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What community measurements can be used to predict bone disease in patients with COPD?

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Summary
Background: Osteoporosis is common in patients with COPD. Previously we have reported that loss of fat-free mass (FFM), measured by dual X-ray absorptiometry (DXA) is associated with loss of bone mineral density (BMD). In addition, in patients with a low body mass index (BMI) and a low FFM, all had evidence of bone thinning, 50% having osteopenia and 50% osteoporosis. We explored the utility of different anthropometric measures in detecting osteoporosis in a community-based COPD population.
Methods: Patients with confirmed COPD and not on long-term oral corticosteroids ($n = 58$) performed spirometry. They underwent nutritional assessment by skinfold anthropometry, midarm circumference, calculation of both % ideal body weight (IBW) and BMI. All had DXA assessment of BMD.
Results: A total of 58 COPD patients had anthropometric measurements taken, with a mean age of 66.8 (SD 8.7) years, 31 (58%) were male, with a forced expiratory volume in 1 s (FEV_1) of 54.17 (20.18)% predicted. Osteoporosis was present at either the hip or lumbar region in 14 patients (24%). The useful anthropometric measurements identifying those with osteoporosis were both % IBW and BMI. The adjusted odds ratio for %IBW was 0.93 (95% confidence interval (CI) 0.87, 0.99), $p = 0.016$ and for BMI: 0.79 (0.64–0.98), $p = 0.03$. The receiver operating characteristics (ROC) score for both was 0.88, indicating a good fit.

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Conclusion: Osteoporosis is common, even in patients with mild airways obstruction. Nutritional assessment, incorporating a calculation of their BMI or %IBW may confer an additional benefit in detecting those at risk of osteoporosis and guide referral for BMD measurement.

Introduction

COPD is associated with considerable morbidity and mortality.[1] Awareness of the associated systemic complications such as loss of skeletal muscle mass and function, osteoporosis, insulin resistance and an increased risk of cardiovascular disease, over and above the risk of smoking is emerging.[2–5] Osteoporosis is an important risk factor for the development of hip, vertebral or long bone fracture which could add further to disability and incapacity. Additionally a hip fracture confers a greater mortality in the following year.[6]

We have previously reported that there is a greater prevalence of osteoporosis (32%) in patients with COPD compared to 13% of controls.[3] The patient population was drawn predominantly from the community and therefore included a large proportion of patients with mild-to-moderate severity airways obstruction. None of them were or had been on oral maintenance corticosteroids. This has been subsequently confirmed in different study populations.[5,7]

The universal standard method of determining bone mineral density (BMD) and hence the presence of osteoporosis is dual energy X-ray absorptiometry (DXA) scanning.[8] In the UK, DXA scanning demand for the service exceeds availability. Diagnosis of COPD does not confer a "blanket" indication to perform a DXA, but identification of a higher risk sub-group is required, given the prevalence of osteoporosis. Body composition appears to be a major determining factor for the presence of osteoporosis in the COPD patient, not reflected to the same extent in lung function, smoking pack years or gender.[3]

There are a number of ways of determining body composition. A low fat-free mass (FFM) may be present in the setting of maintained or a low body mass index (BMI) and can represent a substantial proportion of COPD patients.[1,3] Measurement of body composition in patients with COPD has become an integral part to the COPD guidelines, with both the NICE guidelines and the ATS/ERS guidelines alluding to various methodologies.[9,10] To promote their utility, any nutritional tool needs to be reproducible, reliable and inexpensive in order to facilitate its use within the community. A history of weight loss, whilst being an essential component of nutritional history taking, relies on memory recall of the patient and is renowned for its inaccuracy.

We assessed the utility of anthropometric measures of body composition to identify individuals at risk of osteoporosis and who require a DXA scan in a subset of patients from a larger group in a study of osteoporosis in COPD.[3] We selected the following measures that could be performed in primary care; BMI, midarm circumference (MAC), height squared ratio of FFM from skinfold anthropometry (SFA) and the percentage of ideal body weight (IBW).

Method

We studied a sub-group of 58 patients from a cohort of 81 enrolled in a study of osteoporosis in COPD.[3] A total of 58 patients were selected purely on the grounds that they had anthropometric measurements contemporaneous to DXA determination of BMD. They were recruited when clinically stable from primary care ($n = 51$) and respiratory outpatient clinics ($n = 7$) and represented a sub-group of patients with milder airways obstruction but similar other demographics (age, gender, smoking habit and therapy). All subjects were free from other chronic systemic inflammatory disease, malignant disease, malabsorptive states and none was on maintenance oral corticosteroids. All patients had their diagnosis confirmed by history, examination, spirometry and with a lack of reversibility to β_2-agonist.[11] Patients' age, gender, smoking pack years and daily dose of inhaled steroids (mcg/day) were obtained. The study had South East Wales Research Ethics agreement and all subjects gave written informed consent.

Anthropometry

Height and weight (Seca, Germany) were measured with the subject barefoot and wearing light, indoor clothing. The BMI was calculated (kg/m^2).

Skinfold anthropometry (SFA)

SFA was performed using Holtain callipers (Crymmych, Pembrokeshire) at both the triceps and the sub-scapular region (2 site skinfold measurement) and the subsequent % body fat mass was determined using equations described in detail in Nutrition and health in old age, 1979.[12] From this, the fat mass (FM) (kg) and FFM (body weight−FM) was subsequently calculated. The SFA–FFM was expressed as an index (FFMI)—a height squared ratio, analogous to BMI determination.[13]

Midarm circumference (MAC)

The MAC was measured using a tape measure at the midpoint of the upper arm between the olecranon process and acromion process.

Percentage ideal body weight (IBW)

The IBW was determined from the Metropolitan Life Insurance Table 1983[14] by classing frame size as a ratio of height (cm): wrist circumference (cm). The patient's weight was then classed as a percentage to the IBW. The IBW is

based on height and gender but also accounts for body frame size.

Bone mineral density (BMD) assessment—dual energy X-ray absorptiometry (DXA)

BMD at the lumbar spine and hip were measured by DXA (Hologic Discovery). The BMD is expressed as a *T* score, i.e. the number of reference population standard deviations from a reference mean value for young adults of the same gender. Using WHO guidelines, osteoporosis was classed as a *T* score <-2.5 and osteopenia as a *T* score <-1 but greater than -2.5.[15] *T* scores $\geqslant -1$ were classed as having a normal BMD. A patient was classed as having osteoporosis if the *T* scores suggested osteoporosis at either the lumbar spine or hip.

Spirometry

Spirometry was performed to calculate forced expiratory volume in 1 s (FEV_1), forced vital capacity (FVC) and their FEV_1/FVC ratio (Vitalograph, Bucks, UK).

Statistical analysis

Data analysis was by Statistical Package for Social Science (SPSS) version 14.0. Odds ratios (ORs) with 95% confidence intervals (CIs) were used to investigate the univariate association between each body composition measure performed within the primary care sector and the presence of osteoporosis. All body composition measures significant at the 10% level ($p<0.10$) were entered into a multivariate logistic regression model to evaluate which were independently associated with the presence of osteoporosis, after adjusting for known risk factors of osteoporosis (age, gender, FEV_1, smoking pack years and daily dose of inhaled steroids). The goodness-of-fit of each model was assessed using the Hosmer–Lemeshow test.[16] As a comparison, multivariate linear regression was performed using BMD (using *T* scores) as the main outcome, with R^2 was used as a test of goodness-of-fit.

The ability to discriminate between patients with osteoporosis and patients with normal BMD or osteopenia was quantified by using the area under the receiver operating characteristics curve (ROC area). The ROC area is a suitable measure to summarise the discriminative power of a diagnostic model and can range from 0.5 (no discrimination) to 1.0 (perfect discrimination). A value of 0.7–0.8 is considered to represent reasonable discrimination and values >0.8 suggest good discrimination.[17]

Results

The demographics of the patients are presented in Table 1. Details of the mean BMD measurements, mean *T* scores and numbers with osteoporosis, osteopenia and normal are presented in Table 2. Osteoporosis was found in 14 patients (24%) at either the total hip or the total lumbar spine region and 29 patients (50%) had osteopenia at either of these two sites. The remaining 15 (26%) patients had normal BMD at both sites. Using a BMI of $<20\,kg/m^2$,[13] seven patients (12%) had a low BMI.

The risk of osteoporosis was significantly increased in patients with a lower BMI, %IBW, SFA FFMI or MAC (Table 3). The risk of osteoporosis was significantly increased in female patients and also for those with a low FEV_1. After adjusting for all covariates, COPD patients with a lower BMI or %IBW were both found to be at an increased risk of osteoporosis, whilst statistical significance was lost for MAC and SFA FFMI (Table 4). The Hosmer–Lemeshow statistics of 7.39 ($p = 0.89$) and 3.64 ($p = 0.50$) for both BMI and %IBW, respectively, suggests that there is no significant difference between the predicted values from our models and those observed.

Therefore, the adjusted %IBW and BMI models equally predict the presence of osteoporosis in this sample of patients with COPD, indicating a one unit increase in %IBW or BMI predicts a reduced odds of osteoporosis or conversely

Table 1 Characteristics of patients with COPD.

	All participants ($n = 58$)	Males ($n = 31$)	Females ($n = 27$)
Age (years)	66.8 (8.7)	69.3 (8.3)	63.9(8.5)
Height (m)	1.65 (0.08)	1.69 (0.06)	1.60 (0.06)
BMI (kg/m^2)	25.63 (4.46)	26.24 (4.37)	24.93 (4.55)
Inhaled steroid (mcg/day)*	200 (0–1000)	0 (0–1000)	400 (0–1000)
Smoking habits			
Current smoker *n* (%)	22 (38%)	10 (32%)	12 (44%)
Previous smoker *n* (%)	36 (62%)	21 (68%)	15 (56%)
Smoking pack years*	35 (26.5–50)	40 (30–50)	35 (23–40)
Spirometry			
FEV_1% predicted	54.17 (20.18)	55.52 (20.10)	52.63 (20.54)
FEV_1 (l)	1.36 (0.61)	1.55 (0.66)	1.14 (0.47)

Values are mean (SD) unless stated otherwise.
Inhaled corticosteroid = betamethasone equiv. dose (mcg/day).
*Median (interquartile range).

Table 2 Bone mineral density measurements.

	BMD (g/cm^2)	*T* score	Osteoporosis	Osteopenia	Normal
Total lumbar spine region	0.92 (0.18)	−1.40 (1.55)	13 (22%)	25 (43%)	20 (35%)
Total hip region	0.86 (0.18)	−1.02 (1.29)	5 (9%)	30 (52%)	23 (39%)

Values are mean (SD) unless stated otherwise.

Table 3 Characteristics of COPD patients with and without osteoporosis and results of univariate analysis to investigate predictors of osteoporosis.

	Osteoporosis ($n = 14$)	Non-osteoporosis (osteopenia/ normal) ($n = 44$)	OR (95% CI)	*p*-Value
Age (years)	68.57 (8.0)	66.18 (8.97)	1.03 (0.96–1.11)	0.372
Gender *n* (%)				
Male	4 (29)	27 (61)	Ref.	0.039**
Female	10 (71)	17 (39)	3.97 (1.07–14.70)	
Inhaled steroid (mcg/day)*	400 (0 to 850)	0 (0 to 1000)	1.00 (0.99–1.00)	0.629
Smoking (pack years)	32.57 (23.08)	42.16 (17.75)	0.97 (0.93–1.01)	0.116
FEV_1 (l)	0.98 (0.38)	1.48 (0.63)	0.14 (0.03–0.63)	0.011
BMI (kg/m^2)	22.73 (3.82)	26.55 (4.29)	0.80 (0.67–0.94)	0.009**
SFA FFMI (kg/m^2)	15.44 (1.37)	17.77 (2.37)	0.56 (0.37–0.83)	0.005**
MAC (cm)	27.27 (3.25)	29.53 (3.58)	0.83 (0.68–0.99)	0.047**
IBW (%)	101.72 (13.89)	118.66 (17.29)	0.94 (0.90–0.98)	0.004**

Values are mean (SD) unless stated otherwise.
OR = odds ratio. OR > 1 implies higher probability of osteoporosis, OR < 1 implies lower probability of osteoporosis.
*Median (interquartile range).
**Significant values $p < 0.05$.

Table 4 Results of multivariate analyses to examine the relationship between body composition measured in the community on osteoporosis after adjusting for risk factors.

	Adjusted OR*	95% CI	*p*-Value
BMI (kg/m^2)	0.79	0.64–0.98	0.033**
SFA FFMI (kg/m^2)	0.64	0.39–1.04	0.072
MAC (cm)	0.84	0.67–1.05	0.127
IBW (%)	0.93	0.87–0.99	0.016**

*Adjusted for age, gender, FEV_1, daily dose of inhaled steroids and smoking pack years.
**Significant values $p < 0.05$.

the lower the %IBW or BMI measurement, the higher the risk of osteoporosis. The addition of any of the other body composition measurements did not improve either model.

The same results are shown using the continuous *T* scores as the outcome. The proportion of variation in BMD (using *T* scores) explained by the adjusted %IBW model for both the lumbar spine and hip region, is 28% and 52%, respectively, and for the adjusted BMI model is 27% and 58%, respectively. Again, the addition of any of the other body composition measurements did not significantly improve the model.

Predicted probabilities were calculated from the two adjusted models (%IBW and BMI) The ROC area of the adjusted %IBW and BMI models were 0.88 (95% CI 0.79–0.97), indicating a good fit (Figure 1).

Discussion

We have reported the utility of various anthropometric measurements in determining which patients with COPD are at greater risk of osteoporosis and hence would require a DXA scan. Based on the measures that can be performed in the community, BMI and %IBW are the most informative. The other anthropometric measurements studied did not have a similar predictive value. Thus, BMI and %IBW may offer a method of selecting patients for BMD determination.

The important sequelae to osteoporosis, namely hip, wrist and vertebral fractures are major worldwide problems. Besides the associated discomfort to the patient, the superimposed disability to the already respiratory impaired patient can add to the difficulties encountered, both short and long term. The fiscal enormity of fractures not only encompasses the direct costs of inpatient stay and associated reparative costs of the fracture but the indirect costs

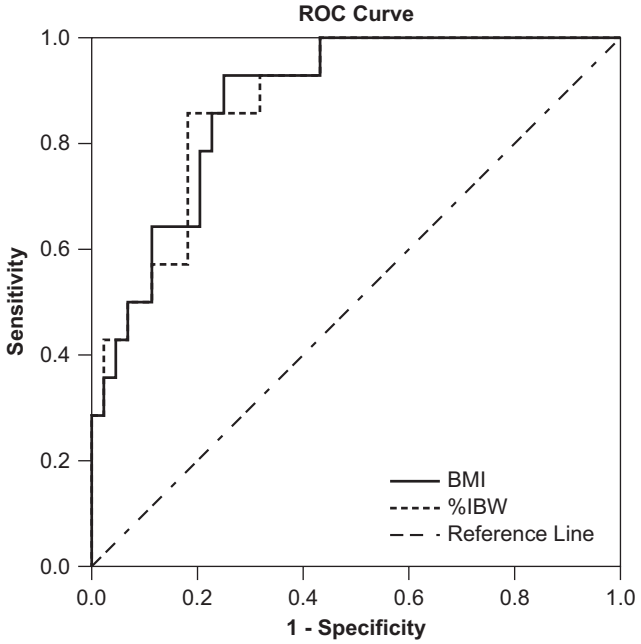

Figure 1 Receiver operating characteristic for %IBW and BMI. BMI and %IBW are adjusted for age, gender, FEV_1, daily dose of inhaled steroids and smoking pack years.

during recuperation in an older population and also to lost working days. The respiratory restrictions of COPD may also complicate or prohibit the anaesthetic procedures associated with managing certain fractures. In itself, vertebral fractures can add to the respiratory dysfunction—reported as a 10% reduction in FVC[18] in patients.

In this population of COPD patients, drawn predominantly from the community, we identified 24% of our patients as having osteoporosis, previously undetected, and a further 50% having osteopenia, compared to a previous report 13% of controls suffering osteoporosis and 22% having osteopenia. Other studies have identified evidence of some bone disease in over 50% of the population,[19] others looked specifically at osteoporosis, found in 33%[20] or vertebral fractures in up to 63% patients.[21,22]

The introduction of the NICE and the ATS/ERS guidelines emphasise the "non-airways" elements of COPD and that a composite picture of COPD includes assessment of exercise ability, nutritional status and quality of life.[9,10] Whilst many studies present body composition as a "secondary care" issue, there are measures that can be performed in the community to assess nutritional status and could be incorporated into the COPD assessment.

The BMI and the related measure of %IBW predicted osteoporosis in these patients, even allowing for other traditional risk factors such as age, gender, lung function and other more controversial factors such as inhaled corticosteroids. The calculation of %IBW relates the subjects' weight not only to a height ratio but also to an assessment of build (based on the wrist circumference) and therefore requires little training. This measurement appeared to contribute only a minor additional benefit to BMI alone. Given the more universal utility of BMI, this appears a more appropriate assessment. Incalzi et al.[23] detected a difference in MAC between those patients with COPD who also had osteoporosis or not but failed to demonstrate its use in predicting osteoporosis. SFA requires training in order to achieve reliable, reproducible results. Inter-observer variation and repeatability of such measurements needs to be borne in mind also, even after training. In addition, as the calipers reach maximal opening in the obese person, the precision of calculations by SFA is less. We used a 2 site evaluation of SFA–FFMI, one of which was a central trunk measurement. This may not detect other areas of FFM loss such as lower limb loss in patients which may account for SFA–FFMI failing to demonstrate what we have previously shown with DXA-based calculation of FFMI,[3] despite the fact that one person with training performed all the measurements. Therefore the robust measures of FFMI by DEXA body composition analysis are not achievable with SFA and cannot be extrapolated to the risk of osteoporosis. Bioelectrical impedance using validated equipment is one method to measure FFM although it is expensive and more cumbersome than other community applied anthropometry tools included in this study.[24] The utility of all of these body composition parameters in risk stratifying patients other than for bone disease is beyond the scope of this paper and we advocate further research to evaluate the inclusion of body composition risk stratification in community patients.

This work highlights that many body composition parameters have been given arbitrary cut-off's and can vary across guidelines.[9,10,25,26] Variation with guidelines may reflect the healthy subject populations which differ across continents and even countries as well as changing socio-environmental factors with time. The NICE/BTS guidelines advocate a BMI of 20 kg/m^2.[9] This demarcation has been shown to have prognostic significance in mortality.[26] More recently, Celli et al.[25] suggested that a BMI of <21 kg/m^2 as equating to worse survival. We found that the lower 5th percentile of this South Wales population for BMI was 20.3 kg/m^2.

The cause for osteoporosis in COPD patients is likely to be multifactorial. It cannot be fully explained by smoking history or by gender. The betamethasone equivalent inhaled corticosteroid dose was not different between those with osteoporosis and those without and our patients were selected for never having received oral maintenance corticosteroids. Systemic inflammation, catabolic intermediary metabolism, hypogonadism, short course "rescue" oral corticosteroid therapy, periods of bed rest during exacerbations and physical inactivity are all likely to play a role.[27–30] Identification of milder forms of BMD loss such as osteopenia may provide an opportunity to readdress nutritional and physical activity optimisation in order to prevent further deterioration in BMD leading to osteoporosis. Risk of fracture is a continuum—Marshall et al.[31] demonstrated that for every 1 standard deviation drop in BMD, the risk of fracture increased by 1.5–2.5 fold. Of note, the presence of vertebral fracture should necessitate the commencement of treatment, regardless of BMD.[32] None of our patients had clinical grounds to suspect osteoporosis or vertebral fracture prior to inclusion in the study. Other measures to limit fracture risk such as maintaining stability are important—a factor that can be influenced by peripheral muscle mass and function, often reduced in patients with COPD.[33]

Currently, within the UK, initiatives are being undertaken to improve spirometry usage and interpretation of the

results.[9,34] Opportunities to address training of a more detailed nutritional and functional assessment need to be advocated. Targets in COPD are becoming more and more orientated to early detection and preventative therapy. COPD by nature is slowly progressive and the earlier the extent of the disease and its related disabling characteristics identified, targeted measures could be implemented. Meanwhile, therapy options in place such as focused smoking cessation, appropriate exercise prescription and pulmonary rehabilitation together with optimal management to reduce exacerbations are to be commended and may also confer additional assistance to bone health.

Limitations

This work is based on a small group of identified patients who were free from chronic oral corticosteroid treatment and other metabolic, neoplastic and inflammatory disease. The Royal College of Physicians offers recommendations on management of the patient on maintenance oral corticosteroids, but identifying osteoporosis in the vast majority of patients with COPD not on maintenance oral corticosteroids has to date not been addressed.[35] In practice, the group we report is select and further larger studies are warranted to explore the possibilities and benefits of simple anthropometry in population studies where patients may be on oral corticosteroids or have additional co-morbidities which may also affect body composition and BMD.

Conclusion

In conclusion, there is a need to detect osteoporosis in patients with COPD, where this associated morbidity is common and present across the spectrum of severity of airways obstruction. A recognised influence on osteoporosis is body composition and this study advocates that BMI or %IBW can identify the high-risk sub-group of patient and strengthens the advice in guidelines on the use of BMI and body weight. Similarly, failure of skin fold or MAC to predict osteoporosis emphasises the current use of BMI. We would encourage further studies to be performed to incorporate a nutritional assessment, into the annual review of the patient with COPD within the community and address targeted approaches to identify patients who may have concurrent osteoporosis.

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