SJIF Impact Factor: 6.711

WORLD JOURNAL OF ADVANCE HEALTHCARE RESEARCH

ISSN: 2457-0400
Volume: 8.
Issue: 10
Page N. 101-107
Year: 2024

Original Article www.wjahr.com

RELATIONSHIP BETWEEN HEART FAILURE AND OSTEOPOROSIS

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Article Received date: 11 August 2024 **Article Revised date:** 01 September 2024 **Article Accepted date:** 21 September 2024

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ABSTRACT

Background: Osteoporosis is a systemic disorder causing bone fragility and fractures, affecting over 200 million people worldwide. It's primarily caused by postmenopausal estrogen loss and secondary by factors like acromegaly, adrenal atrophy, hyperparathyroidism, and drug use. Common etiologic factors include diabetes, smoking, dyslipidemia, hypertension, and estrogen deficiency. **Aims**: To study the Relationship between heart failure and osteoporosis and the association between heart failure & fracture risk in the osteoporotic patient. **Methods**: We collected around 100 patients from the rheumatology outpatient and sent them for the DEXA study in the same hospital. The investigations of these patients were done for Ca, vit. D, Echo, S. Cholesterol, FBS & RFT. The patients were separated into two groups; Control group: persons without heart failure and have DEXA collected from the DEXA unit and Patients group: patient with heart failure sends for DEXA. **Results:** In studying the personal characteristic and medical problems and comparing two groups, the P-value is between (0.06-1.000), so there is no significant difference. Also, by studying the Relationship between heart failure and osteoporosis, P-value is no significant difference (0.680). We also compared the osteoporotic heart failure and non-osteoporotic heart failure regarding diastolic function, the P-value (0.475), so there is no significant difference. Also, regarding biochemical parameters, we compare between patient and control groups and between osteoporotic heart failure and non-osteoporotic heart failure; in general, there is no significant difference because P-value is between (0.06-0.1). **Conclusion:** We conclude that There is no relationship between heart failure and osteoporosis, and just they are sharing some risk factors.

KEYWORDS: Dexa, Heart Failure, Osteoporosis.

INTRODUCTION

Osteoporosis is a systemic disorder defined as decreased bone mass and deterioration of bone tissue's microarchitecture, which leads to the fragility of the bone and increased fractures of the spine, hip and wrist.[1]

Osteoporosis can be classified into primary and secondary forms. Primary osteoporosis, the most common form, occurs due to postmenopausal loss of estrogen and androgen, leading to increased bone turnover and trabecular bone loss and the senile osteoporosis. Secondary osteoporosis, on the other hand, is caused by various factors such as acromegaly, adrenal atrophy, hyperparathyroidism, hyperthyroidism, and drug use.[2]

Osteoporosis can affect more than 200 million of people worldwide. It becomes more common obvious with age and more common in female than in male.[3]

There is increasing awareness of an association between low bone mineral density and cardiovascular disease and increased morbidity and mortality.[4,5] Furthermore, coronary and aortic calcification, endothelial inflammation and dysfunction, which enhance the initiation and development of the atherosclerotic lesion[6], are correlated with low bone mass density and fracture.[7] This may indicate a common pathophysiological mechanism of both conditions, but the basis of mechanism for the Relationship between the two disorders is unclear.[8] However, common etiologic factors can be shared between osteoporosis and cardiovascular disease, especially heart failure; these etiologic factors like diabetes, smoking, dyslipidemia, hypertension, and estrogen deficiency act as a cofounding factor.[9] Medications used to treat heart failure may also play a role, especially loop diuretics because they promote calciuresis and lower bone mineral density, so predispose to osteoporosis and falls because of orthostatic hypotension.[10] In addition, some studies

suggest that warfarin increases fracture risk, but other heart failure treatments (angiotensin-converting enzyme inhibitor, nitrates, angiotensin-receptor blockers, b-blockers, spironolactone, statins, and thiazide diuretics) decrease fracture risk.[11] Regardless, H.F. patients remain at increased osteoporosis and fracture risk even after adjustment for these medications.[12]

Finally, the burden of cardiac disease, especially heart failure in the community in the recent decades, has shifted toward the elderly and women, where osteoporosis is usually prevalent, so any relationship could quickly reflect the co-existence of the disease instead of the causality.[13]

The current study aimed to study the relationship between heart failure and osteoporosis and the association between heart failure and fracture risk in the osteoporotic patient.

PATIENTS AND METHOD

Study Setting

This study had approval from the regional research committee of Mosul health administration, the scientific research committee of collage of medicine, the University of Mosul-Iraq, and performed in a period between September 2020 to March 2021, and done in Ibn-Sina teaching hospital.

Study Design

It is a Case-Control Study; the patients group (case) included Fifty patients with heart failure having echo study with E.F.<50 and diastolic dysfunction, their ages range between 40-80 years old, and of both sexes. Meanwhile, fifty apparently healthy subjects selected as control group and matched for age and sex with patients group.

Data Collection

Data was collected by the direct interview of the researcher with the subjects by

1-A questionnaire form was designed to record the information for each subject, and it included: Name, age, sex, BMI, history of previous osteoporosis, medical history, history of fracture, drug history, especially of H.F. and osteoporosis.

2-Biochemical profile (FBS, S.Ca, S. cholesterol, B. urea, S. creatinine).

3- The subject sent to Echo study.

4- DEXA study: was performed on both patients and control groups.

Instruments

The instruments and calculations

1-Body Mass Index (BMI): It was calculated according to the following equation: BMI=weight (Kg)\ height (m^2).

2-Dual – Energy X-ray Absorptiometry (DEXA): Bone Mineral Density (BMD) was obtained at the lumbar vertebra to all subjects using DEXA apparatus (Osteo-sys 2020) and taking T-score.

T-score classification as normal: 5.5 to -0.9; Osteopenia: -1 to > -2.5; Osteoporosis <= -2.5

3-Echo study: The apparatus used is Philips(model 2006); an echo study was obtained for all subjects. The E.F. and diastolic function was obtained for both groups.

Exclusion criteria

Patients with chronic renal failure, Rheumatic disease, Steroid therapy for an extended period were excluded from the study.

Statistical Analysis

A descriptive statistic is mean and SD. for quantitative data frequency and percentage for categorized data. Analytic statistics chi-squared and independent t-test for 2 means.

RESULTS

Fifty patients with heart failure were collected, and another corresponding 50 patients without heart failure were included as the control group. The personal characteristics of the study sampled population is shown in table (1). The mean age (about 70) of both patients and control group, mean BMI (about 27 of patient group and 29 of control group), gender (male of the patient group was 33(66%), and of the control group was 26(52%), and female of the patient group was about 17(34%) and of the control group was 24(48%), the smokers of the patient group were 12(24%) and of the control group were15(30%). Mean systolic BP of the patient group was 125.3 ± 21.0 mmHg while of the control group was 126.0 ± 12.9 mmHg. The diastolic BP of the patient group was 80.2 ± 12.0 mmHg and 81.3 ± 8.1 mmHg among cases and control respectively. The history of fracture found in 2% of patient group and 5% of control group There were no significant statistical differences for all parameters.

Table 1: Personal characteristics of the study sampled population.

Parameters	Cases "Heart failure" [n = 50]	Control "No heart failure" [n = 50]	P-value*
Mean age (years)	61.3 ± 10.1	61.0 ± 8.9	0.900
Mean BMI (kg/m2)	27.4 ± 5.4	29.4 ± 5.1	0.060
Mean systolic BP (mmHg)	125.3 ± 21.0	126.0 ± 12.9	0.846
Mean diastolic BP (mmHg)	80.2 ± 12.0	81.3 ± 8.1	0.578
Gender	No. (%)	No. (%)	---
Male	33 (66.0)	26 (52.0)	0.155

Female	17 (34.0)	24 (48.0)	
Current smokers	12 (24.0)	15 (30.0)	0.499
History of fractures	2 (4.0)	5 (10.0)	0.240

*** Independent T-test of two means was used for quantitative variables and Chi-square test was used for categoral variables, d.f =1.**

The comparison between the HF patients and the control group regarding other medical problems was shown in table (2). The medical problems were (hypertension, myocardial infarction, diabetes mellitus, cerebrovascular accident, and no medical condition). There are more than one medical problems found in the patients but with no significant statistical differences.

Table 2: Comparison in concurrent other medical problems between H.F. patients and control group.

Medical problems*	Cases "Heart failure"		Control "No heart failure"		P-value**
	No.	%	No.	%	
No	12	24.0	12	24.0	1.000
Hypertension	31	62.0	37	74.0	0.198
Myocardial infarction	12	24.0	12	24.0	1.000
DM	5	10.0	5	10.0	1.000
CVA	3	6.0	0	0.0	0.079
Total	**50**	**100.0**	**50**	**100.0**	---

* **More than one concurrent medical problems found in the patients; ** Chi-square test was used, d.f = 1.**

Among both males and females the comparison between cases and controls concerning the osteoporosis showed no significant statistical differences as shown in table (3).

Table 3: The effect of gender on the Relationship between heart failure and osteoporosis.

Gender		Cases "Heart failure"		Control "No heart failure"		P-value*
		No.	%	No.	%	
Male	Osteoporosis ≤ -2.5	10	30.3	4	15.4	0.181
	No osteoporosis >- 2.5	23	69.7	22	84.6	
Total		33	100.0	26	100.0	---
Female	Osteoporosis ≤ -2.5	10	58.8	14	58.3	0.975
	No osteoporosis >- 2.5	7	41.2	10	41.7	
Total		17	100.0	24	100.0	---
* **Chi-square test was used, d.f = 1.**						

Regarding the Relationship between heart failure and osteoporosis in the study sample groups, the P-value of the DEXA study (T-score) between the patient and control group is 0.68, which meant there were non-significant statistical differences. Nevertheless, the number of heart failure patients having osteoporosis is 20 (40%), and the number of control groups is 18(36%), which means that there are differences in percentage between them. As shown in table (4).

Table 4: The Relationship between heart failure and osteoporosis in the study sampled groups.

DEXA results [T-score]	Cases "Heart failure"		Control "No heart failure"		P-value
	No.	%	No.	%	
Osteoporosis ≤ -2.5	20	40.0	18	36.0	0.680*
No osteoporosis > - 2.5	30	60.0	32	64.0	
Total	50	100.0	50	100.0	---
T-score (Mean ± SD)	- 1.1 ± 1.0		- 0.9 ± 1.3		0.776**
* **Chi-square test was used, d.f = 1.; ** Independent T-test of two means was used.**					

The comparison in diastolic function between osteoporotic HF and non-osteoporotic HF shown in table (5). Grade I of osteoporotic heart failure found in 45%, while non-osteoporotic heart failure in 56%, and the percentage of Grade II of osteoporotic heart failure in 30%, while non-osteoporotic heart failure in 33%. Grade III of osteoporotic heart failure in25%, while non-

osteoporotic heart failure in 10%. The difference statistically not significant.

Table 5: Comparison in diastolic function between osteoporotic H.F. and non-osteoporotic H.F.

Diastolic function	Osteoporotic HF		Non-osteoporotic HF		P-value*
	No.	%	No.	%	
Grade I	9	45.0	17	56.3	0.475
Grade II	6	30.0	10	33.7	
Grade III	5	25.0	3	10.0	
Total	20	100.0	30	100.0	---

* **Chi-square test was used.**

The comparison in biochemical parameters between patients and the control group shown in table (6). S. Ca, was lower in cases while B. Urea and S. Creatinine were higher in cases; these differences were statistically significant.

Table 6: Comparison in biochemical parameters between HF patients and control group.

Biochemical Parameters	Cases "Heart failure" [n = 50] Mean ± SD	Control "No heart failure" [n = 50] Mean ± SD	P-value*
FBS (mmol/l)	6.3 ± 2.7	5.6 ± 1.4	0.088
S. Calcium (mmol/l)	1.4 ± 0.6	1.7 ± 0.6	**0.014**
S. Cholesterol (mmol/l)	7.8 ± 3.4	6.9 ± 2.5	0.145
Bl. Urea (mmol/l)	6.5 ± 3.0	5.0 ± 1.4	**0.001**
S. Creatinine (µmol/l)	99.3 ± 43.0	72.5 ± 15.6	**0.001**

*** Independent T-test of two means was used.**

The comparison in biochemical parameters between osteoporotic HF and non-osteoporotic HF showed that there were no statistically significant differences. As shown in table (7).

Table 7: Comparison in biochemical parameters between osteoporotic HF non-osteoporotic HF.

Biochemical parameters	Osteoporotic HF [n = 20] Mean ± SD	Non osteoporotic HF [n = 30] Mean ± SD	P-value*
FBS (mmol/l)	7.1 ± 3.5	5.8 ± 1.8	0.087
S. Calcium (mmol/l)	1.3 ± 0.6	1.5 ± 0.5	0.062
S. Cholesterol (mmol/l)	6.8 ± 2.8	6.9 ± 2.3	0.925
Bl. Urea (mmol/l)	7.2 ± 3.6	6.1 ± 2.5	0.224
S. Creatinine (µmol/l)	111.2 ± 50.6	91.4 ± 35.9	0.113

* **Independent T-test of two means was used.**

DISCUSSION

The present study was performed to find if there is a relationship between heart failure and osteoporosis, and dealt with many risk factors and biochemical parameters.

The study compared heart failure patients with healthy subjects based on personal parameters like age, sex, BMI, blood pressure, smoking history, and fracture history. Results showed that increasing age is a risk factor for heart failure, with the most prominent risk in older age groups. No statistically significant difference was found between case and control subjects. Like in other studies performed, they found that there is age-related heart failure and was most prominent in the older age group.[14] The study found that men have a higher risk of heart failure compared to women, but this difference is statistically non-significant. The difference diminishes with age. The difference is influenced by Y and X chromosomes and sex hormones, with estrogen being a predominant sex hormone in women. According to mean BMI, Obesity is a significant risk factor for heart failure, with a non-significant difference. Another study found a statistically significant association between obesity and cardiovascular disease, particularly heart failure with age.[14]

This study comparing diastolic and systolic blood pressure between heart failure patients and healthy subjects found that most had normal blood pressure due to anti-hypertensive drugs. However, in another study, the increase in systolic blood pressure was a risk factor associated with the incidence of heart failure by increasing age.[14]

Smoking also we were dealing with it, we found that smoking is a risk factor of incidence of heart failure, but

there was a statistically non-significant difference between case and control groups. Other studies found that smoking in the difference of sex in heart failure risk can be larger than estimated because smoking can also decrease HDL cholesterol level.[14]

The study found no significant relationship between fractures with heart failure and those without, and found no significant difference. Other studies associated fracture risk with BMI, age, and postmenopausal women.[15]

In the current study, the medical conditions were compared, especially cardiovascular diseases like hypertension, myocardial infarction, diabetes mellitus and cerebrovascular accident. It was found that these conditions were causes of heart failure, especially hypertension (62%) but statistically non-significant difference. In other studies, they found that hypertension was a defined independent risk factor for coronary heart disease and accounting for about 47% of ischemic events.[15,16] With an increased mass of left ventricle and diastolic dysfunction, these typical signs in echo study indicating the co-existence of both heart failure and hypertensive heart disease.[16] In concern with myocardial infarction concerning with heart failure, studies have reported that the rate of symptoms and signs of heart failure after myocardial infarction is about 25%, and it is a widespread event after myocardial infarction.[17]

According to diabetes mellitus with heart failure, it was found also, there was no relation statistically, but it remains as a cause of heart failure. Other studies found a relation between the two conditions, and there was a statistically significant difference, and the pathophysiology of heart failure in diabetes mellitus was complex. A cardiovascular complication of diabetes mellitus was represented and significantly contributed to morbidity and mortality.[18]

In concern to the relation of heart failure with a cerebrovascular accident, also, there was a statistically non-significant difference. In other studies, heart failure was an independent marker of unfavorable functional long-term outcome, while the efficacy and safety of mechanical recanalization and thrombolysis appeared unaffected.[19]

In this study, the effect of gender on the relationship between heart failure and osteoporosis was studied. There was a difference in percentage between the osteoporotic male having heart failure, which was about 30% and non-osteoporotic male having heart failure, which was about 69%, while male patients with osteoporosis but no heart failure, which was about 15% and male with osteoporosis but no heart failure which was about 84%. However, there was a statistically non-significant difference. Furthermore, in the female gender, the osteoporotic female with heart failure was about 58% in comparison with a non-osteoporotic female about 41%, while the osteoporotic female without heart failure was about 58% in comparison with non-osteoporotic female was about 41%, this indicates that female gender was a risk factor both osteoporosis and heart failure, but statistically non-significant difference. In other research, about 63% of females have heart failure with osteoporosis, which is significantly higher than that in males because of the prevalence of hypertension and hyperlipidemia in osteoporotic female.[20]

The percentage of patients with heart failure having osteoporosis in the present study was 40%, while the control group is 36%, which means there was a percentage difference but a statistically non-significant difference. Other studies found a borderline statistical difference in the relationship between heart failure and osteoporosis, however, heart failure increases the burden of osteoporosis and osteoporotic fracture. This mean that cardiovascular risk factors like endothelial dysfunction and vascular calcification and inflammation, were associated with low bone mineral density.[21,22] Others reported that the cardiovascular events increased in osteoporotic patients.[23,24]

Dealing with diastolic dysfunction in relation to osteoporosis, the present study found that the percentage of osteoporotic patients having heart failure was increased above the non- osteoporotic heart failure patients, percentage of Grade III of osteoporotic heart failure is 25%, while of non-osteoporotic heart failure was 10%. In other studies, the diastolic dysfunction was present in 21% of the normal bone mineral density group and in 46% of osteoporotic patients; these results revealed that the prevalence of diastolic dysfunction increased as bone mineral density reduced.[25] Also the comparison between heart failure patients and apparently healthy subjects was studied in concern with biochemical parameters and found that there was a statistically non-significant difference in the biochemical parameters (FBS, S. cholesterol, S. calcium), but in concern with B. urea and S. creatinine, there was a statistically significant difference. In other studies found that the relationship between heart failure and glucose was not limited to diabetic patients; also, the degree of hyperglycemia (measured either by plasma level of glucose or HbA1c) seems to be related progressively to the risk for new or recurrent cardiovascular events.[26] While in concern with S. cholesterol level, studies appeared that cholesterol could have a deleterious effect in heart failure, and it was a marker of increased morbidity and mortality.[27,28]

The occurrence of heart failure can be reduced by long-term treatment with anti-lipid drugs.[29] The lipid-lowering agents also enhance the mineralization of bone in patients and can reduce osteoporotic fractures. These effects on bone were attributed to a specific class used, HMG-CoA reductase inhibitors (statin) because it strongly induces lipid clearance. Therefore, it was not possible to know whether the improvement in bone

mineral density was due to the lowering of the lipid or to the direct effect of statins.

In concern with renal function test (B. urea, S. creatinine), other studies concluded that the worsening in renal function in the case of both acute and chronic heart failure was recognized increasingly as an independent predictor of a poor prognosis.[30]

This study found that there is no relationship between the biochemical parameters in osteoporotic heart failure and non-osteoporotic heart failure because of a statistically non-significant difference. In other studies, they could not find any correlation between the calcium concentration and bone mineral density levels, but there was an association between calcium concentrations when patients with clinical conditions of osteoporosis based on bone mineral density assessment. So they showed that patients with elevated calcium concentrations had osteoporosis significantly more than controls with normal calcium concentration (45% vs 29%).[31] In concern with the relationship between the glucose level and osteoporosis, they found that diabetes mellitus is protective, which means that the bone mineral study was higher in diabetic patients than in non-diabetic patients because they found that the insulin resistance and hyper-insulinemia can increase bone mineral density mass. Insulin is an anabolic hormone that increases bone mass through the formation of bone by insulin receptor substrate 1 and 2 on osteoblasts and by sex hormone-binding globulin concentration lowering, which result in increased concentration of testosterone and estradiol.[32]

In concern with the Relationship between S. cholesterol and osteoporosis, many studies showed a negative association between them. Cholesterol and bone mineral density.[33,36] Other studies found no or positive association between bone mineral density and s. cholesterol.[37,38] This indicates an inconsistent relationship between bone mineral density and s. cholesterol.[37,39] The several clinical trials (not in all) found that the use of statin has been associated with a decrease in osteoporosis and osteoporotic fracture.[40,41]

In concern with the Relationship between renal function and bone mineral density, the studies found that the correlation between them after adjustment of age and BMI, negative correlation with lumbar bone mineral density and positive correlation with femur bone mineral density. Generally, it was known that reduced renal function was associated with reduced bone mineral density. Decreasing glomerular filtration rate was associated with increased fibroblast growth factor 23 signaling and parathyroid hormone secretion, which leads to vitamin D synthesis reduction and then associated with bone loss.

CONCLUSION

Finely we notice no direct relationship between heart failure and osteoporosis and osteoporotic fracture, but they share the risk factors, especially age and gender.

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