Vitamin D status and resistance exercise training independently affect glucose tolerance in older adults

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ABSTRACT

We assessed the influence of serum 25-hydroxyvitamin D (25(OH)D) and parathyroid hormone (PTH) concentrations on oral glucose tolerance, body composition, and muscle strength in older, nondiabetic adults who performed resistance exercise training (RT) while consuming diets with either 0.9 or 1.2 g protein kg\(^{-1}\) d\(^{-1}\). We hypothesized that individuals with insufficient 25(OH)D and/or high PTH would have less improvement in glucose tolerance after 12 weeks of RT compared with individuals with sufficient 25(OH)D and lower PTH. Sixteen men and 19 women (aged 61 ± 8 years; range, 50-80 years; body mass index, 26.3 ± 3.6 kg/m\(^2\)) performed RT 3 times/wk for 12 weeks, with oral glucose tolerance tests done at baseline and postintervention. Protein intake did not influence the responses described below. Plasma glucose area under the curve (\(P = .02\)) and 2-hour plasma glucose concentration (\(P = .03\)) were higher for vitamin D-insufficient subjects (25(OH)D <50 nmol/L, \(n = 7\)) vs vitamin D-sufficient subjects (25(OH)D ≥50 nmol/L, \(n = 28\)). These differences remained significant after adjustment for age and body mass index. Resistance exercise training reduced fat mass (mean ± SD, −6% ± 7%; \(P < .001\)) and increased lean body mass (2% ± 3%, \(P < .001\)) and whole-body muscle strength (32% ± 17%, \(P < .001\)) in these weight-stable subjects but did not affect 25(OH)D or PTH concentrations. Oral glucose tolerance improved after RT (−10% ± 16% in glucose area under the curve and −21% ± 40% in 2-hour glucose, \(P = .001\)), but baseline 25(OH)D and PTH did not influence these RT-induced changes. These findings indicate that vitamin D status and RT independently affect glucose tolerance, and a training-induced improvement in glucose tolerance does not offset the negative effect of insufficient vitamin D status in older, nondiabetic adults.

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1. Introduction

Aging is accompanied by a shift in body composition toward an increase in fat mass and a decrease in skeletal muscle mass [1]. The loss of muscle mass and function, termed sarcopenia, is associated with physical impairment and disability [2,3], whereas elevations in fat mass increase the risk for insulin resistance [1,4]. Aging is also a risk factor for vitamin D insufficiency [5], defined by the Institute of Medicine as a serum 25-hydroxyvitamin D (25(OH)D) concentration less than 50 nmol/L [6]. Serum 25(OH)D is positively associated with muscle function [7,8] and glucose tolerance [9-11] in older adults, independent of physical activity. Older adults with vitamin D insufficiency are reported to be more likely to develop sarcopenia and impairments in physical performance compared with adults with sufficient vitamin D status (≥50 nmol/L) [12,13]. Low vitamin D status is often accompanied by an elevation in serum parathyroid hormone (PTH) concentration, which is associated with increased risk for sarcopenia [12] and lower glucose tolerance [14,15]. Research suggests that 1,25(OH)2D, the active vitamin D metabolite, acts directly on the pancreas to stimulate insulin biosynthesis [16,17] and secretion [18]. This is supported by in vivo and in vitro experiments showing severe vitamin D deficiency and disruptions in the vitamin D signaling pathway to result in reductions in glucose-induced insulin secretion and impaired glucose tolerance [16,17]. Vitamin D is also implicated in determining insulin sensitivity by up-regulating the expression of the human insulin receptor (IR) [19] and decreasing obesity-related systemic inflammation through its actions on immune cells [20]. These data suggest that low 25(OH)D and/or high PTH are detrimental to muscle health and glucose tolerance in older adults.

It is recommended that older adults perform moderate- to high-intensity resistance exercise training (RT) 2 to 3 d/ wk to preserve or increase skeletal muscle mass and improve muscle strength and glucose control [21,22]. The influence of serum 25(OH)D and PTH concentrations on RT-induced changes in body composition, muscle strength, and glucose tolerance is not well documented. After a 3-month, low-intensity exercise program that included a combination of supervised group exercises and home-based walking, frail elderly women in the highest quartile for baseline 25(OH)D (≥67.5 nmol/L) improved in more areas of physical performance, but not muscle strength, compared with women in the lower 3 quartiles [23]. The effect of PTH on these outcomes was not evaluated in the previously mentioned study.

The present study evaluated the influence of vitamin D status and serum PTH concentration on changes in body composition, muscle strength, and indices of oral glucose tolerance in nondiabetic, older adults who performed moderate-intensity RT for 12 weeks. The 25(OH)D and PTH data were obtained by analyzing plasma samples saved from a study originally designed to assess the effects of dietary protein intake on resistance training–induced changes in body composition, muscle strength, and glucose tolerance in older adults [24,25]. We reported that RT improved body composition (increased lean body mass and decreased fat mass), muscle strength, and glucose tolerance, independent of dietary protein intake. The rationale for the current study was to retrospectively assess if the participant’s vitamin D status or PTH concentration influenced these metabolic responses to RT. We hypothesized that the magnitude of change in body composition, muscle strength, and glucose tolerance after 12 weeks of RT would be lower in individuals with vitamin D insufficiency and/or high serum PTH concentration.

2. Methods

2.1. Subjects

Older men and women from the greater Lafayette, IN, USA, community were recruited primarily using advertisements in local newspapers and by posting flyers on community and campus bulletin boards. Criteria for eligibility included the following: (1) age range 50 to 80 years; (2) body mass index (BMI) of 20 to 35 kg/m²; (3) nondiabetic; (4) clinically normal kidney, liver, and cardiac functions; (5) not currently using anti-inflammatory steroid medications; (6) no hip replacement; (7) no habitual RT in the past 6 months; (8) postmenopausal (women ≥2 years since last menstruation); and (9) nonsmokers. Fifty subjects were enrolled into the study, 36 subjects completed the protocol, and 35 subjects were included in the final analyses. Details regarding study recruitment, screening procedures, and subject dropout were described previously [24].

The study protocol and informed consent agreement were approved by the Purdue University Institutional Review Board, and this study was conducted according to the guidelines laid down in the Declaration of Helsinki. Subjects provided written informed consent before beginning the protocol and received monetary compensation for their participation.

2.2. Experimental design

The current investigation is a secondary analysis performed using data from a study designed to evaluate the combined effects of RT and dietary protein intake on body composition, muscle strength, and glucose tolerance in older adults [24]. The study consisted of a 14-week protocol that was conducted at Purdue University (40°N latitude) between June and December of the same year. We used a rolling enrollment strategy with subjects starting the protocol between June and September. Subjects were randomly assigned to groups that consumed either a higher- or lower-protein diet, and everyone participated in a moderate-intensity RT program, regardless of protein group assignment. Baseline data were collected during the first 2 weeks of the study, whereas subjects maintained their habitual diet and level of physical activity. The protein and RT interventions were implemented during weeks 3 through 14. Postintervention measurements were obtained during week 14, whereas subjects continued the diet and exercise interventions. Body composition, muscle strength, oral glucose tolerance, blood chemistries, and skeletal muscle insulin signaling protein content were assessed at baseline and postintervention. These data are published [24] and are described in this report as necessary in
conjunction with the 25(OH)D and PTH data. All measurements were made in the morning after an overnight (~10-hour) fast. Subjects were allowed to continue their habitual use of medications and supplements, which was documented throughout the study.

### 2.3. Resistance exercise training intervention

All subjects resistance trained 3 d/wk. Exercise sessions and testing were supervised and completed at the A.H. Ismail Center for Health, Exercise, and Nutrition at Purdue University using pneumatic resistance exercise equipment (Keiser Sports Health Equipment Company, Fresno, CA, USA). Each training session (~1.25 hours) included a 10-minute warm-up, 3 sets of 8 resistance exercises at 80% of the predetermined 1-repetition maximum, and a 10-minute cool down, as previously described [24]. The warm-up and cool-down each included 5 minutes of moderate-intensity treadmill walking or stationary cycling and 5 minutes of stretching. Each training session included an upper back seated row, chest press, latissimus dorsi pull down, leg extension, leg curl, and double-leg press. The seated calf press and shoulder raise were rotated with hip adductor and hip abductor exercises and were performed during every other session, so that participants completed 6 primary exercises and 2 additional exercises for a total of 8 exercises per training session [24]. The first 2 sets of resistance exercises consisted of 8 repetitions with the third set performed to voluntary fatigue or 12 repetitions. Completion of 12 repetitions during the third set of exercises resulted in a 5% increase in resistance for the respective exercise at the next training session.

### 2.4. Dietary intervention

Among all subjects at baseline, dietary protein intake was 1.1 ± 0.6 g protein kg⁻¹ d⁻¹ [24]. Subjects maintained body weight and consumed either a lower-protein (0.9 ± 0.1 g protein kg⁻¹ d⁻¹) or higher-protein (1.2 ± 0.0 g protein kg⁻¹ d⁻¹) diet during the 12-week intervention. The predominant sources of protein for the 2 diets were eggs, striated tissues (beef, poultry, pork, and fish), and dairy products. Diets were individualized to provide 1.5 times the basal energy needs for each subject calculated using sex-specific Harris-Benedict equations [26]. The warm-up and cool-down each included 5 minutes of moderate-intensity treadmill walking or stationary cycling and 5 minutes of stretching. Each training session included an upper back seated row, chest press, latissimus dorsi pull down, leg extension, leg curl, and double-leg press. The seated calf press and shoulder raise were rotated with hip adductor and hip abductor exercises and were performed during every other session, so that participants completed 6 primary exercises and 2 additional exercises for a total of 8 exercises per training session [24]. The first 2 sets of resistance exercises consisted of 8 repetitions with the third set performed to voluntary fatigue or 12 repetitions. Completion of 12 repetitions during the third set of exercises resulted in a 5% increase in resistance for the respective exercise at the next training session.

### 2.5. Body composition and anthropometric assessments

Dual-energy x-ray absorptiometry was used to measure whole-body fat mass and lean mass (GE Lunar Prodigy with EnCORE software version 5.60, Madison, WI, USA). The natural waist circumference was measured with a fiberglass spring tape measure. Height was measured at the beginning of the study with a wall-mounted stadiometer (Holtain Ltd, Crymych, Wales, UK). All measurements were made in the morning after the subject fasted overnight for ~10 hours.
Western blotting [30] (all antibodies purchased from Santa
Cruz Biotechnology, Santa Cruz, CA, USA) at baseline and 
postintervention. Because significant changes from baseline 
post intervention were not detected in total IR or IR
substrate-1 total contents, only a subset of the samples were 
assessed for these proteins (n = 22 and n = 16, respectively).

2.10. Statistical analyses

Serum vitamin D and PTH concentrations were measured as a 
secondary objective of a parent study; therefore, power 
calculations to determine sample size were not performed 
based on these measures. Differences in 25(OH)D and PTH 
concentrations between dietary protein groups, sexes, and 
supplement users (ie, subjects taking a multivitamin, calcium, 
and/or vitamin D supplement) at baseline were evaluated 
with 2-sample t tests. Lafayette, IN, is located above the 35th 
parallel north latitude and is subject to seasonality, which 
could influence serum 25(OH)D and PTH concentrations. 
Repeated-measures analysis of variance was used to assess 
the main effect of month of baseline testing (June through 
September) and interaction between month of baseline 
testing and time to account for a potential influence of season 
on 25(OH)D and PTH concentrations.

A linear regression analysis was conducted to identify 
potential confounders that may influence serum 25(OH)D 
concentrations. Although percentage body fat was highly 
correlated with BMI (r = 0.41, P = .02), only age and BMI were 
identified as significant and analyses were conducted after 
adjusting for the impact of these 2 factors on serum 25(OH)D 
concentrations. In addition, dietary protein group was previously 
found to have independent effects on insulin AUC [24] and 
was included as a covariate for this outcome. Baseline 25(OH)D 
concentration was categorized based on the cutoffs for vitamin 
D status proposed by the Institute of Medicine [6], with a serum 
25(OH)D less than 50 nmol/L classified as insufficient (n = 7) and 
a serum 25(OH)D of 50 nmol/L or greater considered sufficient 
(n = 28). Baseline serum PTH concentrations were divided into 
tertiles (tertile 1: <3.94 pmol/L, n = 11; tertile 2: 3.94-4.77 pmol/L, 
n = 13; tertile 3: >4.77 pmol/L, n = 11). Repeated-measures 
analysis of variance was used to determine the main effects of 
time (ie, RT) and group (ie, vitamin D status and PTH tertile) and 
group-by-time interactions. Tukey-Kramer post hoc test was 
used to explore interactions between group and time and to 
detect interactions between group and 25(OH)D and PTH 
concentrations. Within each vitamin D or PTH group, change 
from baseline was calculated by averaging the individual 
changes among subjects within the respective group.

Relationships for baseline 25(OH)D, PTH, and 25(OH)D/PTH 
ratio with changes in body composition, muscle strength, and 
oral glucose tolerance test outcomes were evaluated with 
Pearson correlations. Pearson correlations were also used for 
the cross-sectional evaluation of relationships at baseline and 
postintervention. Multiple linear regression analyses were

Table 1 – Characteristics of subjects at baseline and postintervention

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Postintervention</th>
<th>P</th>
</tr>
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<tbody>
<tr>
<td>Age (y)</td>
<td>61 ± 8</td>
<td>26.2 ± 3.7</td>
<td>.30</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>26.3 ± 3.6</td>
<td>26.5 ± 3.7</td>
<td>.31</td>
</tr>
<tr>
<td>Waist circumference (cm)</td>
<td>85.8 ± 13.3</td>
<td>84.5 ± 13.0b</td>
<td>.006</td>
</tr>
<tr>
<td>Body weight and composition</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>76.5 ± 14.4</td>
<td>76.2 ± 14.5</td>
<td>.31</td>
</tr>
<tr>
<td>Lean mass (kg)</td>
<td>46.3 ± 11.0</td>
<td>47.5 ± 11.4b</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Fat mass (kg)</td>
<td>27.3 ± 9.1</td>
<td>25.9 ± 9.2b</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Body fat (%)</td>
<td>37.0 ± 10.0</td>
<td>35.1 ± 10.4b</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Whole-body muscle strength (kg)</td>
<td>397 ± 150</td>
<td>512 ± 169b</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Blood analyses</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Calcium (mmol/L)</td>
<td>2.26 ± 0.10</td>
<td>2.25 ± 0.08</td>
<td>.41</td>
</tr>
<tr>
<td>Creatinine (μmol/L)</td>
<td>86.6 ± 13.3</td>
<td>88.4 ± 12.4</td>
<td>.26</td>
</tr>
<tr>
<td>PTH (pmol/L)</td>
<td>4.38 ± 1.20</td>
<td>4.40 ± 1.70</td>
<td>.91</td>
</tr>
<tr>
<td>25(OH)D (nmol/L)</td>
<td>65.4 ± 17.5</td>
<td>63.6 ± 17.5</td>
<td>.26</td>
</tr>
<tr>
<td>25(OH)D/PTH ratio</td>
<td>16.3 ± 7.2</td>
<td>17.4 ± 10.6</td>
<td>.87</td>
</tr>
<tr>
<td>Glucose tolerancea</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fasting glucose (mmol/L)</td>
<td>4.4 ± 0.5</td>
<td>4.4 ± 0.4</td>
<td>.28</td>
</tr>
<tr>
<td>Fasting insulin (pmol/L)</td>
<td>36.8 ± 21.5</td>
<td>42.4 ± 33.3</td>
<td>.84</td>
</tr>
<tr>
<td>Fasting C-peptide (pmol/L)</td>
<td>438 ± 196</td>
<td>450 ± 220</td>
<td>.50</td>
</tr>
<tr>
<td>Glucose AUC (mmol · 2 h/L)</td>
<td>217 ± 102</td>
<td>158 ± 90b</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Insulin AUC (pmol · 2 h/L · 10^3)</td>
<td>30.4 ± 14.8</td>
<td>28.5 ± 18.4</td>
<td>.50</td>
</tr>
<tr>
<td>C-peptide AUC (pmol · 2 h/L · 10^3)</td>
<td>157.4 ± 68.8</td>
<td>155.3 ± 67.6</td>
<td>.61</td>
</tr>
<tr>
<td>2-h glucose (mmol/L)</td>
<td>5.2 ± 1.1</td>
<td>4.7 ± 1.1b</td>
<td>.001</td>
</tr>
<tr>
<td>HOMA-IR</td>
<td>1.04 ± 0.62</td>
<td>1.24 ± 1.14</td>
<td>.76</td>
</tr>
<tr>
<td>ISI</td>
<td>9.05 ± 4.86</td>
<td>9.93 ± 6.29</td>
<td>.17</td>
</tr>
<tr>
<td>Hemoglobin A1c (%)</td>
<td>5.0 ± 0.00</td>
<td>5.0 ± 0.00</td>
<td>.90</td>
</tr>
</tbody>
</table>

a n = 35 (16 men, 19 women). Values are means ± SD.
b Different from baseline.
c n = 31.
performed to further assess associations, and age and BMI were included in the model as confounding variables.

Data points that were missing or outliers (±3 SDs) were not included in the analyses. One man was excluded from the current analysis for having a change in serum PTH concentration (baseline to postintervention) beyond 3 SD of the group mean that could not be explained by change in serum calcium concentration, 25(OH)D, or dietary calcium intake. Baseline and postintervention values for 25(OH)D/PTH ratio, FPI, ISI, and HOMA-IR did not meet the assumptions for normality and were log transformed. Statistical analyses were performed using SPSS (PASW) Statistics 18.0.3 (IBM Corp, Somers, NY, USA). A P value less than .05 was deemed statistically significant. All data are reported as means ± SD, except in the figures where means ± SE are used.

3. Results

3.1. Subjects

Characteristics of subjects at baseline are presented in Table 1. Baseline serum 25(OH)D concentrations ranged from 30.2 to 107.6 nmol/L, with 7 subjects having a concentration less than 50 nmol/L. At baseline, serum PTH ranged from 1.54 to 7.10 pmol/L. Five subjects had secondary hyperparathyroidism classified as a PTH concentration of 5.79 pmol/L or greater in the presence of a normal serum calcium concentration. Serum 25(OH)D, PTH, and 25(OH)D/PTH ratio did not differ by dietary protein group or sex at baseline. Twenty-three subjects (65.7%) reported regularly consuming a multivitamin, calcium, and/or vitamin D supplement. Subjects who consumed supplements had a higher baseline 25(OH)D concentration compared with subjects who did not consume supplements, although this difference was not statistically significant (68.9 ± 18.2 vs 58.4 ± 14.7 nmol/L, P = .09). Baseline PTH was not different between supplement users and nonusers (4.30 ± 1.23 vs 4.42 ± 1.22 pmol/L, P = .76).

3.2. 25-Hydroxyvitamin D and PTH

Serum 25(OH)D and PTH concentrations did not change from baseline to postintervention (Table 1, regardless of protein group, sex, age, and BMI. Neither month of baseline testing nor supplement use influenced change in 25(OH)D or PTH concentrations (data not shown).

3.3. Body composition and muscle strength

As previously reported [24], body weight was maintained throughout the study, whereas body composition and muscle strength improved as a result of RT (Table 1). Waist circumference and fat mass decreased (−1% ± 3% [P = .006] and −6% ± 7% [P < .001], respectively), and lean mass increased (2% ± 3%, P < .001) with RT. Whole-body strength increased

Fig. 1 – Change in body mass and body composition from baseline to postintervention by vitamin D status. The gray bars represent the group of vitamin D–insufficient subjects (<50 nmol/L, n = 7), and the white bars represent the group of vitamin D–sufficient subjects (≥50 nmol/L, n = 28). A main effect of resistance training (P < .05). Vitamin D status did not influence resistance training–induced responses. Data presented as means ± SE.

Fig. 2 – Glucose AUC (A) and 2-hour glucose (B) by vitamin D status at baseline and postintervention. The gray bars represent the group of vitamin D–insufficient subjects (<50 nmol/L, n = 7), and the white bars represent the group of vitamin D–sufficient subjects (≥50 nmol/L, n = 28). A main effect of resistance training (P < .05). A main effect of vitamin D status (P < .05). Vitamin D status did not influence resistance training–induced decreases in glucose AUC and 2-hour glucose. Glucose AUC and 2-hour glucose were higher in vitamin D–insufficient subjects compared with vitamin D–sufficient subjects at baseline and postintervention. Data presented as means ± SE.
of baseline vitamin D status was found for glucose AUC (P = .02) and 2-hour glucose (P = .03; Fig. 2A and B; Supplementary Table 1). Vitamin D–insufficient subjects had higher glucose AUC and 2-hour glucose concentrations than did vitamin D–sufficient subjects at pre– and post–time points, even after adjustment for age and BMI (P = .02).

Change in fasting C-peptide from baseline to postintervention differed among PTH tertiles (group x time, P = .02). The lowest tertile for baseline PTH (<3.94 pmol/L) had a 14% ± 8% decrease in fasting C-peptide, whereas subjects in the highest tertile for PTH (>4.77 pmol/L) had an increase of 15% ± 8% (Fig. 3; Supplementary Table 2). This effect remained significant after adjustment for age and BMI (P = .01). These differences among PTH tertiles were not observed for the change in fasting insulin concentration over time (Fig. 3; Supplementary Table 2).

3.5. Insulin signaling proteins

We previously reported that in this study, skeletal muscle total IR, IR substrate-1, and Akt (n = 30) protein concentrations did not change from baseline to postintervention, whereas aPKC \( \zeta / \lambda \) protein content increased with RT (n = 30, P = .001 [24]). Neither baseline 25(OH)D nor PTH influenced the concentrations of any of these proteins in the skeletal muscle.

3.6. Cross-sectional associations

After adjusting the data for differences in age and BMI, at baseline, only ISI was positively associated with serum 25(OH)D (P = .079; Table 2). However, using postintervention data, age- and BMI-adjusted serum 25(OH)D level was negatively associated with glucose AUC and 2-hour glucose (P < .05). Posttraining, there was also a significant negative relationship between 2-hour serum glucose and 25(OH)D/PTH ratio that remained significant after adjustment for age and BMI (P < .05; Table 2).

4. Discussion

Our finding that vitamin D–insufficient subjects had lower glucose tolerance than did vitamin D–sufficient subjects is in
agreement with previous reports of a negative association between 25(OH)D and glucose AUC [9] or 2-hour serum glucose [10,31,32]. Previous studies reporting an inverse relationship between glucose AUC and 25(OH)D also found that insulin AUC was lower in subjects with higher serum 25(OH)D [9]. However, insulin AUC was not influenced by vitamin D status in our study. In glucose-tolerant adults, ISI (calculated by dividing the average glucose infusion rate by the average plasma insulin concentration during the last hour of a 3-hour glucose tolerance test using hyperglycemic clamps) is a significant predictor of insulin response [31]; therefore, the lack of an effect of vitamin D on insulin AUC in the current study may be caused by the absence of an effect of vitamin D on ISI.

We previously reported that glucose tolerance improved in our subjects after RT [24]. We extend this finding by showing that the impact of RT on glucose tolerance is independent of the beneficial effects of vitamin D on this end point. Research regarding the impact of vitamin D status on exercise-induced changes in muscle strength is limited. The present finding that vitamin D status and PTH concentration did not affect changes in muscle strength with RT contrasts with findings from a study of community-dwelling, frail, elderly Japanese women (n = 80) [23]. After 3 months of low-intensity group and home-based exercises, women in the highest quartile for baseline 25(OH)D (>67.5 nmol/L) had greater improvements in more areas of physical performance than did women in the lower 3 quartiles [23]. Women in the lowest quartile for 25(OH) D (<47.5 nmol/L) experienced no improvement in physical fitness [23]. Among apparently healthy, community-dwelling, elderly Chilean men and women with vitamin D insufficiency (mean serum 25OHD = 31.0 ± 5.5 nmol/L) (n = 96), a 9-month, biweekly regimen of balance, aerobic, and low-intensity strength exercises (<65% 1-repetition maximum) increased quadriceps strength from 11% to 21% above baseline [33]. Supplementation with vitamin D3 (400 IU/d) during the exercise intervention corrected the vitamin D insufficiency (posttreatment serum 25OHD, 64.4 ± 16.2 nmol/L) but did not alter exercise-induced improvements in muscle strength [33]. Collectively, these studies reinforce the use of physical exercise and training to increase muscle strength in community-dwelling older people, whereas the impact of vitamin D status requires further investigation.

Previous research documented positive associations between PTH and indices of insulin resistance [14,15]. We hypothesized that subjects in the lowest tertile for baseline PTH concentration would experience greater improvement in glucose tolerance and insulin sensitivity after RT. We observed that fasting C-peptide decreased in the lowest baseline PTH tertile and increased in the highest baseline PTH tertile after RT. Fasting C-peptide concentration is positively associated with insulin resistance [34] and is higher in type 2 diabetic patients compared with nondiabetic controls [35]. The difference in changes in C-peptide concentration among PTH tertiles may reflect a positive relationship between insulin resistance and PTH concentration. Fasting C-peptide was positively correlated with HOMA-IR and negatively correlated with ISI at both baseline and postintervention (baseline: \( r = 0.62 \) and \( r = -0.69 \), respectively; \( P < .05 \); postintervention: \( r = 0.59 \) and \( r = -0.59 \), respectively; \( P < .05 \)). Although our research showed no relationship between PTH and fasting C-peptide concentration at baseline, a positive relationship was observed postintervention (\( \beta = 0.45, P = .01 \)) that remained marginally significant after adjustment for age and BMI (\( P = .06 \)). Furthermore, cross-sectional correlations suggest the ratio of 25(OH)D to PTH concentration may be a determinant of glucose tolerance with evidence for an inverse relationship with 2-hour glucose and a positive relationship with ISI. Our observations are in agreement with another study that calculated the ratio of PTH/25(OH)D, opposite of our 25(OH)D/PTH ratio, finding HOMA-IR to increase across quartiles for the ratio, indicating lower insulin sensitivity with a higher PTH and lower 25(OH)D concentration [36]. Taken together, these results suggest that higher PTH and lower 25(OH)D/PTH ratio are associated with reduced insulin sensitivity, but this conclusion should be viewed cautiously until validated in future research with larger sample sizes.

Serum 25(OH)D is reported to be inversely associated with body fat mass [37,38], which may be the result of the storage and sequestration of vitamin D in the adipose tissue [39,40]. As a result, we were concerned that serum 25(OH)D could be indirectly reflecting well-established relationships between adiposity and indices of glucose tolerance. However, the BMI of our study group was fairly uniform, and we found that many of our observed relationships were significant after adjusting for differences in BMI and age, another well-established risk factor for glucose intolerance [41]. Collectively, our data are consistent with the hypothesis that maintaining adequate vitamin D status is independently influencing glucose metabolism. The mechanism for this relationship remains to be determined.

This is the first investigation to assess the effect of 25(OH)D and PTH on RT-induced changes in glucose tolerance and skeletal muscle insulin-signaling protein contents. Strengths of this study include the use of a study group that underwent an effective exercise intervention and the availability of data that permits a comprehensive evaluation of the influence of 25(OH)D and PTH on responses to RT. Furthermore, all subjects were apparently healthy and did not meet the diagnostic criteria for prediabetes or diabetes [29]. The current investigation is limited by sample size. The study was not powered to detect differential responses to RT based on vitamin D status and PTH tertile. Related to this, we had fewer subjects with inadequate vitamin D status compared with adequate vitamin D status. As a result of these limitations, the results presented are to be viewed as hypothesis generating and provide preliminary data for future research. Although we do not have data to accurately estimate sunlight exposure or dietary vitamin D intake to assess potential influences of these parameters on 25(OH)D concentration, the overall serum 25OHD concentrations of our subject did not change during the intervention period. This suggests that our results reflect the subjects’ typical 25(OH)D concentrations, thereby increasing the applicability of our findings.

In summary, we reject our hypothesis that individuals with insufficient 25(OH)D and/or higher PTH status will have less improvement in glucose tolerance after 12 weeks of RT than those with adequate vitamin D status and lower PTH. However, we observed that sufficient vitamin D status has a beneficial influence on glucose tolerance in nondiabetic,
weight-stable, older adults. These observations are independent of body mass, suggesting that there are direct effects of vitamin D on glucose-controlling tissues. The basis for this relationship remains to be determined. In addition, we observed that the beneficial impact of RT and vitamin D status on glucose tolerance are independent. Thus, maintaining sufficient vitamin D status provides a complementary approach to RT for maintaining glucose control in adults.

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.nutres.2013.03.005.

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