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Original Investigation

Increasing body fat mass reverses bone loss in osteopenia as detected by dual-energy X-ray absorptiometry scans

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Abstract

Objective: Low body mass index (BMI) is a known risk factor for osteoporosis and is part of the FRAX™ 10-year fracture risk stratification tool for predicting fragility fractures. Little is known regarding the effects of changing body composition on bone mineral density (BMD). However, increasing fat mass (FM) improves BMD in young women with anorexia nervosa. This study aimed to assess whether changes in FM over time affected BMD in the general population.

Material and Methods: Data was collected from patients who underwent dual-energy X-ray absorptiometry (DEXA) assessment between 2004 and 2011. Patients were included if they had multiple scans, including FM measurements. Our scanners limited these to scans of the lumbar spine. Linear regression analysis was performed to identify the relationship between changes in FM and BMD. Backwards stepwise linear regression analysis was performed to identify confounding factors, including sex, risk factors, previous fractures, and baseline BMI.

Results: In this study, 23,239 patients were included, of which 702 met the inclusion criteria. There were 609 (86%) females and 93 (13%) males with a mean age of 64.5 (SD 11.2) years at first scan. We identified a strong positive correlation between increasing FM and BMD between scans (coefficient 28.4; $p<0.01$; 95% CI, 26.6–30.1). Previous pelvic and femur fractures and a history of inflammatory diseases were also associated with increasing FM ($p<0.05$). This relationship was true regardless of patients BMI at their first scan.

Conclusion: These findings suggest that patients at high risk of fragility fractures should be encouraged to increase their FM as long as they are at a low risk for disease states related to high FM.

Keywords: Osteopenia, osteoporosis, bone mineral density, body fat mass, morphometry

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Introduction

Osteoporosis is defined as a systemic skeletal disease characterized by a low bone mass and micro-architectural deterioration of the bone tissue with a consequent increase in bone fragility and susceptibility to fracture (1). It is defined in terms of bone mineral density (BMD) compared with that of a young person by providing a "t-score" (2). It has been recognized as great burden on society by the World Health Organization because of the high associated morbidity and mortality and the increasing incidences. It is estimated that the prevalence of hip fractuvres will be >6 million worldwide by 2050 (1).

Treatment for osteoporosis is largely based on primary prevention. Many tools exist to help estimate the risk of future fragility fractures so that preventative treatment can be appropriately targeted (3, 4). However, while these tools are often very specific, there is doubt regarding their sensitivity compared with BMD measurement alone (5, 6). To accurately predict the future risk of fracture, we need to understand better the factors that affect the change in BMD.

Low body mass index (BMI) has been shown to be an independent risk factor for fragility fractures (7, 8). The effect of change in weight and body composition on fracture risk is not well documented. Data on the effect of change in weight is variable. Some studies reported that increase in weight is a protective feature in BMD (8-12). Others found this was only true for patients with a low starting BMI (13), whereas the reverse was true in other data (14). BMI is an inaccurate tool for measuring body morphology, and an interesting development has been the analysis of changes in body composition and its effect on BMD. This research was largely limited to young women (15, 16), particularly those recovering from anorexia nervosa. These subjects were not a representative of the general population, but preliminary results reveal that BMD increases with increasing body fat mass (FM). No study has

Table 1. Risk factor categories

Risk factor
Drugs
Family history
Gastrointestinal disease
Past medical history
Inflammatory disease (not including rheumatoid arthritis)
Malignancy
Menopause
Metabolic disease
Rheumatoid arthritis
Current smoker
Former smoker
Corticosteroid use

Table 2. Previous fracture locations

Fracture locations
Femur
Forearm
Humerus
Pelvis
Ribs
Spine
Tibia/Fibia

examined the effects of changing FM on BMD in the general population. This data would be helpful when developing new tools to predict future risks of fragility fractures and could help us target preventive treatments more effectively. Therefore, this prompted us to analyze the body composition in patients undergoing dual-energy X-ray absorptiometry (DEXA) scans. DEXA scans are the gold standard method of calculating FM (17).

This study aimed to assess the effect of changes in FM on BMD over time. Moreover, we wished to identify other factors independently associated with change in FM to ensure the accuracy of our results.

Material and Methods

Data was analyzed from patients having DEXA assessment between 2004 and 2011 (in a District General Hospital setting in North West England). Information on patient demographics and referral indications were collected from referral requests.

Table 3. Patient demographics and results for t-score and FM

	Mean	SD	Min.	Max.
Baseline age (years)	64.5	11.3	20.0	86.6
Baseline BMI (kg/cm^2)	26.2	4.6	15.8	45.3
Scan interval (years)	3.0	0.9	0.1	5.3
Baseline t-score	1.1	1.2	- 1.8	5.0
Repeat t-score	1.4	0.5	- 2.4	4.6
t-score change (per year)	0.0	0.5	- 2.4	2.9
Fat mass change (per year)	- 2.9	48.8	- 177.9	202.8

FM: fat mass; BMI: body mass index; SD: standard deviation

Table 4. Prevalence of risk factors and previous fractures in study cohort

	All - 702	Female - 609	Male - 93
Drugs	112 (15.9%)	103 (16.9%)	9 (9.7%)
Family history	151 (21.5)	140 (23.0%)	11 (11.8%)
Gastrointestinal disease	119 (16.9%)	91 (14.9%)	28 (30.1%)
Past medical history	122 (17.4%)	104 (17.1%)	18 (19.4%)
Inflammatory disease	55 (7.8%)	46 (7.6%)	9 (9.7%)
Malignancy	10 (1.4%)	10 (1.6%)	0 (0.0%)
Menopause (early onset)	107 (15.2%)	107 (17.6%)	0 (0.0%)
Metabolic disease	54 (7.7%)	42 (6.9%)	12 (12.9%)
Rheumatoid arthritis	64 (9.1%)	53 (8.7%)	13 (14.0%)
Current smoker	72 (10.2%)	59 (9.7%)	13 (14.0%)
Former smoker	212 (30.2%)	162 (26.6%)	50 (53.8%)
Corticosteroid use	253 (36.0%)	199 (32.7%)	54 (58.1%)
Femur	20 (2.9%)	19 (3.11%)	1 (1.1%)
Forearm	159 (22.6%)	154 (25.3%)	5 (5.4%)
Humerus	33 (4.7%)	31 (5.1%)	2 (2.2%)
Pelvis	3 (0.4%)	3 (0.4%)	0 (0%)
Ribs	40 (5.7%)	38 (6.2%)	2 (2.1%)
Spine	56 (8.0%)	43 (7.1%)	13 (14.0%)
Tibia/Fibia	68 (9.7%)	65 (10.7%)	3 (3.2%)

When patients attended, they were asked regarding their drug history, focusing on medication that could adversely affect the bone density. At every scan, patients were weighed and their height was measured. Risk factors gathered from referral requests were divided into 12 groups (Table 1). Previous fractures were also sub-divided by fracture location (Table 2). This methodology is also detailed elsewhere by Oldroyd et al. (18). The study was approved by the local ethics committee of our hospital. Written consent was not required as per ethics committee guidance.

We performed a longitudinal, population-based study on the basis of the following inclusion criteria. Patients must have had >1 DEXA assessment within the time period. The assessment must also have measured FM of subjects and calculated a t-score. Using our scanner, this restricted results to antero-posterior scans of the lumbar spine. Because this was an observational study, sample size calculation was not required.

Bone density was measured using t-score. Δ t-score was calculated by subtracting the re-

Table 5. Backwards linear regression of fat-mass and t-score with independent risk factors

Variable	Coefficient	Standard error	p	95% Confidence interval
t-score change	28.363	0.876	<0.001	26.643–30.082
Pelvic fracture	16.120	6.807	<0.05	2.756–29.483
Femur fracture	5.580	2.664	<0.05	0.348–10.811
Inflammatory disease	3.454	1.649	<0.05	0.216–6.691

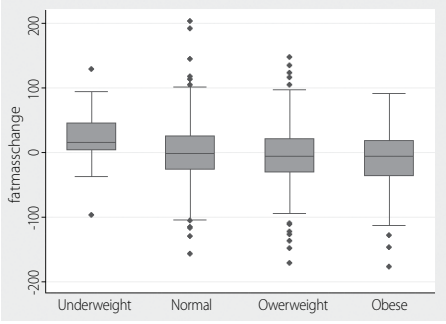

Figure 1. Box and whisker plots of change in fat-mass by body mass index (BMI) weight category

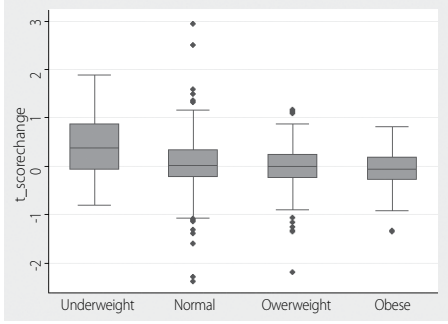

Figure 2. Box and whisker plots of change in t-score by body mass index (BMI) weight category

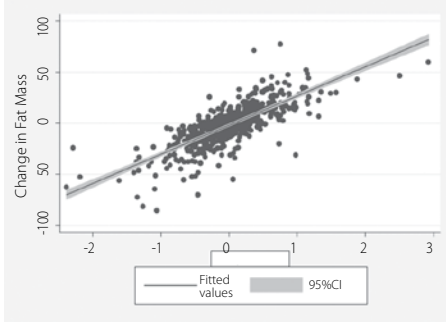

Figure 3. Scatter graph of change in fat-mass vs. change in t-score with trend line and confidence intervals (CI)

sults from the first scan by those in the second and then dividing by the scan interval. Change in FM was also calculated as (fat mass 2–fat mass 1)/interval between scans. This was done because of the variations in scan interval, providing a measure t-score and FM change per unit time.

Statistical analysis

Simple linear regression analysis was performed to identify the correlation between changes in FM and bone density. Forward and backward stepwise linear regression models were fitted to the data with the change in FM as the dependent variable. The change in t-score was treated as an explanatory variable with the following also included as explanatory variables: change in t-score, sex, risk factors, previous fractures, baseline BMI, and age at menopause. Statistical analysis was performed using Stata SE version 11.2 (StataCorp., College Station; Texas, USA).

Results

In this study, 23,239 patients were included, of which 702 met our inclusion criteria. There were 609 females (87%) and 93 males (13%). Data on patient age at the first scan, scan interval, baseline BMI, t-scores and change in FM can be found in Table 3. This table shows a wide age range, with both young-adults and more elderly patients being included. Furthermore, there is a broad spread of baseline BMIs with patients ranging from underweight to obese. At the time of the first scan, 3.4% of patients were underweight, 39.7% were of normal weight, 37.6% were overweight, and 19.2% were obese. There was no significant difference between patients in these different BMI categories in terms of change in FM or change in t-score (Figure 1, 2). Prevalence of risk factors and previous fractures can be found in Table 4. Linear regression analysis identified a strong positive correlation between increasing FM and t-score between scans (Figure 3). Refer to Table 5 for results of backwards stepwise linear regression analysis. There is a statistically significant relationship between increasing FM and increasing t score. However, patients with increasing FM are more likely to have had a previous fracture of the pelvis or femur and are more likely to have a history of inflammatory disease. Results pf the forward stepwise linear regression analysis results were equivocal and have not been included for brevity.

Discussion

Our results would suggest that increasing FM is not just protective of BMD but improves it. This was not limited by the starting BMI of each patient, which goes against previous studies looking at BMD and weight change (13, 14). It may be beneficial to include attempting to gain FM (or at least not lose it) in lifestyle interventions for patients at a high risk of future fragility fractures. However, fragility fractures are not the only cause for morbidity and mortality; therefore, any such advice would be required to be taken in the context of a holistic assessment of patient health (19). Increased cardiovascular disease (CVD) risk is associated with increasing body fat (20). To avoid increasing the risk of CVD, it may be prudent to only recommend increasing fat mass in patients who are underweight (BMI <18.5) and >60 years of age. In this age range, patients who are underweight have the same or higher levels of mortality from CVD and metabolic syndrome than patients with a BMI of 18.5–25 (21). This should maximize the possible benefits from decreasing the risk of fragility fractures, whereas minimizing the other weight associated health risks. These risks dramatically increase in patients of all ages with a BMI >25. This makes increasing FM to improve BMD an unsuitable way to decrease their risk of fragility fractures. However, it is interesting that there is evidence of a link between low BMD and high risk of CVD. This link is not completely understood; however, it is thought to be related to shared pathophysiology (22). The nature of this link could significantly impact where FM-related lifestyle advice should be targeted. If it is possible to reduce the risk of CVD by increasing BMD, then there is less risk attached to getting patients with low BMD to increase their FM. However, if problems, such as atherosclerosis, cause BMD to decrease, then increasing FM is likely to have little effect on increasing BMD and thus, put the patient at much greater risk of CVD. This is an area that must be better understood before we can make any reliable recommendations. As such, we cannot include the effects of FM on BMD in calculations of future fracture risk at this time.

This study does not have a very large sample size, particularly for males. Ideally, we would expand the length of data collection or use results from multiple units to expand the data set. Further-

more, the study only utilizes BMD results from the lumbar spine. This is a weight-bearing area, which has previously been shown to increase BMD with weight gain (8), and change in FM has also been found to affect BMD here in younger patients (15). Both of these suggest that the spine is the best area to focus on. However, it would be better to have data on BMD changes at multiple locations as fragility fractures commonly occur at locations other than the lumbar spine.

The study only analyzed patients who had two scans because of the limited time span of data collection. It would be useful to study how FM change over a longer time period, with more DEXA scans, affects BMD. Moreover, we did not have data on previous weight gain/loss patterns for our patients, which in some patient groups can limit BMD increase related to weight gain (23).

Baseline t scores were fairly high, with few patients with osteopenia. On repeat, some patients who had decreased in FM had become osteopenic. However, none of the patients in the study were osteoporotic at baseline or on their second scan. Although our results demonstrate that osteopenia can be avoided by gaining FM and reversing bone loss, we cannot say if this is true for patients who are already osteoporotic. Future studies should aim to focus on these patients.

Increasing FM appears to improve BMD in males and females, and this is regardless of the patient's initial BMI. However, with the relationship between CVD and low BMD poorly understood, we can not predict how increasing FM would affect the overall morbidity and mortality of patients with low BMD. Therefore, it appears to be sensible to encourage only patients with BMI <18.5 who are aged >60 years to try and increase their FM to reduce fragility fracture risk.

Ethics Committee Approval: Ethics Committee approval was received for this study from the North West Ethics Committee.

Informed Consent: N/A.

Peer-review: Externally peer-reviewed.

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Conflict of Interest: No conflict of interest was declared by the authors.

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