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Original article

# Both basal and post-prandial muscle protein synthesis rates, following the ingestion of a leucine-enriched whey protein supplement, are not impaired in sarcopenic older males

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SUMMARY

*Background:* Studying the muscle protein synthetic response to food intake in elderly is important, as it aids the development of interventions to combat sarcopenia. Although sarcopenic elderly are the target group for many of these nutritional interventions, no studies have assessed basal or post-prandial muscle protein synthesis rates in this population.
*Objective:* To assess the basal and post-prandial muscle protein synthesis rates between healthy and sarcopenic older men.
*Design:* A total of 15 healthy (69 ± 1 y) and 15 sarcopenic (81 ± 1 y) older men ingested a leucine-enriched whey protein nutritional supplement containing 21 g of protein, 9 g of carbohydrate, and 3 g of fat. Stable isotope methodology combined with frequent collection of blood and muscle samples was applied to assess basal and post-prandial muscle protein fractional synthetic rates. Handgrip strength, muscle mass, and gait speed were assessed to identify sarcopenia, according to international criteria.
*Results:* Basal mixed muscle protein fractional synthetic rates (FSR) averaged 0.040 ± 0.005 and 0.032 ± 0.003%/h (mean ± SEM) in the sarcopenic and healthy group, respectively ($P = 0.14$). Following protein ingestion, FSR increased significantly to 0.055 ± 0.004 and 0.053 ± 0.004%/h in the post-prandial period in the sarcopenic ($P = 0.003$) and healthy groups ($P < 0.001$), respectively, with no differences between groups ($P = 0.45$). Furthermore, no differences were observed between groups in muscle protein synthesis rates during the early (0.058 ± 0.007 vs 0.060 ± 0.008%/h, sarcopenic vs healthy, respectively) and late (0.052 ± 0.004 vs 0.048 ± 0.003%/h) stages of the post-prandial period ($P = 0.93$ and $P = 0.34$, respectively).
*Conclusions:* Basal muscle protein synthesis rates are not lower in sarcopenic older men compared to healthy older men. The ingestion of 21 g of a leucine-enriched whey protein effectively increases muscle protein synthesis rates in both sarcopenic and healthy older men.
**Public trial registry number**: NTR3047.


## 1. Introduction

Skeletal muscle mass, function and strength decline with an increasing age, a syndrome that has been coined sarcopenia. The decline in muscle strength and function leads to a reduced ability to perform activities of daily living, and are associated with an increased risk of adverse musculoskeletal outcomes such as falls

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**Abbreviations**

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|---|---|
| AA | Amino acids |
| ANCOVA | Analysis of covariance |
| BMI | Body mass index |
| CRP | C-reactive protein |
| DEXA | Dual-energy X-ray absorptiometry |
| EAA | Essential amino acids |
| En% | Energy percent |
| EndoRa | Endogenous phenylalanine rate of appearance |
| ExoRa | Exogenous phenylalanine rate of appearance |
| FSR | Fractional synthesis rate |
| GC-IRMS | Gas chromatography-combustion isotope ratio mass spectrometry |
| GC–MS | Gas chromatography–mass spectrometry |
| $Hba1_c$ | Glycated haemoglobin |
| iAUC | Incremental area under the curve |
| MMRM | Mixed model for repeated measures |
| MPE | Mole percent excess |
| OGTT | Oral glucose tolerance test |
| Ra | Total rate of appearance |
| Rd | Total phenylalanine rate of disappearance |
| SEM | Standard error of the mean |
| SMMI | Skeletal muscle mass index |
| SPPB | Short physical performance battery |
| TTR | Tracer to tracee ratio |
| UPLC-MS/MS | Ultra-performance liquid chromatography tandem mass spectrometry |

and fractures [1,2]. Since sarcopenia is a strong predictor for mortality [3], it is clinically relevant to unravel the mechanisms underlying the age-related loss of skeletal muscle tissue.

Muscle mass maintenance is believed to be regulated mainly by changes in basal and post-prandial muscle protein synthesis rates (MPS). Age-related declines in basal or post-prandial muscle protein synthesis rates may be responsible for the progressive loss of skeletal muscle mass throughout the lifespan. So far, studies investigating basal muscle protein synthesis rates in older individuals have shown conflicting results. Lower basal muscle protein synthesis rates have been observed in the older populations when compared with younger populations in some studies [4–7]. In contrast, more recent work has been unable to detect significant differences in basal muscle protein synthesis rates between young and older individuals [8–12]. However, none of these studies specifically included older men and women suffering from sarcopenia. Therefore, it is likely that potential differences in basal muscle protein synthesis rates between the young and old have remained undetected, because a heterogeneous older population was selected that included many individuals who had not (yet) shown any signs of (substantial) muscle loss.

In addition to basal muscle protein synthesis, muscle maintenance is also largely determined by the muscle protein synthetic response to food intake. Because of the apparent absence of measurable differences in basal muscle protein synthesis rates between young and older populations, many research groups have shifted their focus to the muscle protein synthetic response to the main anabolic stimuli, such as food intake and physical activity. One of the primary anabolic stimuli for muscle protein synthesis is a systemic hyperaminoacidemia, resulting from the ingestion of dietary protein or essential amino acids [13–17]. A reduced sensitivity of senescent muscle to the anabolic properties of amino acid exposure has been reported by various research groups [8,10,18,19]. The post-prandial muscle protein synthetic response has been shown to be modulated by the type [20], amount [21] and total leucine content [9,22,23] of the protein ingested. Ingestion of ~20 g whey protein has been shown to increase muscle protein synthesis rates in healthy older individuals [17,24–26]. However, the post-prandial muscle protein synthetic response to protein ingestion may be blunted in the sarcopenic compared with the healthy older population. In the present study, we assessed if ingestion of a leucine-enriched whey protein can effectively increase the post-prandial muscle protein synthetic response in both healthy and sarcopenic older men.

We selected 15 healthy and 15 sarcopenic older males to participate in an experiment where we assessed basal and post-prandial muscle protein synthesis rates. Primed continuous infusions with L-[ring-$^{13}C_6$]-phenylalanine were applied with the collection of blood samples and muscle tissue to assess both basal as well as post-prandial muscle protein synthesis rates following the ingestion of a supplement containing 21 g of leucine-enriched whey protein. This is the first study to investigate post-prandial muscle protein synthesis in diagnosed [27] sarcopenic older males and to compare basal and post-prandial muscle protein synthesis rates between healthy and sarcopenic older males.

## 2. Subjects and methods

### 2.1. Subjects

A total of 15 sarcopenic older men (≥65 y) and 15 healthy elderly men (≥65 y) were selected to participate in this study. Subjects responded to advertisements in newspapers and were screened for eligibility at Maastricht University, the Netherlands. We informed all subjects on the nature and possible risks of the experimental procedures before we obtained written informed consent was. This study was approved by the Medical Ethical Committee of the Maastricht University Medical Centre, the Netherlands. The study was conducted in accordance with the Declaration of Helsinki and the International Conference on Harmonization guidelines for Good Clinical Practice as appropriate for nutritional products. The Trial Registration number for this study is NTR3047.

### 2.2. Pre-testing

All subjects participated in a screening session to determine their eligibility for inclusion. The inclusion criteria were male sex, age 65 years or older, and a BMI from 20 through 30 kg/m$^2$. Medical history, medication use, body weight, height, and alcohol use were recorded, and glucose tolerance was assessed by a 2-h oral glucose tolerance test. A basal blood sample was drawn to determine $HbA1_c$, calcidiol and CRP concentrations. Exclusion criteria included: all co-morbidities, the use of medication interacting with muscle metabolism and mobility of the limbs, co-morbidities interacting with gastric-intestinal function, inadequate glycemic control and diabetes mellitus, smoking, weight loss of more than 3 kg in the last three months, the use of protein supplements, and participation in an exercise program. In addition, the criteria derived from the European Working Group on Sarcopenia in Older People [27] and the International Working Group on Sarcopenia [28] were used to determine the presence (or absence) of sarcopenia. The presence of both low skeletal muscle mass index (SMMI,

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