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Low dietary magnesium intake alters vitamin D—parathyroid hormone relationship in adults who are overweight or obese

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ABSTRACT

Vitamin D metabolism is dependent on magnesium (Mg) as a cofactor; therefore, poor Mg status may alter the relationship between vitamin D metabolite serum 25-hydroxyvitamin D (s25OHD) and serum parathyroid hormone (sPTH). We hypothesized that low dietary Mg intake may alter sPTH response to s25OHD in a population with excess body weight, thereby leading to a worsening of cardiometabolic health. To explore this hypothesis, we conducted a cross-sectional study on adults who were either overweight or obese (owt/ob). Dietary Mg intake was measured using a Mg food frequency questionnaire (MgFFQ). Body composition information was measured using Dual Energy X-ray Absorptiometry (DXA). Blood samples were obtained for all biochemical analyses. A total of 57 participants, 22 to 65 years of age, with a body mass index between 25 to 45 kg/m^2 were divided into 3 groups, according to dietary Mg intake percentiles (Low Mg Group = <33 percentile, Medium Mg Group = 33 to 66 percentile, High Mg Group = >66 percentile). Higher s25OHD was negatively associated with lower sPTH in the High Mg Intake group ($r = -0.472$, $P = .041$), but not in other groups. A positive relationship between s25OHD and serum high-molecular weight adiponectin concentrations was observed in the High Mg Group ($r = 0.532$, $r = 0.022$), but not in other groups. Serum Interleukin-6 concentrations were negatively associated with s25OHD ($r = -0.316$, $P = .017$) for the entire study group. Based on these results, our study demonstrated that a low dietary Mg intake may alter PTH response to 25OHD.

Abbreviations: 25OHD, 25-hydroxyvitamin D; BMI, Body mass index; Ca, Calcium; CRP, C-reactive protein; DXA, Dual-energy x-ray absorptiometry; HDL-C, High-density lipoprotein cholesterol; HMW adiponectin, High molecular weight adiponectin; IL-6, Interleukin-6; iMg, Serum ionized magnesium; IU, International Unit; LDL-C, Low-density liproprotein cholesterol; MCP-1, Monocyte chemoattractant protein-1; Mg, Magnesium; MgFFQ, Magnesium Food Frequency Questionnaire; Owt/ob, Overweight or obese; PTH, Parathyroid hormone; s25OHD, Serum concentrations of 25-hydroxyvitamin D; sIL-6, Serum concentrations of interleukin-6; sPTH, Serum concentrations of parathyroid hormone.

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1. Introduction

Magnesium (Mg) is an essential macromineral that serves many important physiological functions and plays an important role in chronic disease prevention [1-3]. The prevalence of poor Mg status due to low dietary intakes is alarmingly high, and it may lead to Mg deficiency and subsequent negative health consequences [2,3]. Magnesium plays critical roles in the regulation of adenosine triphosphate metabolism [1,2,4], deoxyribonucleic acids/ribonucleic acids synthesis [2,5], blood pressure [3,6], and insulin metabolism [7,8]; therefore, adequate Mg intakes are essential in chronic disease prevention and management [2,3]. Poor Mg status is also associated with systemic inflammation [9], a condition that is also commonly observed in individuals who are overweight or obese (owt/ob) [10]. It is well documented that excess body weight is a risk factor for development of hypertension [11], dyslipidemia [12] and systemic inflammation [13]. Obesity may independently and negatively influence cardiometabolic health; moreover, the prevalence of Mg deficiency in the owt/ob population is higher than that in their healthy weight counterparts [14]. Magnesium deficiency and owt/ob can independently lead to poor cardiometabolic health, but the coexistence of both conditions may further increase risk for cardiometabolic diseases such as cardiovascular disease and type 2 diabetes mellitus [9,10].

Magnesium status may influence parathyroid hormone (PTH), a hormone that regulates circulating calcium concentrations [15,16]. Excess production of PTH may cause oxidative stress, leading to systemic inflammation [17,18]. Chronically elevated concentrations of serum PTH (sPTH) have been found to be an independent predictor for both systemic inflammation [17] and prevalence of metabolic syndrome [19]. It is believed that PTH plays a critical role in the pathogenesis of cardiometabolic diseases by promoting atherogenesis [18,20], hypertension [21], and systemic inflammation [17,18,22]. Furthermore, excess body fat accumulation has been associated with elevated sPTH [23]. Treatment for secondary hyperparathyroidism, a condition characterized by elevated sPTH, typically involves using large doses of vitamin D supplementation (up to 50,000 International Units (IU) weekly) and/or calcium supplements [24,25]. However, researchers have recently raised concerns regarding the potential negative effects of large dose vitamin D with or without calcium supplements, including soft-tissue calcification [26] and increased falls in the elderly population [27]. Furthermore, results from the recently published Vitamin D and Omega-3 Trial (VITAL) have shown no improvements of a daily 2000 IU vitamin D_3 supplement on lowering cardiovascular disease risk over 5 years [28], suggesting that improving vitamin D status alone may not offer enough to improve cardiometabolic health parameters. There are also concerns regarding the use of calcium supplements on increased cardiovascular disease risk, with recent research pointing towards a positive association between calcium supplements and myocardial infarction [29]. Thus, it is important to identify other nutrients that may also influence sPTH, either by independently regulating sPTH or by mitigating the influences of vitamin D and calcium on sPTH.

The vitamin D metabolite, 25-hydroxyvitamin D (25OHD), is well understood to exhibit a negative relationship with sPTH [30,31]. However, this relationship may be altered in the owt/ob population [32-36]. Our previous meta-analyses indicated that a vitamin D_3 supplement of 1000 IU per day is ideal to achieve optimal concentrations of sPTH in owt/ob adults [36], which is higher than the current Recommended Dietary Allowances (RDA) for vitamin D for adults (600 IU for women and men between 19 and 70 years of age). Interestingly, Mg influences the secretion of sPTH and the hydroxylation of 25OHD to $1,25OH_2D$ [37-39]. The activating enzyme and transport protein of vitamin D metabolites requires Mg as a cofactor [38-40], which suggests that vitamin D metabolism may be impaired when there is low Mg availability. In a recent clinical study, Dai et al. demonstrated that both vitamin D status and metabolism can be influenced by Mg supplementation [41]. Furthermore, researchers from a clinical trial investigating the effects of Mg therapy have shown that the physiological effects of s25OHD on normalizing sPTH may be influenced by Mg status [37]. However, whether Mg status may influence the 25OHD/PTH axis in a population with excess body weight is unknown.

Previous evidence demonstrated that vitamin D metabolism is dependent on Mg status. A poor Mg status may lead to improper vitamin D metabolism, thereby limiting serum parathyroid hormone response to serum 25-dihydroxyvitamin D. The primary objective of this study was to examine the influence of Mg intake and serum ionized magnesium concentrations (iMg) on the relationship between serum 25-hydroxyvitamin D and serum parathyroid hormone concentrations in adults who are overweight or obese. We hypothesized that low dietary Mg intake will alter the relationship between vitamin D and parathyroid hormone, determined by concentrations of serum 25-hydroxyvitamin D and serum parathyroid hormone. The secondary aim of this study was to determine the influence of Mg status on cardiometabolic disease risk factors in adults with excess body weight. We hypothesized that a poor Mg status will be associated with poor cardiometabolic health in the overweight or obese population, assessed by markers of inflammation, glycemic indices, and lipid profile.

2. Methods and materials

2.1. *Participants and study design*

Women and men who were overweight or obese (BMI >25 kg/m^2) and participated in 2 larger clinical trials (NCT03134417, NCT03600675) at Drexel University were included in our analyses. Exclusion criteria included all major chronic diseases as well as conditions that may alter Mg, vitamin D, and/or calcium metabolism. The parent studies were approved by the Drexel University Institutional Review Board. All participants read and signed informed consent forms prior to participation and were informed of their right to withdraw from the studies at any time. All clinical trials were conducted in accordance with Good Clinical Practice Guidelines, the Declaration of Helsinki [42], and the United States 21 Code of Federal Regulations [43].

2.2. Study questionnaires and dietary assessment

To ensure eligibility, completion of a medical history form was required prior to participation. The following information was obtained from this form: race; date of birth; contact information; disease history; tobacco and alcohol use; recent and current medications; Mg, vitamin D, and calcium supplements use; history of eating disorders; any medical concerns; and any recent weight loss/gain greater than 10 pounds. To obtain dietary intakes, a magnesium food frequency questionnaire (MgFFQ) [44], a calcium food frequency questionnaire (CaFFQ) [45], and a 24-hour dietary recall were administered. The dietary questionnaires were overseen by a trained research assistant and/or registered dietitian in a consistent, reproducible manner. The 5-steps multiple-pass method [46] was used to obtain 24-hour dietary recall information. Dietary calcium to magnesium intake ratio (Ca:Mg ratio) was calculated by dividing dietary calcium intakes by dietary magnesium intakes. Dietary information was analyzed using FoodWorks version 17 software (Long Valley, NJ).

2.3. Anthropometric and physiological measurements

Body weight was measured with minimal clothing and no shoes to the nearest 0.25 kg, using a Seca 700 Physician's Balance Beam Scale (Chino, CA, USA). A stadiometer attached to the scale was used to assess height to the nearest 0.5 cm. Body mass index (BMI) was determined by dividing weight (kg) by height squared (m^2). Waist circumference was measured three times by using a non-stretch tape measure (Health Mobius® Circumference [Girth] measuring Tape-Body Tape Measure) in a horizontal plane around the torso equidistant between the lowest rib and the iliac crest. The average of these measurements was used in data analyses. With participants sitting in an upright position, a registered nurse measured systolic and diastolic blood pressure using a sphygmomanometer once on one arm, measuring to the nearest 0.5 mm Hg.

Trunk fat percent, total lean body mass, total fat-free mass, and total fat mass were assessed using Dual Energy X-ray Absorptiometry (DXA) (Lunar iDXA, enCORE Software Version 15, GE Healthcare, United Kingdom). Lean body mass percentage, fat-free mass percentage, and fat mass percentage were determined by dividing total lean mass, total fat-free mass, and total fat mass, respectively, by total body weight. As a precaution against prenatal radiation exposure, all female participants were required to take a urine pregnancy test (Fisher HealthCare™ Sure-Vue™ Serum/Urine hCG Test) prior to receiving a DXA scan. Sasai et al. [47] verified that the use of DXA provides an accurate measurement of fat percentage with minimal radiation exposure, unlike a computed tomography scan.

2.4. Blood sample collection and analyses

Blood samples were collected via venipuncture after an overnight fast of at least 8 hours. The blood was kept upright at room temperature for at least 1 hour prior to being centrifuged at 1800xg for 12 minutes at 4 °C. All samples were analyzed in duplicates. Serum was stored at –80 °C until analyses, with the exception of iMg analysis, which was performed within 5 hours of the blood sample collection. Concentrations for the assessment of iMg were analyzed with an Ion Sensitive Electrode Method by the NOVA-8 analyzer (NOVA 8 analyzer, NovaMedical, MA). Serum 25OHD concentrations were measured by enzyme immunoassay (EIA) from Immunodiagnostic Systems Inc. (Gaithersbug, MD, coefficient of variation [CV] <8.1%). Serum PTH concentrations were analyzed using an Intact PTH enzyme-linked immunosorbent assay (ELISA) (ALPCO, Salem, NH, coefficient of variation [CV] <6.1%). Markers of inflammation, such as C-reactive protein (CRP), interleukin-6 (IL-6), and Monocyte chemoattractant protein-1 (MCP-1), were assessed using ELISA (R&D Systems, Minneapolis, MN; CV <6.4%, 7.4%, and 7.8%, respectively). Glycemic indices, such as serum osteocalcin concentrations (Immunodiagnostic Systems Inc., Gaithersbug, MD, CV <5.1%) and serum insulin concentrations, were assessed using ELISA (R&D Systems, Minneapolis, MN, CV<7.5%); and serum high molecular weight (HMW) adiponectin concentrations (R&D Systems, Minneapolis, MN; CV <8.6%) and osteocalcin (Immunodiagnostic Systems Inc., Gaithersbug, MD, CV <5.1%) analyses were conducted using ELISA; with the exception of serum fasting glucose, which was measured using the hexokinase method (Sigma-Aldrich, St. Louis, MO, CV <9.0%). Lipid profile, such as serum triglyceride concentrations (Cayman, Ann Arbor, Michigan, CV unavailable), serum concentrations high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), and total cholesterol were analyzed using chemiluminescence assays (Abcam, Cambridge, United Kingdom, CV unavailable).

2.5. Statistical analyses

An a priori power analysis was conducted via G*Power version 3.1.9.2 for sample size estimation. The effect size was calculated based on an article by Atapattu et al. [48], and the lower limit of the confidence interval was chosen as the lowest meaningful effect ($r = 0.60$). To achieve statistical power of 0.80 for a two-tail test with critical criterion set to $\alpha = 0.05$ (assuming an effect size of $r = 0.60$), a sample size of 17 participants per group were needed to achieve sufficient power to detect a correlation of $r \geq 0.60$ to assess the influence of Mg and iMg on the relationship between serum 25-hydroxvitamin D and serum parathyroid hormone.

Descriptive data were obtained, and Mg intakes were used to categorize participants into one of three Mg intake groups in this cross-sectional study: Low Mg Group (lower 33 percentile of the study group for Mg intakes, Mg intakes between 44.5 to 166.9 mg/d); Medium Mg Group (between 33 percentile to 66 percentile of the study group for Mg intakes, Mg intakes between 177.4 to 280.6 mg/d); or High Mg Group (upper 66 percentile of the study group for Mg intakes, Mg intakes between 283.18 to 852.1 mg/d). Assumptions of normality of the data set were examined. Differences between normally distributed variables (trunk fat percent, fat-free mass percent, fat mass percent, iMg, 25OHD, glucose, HDL-C, LDL-C, and total cholesterol) were determined using one-way analysis of variance (ANOVA), and the differences between non-normally distributed variables (age, BMI, Mg intakes, Ca intakes, lean mass percent, PTH, CRP, IL-6, MCP-1, osteocalcin, insulin, HMW adiponectin, and triglyceride concentrations)

were determined using the Kruskal-Wallis test. Correlations between variables were assessed using either Pearson's correlation coefficient or Spearman's rank correlation coefficient tests, to determine the relationship between s25OHD and sPTH with body composition (trunk fat percent, lean mass percent, fat-free mass percent, fat mass percent), markers of inflammation (CRP, IL-6, MCP-1), glycemic indices (osteocalcin, insulin, HMW adiponectin, glucose concentrations), and lipids (triglyceride, HDL-C, LDL-C, total cholesterol concentrations) within each Mg group. The Benjamini-Hochberg procedure was used as the false discovery rate (FDR) [49] control for family-wise error during multiple testing. We rejected the null hypotheses for FDR $q < 0.05$. Analyses were conducted using the IBM SPSS Statistics package (IBM Corporation, Armonk, NY, version 24.0.0).

3. Results

3.1. *Demographics*

A total of 57 adults (29 women and 28 men), 22 to 65 years of age, participated in this study [Fig. 1]. Participants were separated into tertiles, depending on dietary intake of Mg. This included a Low Mg Group (n = 19, median Mg intake = 131.0 mg/d [95% CI: 104.4, 139.9 mg/d]), Medium Mg Group (n = 19, median Mg intake = 216.9 mg/d [95% CI: 203.4, 237.0 mg/d]), and High Mg Group (n = 19, median Mg intake = 376.0 mg/d [95% CI: 347.2, 490.3 mg/d]). Chi-square results did not reveal a statistically significant different between female and male participants within the entire sample ($P = .895$) and within each group ($P = .090$). The exact breakdown of female vs male participants was indicated in Table 1. Within the female participants, there were 22 Caucasians, 2 African Americans, 3 Asians, and 2 of other ethnic backgrounds. Within the male participants, there were 13 Caucasians, 4 African Americans, 9 Asians, and 2 of other ethnic backgrounds. The median age of the participants was 33.7 years (95% CI: 33.0, 39.2 years), and the median BMI was 27.9 kg/m^2 (95% CI: 28.5, 31.4 kg/m^2). There were no statistically significant differences in age and BMI among the 3 groups [Table 1]. Using the Institute of Medicine established vitamin D sufficiency guidelines [50], one participant was vitamin D deficient (25OHD <12 ng/mL), ten participants were vitamin D insufficient (25OHD 12 to <20 ng/mL), and 46 participants were vitamin D sufficient (25OHD ≥ 20 ng/mL).

3.2. *Body composition*

Among the groups, the group mean trunk fat percent was 38.1 ± 10.4% (95% CI: 35.3%, 40.8%), lean body mass percent was 62.1 ± 9.5% (95% CI: 59.4%, 64.6%), fat-free mass percent was 65.3 ± 9.7% (95% CI: 62.7%, 68.0%), and fat mass percent was 34.5 ± 9.8% (95% CI: 31.8%, 37.1%) [Table 1].

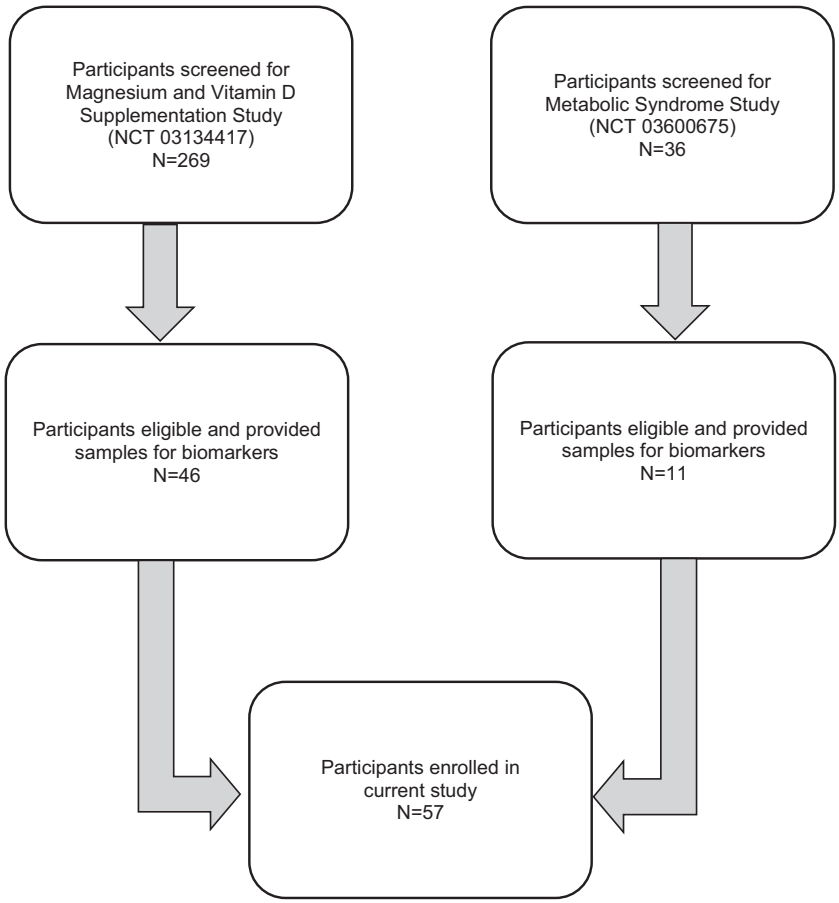

Fig. 1 – Flow chart for the selection of study participants.

Table 1 – Participant body composition, nutrient intakes, and serum biomarkers, separated by magnesium intake tertiles

	Low Mg Group ≤177.4 mg/d (n = 19)	Medium Mg Group 180.6 to 280.6 mg/d (n = 19)	High Mg Group ≥283.18 mg/d (n = 19)	All groups Comparison *P*	Low vs High Mg Groups Comparison *P*
Male/Female[3]	12 M / 8F	5 M / 13F	11 M / 8F	.090	
Participant Characteristics					
Age (years) [2]	37.7 (31.5, 42.2)	33.5 (31.5, 42.6)	27.4 (28.0, 40.8)	.567	.415
BMI (kg/m^2) [2]	27.7 (27.3, 31.8)	27.7 (27.2, 33.4)	29.0 (27.3, 31.0)	.995	.942
Systolic Blood Pressure [1]	115.4 ± 9.9	119.1 ± 12.7	117.4 ± 10.2	.624	.563
Diastolic Blood Pressure [1]	75.1 ± 8.2	77.9 ± 10.2	74.6 ± 10.7	.556	.879
Nutrient Intakes					
Mg Intake (mg/d) [2]	131.0 (104.4, 139.9)	216.9 (203.4, 237.0)	376.0 (347.2, 490.3)	<.001**	<.001**
Ca Intake (mg/d) [1]	604.9 ± 338.8 (436.4, 773.4)	709.6 ± 357.7 (519.0, 900.2)	804.4 ± 413.8 (591.7, 1017.2)	.291	.127
Ca/Mg Ratio [2]	3.67 (2.82, 5.44)	3.16 (2.42, 4.06)	1.85 (1.57, 3.24)	.037*	.023*
Vitamin D, Parathyroid Hormone and Magnesium Status					
iMg (mmol/L) [1]	0.543 ± 0.044 (0.521, 0.565)	0.538 ± 0.036 (0.519, 0.556)	0.537 ± 0.044 (0.514, 0.559)	.896	.681
25OHD (ng/mL) [1]	25.2 ± 7.4 (21.7, 28.6)	24.6 ± 6.2 (21.6, 27.7)	27.1 ± 5.7 (24.3, 29.8)	.489	.377
PTH (pg/mL) [2]	57.6 (49.2, 81.7)	76.3 (58.4, 93.1)	60.0 (51.2, 74.7)	.504	.866
Body Composition					
Trunk Fat % [1]	40.5 ± 11.6 (35.1, 45.8)	39.0 ± 10.6 (33.5, 44.5)	34.7 ± 8.7 (30.5, 38.9)	.204	.084
Lean mass % [1]	60.0 ± 10.2 (55.2, 64.8)	60.8 ± 8.7 (56.3, 65.3)	65.7 ± 8.9 (61.1, 70.3)	.156	.082
Fat-free mass % [1]	63.1 ± 10.6 (58.1, 68.1)	64.1 ± 9.2 (59.4, 68.8)	69.0 ± 8.7 (64.7, 73.3)	.147	.072
Fat mass % [1]	36.6 ± 10.8 (31.5, 41.7)	35.2 ± 10.0 (30.1, 40.4)	31.5 ± 8.3 (27.5, 35.5)	.259	.111
Markers of Inflammation					
IL-6 (pg/mL) [2]	3.36 (2.47, 6.75)	2.30 (1.99, 3.95)	1.89 (1.32, 2.84)	.099	.042*
CRP (mg/dL) [2]	0.214 (0.183, 0.248)	0.217 (0.170, 0.322)	0.200 (0.131, 0.286)	.538	.254
MCP-1 (pg/mL) [1]	372.7 ± 177.2 (289.7, 455.6)	337.6 ± 131.6 (269.9, 405.2)	376.5 ± 111.3 (321.1, 431.9)	.681	.937
Glycemic Indices					
OC (ng/mL) [2]	17.6 (15.9, 30.0)	15.5 (12.8, 19.5)	17.3 (15.2, 25.4)	.475	.977
Insulin (μIU/mL) [2]	8.50 (7.78, 15.04)	9.81 (7.37, 13.0)	7.25 (5.85, 13.0)	.291	.089
Glucose (mg/dL) [1]	86.0 ± 24.6 (71.8, 100.2)	73.0 ± 19.3 (61.3, 84.7)	80.6 ± 31.0 (61.9, 99.4)	.620	.839
Adiponectin (mg/dL) [2]	3.98 (3.19, 6.39)	2.49 (2.15, 5.53)	3.91 (3.17, 6.43)	.468	.863
Lipid Profile					
TGL (mg/dL) [1]	52.9 (36.3, 74.3)	51.5 (50.4, 89.8)	46.4 (36.5, 56.0)	.248	.682
HDL (mg/dL) [1]	44.9 ± 18.0 (36.4, 53.3)	49.0 ± 15.6 (41.0, 57.1)	45.4 ± 17.4 (37.0, 53.8)	.731	.931
LDL (mg/dL) [1]	118.5 ± 38.3 (100.1, 137.0)	140.1 ± 52.4 (114.0, 166.1)	141.5.1 ± 43.3 (120.6, 162.4)	.221	.092
TC (mg/dL) [1]	166.7 ± 41.0 (147.6, 185.9)	203.8 ± 50.8 (178.6, 229.1)	218.8 ± 43.7 (176.7, 218.8)	.030*	.028*

**P <0.01; *P <0.05; [1]Parametric tests were performed, values were presented as means ± Standard deviations; [2]Non-parametric tests were performed, values were presentation as median (95% confidence intervals); [3]Pearson's chi-squared test was performed; BMI, body mass index; Mg, magnesium; Ca, calcium; iMg, serum ionized magnesium; 25OHD, 25 hydroxyvitamin D; PTH, parathyroid hormone; IL-6, interleukin-6; CRP, C-reactive protein; MCP-1, monocyte chemoattractant protein-1; OC, osteocalcin; TGL, triglycerides; HDL, high-density lipoprotein cholesterol; LDL, low-density lipoprotein cholesterol; TC, total cholesterol;

3.3. *Blood biochemical markers analyses for entire study group*

The mean s25OHD was 25.6 ± 6.5 ng/mL (95% CI: 23.9, 27.3 ng/mL). According to the Institute of Medicine's definition of vitamin D status [50], 46 participants (80.7%) had adequate vitamin D statuses (s25OHD> 20 ng/mL), 10 participants were vitamin D insufficient (s25OHD between 12 to 20 ng/mL), and 1 participant was vitamin D deficient (s25OHD <12 ng/mL). The median sPTH was 62.7 pg/mL (95% CI: 60.6, 77.1 pg/mL). There were no statistically significant differences for s25OHD and sPTH, among the groups [Table 1].

Median concentrations of serum IL-6 (sIL-6) were higher (P = .042) in the Low Mg Group, 3.36 pg/mL (95% CI: 2.47, 6.75 pg/mL); as compared to the High Mg Group, 1.89 pg/mL (95% CI: 1.32, 2.84 pg/mL) [Table 1]. For the entire study group, correlation analyses revealed a negative relationship between Mg intake and sIL-6 (r = – 0.295, P = .027). In addition, a negative relationship was also observed between sIL-6 and s25OHD (r = –0.316, P = .017), for the entire study group [Table 2].

Interestingly, the mean total cholesterol concentration was lower (P = .028) in the Low Mg Group at 166.7 ± 41.0 mg/dL (95%CI: 147.6, 185.9 mg/dL), compared to the High Mg Group at 218.8 ± 43.7 mg/dL (95% CI: 176.7, 218.8 mg/dL). There were no other differences observed between blood biomarker variables among the groups [Table 1].

A positive relationship between s25OHD and serum HMW adiponectin concentrations (r = 0.316, P = .017) was also observed for the entire study group. A positive relationship was observed between sPTH and serum LDL-C concentrations (r = 0.499, P = .046), as well as serum total cholesterol (r = 0.366, P = .006, FDR q < 0.05) for all groups [Table 2].

The mean iMg was 0.539 ± 0.041 mmol/L (95% CI: 0.528, 0.550 mmol/L). Concentrations of iMg did not differ between tertiles of Mg intakes [Table 1]. Results from correlation analyses did not reveal a significant relationship between iMg and any variables.

3.4. *Nutrient intakes*

The median Mg intake was 213.1 mg/d (95% CI: 201.3, 262.7 mg/d). In this group of participants, 86.4% did not meet the RDA specific for their age and sex (men, 19 to 30 years of age = 400 mg/d; men, 31 years of age and older = 420 mg/d; women, 19 to 30 years of age = 310 mg/d; women, 31 years of age and older = 320 mg/d). The mean calcium intake was 704.3 ± 373.1 mg/d (95% CI: 599.3, 809.2), and the median Ca:Mg ratio was 3.09 (95% CI: 2.63, 3.75). There were no statistically significant differences in calcium intakes among groups. The Low Mg Group had a significantly higher (P = .023, FDR q < 0.05) Ca:Mg ratio of 3.67 (95% CI: 2.82, 5.44), compared to the High Mg Group at 1.85 (95% CI: 1.57, 3.24). Furthermore, Mg intakes were negatively correlated to the Ca:Mg ratio (r = – 0.324, P = .022), which suggests that higher Mg intakes were a contributor to the lower Ca:Mg ratio in our study.

3.5. *Relationship between 25-hydroxyvitamin D and parathyroid hormone*

The relationship between s25OHD and sPTH concentrations were determined within each tertile. There was no relationship between s25OHD and sPTH, when assessing the entire study group [Table 2]. There was also no relationship between s25OHD and sPTH in the Low Mg Group and Medium Mg Group. Interestingly, the negative relationship between s25OHD and sPTH existed only in the High Mg Group (r = –0.472, P = .041) [Table 3].

3.6. *Relationship between 25-hydroxylvitamin D or parathyroid hormone and body composition*

In the Low Mg Group, sPTH was negatively associated with fat-free mass percent (r = –0.472, P = .036) and positively associated with fat mass percent (r = 0.502, P = .024); however, these relationships were not observed in the High Mg Group [Table 3]. No relationships were observed between s25OHD and body composition measurements in any group, and no relationships were observed between s25OHD and/or sPTH and body composition measurements in the High Mg Group [Table 3].

3.7. *Relationship between 25-hydroxylvitamin D or parathyroid hormone and markers of inflammation*

Interestingly, there was a positive association between s25OHD and serum CRP concentrations in the High Mg Group (r = 0.491, P = .038); however, no relationships were observed between s25OHD and markers of inflammation in the Low Mg Group and Medium Mg Group. No relationships were observed between sPTH and markers of inflammation in any group [Table 3].

3.8. *Relationship between 25-hydroxylvitamin D or parathyroid hormone and glycemic indices*

A positive relationship was detected between s25OHD and serum HMW adiponectin concentrations in the High Mg Group (r = 0.532, P = .022), and a negative relationship was also observed between sPTH and serum insulin concentrations in the High Mg Group (r = –0.488, P = .034). No relationships were observed between s25OHD or sPTH and glycemic indices in the Low Mg Group [Table 3].

3.9. *Relationship between 25-hydroxylvitamin D or parathyroid hormone and lipid profile*

There was a significant negative relationship between sPTH and serum HDL-C concentrations (r = –0.579, P = .009, FDR q < 0.05), and a significant positive relationship was observed between sPTH and serum LDL-C concentrations (r = 0.563, P = .012, FDR q < 0.05) in the High Mg Group. There was a significant negative relationship between s25OHD and serum HDL-C concentrations in the Low Mg Group (r = –0.767, P < .001, FDR q < 0.05) [Table 3].

4. Discussion

Magnesium is an important regulator of vitamin D and PTH metabolism [37-39]. To the best of our knowledge, this is the first study to investigate the influence of dietary Mg intake on the relationship between 25OHD and PTH on cardiometabolic health variables in adults who are overweight or obese. In this cross-sectional study, we assessed the cardiometabolic profile of 57 owt/ob, but otherwise healthy, participants, and we

Table 2 – Relationships between magnesium intakes/25-hydrovitamin D/parathyroid hormone with cardiometabolic outcome variables in the study population

	Mg Intakes		25OHD		PTH	
	r	95% Confidence intervals	r	95% Confidence intervals	r	95% Confidence intervals
Participant characteristics						
Age (years)	–0.127	LL: –0.075, UL: 0.138	0.149	LL: –0.116 UL: 0.394	0.357**	LL: 0.106, UL: 0.565
BMI (kg/m^2)	0.051	LL: –0.212 UL: 0.307	–0.213	LL: –0.449 UL: 0.050	0.033	LL: –0.230 UL: 0.291
Nutrient intakes						
Mg intake (mg/d)	–		0.033	LL: –0.230 UL: 0.291	–0.038	LL: –0.296 UL: 0.225
Ca intake (mg/d)	0.252	LL: –0.009, UL: 0.481	0.058 P	LL: –0.206 UL: 0.314	–0.115	LL: –0.365 UL: 0.150
Ca/Mg ratio	–0.324*	LL: –0.539 UL: –0.069	–0.156	LL: –0.400 UL: 0.109	0.114	LL: –0.151 UL: 0.364
Vitamin D, parathyroid hormone and magnesium status						
iMg (mmol/L)	–0.134	LL: –0.539 UL: –0.069	0.122	LL: –0.143 UL: 0.371	–0.091	LL: –0.343 UL: 0.174
25OHD (ng/mL)	0.033	LL: –0.230 UL: 0.291	–		–0.148	LL: –0.393 UL: 0.117
PTH (pg/mL)	–0.038	LL: –0.296 UL: 0.225	–0.148	LL: –0.393 UL: 0.117	–	
Body composition						
Trunk Fat %	–0.227	LL: –0.460 UL: 0.036	–0.170 P	LL: –0.412 UL: 0.095	0.185	LL: –0.393 UL: 0.117
Lean mass %	0.224	LL: –0.039 UL: 0.458	0.046 P	LL: –0.217 UL: 0.303	–0.245	LL: –0.475 UL: 0.017
Fat-free mass %	0.259	LL: –0.002 UL: 0.487	0.075 P	LL: –0.189 UL: 0.329	–0.266	LL: –0.492 UL: –0.006
Fat mass %	–0.242	LL: –0.473 UL: 0.020	–0.116 P	LL: –0.366 UL: 0.149	0.242	LL: –0.020 UL: 0.473
Markers of inflammation						
IL-6 (pg/mL)	–0.295*	LL: –0.516 UL: –0.037	–0.316*	LL: –0.533 UL: –0.060	0.042	LL: –0.221 UL: 0.299
CRP (mg/dL)	–0.150	LL: –0.395 UL: 0.115	0.104	LL: –0.161 UL: 0.355	–0.209	LL: –0.445 UL: 0.055
MCP-1 (pg/mL)	0.045	LL: –0.218 UL: 0.302	0.049 P	LL: –0.214 UL: 0.306	0.115	LL: –0.150 UL: 0.365
Glycemic indices						
OC (ng/mL)	–0.029	LL: –0.287 UL: 0.233	–0.095	LL: –0.347 UL: 0.170	–0.172	LL: –0.414 UL: 0.093
Insulin (μIU/mL)	–0.213	LL: –0.449 UL: 0.050	–0.053	LL: –0.309 UL: 0.210	–0.285*	LL: –0.508 UL: –0.026
Glucose (mg/dL)	0.002	LL: –0.259 UL: 0.262	–0.191 P	LL: –0.430 UL: 0.073	0.235	LL: –0.027 UL: 0.467
Adiponectin (mg/dL)	–0.131	LL: –0.379 UL: 0.134	0.309*	LL: 0.053 UL: 0.527	0.233	LL: –0.029 UL: 0.465
Lipid profile						
TGL (mg/dL)	–0.087	LL: –0.340 UL: 0.178	–0.042	LL: –0.299 UL: 0.221	0.056	LL: –0.208 UL: 0.312
HDL (mg/dL)	0.007	LL: –0.254 UL: 0.267	–0.186 P	LL: –0.426 UL: 0.078	–0.118	LL: –0.367 UL: 0.147
LDL (mg/dL)	0.116	LL: –0.149 UL: 0.366	0.059 P	LL: –0.205 UL: 0.315	0.499**	LL: 0.274 UL: 0.672
TC (mg/dL)	0.187	LL: –0.077 UL: 0.427	0.119 P	LL: –0.146 UL: 0.368	0.366**	LL: 0.117 UL:0.572

**P < .01; *P < .05; PPearson's correlation coefficients; unmarked correlation coefficient were Spearman's ranked correlation coefficient; BMI, body mass index; Mg, magnesium; Ca, calcium; iMg, serum ionized magnesium; 25OHD, 25 hydroxyvitamin D; PTH, parathyroid hormone; IL-6, interleukin-6; CRP, C-reactive protein; MCP-1, monocyte chemoattractant protein-1; OC, osteocalcin; TGL, triglycerides; HDL, high-density lipoprotein cholesterol; LDL, low-density lipoprotein cholesterol; TC, total cholesterol; LL, lower limit; UL, upper limit.

Table 3 – Relationship between 25-hydroxyvitamin D/parathyroid hormone with cardiometabolic outcome variables identified by magnesium intake groups

	Low Mg Group (n = 19)				High Mg Group (n = 19)			
	25OHD	95% Confidence intervals	PTH	95% Confidence intervals	25OHD	95% Confidence intervals	PTH	95% Confidence intervals
Participant characteristics								
Age (y)	0.272	LL: −0.208, UL: 0.646	0.558*	LL: 0.139 UL: 0.808	0.191	LL: −0.288 UL: 0.594	0.130	LL: −0.345 UL: 0.552
BMI (kg/m^2)	−0.267	LL: −0.643 UL: 0.213	0.178	LL: −0.301 UL: 0.585	−0.053	LL: −0.495 UL: 0.411	−0.025	LL: −0.474 UL: 0.434
Nutrient intakes								
Ca Intake (mg/d)	0.120 P	LL: −0.353 UL: 0.545	−0.449	LL: −0.750 UL: 0.007	0.093 P	LL: −0.377 UL: 0.525	0.196	LL: −0.283 UL: 0.597
Ca/Mg Ratio	−0.207	LL: −0.604 UL: 0.273	−0.196	LL: −0.597 UL: 0.283	−0.012	LL: −0.464 UL: 0.445	0.201	LL: −0.279 UL: 0.600
Body composition measurements								
Trunk Fat %	−0.198 P	LL: −0.598 UL: 0.282	0.389	LL: −0.079 UL: 0.717	−0.226 P	LL: −0.617 UL: 0.254	−0.046	LL: −0.490 UL: 0.417
Lean mass %	0.117 P	LL: −0.356 UL: 0.542	−0.430	LL: −0.740 UL: 0.030	−0.131 P	LL: −0.552 UL: 0.344	0.025	LL: −0.434 UL: 0.474
Fat-free mass %	0.146 P	LL: −0.330 UL: 0.563	−0.472*	LL: −0.763 UL: −0.023	−0.098 P	LL: −0.529 UL: 0.373	0.059	LL: −0.406 UL: 0.500
Fat mass %	−0.151 P	LL: −0.566 UL: 0.326	0.502*	LL: 0.062 UL: 0.779	−0.153 P	LL: −0.568 UL: 0.324	−0.041	LL: −0.486 UL: 0.421
Vitamin D, parathyroid hormone and magnesium status								
iMg (mmol/L)	0.423 P	LL: −0.039 UL: 0.736	−0.176	LL: −0.584 UL: 0.302	−0.247 P	LL: −0.630 UL: 0.233	−0.039	LL: −0.485 UL: 0.423
25OHD (ng/mL)	–		−0.105	LL: −0.534 UL: 0.367	–		−0.472 *	LL: −0.763 UL: −0.023
PTH (pg/mL)	−0.071	LL: −0.509 UL: 0.396	–		−0.472 *	LL: −0.763 UL: −0.023	–	
Markers of inflammation								
IL-6 (pg/mL)	−0.432	LL: −0.741 UL: 0.028	−0.260	LL: −0.639 UL: 0.220	−0.347	LL: −0.692 UL: 0.127	0.147	LL: −0.329 UL: 0.564
CRP (mg/dL)	0.210	LL: −0.270 UL: 0.606	−0.269	LL: −0.644 UL: 0.211	0.491*	LL: 0.047 UL: 0.773	−0.430	LL: −0.740 UL: 0.030
MCP-1 (pg/mL)	0.046 P	LL: −0.417 UL: 0.490	−0.176	LL: −0.584 UL: 0.302	−0.032 P	LL: −0.479 UL: 0.428	0.236	LL: −0.244 UL: 0.623
Glycemic indices								
OC (ng/mL)	−0.171	LL: −0.580 UL: 0.307	−0.392	LL: −0.718 UL: 0.076	−0.212	LL: −0.608 UL: 0.268	−0.245	LL: −0.629 UL: 0.235
Insulin (μIU/mL)	0.054	LL: −0.410 UL: 0.496	−0.209	LL: −0.606 UL: 0.271	−0.053	LL: −0.495 UL: 0.411	−0.488*	LL: −0.771 UL: −0.043
Glucose (mg/dL)	−0.491 P *	LL: −0.773 UL: −0.047	0.327	LL: −0.149 UL: 0.680	−0.065 P	LL: −0.504 UL: 0.401	0.148	LL: −0.587 UL: 0.298
Adipo (mg/dL)	0.067	LL: −0.399 UL: 0.506	0.151	LL: −0.326 UL: 0.566	0.532 *	LL: 0.103 UL: 0.794	0.021	LL: −0.437 UL: 0.471
Lipid profile								
TGL (mg/dL)	0.317	LL: −0.160 UL: 0.674	−0.017	LL: −0.468 UL: 0.441	−0.443	LL: −0.747 UL: 0.014	−0.036	LL: −0.482 UL: 0.425
HDL (mg/dL)	−0.767 P **	LL: −0.906 UL: −0.480	−0.457	LL: −0.755 UL: −0.004	0.041 P	LL: −0.421 UL: 0.486	−0.579**	LL: −0.865 UL: −0.320
LDL (mg/dL)	0.150 P	LL: −0.326 UL: 0.566	0.147	LL: −0.329 UL: 0.564	−0.298 P	LL: −0.663 UL: 0.181	0.563*	LL: −0.271 UL: 0.606
TC (mg/dL)	0.263 P	LL: −0.217 UL: 0.641	−0.152	LL: −0.567 UL: 0.325	−0.423 P	LL: −0.736 UL: 0.039	0.254	LL: −0.480 UL: 0.428

**= $P < .01$;*$P < .05$; PPearson's correlation coefficients; unmarked correlation coefficient were Spearman's ranked correlation coefficient; LL, lower limit; UL, upper limit; BMI, body mass index; Mg, magnesium; Ca, calcium; iMg, serum ionized magnesium; 25OHD, 25 hydroxyvitamin D; PTH, parathyroid hormone; IL-6, interleukin-6; CRP, C-reactive protein; MCP-1, monocyte chemoattractant protein-1; OC, osteocalcin; TGL, triglycerides; HDL, high-density lipoprotein cholesterol; LDL, low-density lipoprotein cholesterol; TC, total cholesterol.

determined that Mg intakes may influence the relationship of s25OHD with sPTH. We were able to observe a negative relationship between s25OHD and sPTH concentrations in the High Mg Group ($r = -0.472$, $P = .041$), whose daily Mg intakes were ≥ 283.18 mg/d, but not in the Medium or Low Mg Groups. In agreement with our hypothesis, low dietary Mg intake may

alter vitamin D metabolism and improve the negative relationship between s25OHD and sPTH. The relationship between 25OHD and PTH on body composition, markers of inflammation, glycemic indices, and lipid profile were also assessed. Our findings suggested that higher Mg intake may be an important determinant and/or a modifier of the 25OHD-PTH axis in the overweight and obese population.

Our results supported the current knowledge that adequate Mg intakes may be necessary for proper vitamin D metabolism. Dai et al. recently published an interventional clinical study using Mg supplementation, and these researchers were able to observe an increase of post-treatment vitamin D metabolites when baseline 25OHD concentration was <30 ng/mL [41]. In our study, the mean 25OHD concentration was 25.6 ± 6.5 ng/mL (95% CI: 23.9, 27.3 ng/mL), which was close to the 30 ng/mL suggested by Dai et al. in which improvement in Mg status may increase vitamin D metabolism. The results from our study suggested that improvement of vitamin D metabolism mediated Mg intakes may have clinical significance. Although the effects of Mg intakes on PTH and 25OHD responses were not entirely clear, our evidence suggests that Mg intakes may affect the relationship between PTH and 25OHD. This is evidenced by the lowering of sPTH with increasing s25OHD only in participants whose Mg intakes were in the higher percentiles (>66 percentile), which suggested proper vitamin D metabolism. In the absence of adequate Mg intakes, the negative relationship between s25OHD and sPTH was not observed. This could be potentially explained by the fact that Mg is a cofactor for the vitamin D activating proteins 25-hydroxylase [40] and 1-alpha-hydroxylase [39], as well as vitamin D binding protein [38], which is the transportation protein for vitamin D metabolites in circulation. Deng et al. [38] previously reported a lower risk of vitamin D deficiency with higher Mg intakes. We demonstrated that low Mg intakes may lower the effectiveness of 25OHD on PTH optimization. Low dietary Mg intake may lead to lower production of 1,25-dihydroxyvitamin D, because the enzyme to convert 25OHD to 1,25-dihydroxyvitamin D, 25-hydroxylase, is Mg dependent [38]. Inadequate production of 1,25-dihydroxyvitamin D leads to a decrease in intestinal calcium absorption [51,52], which in term stimulates PTH production. Although not statistically significant, the mean s25OHD was higher in the High Mg Group (27.1 ± 5.7 ng/mL) compared to the Low Mg Group (25.2 ± 7.4 ng/mL). The lack of a statistically significant difference might also be due to the relatively small sample size of our study, leading to a greater risk for a Type II error. Furthermore, this lack of significant differences of s25OHD among groups might potentially be due to the mean s25OHD for all groups falling within the normal range of 20 ng/mL to 40 ng/mL [50]. It was previously shown in a clinical trial conducted by Sahota et al. [37] that Mg repletion therapy could lower sPTH in participants with vitamin D insufficiency combined with elevated sPTH at baseline [37]. With our results, we further support the emerging hypothesis and mounting evidence that Mg status should be considered to enhance the effectiveness of vitamin D on health outcomes.

The secondary aim of this study was to determine whether Mg intakes and serum iMg concentrations could influence cardiometabolic disease risks in owt/ob adults. We found that although serum iMg concentrations were not significantly correlated with s25OHD, sPTH, and other cardiometabolic health indices, higher dietary Mg intakes might be associated with a more favorable cardiometabolic profile. Although serum iMg concentration is considered a reliable indicator of biologically available Mg, it is important to note that most Mg are stored intracellularly. This may explain why no relationship between iMg concentrations and cardiometabolic health indices were detected. Previous evidence showed a negative relationship between dietary Mg intakes and bodyweight [10]. Contrastingly, the relationship between serum iMg concentrations and bodyweight are lacking. Researchers have previously suggested that the combination of low Mg intakes and poor vitamin D status is associated with an increased risk of cardiometabolic diseases [38]. Consistent with previous research, some protective benefits of Mg on cardiometabolic health mediated via 25OHD were observed when participants were separated by dietary Mg intakes in our study.

Researchers have previously correlated higher vitamin D and Mg status with better glycemic control [8,53,54], but whether Mg status might influence the protective benefits of vitamin D on glycemic control has not been previously determined. In our study, we found a positive relationship between s25OHD and serum HMW adiponectin concentrations in the High Mg Group ($r = 0.532$, $r = 0.022$), but not in other groups. Adiponectin is a hormone produced by adipose tissues that has previously been postulated to improve glucose metabolism and increase insulin sensitivity [45,55,56]. This relationship between s25OHD and serum HMW adiponectin concentrations might suggest that a combination of high Mg intake and high vitamin D status may offer some protective benefits in glycemic control. However, we did not find any other relationships between s25OHD, serum fasting blood glucose, and serum insulin concentrations. The overall benefits of concurrently correcting both vitamin D and Mg deficiencies on glycemic improvements mediated by adiponectin remains to be explored in clinical studies.

The positive relationship between sPTH and fat-mass percent was only observed in the Low Mg Group ($r = 0.502$, $P = .024$), not in other groups, in our study comprised of adults who are owt/ob. This indicated that higher Mg intake may attenuate the increase of sPTH in obesity. Previous researchers have delineated a positive correlation between PTH and body fat mass [23,32], potentially due to renal calcium mishandling commonly observed in obesity [57] and 25OHD sequestration in fat tissue [58]. Furthermore, the lack of differences in s25OHD between the Low Mg Group (25.3 ± 7.6 ng/mL) and High Mg Group (27.1 ± 5.7 ng/mL) suggested that fat-mass percent may be a predictor of PTH, independent of vitamin D status. We postulated that adequate Mg intakes might be protective against obesity related increased PTH production.

Adequate Mg status was previously associated with lower overall systemic inflammation, particularly in an owt/ob population [10]. Indeed, in our study, we found that the inflammatory marker sIL-6 was lower ($P = .042$) in the High Mg Group, 1.89 pg/mL (95% CI: 1.32, 2.84 pg/mL), compared to the Low Mg Group, 3.36 (95% CI: 2.47, 6.75 pg/mL). Although it is well recognized that individuals who are owt/ob are more prone to developing chronic low-grade systemic inflammation, the underlying mechanistic

reasons are not well understood. It has been hypothesized that Mg deficiency may play a role in the manifestation of chronic systemic inflammation by increasing oxidative stress due to changes in calcium handling in obesity [10]. It was postulated that Mg deficiency characterized by low intracellular Mg concentrations might lead to increased blockage of calcium channels [58], leading to an increase of intracellular calcium in adipocytes [59,60].The higher inflammation marker sIL-6 observed in the Low Mg Group in our owt/ob study population could potentially be explained by the sequestration of calcium in adipocytes, which is known to trigger the activation of the pro-inflammatory nuclear factor-kappa B (NFκB) pathway [10,61]. The negative relationship between Mg intakes and sIL-6 concentrations in our study supported the current understanding of Mg on systemic inflammation.

Magnesium deficiency is common among individuals who are owt/ob [62,63]. Consistent with current knowledge, 86% of the owt/ob participants in our study did not consume the RDA for Mg. The RDA for Mg for adults, 19 to 30 years of age, is 310 mg/d for women and 400 mg/d for men. For adults between 31 to 70 years of age, the RDA for Mg is 320 mg/d for women and 420 mg/d for men [64]. Magnesium is found in higher amounts in more healthful foods such as nuts, seeds, legumes, fruits, and green leafy vegetables [65]. Processed foods, often commonly consumed by overweight or obese populations, are not considered good sources of Mg [65]. In a recent analysis of processed food consumption from the National Health and Nutrition Examination Survey) (NHANES) 2007–2012, 57.9% of food consumption in the owt/ob populations was considered ultra-processed, which could be translated to a high prevalence of poor dietary habits and concurrent low Mg intakes in this population [66]. Improving Mg intakes in the owt/ob population should focus primarily on consumption of Mg-rich foods, and secondarily, on supplementation if intake alone is insufficient [65].

The strengths from our study include that all dietary information was collected by either a registered dietitian or a trained research assistant in a consistent, reproducible manner (e.g., the 5-steps multiple-pass method). Another strength is the fact that our participants were owt/ob, but overall healthy adults. Studies conducted in a healthy owt/ob population may reveal more information on chronic disease prevention compared to a diseased population. We also investigated multiple aspects of cardiometabolic health variables, such as body composition, markers of inflammation, glycemic induces, and lipid profile. Assessing multiple aspects of cardiometabolic health variables together might provide a more comprehensive understanding of the influence of Mg on disease prevention, compared to analyzing these aspects separately. To the best of our knowledge, this was the first study where the influence of Mg intakes on the relationship between 25OHD/PTH and cardiometabolic health variables were investigated.

Some limitations of this study included the use of food frequency questionnaires and a single day 24-hour recall. It is important to address the inherent variability of using any dietary recall method. Another limitation was that participants in our study did not exhibit signs of vitamin D deficiency or hyperparathyroidism. Also, serum 1,25-dihydroxyvitamin D concentrations were not measured due to the nature of this study design, and also because calcitriol is not a sensitive indicator of vitamin D status. It may be important to consider this marker in an interventional study. The vast majority of the participants also had normal fasting glucose and insulin concentrations and lipid profile, which made it difficult to determine the clinical significance of how Mg may influence these outcomes variables. Other factors that may affect serum Mg concentrations, such as serum potassium and calcium concentrations, were not measured in this study. However, serum calcium concentration is a poor indicator of calcium status because it is tightly regulated in humans. Dietary calcium intakes were measured as an indicator of calcium status. The overall younger age of the participants might also mean that the clinical consequences on cardiometabolic health of obesity have not yet been manifested. The cross-sectional nature of this study means that the temporal relationship between nutrition status and cardiometabolic health outcome cannot be established. Furthermore, the relatively small sample size of 57 participants may be too small to offer conclusive evidence. We used the Benjamini-Hotchberg method [49] false discovery rate (FDR) to control for any false discovery errors that may occur with the multiple comparisons conducted in the multiple arms of the study. It is plausible that with the number of multiple comparisons conducted, there may be some relationships that are false positives while others may be false negatives. To place our work into context and allow for others to use our results for comparison, we also calculated the 95% confidence intervals for each of the comparisons. Confidence intervals can be compared to the results of other investigations using similar variables. As well, given that there may be an influence of the small sample size and false negatives, insufficient power may be a consequence. Future work may benefit from using the confidence intervals of the effect size in estimating sample size for their research designs.

In conclusion, dietary Mg intake may alter the relationship between 25OHD and PTH, thereby influencing their relationship with cardiometabolic health in an owt/ob population. Future research should focus on investigating the effects of Mg repletion in intervention trials in a vitamin D deficient population or in individuals with hyperparathyroidism, to further understand the role of Mg in improving cardiometabolic health (current ongoing study NCT#03470519).

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