Decreased Bone Density in Chronic Obstructive Pulmonary Disease Patients

Kronik Obstrüktif Akciğer Hastalığı Olan Hastalarda Kemik Dansitesinin Azalması

Emine ARGÜDER, MD,[a]
Demet KARNAK, MD,[a]
Oya KAYACAN, MD,[a]
Sumru BEDER, MD,[a]
Özlem KÜÇÜK, MD[b]

Departments of
[a]Chest Diseases,
[b]Nuclear Medicine,
Ankara University Faculty of Medicine, Ankara

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Yazışma Adresi/*Correspondence:*
Emine ARGÜDER, MD
Ankara University Faculty of Medicine, Department of Chest Diseases, Ankara, TÜRKİYE/TURKEY
drgullu2000@yahoo.com

ABSTRACT Objective: The clinical course of patients with chronic obstructive pulmonary disease (COPD) is often complicated by the development of systemic effects one of which is osteoporosis. The purpose of this study was to investigate potential risk factors for osteoporosis in COPD patients. **Material and Methods:** We conducted a cross-sectional study in 45 consecutive males with COPD recruited from the outpatient clinic. Demographic data were recorded. Pulmonary function tests [percent of predicted forced expiratory volume in 1 second (FEV1%), forced vital capacity (FVC), FEV1/FVC ratio], maximal inspiratory and expiratory pressures (MIP and MEP), arterial blood gas (ABG) analyses, endocrine tests related to bone density and bone mineral density parameters (vertebral "T" scores (VTS) and femoral "T" scores (FTS)) were performed. Patients were allocated into three groups consisting of 15 patients each, according to history of corticosteroid (CS) use: Patients who have never used any CS, subjects who have been on inhaled steroids (fluticasone dose equivalent to at least 250μg.day-1 propionate or 400μg.day-1 budesonide for at least 36 months) or systemic steroids (methylprednisolone mean dose of at least equivalent to 20mg.day-1 of for at least two weeks). **Results:** Three groups were not different regarding osteoporosis. However, in systemic CS group MEP and calcitonin levels were lower than those of inhaled CS group and never CS group ($p<0.05$ for each). VTS was positively correlated with partial arterial oxygen concentration (PaO2), arterial oxygen saturation % (SaO2) and body mass index (BMI) ($r=0.44$, $p<0.01$; $r=0.49$, $p<0.01$, $r=0.34$, $p<0.05$ respectively). FTS was only well correlated with BMI($r=0.34$, $p<0.05$). **Conclusion:** Bone densities were similar into three groups. Parameters related with severity of COPD such as bronchoconstruction and hypoxemia, along with low BMI were found as risk factors in the development of osteoporosis in COPD patients. Preserved MEP and calcitonin levels in inhaled CS group suggested that respiratory muscle strength and bone resorption were not affected by inhaled CS opposite to systemic steroids.

Key Words: Pulmonary disease, chronic obstructive; body mass index; osteoporosis; adrenal cortex hormones

ÖZET Amaç: Kronik Obstrüktif Akciğer Hastalığı (KOAH) tanılı olguların klinik seyri sıklıkla, osteoporoz gibi, hastalığa bağlı sistemik etkilerin görülmesiyle komplike hale gelir. Bu çalışmanın amacı KOAH'lı olgularda osteoporoz gelişimindeki olası risk faktörlerini araştırmaktır. **Gereç ve Yöntemler:** Bu kesitsel çalışmada polikliniğe başvuran 45 sıralı KOAH'lı olgu incelenmiştir. Olguların demografik verileri ve ayrıntılı öyküleri kaydedilmiştir. Solunum fonksiyon testleri (SFT) [1.saniye zorlu akım hızı beklenen yüzdesi (FEV1%), zorlu vital kapasite (FVC), FEV1'in FVC'ye oranı (FEV1/FVC)], maksimal inspiratuar ve ekspiratuar basınçlar (MIP ve MEP), arteriyel kan gazları (AKG), kemik mineral dansitesi ile ilgili endokrin testler ve kemik dansitesi parametreleri (vertebral "T" skor ve femoral "T" skor) ölçümü yapılmıştır. Olgular kortikosteroid (KS) kullanım öyküsüne göre 15 olgudan oluşan üç gruba ayrılmıştır: Hiç KS kullanmamış olanlar, inhale KS (en az 36 ay boyunca günde en az 250μg flutikazon propiyonat ya da 400mg budesonide'e eşdeğer dozda, ya da sistemik kortikosteroid (en az iki hafta süreyle günde ortalama 20mg metilprednizolon eşdeğeri) almış olanlar. **Bulgular:** Gruplar arasında osteoporoz yönünden anlamlı farklılık saptanmamıştır. Sistemik KS, kullanan grupta MEP ve kalsitonin düzeyleri, inhale KS alanlara ve hiç KS kullanmamışlara göre düşük bulunmuştur ($p<0,05$ herbiri için). VTS parsiyel arteriyel oksijen konsantrasyonu (PaO2), oksijen satürasyonu ve vücut kitle indeksi (VKI) ile pozitif ilişkilidir($r=0,44$, $p<0,01$; $r=0,49$, $p<0,01$, $r=0,34$, $p<0,05$ sırasıyla) FTS ise yalnızca VKI ile iyi koreledir ($r=0,34$, $p<0,05$). **Sonuç:** Kemik mineral dansiteleri üç grupta benzerdir. KOAH'ın şiddetiyle ilintili olan parametrelerle (bronkokonstrüksiyon ve hipoksemi) birlikte düşük VKİ osteoporoz gelişiminde risk faktörleri olarak bulunmuştur. İnhale KS alan grupta MEP ve kalsitonin düzeylerinin korunmuş olması bunların ifade ettiği respiratuar kas gücü ve kemik rezorpsiyonunun, sistemik steroidlerin aksine inhale steroidler tarafından etkilenmediğini düşündürmüştür.

Anahtar Kelimeler: KOAH; vücut kitle indeksi; osteoporoz; kortikosteroidler

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Chronic obstructive pulmonary disease (COPD) is characterized by airflow limitation that is not fully reversible. The airflow limitation is usually progressive and associated with an abnormal inflammatory response of the lungs to noxious particles or gases.[1] In the management of COPD patients; physicians are mostly interested in the evaluation of respiratory symptoms. However, inflammatory mechanisms and hypoxemia in COPD may also cause extra-pulmonary consequences such as skeletal muscle weakness and osteoporosis. This, in turn deteriorates the performance status of the COPD patient. The risk of osteoporosis and osteopenia in COPD varies between 36-40% and 35-72%, respectively.[2-5] It is evident that systemic corticosteroids (CS) cause osteoporosis however the effect of inhaled CS on bone metabolism has not yet been clarified.[2,6-9] Various other factors including smoking, alcohol abuse, low body mass index (BMI), vitamin D deficiency due to low exposure to sunlight, hypoxemia, recurrent exacerbations and immobility besides CS use can facilitate the development of osteoporosis in COPD patients. This can cause vertebral or hip fractures further limiting the patient's exercise capacity and worsening the health status.[1,2,10] Thus, early determination of osteoporosis may prevent these conditions.[3]

We aimed to investigate the contribution of clinical and demographic variables to bone loss in COPD patients. We also aimed to show that COPD severity including blood gases, pulmonary functions, and respiratory muscle strength *per se* could be major risk factors for osteoporosis and thus, COPD should be evaluated as a systemic disease.

MATERIAL AND METHODS

STUDY SUBJECTS

Forty-five clinically stable male COPD patients applying to Chest Diseases outpatient clinic of Ankara University School of Medicine were enrolled in the study. They were diagnosed and classified according to "The Global Initiative for Chronic Obstructive Lung Disease" (GOLD) criteria.[1] The patients' age ranged from 40 to 70 years. They were all on regular follow-up for at least three years in our outpatient clinic.

Patients with a history of osteoporosis/osteopenia, any respiratory disease other than COPD, renal, hepatic, endocrine, collagen tissue diseases, diabetes mellitus, malignancy, metabolic bone disease, malabsorption, alcohol abuse, immobilization and the ones on drugs affecting the bone density (bisphosphonate, L-thyroxine, lithium, androgens, etc.) were excluded from the study.

STUDY DESIGN AND METHODS

This study was approved by local ethical committee and conducted according to the principles of the Declaration of Helsinki. Written informed consent was obtained from all patients. The patients' characteristics, including smoking habits (pack-year) and medication history (type of drugs, doses and duration) were recorded. Routine physical examination was performed. Their BMI were calculated. Venous blood samples (10 ml) were obtained in the morning and tested on the same day to obtain complete blood count, biochemical profile and endocrine parameters related to development of osteoporosis. Serum morning plasma cortisol, free testosterone, osteocalcin, calcitonin and urine free cortisol were measured by DSL®, USA ("Diagnostic Systems Laboratory") endocrine immunoassays; serum parathyroid hormone (PTH) was measured by Bio-DPC®, USA ("Diagnostics Products Cooperation"); serum 1.25-OH D_3 was measured by ICN®, USA; and somatomedin was measured by immunotech in all patients. Arterial blood gas (ABG) analyses were done while the patients were breathing ambient air. Pulmonary function tests (PFTs) including forced vital capacity (FVC), forced expiratory volume in 1 second (FEV_1) with its ratio to FVC were measured by Spirolab-II (sensormedics, USA) while the patient was sitting and his/her nose was closed; Maximal inspiratory and expiratory pressures (MIP and MEP) were measured by Vmax-229 (Sensormedics, USA). MIP was obtained at the level of residual volume and MEP was measured at the level of total lung capacity. The measurements were made while the patient was standing. The subjects were verbally encoura-

ged to achieve maximal strength. The measurements were repeated until five values varied by less than 5% and sustained for at least one second; the best value achieved was used in the data analysis. BMD measurements were undertaken by Dual-energy X-ray Absorptiometry (Norland XR-36) detecting local T scores. The scores measured for lumbar spine (L2-L4) (vertebral 'T' score (VTS)), and for femur neck (femur 'T' score (FTS)). According to World Health Organization criteria, osteopenia was defined as a T score measured between -1 and -2.4 South Dakota (SD) and osteoporosis as a T score measured equal or less than -2.5 SD.[11] Bone mineral content (g/cm^2) of femur neck, trochanter and Ward's triangle were also measured.

Patients were allocated into three groups consisting of 15 patients each, according to history of corticosteroid (CS) use: Patients who never used any CS (*never CS group*); subjects who have been on inhaled steroids (*inhaled CS group*), or systemic steroids (*systemic CS group*). *Inhaled CS group* consisted of stable subjects, and the patients were on fluticasone propionate dose equivalent to at least 250μg or 400μg budesonide.day^{-1} for at least 36 months, since the systemic effects such as markers of bone formation can be obvious only during long-term inhaled steroids treatment. *Systemic CS group* was on methylprednisolone, mean dose of least equivalent to 20 mg.day^{-1} due to COPD acute attack, during previous two weeks which is a sufficient time for systemic side effects to occur. Considering VTS levels, the patients were grouped as normal (n:21), osteopathic [osteopenic (n:15) or osteoporotic (n:9)].

STATISTICAL ANALYSIS

The Statistical Package for the Social Sciences version 11.0 for Windows was used to analyze the data on a personal computer. Data were compared by "One-way ANOVA", "Kruskal-Wallis" and "Chi-square" tests. "Spearman" correlation test was used to evaluate the correlations between bone density parameters and other parameters. Any p value <0.05 was considered as statistically significant. Power calculations were performed to eliminate false positive comparison results via NCSS_PASS program.

RESULTS

Characteristics of groups according to history of CS consumption are shown in Table 1. The groups were comparable with respect to their age, smoking habits, BMI, FEV1, FEV1/FVC, PaO_2 and SaO_2 (p>0.05). Mean inhaled steroid dose in *inhaled CS group* was 895.46 ± 45.17 μg.day^{-1} (median: 400 μg.day^{-1}) budesonide or equivalent. In *systemic CS group*, mean and median doses of steroid were 38.34 ± 18.12 mg.day^{-1} and 45 mg.day^{-1}, respectively.

In *systemic CS group*, MEP and calcitonin levels (63.80 ± 16.81 cmH_2O; 9.87 ± 6.89 ng/L) were significantly lower than those of *inhaled CS group* (88.40 ± 32.91 cmH_2O; 19.87 ± 12.37 ng/L) and *never CS group* (72.00 ± 18.56 cmH_2O; 12.56 ± 8.72 ng/L) (p<0.05) (Table 2). In power calculation analyses, powers of > or = 80% for MEP and calcitonin were achieved.

According to VTS, nine subjects (60%) were either osteopenic or osteoporotic (so called osteo-

TABLE 1: Characteristics of the study subjects (mean ±SD).*

	Never CS (n:15)	Inhaled CS(n:15)	Systemic CS(n:15)	p
Age(years)	60.6±8.24	61.6±7.63	56.6±7.08	>0.05
Smoking (pack-years)	50.66±27.04	42.00±28.33	45.60±24.73	>0.05
BMI (weight/height2)	28.47±5.36	26.33±3.50	26.51±5.32	>0.05
FEV1 (% of predicted)	39.26±17.33	39.06±19.93	33.86±17.12	>0.05
FEV1/FVC	55.59±11.11	55.06±10.67	51.62±10.75	>0.05
PaO_2 (mmHg)	56.45±12.08	59.22±12.01	54.66±9.51	>0.05
SaO_2 (%)	86.42±8.75	88.97±5.24	86.84±7.52	>0.05

*: Groups were comparable with each other as these parameters did not show any difference.

TABLE 2: Laboratory findings (mean ±SD) in groups according to corticosteroid use.

	Never CS (n:15)	Inhaled CS (n:15)	Systemic CS (n:15)	p
MIP (cmH_2O)	50.46±13.85	58.40±25.00	55.60±17.29	>0.05
MEP (cmH_2O)	72.00±18.56	88.40±32.91	63.80±16.81	<0.05*
Calcitonin (pg/ml)	12.56±8.72	19.87±12.37	9.87±6.89	<0.05*
VTS	0.4±2.14	-1.15±1.64	1.33±1.81	>0.05
FTS	0.45±1.44	-0.06±1.25	0.04±1.17	>0.05
Femur neck (g/cm^2)	0.91±0.17	0.86±0.14	0.86±0.14	>0.05
Trochanter (g/cm^2)	0.82±0.16	0.79±0.14	0.71±0.11	>0.05
Ward's triangle (g/cm^2)	0.76±0.17	0.75±0.13	0.70±0.15	>0.05

*: Systemic CS vs never CS and inhaled CS.

MIP: Maximal inspiratory pressure; MEP: Maximal expiratory pressure; VTS: Vertebral T score; FTS: Femur T Score; CS: Corticosteroid.

pathic) in *never CS group*, 10 (66.7%) in *inhaled CS group* and eight (53.3%) in *systemic CS group* (Table 3). The number of the study subjects osteopathic with regard to FTS were (13.3%) two in *never CS group*, four (26.7%) in *inhaled CS group* and four (26.7%) in *systemic CS group* (Table 4). The number and the ratio of normal BMD and osteopathic patients did not differ between the groups according to VTS (p>0.05) or FTS score (p>0.05).

Osteopenic or osteoporotic patients according to VTS had lower PaO_2 and SaO_2 than normal BMD subjects (p<0.05) (Table 5). The other characteristics did not differ significantly among the three groups. According to VTS, osteopenic patients had significantly higher blood phosphorus (1.26 ± 0.17 mmol/L) and lower vitamin D values (37.60 ± 15.45 nmol/L) when compared to those of normal (1.06 ± 0.25 mmol/L; 61.12 ± 35.97 nmol/L) and osteoporotic subjects (1.14 ± 0.11 mmol/L; 39.60 ± 13.87 nmol/L) (p<0.05) (Table 5). In power calculation analyses, powers of > 85% were achieved for about all significant parameters given here.

VTS and FTS were both positively correlated with BMI (r=0.34, p<0.05) (Figure 1a). VTS was significantly correlated with PaO_2, FEV_1% (Figure 1b-c) (r=0.34, p<0.05; r=0.30, p<0.05; respectively), and FEV_1/FVC (r= 0.44, p<0.01). Similarly, correlation was also found between VTS and SaO_2 (r= 0.49, p<0.01). VTS was negatively correlated with serum phosphorous level (r= -0.29, p<0.05), while FTS was positively correlated with serum somatomedin level (r= 0.30, p<0.05).

TABLE 3: Normal or osteopathic subject distribution regarding to steroid use according to either vertebral T score. (Groups were not different in number according to VTS).

GR * VTS Crosstabulation					
			VTS		
			Normal	Osteopat	Total
GR	never	Count	6	9	15
		% within GR	40.0%	60.0%	100.0%
	inhaled	Count	5	10	15
		% within GR	33.3%	66.7%	100.0%
	systemic	Count	7	8	15
		% within GR	46.7%	53.3%	100.0%
Total		Count	18	27	45
			40.0%	60.0%	100.0%

p>0.05; GR: group; osteopat: osteopathic; VTS: Vertebral T score.

TABLE 4: Normal or osteopathic subject distribution regarding to steroid use according to either femur T score. (Groups were not different in number according to FTS).

GR * FTS Crosstabulation					
			FTS		
			Normal	Osteopat	Total
GR	never	Count	13	2	15
		% within GR	86.7%	13.3%	100.0%
	inhaled	Count	11	4	15
		% within GR	73.3%	26.7%	100.0%
	systemic	Count	11	4	15
		% within GR	73.3%	26.7%	100.0%
Total		Count	35	10	45
			77.8%	22.2%	100.0%

p>0.05; GR: group; osteopat: osteopathic; FTS: Femur T score.

TABLE 5: According to vertebra 'T' score (VTS), PaO_2, SaO_2, blood phosphorus and 1-25-OH D3 values. (Osteopenics-osteoporotics had low oxygen and saturation levels and osteopenics had low vitamin D/phosphorus levels).

VTS	PaO_2 (median)	SaO_2 (median)	1-25-OH D3 (µg/L) (median)	Phosphorus(mg/dl) (median)
Normal	60.72±9.82	90.22±6.5	24.45±14.39	3.32±0.79
(n:21)	(61.10)	(92.70)	(23.40)	(3.50)
Osteopenic	55.18±12.30&	86.48±5.64&	15.04±6.18*	3.94±0.54*
(n:15)	(53.70)	(88.60)	(14.20)	(4.10)
Osteoporotic	50.22±9.27#	82.38±8.63¥	15.84±5.55	3.58±0.36
(n:9)	(51.40)	(80.40)	(17.50)	(3.50)

&: p<0.05, Osteopenic vs normal,, #: p<0.05, Osteoporotic vs normal, ¥: p<0.01, Osteoporotic vs normal, *: p<0.05, Osteopenic vs normal

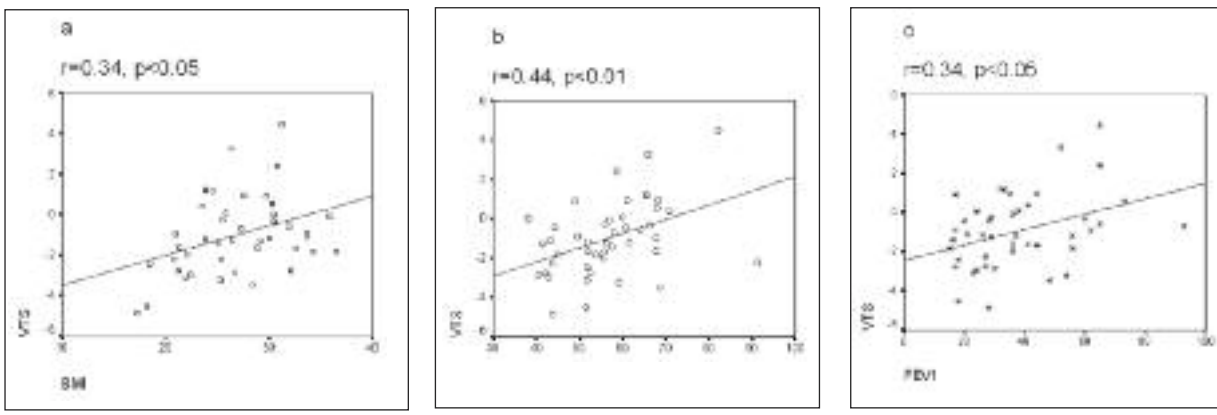

FIGURE 1: Correlations; a) VTS and BMI (r=0.34, p<0.05) b) VTS and PaO2 (r:0.44, p<0.01) c)VTS and FEV1% (r:0.34, p<0.05).
VTS: Vertebral T score; BMI: Body mass index; PaO_2: Arterial oxygen pressure; FEV1: Forced Expiratory volume in 1 second.

DISCUSSION

We examined BMD in COPD patients grouped according to CS consumption; the *never CS*, the *inhaled CS* and the *systemic CS groups*. They were comparable with respect to age, smoking habits, spirometric test results and arterial blood gas analyses.

It was reported that some patients with chronic bronchitis on only bronchodilators had low trabecular BMD while others on oral CS had both lower trabecular and cortical BMD.[12] The present study groups were comparable with respect to BMD parameters, however, independent of the CS use, some of our COPD patients had osteopenia or osteoporosis.

A case-control study involving a large group of subjects has shown an association between the exposure to high doses of inhaled CS and the risk of osteoporotic fractures. The authors have also claimed that patients with severe obstructive airway disease had a high risk of fracture.[13] In the HUNT study, a significant association was observed between inhaled CS use and lower BMD. No dose-response association was observed between inhaled CS and BMD attributed to narrow dose range. No difference in BMD by type of inhaled CS had been observed either.[14] EUROSCOP, one of the largest longitudinal studies showing effects of inhaled CS on BMD, indicated that long-term treatment with inhaled budesonide, at a dose of 800 µg.day^{-1}, had no significant effects on BMD or fracture rate in

COPD patients.[15] Although our study was not performed in a large study group, some patients in our *inhaled CS group* were osteopathic without any fracture history. This inconsistency may be attributable to the limited number of patients in the present study.

CS affect the proximal muscles via reduction of glutamine synthetase activity.[16] Cumulative CS doses have been documented as the most important factor in the development of myopathy in the intubated patients with COPD acute exacerbation.[17] Muscle atrophy frequently occurs in COPD patients limiting the exercise capacity and jeopardizing the quality of life.[18] We measured MEP to evaluate the function of respiratory muscles in the present study. Consistent with the findings in the previous studies, MEP value was significantly lower in *systemic CS group* than that of both *inhaled CS* and *never CS groups,* suggesting respiratory muscle strength was not affected by inhaled CS. Thus inhaled CS can be safely used in COPD patients as needed. As expected, osteoporotic and osteopenic patients accumulated in the *systemic CS group*. These findings suggested that systemic CS not only affect bone mineralization but also impair respiratory muscle strength.

Calcitonin is a protective hormone against the development of osteoporosis due to its anti-resorptive effect.[19] In a study investigating anabolic effects of salmon calcitonin on the skeletal tissue in female rats with CS induced osteopenia, once salmon calcitonin was administered, skeletal resorption decreased and bone formation was stimulated.[20] In our study, *systemic CS group* had lower calcitonin levels than those of *inhaled CS group* and *never CS group* showing that systemic CS might deteriorate the bone resorption/formation equilibrium whereas inhaled CS did not alter calcitonin level resulting in a protective effect on bone resorption.

Regular evaluation of some biochemical markers of bone metabolism such as serum osteocalsin, calcium or alkaline phosphatase levels, and BMD would be helpful for detecting any detrimental changes of bone in COPD patients.[21] There is a reverse mechanism between phosphorus and calcium. When phosphorus reuptake increases, its secretion decreases. Additionally, systemic CS can reduce the calcium reuptake from renal system while increasing the urinary secretion.[22] Osteopenic patients of the present study had higher serum phosphorus values than normals and osteoporotics suggesting that osteopenics were losing calcium more than other groups enhancing the development of osteoporosis. Osteoporotics might have been no longer losing calcium due to lack of calcium storage. In addition, phosphorus was found to be negatively correlated with VTS, showing that serum phosphorus level was directly related to BMD like a promoting factor.

Vitamin D has a primary role in the mineralization of bone matrix. In our country, vitamin D deficiency is reported to be common (%33.4) among elderly people probably due to their clothing habits.[23] In a study investigating the effects of weight and vitamin D on bone density in 71 candidates of pulmonary transplantation for pulmonary diseases, vitamin D deficiency was detected in both thin and normal-weight patients. However, a positive correlation was observed between vitamin D deficiency and low FTS in only thin patients.[24] Osteopenic subjects of the present study had documented vitamin D deficiency.

BMI is a well-known factor influencing the bone density.[25] In postmenopausal women, low BMI has been shown to be a considerable risk factor for the development of osteoporosis.[26] In another study, obesity was shown to protect against osteoporosis.[27] In good agreement with these results, our data demonstrated that BMI of COPD patients was positively correlated with both FTS and VTS. Most of the present patients' BMIs were higher than 18.5 except for two. This may account for its protective effect against osteoporosis in subjects of the present study, despite inhaled and/or systemic CS consumption.

Among 104 COPD patients, ones with osteoporosis had lower FEV_1/FVC than the ones with no osteoporosis at all.[5] Another study show that the extent of pulmonary emphysema significantly cor-

related with reduced bone density.[28] Supporting this, we observed significant correlation with VTS and FEV_1% or FEV_1/FVC showing that osteoporosis risk increased as COPD progresses. The progression of COPD might have led to osteoporosis as such subjects might have needed more CS; these subjects with severe hypoxemia might have decreased mobility and sunlight exposure further affecting the bone metabolism negatively.

Hypoxemia is an important risk factor in the development of osteoporosis. BMD of COPD patients on long-term oxygen therapy for two years has been found significantly lower when compared to the ones who never need oxygen therapy.[29] Compatible with these findings, in the present study, osteopenic or osteoporotic patients with regard to their VTS had lower PaO_2 and SaO_2 compared with normal BMD subjects. As hypoxemia develops in COPD patients, all systems can be affected. Patients on oxygen therapy remain immobile and this further enhances the development of osteoporosis. PaO_2 and SaO_2 values also found to be correlated with VTS. Hence, we suggest that COPD patients with evident hypoxemia should also be evaluated for osteoporosis.

Somatomedin is an important growth factor for bone restoration. Disturbance in the growth hormone (GH)-somatomedin C axis is known to be related with a decreased bone formation. It has been demonstrated that human recombinant GH treatment improves accumulation of bone mineral in patients with cystic fibrosis.[30] Data of a study searching age-related femoral bone loss in men, the major effect has been explained by the age-related increase of PTH and decrease of insulin-like growth factor-1.[31] In the present study we excluded the patients over the age of 70 years to rule out the effect of ageing on bone formation. Although our subjects were not that old, we found a significant correlation between FTS and serum somatomedin level. Thus, the deeper the hypoxemia is, the lower the somatomedin production, further decreasing the BMD.

Significant correlations were observed between VTS and BMI, FEV_1%, PaO_2, SaO_2 and somatomedin. While COPD gets worse, osteoporosis also gets more severe. This interaction can easily be deduced in the correlation analysis of VTS and FTS scores with PFT in the present study. In other words, when VTS and FTS decrease, PFT decreases, too. A number of studies demonstrated that subjects with low values of spirometric parameters were under high risk for osteoporosis.[25,29,32-36] Thus, COPD patients should be followed-up for BMD, BMI and hypoxemia at appropriate periods to avoid possible bone loss.

Development of osteoporosis in COPD is multifactorial. Bronchoconstruction and hypoxemia are contributing risk factors for development of osteoporosis. Immune mechanisms and biochemical changes on bone turnover and physical inactivity causing immobility further promote osteoporosis. Among the drugs, systemic steroids interfere with both skeletal and muscular tissue metabolism resulting in osteopathy and muscle weakness. Therefore, inhaled steroids should be the first choice in COPD since they are free of serious side-effects. COPD patients should be carefully followed up not only for spirometric tests and blood gas analyses but also for osteoporosis and respiratory muscle strength.

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