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Incidence and predictors of new onset atrial fibrillation after single chamber VVI pacemaker implantation in patients with normal baseline cardiac function

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Abstract:
Background: *Atrial fibrillation is a relatively common arrhythmia often seen in patients with permanent pacemakers. In patients with underlying left ventricular dysfunction, single chamber right ventricular pacing increases the incidence of heart failure and atrial fibrillation [1]. But, in patients with normal baseline cardiac function, these effects are not clearly defined. Therefore, with this background in mind we aimed to assess the incidence, predictors and time frame of appearance of new onset atrial fibrillation in patients with normal baseline cardiac function who underwent single chamber VVI pacemaker implantation.*
Material and Methods: *All consecutive patients undergoing VVI pacemaker implantation under the free pacemaker scheme of the State Government, in the Department of Cardiology, Gauhati Medical College and having ACC-AHA Class I indication for PPI and normal cardiac function at baseline were included in the study from September 2010 to August 2011. Each patient was followed up for one year till September 2012. Patients with any form of underlying structural heart disease, ventricular dysfunction, CKD, COPD or any other pacing mode were excluded from the study. They were followed prospectively by echocardiography (left atrial dimension) and ECG which were done at baseline, 1 week, 1 month, 3 months, 6 months and 12 months after implantation till July, 2012. Changes in left atrial dimensions and any documented new onset atrial fibrillation were noted during the follow up period and its time frame of appearance were recorded. At 12 months pacemaker interrogation was done to look for percentage cumulative ventricular pacing.*
Results : *One hundred fifty five (155) consecutive patients with mean age 61±12 (Range 27 - 87), 80.6% males, mean left ventricular Ejection Fraction of 63.59±4.87% (55.7 – 78.0) who undergone VVI pacemaker implantation were enrolled in this study. New onset persistent atrial fibrillation was found in fifteen patients (9.7%). Significant increase in mean left atrial end-diastolic diameter (LAd) was observed as early as 1 month (from 26.72 ± 3.83 mm at baseline to 28.65 ± 2.8 mm at 1 month, p<0.001). Cumulative ventricular pacing percentage was found to be strongly associated with new onset AF.*
Conclusion: *Single chamber VVI pacing in patients with normal baseline cardiac function was associated with 9.7% incidence of new onset atrial fibrillation between 6 to 12 months after implantation. Progressive increase in mean left atrial end-diastolic diameter with LA diastolic dimension > 40 mm and higher percentage of paced beats were strong predictors of new onset atrial fibrillation in our study.*
Keywords: *Atrial fibrillation, cumulative ventricular pacing, Left atrial dimension, normal cardiac function, VVI pacemaker*

I. Introduction

Among the cardiac arrhythmias, atrial fibrillation (AF) is the most common. Apart from being a significant risk factor to predict ischemic stroke, AF may also reduce the quality of life, cardiac performance and the functional status.

The prevention of recurrent syncope and death due to ventricular asystole, the most lethal of all heart rhythm disturbances, using RV pacing stands as one of the greatest medical achievements of the 20th century. Cardiac pacing remains the only effective long-term treatment also for symptomatic bradycardia and chronotropic incompetence. Single chamber ventricular apical pacing continues to be the predominant pacing mode in the developing countries, primarily due to economic constraints. Numerous previous reports have shown that atrial tachyarrhythmias are more likely to occur with ventricular pacemakers (VVI) than with atrial or dual-chamber pacemakers(14% to 57% with VVI versus 0% to 23% with AAI or dual-chamber modes) [2]. It is also well known that in patients with underlying left ventricular dysfunction, single chamber right ventricular pacing increases the incidence of heart failure and atrial fibrillation. Therefore, this study was conducted to

assess the incidence, predictors and time frame of appearance of new onset atrial fibrillation in patients with normal baseline cardiac function who underwent single chamber VVI pacemaker implantation.

II. Material And Methods

Study design : A prospective observational study of one year follow up

Place and duration of study : This study was conducted in the department of Cardiology, Gauhati Medical College and hospital. Patients were enrolled over duration of 12 months from September 2010 to August 2011 and each patient was followed up for one year till September 2012.

Inclusion criteria : All consecutive patients undergoing VVI pacemaker implantation having ACC-AHA Class I indication for Permanent Pacemaker Implantation and normal cardiac function at baseline were included in the study.

Exclusion criteria : Patients with any form of underlying structural heart disease other than the conduction system and sinus node disorder, coronary artery disease, diastolic or systolic ventricular dysfunction, CKD, COPD with pulmonary hypertension, repeat procedure or pulse generator replacement, lack of consent and pacing mode other than VVI were excluded from the study.

Clinical evaluation : A thorough clinical evaluation including detailed history and physical examination, resting 12 lead Electrocardiogram (ECG) and echocardiography were done at admission. Patients were discharged with a programmed Lower rate at 60 per minute. Patients were followed prospectively at 1 week, 1months, 3 months, 6 months and 12 months after PPI. At each of the follow up visits, patients had detailed clinical evaluation and a 12 lead ECG was done.

Clinical outcome measure : The clinical outcome parameter analyzed was new new onset persistent Atrial Fibrillation which was defined as the first episode of AF confirmed by ECG in a patient without previous history of AF. Persistent AF was defined as suspected continuous AF, with ECG evidence, at 2 separate visits >7 days apart [3].

Echocardiography protocol : Baseline echocardiographic evaluation was done within 24 hours of hospital admission using SIEMENS ACCUSON CV70 machine. Left atrial size was measured in systole (LAs) and diastole (LAd) on M-line in parasternal long axis view. Serial changes observed in LA dimensions were recorded to establish a relationship between LA diameter and the risk for development of AF. Echocardiography was repeated at day 7, 1 month, 3 months, 6 months and 12 months after implantation.

Pacemaker interrogation : Percent ventricular pacing was determined from stored pacemaker diagnostic data at one year follow up. Pacemaker interrogation was performed on each patient at the end of one year to note the Percent Cumulative Ventricular Pacing (%Cum VP) over the year.

Statistical analysis : GraphPad Statmate 2 software was used to estimate the sample size and to calculate the power of the study. More than hundred sample size provides adequate power to the study.

The continuous variables are presented as mean (± SD). The One-way ANOVA with post tests and paired 't' test with two way 'p' value were used to compare the means of baseline values of clinical outcome parameter with the values at day 7, 1 month, 3 months, 6 months and 12 months. The effects of confounding parameters such as age, sex, indication of pacing were also analyzed by using one-way ANOVA and unpaired't' test with two way 'p' value. A 'p' value of <0.05 was considered to be significant for all the statistical analysis. Linear regression analysis was used to correlate the values of the systolic and diastolic LA dimensions at the end of one year and percent cumulative ventricular pacing (% Cum VP) over one year. Fisher's exact test was used to compare categorical variables so as to assess the effects of risk factors on clinical outcome measure.

III. Results

Baseline characteristics of the patients (Table 1) : Of 155 patients, 125 (80.6%) were male. Although age ranges from 27 years to 87 years mean age was 61±12 years. Complete Heart Block (CHB) was found to be the commonest indication for permanent pacemaker implantation in this patient population. CHB was the diagnosis in 94 patients (60.6%) followed by Sick Sinus Syndrome (SSS) in 20 cases (12.9%), LBBB and trifascicular block in 17 (10.9%), RBBB with left hemi-block in 16(10.3%) and others in rest 8 cases (5.2%). Baseline mean Left ventricular ejection fraction was 63.59% (range 55.7- 78%) with SD of 4.87 (95% CI was 62.82-64.36).

Clinical outcome measure (Table 2) : New onset persistent atrial fibrillation was found in fifteen patients (9.7%). Six of them presented at the end of six months while rest nine cases were detected at 12^{th} month. Fisher's exact test was used to find out the risk factors and strength of their association. There was equal incidence among all age groups, both sexes and among patients with either sinus nodal disease or AV block.

Echocardiographic parameters (Table 3, Fig. 1) : Significant increase in mean left atrial end-diastolic diameter (LAd) was observed at 1 month (from 26.72 ± 3.83 mm at baseline to 28.65 ± 2.8 mm at 1 month, $p<0.001$) and thereafter, it progressively increased till 1 year. But the left atrial end-systolic diameter (LAs) increased significantly from (19.73 ± 3.96) mm to (23.88 ± 4.3) mm ($p<0.001$) only after 6 months**,** and were progressive thereafter.

Pacemaker interrogation (Table 4, Fig. 2) : At the end of one year follow up pacemaker interrogation was performed in all the cases. At the end of one year follow up pacemaker interrogation was performed in all the cases. It was seen that 41 patients (26.5%) had VVI Cumulative percent ventricular pacing (Cum% VP) ≥ 90%, 83 (53.5%) had Cum% VP ranging from 41 to 89% and 30 (19.4%) had Cum% VP ≤ 40%.

Left atrial diastolic dimension of > 40mm at the time of detection of AF was found to be a strong predictor of atrial fibrillation (Relative risk = 3.01, 95% Confidence Interval: 2.04 to 4.45, P value < 0.0001). Also a higher percentage of paced beats was a strong risk factor for AF. All of them had a > 80% paced complexes. Patients having > 90% paced complexes at the end of 1 year on pacemaker interrogation had a nine fold higher risk of developing AF than those having 80-90% paced complexes (Relative risk = 9.33, 95% Confidence Interval: 4.90 to 17.77, P value < 0.0001).

IV. Figures And Tables

Table 1 : Baseline clinical characteristics of study patients

AGE (YEARS)	61±12 (Range 27 - 87)
GENDER	MALE 125 (80.6%); FEMALE 30 (19.4%)
INDICATIONS OF PACING	
CHB	94 (60.6%)
SSS	20 (12.9%)
LBBB with or without PR prolongation	17(10.9%)
RBBB with left anterior or posterior hemi-block	16(10.3%)
2:1 AV BLOCK	3(1.9%)
RBBB WITH LONG PR	3(1.9%)
SINUS BRADYCARDIA	1(0.6%)
AF WITH SVR	1(0.6%)
LVEF (%)	63.59±4.87 (Range 55.7 – 78.0)

Table 2 : Clinical outcome (New onset atrial fibrillation during follow up (N= 155)

CLINICAL OUTCOME MEASURE	FREQUENCY				
	1 month	3 months	6 months	12 months	TOTAL (%)
NEW ONSET PERSISTENT ATRIAL FIBRILLATION	0	0	6	9	15(9.67)

Table 3 : Changes in LA dimensions by transthoracic two dimensional echocardiography

Parameters (mm)	BaselineN =155	1 week N=155	1 month N=154	3 months N=154	6 months N=154	12 months N=152	P-VALUE
LAd	26.72 ± 3.83	26.93 ± 3.71	28.65 ± 2.8	30.48 ±2.76	33.85 ± 3.76	37.13 ±4.57	ns (0.09) at 1 week, < 0.001 at 1-12 months
LAs	19.73 ± 3.96	19.87 ± 4.09	20.32±4.09	20.71 ± 3.5	23.88 ± 4.3	26.78 ± 6.02	ns (>0.05) at 1 week, 1 month & 3 months; <0.001 at 6& 12 months

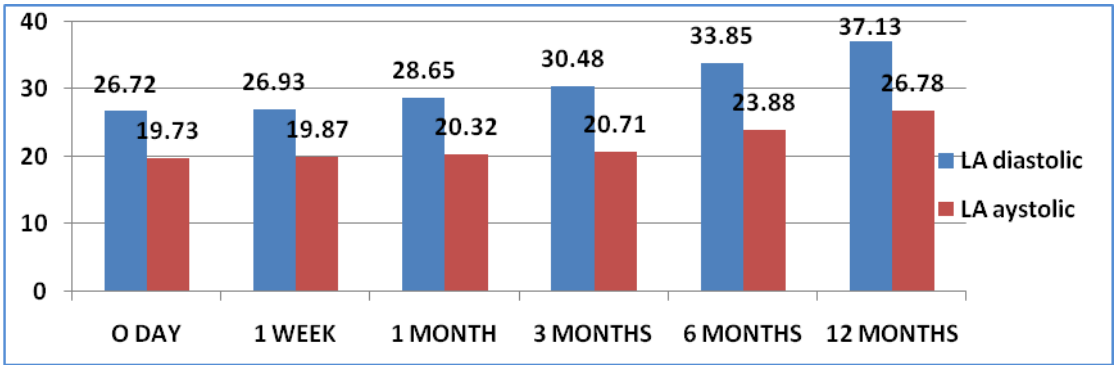

Figure 1 : Bar diagram representing gradual increase in mean LA end-diastolic and end-systolic dimension (mm) with time since pacemaker implantation. P value for LA d was < 0.001 from 1month to 12 months whereas P value for LA s was <0.001 only at 6 and 12 months.

Table 4 : Distribution of patients according to cumulative percentage ventricular pacing during one year

Cum % VP during 1 year (% of total QRS)	Frequency (%) (N=154)
<40	30 (19.4)
40-89	83(53.5)
≥ 90%	41(26.5)

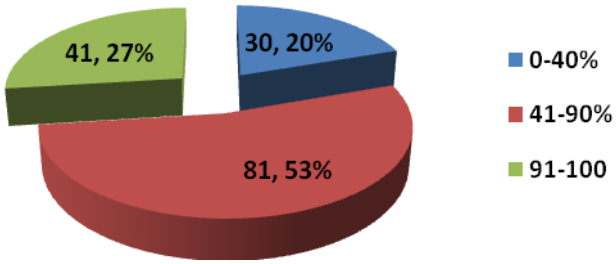

Figure 2 : Distribution of patients according to cumulative percentage ventricular pacing during one year

V. Discussion

Of total 155 patients, Complete Heart Block (CHB) was found to be the commonest indication (in 94 cases, 60.6%) for permanent pacemaker implantation followed by Sick Sinus Syndrome (SSS) in 20 cases (12.9%). In the USA, sinus-node dysfunction is the primary indication for pacemaker implantation in over 50% of patients [4].

Atrial fibrillation is more likely to occur with VVI pacemakers than with atrial or dual chamber pacemakers. Presumably this tendency results from stretching of the atria by a retrograde jet flowing through intermittently incompetent atrioventricular (AV) valves because of asynchronous atrial and ventricular contractions and from the utrial contractions against closed AV valves . The arguments that favor this hypothesis are supported by numerous demonstrations of greater release of atrial natriuretic peptide in single-chamber pacing than in dual-chamber pacing [5-7] . The predisposition to atrial fibrillation has been said to be even more pronounced if atrial tachyarrhythmia was present before the pacemaker was implanted, a situation most typically seen in the sick sinus syndrome [8-10]. But, in our study all patients had normal baseline cardiac function and none had pre-existing atrial fibrillation.

New onset persistent atrial fibrillation was found in fifteen patients (9.7%). Nine of them presented with CHF. Rest six patients had episodes of palpitation. There was equal incidence among all age groups, both sexes and among patients with either sinus nodal disease or AV block. However as expected left atrial diastolic dimension of > 40mm was found to be a strong predictor of atrial fibrillation (Relative risk = 3.01). Also a higher percentage of paced beats was a strong risk factor for AF. All of them had a > 80% paced complexes. Patients having > 90% paced complexes at the end of 1 year on pacemaker interrogation had a nine fold higher risk of developing AF than those having 80-90% paced complexes (Relative risk = 9.33). The incidence of new onset AF with VVI/R pacing varies from as low as 3% per year in UKPACE trial [11], to as high as 19% in elderly by 30 months follow up (PASE trial) [12]. Most studies report in patients with sinus node dysfunction. In the population with all-cause bradycardia (heart block and SND), CTOPP trial [13] finds 6.6% in VVIR arm and a recent trial shows similar frequency (9%) of persistent AF at 9 months follow up in DDDR pacing even with Minimized Ventricular pacing algorithm (MinVPACE study) [14].

This result is also supported by an analysis of the Mode Selection Trial (MOST) where a linearly increasing relationship between Cum% VP and risk of persistent AF was observed, after adjustment for all other predictors of AF in the study population [15]. For each 1% increase in Cum% VP, the relative risk of persistent AF increased by 1% up to 85%. This effect was observed in both the dual-chamber and single-chamber VP modes, but the magnitude was greater in the latter, presumably due to the coexisting loss of AV synchrony. An identical linearly increasing risk relationship between Cum% VP and Atrial Fibrillation (persistent and paroxysmal) was prospectively identified in the SAVEPACe Trial [16].

VI. Conclusion

Single chamber VVI pacing in patients with normal baseline cardiac function was associated with 9.7% incidence of new onset atrial fibrillation between 6 to 12 months after implantation. Progressive increase in mean left atrial end-diastolic diameter with LA diastolic dimension > 40 mm and higher percentage of paced beats were strong predictors of new onset AF in our study.

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