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Bone Loss Accompanying Voluntary Weight Loss in Obese Humans

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ABSTRACT

Dual-energy x-ray absorptiometry was performed in 51 obese patients before and after 15 weeks on a low-calorie diet. Of these patients 39 were scanned 6 months later. Total and regional body bone mineral, fat mass, and fat free mass were measured. In the control group, 9 normal volunteers were scanned with up to 23 kg lard distributed anteriorly, and 9 volunteers were scanned with 15 kg lard posteriorly. The lard was then gradually removed to simulate the fat loss found in the patient group. In the patient group the mean weight loss was 12,273 g, the mean fat loss was 11,014 g, and the mean bone mineral loss was 171.6 g after 15 weeks. Close correlation between the fat loss and the bone loss was found and calculated to be 16.5 g bone mineral per kg fat in the patient group, in contrast with 0.5 g bone mineral per kg fat in the control group. In the control group, 15 kg lard placed posteriorly had no statistically significant effect on the bone measurements. If weight and fat were regained at the scanning time 6 months later, the bone mineral was regained as well. Patients with further weight loss continued to lose bone mineral. One patient lost 754 g bone mineral in 9 months. Her weight loss was 45 kg in that period, and the bone mineral content remained within the range for normal women at her age. Methodologic and pathogenetic problems are discussed. It is concluded that the observed bone loss should be regarded as physiologic normalization accompanying a diet-induced weight loss in the obese.

INTRODUCTION

OBESE PERSONS IN GENERAL are known to have a greater lean body mass (LBM) than persons of normal weight.[1,2] In accordance with this, numerous studies performed with a variety of bioimpedance and scanning techniques have found that during energy restriction a certain proportion—up to 25%—of the weight loss consists of lost LBM.[3–6]

A significant relationship between body weight (BW) and bone mass (BM), as well as a strong correlation between total-body bone mineral (TBBM) and the percentage of body fat in premenstrual women, has been demonstrated in several studies.[7,8] The positive correlation of BM to BW implies that a readjustment of BM must take place after alterations in BW. The measurement of body composition by underwater weighing relies on the assumption that the skeleton is in a constant proportion to LBM. Lindsay et al.[7] demonstrated a variation in this fraction, suggesting significant errors in fat mass (FM) measurements because the skeleton is not in constant proportion to LBM but varies with age.

Some studies have shown that weight loss after intestinal bypass operation for severe obesity may be followed by a loss of bone. The bone mineral content was measured by single-photon absorptiometry of the distal forearm or by x-ray spectrophotometry and metacarpal measurements in these early studies.[9,10] These methods are compromised by the influence of fat tissue on the bone measurements, and the findings were later contradicted.[11,12]

The three body components, TBBM, FM, and LBM, can be measured separately by dual-energy x-ray absorptiometry (DXA).[13] With the development of DXA we now have a method in which the bone mineral measurements are much less influenced by alterations in adjacent fat tissue and therefore convenient for monitoring the skeleton in weight-losing sub-

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jects.[13–16] The method allows evaluation of both regional and total-body bone mineral with high precision and accuracy.[13,17,18] The radiation dose for the entire measurement series is estimated as less than 5 mrem.

Compston et al.[19] recently demonstrated that a diet-induced weight loss is accompanied by a significant decrease in bone mineral density (BMD). Regional bone changes were not measured. The purpose of the present investigation was to measure changes in total and regional body composition in obese patients undergoing rapid weight loss on a low-calorie regimen.

MATERIALS AND METHODS

A group of 51 obese patients (49 women and 2 men), weight 67.4–132.4 kg, age 19–70, body mass index (BMI) 27.1–44.8 kg/m^2, were placed on a low-calorie diet for 15 weeks. Of the women 14 were postmenopausal, and 5 of these received estrogen substitution; 13 women were perimenopausal, and none of these received estrogens. A formula diet (NUPO; Oluf Mørk, Ltd.) yielding 1.9 MJ for women and 2.4 MJ for men was given as a sole source of nutrition for 2 weeks. Thereafter a qualitatively free supplement of food and drink was allowed up to 4.2 MJ for women and 4.7 MJ for men.[20] The daily amount of formula diet for women contained 58 g protein, 800 mg calcium, 800 mg phosphate, and 200 IU vitamin D. For men the corresponding figures were 69 g protein, 960 mg calcium, 960 mg phosphate, and 240 IU vitamin D. Whole-body measurements were performed by a Hologic W-1000 DXA scanner software (Version 5.11) before the diet and after 15 weeks of dieting in 51 patients. Of these 39 were rescanned after 9 months; 2 patients left the study before 15 weeks and were excluded, and 12 patients left the study between 15 weeks and 9 months. The TBBM, FM, and FFM were measured. The software allows a regional calculation, and the total-body measurements were divided into values for the head, trunk, arms, and legs.

The precision of the bone mineral measurements was controlled by daily scanning of standards with known mineral content. The coefficients of variation (CV) for TBBM and soft tissue measurements in the whole-body mode on our system were calculated from a series of double scans performed in 12 volunteers over a period of 18 months. Soft tissue calculations were performed in 9 of these double measurements and TBBM analyses were performed in 12.

To eliminate measurement errors of TBBM caused by varying amounts of fat, the influence of increasing amounts of porcine lard was studied in a control group of nine normal volunteers. The lard was placed anteriorly, with an average distribution of 20% on the arms, 36% on the legs, and 44% on the trunk and neck, to simulate the fat layer in the obese. The lard was then gradually removed to simulate the fat loss found in the patient group. TBBM values were measured at each step of the simulate fat loss (Fig. 1). Nine volunteers were scanned lying on 15 kg lard placed under the back and on the posterior sides of the extremities. The average distribution was 26% behind the arms, 40% behind the legs, and 34% behind the trunk and neck. The lard was then removed and the volunteers rescanned.

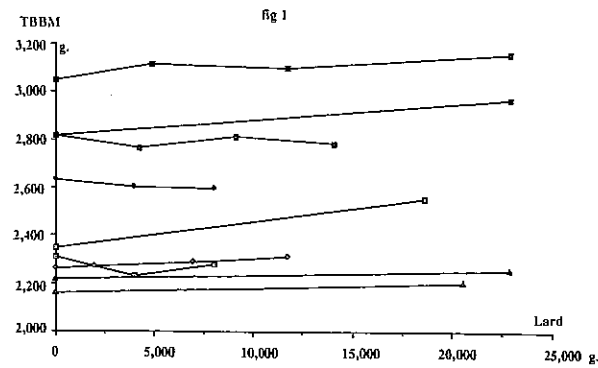

FIG. 1. Nine volunteers were scanned with up to 23 kg lard distributed on hip and trunk, and total-body bone mineral was measured. The lard was removed gradually to simulate fat loss in dieting patients, with four measurements in each volunteer.

RESULTS

The CV values for the bone measurements in normal persons in the whole-body scanning mode were 1.1 and 1.7% for total and regional measurements, respectively. In the obese group the values were 1.7 and 2.4%. The corresponding values for the soft tissue measurements were 1.6 and 3.2% in normal subjects and 2.0 and 3.1% in the obese group.

An amount of 15,000 g lard placed posteriorly accomplished an average change in the TBBM measurements at 0.5 g/kg of lard, but this was not statistically significant ($p = 0.5$), and as shown in Fig. 1 up to 23,000 g lard placed anteriorly had only a minor effect on the TBBM measurements. The alterations in TBBM per kg lost fat in the patient group were 16.5 g bone mineral/kg fat. In contrast, only a minor loss of 0.5 g bone mineral/kg lard was registered in the control group. The total bone loss in the patient group after 15 weeks was statistically significant ($p < 0.0001$), with a mean of 171.6 g (95% confidence interval 142.8–200.4 g; Table 1). The total bone loss was largest in the trunk and smallest in the arms but highly significant at all sites measured, varying from 4.0% in the left arm to 6.9% in the trunk (Table 2). By contrast, the fat losses varied much from region to region, being greatest in the trunk and the legs and smallest in the arms and the head (Table 2).

As shown in Figs. 2 and 3, there was a significant correlation between the losses of TBBM and losses of FM after both 15 weeks and 9 months. There was no correlation between the loss of fat free mass and the loss of TBBM ($r = 0.204$, $p = 0.15$).

At the extreme, one subject lost 754.1 g TBBM (25.4% of her initial TBBM before the diet) in 9 months. The corresponding weight loss was 45.1 kg, which accordingly represented the largest weight loss in our subjects. Her final TBBM and corresponding weight were 2215 g and 59.8 kg, respectively. This TBBM is within the range for normal women of her weight.[7]

There was no difference in bone mineral loss between the pre-, peri-, and postmenopausal women. In the group of postmenopausal women there was a tendency toward a larger bone mineral loss among the women without estrogen replacement compared with those who received estrogen (24 versus 14 g/kg fat loss), but the material size was too small to prove statistically significant ($p = 0.2$).

TABLE 1. ALTERATIONS IN BODY COMPOSITION[a]

	Initial (g)	*15 weeks (g)*	*Changes after 15 weeks (g)*	p *Value*
FFM	52,850 (42,071–85,479)	51,764 (38,809–81,458)	−1,086 (−6208 to 3880)	0.0017
FM	40,611 (20,877–75,663)	29,596 (12,721–54,010)	−11,014 (−25,876 to 2779)	<0.0001
TBBM	2,874 (1942–3,880)	2,702 (1756–3723)	−171.6 (−438.7 to 77.1)	<0.0001

[a]$N = 51$. Ranges are shown in parentheses. Patients were scanned initially and after 15 weeks on a low-calorie diet. There were significant losses in all three compartments measured.

Similar results were found when postmenopausal women receiving estrogen replacement were grouped with premenopausal women and compared with the postmenopausal women without estrogen replacement (16 versus 24 g/kg, $p = 0.07$).

DISCUSSION

The results raise three major questions.

1. Was the bone loss an artifact caused by the radical alterations in the adjacent soft tissues?
2. Why did the patients lose bone?
3. Is the bone loss found in this study greater than expected?

The influence of fat on measurements of bone mineral content (BMC) by dual-photon absorptiometry (DPA)[8,11,16] and DXA[13–16] has been reported as a consistent over- or underestimation. In these reports this local effect was reproduced by covering bone with a suitable amount of alcohol or layers of fat, implying that the over- or underestimation was caused by fat adjacent to the bone merely influencing the measurements directly. In our study we found only minor changes in the TBBM when volunteers were scanned with varying layers of lard, whereas the TBBM losses were much larger in the patient group. We therefore conclude that the bone loss in our study cannot be explained as an error of method. Because different DXA systems contain highly different software and hardware, a control group like ours is recommended when evaluating changes in TBBM in the obese using the DXA method.

The subjects lost on average 5.9% of TBBM during the 15 week period. That the truncal loss and the loss in the legs were larger than the loss in the arms may be explained by the weight relief on the bones in the former regions. However, the loss from

TABLE 2. ABSOLUTE AND PERCENTAGE LOSSES AFTER 15 WEEKS COMPARED WITH START VALUES[a]

	Left arm	*Right arm*	*Trunk*	*Left leg*	*Right leg*	*Head*	*Total*
TBBM, g	8.44	11.65	52.89	34.15	31.86	32.61	171.6
SEM	2.19	1.95	6.34	2.99	2.87	3.26	14.4
Relative loss, %	4.0	5.5	6.9	6.0	5.5	5.3	5.9
Fat, g	636	654	6088	1760	1725	148	11,014
SEM	69.98	53.45	429.35	145.91	140.52	22.29	821.94
Relative loss, %	21.0	22.5	33.9	22.4	22.1	10.9	27.0

[a]($N = 51$). Patients were scanned initially and after 15 weeks on a low-calorie diet. There was a significant loss of bone mineral in all regions, including the cranium. The fat loss varied much from region to region and was significantly smallest in the head.
[b]Standard error of the mean.

TABLE 3. ALTERATIONS IN BODY COMPOSITION[a]

	15 Weeks (g)	*9 Months (g)*	*Changes from 15 weeks to 9 months (g)*
FFM	51,261 (38,809–64,577)	51,441 (40,797–66,995)	181 (−4455 to 6,314)
FM	28,379 (13,633–54,010)	30,002 (11,570–57,138)	1622 (−19,942 to 8977)
TBBM	2,683 (1756–3723)	2,706 (1785–3769)	23 (−343.0 to 191.4)

[a]$N = 39$. Ranges are shown in parentheses. Patients were rescanned after 9 months. No diet was prescribed for the period from 15 to 9 months. There were no significant changes for the whole group, but as the ranges indicate, there were large individual changes.

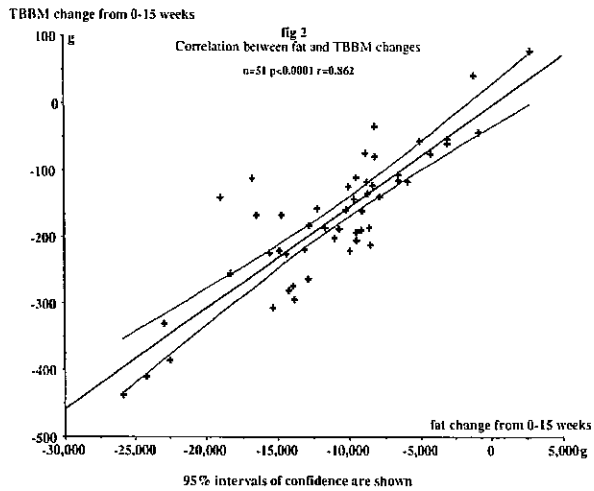

FIG. 2. A group of 51 patients on a low-calorie diet for 15 weeks were scanned before and after the diet. The loss of bone mineral was significantly correlated with the loss of fat.

the cranium, where the bone has very little weight to carry, was as large as the loss in the legs.

From the present study we do not achieve a deep insight into the underlying mechanisms of the bone loss since neither biochemical markers nor calciotrophic hormones were measured. We did not perform calcium metabolic studies, either, but such investigations are now in progress.

The universal nature of the bone loss speaks in favor of a humoral cause. Weight relief may be an initiating factor. Secondary hyperparathyroidism has been described in obese patients.[21,22] In these studies weight loss was followed by an increase in Ca^{2+} and a decrease in parathyroid hormone, and one of the studies also demonstrated a decrease in lactate and free fatty acids.[21] This may cause increased renal calcium loss caused by increased ultrafiltration and decreased reabsorption of calcium. Alterations in extraovarial estrogen synthesis could contribute. In favor speaks the rapidity of the bone loss, which indicates an increase in the activation frequency of bone with a negative balance. This is supported by the tendency to a larger bone loss in the postmenopausal women without estrogen replacement. The lack of difference between pre- and postmenopausal women speaks against this theory, however. Estrogen levels in serum should be further investigated in a larger group of women during the course of a diet.

Malnutrition is not likely. The daily obligatory diet contained 800 mg calcium, 800 mg phosphate, and 200 IU vitamin D. Further studies with estimation of renal loss of calcium and serum levels of calciotrophic hormones are needed if the nature of the negative bone balance is to be elucidated.

A general catabolic state similar to starvation as a cause of the bone loss also seems unlikely because the loss of fat free mass in general was small and was not correlated with the bone loss. It should also be stressed that our diet was qualitatively sufficient by all current standards.

The consequence of the bone loss in dieting is yet to be evaluated. Overweight persons have a larger BMC than average persons,[7,8,23] and the loss of bone during weight loss is likely to be a physiologic readjustment toward normal. This is supported by the findings at the 9 month scanning. The alterations in TBBM were correlated with alterations in weight at 9 months (Fig. 4). If weight was maintained the patients had no further bone loss, and if weight was regained bone was regained as well (Fig. 3).

We conclude that the bone loss in our study should be regarded as a physiologic normalization within acceptable limits accompanying a diet-induced weight loss in the obese.

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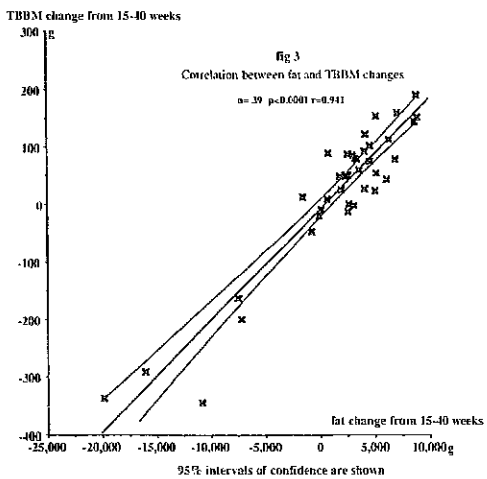

FIG. 3. A group of 39 patients were rescanned after 9 months. No diet was prescribed for the period from 15 weeks to 9 months. The alterations in bone mineral were significantly correlated with the alterations in body fat.

REFERENCES

1. Womersley J, Durnin JVGA, Boddy K, Mahaffy M 1976 Influence of muscular development, obesity, and age on the fat-free mass of adults. J Appl Physiol 41(2):223–229.
2. Foster GD, Wadden TA, Mullen JL, Stunkard AJ, Wang J, Feurer ID, Pierson RN, Yang MU, Presta E, Van Itallie TB, Lemberg PS, Gold J 1988 Resting energy expenditure, body composition, and excess weight in the obese. Metabolism 37:467–472.
3. Kushner FR, Kunigk A, Alspaugh M, Andronis PT, Leitch CA, Schoeller DA 1990 Validation of bioelectrical-impedance analysis as a measurement of change in body composition in obesity. Am J Clin Nutr 52:219–223.
4. Weits T, Van der Beek EJ, Wedel M, Hübben MWA, Koppeschaar HPF 1989 Fat patterning during weight reduction: A multimode investigation. Neth J Med 35:174–184.
5. Westerterp KR, Saris WHM, Soeters PB, Ten Hoor F 1991 Determinants of weight loss after vertical banded gastroplasty. Int J Obes 15:529–534.
6. Ballor DL, McCarthy JP, Wilterdink EJ 1990 Exercise intensity does not affect the composition of diet- and exercise induced body mass loss. Am J Clin Nutr 51:142–146.

7. Lindsay R, Cosman F, Herrington BS, Himmelstein S 1992 Bone mass and body composition in normal women. J Bone Miner Res **7**:55–63.
8. Hassager C, Christiansen C 1989 Influence of soft tissue body composition on bone mass and metabolism. Bone **10**:415–419.
9. Danø P, Christiansen C 1974 Calcium absorption and bone mineral contents following intestinal shunt operation in obesity. Scand J Gastroenterol **9**:775–779.
10. Parfitt AM, Chir B, Miller MJ, Frame B, Villanueva AR, Oliver I, Thomson DL 1978 Metabolic bone disease after intestinal bypass for treatment of obesity. Ann Intern Med **89**:193–199.
11. Rickers H, Balslev I, Foldtved H, Rødbro P 1981 Bone mineral content before and after intestinal bypass operation in obese patients. Acta Med Scand **209**:203–207.
12. Danø P, Christiansen C 1978 Calcium malabsorption and absence of bone decalcination following intestinal shunt operation for obesity. Scand J Gastroenterol **13**:81–85.
13. Haarbo J, Godtfredsen A, Hassager C, Christiansen C 1991 Validation of body composition by dual energy x-ray absorptiometry (DEXA). Clin Physiol **11**:331–341.
14. Hansen MA, Hassager C, Overgaard K, Marslew U, Riis BJ, Christiansen C 1990 Dual-energy x-ray absorptiometry: A precise method of measuring bone mineral density in the lumbar spine. J Nucl Med **31**(7):1156–1162.
15. Charles PH, Richard WK, Mitchell BS, Sartoris DJ 1990 Accuracy of dual-energy radiographic absorptiometry of the lumbar spine: Cadaver study. Radiology **176**:171–173.
16. Hangartner TN, Johnston CC 1990 Influence of fat on bone measurements with dual-energy absorptiometry. Bone Miner **9**:71–81.
17. Mazess RB, Barden HS, Bisek JP, Hanson J 1990 Dual-energy x-ray absorptiometry for total-body and regional bone-mineral and soft-tissue composition. Am J Clin Nutr **51**:1106–1112.
18. Slosman DO, Casez JP, Pichard C, Rochat T, Fery F, Rizzoli R, Bonjour JP, Morabia A, Donath A 1992 Assessment of whole-body composition with dual-energy x-ray absorptiometry. Radiology **185**:593–598.
19. Compston JE, Laskey MA, Croucher PI, Coxon A, Kreitzman S 1992 Effect of diet-induced weight loss on total body bone mass. Clin Sci **82**:429–432.
20. Hey H, Petersen HD, Andersen T, Quaade F 1987 Formula diet plus free additional food choice up to 1000 Kcal (4.2 MJ) compared with an isoenergetic conventional diet in the treatment of obesity. A randomized clinical trial. Clin Nutr **6**:195–199.
21. Andersen T, McNair P, Hyldstrup L, Fogh-Andersen N, Nielsen TT, Astrup AS, Transbøl I 1988 Secondary hyperparathyroidism of morbid obesity regresses during weight reduction. Metabolism **37**(5):425–428.
22. Atkinson RL, Dahms WT, Bray GA, Schwartz AA 1978 Parathyroid hormone levels in obesity. Miner Electrolyte Metab **1**:315–320.
23. Dalen N, Hallberg D, Lamke B 1975 Bone mass in obese subjects. Acta Med Scand **197**:353–355.

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