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Original Research Article

Measurement of bone mineral density in stable COPD patients using ultrasound densitometry: prevention is better than cure

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ABSTRACT

Background: COPD is a multisystem disorder and three or more comorbidities are associated with poor prognosis. Osteoporosis is one of the major comorbidity and is associated with an impact on the primary dysfunction in COPD. Bone Mineral density measures strength of the skeletal system and ultrasound based BMD measurement is a cheap, cost effective intervention which is also free from ionizing radiation. Ultrasound densitometer BMD measurement can be utilized for screening of osteoporosis in COPD patients.
Methods: 50 stable COPD (diagnosed as per GOLD guideline) patients attending a post graduate institute in Mumbai were enrolled for the study and bone mineral density was measured using ultrasonography BMD scan of calcaneum.
Results: Among 50 enrolled COPD patients, 27 (54%) patients had osteopenia and 14 (28%) were osteoporotic.9 (64.3%) female and 18 (50%) male COPD patients had osteopenia. 4 (28.6%) females and 10 (27.8%) males were osteoporotic.
Conclusions: Considering the additional burden of osteoporosis on management of COPD, it is advisable to measure BMD to formulate strategies to prevent fractures in COPD patients.

Keywords: Stable COPD, Bone mineral density, Osteopenia, Osteoporosis

INTRODUCTION

COPD is a preventable and treatable, condition which consists of persistent airflow limitation, and is characterized by chronic respiratory symptoms caused by significant exposure to noxious gases and particles and is associated with various comorbidities. Osteoporosis is a major comorbidity associated with COPD and is underdiagnosed and associated with poor health status and prognosis (GOLD 2017).[1]

Osteoporosis in COPD is associated with low BMI, low fat free mass, and emphysema, smoking and regular use of steroids. Systemic use of steroids is associated with significant risk of osteoporosis in COPD (GOLD 2017).[1]

Osteoporosis is associated with an increased risk of fracture.[2] Osteopenia is a preclinical stage of osteoporosis. A large study, "The National Health and Nutrition Examination Survey" (NHANES) showed, a 16.9% prevalence of osteoporosis in 995 COPD subjects and an 8.9% prevalence in 14,828 non-COPD subjects aged 45 years and above.[3] Inhaled corticosteroids with or without long acting beta 2 agonists in stable COPDs and systemic steroids during exacerbation are cornerstones of treatment along with, short acting beta 2 agonist, anticholinergic, theophyllines and non-pharmacological treatment. A recent meta-analysis of 16 randomized controlled trials (RCTs) (14 Fluticasone and 2 Budesonide) with 17,513 subjects and seven observational studies with 69,000 subjects indicated that

ICS was associated with a small but significant fracture risk (OR=1.27 in the RCTs and 1.21 in observational studies).[4] Two studies have suggested a dose-dependent decrease in BMD in asthmatics on regular ICS use. (Results were confounded by the past use of oral corticosteroids).[5,6]

COPD patients with lower BMD have been shown to exhibit higher levels of CRP and inflammatory cytokines such as TNF-α, IL-1, and IL-6 showing systemic inflammation in COPD-associated osteoporosis.[7] These three cytokines are inducers of osteoclasts both in vitro and in vivo and have been considered to be involved in the pathogenesis of both primary and secondary osteoporosis, such as that associated with rheumatoid arthritis.[8,9]

Osteoporosis is a multifactorial disease characterized by a reduction in bone mass and by abnormalities in the architecture of bones making the skeleton more prone to fracture. Immobility, low BMI, Vitamin D deficiency, hypogonadism, steroid therapy and systemic inflammation are responsible factors for osteoporosis in COPD. Exact pathophysiological mechanism of low bone mass is not clear, but one study showed poor gastrointestinal absorption of calcium and another study attributed low estrogen level for osteoporosis as an etiology.[10,11]

Measurements of bone mineral density (BMD) have been found to be an accurate parameter of measurement for osteoporosis.

Measurement of BMD is done with dual energy X-ray absorptiometry- (DEXA scan) but is not free from ionizing radiations and is an expensive investigation. Ultrasound based densitometry is considered as a cheap, ionizing radiation free and easy to use alternative indicator of skeletal status in the trabecular bone of the calcareous.[12] Osteoporosis in COPD patients is often underdiagnosed.[13]

Smoking has been shown to be an independent risk factor for osteoporosis among both genders.[14-16] COPD is associated with smoking, thus it is a common etiological agent for both.

The purpose of this article is to make observations available about extra pulmonary manifestations of COPD in order to develop more effective preventive and curative strategies ultimately reducing the healthcare cost.

Aims and objectives

1. To screen COPD patients for osteopenia and osteoporosis.

2. To study the association of osteoporosis with COPD, BMI and smoking.

METHODS

50 diagnosed stable COPD patients (As per GOLD guidelines) attending chest OPD at ESI postgraduate institute at MGM hospital, Mumbai, was included in the study. It was a prospective observational study and the period was from May 2013 to July 2014.

Inclusion criteria

An inclusion criterion was stable COPD patients between 35 to 80 years of age.

Exclusion criteria

Exclusion criteria were pregnant women, patients less than 35 years of age, history of recent AMI, stroke and moribund patients.

Written informed consent was obtained from every patient who fulfilled the inclusion and exclusion criteria. A case study proforma was filled for each patient. Standard medical history and physical examination were undertaken for each enrolled patient. Diagnosis of COPD was made as per standard guidelines (GOLD). The study was approved by Institutional Ethics Committee.

All patients were subjected to:

- Chest X-ray and CT chest in select cases.
- Spirometry with bronchodilator reversibility test.
- Classification of severity of airflow limitation in COPD.
- Mild COPD: FEV1>80% of predicted- GOLD I.
- Moderate COPD: FEV1 50% to 80% of predicted- GOLD II.
- Severe COPD: FEV1 30% to 50% of predicted- GOLD III.
- Very severe COPD_FEV1 less than 30% of predicted- GOLD IV.

Ultrasonography BMD scan was used. Gel was applied to heel of one of the feet and placed on the ultrasonic device. The device measured the mineral density of calcaneum (cancellous bone) using ultrasonic waves, the results were displayed as below (WHO classification-Bone Densitometry)

Up to -1 S.D. considered normal
From -1 to -2.5 S.D. considered osteopenia.
Below -2.5 S.D. considered osteoporotic.

BMI grades[17]

1) BMI less than 18.5- underweight range.
2) BMI- 18.5 to <25- within the normal.
3) BMI- 25.0 to <30- overweight range.
4) BMI- 30.0 or higher- obese.

Statistical methods

SPSS software was used to analyze the data and appropriate statistical tests were used and results were compared with the data from studies in the literature available.

RESULTS

There were 36 males and 14 females. 19 patients were in the age group of 50-59. 18 patients were from 60-69 years, 6 patients from 70-80 years of age and 7 patients were from 40-49 years of age. There were 6 current smokers and 18 former smokers. GOLD II- 27 patients, GOLD III- 16 patients, GOLD-IV- 7 patients (Table 1).

Gender wise distribution was given in Table 2. 9 (64.3%) and 4 (28.6%) females had osteopenia and osteoporosis respectively. 18 (50%) males had osteopenia and 10 (27.8%) males were osteoporotic.

16 patients from GOLD II- were osteopenic and 9 patients had BMD in the normal range. 2 patients had osteoporosis. 10 (62.5%) patients (GOLD III) had osteopenia and 6 (37.5%) patients had osteoporosis. In GOLD IV, 6 (85.7%) out of 7 patients were osteoporotic (Table 3A and 3B).

6 (50%) patients from low BMI grade had osteopenia and 5 (41.7%) were osteoporotic. 10 (76.9%) from normal BMI grade had osteopenia. 5 (50%) patients from overweight grade had osteopenia and 2 patients were osteoporotic. Out of 15 obese patients according to WHO grades of BMI, 6 (40%) had osteopenia and another 6 (40%) had osteoporosis as given in Table 4.

Table 1: Baseline characteristics of the patients enrolled for the study.

Characteristics	No. of patients (n=50)
1) Gender	Males-36, Females-14
2) Age distribution	
40-49	07
50-59	19
60-69	18
70-80	06
3) Smoking history and history of exposure to noxious gases, particles and other agents	
Current smokers	06
Former smokers and patients with exposure to other agents.	18 (13+5)
No obvious history of exposure to noxious gases/particles.	18
Biomass fuel exposure	08
4) Mean BMI	22.62
5) GOLD I, II, III, IV	II-27, III-16, IV-07

Table 2: Gender vs. BMD grade cross table.

Crosstab						
			BMD CAT			Total
			Normal	Osteopenia	Osteoporosis	
Gender	F	Count	1	9	4	14
		% within gender	7.1%	64.3%	28.6%	100.0%
		% within BMD CAT	11.1%	33.3%	28.6%	28.0%
		Residual	-1.5	1.4	0.1	
	M	Count	8	18	10	36
		% within gender	22.2%	50.0%	27.8%	100.0%
		% within BMD CAT	88.9%	66.7%	71.4%	72.0%
		Residual	1.5	-1.4	0.0	
Total		Count	9	27	14	50
		% within gender	18.0%	54.0%	28.0%	100.0%
		% within BMD CAT	100.0%	100.0%	100.0%	100.0%

Table 3A: COPD GOLD grade vs. BMD grade- cross table.

Crosstab						
			BMD CAT			Total
			Normal	Osteopenia	osteoporosis	
COPD GOLD-grades	Moderate GOLD II	Count	9	16	2	27
		% within COPD grade	33.3%	59.3%	7.4%	100.0%
		% within BMD CAT	100.0%	59.3%	14.3%	54.0%
		Residual	4.1	1.4	-5.6	
	Severe GOLD III	Count	0	10	6	16
		% within COPD grade	0.0%	62.5%	37.5%	100.0%
		% within BMD CAT	0.0%	37.0%	42.9%	32.0%
		Residual	-2.9	1.4	1.5	
	very severe GOLD IV	Count	0	1	6	7
		% within COPD grade	0.0%	14.3%	85.7%	100.0%
		% within BMD CAT	0.0%	3.7%	42.9%	14.0%
		Residual	-1.3	-2.8	4.0	
Total		Count	9	27	14	50
		% within COPD grade	18.0%	54.0%	28.0%	100.0%
		% within BMD CAT	100.0%	100.0%	100.0%	100.0%

Table 3B: COPD GOLD grade vs. BMD grade- Chi-square tests.

	Value	df	Asymp. sig. (2-sided)
Pearson chi-square	22.996[a]	4	0.000
Likelihood ratio	25.942	4	0.000
Linear-by-linear association	18.846	1	0.000
N of valid cases	50		

[a]6 cells (66.7%) have expected count less than 5. The minimum expected count is 1.26.

Table 4: BMI category vs. BMD grade- cross table.

Crosstab						
			BMD CAT			Total
BMI grade-WHO			Normal	Osteopenia	Osteoporosis	
BMI grade	Under weight (low BMI)	Count	1	6	5	12
		% within BMI grade	8.3%	50.0%	41.7%	100.0%
		% within BMD CAT	11.1%	22.2%	35.7%	24.0%
		Residual	-1.2	-0.5	1.6	
	Normal	Count	2	10	1	13
		% within BMI grade	15.4%	76.9%	7.7%	100.0%
		% within BMD CAT	22.2%	37.0%	7.1%	26.0%
		Residual	-.3	3.0	-2.6	
	Overweight	Count	3	5	2	10
		% within BMI grade	30.0%	50.0%	20.0%	100.0%
		% within BMD CAT	33.3%	18.5%	14.3%	20.0%
		Residual	1.2	-.4	-.8	
	Obese	Count	3	6	6	15
		% within BMI grade	20.0%	40.0%	40.0%	100.0%
		% within BMD CAT	33.3%	22.2%	42.9%	30.0%
		Residual	0.3	-2.1	1.8	
Total		Count	9	27	14	50
		% within BMI grade	18.0%	54.0%	28.0%	100.0%
		% within BMD CAT	100.0%	100.0%	100.0%	100.0%

DISCUSSION

Osteoporosis is characterized by low bone mass and microarchitectures changes in bone that increase the susceptibility to fracture.[18,19] Bone mass is directly correlated with BMI.[18,20] The fracture risk depends on bone strength, which is determined by bone mineral density (BMD) and bone quality.[21] Since there is no tool available, for precise evaluation of bone quality, for the diagnosis of osteoporosis BMD is utilized as an investigation.[21]

In a systematic review of 13 studies from the period of 1998 to 2008 (775 COPD patients), the prevalence of osteoporosis was between 24%-69%. The COPD patients with osteoporosis had lower FEV1 and BMI values than the patients without osteoporosis.[22] In a retrospective review on 234 male patients referred for osteoporosis, revealed that COPD was the leading cause of secondary osteoporosis.[23]

In the current study, out of total number of COPD (n=50), 27 (54%) patients (18 males and 9 females) had osteopenia and 14 (28%) patients (10 males and 4 females) had osteoporosis. 16 patients (59.3%) were osteopenic within GOLD II- COPD, 10 (62.5%) patients within GOLD III had osteopenia, whereas 6 (85.7% within GOLD IV group patients from very severe obstructive category (FEV1-less than 30%)were osteoporotic, suggesting strong relationship of severity of obstruction and osteoporosis. Considering gender wise distribution 9 (64.3%) and 4 (28.6%) females had osteopenia and osteoporosis respectively. 18 (50%) males had osteopenia and 10 (27.8%) males were osteoporotic.

A recent study of 104 consecutive patients' hospitalized for a COPD exacerbation revealed a prevalence of osteoporosis of 60% and out of these, 60% patients were males. The majority of patients (79%) with osteoporosis had received inhaled corticosteroids for at least 4 months, and 45% patients had received oral steroids for at least 4 months.[24]

In a study conducted by Abu-Bakr and his colleagues, the prevalence of osteopenia was 50% and osteoporosis was 30% in COPD patients.[25] The prevalence of osteopenia and osteoporosis in a similar study in COPD patients was 31.5% and 52.8%.[26]

In the evaluation of obstructive lung disease and osteoporosis (EOLO) study, the prevalence of vertebral fractures in COPD patients was 41%, and correlated with COPD severity.[27] In a study by Mineo et al, bone density of 40 patients before and 1 year after lung volume reduction surgery for emphysema was measured. In spite of oral steroid therapy, bone density improved after the surgery, which was maintained after surgery in about 50% of patients, suggesting association of emphysema and osteoporosis.[28]

Low BMI has shown to be predictive of osteoporosis among COPD patients.[29-31] 6 (50%) of patients out of 12 from our study, having low BMI had osteopenia, and 5 (41.7%) were osteoporotic. But 76.9% (10 out of 13) patients having BMI in normal range, had osteopenia. 50% out of 10 overweight patients had osteopenia and 2 patients had osteoporosis. Out of 15 obese patients (BMI 30 or higher) 6 (40%) of the patients had osteopenia and another 6 (40%) were osteoporotic. Similar study from South India, showed 67% prevalence of osteopenia and osteoporosis among COPD. There was a large difference in the prevalence of osteoporosis between patients with moderate and severe obstruction (18.6% vs. 81.2% $p<0.001$).[32] Another recent study of osteoporosis in COPD found that BMI was the strongest predictor of osteoporosis, with a BMI equal to and above 22 having an odds ratio of 4.18 (95% CI, 1.19 to 14.71).[24]

In another similar study, out of the 37 COPD (GOLD III/IV category) patients, the BMD was found to be normal in 10 (27%) patients, while 27 (73%) patients were found to have osteopenia/osteoporosis 19 (51.35%) patients had osteopenia and 8 (21.62%) patients were osteoporotics.[33]

Meta-analysis of 29 studies revealed that roughly one in eight hip fractures was attributable to cigarette smoking. Current smokers lose bone at faster rates than non-smokers, and by age 80, bone mineral density declines by 6%.[34] Seeman et al reported a 2.3 fold increased risk of vertebral fractures among long term smokers.[14]

Out of 18, (13 former smokers and 5 patients exposed to other etiological agents) from our study, 3 current smokers and 5 former smokers had osteopenia and 1 smoker and 4 (36.4%) former smokers were osteoporotic. Slemenda et al reported that lumbar spine BMD was 12% lower in smokers who have smoked 20 pack-years compared to nonsmokers.[35]

In a study on age related manifestations in COPD and smoking, female smokers with normal spirometry but low KCO (suggestive of emphysema), with decreased BMD and Telometer length shortening. KCO values lower than 80% were associated with systemic manifestations in female smokers and, to a lesser degree, in male smokers.[36] In one more similar study, 43.4% current smokers had osteopenia and 60% current smokers hadosteopenia.[37]

Limitations of the study

1) Small sample size. 2) Fracture risk depends on bone strength and bone quality. BMD measures are not considered as 100% accurate measurement of susceptibility for fracture. 3) Ultrasound based BMD measurement is not the gold standard (DEXA scan is considered as a gold standard for BMD measurement).[38,] for the diagnosis of reduced bone mass and increased susceptibility to fracture.

CONCLUSION

As osteoporosis is one of the major comorbidity in COPD, affecting prognosis. COPD patients with low BMI are more prone for fractures, especially on frequent/regular use of systemic steroids and even if the patients are on long term high dose of inhaled corticosteroids. Screening with ultrasound based bone mineral density which is cheap, free from ionizing radiations, may be undertaken for COPD patients.

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