EFFECTS OF A VITAMIN D AND LEUCINE-ENRICHED WHEY PROTEIN NUTRITIONAL SUPPLEMENT ON MEASURES OF SARCOPENIA IN OLDER ADULTS

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CONTENTS

BACKGROUND

- Preserving physical mobility, function, and independent living is vital for frail older adults.
- Sarcopenia, the age-related loss of muscle mass, strength, and function pose significant threats to physical performance, independence, and quality of life, contributing to a large part of physical frailty.
- In addition, it is a strong risk factor for reduced mobility, falls and fractures and is directly related to rates of hospital and long-term care admissions.
- The onset and progression of sarcopenia is multidimensional, involving physical inactivity, altered metabolism, neuromuscular deterioration, and marginal nutrient intakes and absorption.
- Marginal nutrient intake is a modifiable risk factor of sarcopenia, particularly protein, essential amino acids, leucine, and vitamin D.

PROBLEM

Could nutritional supplementation positively influence aspects of sarcopenia and thereby prevent mobility disability?

HYPOTHESIS

- A specific oral nutritional supplement can result in improvements in measures of sarcopenia.
- A targeted nutritional supplement containing whey protein, enriched with leucine and vitamin D in a timely bolus amount, would result in the accretion of muscle protein and improvements of muscle strength and function independent of physical exercise among non-malnourished sarcopenic older adults at high risk for disability.

METHODOLOGY

Design:

- randomized, controlled, double-blind, 2 parallel-group study

Randomization:

- The randomization sequence was computer-generated by a blinded statistician not involved in data collection or analysis.
- All investigators, study staff, and participants were blinded to group allocations, and the randomization code was not broken until statistical modeling of the primary and secondary outcomes was complete.

Primary Outcome Measures

1. Handgrip strength

- measured using a hydraulic hand dynamometer: Two consecutive measures of grip strength in both hands were recorded to the nearest kilogram with the participant in an upright position and the arm of the measured hand parallel to the body. Maximum grip strength was calculated by taking the average of the highest measurement from both hands.

2. SPPB

- 3 components: gait speed (4-meter walk at a usual pace), chair stand test (time required to rise 5 consecutive times from a chair without arm rests), and balance (3 different standing balance tests) Each component was scored from 0 (not possible) to 4 (best performance) and summed in a total score ranging from 0 to 12.

Secondary Outcome Measures

- The individual outcomes related to physical function: chair rise test, gait speed, and balance score, were predefined as separate secondary outcomes.

Other secondary outcomes were appendicular muscle mass (by DXA) and questionnaires of self-reported physical activity, activities of daily living, and health-related quality of life.

Primary outcomes of handgrip strength and SPPB score, and secondary outcomes of chair-stand test, gait speed, balance score, and appendicular muscle mass (by DXA) were measured at baseline, week 7, and week 13 of the intervention.

Participants:

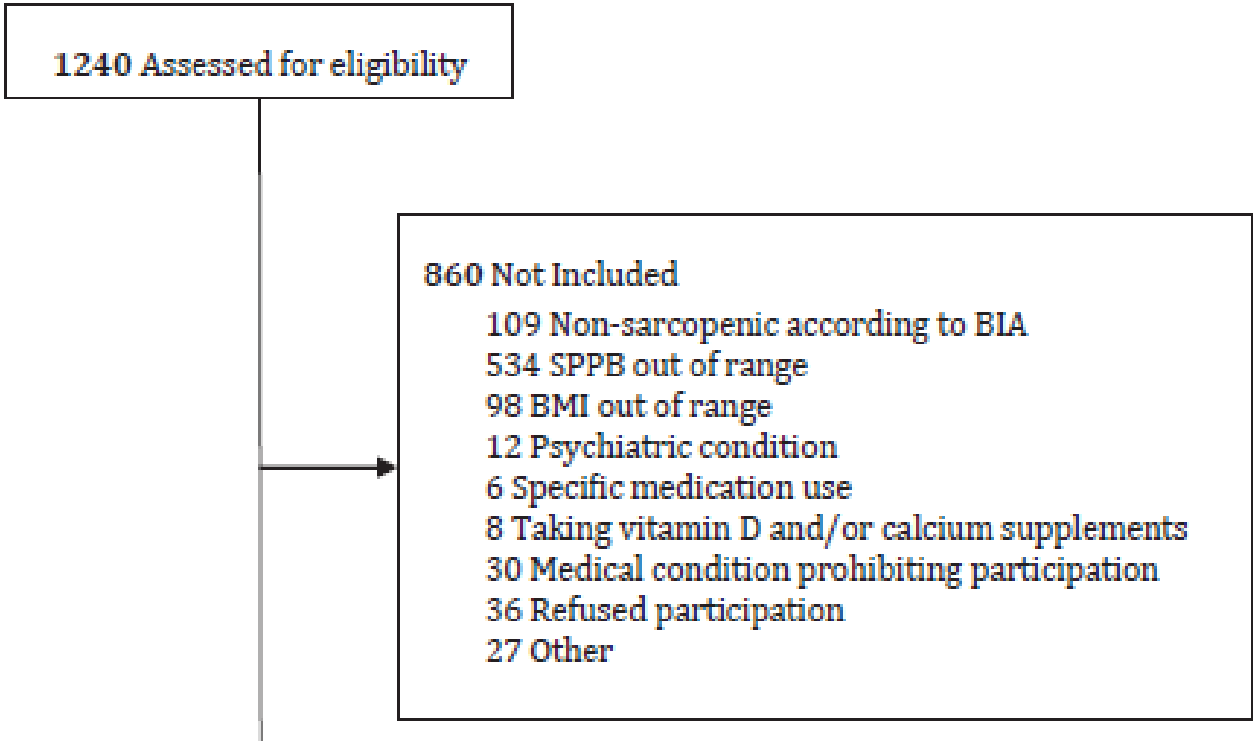
- recruited from 18 study centers in 6 European countries: Belgium, Germany, Ireland, Italy, Sweden, and the United Kingdom

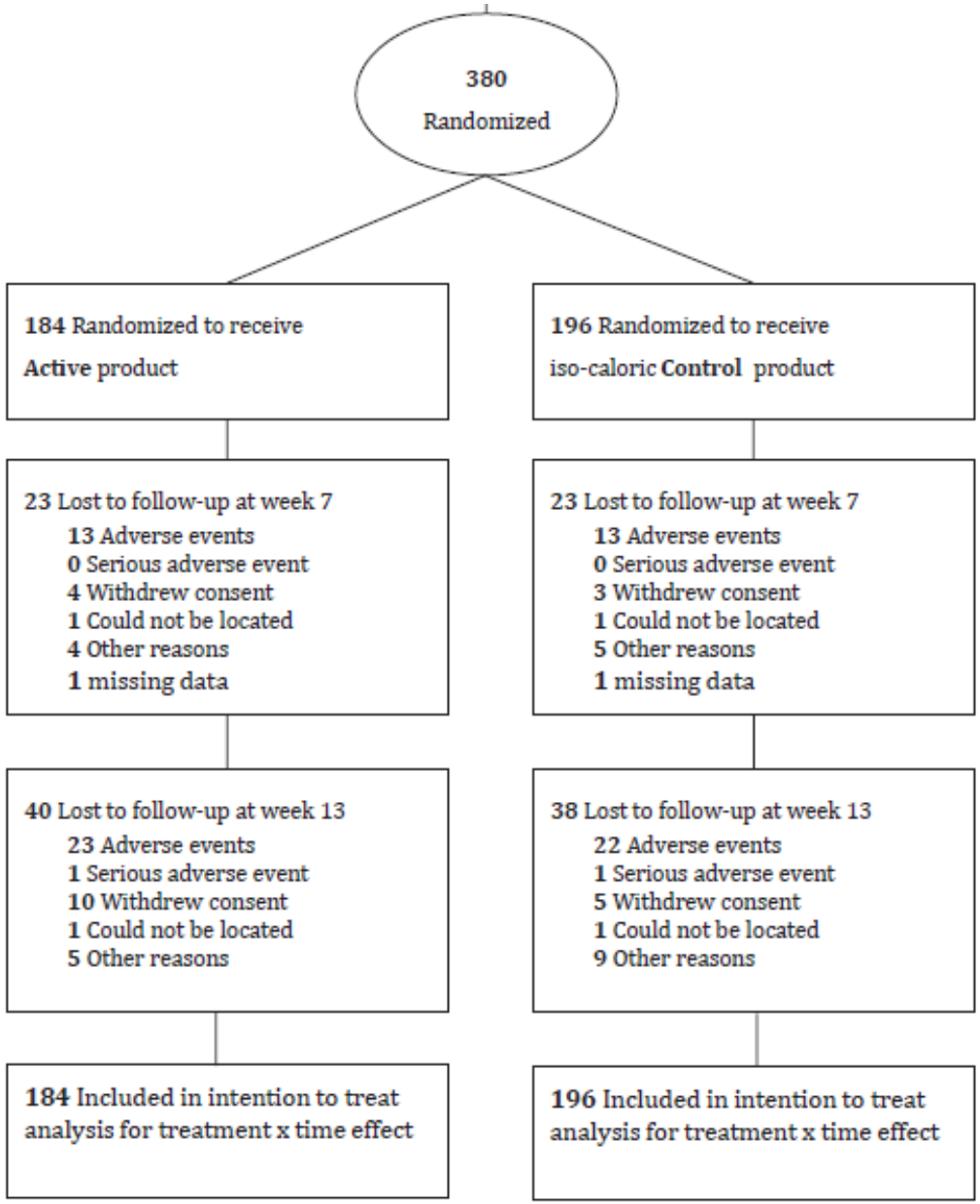
Inclusion criteria:

- non-protein-energy malnourished older participants (>65 years) with mobility limitations: screened for mild to moderate limitations in physical function (SPPB score 4e9), and for low skeletal muscle mass index [SMI; (skeletal muscle mass/BW * 100) 37% in men and 28% in women] using bioelectric impedance analysis
- a body mass index (BMI) between 20 and 30 kg/m
- no major cognitive impairment (Mini Mental State Examination score 25)
- able and willing to provide informed consent

Excluded if:

- had comorbidities such as kidney or liver failure, malignancies over the past 5 years, anemia, or acute inflammation (C-reactive protein concentration >10 mg/L), or
- presented with contraindications for calcium/vitamin D supplementation and/or
- were using medication interfering with the nutritional intervention


1240 Assessed for eligibility
860 Not Included
109 Non-sarcopenic according to BIA
534 SPPB out of range
98 BMI out of range
12 Psychiatric condition
6 Specific medication use
8 Taking vitamin D and/or calcium supplements
30 Medical condition prohibiting participation
36 Refused participation
27 Other


380
Randomized
184 Randomized to receive
Active product
196 Randomized to receive
iso-caloric Control product
23 Lost to follow-up at week 7
13 Adverse events
0 Serious adverse event
4 Withdrew consent
1 Could not be located
4 Other reasons
1 missing data
23 Lost to follow-up at week 7
13 Adverse events
0 Serious adverse event
3 Withdrew consent
1 Could not be located
5 Other reasons
1 missing data
40 Lost to follow-up at week 13
23 Adverse events
1 Serious adverse event
10 Withdrew consent
1 Could not be located
5 Other reasons
38 Lost to follow-up at week 13
22 Adverse events
1 Serious adverse event
5 Withdrew consent
1 Could not be located
9 Other reasons
184 Included in intention to treat analysis for treatment x time effect
196 Included in intention to treat analysis for treatment x time effect

Intervention:

- Participants were randomized to receive either the active or an iso-caloric control product.

-The active product contained, per serving, 20 g whey protein, 3 g total leucine, 9 g carbohydrates, 3 g fat, 800 IU vitamin D, and a mixture of vitamins, minerals, and fibers

-The iso-caloric control product did not contain any protein or micronutrients, and only carbohydrates, fat, and some trace elements

- Both were delivered as 40 g powder reconstituted with 100 to 150 mL water and consumed twice daily before breakfast and lunch to provide an adequate bolus of protein in addition to the meals.

DATA ANALYSIS

- This study was powered to detect an effect size of 1.9 kg for handgrip strength and a 0.5-point difference in SPPB. Assuming an a-value of 0.025, a 2-sided effect, and using the Hochberg principle for 2 primary outcomes, a sample size of 300 gave 80% power to observe an effect.
- A mixed model for repeated measures (MMRM) was performed. In this model, the treatment by time interaction coefficient estimates the potentially differential change in outcomes over time between active and control group.
- The Mann-Whitney U test was used for categorical variables that could not be used in the MMRM model.
- All statistical analyses were done using SAS software (version 9.4; SAS, Inc, Cary, NC) according to the predefined statistical analysis plan and were repeated by independent statisticians who confirmed the findings.

RESULTS

- Handgrip strength and SPPB improved in both groups without significant between-group differences.
- The active group improved more in the chair-stand test compared with the control group, between-group effect (95% confidence interval): -1.01 seconds (-1.77 to -0.19), P = .018.
- The active group gained more appendicular muscle mass than the control group, between-group effect: 0.17 kg (0.004-0.338), P = .045.

Muscle Strength and Function Outcomes

	Mean (SD)	Change From Baseline, Mean (SD)		Estimated Between-Group DifferenceMean (95% CI)Active − Control	*P**
	Baseline	Week 7	Week 13		
Handgrip strength, kg					
Active†	20.9 (7.9)	0.20 (3.2)	0.79 (3.6)‡	0.30§ (−0.46–1.05)	.44
Control‖	20.6 (7.5)	0.34 (2.8)	0.54 (3.2)		
SPPB					
Active¶	7.5 (1.9)	0.50 (1.26)	0.86 (1.38)**	0.11§ (−0.21–0.42)	.51
Control††	7.5 (2.0)	0.51 (1.21)	0.77 (1.45)**		
Chair-stand time, s‡‡					
Active§§	17.1 (15.2, 21.2)	−1.4 (−3.3–0.4)	−2.5 (−4.2 to −0.6)**	−1.01§ (−1.77 to −0.19)	.018
Control‖‖	17.6 (14.6, 20.6)	−1.0 (−3.0–1.1)	−1.2 (−3.3–0.8)**		
Balance test¶¶					
Active¶	3.0 (2.0, 4.0)	0.0 (0.0–0.0)	0.0 (0.0–1.0)	N.A.	.89
Control††	3.0 (2.0, 4.0)	0.0 (0.0–1.0)	0.0 (0.0–1.0)		
Gait speed, m/s					
Active¶	0.8 (0.2)	0.03 (0.11)	0.07 (0.12)**	0.01§ (−0.02–0.04)	.46
Control***	0.8 (0.2)	0.03 (0.10)	0.05 (0.12)**		

N.A., not applicable; SPPB, Short Physical Performance Battery.

The chairstand test is a robust measure of lower-extremity function because it requires lower-body strength, power, and good balance and coordination. Poor chair-stand performance is an independent risk factor for physical disability, hospitalization, and mortality.

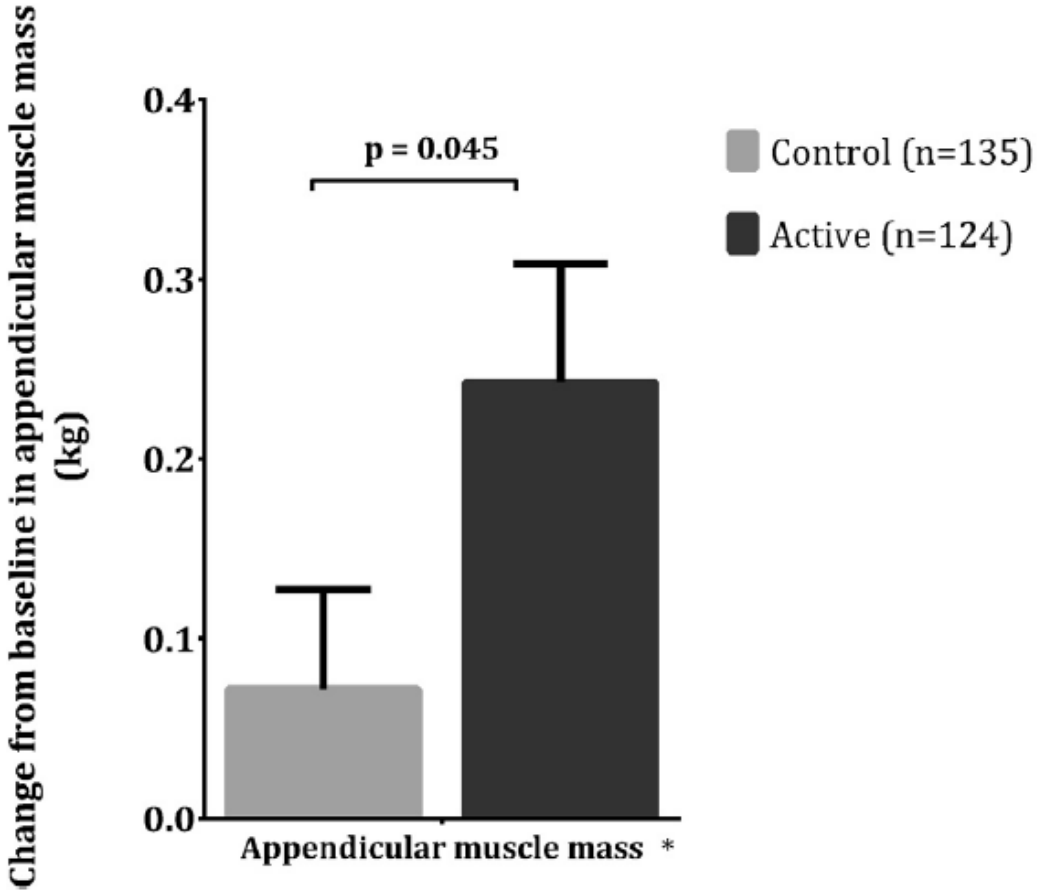


Fig. 2. Change (kg) in appendicular muscle mass from baseline to week 13 follow-up. *The raw mean change from baseline to week 13 and SE. The *P* value represents the time × treatment interaction derived from a mixed model (MMRM) adjusting for age, sex, and baseline protein intake.

LIMITATIONS

- An intervention effect was not observed in SPPB. The SPPB is by nature a categorical score, thus less sensitive to changes than a continuous numerical scale. As such, the sarcopenic screening measures of handgrip strength and SPPB may not be appropriate outcomes for measuring effects of sarcopenia intervention: Improve? Select sensitive and specific outcomes for sarcopenia, such as lower extremity strength and function.
- Although this study was performed among a robust sample of independently living older adults with mobility limitations, the full spectrum of older adults in the population at large, like those recovering from hospitalization and immobilization, could not be included.

SUMMARY AND CONCLUSION

- This 13-week intervention of a vitamin D and leucine-enriched whey protein oral nutritional supplement resulted in improvements in muscle mass and lower-extremity function among sarcopenic older adults.
- This study shows that specific nutritional supplementation alone might benefit geriatric patients, especially relevant for those who are unable to exercise.
- These results warrant further investigations into the role of a specific nutritional supplement as part of a multimodal approach to prevent adverse outcomes among older adults at risk for disability.