

## An association between respiratory function and hip bone mineral density in older men: a cross-sectional study

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**Abstract** The association between respiratory function and bone mineral density (BMD) among women living in the community has been reported previously. We examined the association between forced expiratory volume in 1 s (FEV<sub>1</sub>) and BMD measured at hip using dual-energy X-ray absorptiometry in a group of 947 men (aged 65 to 76 years) recruited from general practice age-sex registers in Cambridge between 1991 and 1995. A positive and significant correlation was seen between FEV<sub>1</sub> and BMD measured at total hip, femoral neck, and trochanter. A unit change (1 l) in FEV<sub>1</sub> was associated with a change of BMD by 0.019, 0.017, and 0.026 g/cm<sup>2</sup> in the total hip, femoral neck, and trochanteric region, respectively. These associations were independent of possible confounding factors such as age, height, weight, smoking habit, major disease prevalence, and medications, which might affect bone metabolism. In categorical analyses, the highest BMD was seen in the highest FEV<sub>1</sub> quartile, while the lowest BMD was seen in the lowest FEV<sub>1</sub> quartile. This pattern was seen in all three skeletal sites and was independent of covariates listed above. Compared with the bottom FEV<sub>1</sub> quartile, mean hip BMDs in the top quartile were 2–3.5% higher. The exact mechanism of this association is not clear to us. One plausible explanation is that respiratory function and bone health both reflect common but as yet unknown determinants.

**Keywords** Bone density · Community · Forced expiratory volume · Men · Osteoporosis · Respiratory function

### Introduction

The association between respiratory function and bone mineral density among patients with chronic respiratory diseases has been reported previously [1]. Further, higher risk of osteoporosis among subjects with airflow limitation has been demonstrated in a recent study [2]. We have previously reported a positive and continuous association between forced expiratory volume in 1 s (FEV<sub>1</sub>) and bone mineral density (BMD) of the proximal femur in women living in the general community in the UK [3]. This association was independent of age, height, weight, smoking habit, medication use, and presence of chronic diseases, which can affect bone metabolism. We wished to examine the association between respiratory function FEV<sub>1</sub> and hip BMD in a group of older men living in the community.

### Methods

This study involved men who participated in the Cambridge General Practice Health Study, which invited men aged 65 or above, resident in the community, and identified using general practice age and sex match registers between 1991 and 1995. Those who consented for the health survey completed the health and lifestyle questionnaire, which gathered information on their current and past medical history. Height and weight were measured in light clothing without shoes during the physical examination by trained personnel at Addenbrooke's Hospital, Cambridge. History of cancer, heart disease, stroke, and respiratory disease, were assessed using self-completed questionnaires. The use of systemic corticosteroids was recorded as "never" or "ever," while participants were categorized into three groups on their smoking habits: "current smokers," "past smokers," and "never smoked." BMD of the nondominant proximal femur was measured using the Hologic QDR 1000 densitometer (Hologic, Waltham, MA, USA). The

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**Table 1** Descriptive data of 947 men aged 65–76 years, according to FEV<sub>1</sub> quartiles in the Cambridge General Practice Study

| Parameter                           | Quartile 1 (n=234) | Quartile 2 (n=234) | Quartile 3 (n=240) | Quartile 4 (n=236) | p Value |
|-------------------------------------|--------------------|--------------------|--------------------|--------------------|---------|
| Characteristics                     | Mean (SD)          | Mean (SD)          | Mean (SD)          | Mean (SD)          |         |
| Age, years                          | 69.9 (2.8)         | 69.5 (2.8)         | 69.1 (2.7)         | 68.4 (2.5)         | < 0.001 |
| Height, cm                          | 169.9 (6.5)        | 177.7 (6.2)        | 172.3 (6.4)        | 175.5 (6.1)        | < 0.001 |
| Weight, kg                          | 76.2 (11.9)        | 77.3 (10.5)        | 78.5 (11.5)        | 79.4 (9.7)         | 0.009   |
| BMI, kg/m <sup>2</sup>              | 26.3 (3.8)         | 26.5 (3.2)         | 26.4 (3.2)         | 25.7 (2.6)         | 0.008   |
| FEV <sub>1</sub> , liter            | 1.79 (0.31)        | 2.45 (0.12)        | 2.83 (0.11)        | 3.37 (0.28)        | < 0.001 |
| Total hip BMD, g/cm <sup>2</sup>    | 0.935 (0.151)      | 0.959 (0.141)      | 0.963 (0.146)      | 0.982 (0.133)      | 0.004   |
| Femoral neck BMD, g/cm <sup>2</sup> | 0.759 (0.133)      | 0.778 (0.117)      | 0.782 (0.126)      | 0.803 (0.121)      | 0.003   |
| Trochanter BMD, g/cm <sup>2</sup>   | 0.712 (0.124)      | 0.746 (0.123)      | 0.751 (0.131)      | 0.766 (0.119)      | < 0.001 |
| Percentage of men with              | Number (%)         | Number (%)         | Number (%)         | Number (%)         |         |
| COAD/asthma                         | 88 (37.6)          | 42 (17.7)          | 31 (12.9)          | 22 (9.3)           | < 0.001 |
| Cancer                              | 14 (6.0)           | 11 (4.6)           | 12 (5.0)           | 14 (5.9)           | 0.890   |
| Cardiovascular disease              | 43 (18.4)          | 37 (16.0)          | 24 (10.0)          | 28 (11.9)          | 0.035   |
| Current smoking habit               | 41 (17.5)          | 27 (11.4)          | 13 (5.4)           | 9 (3.8)            | < 0.001 |
| Steroid use                         | 20 (8.5)           | 5 (2.1)            | 12 (5.0)           | 4 (1.7)            | 0.001   |

coefficient of variance for hip BMD measurements in our unit was 1.6% for the femoral neck, 1.5% for the trochanter, and 3.0% for Ward's triangle [4].

Forced expiratory volume in the 1st second (FEV<sub>1</sub>) was measured twice using a portable spirometer (Micromedical, UK) [5]. The higher reading of the two measurements was used in the analysis.

#### Statistical analyses

Men were divided into quartiles according to FEV<sub>1</sub>, and descriptive data of each quartile were given as mean (SD) or percentages (number). Correlations between hip BMD, age, weight, height, and FEV<sub>1</sub> as continuous variables were examined using Pearson correlation coefficients. Mean BMDs at total hip, femoral neck, and trochanter were compared using multivariate analysis of variance, initially adjusted for age, height, and weight, and then additionally for possible confounders such as respiratory disease, cardiovascular disease, and smoking habit. A linear regression model was fitted to examine the relationship of FEV<sub>1</sub> (independent variable) on BMD (dependent variable) with and without covariates

in the model. Data were analyzed using SPSS software, version 10 for Windows.

## Results

### Descriptive data

The descriptive data of 947 men aged 65 to 76 years (mean 69.2 years, SD=2.8) are shown in Table 1. Compared with men in the highest quartile of FEV<sub>1</sub>, men in the lowest quartile were older, shorter, and lighter, and had lower average BMDs in all hip regions. The percentage of current smokers, corticosteroid users, and men with history of cardiovascular disease and respiratory disease were significantly higher in the lowest FEV<sub>1</sub> quartile when compared with the highest.

### Association between FEV<sub>1</sub> and BMD

Significant and positive correlations were observed between FEV<sub>1</sub> and BMD measured in all three hip sites. Age, weight, and height also showed significant correlations with both BMD and FEV<sub>1</sub> (Table 2).

**Table 2** Correlations between

|                  | Weight            | Height           | Total hip BMD    | Femoral neck BMD | Trochanteric BMD | FEV <sub>1</sub>  |
|------------------|-------------------|------------------|------------------|------------------|------------------|-------------------|
| Age              | -0.124<br>< 0.001 | -0.087<br>0.007  | -0.106<br>0.001  | -0.105<br>0.001  | -0.073<br>0.026  | -0.198<br>< 0.001 |
| Weight           | -                 | 0.482<br>< 0.001 | 0.441<br>< 0.001 | 0.376<br>< 0.001 | 0.339<br>< 0.001 | 0.128<br>< 0.001  |
| Height           | -                 | -                | 0.208<br>< 0.001 | 0.192<br>< 0.001 | 0.233<br>< 0.001 | 0.301<br>< 0.001  |
| Total hip BMD    | -                 | -                | -                | 0.854<br>< 0.001 | 0.910<br>< 0.001 | 0.137<br>< 0.001  |
| Femoral neck BMD | -                 | -                | -                | -                | 0.781<br>< 0.001 | 0.132<br>< 0.001  |
| Trochanteric BMD | -                 | -                | -                | -                | -                | 0.167<br>< 0.001  |

age, weight, height, hip BMD, and FEV<sub>1</sub>. All variables were entered as continuous measures

**Table 3** Adjusted mean (SD) BMD values in FEV<sub>1</sub> quartiles in men aged 65–76 years, in the Cambridge General Practice Study. *Fem neck BMD* femoral neck BMD, *Troch BMD* trochanteric BMD

|                            | Quartile 1    | Quartile 2    | Quartile 3    | Quartile 4    | <i>p</i> Value |
|----------------------------|---------------|---------------|---------------|---------------|----------------|
| Total Hip BMD <sup>a</sup> | 0.945 (0.012) | 0.963 (0.012) | 0.959 (0.012) | 0.973 (0.012) | 0.18           |
| Total Hip BMD <sup>b</sup> | 0.950 (0.012) | 0.963 (0.012) | 0.957 (0.012) | 0.970 (0.012) | 0.45           |
| Fem neck BMD <sup>a</sup>  | 0.768 (0.012) | 0.781 (0.012) | 0.779 (0.012) | 0.795 (0.012) | 0.15           |
| Fem neck BMD <sup>b</sup>  | 0.773 (0.012) | 0.782 (0.012) | 0.777 (0.012) | 0.792 (0.012) | 0.41           |
| Troch BMD <sup>a</sup>     | 0.721 (0.012) | 0.748 (0.012) | 0.749 (0.012) | 0.756 (0.012) | 0.01           |
| Troch BMD <sup>b</sup>     | 0.725 (0.012) | 0.74 (0.012)  | 0.748 (0.012) | 0.752 (0.012) | 0.09           |

<sup>a</sup>Adjusted for age, weight, and height

<sup>b</sup>Adjusted for age, weight, height, respiratory diseases, cardiovascular diseases, smoking, and steroid use

Mean (and SD) BMDs of total hip, femoral neck, and trochanter in FEV<sub>1</sub> quartiles are shown in Table 3. After adjusting for possible confounding factors, the highest BMDs were observed in the highest FEV<sub>1</sub> quartile, while the lowest BMDs were seen in the lowest FEV<sub>1</sub> quartile, and this pattern was seen in all three hip regions. Mean BMDs generally showed an upward trend with increasing FEV<sub>1</sub>.

Results of the regression analysis are shown in Table 4. A significant and positive relationship, independent of the effects of age, height, weight, smoking habits, prevalent disease, or steroid medication was observed between FEV<sub>1</sub> and hip BMD. A unit change in FEV<sub>1</sub> (1 l) was associated with a statistically significant 0.031, 0.027, and 0.034 g/cm<sup>2</sup> change in BMD in total hip, femoral neck, and trochanter, respectively. Including the potential confounding factors in the model attenuated these associations but they still remained significant. Excluding current smokers or steroid users in the regression model did not materially alter the regression slopes (data not shown).

## Discussion

We previously reported a continuous and positive association between FEV<sub>1</sub> and hip BMD among community-living women who participated in the same study. These women were recruited from the same community and were assessed by the same team in the same manner. The association seen in these women was independent of age, body mass index, smoking habit,

**Table 4** Regression coefficients of BMD with FEV<sub>1</sub> in men aged 65–76 years, in the Cambridge General Practice Study

|   | Coefficient<br>(per 1 l/s) | SE    | <i>p</i> Value |
|---|----------------------------|-------|----------------|
| Total hip BMD, unadjusted               | 0.031                      | 0.008 | <0.001         |
| Total hip BMD, adjusted <sup>a</sup>    | 0.019                      | 0.007 | 0.006          |
| Femoral neck BMD, unadjusted            | 0.027                      | 0.007 | <0.001         |
| Femoral neck BMD, adjusted <sup>a</sup> | 0.017                      | 0.006 | 0.005          |
| Trochanter BMD, unadjusted              | 0.034                      | 0.008 | <0.001         |
| Trochanter BMD, adjusted <sup>a</sup>   | 0.026                      | 0.006 | <0.001         |

<sup>a</sup>Adjusted for age, weight, height, respiratory diseases, cardiovascular diseases, smoking, and steroid use

and history of diseases or medications which might influence bone metabolism [3]. The association was evident in young, middle, and older age groups almost to the same extent. Although the exact mechanism of this association was not clear, a common underlying determinant, such as physical activity was a plausible explanation.

In the current study, a positive correlation was seen between respiratory function measured by FEV<sub>1</sub> and hip BMD measured at total hip, femoral neck, and trochanter in men aged 65–76 years. The association was independent of age, weight, height, smoking habits, steroid use, and prevalent diseases, which might affect bone metabolism. After adjusting for above potential confounding factors, mean hip BMD of men in the highest FEV<sub>1</sub> quartile was approximately 2.0–3.5% higher when compared with mean BMD in those in the lowest quartile. This is somewhat less than what was seen in women previously [3]. BMD in all three hip regions showed a general upward trend from the lowest to the highest FEV<sub>1</sub>. In contrast to women, the mean differences in BMD in FEV<sub>1</sub> quartiles were not statistically significant except in the trochanteric area. However, more sensitive regression analyses showed statistically significant relationships.

In the regression analysis, the magnitude of the association seen between respiratory function and BMD in men was weaker than that seen in the subgroup analysis of women over 65 years [3]. In older women (*n* = 1,195), a unit (1 l) change in FEV<sub>1</sub> was associated with a change in BMD of 0.039, 0.029, and 0.040 g/cm<sup>2</sup> in total hip, femoral neck, and trochanter, respectively. In the current study involving men of a similar age group, corresponding figures were 0.019, 0.017, and 0.026 g/cm<sup>2</sup>. Nevertheless, while these differences were small, and observed mean BMDs for men did not reach osteoporosis or osteopenia thresholds in the lowest quartiles, they may still be of interest in terms of understanding the mechanisms involved in bone loss.

The differences we observed in the association between respiratory function and BMD between men and women could partly be due to differences in sample sizes and, hence, lack of power, although a real gender difference cannot be excluded. Gender differences were observed in both BMD and hip geometry [6, 7]. Gender differences in BMD were observed early in life, between

prepubertal men and women [8] and also in forearm bones among Japanese [9]. If physical activity is the link between BMD and respiratory function, the association might be expected to be greater among men, who are more physically active than women. Other possible factors such as smoking, alcohol consumption, prevalence of diseases, and use of drugs which can affect bone metabolism may also differ in men and women. Although recruited from the same community, considerable differences in the prevalence of current smokers and in the number of patients with a history of cancers and other relevant diseases were seen between men in the current study and women in our previous study [3], reflecting the well-recognized sex differences in health.

Our study has several limitations. Selection bias is unlikely to explain the relationship unless nonresponders differed from responders with respect to the relationship between respiratory function and BMD. That is, that nonresponders were more likely to have good respiratory function and low BMD or vice versa, which does not seem plausible. There are measurement errors in assessment of BMD and respiratory function, but random measurement error would attenuate any relationship. We did not quantify smoking and corticosteroid use, and they were used as categorical variables in the analysis. The effects of smoking and corticosteroids both on BMD and lung functions are dose related, so we may not have adjusted adequately for smoking and steroid use. Nevertheless, regression analyses after excluding steroid users and current smokers found similar relationships between respiratory function and BMD. We did not include spine BMD in the analysis, since spine BMD is influenced by the presence of degenerative changes and vertebral fractures. Vertebral fractures reduce lung function, and the extent of this problem was not known to us in this study.

The association between respiratory function and BMD seen in these studies need further exploration. Whether respiratory function has a direct influence on

BMD or both measures reflect a common predisposing factor is unknown. Elucidating the nature of the relationship may help in the understanding of the determinants and prevention of bone loss in later life.

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