. This was statistically significant (p = 0.003). Patients with VVI pacemakers had a 7-8-fold higher risk of developing permanent AF than patients who had DDD pacemakers.

Comparison of echocardiographic changes in DDD (physiological) and VVI (ventricular) pacemaker groups

In the DDD pacemaker group, the mean initial LAD was 3.65 ± 0.129cm, while the last LAD average was 3.84 ± 0.3cm (Table 3). Change in LAD was calculated as 0.185 ± 0.34cm. While the first LVSD mean was 3.13 ± 0.38cm, the last LVSD mean was 3.29 ± 0.36cm. The diameter change in LVS was 0.15 ± 0.16cm. Similarly, comparison of initial (4.7 ± 0.41cm) and end (4.85 ± 0.38cm) LVDD showed a slight change (0.13 ± 0.26cm). This is also reflected by LV ejection fraction where the change was measured as 1.875 ± 3.3%.

Table 3. Echocardiographic characteristics of patient groups with DDD and VVI pacemaker

	Echocardiographic features	DDD (n=56)	VVI (n=53)
Ejection fraction (%)	Initial LV EF	61.16±4.8	60.2±5
	Final LV EF	59.29±4.6	57.23±5.5
Left Atrium Diameter (cm)	Initial LAD	3.65±0.29	3.68±0.3
	Final LAD	3.83±0.3	4.02±0.35
Left Ventricular Systolic Diameter (cm)	Initial LVSD	3.13±0.38	3.068±0.4
	Final LVSD	3.29±0.36	3.29±0.44
Left Ventricular Diastolic Diameter (cm)	Initial LVDD	4.7±0.41	4.66±0.38
	Final LVDD	4.85±0.38	4.82±0.4

While the mean diameter of the initial LA was 3.68 ± 0.3 cm, the end LAD was 4.02 ± 0.35 cm in the VVI group. The change LAD was calculated as 0.343 ± 0.36cm. The initial (3.06 ± 041 cm) and end (3.29 ± 0.44 cm) LV systolic measurements revealed a slight alteration in LV (0.224 ± 0.25 cm). Similarly, initial (4.82 ± 0.4 cm) and end (4.66 ± 0.38 cm) LVDD was determined, which showed a minor change (0.152 ± 0.20 cm). Lastly, initial and end LVEF was determined and compared. The LVEF only presented a slight change of 2.98 ± 3.1% over the course of the study.

These echocardiographic parameters of patients with DDD and VVI pacemakers showed that there were no statistically significant differences in both groups in terms of EF change, LV systolic, and diastolic diameter changes. However, the mean diameter change or increase in the LA, was statistically significant in the VVI permanent pacemaker group compared to the DDD permanent pacemaker group (respectively 0.185±0.34 vs 0.343±0.36, P = 0.022) (Table 4), indicating the advantages of DDD over the VVI pacemaker.

Table 4. Comparison of echocardiographic changes in patients with DDD and VVI pacemaker

Basal features	DDD (n=56)	VVI (n=53)	v
Initial and last left atrium diameter change (cm)	0.185±0.34	0.343±0.36	0.022
Initial and last left ventricular systolic diameter change (cm)	0.159±0.16	0.224±0.24	0.11
Initial and last left ventricular diastolic diameter change (cm)	0.132±0.26	0.153±0.20	0.649
Initial and final ejection fraction change (%)	1.88±3.3	2.98±3.1	0.081

Discussion

In this study, we have investigated the effect of pacemaker mode selection on echocardiographic (alterations in EF, LV systolic and diastolic diameter and LA diameter) parameters concerning permanent AF development in patients who were admitted to our hospital's cardiology pacemaker polyclinic.

As known, permanent AF is the most common supraventricular arrhythmia with increased age. Permanent AF leads to thromboembolic events, heart failure, poor quality of life, and recurrent hospitalizations.

The effect of pacemaker mode selection on the development of permanent AF has been investigated in many studies, since it affects morbidity and mortality significantly and is frequently encountered in clinical practice. The incidence of AF was shown to occur higher in patients with VVI (R) pacing than patients with atrial-based pacing (AAI (R) or DDD (R). However, in the UKPACE study, no significant difference was observed in the development of AF between DDD and VVI modes in Complete AV-block patients. In the study reported by Andersen et al. 23% of patients with VVI pacing developed at AF after 3 years, this rate was found to be 14% in patients with AAI pacing, which did not reach statistical significance, probably due to the small number of patients examined [3,4].

In CTOPP, AF was significantly less common in the atrial-based pacing group than in the group with VVI (R) pacing, and relative risk of developing AF in the DDD pacing group compared to the group with VVI (R) pacing decreased significantly by 21% in 2.7 years (p= 0.008). This relative risk reduction was in agreement with the 20.1% risk reduction observed after 6.4 years of CTOPP and 27.1% relative risk reduction in favour of atrial-based pacing in permanent AF [5, 6]. These studies have identified the following risk markers for permanent AF: being over the age of 74, sinoatrial node disease, and a history of AF attacks [7, 8].

Thus, there is consistent evidence that atrial-based pacing reduces the risk of permanent AF in patients with sinus node disease. A number of mechanisms such as suppression of early atrial beats that will trigger the development of permanent AF and preservation of optimal ventricular diastolic filling through preservation of timely atrial contraction have been proposed. Follow-up echocardiographic measurements performed by Andersen and co-workers 5.5 years after pacemaker implantation also showed that left atrial diameter increased less in the group with AAI pacing than in the group with VVI pacing [9].

Similar observations apply to the risk of thromboembolism or stroke. Andersen et al reported a significant increase in thromboembolic events in patients with sick sinus syndrome in the VVI group compared with the AAI group after 3.3 years of observation (6/110 vs. 20/115 events, P = 0.0083). This was confirmed 5.5 years later (19/110 vs. 39/115 events, P = 0.0065) [4]. In a comparison of DDD(R) and VVI(R) pacing in other studies, no significant relationship was found with thromboembolism and stroke, neither after 2.5-3 years of treatment nor in the extension of the study after 6.4 years [3,5,6,10,11]. Furthermore, annual stroke rates ranged from 1% in the CTOPP to 2.2% at MOST in the two largest endpoint studies published to date in patients with permanent pacemakers [6, 11].

There are contradictory results in these studies because coronary artery disease and advanced age, which are effective in the development of permanent AF, have not been excluded in these studies. Furthermore, patients in the studies had predominantly sinus syndrome. However, all patients in our study were Complete AV-block patients and elderly patients (over 75 years old) who were considered as risk factors for the development of permanent AF detected in other studies were not included in our study. Although those with sinus node disease, advanced age, and coronary artery disease were excluded in our study, the atrial-based pacing (DDD) group developed significantly less permanent AF than the ventricular pacing group. Less permanent AF was observed in the atrial-based pacemaker mode, independent of other risk factors for the development of permanent AF (DDD: 3/81, VVI: 13/67, P = 0.003). Recent studies also support that the closest pacing to heart conduction physiology has drastically reduced development of permanent AF thereby reducing stroke and embolic events to lower levels [12-14].

According to our findings, the reason for the development of permanent AF in the ventricular-based pacemaker mode may be due to atrial dilatation as a result of the disruption of AV synchronization. This finding is consistent with an increased occurrence of permanent AF in patients with VVI pacing. Our study did not include anticoagulant therapy in patients with permanent AF with a pacemaker. Stroke and thromboembolism rates were not evaluated in patients with AF or without, which is one of the limitations of our study. This is rational because even large clinical studies may not be able to adequately demonstrate that one pacing mode is superior to another in terms of stroke risk, given that there are many possible cardiac and non-cardiac etiology of stroke in elderly patients and the variable use of antiplatelet therapy.

After revealing the effects of pacemaker mode selection on permanent AF, we also investigated the variations in echocardiographic (EF change, LV systolic and diastolic diameter change and LA diameter change) parameters in our study. The studies have shown that one of the effects of ventricular pacing is the stimulus for a remodeling process that leads to the development of new or worsening heart failure, especially with right apex stimulation. However, heart failure is a slowly progressing disease and most of the patients enrolled in pacemaker endpoint studies had normal EF. In the study by Andersen et al., compared with 19/109 patients in the AAI pacing group, 35/113 patients in the VVI pacing group experienced a deterioration in the New York Heart Association class over 5.5 years, which is a significant difference in favor of AAI pacing [9].

Also, the increase in the diuretic dose was significantly higher in the VVI group than in the AAI group, and the LVEF decreased in the VVI group (-5% compared to baseline in 5.5 years, P <0.0005), but not in the AAI group. In the MOST study, compared to the VVI (R) group, DDD (R) reported a significant decrease in the incidence of hospitalization due to heart failure in the pacing group (10.3% vs. 12.3%, P = 0.021 over 2.7 years). However, the other studies without normalization procedure observed no difference between the two groups [3, 6, 10, 11]. Recent experimental evidence has shown that electrical stimulation of the myocardium has a significant effect on structural and metabolic properties [15, 16].

In our study, non-statistical changes in both pacemaker modes were observed on mean LVEF, LV systolic, and diastolic mean diameters. However, there was a statistically significant increase in initial mean LAD in VVI (ventricular pace) pacing compared to DDD (physiological pace) pacing ($p = 0.022$). This may explain why AF is more common in VVI pacing.

Limitations of the study

Although our study was conducted in a hospital serving a large geographic area and a heterogeneous patient population, being a single medical center may be considered a limitation. The fact that the majority of the patients admitted to our hospital have low education levels and the patients evaluated in a single visit may have had a negative effect on our health information.

Conclusion

In this study, we have shown that the pacemaker mode selection is very important in patients who had initial P activity and who required Complete AV block permanent pacemaker in order to prevent permanent AF which is the most common type of arrhythmia. Physiologic (DDD) pacing has become more important for the prevention of the development of permanent AF. In our study, the risk of permanent AF was found to be 7-8 times higher in patients with VVI pacemaker insertion compared to DDD pacemaker insertion. Echocardiographic parameters of patients with DDD and VVI pacemaker insertion: No statistically significant difference was found in both groups in terms of EF change, LV systolic and diastolic diameter changes. However, the LA mean diameter change, i.e. increase, was statistically significant in the VVI permanent pacemaker group compared to the DDD permanent pacemaker group ($P = 0.022$). In the light of these findings, we recommend DDD permanent pacemaker insertion to patients with P-wave activity with AV block.

Conflict of interests
The authors declare that they have no competing interests.

Financial Disclosure
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Ethical approval
Ethics committee approval was obtained from Local Ethics Committee with protocol number 0446.

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