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Bone mineral density among cases with chronic Cardiac arrythmias

Rheumatology and Rehabilitation

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ABSTRACT

Background: In spite of growing suggestion of a mutual connection among bone and heart health, the association among bone mineral density (BMD) and chronic cardiac arrhythmia remains insufficiently studied.

Aim of The Work: to investigate BMD among cases with chronic cardiac arrhythmias especially Atrial fibrillation (AF) (the commonest chronic cardiac arrhythmia) , its medications.

Patients and Methods: This was a case-control study carried out at Outpatient clinics and Inpatient of Cardiology and Rheumatology Rehabilitation Departments of Al Hussein and Bab El Sharia University Hospitals- Al-Azhar University – Cairo from March 2021 till October 2021.

Results: a highly significant change was found among Vit-D and T score (AP spine, Lt Femur and Lt Forearm) in study group, a highly significant change was found among disorder duration and T score (AP spine, Lt Femur and Lt Forearm) and Vit-D in study group.

Conclusion: Cases with AF were at an elevated risk of osteoporotic fractures than were cases with no AF in this work.

Keywords: *Open angle glaucoma; Retinal nerve fiber layer thickness; Ganglion Cell Layer Thickness; Corneal Thickness.*

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INTRODUCTION

Cardiac arrhythmias & osteoporotic fractures are mutual in the ageing people.

There is a rising number of cases receiving medical medications for cardiac arrhythmia. This is because of the advance in age of the people and the upgraded survivals of cases with ischemic heart disorders. AF is the commonest chronic cardiac arrhythmia. New reports have proposed that conversions to sinus rhythm doesn't upgrade survival in cases with AF in comparison to rate controlling and anti-coagulation.[1] Subsequently, the number of cases on medical management for cardiac arrhythmia can rise still more.

In a case-control report utilizing data from the British General Practice Research Database (GPRD), the usage of anti-arrhythmics was significantly correlated to the danger of fractures [OR: 1.5; 95.0% ,95.0%CI: 1.4–1.6], but the sub-types of anti-arrhythmic medications weren't described.[2]

AF can rise the falling danger of and thus the danger of fractures, counting, chest pains, dyspnea, palpitations, dizziness, light-headedness, and fatigue. [3, 4]

Amiodarone is a mutual anti-arrhythmic utilized for management of Arrythmia. Amiodarone is recognized to impact thyroid functions and can thus impact osteoprotic fractures risk. [5, 6] Cutaneous photo-sensitivity is a recognized complication of amiodarone, and cases using this medication are frequently encouraged to shield their skin from intense sun-light exposures.[7] For the majority of people, >80% of their Vit-D needs produced from sun-light exposures.[8] Subsequently, cases received amiodarone can simply advance a Vit-D deficit that in order can rise the danger of osteoprosis [9, 10] and fractures. [11]

Present standard method for detecting osteoporosis is the estimations of BMD by means of dual energy X-ray absorptiometry (DEXA). [12]

This study aimed to study BMD among cases with chronic cardiac arrhythmias especially AF (the commonest chronic cardiac arrhythmia), its medications.

PATIENTS AND METHODS

This report was a case-control carried out at Outpatient clinics and Inpatient of Cardiology and Rheumatology Rehabilitation Departments of Al

Hussein and Bab-ElSharia University Hospitals- Al-Azhar University – Cairo from March 2021 till October 2021

One hundred and fifty persons enrolled in this report were subdivided into 2 groups: Group (A): 100 cases with established diagnosis of Arrythmia 2 year ago at least. Group (B): 50 apparently healthy Persons as a control group.

Inclusion criteria: These included an established diagnosis of Arrythmia by ECG for at least 2 years.

Exclusion criteria: Age below 30 or above 60 years old, diagnosis of endocrine disorders (primary hyperparathyroidism, hyperthyroidism, etc.), diagnosis of Rheumatologic disorder (RA, SLE, AS, etc.), those Cases on glucocorticoids more than 7.5-mg every day for more than 6-mths, cases with a creatinine clearance ≤50 ml/minute. Under this level, there is decreased hydroxylation of 25(OH) D to 1, 25-di-hydroxy-Vit-D, gravid or lactating females and post-menopausal females.

Methods:

Clinical assessment: History: complete history taking: In history-taking, age, gender, residence, job, smoking or former smoker, presenting complaints, jaundice, itching, existence of risk-factors, like DM or HPT were assessed. Clinical examinations: General examinations: Pulse BP, temp. and musculoskeletal examination, Cardiac examination. The following laboratory investigations were done for all cases: TSH, free T3, free T4 and PTH, total & ionized calcium, Vit-D, serum phosphorus, alkaline phosphatase, liver enzymes as ALT – AST and kidneys functions examinations as s-Cr, s-urea & creatinine clearance. BMI and Waist circumference were determined. Measurements of BMD by DEXA scans: We evaluated BMD via DEXA scans densimeter by means of X-ray equipment and a computer to calculate bone densities of AP lumbar spine & RT neck femur. The investigated parameters were age, time since menopause, sex, BMI and DM period. BMD was determined in the Rt proximal femur and AP lumbar spine and the statistics were investigated on the basis of T-score & Z-score and areal BMD by means of the WHO criteria. T-scores from −1 to −2.5 were measured to indicate osteopenia, and those equal or <−2.5 were measured to indicate osteoporosis. Electro-cardiograph (ECG): ECG has been accomplished to cases as next: 7 electrodes have been located in a diagonal arrangement, with 3 of them on the right-side of the chest, and 4 on the left-side. The recorders utilized comprised analogical (Dynamis)1 and digital (DMS 300-6)2 apparatuses. Decoding of the records has been done by means of particular program (Cardio-Scan 10). So as to lessen digital errors, all of the beats indicated as ectopic by the program were manually reviewed by the investigators. Ethical committee: agreement from the faculty of medicine ethics committee and IRB has been attained.

Statistical analysis: the results were analyzed via SPSS-20 software (IBM, USA). Quantitative variables have been introduced as mean and SD. Qualitative variables have been introduced as numbers and percentages. So as to compare parametric quantitative variables among 2 groups, Student t-test has been used. Qualitative parameters comparisons were performed via chi-square (X2) testing or Fisher's exact testing when frequencies less than 5. Pearson correlation coefficients have been utilized to evaluate the correlation among 2 variables with normal distribution. When a variable hasn't a normal distribution, At $P < 0.05$ the result was significant

RESULTS

The current study included One hundred and fifty persons; were subdivided into 2 groups: Group (A): 100 cases with established diagnosis of arrhythmia 2 year ago at least . Group (B): 50 apparently healthy Persons as a control group.

41% of cases were males and 59% were females with a mean age of 48 years.

There was a significant change was found among the study groups as (cases and control) and the demographic data (age), A non-significant change was found among the study groups as (cases and control) and the demographic data (sex and BMI). (Table 1).

This study shows that a highly significant change was found among the study groups as (cases and control) and Vit-D as (deficient, insufficient and normal), with mean cases 18.44 (±10.89 SD) with range (2.60-48.40) and mean control 36.63 (±5.84 SD) with range (30 -50). (Table 2).

There were only 12 (100%) with diagnosis of AF have osteoporosis, There were 5 (16.1%) with diagnosis of A. flutter, 20 (64.5%) with diagnosis of AF, 5 (16.1%) with diagnosis of SVT and 1 (3.2%) with diagnosis of VT have osteopenia, There were 10 (17.5%) with diagnosis of A. flutter, 31 (54.4%) with diagnosis of AF, 12 (21.1%) with diagnosis of SVT, 1 (1.8%) with diagnosis of Sinus tachycardia, 1 (1.8%) with diagnosis of VT and 2 (3.5%) with diagnosis of Atrial flutter have normal AP spine. There were only 9 (100%) with diagnosis of AF have osteoporosis, There were 4 (16.0%) with diagnosis of A. flutter, 17 (68.0%) with diagnosis of AF, 2 (8.0%) with diagnosis of SVT, 1 (4.0%) with diagnosis of VT and 1 (4.0%) with diagnosis of Atrial flutter have osteopenia, There were 11 (16.7%) with diagnosis of A. flutter, 37 (56.1%) with diagnosis of AF, 15 (22.7%) with diagnosis of SVT, 1 (1.5%) with diagnosis of Sinus tachy, 1 (1.5%) with diagnosis of VT and 1 (1.5%) with diagnosis of Atrial flutter have normal Lt Femur. (Table 3).

A high significant change was found among BMI and Vit-D and T score (AP spine, Lt Femur and Lt Forearm) in study group. This table shows that a highly significant change was found among Vit-D and T score (AP spine, Lt Femur and Lt Forearm) in study group. (Table 4).

A highly significant change was found among disorder duration and T score (AP spine, Lt Femur and Lt Forearm) and Vit-D in study group (Table 5).

Demographic data	Cases (n = 100)		Controls (n = 50)		Test of Sig.	p
	No.	%	No.	%		
Sex						
Male	41	41.0	12	24.0	χ^2= 4.216*	0.040*
Female	59	59.0	38	76.0		
Age						
30 - <40	14	14.0	9	18.0	χ^2= 6.647*	0.036*
40-<50	32	32.0	25	50.0		
≥ 50	54	54.0	16	32.0		
Min. – Max.	30.0 – 59.0		32.0 – 59.0		t= 2.026*	0.045*
Mean ± SD.	48.39 ± 7.32		45.94 ± 6.23			
Median (IQR)	50.0 (45.0 – 54.0)		45.50(41.0 – 51.0)			
BMI						
Normal (18.5-24.9)	7	7.0	4	8.0	χ^2= 0.374	0.829
Overweight (25-29.9)	37	37.0	16	32.0		
Obese (≥ 30)	56	56.0	30	60.0		
Min. – Max.	20.60 – 47.90		23.30 – 44.50		t= 0.870	0.386
Mean ± SD.	32.89 ± 6.01		32.02 ± 5.24			
Median (IQR)	31.20 (28.60–36.60)		32.60(27.90 – 34.90)			

IQR: Inter quartile range SD: Standard deviation
χ2: Chi square testing t: Student t-test
*: Statistically significance at p value≤ 0.05

Table 1: Comparing among the study groups as regard demographic data

Vit-D	Cases (n = 100)		Control (n = 50)		Test of Sig.	p
	No.	%	No.	%		
Deficient (0- 20)	54	54.0	0	0.0	χ^2= 62.726*	<0.001*
Insufficient (20 -30)	30	30.0	11	22.0		
Normal (30 – 100)	16	16.0	39	78.0		
Min. – Max.	2.60 – 48.40		20.0 – 49.0		U= 486.0*	<0.001*
Mean ± SD.	18.44 ± 10.89		36.51 ± 7.76			
Median (IQR)	19.26 (8.75 – 26.25)		38.0(31.0 – 42.0)			

IQR: Inter quartile range SD: Standard deviation
U: Mann Whitney test χ2: Chi square test
p: p value for comparison among study groups
*: Statistical significance at p ≤ 0.05

Table 2: Comparing among the study groups as regard d Vit-D

	AP spine						χ^2	MCp
Diagnosis	**Osteoporosis (< -2.5) (n = 12)**		**Osteopenia (-2.5 to -1) (n = 31)**		**Normal (>-1) (n = 57)**			
	No.	**%**	**No.**	**%**	**No.**	**%**		
A. flutter	0	0.0	5	16.1	10	17.5	10.436	0.336
AF	12	100.0	20	64.5	31	54.4		
SVT	0	0.0	5	16.1	12	21.1		
Sinus tachy	0	0.0	0	0.0	1	1.8		
VT	0	0.0	1	3.2	1	1.8		
Atrial flutter	0	0.0	0	0.0	2	3.5		
	Lt Femur						χ^2	MCp
Diagnosis	**Osteoporosis (< -2.5) (n = 9)**		**Osteopenia (-2.5 to -1) (n = 25)**		**Normal (>-1) (n = 66)**			
	No.	**%**	**No.**	**%**	**No.**	**%**		
A. flutter	0	0.0	4	16.0	11	16.7	10.763	0.334
AF	9	100.0	17	68.0	37	56.1		
SVT	0	0.0	2	8.0	15	22.7		
Sinus tachy	0	0.0	0	0.0	1	1.5		
VT	0	0.0	1	4.0	1	1.5		
Atrial flutter	0	0.0	1	4.0	1	1.5		

χ2: Chi square test MC: Monte Carlo

Table 3: Relation between arrhythmia and T score (normal - osteopenia - osteoporosis) in study groups

	BMI	
	r	**P**
Vit-D	0.398*	<0.001*
T score		
AP spine	0.238*	0.017*
Lt Femur	0.318*	0.001*
Lt forearm	0.331*	0.001*
	Vit-D	
	r	**P**
T score		
AP spine	0.514*	<0.001*
Lt Femur	0.517*	<0.001*
Lt forearm	0.688*	<0.001*

r: Pearson coefficient

*: Statistical significance at $p \leq 0.05$

Table 4: Correlation between BMI and Vit-D and T score in study group

	Disorder duration	
	r	**P**
T score		
AP spine	-0.447*	<0.001*
Lt Femur	-0.343*	<0.001*
Lt forearm	-0.576*	<0.001*
Vit-D	-0.462*	<0.001*

r: Pearson coefficient

*: Statistical significance at $p \leq 0.05$

Table 5: Correlation between disorder duration and t score and Vit-D in study group

DISCUSSION

Elderly is a complex process that eventually causes morbidities, that was considered as the main risk-factor for several disorders comprising cardio-vascular diseases, neurological disorders, metabolic disturbances, and tumor. As persons age, can change in body compositions happen; for instance, the body muscles, bones losing, and body fat rise and lean mass and BMD reduction. Furthermore, variations in the body compositions are because of changes in energy balances, with a positive energy balance causing weight gains and a negative balance causing weight losing. The resting metabolic rates decreases in the age advancing process, that can as well cause variations in body compositions and contrariwise. In contrast, the cardio-protective systems decline throughout the aging age advancing, contributed to the progress of heart failures.[13]

The current report revealed that a highly significant change was found among the study groups as (cases and control) and Vit-D as (deficient, insufficient and normal), with mean cases 18.44 (±10.89 SD) with range (2.60-48.40) and mean control 36.63 (±5.84 SD) with range (30 -50). There was statistically insignificant difference between arrhythmia and Vit-D in study group.

In accordance with our results, metanalysis conducted by Liu et al., (95) as they reported that 13 reports were comprised with 6518 cases of AF among 74,880 contributors. Vit-D insufficiency (less than 20 ng/ml) was accompanying with elevated risk of AF (RR:1.2, 95% CI: 1.0–1.4).

Also, Demir et al., [14] revealed that a number of 102 cases with non-valvular chronic AF without any other cardio-vascular disorders (ages mean 62.51 ± 5.88; group-I) and 96 cases with AF, which is accompanied with mitral-valve disorder (ages mean 61.51 ± 5; group-II) have been enrolled. Of all, 100 age-matching controls with sinus rhythm (ages mean 61.35 ± 5.44). Group-I cases had lower Vit-D levels than group-II and the controls (6.5 ± 4.9, 9.2 ± 7.4, and 11.2 ± 6.9 ng/mL, P value< .001, respectively). Furthermore, meta-analysis held by Zhang et al., [15] reported a weak but positive correlation among Vit-D insufficiency and AF.

Osteoporotic fractures are accompanying with elevated death rate and decreased quality of life (QoL) in old people. Numerous reports revealed an elevated danger of fractures among cases managed with oral anti-coagulants (OACs). The majority of cases with non-valvular AF are managed with OAC for strokes avoidance. The vit-K antagonists (VKAs) were the only real choice for thromboprophylaxis in AF cases for several years; but, in lately, Direct-OACs have appeared as substitutes. Warfarin is a VKA, and by adaptable Vit-K, warfarin constrains the g-carboxylation of numerous proteins, comprising coagulation factor II, VII, IX, and X. [16]

In the current work, a highly significant change was found among the studied groups as (cases and control) and AP spine (EBMD and T score), With mean EBMD cases 1.10 (±0.17 SD) with range (0.74 - 1.52) and mean EBMD control 1.20 (±0.14 SD) with range (0.91 – 1.48), and mean T score cases -0.65 (±1.42 SD) with range (-3.70 – 2.80) and mean T score control 0.41 (±0.97 SD) with range (-1.70 – 2.50). A highly significant change was found among the studied groups as (cases and control) and Lt Femur (BMD and T score), With mean BMD cases 0.98 (± 0.23 SD) with range (0.53 – 2.09) and mean BMD control 1.07 (±0.11 SD) with range (0.78 – 1.26), and mean T score cases -0.16 (±1.84 SD) with range (-3.70 – 9.10) and mean T score control 0.65 (±0.76 SD) with range (-1.10 – 2.20). A highly significant change was found among the studied

groups as (cases and control) and Lt Femur (T score), with mean T score cases -0.48 (±1.99 SD) with range (-4.60 – 4.80) and mean T score control 0.83 (±1.30 SD) with range (-1.10 – 3.0). A nonsignificant change was found among the study groups as (cases and control) and Lt Femur (BMD), with mean BMD cases 1.48 (±7.93 SD) with range (0.26 – 80.0) and mean BMD control 0.67 (±0.12 SD) with range (0.48 – 0.97).

In accordance with our results, Kim et al., [17] revealed that throughout a median following-up of 48-mths, the frequency of bone fractures was elevated in AF cases than in non-AF cases (3.20 vs. 2.18 per 100-person yearly), resp. AF was accompanying with fracture non-dependently of other comorbidities with an adjusted hazard-ratio (HR) of 1.21 (95% CI, 1.02–1.41; P<0.05). AF was consistently accompanied with an elevated risk of osteoporotic fractures and following mortality thereafter fractures.

Previous studies conducted by Rice et al., [18] have revealed that bone fractures are accompanying with multi-exogenous and endogenous influences that rise falling danger and weaken bony structures. Sanders et al., [19] revealed that AF is non-dependently correlated with elevated fallings.

Potential clarifications for this associations included haemodynamic variations in accordance to reduced cardiac output from losing of the atrial kick and asymmetrical ventricular responding; these variations may damage brain perfusions, leading to losses of postural tone, which in order, could cause falls. Cases with AF frequently have sinus node disorders, that could cause bradycardia, and even asystole post-AF terminations. Regarding bone strength, AF may impact the micro-vasculature in bones through thromboembolism, consequently influencing bone formations. [20]

The study carried out by Wong et al., [21] from Taiwan and Australia revealed that persons with AF have a 2-fold elevated in danger of fractures, but Wallace et al., [22] reported nonsignificant correlation among AF and fractures danger.

The present findings in line with the study of Binding et al., [23] as they revealed that the standardized absolute 2-yrs danger of any fracture was less between Direct-OACs managed cases (3.10%; 95.0% CI: 2.91% to 3.31%) and between VKA-managed cases (3.80%; 95% CI: 3.40% to 4.20%). DOAC was correlated with a significantly low relative risks of any fracture (HR: 0.849; 95.0% CI: 0.74 to 0.96), main osteoporotic fractures (HR: 0.85; 95% CI: 0.72 to 0.99), and starting osteoporotic medications (HR: 0.820; 95% CI: 0.70 to 0.95). A mutual endpoint revealed that cases managed with DOAC had a significantly lesser relative risks of experiencing any fractures or starting osteoporosis medications (HR: 0.84; 95% CI: 0.76 to 0.93).

In the study of Lutsey et al., [24] rivaroxaban usage in comparison to warfarin was correlated with less fractures- risks necessitating hospital-stay (HR, 0.80; 95% CI, 0.69-0.93) and all clinical fractures (HR, 0.82; 95% CI, 0.76-0.90), while the estimation for hip fracture (HR, 0.89; 95% CI, 0.71-1.12) was nonsignificant. Apixaban usage was accompanying with less danger of all fracture outcomes in comparison to warfarin, counting hip fracture (HR, 0.67; 95% CI, 0.45-0.98), fractures needing hospital-stay (HR, 0.61; 95.0% CI, 0.47-0.79), and all clinical fracture (HR, 0.85; 95.0% CI, 0.75-0.99).

According to Huang et al., [25] significantly inferior risks of osteoporosis were found in the rivaroxaban (HR=0.688; 95% CI=0.55–0.82) and apixaban (HR=0.38; 95.0% CI=0.22–0.66) sub-groups, but not in the dabigatran sub-group (HR=1.04; 95.0% CI=0.85–1.27).

Huang et al., [26] revealed that the median following-up period was 2.4 yrs. In comparison to warfarin, NOACs were accompanying with a decreased fractures danger [HR = 0.84, 95% CI = 0.769–0.929; Pvalue < 0.001]. Sub analyses showed that every NOAC, explicitly dabigatran (HR = 0.87, 95.0% CI = 0.78–0.98; P = 0.028), rivaroxaban (HR = 0.82, 95% CI = 0.73–0.91; P value< 0.001), and apixaban (HR = 0.67, 95.0% CI = 0.52–0.87; P value= 0.003), had a decreased fractures danger.

AF is on of the possible risk-factors for fracture, as it not only results in structural and functional changes in the cardio-vascular system, but as well exerted thromboembolic influences on the nervous system, and interrupts postural stability. Consequently, AF is now known as a non-dependent risk-factor for nonaccidental fallings. Vit-K antagonists, are utilized in preventing strokes in AF, may be accompanied with decreased BMD and elevated danger of osteoporotic fractures. Regarding bones strength, the thromboembolic impacts of AF can decrease bones mass through decrease in the osseous blood supplies. [27]

The present findings revealed that a highly significant change was found among BMI and Vit-D and T score (AP spine, Lt Femur and Lt Forearm) in study group. A highly significant change was found among Vit-D and T score (AP spine, Lt Femur and Lt Forearm) in study group. There was nonsignificant change among arrhythmia (A. flutter, AF, SVT, Sinus tachy, VT and Atrial flutter) and (forarm t score / femur t score / spine t score) in study group.

Our results were supported by study of Vimaleswaran et al., [28] as they revealed that correlations among Vit-D scores and BMI were established.

CONCLUSION

Cases with AF were at an elevated danger of osteoporotic fractures than were cases without AF in this work.

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