Osteoporosis in Patients with COPD

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Definitions of Osteoporosis

Osteoporosis

: Progressive skeletal disease that is characterized by low bone mass, skeletal fragility and susceptibility to fracture.

WHO criteria

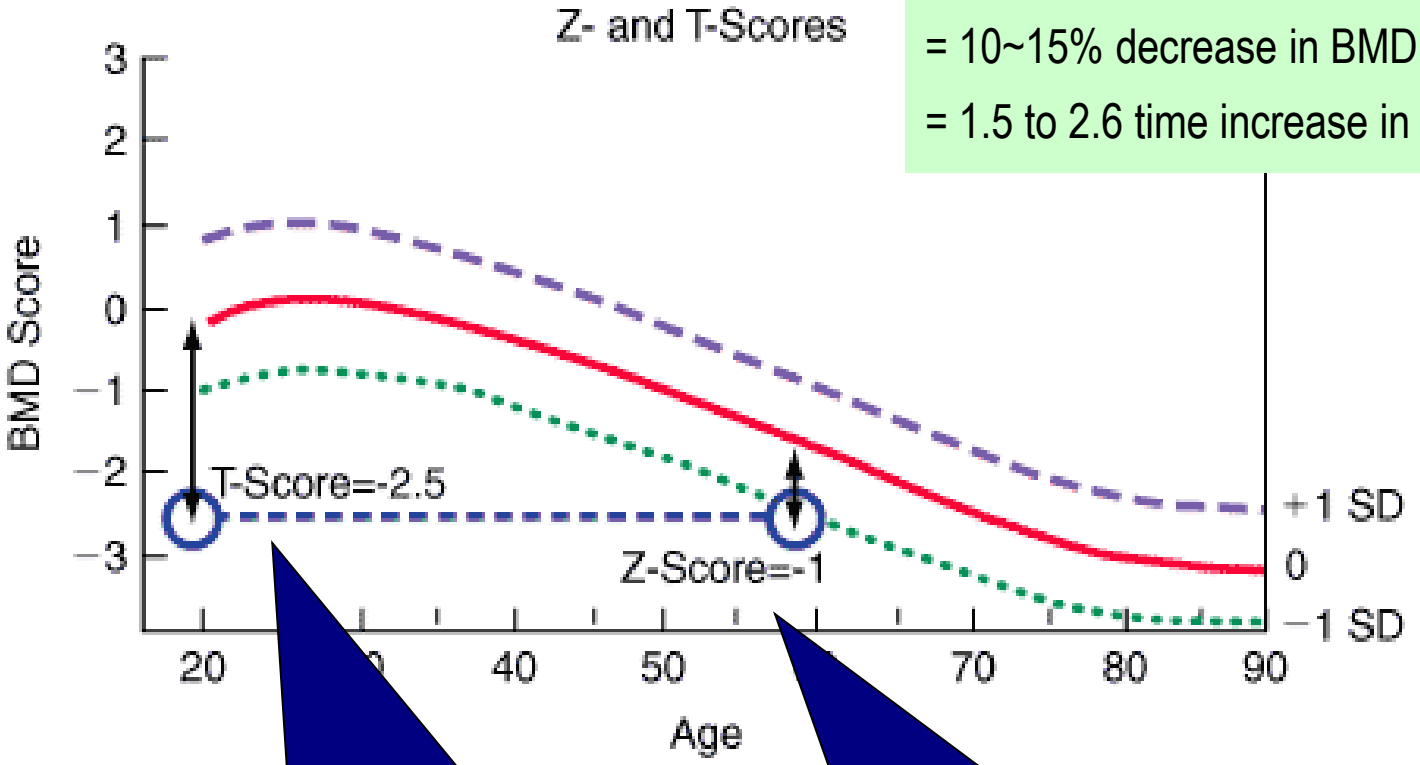
Terminology	T-score definition
Normal	T ≥ -1.0
Osteopenia	-2.5 < T < 1.0
Osteoporosis	T ≤ -2.5
Established osteoporosis	T ≤ -2.5 in the presence of one or more fragility fractures

Eastell R et al. N Engl J Med 1998; 338:736
Blake et al. Semin Nucl Med 2010;40:62

1 SD decrease

= 10~15% decrease in BMD (g/cm^2)

= 1.5 to 2.6 time increase in fracture risk



- Comparing to the mean peak BMD of a normal, young adult population
- For women, reference database is white women aged 20 to 29 years
- Preferred choice for postmenopausal women

- Difference between the woman's BMD & the mean BMD of a reference population of the same gender, age, and ethnicity

Risk Factors of Osteoporosis

Table 1. Osteoporosis Risk Factors*

Not modifiable	Potentially modifiable
Female sex	Oral corticosteroid use
Advanced age	Low body weight (<60 kg)
White race	Sedentary lifestyle
History of previous fracture as an adult	Excessive caffeine intake
Estrogen deficiency or oophorectomy before the age of 45 years	Smoking
Orchiectomy or testosterone deficiency	Heavy alcohol use
Family history of osteoporosis	Lifelong low calcium or vitamin D intake
History of nontraumatic fracture in first-degree relative	Lactose intolerance or milk allergy
Endocrine disease: diabetes mellitus, Cushing syndrome, Addison disease, hyperthyroidism, hyperparathyroidism	Certain antiepileptics and anticoagulants, other medications*†
Hematologic disease: multiple myeloma, mastocytosis, pernicious anemia	Lifelong low calcium or vitamin D intake
Malabsorption syndromes	

* Adapted from National Institutes of Health Consensus Development Panel on Osteoporosis Prevention, Diagnosis, and Therapy,[5] Tangsinmankong et al,[6] Maricic,[7] and Campion and Maricic.[8]

† Includes phenytoin, heparin, warfarin, cyclosporine, methotrexate, and excessive thyroid hormone replacement.

COPD

- A common preventable and treatable disease
  - Characterized by

    persistent airflow limitation

    that is usually progressive
  - Associated with

    an enhanced chronic inflammatory response in the airways and lung to noxious particles or gases.
  - Exacerbations and co-morbidities

    contribute to the overall severity in the individual patients.

GOLD, 2011

Common Comorbidities in COPD

Cardiovascular Disorders

- Pulmonary hypertension
- Right heart failure, Cor pulmonale
- Vascular disease
  - -Coronary artery disease
  - -Cerebrovascular disease
  - -Periferal vascular disease
- Systemic hypertension

Nutritional Disorders, Cachexia

Musculoskeletal Disorders

- Muscle dysfunction
- Osteoporosis

Cancer

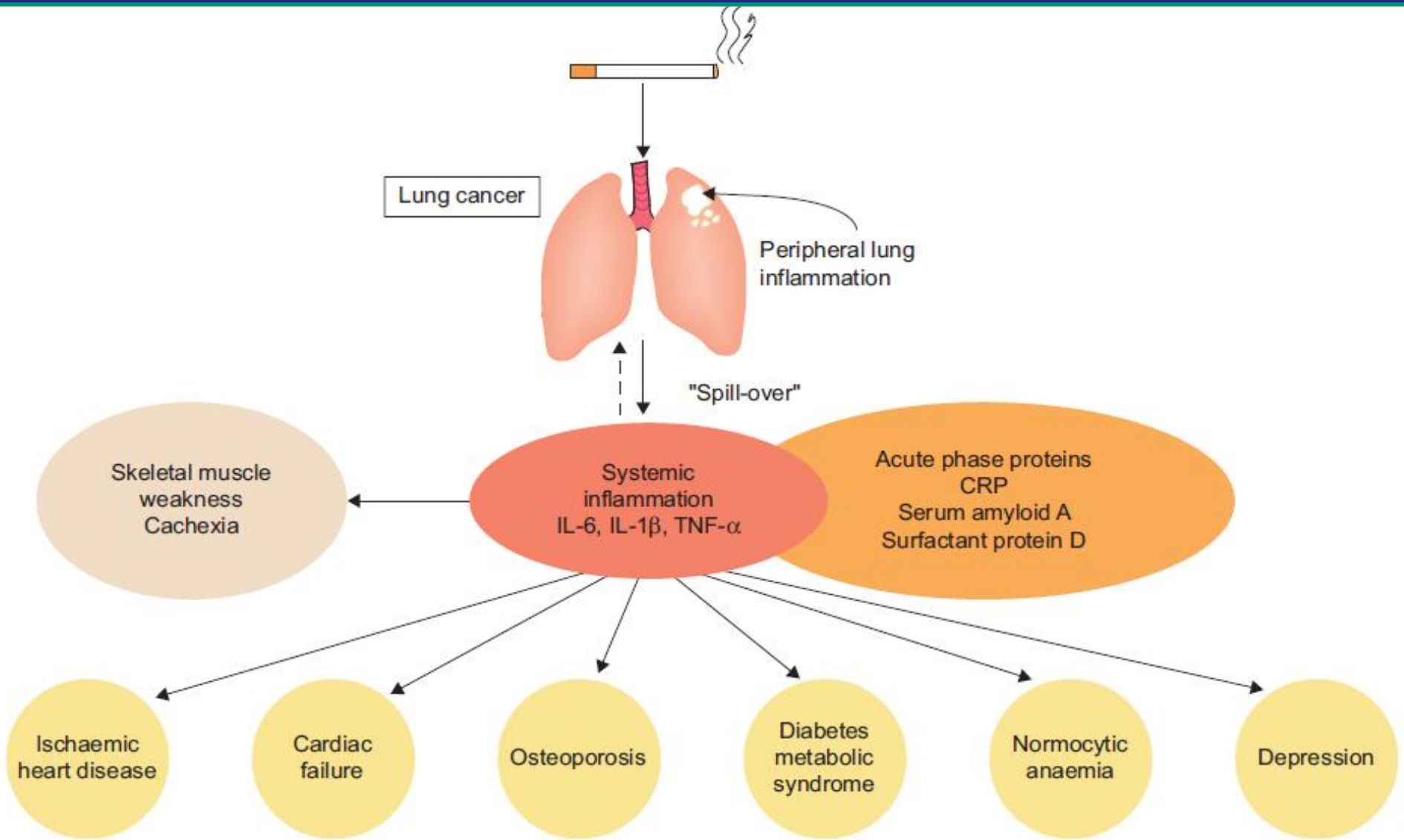
Other

- Sleep disorders
- Sexual dysfunction
- Diabetes
- Depression, anxiety
- Anaemia
- Peptic ulcus
- Glocoma

COPD, Comorbidity, and Mortality

Chatila WM, et al. Proc Am Thorac Soc. 2008;5:549

Systemic Inflammation & COPD



Barnes PJ et al. Eur Respir J. 2009

Prevalence of Osteoporosis in COPD

- As many as 35 to 72% of patients with COPD have been reported to be **osteopenic**, and 36 to 60% of patients with COPD have **osteoporosis**

(Incalzi RA et al Respir Med 2000; 94:1079)

- 32.5% in COPD vs. 11.4% in control subjects matched for age

(Graat-Verboom, L, et al. Eur Respir J 2009; 34: 209)

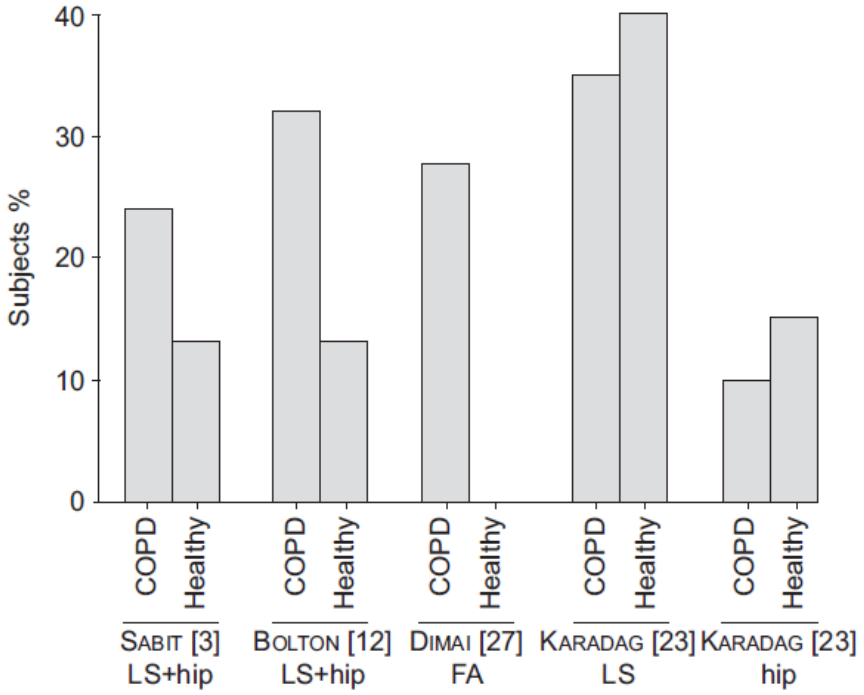


FIGURE 1. Prevalence of osteoporosis in patients with chronic obstructive pulmonary disease (COPD) *versus* healthy subjects. Absolute numbers included in the studies: Sabit [3] n=75 COPD patients, n=42 healthy subjects; Bolton [12] n=81 COPD patients, n=38 healthy subjects; Dimai [27] n=71 COPD patients, n=40 healthy subjects; Karadag [23] n=28 COPD patients, n=20 healthy subjects. For Karadag *et al.* [23] prevalence for lumbar spine (LS) and hip are displayed separately (the author provided us with the combined prevalence of osteoporosis in the COPD patients (40%); however, this combined prevalence in the healthy subjects was not provided). FA: forearm.

Systemic Manifestations and Comorbidities of COPD

TABLE 1. PREVALENCE OF SELF-REPORTED COMORBIDITIES AT BASELINE IN THE ECLIPSE STUDY*

	COPD ($n = 2,164$)	Smoking Control Subjects ($n = 337$)	Nonsmoking Control Subjects ($n = 245$)	P Value
Heart trouble, %	26†,‡	11	9	<0.001
Heart attack, %	9†,‡	3	1	<0.001
Stroke, %	4§	2	1	0.018
Heart failure, %	7†,‡	1	0	<0.001
Arrhythmia, %	12†,§	5	7	<0.001
Osteoporosis, %	14†,‡	5	5	<0.001
Diabetes, %	10‡	7	5	0.003
Inflammatory bowel disease, %	5‖	2	4	0.127
Peptic ulcer, %	11‡	7§	3	<0.001
Reflux/heartburn, %	27§	29§	19	0.031
Depression requiring treatment, %	17	15	14	0.506

Definition of abbreviation: COPD = chronic obstructive pulmonary disease.
*Adapted by permission from Reference 8.
† $P < 0.01$ vs. smoking control subjects.
‡ $P < 0.01$ vs. nonsmoking control subjects.
§ $P < 0.05$ vs. nonsmoking control subjects in the year before the study.
‖ $P < 0.05$ vs. smoking control subjects in the year before the study.

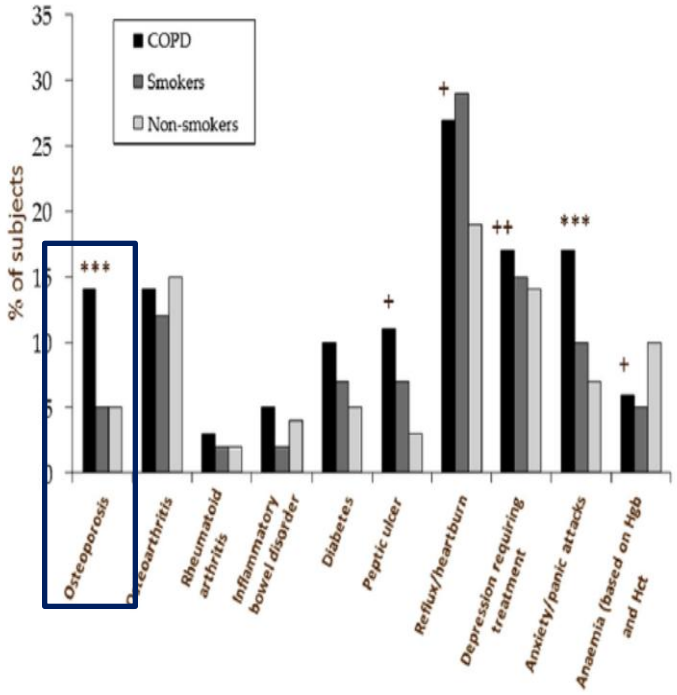
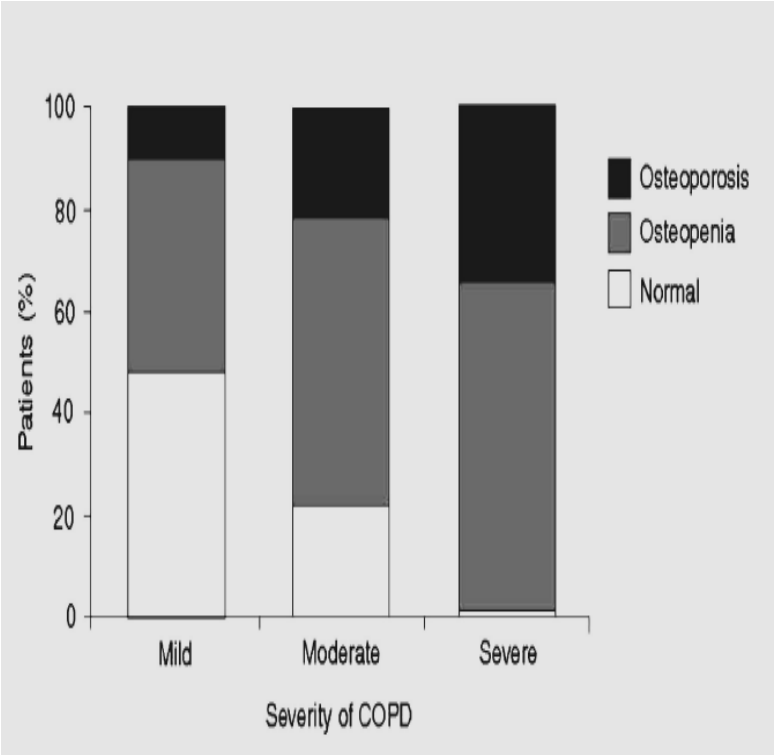


Figure 1 Percentage of COPD subjects, smokers and non-smokers with general comorbidities – ***$P < 0.001$ comparing COPD with smokers and non-smokers; ++ $p < 0.01$, +$p < 0.05$ comparing COPD with control non-smokers (p values adjusted for age and gender).

Augusti A, Proc Am Thorax Soc 2012;9:43
Miller J, et al. Respiratory Medicine 2013; 107: 1376

Osteoporosis in COPD



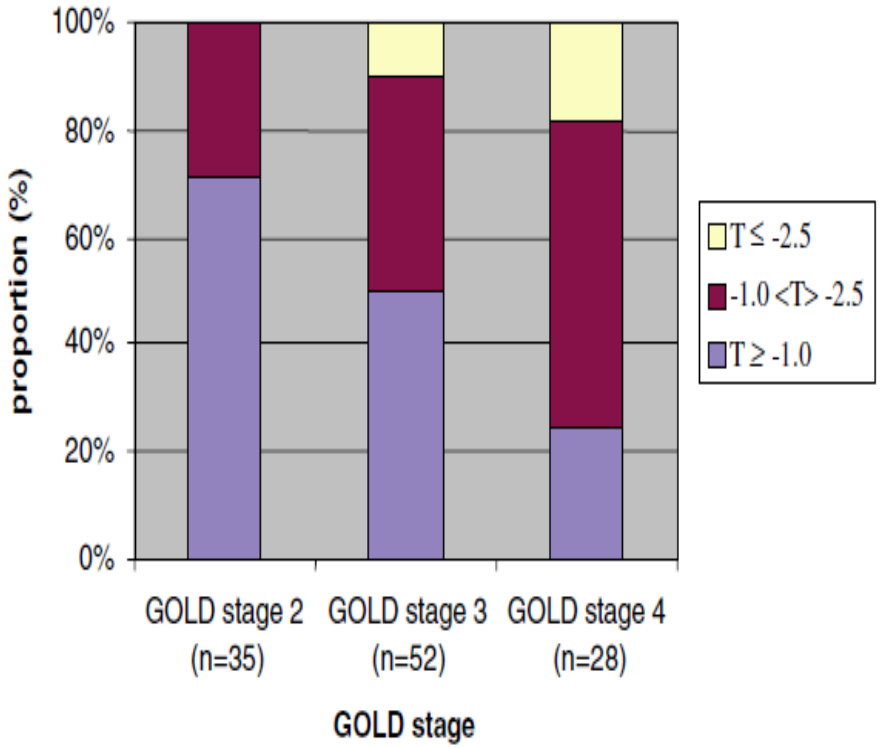
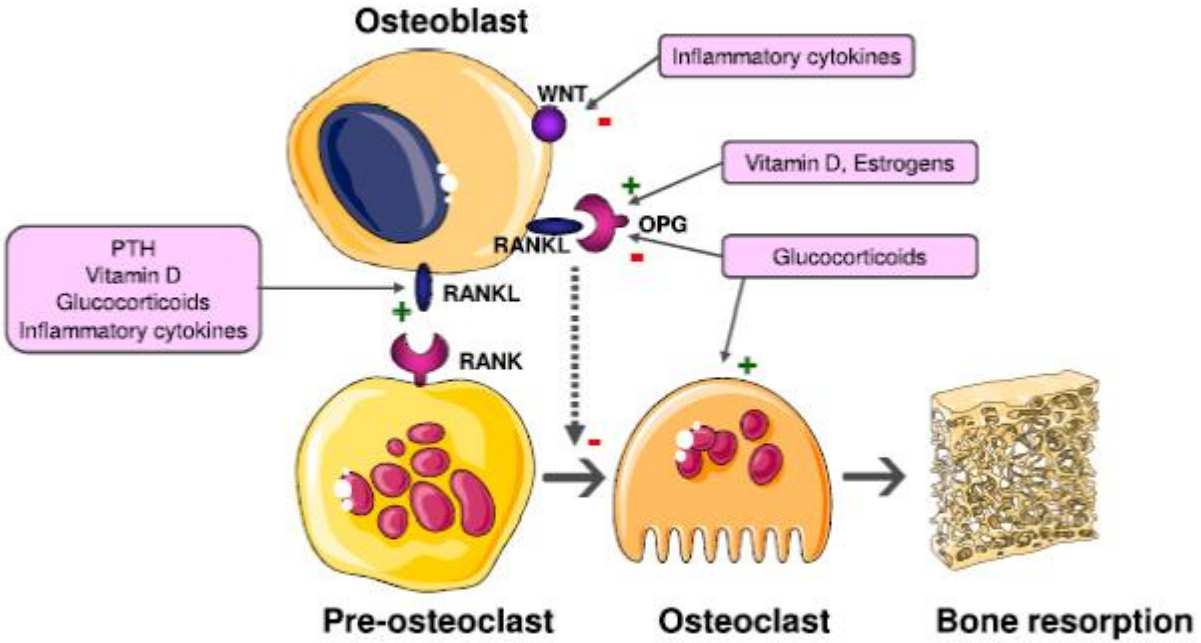


Fig. 1 Bone mineral density for the different GOLD stages

Decramer M, et al. Journal of Chronic Obstructive Pulmonary Disease, 5:235–256
Vrieze A, et al. Osteoporos Int 2007;18:1197–1202

Pathophysiology of Osteoporosis

Figure 3: Key mechanisms in the pathogenesis of osteoporosis in COPD



Adapted with permission from: Lehouck and colleagues, Chest 2011;139(3):648-657

Osteoporosis in COPD and BA

A Comparison of Bone Mineral Density in Elderly Female Patients With COPD and Bronchial Asthma*

Hideki Katsura, MD; and Kozui Kida, MD, FCCP

Table 2—*Bone Densitometry Data**

Bone Data	COPD (n = 20)	Bronchial Asthma (n = 24)	p Value
Total body BMD, g/cm^2	0.89 ± 0.02	0.98 ± 0.02	< 0.01
Spine BMD			
g/cm^2	0.80 ± 0.04	1.01 ± 0.04	< 0.001
Z score	− 0.33 ± 0.27	1.08 ± 0.34	< 0.01
T score	− 2.54 ± 0.32	− 1.01 ± 0.35	< 0.01

*Data are presented as mean ± SEM.

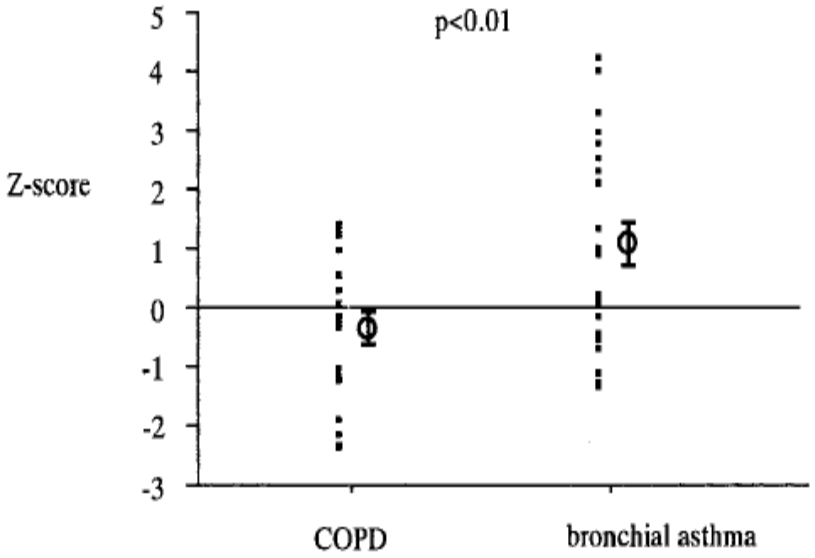


FIGURE 1. Comparison of BMD of the lumbar spine by Z score. The Z score represents a SD from the weight-adjusted average BMD of each age based on the data of Japanese women. BMD of patients with COPD expressed by Z score was significantly lower than that of patients with bronchial asthma.

CHEST 2002; 122:1949–1955

Associations between Airflow Obstruction and Osteoporosis

Table 3. Associations between Airflow Obstruction and Hip Osteoporosis and Osteopenia of the Total Femur*

Category	Osteoporosis		Osteopenia	
	Odds Ratio (95% Confidence Interval)	*P* for Trend†	Odds Ratio (95% Confidence Interval)	*P* for Trend†
Normal	Reference	0.005	Reference	0.005
Mild airflow obstruction	1.3 (0.8 to 2.1)		0.9 (0.7 to 1.1)	
Moderate airflow obstruction	2.1 (1.4 to 3.3)		1.3 (0.9 to 1.7)	
Severe airflow obstruction	2.4 (1.3 to 4.4)		1.7 (1.0 to 2.6)	

* Adjusted for age, smoking status, medications, physical activity, and body mass index (see Methods).
† *P* values reflect linear trend across the lung function categories starting from "none" to "severe."

Airway obstruction increases the risk of osteoporosis.

Sin et al, Am J Med 2003;114:10 –14

Osteoporosis in COPD

Relationship Between Pulmonary Emphysema and Osteoporosis Assessed by CT in Patients With COPD*

Tadashi Ohara, MD; Toyohiro Hirai, MD, PhD; Shigeo Muro, MD, PhD; Akane Haruna, MD; Kunihiko Terada, MD; Daisuke Kinose, MD; Satoshi Marumo, MD; Emiko Ogawa, MD, PhD; Yuma Hoshino, MD, PhD; Akio Niimi, MD, PhD; Kazuo Chin, MD, PhD; and Michiaki Mishima, MD, PhD

Table 2—*Linear Regression Analyses of BMD at Each Vertebral Level*

Variables	Average of Thoracic Vertebra	Vertebrae			
		T4	T7	T10	L1
Age	− 0.390*	− 0.316†	− 0.349*	− 0.449‡	− 0.494‡
BMI	0.363*	0.409‡	0.303†	0.322*	0.227
Smoking index	− 0.072	− 0.053	− 0.001	− 0.147	− 0.114
FEV_1 absolute	0.286†	0.263†	0.238	0.314†	0.327*
FEV_1 % predicted	0.181	0.194	0.141	0.179	0.181
RV/TLC ratio	− 0.241	− 0.216	− 0.209	− 0.263†	− 0.229
DLCO/VA ratio	0.522‡	0.472‡	0.435*	0.575‡	0.487‡
PaO_2	0.266†	0.219	0.243	0.296†	0.418*
LAA%	− 0.522‡	− 0.504‡	− 0.412*	− 0.569‡	− 0.543‡

*$p < 0.01$.
†$p < 0.05$.
‡$p < 0.001$.

CHEST 2008; 134:1244–1249

Steroid and Osteoporosis in COPD

Positive correlation between chronic oral steroid therapy and fracture rate

TABLE 2

ASSOCIATION BETWEEN STEROID USE AND VERTEBRAL FRACTURES*

	Age-adjusted Odds Ratio (95% CI)	Multivariate-adjusted Odds Ratio† (95% CI)
Inhaled steroid users	1.35 (0.77–2.56)	1.38 (0.71–2.69)
Systemic steroid users	1.80 (1.08–3.07)	2.16 (1.14–4.11)
Intermittent, n = 52	1.25 (0.66–2.54)	1.55 (0.72–3.32)
Continuous, n = 73	2.36 (1.26–4.38)	2.99 (1.38–6.49)

* Vertebral fractures defined as one or more radiographic fractures. Referent group in each case is Never Users.

† The odds ratio adjusted for age, age of onset of smoking, weight, current smoking status, pack-years of tobacco, FEV_1%, Baseline Dyspnea Index, Activity Limitation Score, and General Health Status Index.

McEVOY C, et al. AM J RESPIR CRIT CARE MED 1998;157:704–709.

Inhaled budesonide did not increase new lumbar fractures

TABLE 3. SERIOUS ADVERSE EVENTS, DISCONTINUATIONS DUE TO ADVERSE EVENTS, DEATHS, AND GLUCOCORTICOID-RELATED SIDE EFFECTS.

EVENT*	SUBJECTS WITH AT LEAST ONE ADVERSE EVENT		P VALUE
	PLACEBO GROUP	BUDESONIDE GROUP	
Serious adverse event — no.	161	177	0.37
Neoplasm	25	21	
Cardiovascular disorder	32	28	
Gastrointestinal disorder	15	17	
Respiratory disorder	14	17	
Musculoskeletal disorder	16	14	
New lumbar fractures			0.50
No. of subjects	3	5	
No. of fractures	3	8	
Coughing	1	3	
Urinary-bladder carcinoma	4	3	
Deaths — no.†	10	8	0.64
Glucocorticoid-related side effects			
Oropharyngeal candidiasis — no.	10	31	<0.001
Pharyngeal irritation or hoarseness — no.	28	46	0.04
New lumbar fractures			0.50
No. of subjects	3	5	
No. of fractures	3	8	
Skin bruises — no. of subjects (%)	27 (4)	63 (10)	<0.001
Cumulative no. of bruises	42	364	<0.001

Pauwels RA et al. New Engl J Med 1999; 340:1948

Inhaled triamcinolone decreased bone mineral density

TABLE 3. BONE MINERAL DENSITY OF PARTICIPANTS FOR WHOM ALL THREE MEASUREMENTS WERE AVAILABLE.*

MEASUREMENT	TRIAMCINOLONE	PLACEBO	P VALUE
Lumbar spine			
No. of participants	158	170	
Base line (g/cm²)	0.988±0.013	0.979±0.013	0.60
12 mo (g/cm²)	0.988±0.013	0.973±0.013	0.43
36 mo (g/cm²)	0.985±0.013	0.988±0.014	0.89
% Change from base line to 36 mo	−0.35±0.33	0.98±0.36	0.007
Femoral neck			
No. of participants	176	183	
Base line (g/cm²)	0.762±0.010	0.754±0.010	0.54
12 mo (g/cm²)	0.760±0.010	0.751±0.010	0.53
36 mo (g/cm²)	0.747±0.010	0.752±0.010	0.73
% Change from base line to 36 mo	−2.00±0.35	−0.22±0.32	<0.001

Lung Health Study Groups. New Engl J Med 2000;28:343

TORCH safety data: Osteoporosis

Table 4. Adverse Events among 6184 Patients in the Safety Population and 658 Patients in the Substudy of Bone Mineral Density.

Adverse Event	Placebo Group (N = 1544)	Salmeterol Group (N = 1542)	Fluticasone Group (N = 1552)	Combination-Therapy Group (N = 1546)
Bone mineral density¶				
Hip — no. of patients/total no.	52/164	78/166	65/163	82/165
Change from baseline — %‖	−3.1	−1.7	−2.9	−3.2
Lumbar spine — no. of patients/total no.	50/164	76/166	63/163	81/165
Change from baseline — %‖	0	1.5	−0.3	−0.3

Calverley PMA et al. N Eng J Med 2007;356:775

Steroid and Osteoporosis in COPD

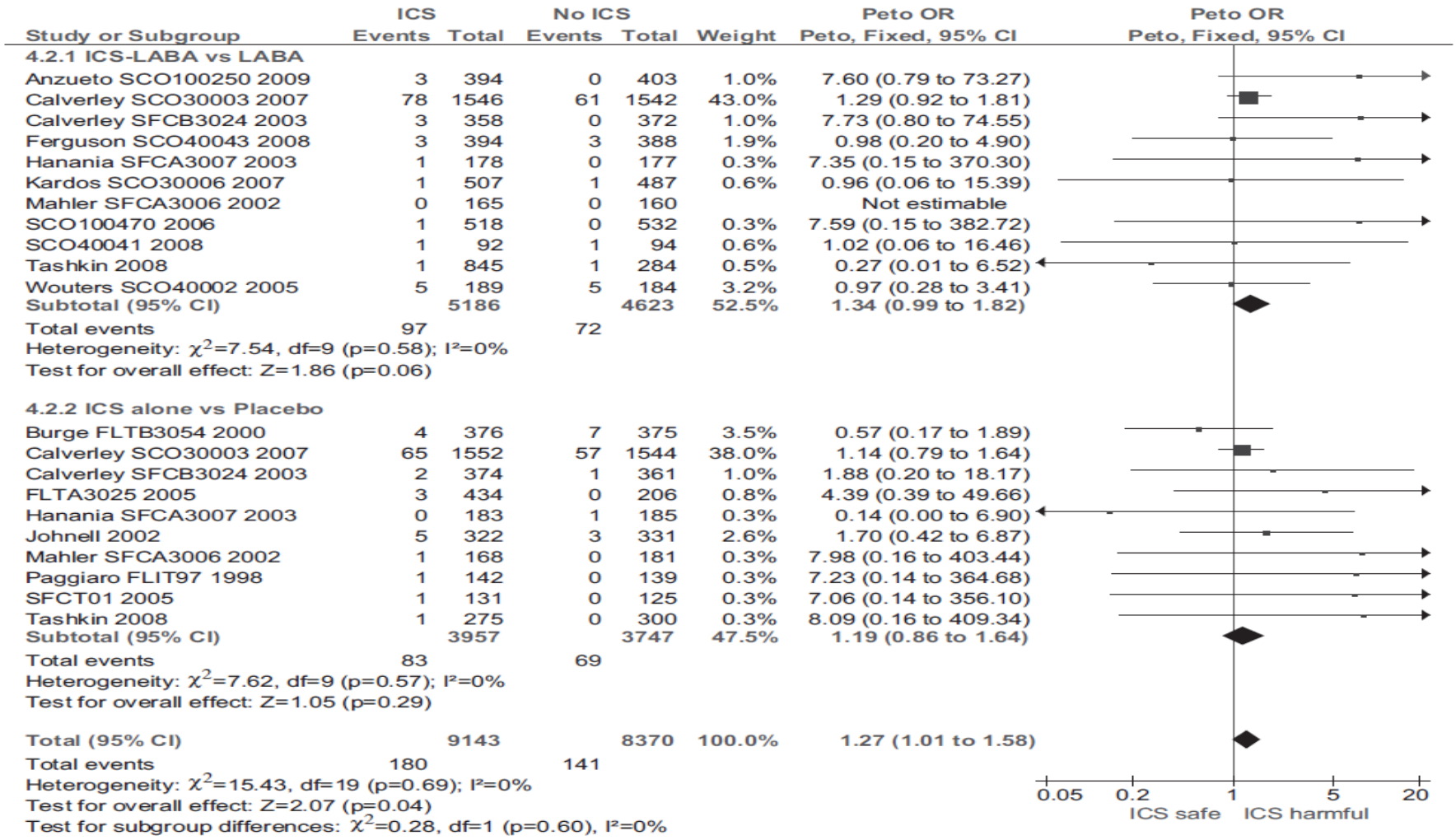
TABLE 3. INCIDENCE OF FRACTURES ACCORDING TO INHALED CORTICOSTEROID DOSE

	Low dose (n = 46,797)			*Medium dose (n = 43,070)*			*High dose (n = 28,815)*		
	No. of cases	*Inhaled corticosteroid versus bronchodilator group Adjusted RR (95% CI)*	*Inhaled corticosteroid versus control group Adjusted RR (95% CI)*	*No. of cases*	*Inhaled corticosteroid versus bronchodilator group Adjusted RR (95% CI)*	*Inhaled corticosteroid versus control group Adjusted RR (95% CI)*	*No. of cases*	*Inhaled corticosteroid versus bronchodilator group Adjusted RR (95% CI)*	*Inhaled corticosteroid versus control group Adjusted RR (95% CI)*
Nonvertebral	1643	0.98 (0.91–1.05)	**1.11 (1.03–1.20)**	1315	0.99 (0.92–1.06)	**1.16 (1.07–1.26)**	806	1.09 (1.00–1.19)	**1.28 (1.15–1.42)**
Forearm	327	0.98 (0.84–1.15)	**1.06 (0.90–1.24)**	306	1.06 (0.91–1.24)	**1.19 (1.00–1.41)**	188	1.14 (0.96–1.37)	**1.15 (0.94–1.42)**
Hip	67	0.93 (0.69–1.24)	**0.95 (0.67–1.34)**	110	1.06 (0.83–1.36)	**1.06 (0.80–1.40)**	107	1.59 (1.24–2.03)	**1.77 (1.31–2.40)**
Vertebral	63	0.77 (0.56–1.06)	**1.31 (0.89–1.92)**	64	0.80 (0.59–1.09)	**1.39 (0.95–2.04)**	61	1.23 (0.90–1.68)	**2.50 (1.63–3.83)**

Figures in bold show adjusted relative rate for fracture when subjects using inhaled corticosteroids were compared with control subjects.

J Bone Miner Res 2001;16:581

Inhaled steroid increased fracture risk



Study or Subgroup	ICS Events	ICS Total	No ICS Events	No ICS Total	Weight	Peto OR Peto, Fixed, 95% CI
4.2.1 ICS-LABA vs LABA						
Anzueto SCO100250 2009	3	394	0	403	1.0%	7.60 (0.79 to 73.27)
Calverley SCO30003 2007	78	1546	61	1542	43.0%	1.29 (0.92 to 1.81)
Calverley SFCB3024 2003	3	358	0	372	1.0%	7.73 (0.80 to 74.55)
Ferguson SCO40043 2008	3	394	3	388	1.9%	0.98 (0.20 to 4.90)
Hanania SFCA3007 2003	1	178	0	177	0.3%	7.35 (0.15 to 370.30)
Kardos SCO30006 2007	1	507	1	487	0.6%	0.96 (0.06 to 15.39)
Mahler SFCA3006 2002	0	165	0	160		Not estimable
SCO100470 2006	1	518	0	532	0.3%	7.59 (0.15 to 382.72)
SCO40041 2008	1	92	1	94	0.6%	1.02 (0.06 to 16.46)
Tashkin 2008	1	845	1	284	0.5%	0.27 (0.01 to 6.52)
Wouters SCO40002 2005	5	189	5	184	3.2%	0.97 (0.28 to 3.41)
Subtotal (95% CI)		5186		4623	52.5%	1.34 (0.99 to 1.82)
Total events	97		72			
Heterogeneity: χ^2=7.54, df=9 (p=0.58); I^2=0%						
Test for overall effect: Z=1.86 (p=0.06)						
4.2.2 ICS alone vs Placebo						
Burge FLTB3054 2000	4	376	7	375	3.5%	0.57 (0.17 to 1.89)
Calverley SCO30003 2007	65	1552	57	1544	38.0%	1.14 (0.79 to 1.64)
Calverley SFCB3024 2003	2	374	1	361	1.0%	1.88 (0.20 to 18.17)
FLTA3025 2005	3	434	0	206	0.8%	4.39 (0.39 to 49.66)
Hanania SFCA3007 2003	0	183	1	185	0.3%	0.14 (0.00 to 6.90)
Johnell 2002	5	322	3	331	2.6%	1.70 (0.42 to 6.87)
Mahler SFCA3006 2002	1	168	0	181	0.3%	7.98 (0.16 to 403.44)
Paggiaro FLIT97 1998	1	142	0	139	0.3%	7.23 (0.14 to 364.68)
SFCT01 2005	1	131	0	125	0.3%	7.06 (0.14 to 356.10)
Tashkin 2008	1	275	0	300	0.3%	8.09 (0.16 to 409.34)
Subtotal (95% CI)		3957		3747	47.5%	1.19 (0.86 to 1.64)
Total events	83		69			
Heterogeneity: χ^2=7.62, df=9 (p=0.57); I^2=0%						
Test for overall effect: Z=1.05 (p=0.29)						
Total (95% CI)		9143		8370	100.0%	1.27 (1.01 to 1.58)
Total events	180		141			
Heterogeneity: χ^2=15.43, df=19 (p=0.69); I^2=0%						
Test for overall effect: Z=2.07 (p=0.04)						
Test for subgroup differences: χ^2=0.28, df=1 (p=0.60), I^2=0%						

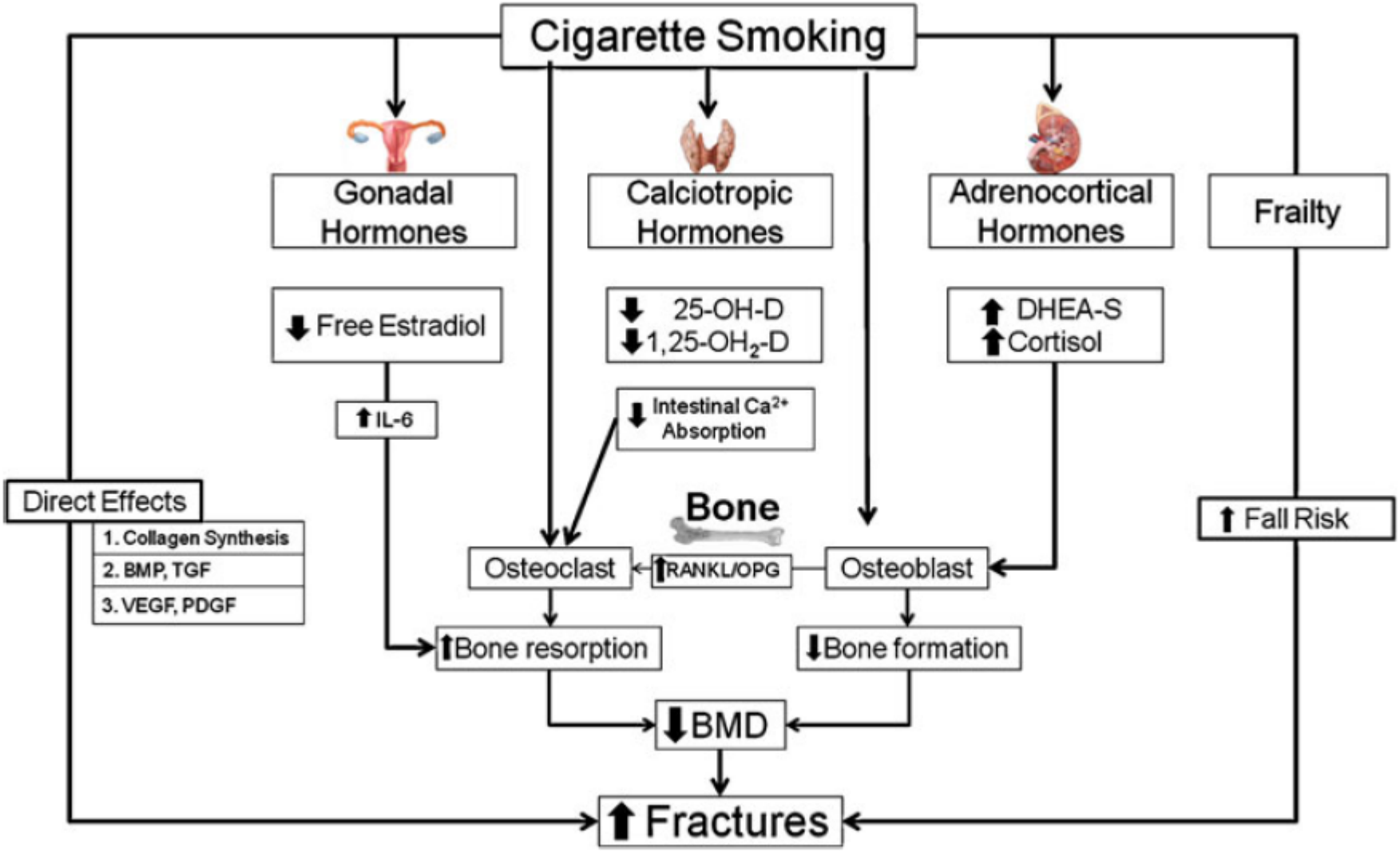
Figure 2 Meta-analysis of odds of fracture with inhaled corticosteroid (ICS) exposure trials of patients with chronic obstructive pulmonary disease. LABA, long-acting β_2-agonist.

Lork Y, et al. Thorax 2011;66:699

Smoking and Osteoporosis

- Slemenda et al. reported that lumbar spine BMD was 12% lower in smokers who have smoked 20 pack-years compared to nonsmokers. (J Bone Miner Res 1989; 4:737–741)
- Risk of vertebral fractures increases 2.3 fold among long term smokers. (Seeman et al. Am J Med 1983; 75:977–983)

Smoking and Osteoporosis



BMI and Osteoporosis in COPD

- In COPD, BMI was the strongest predictor of osteoporosis, with a BMI ≤ 22 having an odds ratio of 4.18 (95% CI, 1.19 to 14.71)

TABLE 3. Logistic regression analysis having osteoporosis as outcome

Variables	Odds ratio	95% Confidence intervals	Coefficient	Standard error	*P*-value
BMI ⩽ 22 kg m^{-2}*	4·18	1·19–14·71	1·43	0·64	0·026
$Paco_2$ > 6·93 kPa†	0·60	0·23–1·61	−0·50	0·49	0·313
FEV_1/FVC < 34%*	1·65	0·62–4·37	0·49	0·49	0·318
MAMC < 201·34 mm*	1·34	0·55–3·26	0·29	0·45	0·512
Age	1·01	0·95–1·08	0·01	0·03	0·679
Male gender	0·54	0·21–1·38	−0·61	0·47	0·199

Abbreviations as in Tables 1 and 2.
*Corresponding to the lowest quartile of the distribution of BMI, FEV_1/FVC and MAMC.
†Corresponding to the highest quartile of the distribution of $Paco_2$.

Incalzi RA et al. Respir Med 2000; 94:1079–1084

Associations between FFM and Osteoporosis

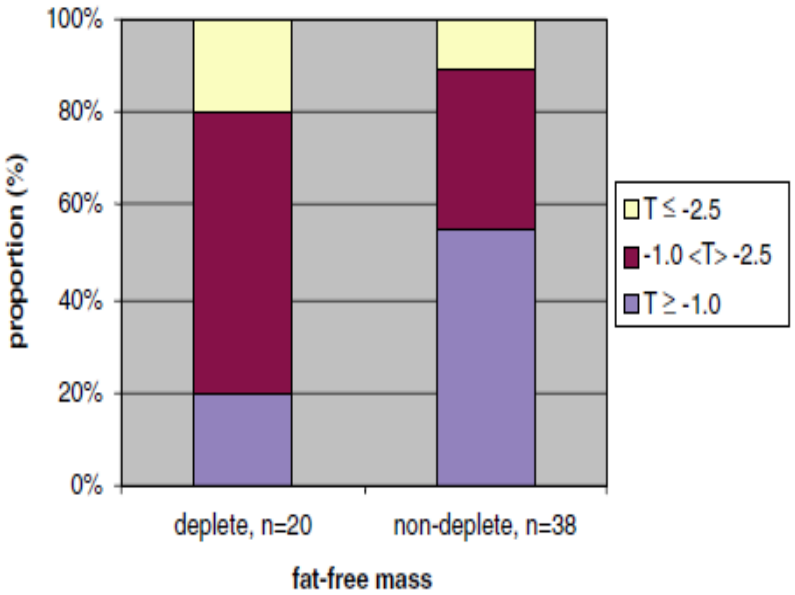


Fig. 3 Bone mineral density for patients with low FFM (depleted) and normal FFM (non-depleted)

Table 3 Logistic regression model with covariates: age, gender, FEV_1 and FFMI

	B(SE)	Exp (B)	95% CI
Constant	9.010(3.144)		
Age	−0.044(0.034)	0.957	0.896–1.02
Gender	−0.954(0.682)	0.385	0.101–1.47
FFMI, kg/m^2	−0.235 (0.107)*	0.791	0.642–.975
FEV_1, l	−1.290 (0.620)*	0.275	0.082–.927

Dependent is abnormal bone mineral density (T-score < −1 SD)
R^2 =0.20 (Cox & Snell), 0.27(Nagelkerke)
*p<0.05

Vrieze A, et al. Osteoporos Int 2007;18:1197–1202

Diagnosis of Osteoporosis in COPD

✓ **Identify individuals at high risk of osteoporosis**

: Similar recommendations should be applied to patients with COPD

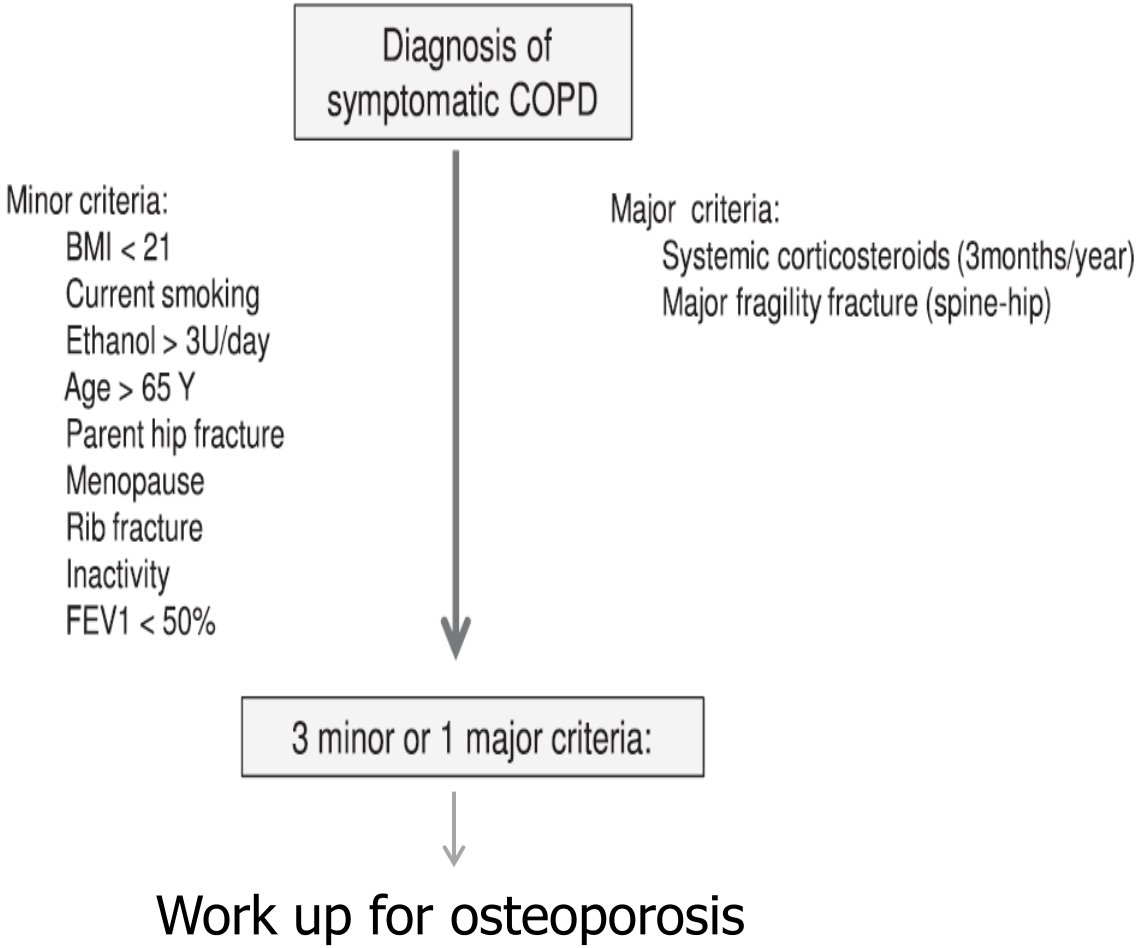
✓ **GOLD (2014)**

: Usual osteoporosis guidelines

Indications for Bone Mineral Density Testing
All women 65 y of age or older
All postmenopausal women
With a history of fracture(s) without major trauma after age 40 to 45 y
With osteopenia identified radiographically
Starting or taking long-term systemic glucocorticoid therapy (≥3 mo)
Other perimenopausal or postmenopausal women with risk factors for osteoporosis if willing to consider pharmacologic interventions
Low body weight (<127 lb or body mass index <20 kg/m^2)
Ever use of long-term systemic glucocorticoid therapy (≥3 mo)
Family history of osteoporotic fracture
Early menopause
Current smoking
Excessive consumption of alcohol
Secondary osteoporosis (see Table 9)

AACE guideline 2010

Diagnosis of Osteoporosis in COPD



Lehouck et al. Chest 2011:139:648-57

Management of Osteoporosis

Goals of Treatment

- To prevent fractures by improving bone strength
- To relieve symptoms of fractures and skeletal deformity
- To maximize physical function

Table 12
Recommendations
Regarding Lifestyle Issues

Ensure adequate intake of calcium throughout life
Ensure adequacy of vitamin D intake
Consume a balanced diet
Regularly perform weight-bearing exercises
Avoid use of tobacco
Limit alcohol consumption
Take measures to avoid falls
Consider use of hip protectors

AACE guideline 2010

Chest 2011;139:648-57

Drugs approved by FDA for Prevention & Treatment of Osteoporosis

	Postmenopausal osteoporosis		Glucocorticoid-induced osteoporosis		In men
	Prevention	Treatment	Prevention	Treatment	
Estrogen	Multiple regimens				
Calcitonin		200 IU IN daily or 100 IU SQ qod			
Denosumab		60 mg SQ q6mo			
Raloxifene	60 mg PO daily	60 mg PO daily			
Ibandronate	2.5 mg PO daily 150 mg PO monthly	2.5 mg PO daily 150 mg PO monthly 3 mg IV q3mo			
Alendronate	5 mg PO daily 35 mg PO weekly	10 mg PO daily 70 mg PO weekly		5 mg PO daily 10 mg PO daily	10 mg PO daily 70 mg PO weekly
Risedronate	5 mg PO daily 35 mg PO weekly 150 mg PO monthly	5 mg PO daily 35 mg PO weekly 150 mg PO monthly	5 mg PO daily	5 mg PO daily	35 mg PO weekly 150 mg PO monthly
Zoledronic acid	5 mg IV q2yr	5 mg IV yearly	5 mg IV yearly	5 mg IV yearly	5 mg IV yearly
Teriparatide		20 μg SQ daily		20 μg SQ daily	20 μg SQ daily

AACE Guideline. 2010

Summary of Evidence for Fracture Risk Reduction

	Fracture risk reduction		
	Vertebral	**Non-vertebral**	**Hip**
Calcitonin	Yes	No effect demonstrated	No effect demonstrated
Raloxifene	Yes	No effect demonstrated	No effect demonstrated
Denosumab	Yes	Yes	Yes
Ibandronate	Yes	No effect demonstrated (?)	No effect demonstrated (?)
Alendronate	Yes	Yes	Yes
Risedronate	Yes	Yes	Yes
Zoledronic acid	Yes	Yes	Yes
Teriparatide	Yes	Yes	No effect demonstrated

AACE Guideline. 2010

Diagnosis and Treatment of Osteoporosis in COPD

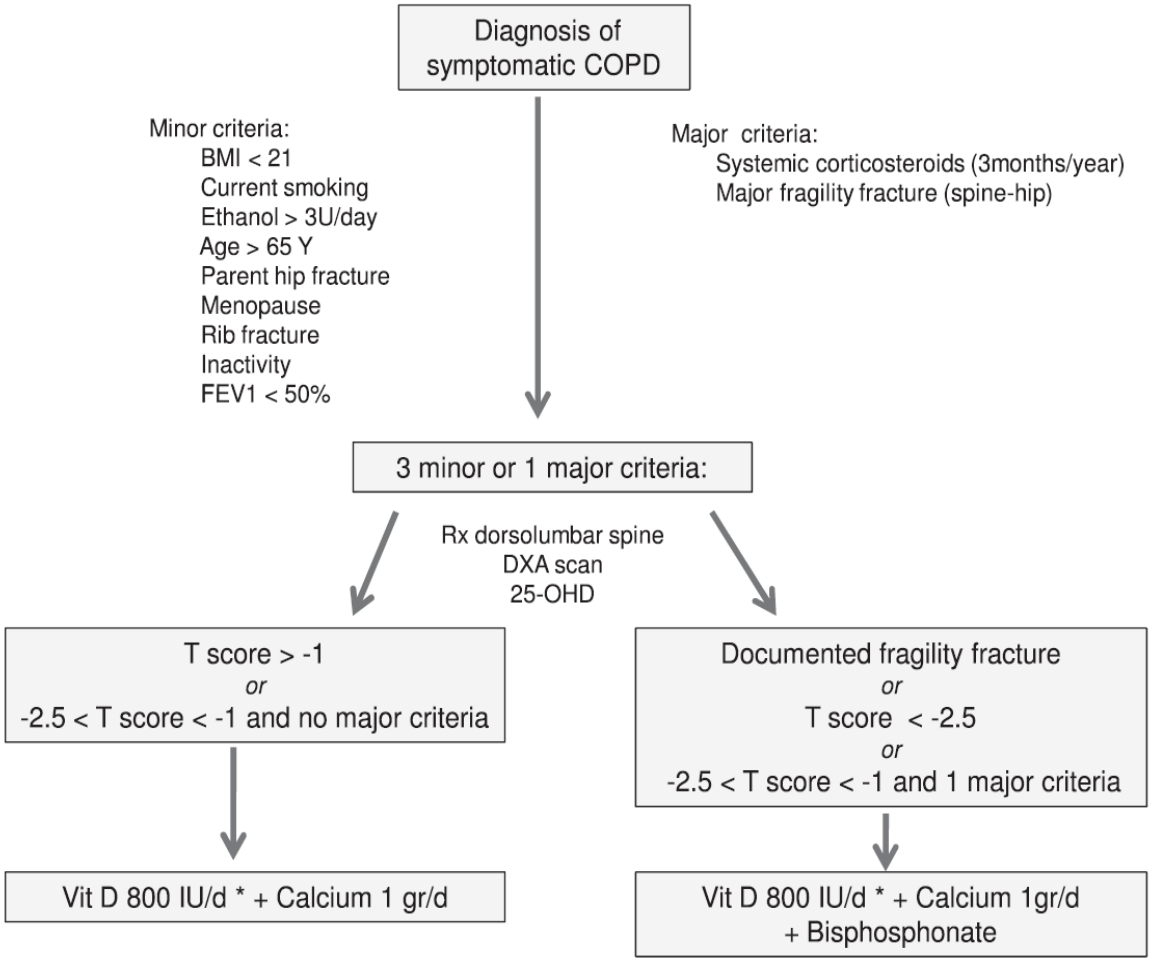


FIGURE 3. Flow diagram summarizing risk assessment, diagnosis, and therapy of osteoporosis in COPD
*25-OHD < 10 ng/mL: start high dose vitamin D supplements with control of 25-OHD after 3 months.
25-OHD = 25 hydroxyvitamin D; DXA = dual-energy x-ray absorptiometry; Vit D = vitamin D.

Lehouck et al. Chest 2011:139:648-57

Summary

- ✓ Patients with COPD are at increased risk of osteoporosis and fractures.

- ✓ Osteoporosis in COPD

  : Already present in the early stages of COPD

  : Associated with airflow obstruction

  : May be more closely associated with emphysema than other subgroups of COPD

  : Risk factor -smoking, oral steroid, high dose ICS, ↓ BMI, ↓ FFMI

- ➢ Multidimensional treatment strategy and comprehensive approach to comorbidity are required in the management of COPD

- ➢ Early prevention and treatment of osteoporosis in COPD is important