Original Article

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Osteoporosis and Correlates in Chronic Obstructive Pulmonary Disease

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ABSTRACT

Introduction: Osteoporosis is one of the extra-pulmonary effects of chronic obstructive pulmonary disease (COPD). Osteoporosis is characterized by low bone mineral density (BMD) resulting in an increased risk of fracture thereby causing significant morbidity and mortality. The aim of the study was to determine prevalence of osteoporosis among stable COPD patients and association between bone mineral density with severity of COPD and body mass index.

Methodology: A total of 100 stable new COPD patients were recruited in this study. Diagnosis and severity grading of COPD patients were made according to the GOLD guidelines. Height and weight were measured and body mass index (BMI) was calculated. Bone mineral density (BMD) was performed using dual energy X-ray absorptiometry (DEXA). BMD was expressed in g/cm^2 and standardized T-score and Z-score.

Results: The increase of COPD severity correlates with the decrease of average values of BMD (lumbar spine: 0.769±0.21 g/cm^2, p=0.012, femoral neck: 0.698±0.12 g/cm^2, p=0.013) as well as T-score (lumbar spine: -2.81± 1.96, p=0.005, femoral neck: -2.09±0.92, p=0.022) and Z-score. Also, the decrease of BMI correlates with the decrease of average values of BMD (lumbar spine p=0.019, femoral neck p=0.0004), T-score (lumbar spine p=0.013, femoral neck p=0.008) and Z-score and increase of total osteoporosis.

Conclusion: Patients with severe COPD and lower BMI have reported low values of BMD parameters (i.e. T-score and Z-score). Therefore it can be concluded that measurement of BMD parameters cannot be ignored in patient with COPD. Detection of osteoporosis and osteopenia and its correction can be used as effective tool in pulmonary rehabilitation program for better management of COPD patients.

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is associated with significant concomitant comorbidities, which increase its morbidity and mortality.[1] Osteoporosis is one of the major comorbidity in COPD which is often under-diagnosed and associated with poor health status and prognosis.[1] The prevalence of osteoporosis depends on the patients under study, the method used to assess bone mineral density, and definition used to define osteoporosis.

World Health Organization (WHO) definition for osteoporosis is based on the measurement of bone mineral density (BMD).[2] Dual energy X-ray absorptiometry (DEXA) is currently the "gold standard" and the most frequently used method of BMD measurement. BMD is expressed as standard deviation of means, T and Z scores. The T-score is a standard deviation (SD) compared to a young adult sex matched control population. The Z-score is a standard deviation compared to an age and sex matched control population. Osteopenia is defined as BMD between -1 and -2.5 standard deviations (SDs) below the mean for young adults (i.e. the T score), while osteoporosis is defined as a BMD of -2.5 SDs below the mean for young adults.[3] Potential risk factors for osteoporosis may be life style, genetics, treatment with corticosteroids, endocrine abnormalities, or impairment of the body composition and peripheral skeletal muscles.

Fractures of the hip, vertebrae, and forearm are the most common fractures in patients with osteoporosis, although fractures of other body parts can also be the result of osteoporosis. The most common type of osteoporosis induced fracture is the vertebral compression fractures (VCFs).[4] VCFs are associated with back pain and kyphosis. Kyphosis can cause loss of height, resulting in

impaired lung function.[5] Every single VCF decreases the vital capacity by 9%, and the lung function impairment is most notable when kyphotic angle is more than 55°.[6] The impact of reduced lung function would be more pronounced in COPD patients with already poor lung reserve.

Osteoporosis deserves special attention in COPD patients, as it is a secondary development that appears as a result of systemic inflammatory process, metabolic disorders, long term hypoxia arising on the background of respiratory failure, decreased physical activity and is systemic in its nature.[7,8] In COPD, the prevalence of osteoporosis is assumed to be two to five fold higher than in age-matched subjects without airflow obstruction.[9,10] The aim of the study was to find out prevalence of osteoporosis in stable COPD patients as well as to determine the association of bone mineral density (based on DEXA) with severity of COPD and body mass index.

METHODS

The present study was a descriptive type of observational study. 100 stable new COPD patients were recruited at the Institute of Respiratory Diseases, in a Government Medical College in Jaipur, Rajasthan. Diagnosis and grading of COPD was made according to the GOLD 2016 guidelines. Lung function parameters were assessed using the RMS (Helios 401, India) Pc based spirometer. Post bronchodilatation (after administration of 400 µg salbutamol) forced expiratory volume in the first second (FEV1) and forced vital capacity (FVC) were measured, and FEV1/FVC was calculated. All included patients had a FEV1/ FVC of <0.70. According to the GOLD 2016 guidelines, patients with a FEV1 ≥ 80% of predicted were classified as GOLD I (mild), patients with a FEV1 between 50% and 80% of predicted were classified as GOLD II (moderate), patients with a FEV1 between 30% and 50% were classified as GOLD III (severe), and patients with a FEV1<30% were classified as GOLD IV(very severe).[1] Height and weight were measured and body mass index (BMI) was calculated and defined as low (≤ 20 kg/m^2), normal (20–24.9 kg/m^2), overweight (25–29.9 kg/m^2), and obese (≥ 30 kg/m^2).

BMD parameters were performed using Lunar Explorer (S/N 91395) bone densitometer manufactured by Hologic, Inc. of Germany. BMD was measured at the lumbar spine (vertebrae L2, L4) and at the femoral neck. BMD was expressed in standard globally accepted term (g/cm^2), and as T-score. According to WHO, T-score values between -1.0 and -2.5 are definable for osteopenia, T-scores below -2.5 are definable for osteoporosis and T-score above -1 definable as normal bone mass.[2] All statistical analyses were performed using the statistical software R version 3.4.1. Student t test was used to compare a continuous variable between two study groups. Chi square test was used to compare categorical responses between two (or more) independent groups. Linear regression analysis statistical test was used to find out association between different parameters (i.e. BMD, T-score, severity of COPD and BMI) of this study population. A significance level of $p < 0.05$ was used.

Table 1: Regression analysis of bone mineral density (BMD) parameters and severity of COPD

BMD Parameters	Mild Mean±SD (n=5)	Moderate Mean±SD (n=11)	Severe Mean±SD (n=43)	Very Severe Mean±SD (n=41)	Linear Regression Analysis	
					F	P
BMD femoral neck (g/cm^2)	0.687±0.073	0.689±0.113	0.679±0.139	0.596±0.105	6.36	0.0133
T-score femoral neck	-1.700±0.620	-1.718±0.829	-1.653±1.275	-2.456±0.801	5.35	0.0229
BMD lumbar spine (g/cm^2)	0.862±0.363	0.863±0.182	0.79±0.231	0.741±0.171	6.48	0.0125
T-score lumbar spine	-2±3.233	-1.79±1.558	-2.572±2.091	-3.119±1.48	8.22	0.0051

Table 2: Correlation among body mass index (BMI) and bone mineral density (BMD) parameters at femoral neck and lumbar spine

BMD Parameters	BMI Low Mean±SD	Normal Mean±SD	Obese Mean±SD	Overweight Mean±SD	Linear Regression Analysis F	p
BMD femoral neck (g/cm^2)	0.623±0.125	0.693±0.108	0.707±0	0.836±0.115	13.58	0.0004
T-score femoral neck	-2.147±1.132	-1.707±0.813	-1.6±0	-0.35±1.344	7.26	0.0083
BMD lumbar spine (g/cm^2)	0.757±0.232	0.839±0.142	0.843±0	0.889±0.076	5.61	0.0198
T-score lumbar spine	-2.925±2.078	-2.107±1.238	-2.5±0	-1.6±0.99	6.27	0.0139

Table 3: **Distribution of categories of BMD parameters in COPD patients in relation to BMI**

		Undernourished	Normal	Overweight	Obese	
Femoral neck	Normal	8	5	0	1	
Osteoporosis	Osteopenia	39	19	1	1	χ^2=10.01
	Osteoporosis	24	2	0	0	p=0.123
	Total	71	26	1	2	100
Lumbar spine	Normal	7	4	0	1	
Osteoporosis	Osteopenia	16	13	1	1	χ^2=14.88
	Osteoporosis	48	9	0	0	p=0.021
	Total	71	26	1	2	100
Total	Normal	3	2	0	1	
Osteoporosis	Osteopenia	17	14	1	1	χ^2=19.09
	Osteoporosis	51	10	0	0	p=0.004
	Total	71	26	1	2	100

Table 4: Distribution of T-score at femoral neck and lumbar spine in relation to steroid use

		Inhaled Steroid Mean±SD (n=89)	Oral Steroid Mean±SD (n=7)	p value
\	T-Score femoral neck	-2.13±1.05	-3.73±0.78	0.00014
	T-Score lumbar spine	-2.90±1.76	-5.6±0.28	0.00011

RESULTS

The mean age of COPD patients was 62±10.60 years, 87 patients were male and 13 patients were female. Patients had history of an average 49.16±21.21 pack years of smoking. Out of total patients 5 were mild, 11 were moderate, 43 were severe, and 41 were very severe as per GOLD guidelines. Severity of COPD increased proportionately with pack years of smoking but mean smoking history (in pack years) was not significantly different with regard to the categories of COPD (F=1.431, p=0.238). The male patients had often severe and very severe COPD but this was also not statistically significant (p value > 0.05).

At lumbar spine, 57 patients had osteoporosis and 31 patients had osteopenia and at femoral neck 26 patients had osteoporosis and 60 patients had osteopenia. BMD and T-score at both lumbar spine and femoral neck were significantly decreased with increase in severity of COPD ($p < 0.05$) (Table 1).

BMD and T-scores at both lumbar spine and femoral neck were decreasing with a decrease in values of BMI. All these results were statistically significant (p value< 0.05) (Table 2). Proportion of osteoporosis at both femoral neck and lumbar spine as well as total osteoporosis was increasing with decreased values of BMI i.e. low BMI patients had more osteoporosis. These observations were statistically significant for lumbar spine as well as for total osteoporosis (p value <0.05) but not for femoral neck osteoporosis (p value >0.05) (Table 3). Patients with severe and very severe disease had low BMI which shows that increasing severity of COPD was associated with negative impact on BMI of COPD patients, but this was statistically insignificant (p value >0.05).

Prevalence of total osteoporosis among study population was 61% which was higher than previously reported studies. 89 patients had history of long term use of inhaled steroid and seven patients had history of long term (>3 months) oral corticosteroid use. T-score at lumbar spine and femoral neck had more negative values in patients who had history of oral steroid use and the result was statistically significant ($p < 0.05$) (Table 4).

DISCUSSION

There is paucity of Indian studies targeting osteopenia and osteoporosis in COPD patients. Osteoporosis leads to increased risk for fracture and impaired quality of life. The present study showed high prevalence of osteoporosis (61%) in COPD patients. Prevalence of osteoporosis varies from 9-69% in various studies.[6,9,11] Probable reason for this high number in the present study may be long term use of oral and inhaled corticosteroid. Patients with history of long term use of oral corticosteroids had more negative values of T-scores at both lumbar spine and femoral neck when compared to inhaled steroids. Systemic glucocorticosteroids (GCSs) are used as evidence-based treatment of COPD exacerbations despite their deleterious effect on BMD. A meta-analysis by Van Staa et al[10] showed a strong inverse correlation between bone mineral density and total cumulative dose of glucocorticosteroids (GCSs). A study reported mild effects of high doses of inhaled corticosteroids (ICSs) on bone turnover.[11]

The finding of the study has revealed that increase of COPD severity correlates with decrease of BMI. Increasing severity of COPD had significant negative correlation with BMD parameters (T-score and BMD) which was responsible for osteoporosis and osteopenia in the present study. COPD patients with low BMI had more negative values of T-scores and BMD.

These relationships between lung function parameters and BMD are complex and not yet clear. In COPD patients, reduced lung function has been found to be associated with increased inflammatory markers, which is a risk factor for osteoporosis.[13] It is also possible that reduced physical activity because of impaired lung function is the reason for reduced BMD.[9]

Analysis of the present study shows that with the increase of COPD severity the average values of BMD and T-score decreased significantly and percentage of patients with osteoporosis of not only lumbar spine and femoral neck but of total osteoporosis is also increased. The study gives an idea that BMI also has a significant negative correlation with BMD parameters (T-score and BMD) similar to several studies reported earlier.[11,14]

Weight loss and a low BMI has been reported in patients with COPD. The link between low BMI and osteoporosis in COPD patients is not yet entirely clear. It might be due to decreased physical activity, increased inflammation, or other mechanisms leading to proteolysis.[15] Another explanation for more osteoporosis in patients with lower BMI could be that bone formation is decreased because there is relatively low mechanical loading on these bones.

Considering that COPD is a secondary cause of osteoporosis, it was suggested that COPD men with three

minor (BMI <21kg/m^2, current smoking, use of ethanol >3 units/day, age >65 years, parent hip fracture, rib fracture, inactivity, FEV_1 <50% predicted) or one major (systemic corticosteroids for three months/year, major fragility fracture spine-hip) criteria were at increased risk for osteoporosis and therefore candidates for routine DEXA. As a general rule, every COPD man or woman with or without diagnosed osteoporosis should receive calcium (1000 mg/day) and vitamin D (800 IU/day) as a standard supplementation, considering that calcium and vitamin D have been shown to reduce fracture risk in men and women (target serum level of 25-OHD ≥30 ng/mL). Pharmacologic therapy is indicated in COPD men with documented fragility hip or vertebral (clinical or morphometric) fracture, or T-score below −2.5 SD or with less marked bone loss (−1 <T-score <−2.5) and one major criteria, as mentioned above.[15]

CONCLUSION

The present study showed significant derangement in bone mineral density and T-Score in COPD patients especially who had history of long term use of steroid, low BMI, and severe to very severe COPD. Based on the current results it seems reasonable to advise physicians to screen for osteoporosis in COPD patients with a low BMI and who had severe and very severe disease.

Limitation of the study: There was no monitoring of the effect of intervention on the prevention and treatment of osteoporosis and fractures. So randomized placebo controlled trials are required to assess the effect of intervention for subgroup of COPD patients with osteoporosis.

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