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Assessment of Atrial Fibrillation in Patients with Pacemaker Implantation

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ABSTRACT

Background: Atrial fibrillation (AF) is the commonest sustained disorder of cardiac rhythm. Permanent pacemaker (PPM)-detected atrial high-rate episodes (AHREs) of even 5-minute duration may identify patients at increased risk for death.

Objective: This study aimed to investigate the association of echocardiographic and clinical parameter with the occurrence of AHREs in patients with a dual-chamber pacemaker.

Patients and methods: this retrospective study included 208 patients. It was conducted in the Cardiology Department, Faculty of Medicine, Zagazig University Hospitals. The patients were classified according to development of AF into 2 groups: Group (A) involved 77 patients with AF and group **(B)** involved 131 patients without AF.

Results: The mean age of the studied cases was 61.67 ± 8.13 years and 53.4% were females. Mean SBP was 122.6 ± 16.8 mmHg while mean DBS was 76.9 ± 10.14 mmHg**.** There was a high statistically significant increase in LA volume index, E/é and a high statistically significant decrease in SV index and EF among AF group compared to non AF group**.**

Conclusion: In our opinions patients with CIED detected AHREs need oral anticoagulation to prevent thromboembolic events and decrease burden of ischemic stroke**.**

Keywords: Pacemaker implantation, Atrial fibrillation, Echocardiography.

INTRODUCTION

Atrial fibrillation (AF) is the most common arrhythmia encountered in clinical practice and is associated with high morbidity and mortality [(1)]. Some patients suffering from AF might have mild symptoms or short duration (caused by missed diagnosis) or the episodes only occur at night/during sleep, which results in a significant underestimation of the incidence of AF [(2)]. Current dual-chamber permanent pacemakers (PPMs) are capable of detecting and storing atrial high-rate episodes (AHREs), which have been shown to be a reliable surrogate of atrial tachyarrhythmias, especially for AF [(3, 4)]. Moreover, prior studies have verified the risk factors associated with AF, i.e., age, congestive heart failure, sinus node dysfunction, and higher ventricular pacing ratio [(5)].

Subclinical atrial tachyarrhythmias occur frequently in patients with pacemakers. These arrhythmias have been reported to be associated with an increased risk of thromboembolism [(6)]. Symptoms of atrial fibrillation (AF) are variable, and approximately 20% of patients with persistent AF are asymptomatic [(7)]**.** Asymptomatic AF is correlated with thromboembolic risks and the 1-year mortality rate was found to be higher in asymptomatic AF patients [(8)].

Cardiac implantable electronic devices (CIED) have been developed, and most dual-chamber pacemakers have specific algorithms to detect atrial high-rate episodes (AHREs) [(9)]. Increased left ventricular (LV) stiffness estimated by LV diastolic wall strain (DWS) has been reported to be a strong determinant of AF prevalence in structurally normal patients [(10)]**.**

The present study aimed to investigate the association of echocardiographic and clinical parameter with the occurrence of AHREs in patients with a dual-chamber pacemaker.

PATIENTS AND METHODS

Our retrospective study (record-based) was performed in the Cardiology Department, Faculty of Medicine, Zagazig University Hospitals. The patients were classified according to development of AF into 2 groups: Group (A) involved 77 patients with AF and group (B) that involved 131 patients without AF.

Inclusion criteria: Patients with previous history of cardiac implantable.

Exclusion criteria: Patients without follow-up data/echocardiographic findings (including poor-quality images) before the implantation during sinus rhythm. Patients who had undergone cardiac surgery.

Ethical Consideration:

The study was approved by the Local Ethical Committee of Zagazig University. Written consent was obtained from every patient prior to the procedures. This study has been carried out in accordance with the code of Ethics of The World Medical Association (Declaration of Helsinki) for studies involving humans.

Basic demographic information including age, gender was recorded. Full general and local examination with special emphasis on Systolic blood pressure, diastolic blood pressure and pulse pressure are measured in standard conditions. Laboratory tests included, serum creatinine, blood urea, uric acid, CRP and complete blood count (CBC).

Echocardiographic data:

All patients had been subjected to transthoracic echocardiography (TTE) during 12-month follow up period after permanent pacemaker implantation.

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The LA volume at the time just before mitral valve opening on the apical 4- and 2-chamber views was determined offline using Simpson's biplane disc summation method. LA volumes were indexed for body size by dividing the LA volume by body surface area calculated using the Dubois formula [(11)]. A patient with an LV mass index > 95 g/m^2 (female) or 115 g/m^2 (male) was considered to have LV hypertrophy (LVH) [(12)]. Concentric LVH is an increased left ventricular mass index with a relative wall thickness ≥ 0.45. Eccentric LVH is an increased left ventricular mass index with a relative wall thickness < 0.45 [(13)]. The measurement of (E) velocity is derived from pulsed-wave (PW) Doppler, usually in the apical 4-chamber view. Annular pulsed wave Doppler tissue imaging is also obtained from the apical 4-chamber view, using a 1- to 2-mm size sample volume. Averaging of (é) velocity from the septum and lateral side of the mitral annulus is desirable [(14)].

Statistical analysis

The collected data were coded, processed and analyzed using the SPSS (Statistical Package for Social Sciences) version 22 for Windows® (IBM SPSS Inc., Chicago, IL, USA). Data were tested for normal distribution using the Shapiro Walk test. Qualitative data were represented as frequencies and relative percentages. Chi square test (χ^2) was used to calculate difference between two or more groups of qualitative variables. Quantitative data were expressed as mean ± SD (Standard deviation). Differences between quantitative independent multiple was tested by

ANOVA. Independent samples t-test was used to compare between two independent groups of normally distributed variables (parametric data). P value ≤ 0.05 was considered significant.

RESULTS

The present study showed that the mean age of the studied cases was 61.67 ± 8.13 years and 53.4% of them were female. They were older in AF group (p = 0.02), but with no statistical significant difference in gender distribution. Also, the mean SBP among the studied cases was 122.6 ± 16.8 mmHg while mean diastolic was 76.9 ± 10.14 mmHg with no statistical significant differences between the studied groups regarding SBP or DBP **(Table 1).** There was no significant difference between the studied groups regarding laboratory examination **(Table 2).** Regarding, medical treatments, AF group used more anticoagulants, BBs and diuretics **(Table 3).**

The mean LA volume index among the studied cases was 32.89 ml/m^2, mean EDD was 43.3 mm, mean PWs was 1.3 mm, mean EDV was 145.12 ml, mean SV was 91.13 ml, mean EF was 62.67%, mean E/é was 8.48, mean LV mass index was 64.16 g/m^2, and mean ESP was 124.67 mmHg. There were no statistical significance differences between the studied groups in EDD and LV mass index but there was a high statistically significant increase in LA volume index, E/é and a high statistically significant decrease in SV index and EF among AF group compared to non AF group **(Table 4).**

Univariate analysis indicated reduced EDV and SV index together with older age, larger LA volume index and high P wave dispersion as significant variables **(Table 5).**

Table (1): Demographic data of the studied groups

Variable		Total (n=208)		AF (n=77)		Non AF (n=131)		t	P
Age (years)		**61.67±8.13 44-81**		**63.34±7.91 44-81**		**60.69±8.13 48-81**		**2.29**	**0.02**
SBP (mmHg)		**122.6±16.8**		**121.88±16.22**		**123.02±17.18**		**0.47**	**0.64 NS**
DBP (mmHg)		**76.9±10.14**		**76.69±10.28**		**77.02±10.09**		**0.23**	**0.82 NS**
		No	**%**	**No**	**%**	**No**	**%**	**χ^2**	**P**
Gender	Female	**111**	**53.4**	**42**	**54.5**	**69**	**52.7**	**0.07**	**0.79**
	Male	**97**	**46.6**	**35**	**45.5**	**62**	**47.3**		**NS**

SD: Standard deviation; t: Independent t test; NS: Non-significant (P>0.05); SBP (Systolic Blood pressure); DPB (Diastolic blood pressure)

Table (2): Laboratory investigation & drugs used among the studied patients

Variable	Total (n=208)	AF (n=77)	Non AF (n=131)	χ^2	P
Serum creatinine(mg/dl)	**1.18±0.26**	**1.21±0.25**	**1.17±0.27**	**0.9**	**0.37**
Creatinine clearance (ml/min)	**67.14±7.84**	**66.87±7.9**	**67.29±7.83**	**-0.38**	**0.71**
HBA1C (%)	**5.99±0.33**	**6.03±0.32**	**5.96±0.32**	**1.35**	**0.18**
Hb (g/dl)	**12.63±1.11**	**12.56±1.14**	**12.67±1.09**	**-0.7**	**0.49**
WBCs (10^3/ul)	**5.39±1.51**	**5.35±1.08**	**5.42±1.73**	**-0.39**	**0.69**
Platelets (10^3/ul)	**214.88±29.16**	**218.92±42.29**	**212.51±17.13**	**1.3**	**0.21**
CRP (mg/L)	**5.06±1.83**	**5.07±2.39**	**5.06±1.41**	**0.013**	**1**
Cardiac enzymes (ng/ml)	**56.52±22.77**	**58.35±26.22**	**55.45±20.51**	**0.83**	**0.41**

χ^2: Chi square test; HBA1c (glycosylated hemoglobin), Hb (Hemoglobin), WBCs (white blood cells), CRP (C-reactive protein).

Table (3): Drugs used among the studied patients

Variable		Total (n=208)		AF (n=77)		Non AF (n=131)			
		No	%	No	%	No	%	χ^2	P
Drugs	Antiplatelet	63	30.3	23	29.9	40	30.6	13.89	0.02
	Anticoagulant	8	3.9	5	6.5	3	2.3		
	ACEI/ARBS	77	37.1	28	36.4	49	37.5		
	BBs	33	15.9	20	26	13	10		
	Statins	47	22.6	18	23.4	29	22.2		
	Diuretics	21	10.1	10	13	11	8.4		

χ^2: Chi square test; ACEI: angiotensin convertase enzyme inhibitor, BB: beta blockers), ARBS: angiotensin receptor blockers.

Table (4): Echo results among the studied groups

Variable	Total (n=208)	AF (n=77)	Non AF (n=131)	t	P
LA volume index (ml/m^2)	32.89±10.25 16-62	40.65±11.24 16-62	28.34±6.07 18-38	10.26	<0.001 **
EDD(mm)	43.3±5.72 35-67	42.96±5.45 35-55	43.5±5.89 35-67	0.65	0.52 NS
ESD(mm)	42.73±3.15 36-48	42.96±3.3 38-48	42.59±3.06 36-45	0.79	0.43
EDV(ml)	145.12±16.21 120-175	128.64± 5.59 120-137	154.81±11.99 135-175	-21.34	<0.001 **
ESV(ml)	54±6.46 40-65	54.8±3.74 48-60	53.52±7.59 40-65	1.63	0.11
SV index (ml/m^2)	53.6±10.9 35.91-78.82	43.43±3.88 35.91-50.59	59.61±9.12 41.18-78.82	-17.72	<0.001 **
EF (%)	62.67±6.47 51-77	57.78±3.39 51-64	65.56±6.1 52-77	-11.80	<0.001 **
E/A ratio	1.14±0.17	1.13±0.12	1.20±0.16	10.65	0.2
E/é	8.48±2.99 4.6-13	12.19±0.83 11-13	6.3±0.98 4.6-8	44.26	<0.001 **
LV mass index (g/m$^{2)}$	64.16±10.59 42-94	63.87±7.47 49-82	64.34±12.08 42-94	-0.34	0.73 NS

SD: Standard deviation, t: Independent t test, NS: Non-significant (P>0.05) , **: highly significant(P<0.001) DWS(diastolic wall strain assessed by PWs-PWd/PWs), E/é (ratio between early mitral inflow velocity and mitral annular early diastolic velocity), EDD (end diastolic diameter), ESD (end systolic diameter), EDV(end diastolic volume), ESV(end systolic volume), EF (ejection fraction), LA (left atrium), LV (left ventricle), PWd (Post wall diameter at end-diastole) , PWs (Post wall diameter at end-systole) , SV(stroke volume).

Table (5): Univariate regression analysis for independent predictors of AF after the implantation of dual-chamber pacemaker

Variable	Univariate	
	t	P value
Age(years)	2.29	**0.02**
SBP(mmHg)	0.47	0.64
DBP(mmHg)	0.23	0.82
Heart rate(beat/min)	1.36	0.18
P wave dispersion(msec)	39.1	**<0.001**
EDD(mm)	0.65	0.52
EDV(ml)	-21.34	**<0.001**
SV index (ml/m^2)	-17.72	**<0.001**
LA volume index(ml/m^2)	10.26	**<0.001**
Serum creatinine(mg/dl)	0.9	0.37
HBA$_1$C(%)	1.35	0.18
CRP(mg/L)	0.013	1

t: Independent t test , HR: hazard ratio , CI(Confidence interval) NS: Non-significant (P>0.05) , * p<0.001 highly significant

DISCUSSION

Atrial fibrillation (AF) is the commonest sustained disorder of cardiac rhythm, which is usually associated with an increased risk of both morbidity and mortality from heart failure, stroke, and thromboembolic complications. The mortality rate in AF is about twice that of patients with normal sinus rhythm [15,16].

Our retrospective study (record based) was conducted in the Cardiology Department, Faculty of Medicine, Zagazig University Hospitals. 208 patients 97 males (46.6 %) and 111 females (53.4 %) with mean age of 61.67 ± 8.13 years, 87 of them with SND and 121 with AVB. Patients were enrolled in the study according to the aforementioned inclusion and exclusion criteria. They were classified according to development of AF into 2 groups: Group (A) included patients with AF (77 patients 37%) and group (B) that included patients without AF (131 patients 63%).

We found that AF group was older in age and this is in agreement with **Skanes *et al.*** [17] who reported that older age, higher prevalence of SND, and prior AF could predict the development of chronic AF in patients with a pacemaker.

In this study, the mean SBP among the studied cases was 122.6 mmHg and mean DBP was 76.9 mmHg with no significant differences between the studied groups. These results are in agreement with **Kishima *et al.*** [18].

The mean serum creatinine among the studied groups was 1.18 mg/dl, mean HBAIc was 5.99%, mean CRP was 5.06 mg/l and mean cardiac enzymes (troponin T hs) was 56 ng/ml. There were no statistical significance differences between the studied groups in laboratory results and this is in agreement with **Wu *et al.*** [19].

Also, in our study an analysis regarding other comorbidities like ischemic stroke, myocardial infarction and peripheral vascular disease was carried out and it was observed that there were no statistical significant differences between the studied groups. This are in agreement with **Kishima *et al.*** [18] **and Chen *et al.*** [20]**.** But, different results were found by **Uetake *et al.*** [15] who stated that AF group had significant increase in TIAs, or stroke risk compared to no AF group.

In addition, as part of our research, we looked into a variety of drug consumption and observed that there were statistical significant differences in anticoagulants, beta blockers and diuretics use in AF group. This is in agreement with **Kishima *et al.*** [18] but different results were found by **Uetake *et al.*** [15] who observed no significant difference between studied groups in medications.

We found that LA volume index was higher among AF group. This is in agreement with **Antoni *et al.*** [21]. The PWs was lesser among AF group compared to non-AF group. This is in agreement with **Takeda *et al.*** [11] and **Kishima *et al.*** [18]**.** We found that mean E/A ratio recorded during sinus rhythm was 1.14 with no statistical significant difference between the studied groups. This is in agreement with **Uetake *et al.*** [15]. However, we discovered that the mean E/é ratio was 8.48, with a highly statistically significant difference across the studied groups, with the AF group having the highest level of E/é ratio. This is in agreement with **Kishima *et al.*** [18]**.**

Our study went with other many studies that evaluated CIED detected AHREs as **Uittenbogaart *et al.*** [22] who described the relationship between CIED-detected AHRE and risk of thrombo-embolic events. In their study, patients with an AHRE burden lasting over 6 min had an increased risk of thromboembolic events that was similar to patients with an AHRE burden lasting over 6 h**.**

Also, **Pioger *et al.*** [23] reported that an atrial fibrillation episodes were documented by the fallback mode switch (FMS) provided by implanted pacemakers. They included 377 patients. At least one AF episode was stored during follow-up in the memory of 169 pacemakers (45%). A significant higher incidence of premature atrial beats was observed in patients with AF than in patients without AF ($P < 0.0002$). Patients with AF had a lower atrial percentage of paced events (55%) than patients without AF (63%). These results confirm the high incidence of AF in paced patients and suggest a preventive effect of atrial pacing**.**

Our findings may provide additional prognostic information for other factors. However, the management of patients with CIED-detected AHREs and low diastolic wall strain remains controversial.

CONCLUSION

In our opinions patients with CIED detected AHREs need oral anticoagulation to prevent thromboembolic events and decrease burden of ischemic stroke**.** Current guidelines do not address in detail the management of these patients. Further investigations to confirm the benefit of oral anticoagulants.

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