The relationship between weight change history and 25(OH)D concentrations in adults
La relación entre la historia del cambio ponderal y las concentraciones de 25(OH)D en los adultos

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Abstract

Background: although obesity has been consistently associated with lower 25-OH hydroxyvitamin D-25(OH)D-levels, little is known about the effect of weight change on serum 25(OH)D levels.

Methods: the present analysis was based on data from the National Health and Nutrition Examination Survey. Percent weight changes were calculated from participant-reported maximum lifetime weight and weight in the past year and 10 years ago. Subsequently, general linear models adjusted for potential confounders were assembled to examine 25(OH)D concentrations across percent weight change categories.

Results: a total of 6,237 participants with a mean age of 57.5 (SE, 0.2) years comprised the study sample. After adjustment for potential confounders, subjects who have gained weight ≥ 5% in the past year and 10 years before had on average 4.5 and 5.1 nmol/L lower 25(OH)D levels than those with a stable weight, respectively. Moreover, this association persisted even among participants with adequate vitamin D intake. Notably, subjects who lost weight > 5% from their maximum reported weight had significantly higher 25(OH)D levels than those who did not.

Conclusion: subjects with a stable weight and those who lost weight ≥ 5% from their maximum reported lifetime weight had significantly higher 25(OH)D concentrations than those who did not. Thus, maintaining a healthy weight over time may be an effective strategy to reach optimal serum 25(OH)D levels.

Keywords: Weight change. Vitamin D. Maximum weight. NHANES.

Resumen

Antecedentes: aunque la obesidad se ha asociado consistente con niveles más bajos de 25-OH-vitamina D (25(OH)D), poco se sabe sobre el efecto del cambio de peso en los niveles de 25(OH)D.

Métodos: el presente análisis se basó en datos de la Encuesta Nacional de Examen de Salud y Nutrición. Los cambios porcentuales en el peso se calcularon a partir del peso medido actual y el peso máximo reportado, peso en el último año, y hace 10 años. Se usaron modelos lineales generales ajustados por posibles cofactores para examinar las concentraciones de 25(OH)D de acuerdo con el porcentaje de cambio ponderal.

Resultados: un total de 6.237 participantes con una edad promedio de 57.5 años conformaban la muestra del estudio. Los sujetos que aumentaron de peso ≥ 5% en el año anterior y en los 10 años previos tuvieron en promedio 4,5 y 5,1 nmol/L menos de 25(OH)D que aquellos con peso estable, respectivamente. Además, esta asociación persistió incluso entre los participantes con una ingesta adecuada de vitamina D. Por el contrario, los sujetos que perdieron ≥ 5% de su peso máximo reportado tuvieron niveles más altos de 25(OH)D comparados con aquellos que no perdieron peso.

Conclusion: los sujetos con un peso estable y aquellos que perdieron ≥ 5% de su peso máximo reportado tuvieron concentraciones significativamente más altas de 25(OH)D frente a aquellos que aumentaron de peso. Por lo tanto, mantener un peso saludable con el tiempo puede ser una estrategia eficaz para alcanzar niveles óptimos de 25(OH)D.
INTRODUCTION

The prevalence of obesity is increasing worldwide and accounts for the expanding prevalence of chronic comorbidities (1). Although low serum 25-hydroxyvitamin D (25(OH)D) concentrations have been consistently reported among obese subjects across different races and latitudes, the precise mechanism of this association has not been fully elucidated (2-6). However, previous studies have concluded that limited sun exposure, inadequate use of vitamin D supplements, decreased bioavailability of vitamin D once in fat tissue, or simply dilution of ingested or synthesized vitamin D in fat mass may explain low vitamin D status in subjects with obesity (7-9).

Clinical trials of restricted calories and exercise interventions among children and women with overweight and obesity have reported increasing serum 25(OH)D concentrations among those who achieved moderate weight loss. Similarly, a recent systematic review and meta-analysis of randomized and nonrandomized weight-loss trials reported that 25(OH)D concentrations were marginally increased with weight loss in comparison with weight maintenance under similar conditions of supplemental vitamin D intake (10-14).

Despite these facts, no previous population-based study has reported the effect of weight history on serum 25(OH)D and its metabolites concentrations. Therefore, the present study aimed to examine the relationship between short- and long-term weight change and weight loss from the maximum reported weight, and 25(OH)D concentrations in a nationally representative sample of adults.

METHODS

STUDY PARTICIPANTS

The National Health and Nutrition Examination Survey (NHANES) is a biannual cross-sectional study conducted by the National Center for Health Statistics of the Centers for Disease Control and Prevention. The purpose of the NHANES is to collect data about the health, nutritional status, and health of the noninstitutionalized civilian resident population of the U.S. Information about the analysis and reporting guidelines of the NHANES are described elsewhere (15).

WEIGHT HISTORY

In the Weight History section, participants aged 40 years and older were asked “How much did you weigh in pounds a year and 10 years ago? If you don’t know your exact weight, please make your best guess.” In the mobile examination center, body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared, and then rounded to one decimal place. For this analysis, weight in pounds was converted to kg. Weight change was calculated by subtracting baseline measured weight from self-reported weight in the past year and 10 years ago. Then, this result was divided by the baseline weight and reported as percent weight change. As previously described, weight change was defined as weight loss ≥ 5 %, stable weight as a change of < 5 %, and weight gain as an increase of ≥ 5 % (16).

Weight change from subjects who reported their maximum weight was calculated based on the following question: “Up to the present time, what is the most you ever weighed?” Percent change in weight from the patients’ reports of their maximum reported lifetime weight was calculated, and weight loss was categorized as previously defined (< 5 % loss, 5%-10 % loss, and > 10 % loss). Percent change from reported maximum weight was corrected to 0 % if maximum weight was observed at the current evaluation (17). Obesity history was also categorized according to the subject’s baseline BMI and estimated BMI 10 years ago, which was calculated by using subjects baseline measured height and reported weight 10 years ago. Subjects were then classified as never obese, previously obese and presently non-obese, previously non-obese and presently obese, and always obese (18).

COVARIATES

In the demographic file, data on the following variables were obtained: examination period, age, gender, race/ethnicity, education, and ratio of family income to poverty threshold as a measure of socioeconomic status. Moreover, participants reported their smoking status and general health, which was grouped as good to excellent or fair to poor. Based on the 2018 Physical Activity Guidelines for Americans, the participants’ leisure-time physical activity was classified as physically active, insufficiently active, or inactive (19). The NHANES dietary data were used to estimate vitamin D intake from the types and amounts of foods and beverages consumed during the 24-hour period prior to the interview. Similarly, the 30-day dietary supplement file was used to provide a summary record of the mean daily vitamin D intake from all supplements and antacids. Data were routinely examined for discrepancies and erroneous entries.

25(OH)D CONCENTRATIONS

The CDC developed the standardized liquid chromatography-tandem mass spectrometry (LC-MS/MS) to measure 25(OH) D3, 25(OH)D2, and total 25(OH)D. For the LC-MS/MS method, total 25(OH)D (in SI units of nmol/L) was defined as the sum of 25(OH) D3 and 25(OH)D2, and excluded the C3 epimer of 25(OH)D2. The LC-MS/MS method has better analytical specificity and sensitivity compared to immunosassay methods, and fixed analytical goals for imprecision (≤ 10 %) and bias (≤ 5 %) (20).

STATISTICAL METHODS

The characteristics of participants were reported as weighted percentages and mean values with their corresponding standard
errors. General linear models adjusted for possible confounders were used to examine the associations between percent weight change categories (≥ 5 % weight loss, loss or gain weight < 5 %, and gain weight ≥ 5 %) in the past year and 10 years, and 25(OH)D concentrations. Similarly, 25(OH)D and its metabolites levels, stratified according to age groups, were compared by obesity history status in the previous 10 years. Moreover, the effect of progressive weight loss (> 10 %, 5 to 10 %, < 5 %, and 0 %) from the participants’ maximum lifetime weight on 25(OH)D concentrations was also examined. Statistical analyses were performed using the SPSS Complex Sample software, V.17 (SPSS Inc, Chicago, Illinois, USA) to incorporate constructed weights and obtain unbiased, national estimates. A p-value < 0.05 was considered statistically significant.

RESULTS

A total of 6,237 participants with a mean age of 57.5 (SE, 0.2) years comprised the study sample. As shown in table I, the majority of participants were examined between May 1st to Oct 31st, were non-Hispanic whites, had some college education, and reported a sedentary lifestyle. Notably, 21 % and 47 % of participants had gained weight ≥ 5 % in the past year and 10 years, respectively. In contrast, an estimated 56 % of subjects had lost weight ≥ 5 % from their maximum weight, which was reported on average at 90.2 kg. Overall, 47.5 % (SE, 1.0) and 19.7 % (SE, 1.4) of adults aged 40 years and older reported taking vitamin D supplements and had evidence of vitamin D deficiency, respectively.

As shown in table II, participants who had gained weight ≥ 5 % in a year and in the past 10 years had considerably lower 25(OH)D and 25(OH)D concentrations than those with a stable weight. Indeed, mean 25(OH)D level differences between subjects who gained weight and those with stable weight in the previous year and 10 years were 4.5 and 5.1 nmol/L, respectively. As expected, 25(OH)D concentrations were higher among participants with vitamin D intake ≥ 400 IU/day than among those without it. However, subjects who gained weight ≥ 5 % in the past year had significantly lower mean 25(OH)D levels than those with stable weight, irrespective of their daily vitamin D intake. In fact, the lowest mean 25(OH)D level was seen among participants who gained weight and had a vitamin D intake < 400 IU/day (Fig. 1).

Table III shows 25(OH)D and its metabolites concentrations according to obesity history in the previous 10 years and stratified by age groups. In general, mean 25(OH)D and its metabolites levels were lower among middle-aged than in older adults. After adjustment for potential confounders, participants defined as always obese and those previously non-obese but presently obese had significantly lower 25(OH)D, and 25(OH)D levels compared with their never obese counterparts. Notably, mean 25(OH)D, and 25(OH)D levels were 10.6 and 10.0 nmol/L lower among subjects with obesity in the previous 10 years than among those never obese, respectively.

| Table I. Demographic characteristics of participants in the NHANES 2011-2014 |
|---------------------------------|-----------------|----------------|
| No. participants                | Weighted % (SE) |
| **Six-month period**           |                 |
| Nov 1st to Apr 30th            | 2,952           | 42.9 (4.7)    |
| May 1st to Oct 31st            | 3,285           | 57.1 (4.7)    |
| **Age (years)**                |                 |
| 40-59                          | 3,280           | 59.6 (0.8)    |
| ≥ 60                           | 2,957           | 40.4 (0.8)    |
| **Gender**                     |                 |
| Male                           | 3,048           | 48.9 (0.7)    |
| Female                         | 3,189           | 51.1 (0.7)    |
| **BMI (kg/m²)**                |                 |
| Normal-weight                  | 1,677           | 25.7 (0.7)    |
| Overweight                     | 2,134           | 35.5 (0.8)    |
| Obese                          | 2,426           | 38.8 (1.0)    |
| **Race/ethnicity**             |                 |
| Hispanic                       | 1,261           | 10.5 (1.4)    |
| Non-Hispanic white             | 2,682           | 73.0 (2.3)    |
| Non-Hispanic black             | 1,451           | 10.0 (1.3)    |
| Other races                    | 843             | 6.6 (0.6)     |
| **Education**                  |                 |
| Less than high school          | 2,218           | 26.9 (1.6)    |
| High school graduate           | 1,597           | 26.1 (1.1)    |
| Some college or AA degree      | 1,679           | 31.6 (1.3)    |
| College graduate or above      | 740             | 15.5 (1.4)    |
| **RIP**                        |                 |
| < 1.00                         | 1,125           | 11.9 (1.1)    |
| ≥ 1.00                         | 4,648           | 88.1 (1.1)    |
| **Smoking status**             |                 |
| Never                          | 3,285           | 52.0 (1.1)    |
| Former                         | 1,795           | 29.7 (0.9)    |
| Current                        | 1,153           | 18.2 (0.9)    |
| **Physical activity status**   |                 |
| Inactive                       | 3,387           | 50.2 (1.4)    |
| < 150 min/week                 | 1,001           | 16.6 (0.9)    |
| ≥ 150 min/week                 | 1,845           | 33.2 (1.2)    |
| **Self-reported health status**|                 |
| Good to excellent              | 4,586           | 80.4 (1.0)    |
| Fair to poor                   | 1,649           | 19.6 (1.0)    |
| **Vitamin D intake**           |                 |
| < 400 IU                       | 3,571           | 53.3 (1.0)    |
| ≥ 400 IU                       | 2,666           | 46.7 (1.0)    |
| **25(OH)D level**              |                 |
| < 50 nmol/L                    | 1,646           | 19.7 (1.4)    |
| ≥ 50 nmol/L                    | 4,591           | 80.3 (1.4)    |

SE: standard error. AA: Associates of Arts; RIP: ratio of family income to poverty.
### Table II. Serum 25(OH)D and metabolite levels across weight change history among adults

| Vitamin D (nmol/L) | Weight loss (≥ 5 %) (n = 1,475) | Stable weight a (n = 3,382) | Weight gain (≥ 5 %) (n = 1,380) |
|--------------------|---------------------------------|-----------------------------|-------------------------------|
| 25(OH)D<sub>3</sub> | 71.7 (1.4)                      | 70.9 (1.0)                  | 65.9 (1.0)*                   |
| 25(OH)D<sub>2</sub> | 5.5 (0.8)                       | 4.4 (0.4)                   | 4.9 (0.8)                     |
| 25(OH)D            | 77.2 (1.0)                      | 75.4 (0.9)                  | 70.9 (1.1)*                   |

#### Weight change in 10 years

| Vitamin D (nmol/L) | Weight loss (≥ 5 %) (n = 1,473) | Stable weight a (n = 1,812) | Weight gain (≥ 5 %) (n = 2,952) |
|--------------------|---------------------------------|-----------------------------|---------------------------------|
| 25(OH)D<sub>3</sub> | 77.7 (1.1)                      | 73.2 (1.1)                  | 67.1 (1.0)*                     |
| 25(OH)D<sub>2</sub> | 5.2 (0.8)                       | 4.0 (0.3)                   | 5.1 (0.6)                      |
| 25(OH)D            | 76.9 (0.9)                      | 77.3 (1.1)                  | 72.2 (0.9)*                     |

Models adjusted for six-month study period, age, gender, race/ethnicity, education, poverty level, smoking status, physical activity, self-reported health, and vitamin D intake. a: Reference category (loss or gain weight < 5 %); *: p-value < 0.05

### Figure 1.

25(OH)D levels according to vitamin D intake and percent weight change in the past year.

Figure 2 shows adjusted 25(OH)D levels across the participants’ percent weight change categories from their maximum weight. Notably, participants who lost weight had significantly higher total 25(OH)D levels than those with a present maximum weight. For instance, participants who lost weight > 10 %, 5 to 10 % or < 5 % from their maximum had an average 5.2, 4.8, and 2.4 nmol/L higher 25(OH)D levels than those who did not, respectively.
The present findings suggest that adults who maintained a stable weight over time had significantly higher 25(OH)D3 and 25(OH)D concentrations than their counterparts who gained weight. Notably, 25(OH)D and its metabolites concentrations were similarly distributed across weight change in the past year and over the past 10 years. For instance, 25(OH)D levels were 4.5 and

| Table III. | The association between obesity status in the previous 10 years and 25(OH)D concentrations among middle-aged and older adults |
|------------|------------------------------------------------------------------------------------------------------------------|
|            | Never obese (reference)                                      | Previously obese and presently non-obese | Previously non-obese and presently obese | Always obese |
| 40-59 years | 25(OH)D3 70.1 (1.0) 68.0 (3.5) 61.7 (1.7)* 60.1 (1.1)* | 3.3 (0.3) 3.2 (0.8) 4.4 (0.7) 4.1 (0.6) | 73.4 (0.9) 71.3 (3.1) 66.1 (1.5)* 64.2 (1.1)* |
|            | ≥ 60 years | 25(OH)D3 79.4 (1.3) 74.8 (1.7) 71.4 (1.9)* 68.6 (1.4)* | 6.4 (1.0) 5.8 (1.2) 6.2 (1.2) 6.8 (1.0) | 85.9 (1.2) 80.7 (3.0) 77.6 (2.3)* 75.5 (1.2)* |
|            | Total      | 25(OH)D3 73.9 (1.0) 70.7 (2.1) 65.7 (1.4)* 63.3 (1.0)* | 4.5 (0.5) 5.2 (0.6) 4.3 (0.8) 5.2 (0.6) | 78.5 (0.8) 74.9 (1.4) 70.9 (1.4)* 68.5 (1.0)* |
| ≥ 60 years | 25(OH)D3 | 70.1 (1.0) 68.0 (3.5) 61.7 (1.7)* 60.1 (1.1)* | 3.3 (0.3) 3.2 (0.8) 4.4 (0.7) 4.1 (0.6) | 73.4 (0.9) 71.3 (3.1) 66.1 (1.5)* 64.2 (1.1)* |
|            | ≥ 60 years | 25(OH)D3 | 79.4 (1.3) 74.8 (1.7) 71.4 (1.9)* 68.6 (1.4)* | 6.4 (1.0) 5.8 (1.2) 6.2 (1.2) 6.8 (1.0) | 85.9 (1.2) 80.7 (3.0) 77.6 (2.3)* 75.5 (1.2)* |
| Total      | 25(OH)D3 | 73.9 (1.0) 70.7 (2.1) 65.7 (1.4)* 63.3 (1.0)* | 4.5 (0.5) 5.2 (0.6) 4.3 (0.8) 5.2 (0.6) | 78.5 (0.8) 74.9 (1.4) 70.9 (1.4)* 68.5 (1.0)* |

*: Model 1 adjusted for six-month study period, gender, race/ethnicity, education, poverty level, smoking status, leisure-time physical activity, self-reported health, and vitamin D intake; **: Model 2 adjusted for age and all variables in model 1; *: p-value < 0.05.

**Figure 2.**
Percent weight change from self-reported maximum weight and 25(OH)D levels.

**DISCUSSION**

The present findings suggest that adults who maintained a stable weight over time had significantly higher 25(OH)D3 and 25(OH)D concentrations than their counterparts who gained weight. Notably, 25(OH)D and its metabolites concentrations were similarly distributed across weight change in the past year and over the past 10 years. For instance, 25(OH)D levels were 4.5 and
5.1 nmol/L lower among participants who gained weight ≥ 5 % in the previous year and since 10 years ago when compared with those with stable weight, respectively. In contrast, 25(OH)D levels were marginally increased in participants who had lost weight ≥ 5 % in the previous year.

The study results are consistent with those from a recent systematic review and meta-analysis of 4 randomized and 11 nonrandomized clinical trials of caloric restriction and exercise in which 25(OH)D levels slightly improved with weight loss in comparison with weight maintenance under similar conditions of supplemental vitamin D intake (14). Likewise, Panu et al., in a meta-regression analysis of clinical trials, reported a small increase in 25(OH)D levels after weight loss in obese subjects not taking vitamin D supplements (21). Moreover, participants who gained weight ≥ 5 % in the past year had significantly lower 25(OH)D levels than their counterparts with stable weight, irrespective of their daily vitamin D intake. However, subjects who gained weight and reported taking vitamin D ≥ 400 IU/d had on average 23.9 nmol/L higher 25(OH)D levels than those who did not.

Notably, participants who lost weight from their maximum reported weight had significantly higher 25(OH)D levels than those who did not, which was more marked among subjects who lost weight ≥ 5 %. The present findings are consistent with the results from the diabetes prevention program, in which participants in the lifestyle intervention who lost a mean body percent of 7.3 % in the first 6 months had mean 25(OH)D levels 0.8 ng/mL higher than those in the placebo group who lost only 0.4 % (22). Thus, the study findings suggest that adipose tissue is a storage site for vitamin D, which may be slowly released into the circulation in subjects who lose weight through lifestyle interventions. Since exercise is a powerful stimulus for lipolysis, it is feasible that the vitamin D deposited in adipocytes may be mobilized by increasing physical activity (23). Moreover, the increased 25(OH)D levels across weight loss categories from the subjects’ maximum reported weight found in the present study do not support the hypothesis of sequestration of dietary or endogenous synthesis of cholecalciferol in the fatty tissue in subjects with obesity (7).

For instance, a recent study conducted to examine the association between leisure-time physical activity and 25(OH)D concentrations among older adults demonstrated that obese subjects physically active had on average 9.2 nmol/L higher 25(OH)D levels than their counterparts with a sedentary lifestyle (24).

The study results are in agreement with the vitamin D dilutional model previously described by Drincic et al., in which any given increment of cholecalciferol would be distributed not only in the serum, but also in the totality of body fat. Accordingly, if the fat mass is twice as much in an obese subject as compared to a normal-weight subject, then the induced rise in serum cholecalciferol would be roughly predicted as half as much (8). Similarly, a cross-sectional study designed to compare vitamin D concentrations in subcutaneous and omental adipose tissue between women with obesity and those without obesity scheduled for surgery concluded that the enlarged adipose mass in subjects with obesity serves as reservoir for vitamin D, and that the increased amount of vitamin D required to saturate this compartment may predispose individuals with obesity to inadequate serum 25(OH)D levels (25).

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Of relevance, Ganloff et al., in a 1-year lifestyle interventional study among men with obesity not taking vitamin D supplementation, described that the visceral adipose tissue was the adipose depot most correlated with increasing 25(OH)D levels (26).

Several limitations should be mentioned while interpreting the results. First, percent weight change over time was calculated from participants’ self-reported weight, which may have been a source of recall bias. Nevertheless, a recent report from the Finnish twin study demonstrated high correlations between self-reported and measured anthropometric values (27). Second, sunlight exposure and sun protection measures were not included in the present analysis, which may have affected the synthesis of vitamin D. Third, the effect of latitude on subject 25(OH)D levels was undetermined. Despite these limitations, the present population-based study is the first to demonstrate a significant relationship between weight change history and 25(OH)D concentrations.

In conclusion, subjects with a stable weight or those who lost weight ≥ 5 % from their maximum lifetime weight had significantly higher 25(OH)D concentrations than their counterparts who gained weight over time. Thus, maintaining a healthy weight may be an effective strategy to reach optimal serum 25(OH)D levels.

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