Case Study
JOURNAL OF UNIVERSITY OF BABYLON
For Pure and Applied Sciences (JUBPAS)
Vol.32; No.3.| 2024

ISSN: 2312-8135 | Print ISSN: 1992-0652

مجلة جامعة بابل للعلوم الصرفة والتطبيقية مجلة جامعة بابل للعلوم الصرفة والتطبيقية

Assessment of Bone Mineral Density in Chronic Obstructive Pulmonary Disease Patients

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تقييم كثافة المادة العظمية لدى المرضى المصابين بأمراض الرئة الانسدادية المزمنة

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Accepted: 5/6 /2024 **Published:** 30/9/2024

ABSTRACT

Background:

Main co-morbidities of chronic obstructive pulmonary disease that restricts physical exercise is osteoporosis. In this study we assess chronic obstructive pulmonary disease patients for osteoporosis, osteopenia and determine correlation of body mass index, number of pack years, severity of chronic obstructive pulmonary disease with bone mineral density

Method and patients:

This cross-sectional study was carried out on 61 chronic obstructive pulmonary disease patients.. Dual energy x-ray absorptiometry was used to evaluate the bone mineral densities at lumbar spine. According to WHO guidelines, patients with a T score greater than -1 were classified as having normal bone density, those with a T score of (-1)to (-2) as having osteopenia, and those with a T score of less than -2.5 as having osteoporotic bone density.

Results:

Sixty - one chronic obstructive pulmonary disease patients were included in this study, 11 patients (18%) had normal bone mineral density, fifty patients had abnormal bone mineral density .Also thirty - two patients had osteoporosis(52.5%) and 18 (29.5%) had osteopenia. .BMD correlated directly with BMI (P value=0.009) and inversely with number of pack years (P = 0.000), ,BMD correlated inversely with severity of COPD (P = 0.001) .

Conclusion:

Patients with chronic obstructive lung disease had a higher chance of osteoporotic fractures and decreased bone mineral density.A lower BMI, more pack years, and a rise in the severity of the condition raised chance of osteoporosis..

Key words:

Chronic obstructive pulmonary disease(COPD) ; Bone Mineral Density(BMD) ;osteoporosis; dual energy x-ray absorptiometry (DEXA);Body mass index (BMI).

Abbreviations:

COPD: Chronic obstructive pulmonary disease, BMD: Bone mineral density, BMI: Body mass index, DEXA: Dual energy x-ray absorptiometry, FEV1: Forced expiratory volume for 1 second, FVC: Forced vital capacity, SD: Standard deviation, WHO: World health organization, TNF: Tumor necrosis factor, GOLD: Global dissociative for Chronic obstructive pulmonary disease.

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INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) is a chronic, inflammatory disease characterized by progressive and irreversible airway restriction. COPD is associated with various systemic comorbidities, including osteoporosis, ischemic heart disease, sarcopenia, and anxiety/depression [1] .

COPD comprises emphysema, which is defined anatomically as a condition characterized by destruction and enlargement of alveoli and Chronic bronchitis is defined as the presence of cough and sputum production for the majority of days over three months for two consecutive years and small airways disease, a condition in which small bronchioles are narrowed[2].

The prevalence of tobacco usage and the use of biomass fuels in low- and middle-income countries are directly correlated with the prevalence of COPD. Because of their rising tobacco use, Asian and African nations will see the biggest increases in COPD-related morbidity and mortality .The most important risk factor is cigarette smoking, and both the quantity and duration of smoking are associated with an increased risk of COPD. Not all smokers acquire COPD, and developing the illness with fewer than 10 pack years is uncommon, indicating the significance of individual susceptibility factors, Additional risk factors for COPD include HIV infection was associated with emphysema, occupational exposures to silica, coal dust, and cadmium, Low socioeconomic status, Genetic variables as α1-antiproteinase deficiency, Airway hyper-reactivity . Any patient over 40 years of age who exhibits signs of dyspnea or chronic bronchitis should be suspected of having COPD [3].

The three most typical signs of COPD are exertional dyspnea, sputum production, and cough. Many people wait months or even years to seek medical care despite experiencing symptoms. Even though airflow restriction develops gradually, the majority of patients attribute the start of their condition to an acute sickness or exacerbation. [2].

Spirometry is required to rule out other differential diagnoses that may present with similar spirometric patterns, such as severe asthma, bronchiectasis, and obliterative bronchiolitis, and to make a confident diagnosis of irreversible Airways obstruction (post bronchodilator FEV1/FVC≤0.7, per GOLD guidelines). It is also necessary to evaluate the severity of the condition based on the expected post-bronchodilator FEV1%.Classification of airflow limitation severity in COPD (based on post bronchodilator FEV1 %):

GOLD 1Mild COPD: post bronchodilator FEV1/FVC<70%, FEV1 ≥ 80% predicted

GOLD2 Moderate COPD: post-bronchodilator FEV1/FVC< 70% , FEV1 50% -80% predicted.

GOLD3 Severe COPD:post bronchodilator FEV1/FVC< 70% FEV1 of 30%–50% .predicted

GOLD 4: Severe COPD:post bronchodilator FEV1/FVC < 70%, FEV1 < 30% predicted.

Cachexia, skeletal muscle abnormalities, osteoporosis, coronary artery disease, heart failure, pulmonary vascular disease, pulmonary infections, metabolic syndrome, and cancer are the most significant co-morbidities that contribute to the natural history of COPD [4].

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When osteoporosis is not exacerbated by fractures, it is a quiet illness. Individuals who suffer from osteoporosis are particularly vulnerable to fragility fractures. The injury that causes fragility fractures is too small to shatter a regular bone[5]. osteoporosis affects both the microarchitecture and bone mass. BMD measurements are used to measure bone mass. In contrast, the assessment of bone microarchitecture only through bone biopsy which is not a common practice in developing countries. The gold standard for diagnosing osteoporosis is the dual-energy X-ray absorptiometry (DEXA) scan, which measures BMD [6]. It can also be used to monitor how well a treatment is working. BMD is expressed as the Z, T, and SD of means. The difference in the number of standard deviations between the patient's mean BMD value and the mean BMD of a young, sex-matched adult control group is known as the T-score. However, the Z-score is the difference in the number of standard deviations between the patient's mean BMD value and the mean BMD of a reference group that is age, sex, and race-matched [7] . Fracture risk increases 1.5–3 times for every 1 SD decrease in BMD [8] .

The International Society for Clinical Densitometry recommends measuring BMD in the hip and lumbar spine and using the lowest T-score of the tested areas to diagnose osteoporosis [9] . lumber spine is preferred for Early identification as it contain high significant amount of trabecular bone. Patients who are extremely obese, have significant degenerative disease, require extensive surgical equipment, or whose BMD of the hip or spine is not measurable or interpretable, should have their forearm BMD tested [10] . When combined with other technologies like calcaneal ultrasound, peripheral DEXA, quantitative computed tomography, single or dual-photon radionuclide absorptiometry, or magnetic resonance imaging, dual-energy x-ray absorptiometry measurements of bone mineral density (BMD) at sites like trochanter, lateral lumbar spine, other forearm regions, heel, or entire body may be helpful in assessing fracture risk, but they are not advised for use in diagnosing osteoporosis[11].

Numerous risk factors, such as aging, smoking, physical inactivity, systemic inflammation, malnutrition, low body-mass index (BMI), hypogonadism, vitamin D insufficiency, and frequent corticosteroid use, contribute to the occurrence of osteoporosis in COPD patients [12,13] Compared to healthy persons, patients with COPD are more likely to develop osteoporosis, and bone loss happens gradually over years [14]. The effects of osteoporosis and fractures caused by osteoporosis on COPD patients are profound. The most frequent kind of fracture caused by osteoporosis is a vertebral compression fracture [15]. vertebral compression fractures are linked to kyphosis and back discomfort. Loss of height due to kyphosis might affect lung function [16] .

Vital capacity is reduced by 9% for each VCF, with the greatest harm to lung function occurring at kyphotic angles greater than 55°.Those with COPD who already have low lung reserve would be especially affected by the decline in lung function [17]. Patients with COPD may experience exacerbations of rib fractures as a result of hypoventilation brought on by chest discomfort and a diminished capacity for expectoration. Additionally, osteoporotic fractures in COPD patients might make them less mobile and increase their risk of pulmonary embolism and deep vein thrombosis (DVT)[16] . Therefore Osteoporosis is recognized as a major comorbidity

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of chronic obstructive pulmonary disease (COPD), should be diagnosed by appropriate methods and properly treated [18].

MATERIALS AND METHOD:

Study design, setting and timing:

Cross sectional study was conducted on 61 COPD patients including patients of respiratory consultant clinic and patients who were admitted in the respiratory ward at 9th floor of Baghdad teaching hospital from october2016 to July of 2017 .

The study included all individuals who diagnosed as COPD was proved by clinical examination and subsequent spirometry in accordance with GOLD guideline.

Exclusion criteria:

Patients with underlying pulmonary diseases such as broncheictasis and asthma ,tuberculosis, so as to patients on long term oral steroid or with co morbidities such as chronic liver disease congestive heart failure, bronchogenic carcinoma ,rheumatic disease, thyroid dysfunction or other endocrine disorders.

Sampling and patients:

Data Collection: -

After taking permission from all patients ,detailed history regarding (Age , sex, Residence, marital status, occupational state and smoking state ((current, x Smoker, passive smoking)), number of cigarettes per day then pack/ year was calculated for every patient (number of cigarettes per day was multiplied by their number of smoking years , and the result was divided by 20), duration of smoking, age of starting smoking, and duration of quitting in ex-smokers) past medical Diseases, then clinical examination followed by spirometery .Reversibility was performed after 20 minutes following the administration of Salbutamol (5mg) nebulisation for all patients to exclude asthma .

The diagnosis of COPD confirmed with post bronchodilator FEV1/FVC <70% and staging according FEV1 values .Bone mineral density assessed by DEXA (dual energy X ray absorptiometry), using osteosys,B2R10911p12, DEXUM32011,korea, which is the gold standard for diagnosis of osteoporosis. Patients with T scores greater than(-1)were classified as normal bone density, those with T scores between(-1)and (-2) as having osteopenia, and those with T scores less than -2.5 as having osteoporotic bone density, according to WHO guidelines [8] .

Body mass index was measured by dividing weight over squared height . copd patients were classified into underweight with a BMI of less than 18.5, a normal BMI of 18.5–24.9, an overweight BMI of 25–29.9, and when obese BMI of ≥30.

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STATISTICAL ANALYSIS:

Descriptive statistics including mean and standard deviation were used to summarize the baseline characteristics of the patients .us Pearson's Chi Square test to assess the difference in BMD score according to illness, body mass index, gender and smoking status and pack year .

RESULTS AND DISCUSSION

This study sample were 61 patients. Most of the them were males (54) ,the females were (7) . All of the patients had positive smoking history (current 33 , reformed 28).Mean age of the male patients was 60.7 years and that of female patients was 61.2 years.

Table (1) Descriptive Statistics

	No.	*Minimum*	*Maximum*	*Mean*	*Std. Deviation*
Age	***61***	***43.00***	***82.00***	***60.8032***	***10.06083***
Pack year	***61***	***15.00***	***100.00***	***54.3934***	***25.88647***
Valid N (list wise)	***61***				

Table(2) mean age of our patients sample

AGE	NUMBER	PERCENTAGE
40-49	**5**	**8.10%**
50-59	**21**	**34.40%**
60-69	**20**	**32.70%**
70-79	**14**	**22.90%**
>80	**1**	**1.63%**
TOTAL	**61**	**100%**

Based on FEV1 values 26(42.6%) of patients had moderate obstruction,17(27.9%) of patients had severe obstruction while 18(29.5) had very severe obstruction. There is patients with mild obstruction (figure 1). 32.8% of the patients were underweight (BMI <18.5) as in (table 3).

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Table 3 BMI of COPD patients

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	<18.5	20	20.6	32.8	32.8
	18.5-24.9	24	24.7	39.3	72.1
	25-29.9	10	10.3	16.4	88.5
	30-34.9	7	7.2	11.5	100.0
	Total	61	62.9	100.0	

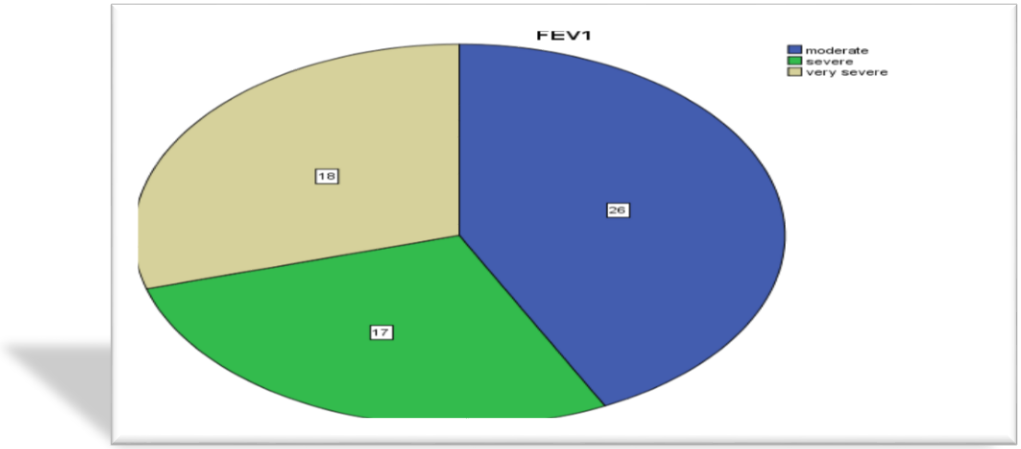

Figure (1) Distribution of COPD severity among sample.

Overall, fifty patients included individuals with abnormal BMD, of whom 32 (52.5%) had osteoporosis and 18 (29.5%) had osteopenia. while only 11(18%) patients had normal BMD figure 2.

Six patients (19%) had moderate obstruction, 10 patients (31%) had severe obstruction, and 16 patients (50%) had very severe obstruction among the osteoporotic patients. Twelve (67%), five (27.4 %), and one (5.6%) of the osteopenic patients had moderate obstruction, very severe obstruction, and very severe obstruction, respectively.

Of the 11 individuals with normal BMD values, 2 (18.18%) had very severe obstruction, 1 (9.09%) had very severe obstruction, and 8 (72.7%) had moderate obstruction. Among the various stages of COPD, BMD revealed a significant difference (P = 0.001) [fig3]. The BMD dropped as the COPD stage became more severe.

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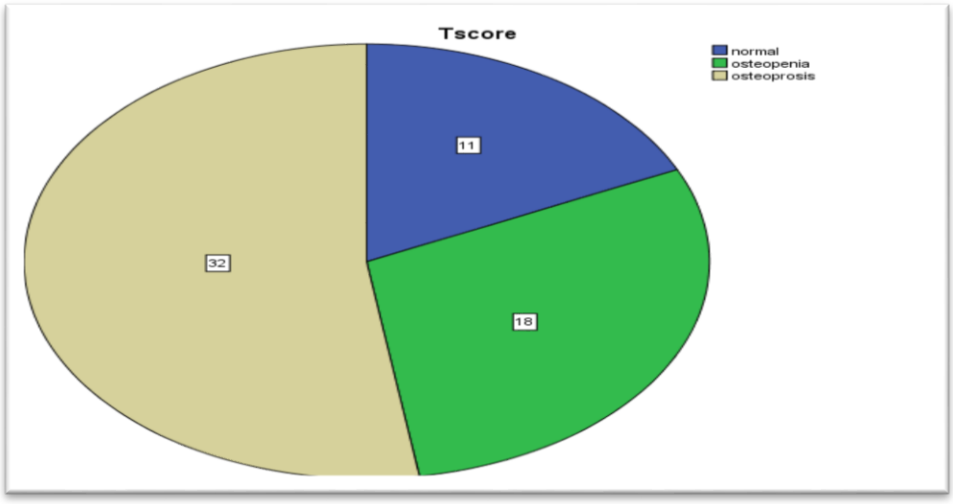

Figure 2 Bone mineral distribution among sample

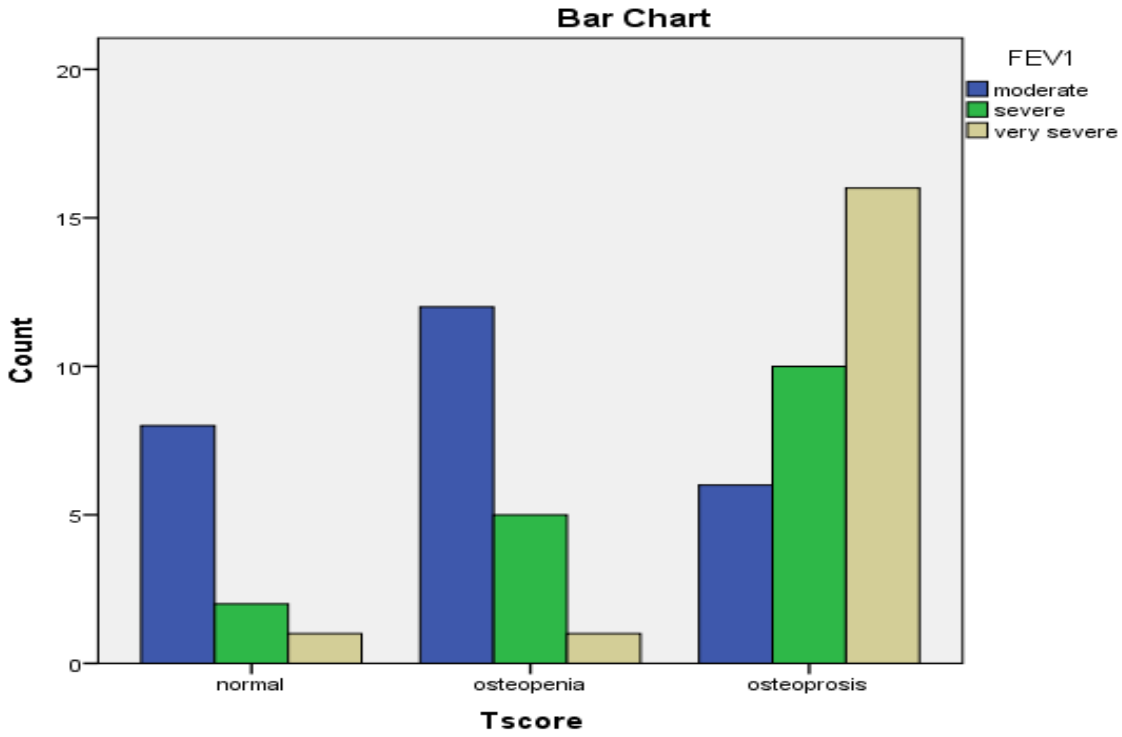

Fig 3 T score and FEV1 (P value =0.001)

Osteoporosis was shown to be more common in people with low BMI (46.8%) than in overweight persons (15.6%). while 6.25 percent of people are obese. There was statistical significance in this connection. (P value0 =.009) [fig 4].

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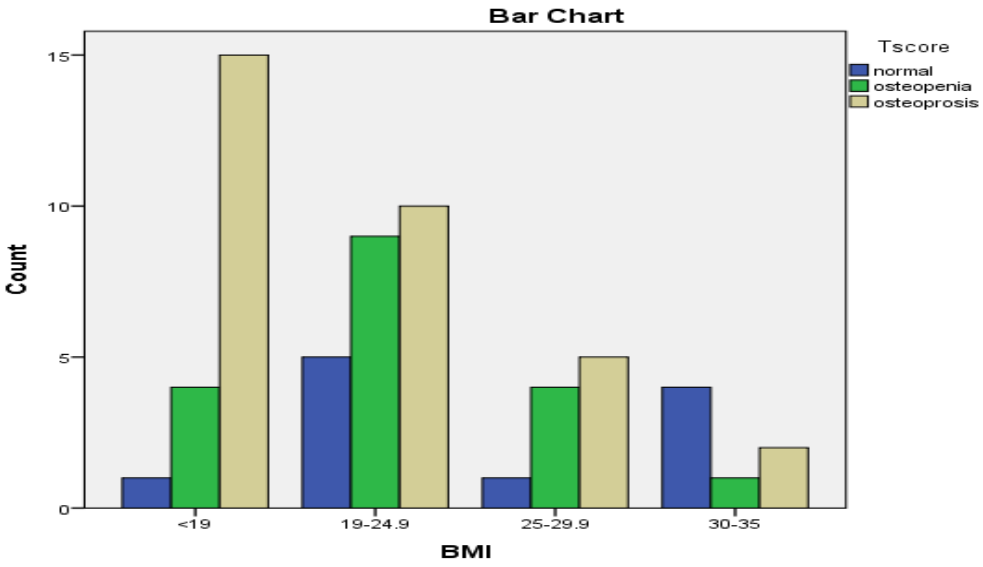

Fig 4 T score and BMI (P value =0.009)

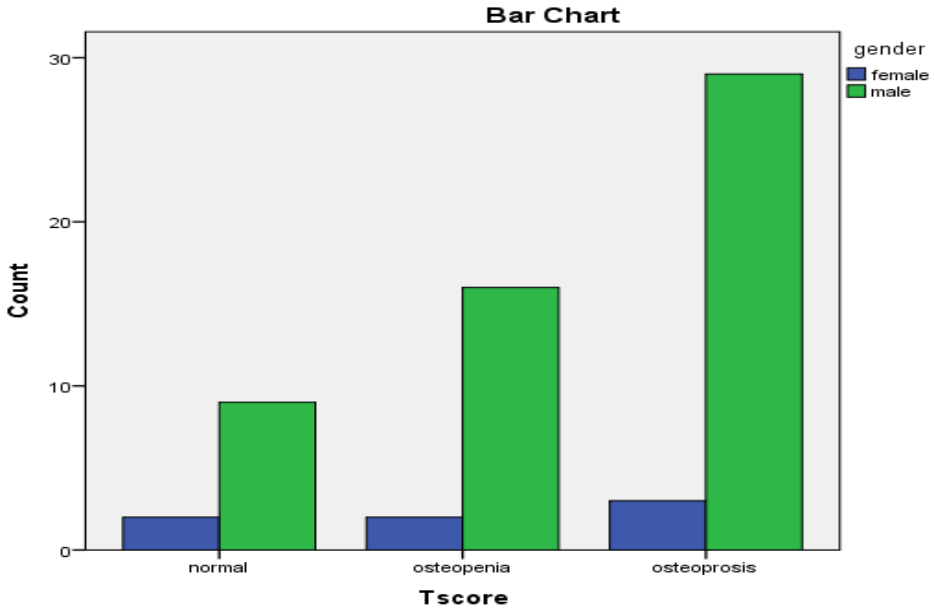

Fig 5 T score and gender (P value =0.75)

Only three female patients exhibited osteopenia and two patient had osteoporosis (Fig 5) .Smoking status was found to have no association with BMD score (P value =0.9)

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(Fig6),while the amount of smoking(pack year) had strong significant Association(inversely related) with BMD score (p value= 0.000).

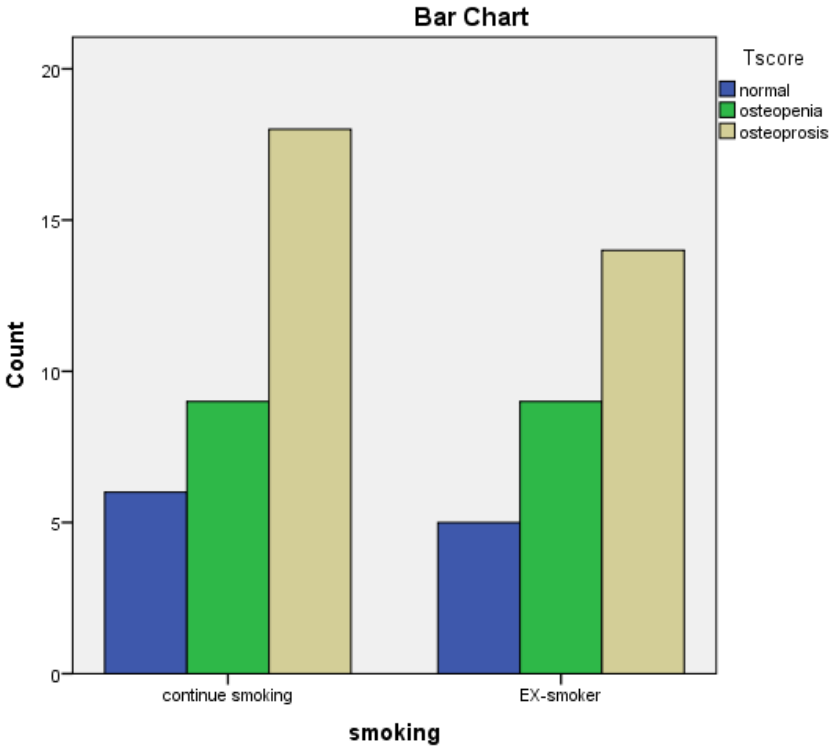

Fig 6 T score and smoking status(P value =0.9)

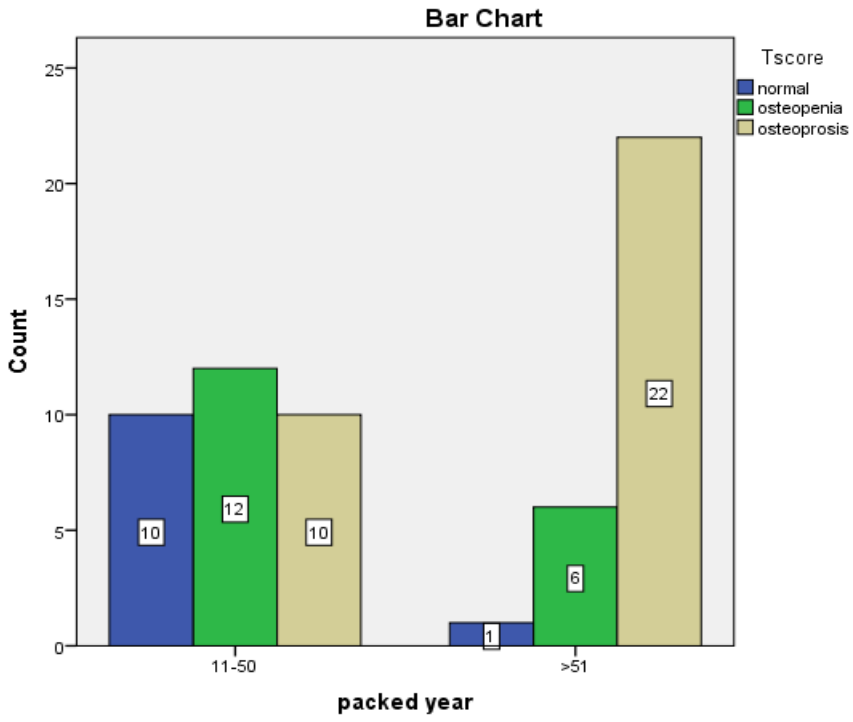

Fig 7 T score and pack year (P value =0.000)

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This study shows **81.5**% of patients had abnormal bone mineral density ,**52.5%** had osteoporosis, **29.5%** had osteopenia. In a comprehensive evaluation of 13 studies involving 775 people with COPD revealed a prevalence of osteoporosis of 35.1 (9-69%) and osteopenia of 38.4% (range 27-67%) [14]. Another study found that 30% of people had osteopenia and 50% of people had osteoporosis [19]. A prevalence of osteoporosis and osteopenia was 52.8%,31.5 in other study [20]. And the prevalence of osteoporosis was 66.6% and of osteopenia 19.6% [21]. Cross sectional study of clinical stable 95 COPD patients reported that the prevalence of osteoporosis and osteopenia measured by DEXA scan each in 42% of patients[22] . In a study of a small number of advanced COPD patients(37 Indian COPD patients) found Osteoporosis prevalence was 21.6 and osteopenia prevalence was 27% [23].However, he did not employ the gold standard DEXA scan for osteoporosis diagnosis; instead, he used ultrasound densometry. Another limitation of his study was that he only measured one heel.Variations in osteoporosis prevalence across studies may be caused by methodological variations in BMD assessment as well as patient population characteristics (age, sex, history of bone medication use, GOLD stages, stable COPD patients, physical activity, genetic susceptibility to osteoporosis) selected for the study.

The prevalence of osteoporosis varied between moderate, severe, and very severe obstruction(19%, 31%, and 50%), as demonstrated by this study. This suggests a strong positive link between BMD scores and severity (FEV1 values; p=0.001). Since our study was hospital-based and patients with mild obstruction with mild obstruction may be asymptomatic or have mild symptoms might not need hospital care, we did not include them in our analysis. A similar findings of increased risk of osteoporosis in severe air flow obstruction was observed [24]. another study observed the risk of osteoporosis and bone fractures in COPD patients increased with more severe obstruction when compared with non COPD patients, he reported a high prevalence of osteoporosis in stage III and stage IV COPD disease when compared to stage I and stage II COPD [25] .

In healthy people, a low body mass index is an established risk factor for osteoporosis [26,27,28] . Fractures were becoming more common in those with BMIs under 25.For each standard deviation fall in BMI, the age-adjusted risk of fractures increased by 18% [29] . Low BMI is common in COPD patients [30]. The dangers of a low body mass index was higher with advance COPD this may be due to systemic inflammation and release of proinflamatory TNF-α and other cytokines in COPD lead to malnourishment and malfunctioning of the peripheral muscles [31] . Studies revealed that, in comparison to weight-stable COPD patients and normal individuals, peripheral blood monocytes in COPD patients experiencing weight loss produced higher levels of serum TNF-α and lipopolysaccharide-stimulated TNF-α. TNF-α is a well-known strong inhibitor of collagen synthesis and an osteoclastic bone resorption stimulant, suggesting that patients with COPD experience weight loss and bone loss due to systemic inflammatory response and increased TNF-α production [32]. weight

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loss in COPD occur with more advance stages because of decrease intake and increase energy requirement. in addition to that persons with high BMI had protection against osteoporosis due to weight bearing load effect and effect of higher estrogen level [26]. Owing to increased testosterone aromatization to estradiol in adipose tissue, obese people have higher bone mineral density [33] . this explain what we found in our study of higher prevalence of osteoporosis in low BMI individuals (46.8%) as compared to overweight 15.6% while in obese individuals the prevalence was only (6.25%),this indicating appositive correlation between BMI and bone mineral density and this association was statistically significant (P value =0.009).Many studies showing that majority of COPD patients with low body mass index had low bone mineral density [34,35]. High frequency of 50% osteopenia and 50% osteoporosis in patients with cachectic COPD was observed [36] .

All patients in the current study had a positive smoking history, and we discovered a strong inverse relationship (p value 0.000) between BMD scores and the number of pack years patients with osteoporosis had more pack years fig. 7.

The reference showed that smoking had a cumulative dose-dependent effect and was an independent risk factor for low bone mineral density [37] .Numerous studies revealed that smokers had a higher rate of bone loss [31,33,38,39] . And increased hip and vertebral fractures risk in smoker [40] .The mechanism of bone loss in smokers consisting of changed adrenal cortical hormone metabolism, dysregulation of synthesis and estradiol binding, altered calcitrophic hormone metabolism, impact on collagen metabolism, and bone angiogenesis . It was observed decrease absorption of calcium in gastrointestinal tract in smokers compared to nonsmoker [41]. Female gender is recognized risk factors for osteoporosis and fractures [42] .in our study 90.6 of osteoporotic patient was male and only 9.3 % was female (p value =0.75) this is due to small female sample in our study (only seven females were included ,three were osteoporosis ,two were osteopenia and two was normal) .

CONCLUSION

This study demonstrated that low bone mineral density is common in COPD patient and this risk increase with increased severity of disease and smoking amount (pack year), and with decreasing body mass index.

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Conflict of interests

There are non-conflicts of interest

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ISSN: 2312-8135 | Print ISSN: 1992-0652
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الخلاصة

المقدمة: هشاشة العظام من الامراض المصاحبة لمرض الانسداد الرئوي المزمن التي تحد من النشاط البدني للجسم. لدراسة حدوث قلة كثافة العظام (الهشاشة والليونة) لدى مرضى الانسداد الرئوي المزمن وتحديد العلاقة بين كثافة العظام مع شدة الانسداد ومع مؤشر كتلة الجسم.

طريقة العمل: تم اجراء دراسة مقطعية تتضمن 61 مريضا يعانون من مرض انسداد الرئوي المزمن، تم قياس كثافة العظام بواسطة الامتصاص ثنائي الطاقة لاشعة اكس، وتم: تصنيف المرضى حسب معايير منظمة الصحة العالمية لتعريف هشاشة العظام حسب الدرجة (ت) اذا كانت اكثر من (−1) يعتبر طبيعي اما اذا كانت بين (−1) الى (−2) فيعتبر لدية قلة في كثافة العظم, اما اذا كانت اقل من −5.2 يعتبر لدية هشاشة عظام .

النتائج: تكونت عينة الدراسة من (61) مريضا؛ (50) مريضا منهم كانت كثافة عظامهم غير طبيعية من بينهم (32) مريضا كان لديهم هشاشة بالعظام، (18) لدية قلة كثافة العظام. بينما(10) فقط كثافة عظامهم طبيعية .

كما لوحظ ان مستوى كثافة العظام كانت تتناسب عكسيا مع شدة الانسداد لمرض الانسداد الرئوي المزمن ومع عدد السنوات وكمية التدخين وطرديا مع مؤشر كتلة الجسم (BMI).

الاستنتاج: ان مرضى الانسداد الرئوي المزمن هم اكثر عرضة لخطر الاصابة بنقص كثافة العظام وماتتبعها من مضاعفات الكسور الناتجة من هشاشه العظام. كذلك استنتجت الدراسة انه كلما زادت شدة الانسداد لمرض الانسداد الرئوي المزمن وكلما زادت عدد السنوات وكمية التدخين تقل كثافة العظام ويزداد خطر الهشاشة كما ثبت من خلال الدراسة ايضا بانخفاض مؤشر كتلة الجسم يزيد من خطر الهشاشة.

الكلمات المفتاحية: الانسداد الرئوي المزمن, كثافة العظام,هشاشة العظام , الامتصاص ثنائي الطاقة لاشعة اكس. مؤشر كتلة الجسم .