Physical Activity Modifies the Association between Dietary Protein and Lean Mass of Postmenopausal Women

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ABSTRACT

Background Maintenance of lean muscle mass and related strength is associated with lower risk for numerous chronic diseases of aging in women.

Objective Our aim was to evaluate whether the association between dietary protein and lean mass differs by physical activity level, amino acid composition, and body mass index categories.

Design We performed a cross-sectional analysis of a prospective cohort.

Participants/setting Participants were postmenopausal women from the Women's Health Initiative with body composition measurements by dual-energy x-ray absorptiometry (n=8,298).

Main outcome measures Our study measured percent lean mass, percent fat mass, and lean body mass index.

Statistical analyses performed Linear regression models adjusted for scanner serial number, age, calibrated energy intake, race/ethnicity, neighborhood socioeconomic status, and recreational physical activity were used to determine the relationship between protein intake and body composition measures. Likelihood ratio tests and stratified analysis were used to investigate physical activity and body mass index as potential effect modifiers.

Results Biomarker-calibrated protein intake was positively associated with percent lean mass; women in the highest protein quintile had 6.3 percentage points higher lean mass than the lowest quintile ($P<0.001$). This difference rose to 8.5 percentage points for physically active women in the highest protein quintile ($P_{interaction}=0.023$). Percent fat mass and lean body mass index were both inversely related to protein intake (both $P<0.001$). Physical activity further reduced percent fat mass ($P_{interaction}=0.022$) and lean body mass index ($P_{interaction}=0.011$). Leucine intake was associated with lean mass, as were branched chain amino acids combined (both $P<0.001$), but not independent of total protein. All associations were observed for normal-weight, overweight, and obese women.

Conclusions Protein consumption up to 2.02 g/kg body weight daily is positively associated with lean mass in postmenopausal women. Importantly, those that also engage in physical activity have the highest lean mass across body mass index categories.
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Obesity and loss of lean mass, or sarcopenia, are thought to act jointly to increase risk for all-cause mortality.[1] The loss of lean mass is hypothesized to contribute to the loss of insulin sensitivity and disturbances in metabolism that are common in overweight and obese individuals.[2] Several studies suggest that protein intake is an independent dietary factor important for maintenance of lean mass and its function in glucose homeostasis, energy expenditure, and fat oxidation.[3,4] High protein intake during weight loss has been shown to preserve lean mass and its function.[5,6] In a recent overfeeding trial,

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individuals randomized to high-protein diets containing 15% or 25% of total calories from protein experienced weight gain due to increases in both lean and fat mass, whereas those randomized to low-protein (5%) diets gained fat mass but lost lean mass with attenuated total weight gain.[7] More recent work on the effects of individual dietary and supplemental amino acids suggests an important role for specific amino acids on body composition. The branched-chain amino acid (BCAA) leucine has been shown to stimulate muscle protein synthesis, improve insulin sensitivity,[8] and may prevent diet- and age-related adiposity.[9,10] Collectively, these findings support a beneficial role for total protein and specific amino acids on lean mass across a spectrum of behaviors, including overeating and inactivity. Given the potential benefits of dietary protein, the current recommendations for daily protein intake in older adults (0.8 g protein/kg body weight) have recently been questioned for being insufficient for optimal lean mass health,[11] and the European Society for Clinical Nutrition and Metabolism has recommended at least 1.0 to 1.2 g protein/kg body weight daily for healthy, older individuals.[12]

Despite evidence favoring the metabolic benefits of maintaining a high lean mass, and potential benefits of high-protein diets, the relationship between lean mass and metabolic health is less clear for overweight/obese women. The Monet Study of postmenopausal women supports an adverse relationship between lean mass and metabolic parameters in obese, sedentary older women. These investigators showed that the presence of a high lean body mass index (LBMI; calculated as lean body mass [kg]/height [m^2]) in sedentary postmenopausal women was independently associated with reduced insulin sensitivity, poor glucose disposal, and higher levels of circulating pro-inflammatory C-reactive protein.[13] These observations suggest caution in recommending higher protein intakes in the absence of other behavioral modifications.

Physical activity is a well-established, independent determinant of both muscle mass and insulin sensitivity, though the intensity, frequency, and duration required for individual benefit remain unclear.[14] Further, there is a lack of epidemiological evidence on the impact of physical activity as a modifier of body composition in response to different levels of dietary protein intake, despite evidence that protein demands increase with physical activity.[6]

To the knowledge of the authors, no studies have evaluated the relationship between dietary protein on muscle and fat mass by physical activity levels or considered the potential impact of body mass index (BMI; calculated as mass [kg]/height [m^2]) on these associations. Associations between total dietary protein (or amino acids, specifically leucine) and lean mass, fat mass, or LBMI were tested, and potential interactions with physical activity were investigated in 8,298 postmenopausal women who participated in the Women's Health Initiative (WHI) and for whom body composition was assessed by dual-energy x-ray absorptiometry (DXA). Secondarily, these associations were then assessed for differences by BMI category.

METHODS

Participants

The WHI included three clinical trials and an observational study comprising 161,808 postmenopausal women, aged 50 to 79 years, that launched in 1991 and completed enrollment in 1998.[15] Human subjects review committees at 40 participating institutions across the United States reviewed and approved each study, and individual participants provided written informed consent. Of 11,020 women who participated in the DXA cohort (conducted at the Arizona; Pittsburgh, PA; and Alabama sites), 10,635 had baseline body composition measures available. Of these, 403 women were excluded from the analysis due to implausible reported energy intake (<600 kcal/day or >5,000 kcal/day), an additional 816 women were excluded for missing data needed to calculate calibrated protein,[16] and another 1,118 women were excluded for missing data on physical activity. The final study population comprised 8,298 postmenopausal women.

Body Size Measurements

Height and weight were measured using standardized protocols by trained study personnel in study clinics, and BMI and LBMI were calculated. Body composition was assessed using whole-body DXA scans, which included measurements of lean (soft tissue) mass and fat mass. All DXA scans were operated by a trained technician certified by the manufacturer. Percent lean mass and percent fat mass were calculated and served as the primary outcome measures throughout the analysis. Detailed methods and quality control are described elsewhere.[17]

Dietary Assessment

Total energy and protein intake at baseline (total as well as animal and plant-based protein) were calculated from the self-administered, 122-item WHI food frequency questionnaire.[18] Intakes of individual amino acids were computed using estimates derived from the Nutrition Data System for Research nutrient database developed by the Nutrition Coordinating Center, University of Minnesota, Minneapolis.[19] Protein intake was evaluated using grams of protein per kilogram body weight to be consistent with the current recommended daily allowance (RDA).[20] Calibrated energy and calibrated protein intake were calculated according to the WHI Nutritional Biomarkers Study.[16] Briefly, the Dietary Modification trial (n=544) used a doubly labeled water protocol to estimate total energy expenditure and a urinary nitrogen protocol to estimate protein consumption. These results showed that food frequency questionnaire estimates for total energy were considerably underestimated, and protein was modestly underestimated. The calibrated protein and energy equations correct for these estimations and are therefore considered more accurate. The regression model for calibrated energy equation includes age, BMI, race/ethnicity, income, and physical activity. The calibration equation for protein includes age, BMI, race/ethnicity, income, and education.

Physical Activity and Other Participant Characteristics

Recreational physical activity was measured using a validated questionnaire developed for the WHI that determines frequency and duration of several types of activities. In this study, total activity measured is reported as the ratio of work metabolic rate to resting metabolic rate according to