The impact of protein supplementation to maximize the skeletal muscle adaptive response to resistance type exercise training in healthy elderly men

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Primary Objective: To examine how protein supplemented after exercise and before each night of sleep augments the resistance type exercise training-induced changes in quadriceps muscle size (CSA) in healthy elderly men. Secondary Objective:...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON44031

Source
ToetsingOnline

Brief title
Active Aging Training Study

Condition

- Other condition
- Muscle disorders

Synonym
Muscle loss, Sarcopenia

Health condition

Aging - Sarcopenia

Research involving
Human

Sponsors and support

Primary sponsor: Universiteit Maastricht
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Aging, Dietary protein, Resistance exercise, Skeletal muscle

Outcome measures

Primary outcome

Quadriceps CSA (CT Scan)

Secondary outcome

* Skeletal muscle fibre size (Muscle Biopsy)

* Whole-body and regional body composition (DEXA)

* Muscular strength (1 RM * each exercise machine)

* Diurnal rates of muscle protein synthesis (Muscle Biopsy - Heavy water)

Study description

Background summary

From p10-11 of C1 protocol document:

Aging is accompanied by the progressive decline in skeletal muscle mass and strength, a process termed sarcopenia. As the regulation of muscle mass is associated with nutrition and, more importantly, levels of physical activity, it appears as though long-term alterations in life-style play a central role in the progression of sarcopenia. As such, it is understood that effective interventional strategies for counteracting or slowing the progression of sarcopenia should be focused on optimal exercise programs and supportive nutrition. Currently, resistance exercise is considered to be the most effective strategy for improving muscle mass and strength. It has been demonstrated that protein ingestion enhances the hypertrophic effects of

exercise, yet this effect is not ubiquitously observed. A recent meta-analysis conducted within our research group compiled applicable exercise training studies conduct with the elderly population and demonstrated that protein ingestion is indeed efficacious, although having a smaller effect than what was previously thought (11). As such, current work is directed at optimizing the effect of nutritional support on enhancing exercise-based gains in muscle mass in the elderly.

Mechanistically, the age-related loss in muscle mass is the result of a persistent imbalance in muscle protein turnover, whereby rates of protein breakdown chronically exceed rates of protein synthesis. It has been repeatedly observed that the elderly are unable to stimulate muscle protein synthesis as effectively as younger individuals following the provision of anabolic stimuli (i.e., exercise and protein intake). Since basal rates of synthesis seem to be unaffected by aging and rates of muscle protein breakdown respond minimally to anabolic stimuli, research emphasis is placed upon enhancing the extent to which muscle protein synthesis is stimulated in the elderly. It has been demonstrated in acute (6hr) studies that modifying the amount, type, source and amino acid composition of protein intake can rescue the inadequate stimulation of muscle protein synthesis in the elderly (34, 35). Resistance type exercise stimulates both muscle protein synthesis and breakdown rates (7, 37, 48). It has recently been shown that in the absence of post-exercise protein intake, net protein balance remains negative, since the increase in protein synthesis is compensated by an increase in protein breakdown (4, 27). Hence, provision of protein and/or amino acids is required for resistance exercise to be effective (i.e. resulting in net protein accretion). Whereas some studies report beneficial effects of protein supplementation during long-term resistance type exercise training in healthy old men (44, 45), others did not find any positive effects of protein supplementation on skeletal muscle fiber size and/or mass following long-term resistance type exercise training (13, 49). This discrepancy might, in part, be explained by the fact that the timing of the post-exercise protein intake plays an important regulatory role in its effectiveness in augmenting the response to resistance type exercise intervention (12, 13, 46). The intake of protein before and/or immediately after exercise has been shown to be effective to facilitate skeletal muscle reconditioning in some (13, 20, 33), but not all training intervention studies (1-3). In addition, most training studies only supplement on training days (i.e. only three times a week). Little is known about the effects of protein supplementation on non-training days during a long-term training intervention period. Providing additional dietary protein on non-training days will likely aid the skeletal muscle adaptive response on the days of recovery thereby augmenting muscle mass gains. Recently, the impact of exercise in the evening and the efficacy of protein ingestion immediately after exercise on protein synthesis during subsequent overnight recovery was evaluated (5). An increase in protein synthesis during the first few hours of post-exercise recovery was observed when protein was ingested. In addition, whole body protein synthesis was improved after protein administration in the

evening (5). It might be speculated that repeated periods of protein induced stimulation of whole body protein synthesis during overnight recovery will lead to increased muscle mass and strength over time.

In the proposed study, the effects of protein supplementation immediately after exercise and before sleep on muscle fiber size, body composition, and muscle strength will be assessed during a 12 weeks resistance type exercise-training program in healthy elderly men. The protein supplement is based on a practically applicable supplement, which could commercially become available for the general population (Fortifit, Nutritia, The Netherlands). Previous studies show that the ingestion of at least 30g protein is in the optimal range to stimulate the muscle protein synthetic response following resistance type exercise (31, 54). Carbohydrates are added to further stimulate the anabolic response through the insulin stimulated pathways (14, 15). The placebo group will ingest supplements identical to the protein group except with the protein content replaced by carbohydrate to equate the energy content of the supplements. The results of this study will have a practical implication in the development of new dietary strategies in resistance type exercise regimes to increase muscle mass and strength in older people. Furthermore, we aim to underpin the physiological efficacy for sufficient protein supplementation to enhance exercise-based gains in muscle mass and strength by demonstrating an increase in muscle protein synthesis during exercise training. Overall, the main aim of this study is to examine whether protein supplementation after each exercise session and daily before sleep, on both training and non-training days, during a 12 weeks resistance type exercise-training program, augments the increase in skeletal muscle fiber size, body composition and muscle strength in healthy old men.

Study objective

Primary Objective: To examine how protein supplemented after exercise and before each night of sleep augments the resistance type exercise training-induced changes in quadriceps muscle size (CSA) in healthy elderly men.

Secondary Objective: Differences in skeletal muscle fiber size and distribution (biopsy), whole body- and regional body composition (DEXA scan), muscle strength and physical performance (1RM, SPPB) and oral glucose tolerance (OGTT) will be secondary parameters. Diurnal rates of muscle protein synthesis will be compared between groups for one week (week 12) to establish the physiological relevance for enhancing exercise-based muscle mass with protein supplementation.

Study design

This study will be a double blind, randomized, placebo-controlled intervention

trial. The total study consists of a screening and an experimental part in which we will focus on the effects of an exercise intervention program with nutritional support on skeletal muscle mass and function in healthy elderly men. We will assess the effects of a 12 weeks resistance type exercise training program (3x/week) with or without additional protein supplementation (provided after each exercise session and daily before sleep) on skeletal muscle mass and function on whole body-, muscle- and myocellular level. A 12 week time period with training performed 3x/week has previously been shown to be required to establish a measurable increase in skeletal muscle mass and function (18, 49). In the present study, we aim to determine whether we can further increase the gain in muscle mass and function by providing protein supplementation after exercise and prior to sleep. This approach may prove an effective nutritional strategy to augment the benefits of resistance type exercise training. A one-week *heavy water* dosing protocol will be conducted in both groups during the last week of exercise training to demonstrate the effect of dietary protein supplementation on diurnal rates of muscle protein synthesis while undergoing an exercise training program.

Intervention

From p 17 of C1 protocol document:

Exercise Training:

Participants will perform a 12-week resistance type exercise-training program, consisting of six different exercises. Leg press, leg extension, chest press, shoulder press, horizontal row and vertical lat pull exercise will be performed on regular weight lifting machines (Technogym, Rotterdam), 3 days per week (Monday-Wednesday-Friday). In the first week, intensity will gradually increase from 70% to 75% of 1RM. Thereafter, training will be performed at 80% of 1RM. During each session, 4 sets of 8-10 repetitions will be performed on both the leg press and leg extension machines. In addition, 2 sets of 8-10 repetitions will be performed for either the chest-press/vertical lat pull or shoulder press/horizontal row exercises. The exercises of the upper extremities will alternate between subsequent exercise days. Training intensity (weight lifted) will be adapted if more than 10 repetitions can be performed. In addition, 1RM strength will objectively be measured at 4 and 8 weeks during the intervention period, to ensure progressive training loads (49). Sets will be separated by 90 seconds rest and exercises will be separated by 3 min of rest. Before and after each session, a 5-10 min warm up / cooling down at low intensity will be performed on a cycle ergometer. All training sessions will be performed under the supervision of an experienced investigator. Following every exercise session participants will receive their test beverage (either protein or placebo).

Protein Supplementation:

All participants will be randomly assigned to the protein supplementation or the placebo group. During the 12 week resistance type exercise program participants allocated to the protein group will receive a protein drink after each exercise session and prior to sleep at night, on both training and non-training days. Participants assigned to the placebo group will receive a placebo drink after each exercise session and prior to sleep at night, on both training and non-training days. Supplementation during the intervention period will consist of 300 ml beverages (Fortifit, Danone). Beverages will contain flavour additives, protein and carbohydrates (protein-group), dissolved in water. The protein beverage will contain a total of 21 g protein, as 20 g whey protein and 1 gram leucine along with 10 g CHO and 3 g fat (document D4.1). To control for different energy intake between the groups from differences in the macronutrient contents of the drinks, the control group will ingest an iso-caloric drink, whereby the absent protein is replaced by carbohydrate (document D4.2). Beverages will be masked for taste and smell by adding citric and vanilla additives.

Study burden and risks

The burden and risks associated with participation are minimal. Insertion of the catheters is comparable to a blood draw and could result in a small hematoma. Muscle biopsies will be taken under local anesthesia by an experienced physician, but may cause some minor discomfort for maximally up to 24 h after completion. The discomfort is comparable to muscle soreness or the pain one has after bumping into a table. We will take a total of 19 blood samples (200 mL) over the entire course of the study. We will take 1 during the screening visit, 5 on each of the two OGTT tests (pre and post training) and 9 during the heavy water assessment. Participants have to be fasted and rested for the screening and for both of the OGTT assessments, so they are not allowed to eat and drink (except for water) from 22h00 the evening before. Also, participants should not perform any type of intense physical exercise outside of the training protocol. Furthermore, we will ask the participants to fill out a dietary and activity record for 3 days prior to (week -1) and during (week 11) the 3-month exercise-training program.
There is no risk associated with the DEXA scan. The radiation dose emitted during a DEXA scan is 0.001 mSv. This is a very low exposure compared to the total background radiation in the Netherlands, which is ~2.5 mSv/year. For comparison, the radiation dose during a flight higher than 10 km is 0.005 mSV·h-1. The level of radiation emitted during a CT scan is also minimal since only single-slice scans will be taken at the level of mid-thigh (0.15 mSv per scan). Both the DXA and CT-scan will be performed twice. Consequently, every participant will be subjected to a total radiation dose of 0.302 mSv on completion of the study. This is very minimal exposure compared to the total background radiation level per year in the Netherlands, which is approximately 2.5 mSv/year.
The ingested protein supplement is a regular food and food supplementation substance and therefore part of the normal diet.

Performing exercise will pose little risk as the possibility for adverse health events will be evaluated during the screening (ECG) and subjects will be closely monitored throughout all exercise sessions. The exercise sessions might result in feelings of muscle soreness. Exercise intensity will gradually be increased in the first week to ensure familiarization of the muscles involved and to minimize the risk for muscle soreness and/or muscle injuries. Therefore, an experienced investigator will supervise all training sessions.
Isotopically-labelled water (deuterium oxide or *heavy water*) ingestion has been previously used in numerous published studies and is entirely safe and non-toxic when body water enrichments are below approximately 20 mol%. For the current study, body water enrichment will be approximately 1-2 mol%.
There is no direct benefit for the participants, only their contribution to scientific knowledge and nutritional strategies that prevent muscle loss in the elderly, which will be obtained from this study and can be used in the future.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Elderly (65 years and older)

Inclusion criteria

* Healthy males
* Age between 65 and 80 y
* BMI between 18.5 and 30 kg/m2
* Moderately active, performing fitness or sports on a non-competitive basis 1 time or less than 2 hours per week

Exclusion criteria

* HbA1C level above 6.5%
* Fasted blood glucose level above 6.9 mmol/L
* Celiac disease
* Lactose intolerance
* Smoking
* Diabetes
* Cancer
* Cardiovascular Disease
* Diagnosed GI tract diseases
* Arthritic conditions
* A history of neuromuscular problems
* Cognitive Impairment
* COPD
* Renal disorder
* Any medications known to affect protein metabolism (i.e. corticosteroids, non-steroidal anti-inflammatories, or prescription strength acne medications).
* Participation in exercise program
* Hypertension, high blood pressure that is above 140/90 mmHg.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo

Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	15-07-2015
Enrollment:	46
Type:	Actual

Ethics review

Approved WMO

Date:	10-06-2015
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL52214.068.15