

Prevalence, risk assessment, and predictors of osteoporosis among chronic obstructive pulmonary disease patients

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J. Adv. Pharm. Technol. Res.

ABSTRACT

The link between chronic obstructive pulmonary disease (COPD) and osteoporosis is unclear and yet to be understood. The study goals were to detect the prevalence of osteoporosis and investigate its predictors among COPD patients. This is a longitudinal study conducted in a tertiary care setting. During the study, patients' bone mineral density was checked, pulmonary parameters were recorded, and a risk assessment tool was validated. Based on T-score, more than 50% of subjects were osteoporotic. Spirometric parameters were significantly lower among osteoporotic patients. For the risk assessment tool, a cutoff point of 34 made the optimum balance between sensitivity and specificity (0.867 and 0.087, respectively) with a generated area under the curve of 0.934. Severe COPD patients were four times at higher risk of getting osteoporosis, forced expiratory volume (FEV) % predicted, and FEV/forced vital capacity was inversely related to the risk of osteoporosis. Patients with severe dyspnea had twice the risk of getting osteoporosis. Osteoporosis was prevalent among COPD patients, and severe COPD patients were at higher risk of getting osteoporosis.

Key words: Chronic obstructive pulmonary disease, osteoporosis, predictors, prevalence, risk assessment

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is among the leading causes of death worldwide.^[1] It is a serious lung

disease known for causing irreversible and progressive airway obstruction and severe breathing limitation that can lead to emergency intervention and hospital admission. COPD is often underdiagnosed. It is estimated that more than 300 million patients are suffering from COPD worldwide, and it is considered among the most common respiratory conditions in the world.^[2] It can be associated with an exaggerated chronic inflammatory response in the airways after contact with smoke, air pollution, noxious fumes or gases, and cigarette smoking.^[3,4]

Osteoporosis is one of the comorbidities that can be associated with COPD. The national osteoporosis foundation in the United States of America has described osteoporosis as "a

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Submitted: 19-Apr-2021

Revised: 27-Jul-2021

Accepted: 31-Jul-2021

Published: 20-Oct-2021

Access this article online

Quick Response Code:



Website:

www.japtr.org

DOI:

10.4103/japtr.japtr_98_21

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How to cite this article: Bitar AN, Sulaiman SA, Ali IA, Khan AH. Prevalence, risk assessment, and predictors of osteoporosis among chronic obstructive pulmonary disease patients. *J Adv Pharm Technol Res* 2021;12:395-401.

bone disease that occurs when the body loses too much bone, makes too little bone, or both.^[6] The link between these two diseases remains unclear; a recent meta-analysis indicated that osteoporosis is more prevalent among COPD patients than anticipated.^[6] Osteoporosis can be asymptomatic; the low bone mineral density (BMD) among osteoporotic patients increases the risk of fractures, most common of which are the wrist, hip, and spinal.^[7] The impaired capacity to move due to osteoporotic fractures was linked to a faster decline in COPD patients' pulmonary function.^[8]

The link between COPD and osteoporosis is unclear and yet to be understood. In this study, we tried to detect the prevalence of osteoporosis among COPD patients, and we clinically evaluated the cases. We also tested and validated a novel osteoporosis risk assessment tool designed to identify patients at high risk of osteoporosis.

METHODOLOGY

Study design and setting

This study is a longitudinal study conducted in a tertiary care setting in Malaysia. Participants were divided into groups with osteoporosis and without osteoporosis. Ethical approval for the study was obtained from the Medical Research and Ethics Committee, Ministry of Health Malaysia, with the following number: KKM/NIHEC/P19-528(11).^[9]

Participants selection

Cases that met the inclusion criteria were coded and shuffled by an independent staff, then samples were selected randomly, and then subjects were invited to participate in the study. A competent pulmonologist and an investigator clinically examined all recruited subjects. In the prerecruitment interview, written informed consent was obtained from all participants.

Tests and measurements

Data collection tool was used to collect patients' information, including demographics, socioeconomic data, medical history, and clinical test results: the modified Medical Research Council (mMRC) dyspnea scores, COPD assessment test scores, spirometry results [Supplementary File 1]. A well-trained nurse conducted the spirometry based on the American Thoracic Society guidelines;^[10] all recruited subjects were professionally diagnosed with COPD according to the latest GOLD guidelines.^[11] The patients' BMD was tested every visit using quantitative ultrasonography (QUS) at the calcaneus area (SONOST 3000, by OsteoSys Co., Ltd. Guro-Dong 152-848, Seoul, South Korea).

Clinical evaluation tool for bone health

A closed-ended risk assessment tool was used; then, patients' risk for osteoporosis was estimated based on a

simple additive scoring system in the tool. This tool was divided into two sections; the first one consisted of 18 questions related to bone health, each of which carries specific points; from 1 to 3 (1: No, 2: I do not know/Not sure, 3: Yes), [Supplementary File 2]. The lowest possible is 18, while the highest possible score is 54. Based on the obtained scores in the first section, the cases were divided into two categories: 1 – Nonosteoporotic: (18–34) points, 2 – Osteoporotic: (35–54) points.

Validation of the designed tool

The designed tool's components and items were examined and evaluated by a panel of experts. Receiver operator characteristic analysis was conducted to determine the constructed diagnostic tool's sensitivity, specificity, and precision. Results were analyzed to determine the best cutoff point of the obtained scores using (SPSS 24, Inc., Chicago, IL, USA). The generated area under the curve (AUC) was used to evaluate the tool's overall performance compared to QUS results; AUC should not be ≤ 0.500 .^[12]

Inclusion and exclusion criteria

All male COPD patients above 40 years old who visited the respiratory clinic or the ward were included in the study. Female patients were excluded because of the drastic postmenopausal hormonal effect on osteoporosis development and prognosis. Patients with other severe conditions that might significantly impact bone health were excluded (cancerous diseases, hepatic malfunction, kidney disease, Paget's disease, mastocytosis, osteogenesis imperfecta, and severe malabsorption), Patients with severe endocrinal disorders such as Addison's disease, Cushing's syndrome, and Graves' disease were also excluded. Patients who were already diagnosed with a bone disease or who were on bone treatment were excluded.

Statistical analysis

The statistical analysis was conducted using the latest version of the Statistical Package for the Social Sciences (SPSS) (Version 27.0; IBM corp.). Descriptive statistics were done. Chi-square test was performed for categorical variables and *t*-test to compare the means in continuous variables. Linear regression was conducted to examine the relationship between the common extensor tendon and T-score during the study. Logistic regression was performed to calculate the risk of having osteoporosis among COPD subjects. The adopted statistical significance cut point was at $P < 0.05$.

RESULTS

The total number of invited subjects was 469. Ninety-three were reluctant, and we lost contact with 61 subjects, so 65 more were enrolled to compensate, and the total number was 380 participants [Figure 1]. Based on QUS T-score results, osteoporotic subjects accounted for 51.6% of

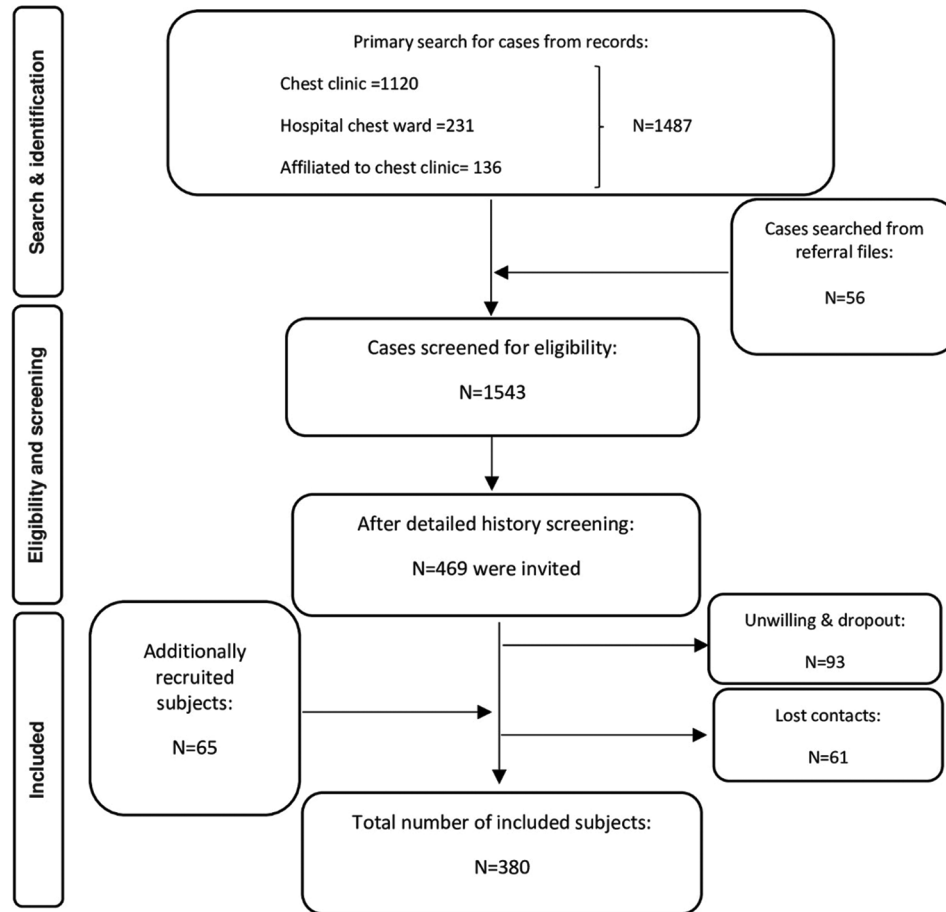


Figure 1: Flow chart of search, screening, and recruitment of subjects in the study

patients. The overall mean \pm standard deviation (SD) for patients' age was 65.4 ± 10.04 . The overall mean \pm SD for patients' body mass index (BMI) was 23.32 ± 5.43 [Table 1].

Chronic obstructive pulmonary disease among osteoporotic and nonosteoporotic patients

The overall mean SD of forced expiratory volume (FEV) 1% predicted and FEV1/forced vital capacity (FVC) ratios showed no significant difference between the baseline and final follow-up. However, during the study, both were significantly lower in osteoporotic subjects compared to the nonosteoporotic ones (FEV1% pred [baseline]: 51.45 ± 14.8 vs. 61.85 ± 16.1 , FEV1% pred [final]: 51.13 ± 14.6 vs. 61.79 ± 15.7 , FEV1/FVC [baseline]: 62.9 ± 16.2 vs. 68.32 ± 15.6 , and FEV1/FVC [final]: 62 ± 16 vs. 67.87 ± 15.1) [Table 2]. Patients' T-score was significantly lower in the last visit of the study, while the risk assessment tool showed higher scores among osteoporotic subjects.

The risk assessment tool

Most of the risk assessment tool components showed a significant association with osteoporosis [Figure 2]. The best cutoff point to optimize the tool's sensitivity and precision was between 34 and 35 points (34.5) of the score obtained.

Where 86.7% of positive outcomes are correctly predicted or classified by the tool, while the 1-specificity at this point was 0.087, which means that around 9% of negative outcomes are incorrectly classified or identified as positive at this point [Figure 3a]. For the exact cutoff point, the precision was 0.914, and the recall was also 0.867 [Figure 3b]. The AUC for the conducted test was 93.4%, and the overall model quality was above 0.5 (0.91) [Figure 3c].

Relationship between the risk assessment tool and quantitative ultrasonography's T-score

In Figure 4a, the data showed positive linearity and homoscedasticity. As the tool's scores go up, the T-score goes down with a statistically significant correlation ($P < 0.01$). The linear regression correlation was statistically significant between the tool's overall score and the overall T-score, $r(378) = 0.832$, $P < 0.001$. The bootstrapped 95 confidence interval (CI) for the slope to predict T-score from the evaluation score ranged from 0.1 to 0.12; thus, for each point increased score of the tool, the patients' T-score score increased by about 0.10–0.12 points. The Durbin-Watson statistics were 1.4, which meets the assumption of dependence; the normal p-p plot of the standardized residual of the performed regression showed that the dots

Table 1: Sociodemographic characteristics of patients

	Nonosteoporotic (n=184; 48.4%)	Osteoporotic (n=196; 51.6%)	Total (n=380; 100)
Age	66.9±10.9	64.30±9.4	65.4±10.04
BMI	23.86±4.31	22.81±6.27	23.32±5.43
Material status			
Married	117 (63.5)	129 (65.8)	246 (64.7)
Single	28 (15.2)	25 (12.7)	53 (13.9)
Divorced/widowed	39 (21.2)	42 (21.4)	81 (21.3)
Residential area			
Rural	33 (17.9)	57 (29.1)	90 (23.7)
Urban	151 (82.1)	139 (70.9)	290 (76.3)
Education			
Nonuniversity	113 (61.4)	117 (59.7)	230 (60.5)
University	71 (38.6)	79 (40.30)	150 (39.5)
Average income (USD)			
≤400	19 (10.3)	22 (11.2)	41 (10.8)
>400	165 (89.7)	174 (87.8)	339 (89.2)
Alcohol consumption			
Yes	6 (3.3)	10 (5.1)	16 (4.2)
No	178 (96.7)	186 (94.9)	364 (95.6)
Smoking history			
Yes	154 (83.7)	167 (85.2)	321 (84.5)
No	30 (16.3)	29 (14.8)	59 (15.5)
Comorbidities			
Yes	106 (57.6)	104 (53)	210 (55.3)
No	78 (42.4)	92 (47)	170 (44.7)

BMI: Body mass index

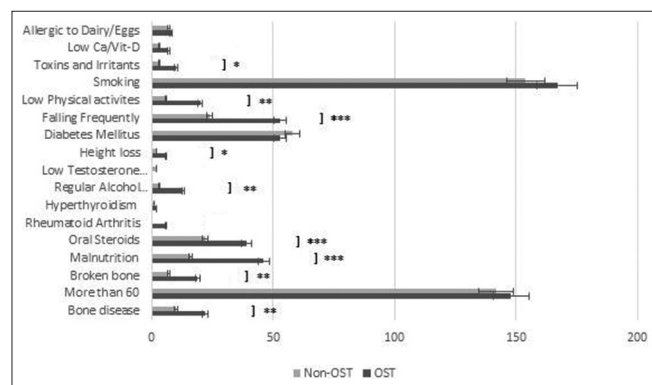


Figure 2: Osteoporosis risk factors. OST: Osteoporotic group, Non-OST: Non-osteoporotic group, *: $P < 0.05$, **: $P < 0.01$, ***: $P < 0.001$

generally line up around the slop, so we have normality of residuals [Figure 4b].

Predictors for osteoporosis among chronic obstructive pulmonary disease patients

Patients with severe COPD were four times at higher risk of getting osteoporosis (odds ratio [OR]: 3.917, 95 CI: [2.430–6.314], $P < 0.001$) [Table 3]. FEV1% predicted and FEV1/FVC ratio results were inversely statistically significant; the lower the spirometric values, the higher the risk of osteoporosis to predict osteoporosis (OR:

0.970, 95 CI: [0.954–0.986], $P = 0.001$ and OR: 0.984, 95 CI: [0.970–0.999], $P = 0.035$, respectively). Those who had more severe dyspnea were at higher risk of osteoporosis; the mMRC dyspnea scale demonstrated a reasonable predictability power (OR: 2.046, 95 CI: [1.122–3.733], $P = 0.02$).

DISCUSSION

Osteoporosis was highly prevalent among COPD patients. According to a recent meta-analysis, the pooled prevalence of osteoporosis among COPD patient was 37.62%; however, looking at the included studies, we found that the range was wide from 14% up to 66%.^[6] Liao *et al.* found that osteoporosis was underdiagnosed among COPD patients.^[9] The FEV1% predicted and FEV1/FVC ratios were significantly lower among osteoporotic patients than the nonosteoporotic ones, similar to a recent Taiwanese study.^[13]

A significant association with osteoporosis has been observed in most of the risk factors. In Shanghai, they found that being underweight or malnourished and low-level activities were significantly associated with osteoporosis, which matches our findings.^[14] A recent study from Sweden indicated that smoking was associated with an increased risk of osteoporosis and fractures;^[15] however,

Table 2: Chronic obstructive pulmonary disease among osteoporotic and nonosteoporotic patients

	Mean±SD		
	Nonosteoporotic (n=184; 48.4%)	Osteoporotic (n=196; 51.6%)	Overall (n=380; 100%)
FEV ₁ % pred			
Baseline	61.85±16.1	51.45±14.8*	56.5±16
Final	61.79±15.7	51.13±14.6*	56.29±16.1
FEV ₁ /FVC ratio			
Baseline	68.32±15.6	62.9±16.2*	65.54±16.3
Final	67.87±15.1	62±16*	65.37±15.7
SpO ₂ %			
Baseline	96.4±0.8	96±1.2	96.23±1.1
Final	96.5±0.9	96.1±0.9	96.31±0.9
mMRC dyspnea scale			
Baseline	1.94±0.65	2.38±0.81*	2.1±0.77
Final	1.98±0.67	2.46±0.87*	2.33±0.82 [#]
CAT score			
Baseline	10.4±8.47	9.9±8.15	10.3±8.32
Final	16.16±7.69 [#]	14.4±7.43 [#]	15.2±7.6 [#]
Exacerbation (year)			
Baseline	1.07±0.6	1.21±0.49*	1.14±0.58
Final	1.14±0.58	1.2±0.55*	1.18±0.62
T-score			
Baseline	-1.51±0.66	-3.17±0.47	-2.37±1
Final	-1.67±0.67 [#]	-3.3±0.46 [#]	-2.51±1 [#]
CET-score			
Baseline	26.8±5.2	38.13±4.53*	32.65±7.45
Final	26.7±5.1	37±5.74*	31.97±7.51

*Statistically significant, [#]Statistically significant difference between baseline and the final visit. FEV₁: Forced expiratory volume in the 1 s, FEV₁% pred: Predicted FEV₁, FVC: Forced vital lung capacity, SpO₂ %: Oxygen saturation, mMRC dyspnea scale: Modified Medical Research Council dyspnea scale, COPD: Chronic obstructive pulmonary disease, CAT score: COPD assessment test score, CET Score: The clinical evaluation tool score, SD: Standard deviation

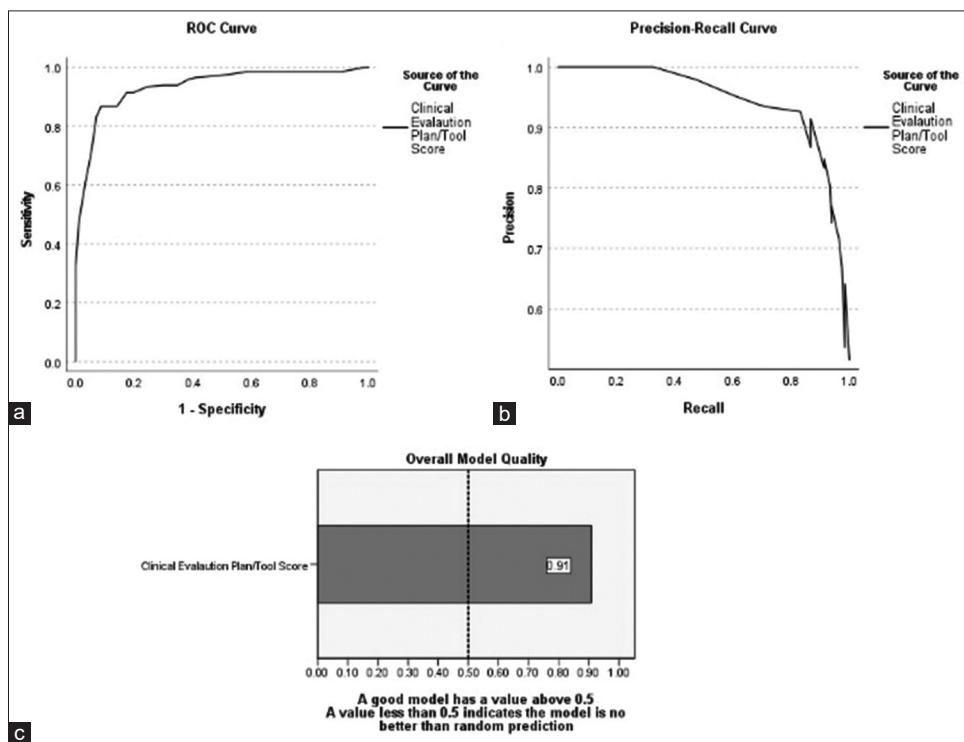


Figure 3: Risk assessment tool’s validation (the clinical evaluation tool). (a) Receiver operator characteristic (sensitivity-specificity curve). (b) Precision-recall curve. (c) Overall model quality

Table 3: The results of predictors analysis

Variable	Crude OR (95% CI)	P
Age	0.982 (0.960-1.005)	0.116
BMI	0.974 (0.928-1.022)	0.289
GOLD category	3.917 (2.430-6.314)	0.001*
FEV ₁ % pred	0.970 (0.954-0.986)	0.001*
FEV ₁ /FVC ratio	0.984 (0.970-0.999)	0.035*
mMRC	2.046 (1.122-3.733)	0.020*
SpO ₂	0.900 (0.708-1.144)	0.391
CAT-score	0.989 (0.944-1.035)	0.632

*P<0.001. FEV₁: Forced expiratory volume in the 1 s, FEV₁% pred: Predicted FEV, mMRC dyspnea scale: Modified Medical Research Council dyspnea scale, COPD: Chronic obstructive pulmonary disease, CAT score: COPD assessment test score, FVC: Forced vital capacity of the lungs, SpO₂%, Oxygen saturation, BMI: Body mass index, OR: Odds ratio, CI: Confidence interval

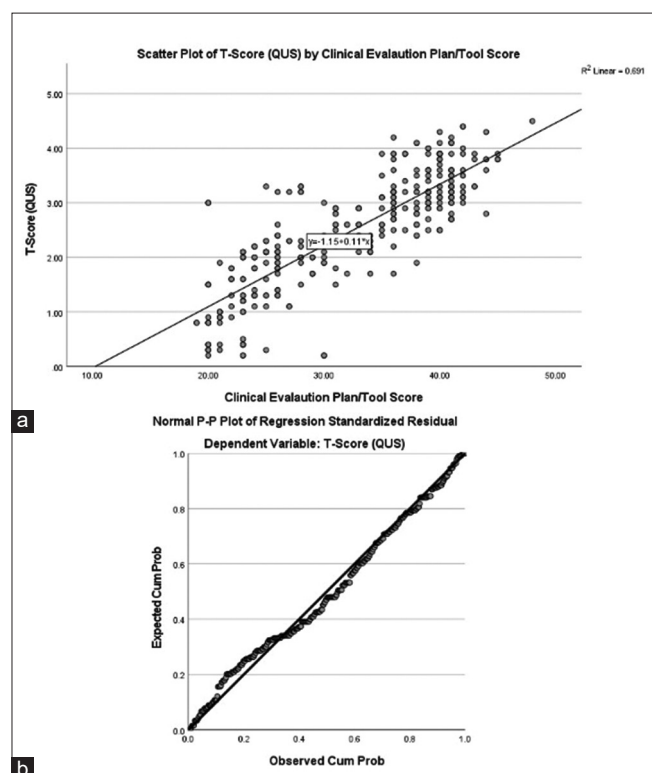


Figure 4: The relationship between the clinical evaluation tool and T-score. (a) Scatter plot of T-score by clinical evaluation plan score with total regression fit line. (b) Normal P-P plot of regression standardized residual

in a regression meta-analysis, the researchers have reached inconclusive results regarding the effect of smoking.^[16] The significant risk factors for osteoporosis among COPD patients included low BMI, frequent exacerbations, the use of steroids, systemic inflammation, low vitamin D, lack of physical activities, and hyperthyroidism.^[16] Similar to our findings, among male subjects in Taiwan, a higher prevalence of osteoporosis was observed among COPD patients, and lower BMI was associated with osteoporosis; after binary regression, low BMI was an insignificant risk factor,^[13] which is in contrast with Chuealee *et al.* findings.^[17]

A few risk assessment tools for osteoporosis were developed in the past. Recent research has shown that most of these tools were lacking precision (ranging from 0.04 to 0.12), and the simple calculated osteoporosis risk estimation (SCORE) had the best balance between recall and precision among the tested tools, and the AUC was the highest (0.072–0.161).^[18] A study has tested FRAX without BMD, and they found its sensitivity to be 33.3% with a specificity of 86.4% and an AUC of 60% at a threshold of $\geq 9.3\%$,^[19] while the AUC in our findings was around 90%. Ettinger *et al.* found that FRAX was the predictability of fractures varied a lot. Although the addition of BMD test results to the tool's calculations improved the FRAX risk estimate, it did little to improve its predictive performance.^[20]

Our results have shown that severe COPD patients were at higher risk of osteoporosis. Similarly, Graumam *et al.* found that patients with more advanced COPD stages were at higher risk of osteoporosis.^[21] Furthermore, in a longitudinal study, it has been noticed that the increased exacerbation rates were independently associated with the progression of osteoporosis among COPD patients.^[22] This was attributed to the exaggerated inflammatory response among COPD patients and increased hypoxia and oxidative stress, besides the imbalanced protease/antiprotease system.

CONCLUSIONS

Osteoporosis was prevalent among COPD patients. The risk assessment tool was sensitive, and severe COPD patients were at higher of getting osteoporosis.

Acknowledgments

The authors would like to thank the Director-General of Health Malaysia for permission to publish this paper. The authors acknowledge that this project was partially sponsored by Bridging/ Bridging-Incentive Grants by Universiti Sains Malaysia (Grant Number: 304. PFARMASI.6316508).

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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SUPPLEMENTARY FILE 1

PATIENT MEDICAL PROFILE FORM

I. Personal information			
Patient Code			
Age (Yrs)	<input type="checkbox"/> 35-44	<input type="checkbox"/> 45-54	<input type="checkbox"/> 55-64
	<input type="checkbox"/> 65-74	<input type="checkbox"/> 75-84	<input type="checkbox"/> 85+
Residence	<input type="checkbox"/> Rural		<input type="checkbox"/> Urban
Marital status	<input type="checkbox"/> Single		<input type="checkbox"/> Divorced/ widowed
	<input type="checkbox"/> Currently married		
BMI (kg/m²)	<input type="checkbox"/> Severely underweight (15-16)		<input type="checkbox"/> Underweight (16-18.5)
	<input type="checkbox"/> Normal (18.5-24.9)		<input type="checkbox"/> Over weight (25-29.9)
	<input type="checkbox"/> Obese (>30) (Class I-II-III-IV-V-VI)		
Ethnicity	<input type="checkbox"/> Malay	<input type="checkbox"/> Indian	<input type="checkbox"/> Chinese <input type="checkbox"/> Other
Exercise	<input type="checkbox"/> Yes		<input type="checkbox"/> No
Alcohol & Drug addiction	<input type="checkbox"/> Yes		<input type="checkbox"/> No
	(If any, please clarify the route, quantity and method of intake.....)		
Family history of chronic disease	<input type="checkbox"/> COPD		<input type="checkbox"/> Osteoporosis
	<input type="checkbox"/> Other.....		
II. Socio-economic information			
Education	<input type="checkbox"/> No formal education	<input type="checkbox"/> Primary	<input type="checkbox"/> Secondary
	<input type="checkbox"/> College	<input type="checkbox"/> Graduation	<input type="checkbox"/> Post-graduation
Work status	<input type="checkbox"/> Unemployed		<input type="checkbox"/> Employed <input type="checkbox"/> On social aid
Nature of work (If employed)	<input type="checkbox"/> Government sector	<input type="checkbox"/> Private sector	<input type="checkbox"/> Office work
	<input type="checkbox"/> Self-employed	<input type="checkbox"/> Labor Intense	<input type="checkbox"/> Other.....
Average income per month. (RM)	<input type="checkbox"/> 500-2000		<input type="checkbox"/> 2000-5000
	<input type="checkbox"/> 5000-10000		<input type="checkbox"/> more than 10000
Impact of disease on life	<input type="checkbox"/> Activity limitation	<input type="checkbox"/> Missing work	<input type="checkbox"/> Missing social events
	<input type="checkbox"/> Lack of wellbeing		<input type="checkbox"/> Affect family routine
III. Medical history			
Co-morbidity	<input type="checkbox"/> Dyslipidemia	<input type="checkbox"/> Hypertension	<input type="checkbox"/> DM
	<input type="checkbox"/> HIV	<input type="checkbox"/> Pneumonia	<input type="checkbox"/> T.B
	<input type="checkbox"/> ESRD	<input type="checkbox"/> IHD	<input type="checkbox"/> URTI/LRTI
	<input type="checkbox"/> Other.....		
Exposure to risk factors	<input type="checkbox"/> Occupational	<input type="checkbox"/> Environmental	<input type="checkbox"/> Non /Ex/Smoking
Past medical history	<input type="checkbox"/> Allergy	<input type="checkbox"/> Asthma	<input type="checkbox"/> Sinusitis <input type="checkbox"/> Bronchiectasis
	<input type="checkbox"/> Emphysema	<input type="checkbox"/> Bronchitis	<input type="checkbox"/> Other.....
Vaccination history	<input type="checkbox"/> Influenza vaccine		<input type="checkbox"/> Pneumococcal vaccine
Allergic to dairy products	<input type="checkbox"/> Yes		<input type="checkbox"/> No
IV. Clinical history			
COPD stage	<input type="checkbox"/> GOLD-1	<input type="checkbox"/> GOLD-2	<input type="checkbox"/> GOLD-3 <input type="checkbox"/> GOLD-4
Osteoporosis T-score	<input type="checkbox"/> 0 to -0.99	<input type="checkbox"/> -1 to -2.4	<input type="checkbox"/> below -2.5 <input type="checkbox"/> below -2.5 with fracture
Previous treatment History	Start date/End date	Regimens	Outcome
COPD			
Osteoporosis			

V. COPD diagnosis tests	
Pulmonary Function Test (PFT)& Spirometry	<input type="checkbox"/> FEV1..... <input type="checkbox"/> FVC..... <input type="checkbox"/> FEV1/FVC..... <input type="checkbox"/> Other (if needed).....
Transfer factor for carbon monoxide (TLCO)	
CT scan of the thorax/X-ray	
ECC	
Echocardiogram	
Pulse oximetry	
VI. Patient clinical status of COPD	
Signs and symptoms	<input type="checkbox"/> Dyspnoea <input type="checkbox"/> weight loss <input type="checkbox"/> Fatigue <input type="checkbox"/> anorexia <input type="checkbox"/> Cough <input type="checkbox"/> Wheezing <input type="checkbox"/> Chest tightness <input type="checkbox"/> Syncope Ankle swelling <input type="checkbox"/> Sleeping apnoea <input type="checkbox"/> Others..... <input type="checkbox"/> mMRC Grade 0 <input type="checkbox"/> mMRC Grade 1 <input type="checkbox"/> mMRC Grade 2 <input type="checkbox"/> mMRC Grade 3 <input type="checkbox"/> mMRC Grade 4
mMRC (Modified Medical Research Council) Dyspnoea Scale	
Surgical Interventions (if any)	
CAT Score	
GOLD Category	<input type="checkbox"/> GOLD-A <input type="checkbox"/> GOLD-B <input type="checkbox"/> GOLD-C <input type="checkbox"/> GOLD-D
VII. Laboratory results	
Haemoglobin level	<input type="checkbox"/> Below normal <input type="checkbox"/> Normal
HCT ratio	<input type="checkbox"/> Below normal <input type="checkbox"/> Normal
Erythrocyte sedimentation rate	<input type="checkbox"/> Normal <input type="checkbox"/> Above normal
CD4 Count	<input type="checkbox"/> Baseline (<200)(>200) <input type="checkbox"/> During Study(<200)(>200)
Eosinophil count	<input type="checkbox"/> Normal <input type="checkbox"/> Above normal
Viral load	<input type="checkbox"/> Baseline (<400)(>400) <input type="checkbox"/> During Study(<400)(>400)
ALT level	<input type="checkbox"/> Normal <input type="checkbox"/> Above normal
Serum creatinine	<input type="checkbox"/> Normal <input type="checkbox"/> Above normal
Blood Urea Nitrogen	<input type="checkbox"/> Normal <input type="checkbox"/> Above normal
Potassium level	<input type="checkbox"/> Normal <input type="checkbox"/> Below normal
Full blood count	
Erythrocyte sedimentation rate (ESR)	
serum phosphate	
serum calcium	
serum albumin	

XIII. Clinical status of bone fracture

Signs and symptoms	<input type="checkbox"/> Pain <input type="checkbox"/> Low trauma fracture <input type="checkbox"/> Back pain <input type="checkbox"/> Swelling <input type="checkbox"/> Loss of function <input type="checkbox"/> Loss of height <input type="checkbox"/> tenderness <input type="checkbox"/> unnatural movements <input type="checkbox"/> Others..... <input type="checkbox"/> deformity <input type="checkbox"/> shock
Risk for Osteoporosis	<input type="checkbox"/> Previous fracture <input type="checkbox"/> arthritis osteoporosis <input type="checkbox"/> FT4 <input type="checkbox"/> Serum protein electrophoresis <input type="checkbox"/> Family fractures history <input type="checkbox"/> Current smoking <input type="checkbox"/> TSH <input type="checkbox"/> Glucocorticoids <input type="checkbox"/> Alcohol 3 or more units/day <input type="checkbox"/> Testosterone <input type="checkbox"/> urine Bence John protein <input type="checkbox"/> Rheumatoid -Secondary <input type="checkbox"/> LH

IX. Previous Assessment of bone health (if any)

Type of test	<input type="checkbox"/> screening <input type="checkbox"/> diagnosis				
Type of diagnosis	Frax tool	cDEXA	pDEXA	Quantitative ultrasound (QUS)	Peripheral quantitative computed tomography (pQCT)

IX. Assessment Bone Mineral Density (If Any)			
Site of BMD	Classification of BMD (g/cm ²)	At Base Line	At the end of treatment Completion
Distal Radius	1. 0 to -0.99 2. -1 to -2.499 3. below -2.5 4. below -2.5 with fracture		
Lumber spine (L1 - L4)	1. 0 to -0.99 2. -1 to -2.499 3. below -2.5 4. below -2.5 with fracture		
Femoral neck / Total hip	1. 0 to -0.99 2. -1 to -2.499 3. below -2.5 4. below -2.5 with fracture		
Calcaneus	1. 0 to -0.99 2. -1 to -2.499 3. below -2.5 4. below -2.5 with fracture		

Flow up notes and comments:.....

- **DECLARATION:** All patients' information are to remain confidential and are not to be used for any purposes other than the intended research.

SUPPLEMENTARY FILE 2

CLINICAL EVALUATION TOOL

- Patient Code:

-Group Number:

-Case Number:

1st Assessment Step:

1. Diagnosed parents/siblings with osteoporosis?	<u>No</u>		<u>Yes</u>	<u>Comments</u>
	1	2	3	
2. Is there a family history of bone disease?	<u>No</u>		<u>Yes</u>	<u>Comments</u>
	1	2	3	
3. Is the patient above 60 years of age?	<u>No</u>		<u>Yes</u>	<u>Comments</u>
	1	2	3	
4. History of broken bones due to minor fall?	<u>No</u>		<u>Yes</u>	<u>Comments</u>
	1	2	3	
5. Being frail and falling frequently (1-5 years)?	<u>No</u>		<u>Yes</u>	<u>Comments</u>
	1	2	3	
6. History of height loss (1 inch at least)?	<u>No</u>		<u>Yes</u>	<u>Comments</u>
	1	2	3	
7. History of malnutrition or severely underweight?	<u>No</u>		<u>Yes</u>	<u>Comments</u>
	1	2	3	
8. A History of oral steroids (2 consecutive months)?	<u>No</u>		<u>Yes</u>	<u>Comments</u>
	1	2	3	
9. History of rheumatoid arthritis?	<u>No</u>		<u>Yes</u>	<u>Comments</u>
	1	2	3	
10. Is there a history of Hyperthyroidism?	<u>No</u>		<u>Yes</u>	<u>Comments</u>
	1	2	3	
11. Any history of metabolic disorders or DM?	<u>No</u>		<u>Yes</u>	<u>Comments</u>
	1	2	3	
12. Female/History of low testosterone levels?	<u>No</u>		<u>Yes</u>	<u>Comments</u>
	1	2	3	
13. Regular alcohol consumption (>2 units/day)?	<u>No</u>		<u>Yes</u>	<u>Comments</u>
	1	2	3	

14. Is the patient smoker or has a smoking history?	<u>No</u>		<u>Yes</u>	<u>Comments</u>
	1	2	3	
15. Level of physical activity less than 30 min/day?	<u>No</u>		<u>Yes</u>	<u>Comments</u>
	1	2	3	
16. Allergic history to dairy products?	<u>No</u>		<u>Yes</u>	<u>Comments</u>
	1	2	3	
17. History of low calcium or Vit-D levels?	<u>No</u>		<u>Yes</u>	<u>Comments</u>
	1	2	3	
18. Is there exposure to toxins, irritants, allergens?	<u>No</u>		<u>Yes</u>	<u>Comments</u>
	1	2	3	

Total Score: _____

2nd Assessment Step:

19. Osteoporosis Risk Evaluation Scale:

Non Osteoporotic
(18-34)

Osteoporotic
(35-54)