Improved nutritional status and bone health after diet-induced weight loss in sedentary osteoarthritis patients: a prospective cohort study

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BACKGROUND/OBJECTIVES: Obese subjects are commonly deficient in several micronutrients. Weight loss, although beneficial, may also lead to adverse changes in micronutrient status and body composition. The objective of the study is to assess changes in micronutrient status and body composition in obese individuals after a dietary weight loss program.

SUBJECTS/METHODS: As part of a dietary weight loss trial, enrolling 192 obese patients (body mass index >30 kg/m²) with knee osteoarthritis (>50 years of age), vitamin D, ferritin, vitamin B₁₂ and body composition were measured at baseline and after 16 weeks. All followed an 8-week formula weight-loss diet 415–810 kcal per day, followed by 8 weeks on a hypo-energetic 1200 kcal per day diet with a combination of normal food and formula products. Statistical analyses were based on paired samples in the complete population.

RESULTS: A total of 175 patients (142 women), 91%, completed the 16-week program and had a body weight loss of 14.0 kg (95% confidence interval: 13.3–14.7; P<0.0001), consisting of 1.8 kg (13.3–2.3; P<0.0001) lean body mass (LBM) and 11.0 kg (10.4–11.6; P<0.0001) fat mass. Bone mineral content (BMC) did not change (-13.5 g; P=0.18), whereas bone mineral density (BMD) increased by 0.004 g/cm² (0.001–0.008 g/cm²; P=0.025). Plasma vitamin D and B₁₂ increased by 15.3 nmol/l (13.2–17.3; P<0.0001) and 43.7 pmol/l (32.1–55.4; P<0.0001), respectively. There was no change in plasma ferritin.

CONCLUSIONS: This intensive program with formula diet resulted in increased BMD and improved vitamin D and B₁₂ levels. Ferritin and BMC were unchanged and loss of LBM was only 13% of the total weight loss. This observational evidence supports use of formula diet-induced weight loss therapy in obese osteoarthritis patients.

Keywords: nutritional status; weight loss; formula diet; osteoarthritis

INTRODUCTION

Obese subjects often show micronutrient deficiencies. The reason for this is complex. Obesity reduces the bioavailability of several vitamins and there may be an alteration in nutrient metabolism. Furthermore, the quality of ingested foods may be poor. Obesity and being overweight represent a rapidly growing threat to the health of populations in an increasing number of countries. Positive energy balance deriving from excessive food intake in relation to energy expenditure is the pathophysiological basis of obesity in most cases. Weight loss is expected to result in a significant reduction in risk of the majority of these comorbid conditions. Weight loss has, however, also been associated with (a potentially harmful) loss of muscle mass and bone in obese individuals.

A variety of weight loss methods are available today, including diet therapy approaches such as low-calorie diets and lower-fat diets, change in physical activity patterns, behavior therapy techniques, pharmacotherapy, surgery and combinations of these techniques. Among these, bariatric surgery is the most effective but it is found to aggravate the insufficient state of several micronutrients. As obesity and micronutrient deficiencies are related to and associated with increased risk of morbidity, one must consider the nutritional value and capacity of weight-loss treatments to secure adequate amounts of nutrients and prevent detrimental effects while losing weight. In the current study, we used a prospective cohort of sedentary obese knee osteoarthritis patients, who completed a weight loss trial to look at the effect of a formula low-energy diet on micronutrient status, that is, vitamin D, vitamin B₁₂, ferritin as well as on body composition. Clinically, osteoarthritis causes painful joints and is a leading cause of impaired mobility in the elderly; most patients with symptomatic knee osteoarthritis have limitations in function that prevent them from engaging in their usual activities.

Our objective was to assess and evaluate changes in micronutrient status (vitamin D, B₁₂ and ferritin) and body composition in obese knee osteoarthritis patients after 8 weeks of low-energy diet followed by 8 weeks of a hypo-energetic diet, including two formula diet products daily.

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Contributors: RC had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. PC, EMB, BFR, HB, ARL, AA, KW and RC contributed to study concept and design. PC, EMB, HB and RC analysed and interpreted the data. PC, EMB, HB and RC drafted the manuscript. PC, EMB, BFR, HB, ARL, AA, KW and RC revised the manuscript for important intellectual content.

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PARTICIPANTS AND METHODS

The results presented in this paper are from a prospective cohort of 192 well-characterized obese knee osteoarthritis patients over 50 years of age. In this study, we assessed micronutrient status and body composition, including total body bone mineral content (BMC) and bone mineral density (BMD) in the complete population, that is, all the participants who entered and completed the weight loss trial, using data from the baseline and 16-week assessment. The CAROT study (‘Influence of weight loss or exercise on CARTilage in Obese knee osteoarthritis patients Trial’) was a randomized controlled trial designed to answer the question of how to modify long-term habitual eating patterns. The current study is looking into the nutritional benefit and harm following the 16-weeks diet scheme.

Setting

Participants included in this pragmatic trial were recruited between November 2007 and August 2008 from the outpatient clinic at the Department of Rheumatology, Frederiksberg Hospital, Frederiksberg, Denmark, through advertisements in newspapers and on the website of the Parker Institute. Additionally, local general practitioners were informed about the possibility of assigning patients to the project.

Participants

Individuals who were >50 years of age with confirmed knee osteoarthritis according to standing radiographs were eligible for inclusion, and obese as defined by a body mass index (BMI) ≥30 kg/m². Exclusion criteria were: lack of motivation to lose weight, inability to speak Danish, planned antiobesity surgery, total knee arthroplasty and receiving pharmacological therapy for obesity. In all, 192 patients were enrolled in the trial. The participants were asked not to change any medication or nutritional supplement during the study. The study was approved by the ethics committee of the Capital Region of Denmark (H-B-2007-088) and all participants having lower values than 50 nmol/l, which is the limit of 7.3 essential amino acids, fatty acids, vitamins and minerals. Daily intake of milk using 7.5 dl of milk per day and one in water (total: 3402 kJ per day, 8.7 kg protein). The LED program consisted of powdered formula mixture dissolved in water. Women below a height of 173 cm were given three sachets a day ≈415 kcal per day (1743 kcal per day, 43.2 g protein). Men and women taller than 173 cm were given four sachets a day ≈520 kcal per day (2327 kcal per day, 56.7 g protein). The LED program consisted of powdered formula mixture dissolved in skimmed milk and water. Participants were given four sachets a day, three of which were dissolved in milk using 7.35 dl of milk per day and one in water (total: 3402 kcal per day, 83.9 g protein). Both programs met all recommendations for daily intake of essential amino acids, fatty acids, vitamins and minerals. Daily intake of vitamin D was 5 μg, B₁₂ vitamin was 2 μg, iron was 14 mg and calcium was 912 mg in the VLED group. In the LED group, daily intake of vitamin D was 7.3 μg, B₁₂ vitamin was 6.4 μg, iron was 19 mg and calcium was 2146 mg. Daily intake of protein was at least 43.2 g, and of essential fatty acids, with the guidelines for healthy eating issued by the Danish National Board of Health, that is, low fat, low sugar and high fiber. The two daily diet products supplied 3.4 μg of vitamin D, 1.4 μg of vitamin B₁₂, 9.4 mg of iron and 608 mg calcium. The aim and focus of the dietary education was to modify long-term habitual eating patterns.

Variables

Body weight was measured on digital scales (TANITA BW-800, Frederiksberg Vægtfabrik, Frederiksberg, Denmark). Other outcome measures were changes in BMI calculated by a person’s weight (in kg) divided by the square of his/her height (in m), where height was measured to the nearest 0.01 m, blood-hemoglobin, plasma-parathyreoidea hormone (PTH), plasma-25-OH-vitamin D3 (vitamin D), plasma-cobalamin (B₁₂ vitamin) and plasma-ferritin (iron). All were measured at baseline and at week 16. All blood samples were analyzed at The Clinical Chemistry Department at Frederiksberg Hospital. Plasma-25-OH-vitamin D3 was measured on a Abbott Architect iSR using micro particle chemiluminescens immunoassay, plasma-cobalamin and plasma-ferritin was measured on a Abbott Architect i2000SR using two step immunoassay with chemiluminescens micro particle technology and PTH was measured on a Cobas-HR using sandwich immunoassay with chemiluminescens detection. Micronutrient deficiency was defined according to the guidelines for the Clinical Chemistry Laboratory at Frederiksberg Hospital: cutoff values were P-25-OH-vitamin D3 <50 nmol/ml, P-cobalamin <200 pmol/ml and P-ferritin <12 μg/l. The rationale for selecting these three micronutrients is that these three are linked to important processes in the body, and both obesity as well as older age increases the risk of deficiency. The cutoff value for too high levels of PTH was 6.9 pmol/l.

Lean body mass (LBM, kg), body fat (kg), BMI (g/cm²) and BMC (g) were determined by dual energy X-ray absorptiometry using a Lunar DPX IQ Full Body Bone Densitometer (GE Medical Systems, Madison, WI, USA) and was measured at baseline and after 16 weeks’ diet therapy. The cohort was analyzed in total, as well as stratified by sex. The rationale for this is that both blood levels of certain vitamins and minerals, as well as body composition, are dependent on gender.

Statistics

The overall statistical analysis plan scrutinized the null hypothesis that none of the outcome measures included had changed significantly during an intensive weight-loss program. Thus: H₀ = 0, which was tested using 1-sample, paired t-tests. A priori we considered a P-value <0.05 (two-sided) as indicating a rejection of the null hypothesis. For sensitivity, in order to support the results from the group level of the 1-sample t-tests, we also applied Spearman’s correlation analyses to assess whether there was an association between the weight change and subsequent change in nutritional status and/or bone health on the level of the individual patient. The SAS statistical package (version 9.2; SAS Institute Inc., Cary, NC, USA) was used for all statistical analyses.

RESULTS

Of the 192 participants randomized to the trial, 175 (91%) completed the study (returned for final data collection at week 16). Only participants returning for the final examination are included in these analyses. The baseline characteristics of the cohort are presented in Table 1.

The mean age of the participants (± s.d.) was 62.6 ± 6.3 years. The majority of the participants were women, which is typical for knee osteoarthritis (142 of the 175). The mean weight at baseline was 102.4 ± 14.5 kg, corresponding to a BMI of 37.1 ± 4.4 kg/m². LBM was 50.6 ± 8.7 kg and fat mass was 46.6 ± 9.2 kg. The mean P-25-OH-vitamin D3 was 48.9 ± 20.1 nmol/l at baseline with 84 (48%) participants having lower values than 50 nmol/l, which is the limit for insufficiency, a threshold applied by the hospital laboratory. The mean value of B₁₂ at baseline was 293.2 ± 120.1 pmol/l; 34 (19.4%) participants had values below the recommended level at 200 pmol/l, a threshold applied by the hospital laboratory. The mean ferritin was 117.1 ± 94.6 μg/l with two (1.1%) participants

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having values lower than the threshold of 12 µg/l. The mean parathyroid hormone was 6.4 ± 2.2 pmol/l with 55 (31.4%) participants having excessive values, that is, above 6.9 pmol/l. The mean BMC was 2780.7 ± 462.5 g and the mean BMD was 1.20 ± 0.09 g/cm².

After the first 8 weeks, the participants had lost 12.0 kg (95% confidence interval (CI): 11.4 - 12.5 kg; P < 0.0001) and an increase in BMD of 0.004 g/cm² (95% CI: 11.4 - 12.5 kg; P < 0.0001). The participants had lost a mean of 14.0 kg (95% CI: 13.3 - 14.7 kg; P < 0.0001). The BMI was reduced by 5.1 kg/m² (95% CI: 4.8 - 5.3 kg/m²; P < 0.0001). Sixty-two participants (35.4%) had a BMI that had fallen to 38 (21.7%). The mean value of vitamin B12 had increased and none of the participants presented ferritin values that were below the recommended level at 13.7% to a large extent because of loss, on the individual patient rather than the group level, as fat is a known storage location for vitamin D. A strong correlation between weight loss and vitamin D increase was found, whereas a lesser, but still statistically significant, correlation was seen between fat loss and vitamin D increase (see Appendix II).

In order to prospectively explore whether it is reasonable to accept the null hypothesis that the intensive weight loss does not change the BMC level, we performed a prospective power analysis under the assumption that 175 patients were in a new study (like the present): For a paired t-test of a normal mean difference with a two-sided significance level of 0.05, assuming from Table 1 a (conservative) common s.d. of 475 g and correlation r = 0.95, a sample size of 175 pairs has a power of 0.80 (that is, statistical power > 80%) to detect a mean difference of 13.5 g. This is also supported by the width of the 95% CIs, with the lower limit (−33.3 g) implying a potentially clinically relevant loss in BMC.

In a study concerning vitamin D one will always be aware of possible differences in sun exposure with time of year, when in a Northern country. Looking at this aspect in our population, we consider the vitamin D status of our patients to be important.

Ancillary analyses

Spearman’s correlation analyses were carried out to answer the question concerning release of vitamin D bound in fat with weight loss, on the individual patient rather than the group level, as fat is a known storage location for vitamin D. A strong correlation between weight loss and vitamin D increase was found, whereas a lesser, but still statistically significant, correlation was seen between fat loss and vitamin D increase (see Appendix II).

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### Table 1. Demographic and clinical characteristics at baseline

| Characteristic/variable | Males (n = 33) | Females (n = 142) | Total (n = 175) |
|-------------------------|---------------|------------------|----------------|
| Age, years              | 62.4 ± 6.4 (51 - 74) | 62.6 ± 6.3 (50 - 77) | 62.6 ± 6.3 (50 - 77) |
| Height, cm              | 176.8 ± 6.7 (168 - 191) | 163.6 ± 6.2 (148 - 184) | 162.6 ± 6.1 (148 - 191) |
| Weight, kg              | 113.8 ± 14.8 (88.5 - 145) | 99.8 ± 13.2 (76 - 144) | 102.4 ± 14.5 (76 - 145) |
| Body mass index, kg/m²  | 36.3 ± 4.0 (31.0 - 46.8) | 37.2 ± 4.5 (30.1 - 51.6) | 37.1 ± 4.4 (30.1 - 51.6) |
| BMI > 40 kg/m², n (%)   | 30 (15.2) | 30 (21.1) | 35 (20.0) |
| P-parathyroid hormone, pmol/l | 9.2 ± 0.7 (7.3 - 10.5) | 8.6 ± 0.6 (6.5 - 10.0) | 8.7 ± 0.6 (6.5 - 10.5) |
| Vitamin B12, pmol/l    | 5.3 ± 1.6 (3.0 - 12.1) | 6.6 ± 2.3 (2.5 - 14.6) | 6.4 ± 2.2 (2.5 - 14.6) |
| P-parathyroid hormone > 6.9 pmol/l, n (%) | 3 (9.1) | 52 (36.6) | 55 (31.4) |
| P-25-OH-vitamin D3, nmol/l | 58.0 ± 19.5 (10 - 91) | 46.7 ± 19.7 (10 - 92) | 48.9 ± 20.1 (10 - 92) |
| P-25-OH-vitamin D3 < 50 nmol/l, n (%) | 10 (30.3) | 74 (21.1) | 84 (48.0) |
| P-cofamolin (vitamin B12), pmol/l | 274.7 ± 100.5 (105 - 509) | 297.5 ± 124.1 (94 - 1159) | 293.2 ± 120.1 (94 - 1159) |
| P-cobalamin (vitamin B12) < 200 pmol/l, n (%) | 8 (24.2) | 26 (18.3) | 34 (19.4) |
| P-ferritin, lg/l        | 173.8 ± 127.5 (12 - 558) | 103.9 ± 80.2 (5 - 533) | 117.1 ± 94.6 (5 - 558) |
| P-ferritin < 12 lg/l, n (%) | 2 (1.4) | 2 (1.1) | 2 (1.1) |
| Lean body mass, kg      | 65.2 ± 6.5 (54.6 - 78.4) | 47.2 ± 4.6 (37.1 - 59.5) | 50.6 ± 8.7 (37.1 - 78.4) |
| Fat mass, kg            | 41.5 ± 3.0 (30.7 - 57.8) | 47.8 ± 3.9 (31.1 - 80.7) | 46.6 ± 9.2 (30.7 - 80.7) |
| Bone area, cm²          | 2659 ± 207 (2202 - 3051) | 2232 ± 185 (1837 - 2733) | 2312 ± 253 (1837 - 3051) |
| Bone mineral content, g | 3384.1 ± 473.1 (2151 - 4134) | 2640.5 ± 329.0 (1931 - 3840) | 2780.7 ± 462.5 (1931 - 4134) |
| Bone mineral density, g/cm² | 1.27 ± 0.11 (0.98 - 1.46) | 1.18 ± 0.08 (0.94 - 1.43) | 1.20 ± 0.09 (0.94 - 1.46) |

Data are mean ± s.d. and (min - max), except when otherwise indicated. Dichotomous data are reported as number of observations and proportions (%).
Table 2. Changes and critical thresholds following intervention (16 weeks)

| Characteristic/variable | Males (n = 115) | Females (n = 142) | Total (n = 177) |
|-------------------------|----------------|------------------|----------------|
| ΔWeight, kg | -14.7 (-16.9 to -12.6) | -13.8 (-14.6 to -13.1) | -14.0 (-14.7 to -13.3) |
| ΔBody mass index, kg/m² | -4.7 (-5.4 to -4.0) | -5.2 (-5.4 to -4.9) | -5.1 (-5.3 to -4.8) |
| BMI >40 kg/m², n (%) | 2 (6.0) | 7 (4.9) | 9 (5.1) |
| ΔB-haemoglobin, mmol/l | -0.20 (-0.37 to -0.04) | 0.03 (-0.04 to 0.09) | -0.02 (-0.08 to 0.04) |
| AP-parathyroid hormone, pmol/l | -0.53 (-0.98 to -0.09) | -0.95 (-1.24 to -0.66) | -0.87 (-1.12 to -0.62) |
| P-parathyroid hormone >6.9 pmol/l, n (%) | 4 (12.1) | 24 (16.9) | 28 (16.0) |
| AP-25-OH-vitamin D3, nmol/l | 15.2 (9.9 to 20.4) | 15.3 (13.0 to 17.5) | 15.3 (13.2 to 17.3) |
| P-25-OH-vitamin D3 <50 nmol/l, n (%) | 4 (12.1) | 34 (23.9) | 38 (21.7) |
| AP-cobalamins, pmol/l | 16.7 (-8.8 to 42.1) | 50.0 (37.0 to 63.0) | 43.7 (32.1 to 55.4) |
| P-cobalamins <200 pmol/l, n (%) | 6 (18.2) | 15 (10.6) | 21 (12) |
| ΔP-ferritin, ìg/l | -18.7 (-57.3 to 19.9) | 12.2 (5.9 to 18.5) | 6.4 (-2.5 to 15.2) |
| P-ferritin <12 ìg/l, n (%) | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| ΔLean body mass, kg | -2.2 (-3.1 to -1.2) | -1.7 (-2.2 to -1.2) | -1.8 (-2.3 to -1.3) |
| ΔFat mass, kg | -11.0 (-12.9 to -9.0) | -11.0 (-11.6 to -10.5) | -11.0 (-11.6 to -10.4) |
| ΔBone area, cm² | -32.1 (-64.7 to 0.4) | -17.8 (-36.3 to 0.6) | -20.5 (-36.6 to -4.5) |
| ΔBone mineral content, g | 16.4 (-31.3 to 64.1) | -20.5 (-42.3 to 1.3) | -13.5 (-33.3 to 6.2) |
| ΔBone mineral density, g/cm² | 0.020 (0.011 to 0.030) | 0.000 (-0.003 to 0.004) | 0.004 (0.001 to 0.008) |

Data are mean values (95% confidence interval; P-value associated with test for no change from baseline), except when otherwise indicated. Dichotomous data are reported as number of observations and proportions (%).

Carried out a post hoc analysis of variability of vitamin D between the groups who started treatment between January and April, and the groups who started treatment between May and August. No difference between the groups was found.

**DISCUSSION**

Our study showed that intensive weight loss achieved by use of a low-energy formula diet was accompanied by significant increases in vitamin D and B₁₂ levels. This is striking, as nearly half of our participants had a deficiency of vitamin D at baseline and about one in five showed deficiency in vitamin B₁₂. At week 16, the percentage of participants being deficient in vitamin D and B₁₂ had decreased significantly. The correction of these vitamin deficiencies may very likely have been due to the formula products given, as the intake of both vitamin D and calcium was sufficient to cause an increase in vitamin D status and prevent bone loss. This supports that by making sure that the diet applied includes all essential vitamins and minerals, and the participants did not experience any negative effect on bone status with weight loss.20

In a calorie restriction study by Redman et al., (2008) the participants were offered diets providing the recommended daily intake of all essential vitamins and minerals, and the participants did not experience any negative effect on bone status with weight loss.20 This supports that by making sure that the diet applied includes all essential nutrients (like vitamin D and calcium) it is possible to minimize or prevent loss from the muscle and bone. The formula diet program provided at least 100% of the daily-recommended intake of calcium and vitamin D for adults between 18 and 65 years of age at the time the study was conducted. The Danish guidelines recommended a daily intake of vitamin D of 5 ìg and of calcium 800 mg. It has previously been shown that diets high in calcium or dairy products can suppress bone resorption.21 As calcium absorption is dependent on the presence of 1.25 (OH)₂ vitamin D, the requirement of calcium can only be meaningfully discussed if the vitamin D status is sufficient. The optimal vitamin D intake is not known and there is evidence suggesting that the present recommended intake is actually inadequate and needs to be increased.22 However, based on our data we can conclude that the intake of both vitamin D and calcium was sufficient to cause an increase in BMD and to prevent loss of BMC. With their weight loss, >60% of the participants experienced clinically significant improvements in pain and disability.1 This could also have caused an increase in physical activity and, if this was the case, increased physical activity could explain the relatively low loss of LBM as well.
as low loss of bone observed in our participants. The participants were though not advised to change their physical activity pattern during the study, but were advised to stick to their usual routines.

Measurements of BMC and BMD by dual energy X-ray absorptiometry are known to be affected, although to a minor degree, by layer of excessive fat. There are also differences between dual energy X-ray absorptiometry scanners used. In general, Hologic scanner measurements show an increase in BMD whereas Lunar scanner measurements show a decrease in BMD with weight loss.

In our study, we used a Lunar scanner (GE Medical systems). Despite of this we found an increase in BMD with weight loss. We therefore must conclude that this observation is real and if anything the increase in BMD is measured as too low.

In this study we measured the blood levels of the micronutrients, we expected to be of clinical importance in relation to our study population. However, it would have been interesting to measure changes in a wider panel of micronutrients in connection to this type of weight loss program, as it is well known that obesity is often accompanied by a low status.

General implications

Obesity may be associated with nutrient deficiencies and the average overweight subject may suffer from a nutritionally inadequate diet. When trying to lose weight by consuming less food, individuals may unwittingly reduce essential nutrient intake even further. This creates an important role for nutrient-dense foods like formula diets, which allow adequate intake of macro- and micronutrients although still providing smaller amounts of energy. Given the growing rate of obesity, it is important for subjects deciding to reduce their energy intake to maintain a nutritionally sound diet, providing adequate vitamins, minerals and macronutrients.

Our data suggest that weight loss can be achieved effectively and safely with low-energy formula products, as long as this diet contains a sufficient amount of nutrients. This is supported by the Look Ahead Study, where the number of meal replacements consumed in the first 6 months was significantly related to weight loss at week 26 ($r = 0.32, P < 0.001$), as was the total number consumed for the year to weight loss at week 52 ($r = 0.30, P < 0.001$). As our obese patients need support to keep to a healthy diet, the formula diet may take the burden of having to deliberately choose the low-fat healthy option at each meal time, and replacement of one or two meals a day with the low-calorie formula diet may be the ‘medicine’, which helps the patients to keep their micronutrients at acceptable levels as well as the obtained weight loss on a more permanent scale.

CONFLICT OF INTEREST

AR Leeds is employed as medical director of the Cambridge Manufacturing Company (Cambridge Weight Plan). Pia Christensen, Henning Bliddal, Birgit Falk Riecke, Robin Christensen and Arne Astrup received travel grants to attend scientific meetings from the Cambridge Manufacturing Company.

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Appendix II. Spearman’s correlations between changes in body weight and fat mass (n = 175)

| Characteristic/variable          | ΔWeight, kg | ΔFat mass, kg |
|----------------------------------|-------------|---------------|
| ΔP-25-OH-vitamin D3, nmol/l      | r = −0.21   | r = −0.16     |
|                                  | P = 0.006   | P = 0.03      |
| ΔP-cobalamins, pmol/l           | r = 0.08    | r = 0.08      |
|                                  | P = 0.28    | P = 0.29      |
| ΔP-ferritin, μg/l               | r = −0.33   | r = −0.27     |
|                                  | P < 0.0001  | P = 0.0003    |
| ΔLean body mass, kg             | r = 0.39    | r = 0.01      |
|                                  | P < 0.0001  | P = 0.90      |
| ΔFat mass, kg                   | r = 0.82    | r = 1.00      |
|                                  | P < 0.0001  |               |
| ΔBone area, cm²                 | r = −0.03   | r = 0.22      |
|                                  | P = 0.70    | P = 0.003     |
| ΔBone mineral content, g        | r = 0.02    | r = 0.31      |
|                                  | P = 0.82    | P < 0.0001    |
| ΔBone mineral density, g/cm²    | r = −0.01   | r = 0.12      |
|                                  | P = 0.86    | P = 0.11      |