

Top 10 Supportive Studies for Pro-Stat MAX

1. Weijs, PJM, et al. Optimal Protein and Energy Nutrition Decreases Mortality in Mechanically Ventilated, Critically Ill Patients: A Prospective Observational Cohort Study. *JPEN*. 2012;36:60-68. [pubmed](#)

Background: Optimal nutrition for patients in the intensive care unit has been proposed to be the provision of energy as determined by indirect calorimetry and the provision of protein of at least 1.2 g/kg.

Methods: Prospective observational cohort study in a mixed medical-surgical intensive care unit in an academic hospital. In total, 886 consecutive mechanically ventilated patients were included. Nutrition was guided by indirect calorimetry and protein provision of at least 1.2 g/kg. Cumulative intakes were calculated for the period of mechanical ventilation. Cox regression was used to analyze the effect of protein + energy target achieved or energy target achieved versus neither target achieved on 28-day mortality, with adjustments for sex, age, body mass index, Acute Physiology and Chronic Health Evaluation II, diagnosis, and hyperglycemic index.

Results: Patients' mean age was 63 ± 16 years; body mass index, 26 ± 6 ; and Acute Physiology and Chronic Health Evaluation II, 23 ± 8 . For neither target, energy target, and protein + energy target, energy intake was $75\% \pm 15\%$, $96\% \pm 5\%$, and $99\% \pm 5\%$ of target, and protein intake was $72\% \pm 20\%$, $89\% \pm 10\%$, and $112\% \pm 12\%$ of target, respectively. Hazard ratios (95% confidence interval) for energy target and protein + energy target were 0.83 (0.67–1.01) and 0.47 (0.31–0.73) for 28-day mortality.

Conclusions: Optimal nutritional therapy in mechanically ventilated, critically ill patients, defined as protein and energy targets reached, is associated with a decrease in 28-day mortality by 50%, whereas only reaching energy targets is not associated with a reduction in mortality.

2. Pennings et al. Whey protein stimulates postprandial muscle protein accretion more effectively than do casein and casein hydrolysate in older men. *Am J Clin Nutr*. 2011;1-9. [pubmed](#)

Background: Differences in digestion and absorption kinetics of dietary protein, its amino acid composition, or both have been suggested to modulate postprandial muscle protein accretion.

Objective: The objective was to compare protein digestion and absorption kinetics and subsequent postprandial muscle protein accretion after ingestion of whey, casein, and casein hydrolysate in healthy older adults.

Design: A total of 48 older men aged 74 ± 1 y were randomly assigned to ingest a meal-like amount (20 g) of intrinsically L-phenylalanine-labeled whey, casein, or casein hydrolysate. Protein ingestion was combined with continuous intravenous L-phenylalanine infusion to assess in vivo digestion and absorption kinetics of dietary protein. Postprandial mixed muscle protein fractional synthetic rates (FSRs) were calculated from the ingested tracer.

Results: The peak appearance rate of dietary protein-derived phenylalanine in the circulation was greater with whey and casein hydrolysate than with casein ($P < 0.05$). FSR values were higher after whey than after casein ($P < 0.01$) and casein hydrolysate ($P < 0.05$) ingestion. A strong positive correlation ($r = 0.66$, $P < 0.01$) was observed between peak plasma leucine concentrations and postprandial FSR values.

Conclusions: Whey protein stimulates postprandial muscle protein accretion more effectively than do casein and casein hydrolysate in older men. This effect is attributed to a combination of whey's faster digestion and absorption kinetics and higher leucine content.

3. Katsanos, C, et al. Whey protein in elderly results in greater muscle protein accrual than taking its constituent essential amino acid content. *Nutr Res.*2008;28:651-658. [pubmed](#)

Background: It is recognized that both whey protein (WY) and essential amino acids (EAA) are stimuli for muscle protein anabolism. The aim of the present study was to determine if the effects of WY ingestion on muscle protein accrual in elderly persons are due solely to its constituent EAA content.

Methods: Fifteen elderly persons were randomly assigned to ingest a bolus of either 15 g of WY, 6.72 g of EAA, or 7.57 g of nonessential amino acids (NEAA). We used the leg arteriovenous model to measure the leg phenylalanine balance, which is an index of muscle protein accrual.

Results: Phenylalanine balance during the 3.5 hours after the bolus ingestion improved in the WY ($P < .05$) but not in the EAA or NEAA groups. The insulin response during the same period was lower in both the NEAA (48 ± 40) and EAA (213 ± 127) when compared to the WY (1073 ± 229 ; $P < .05$).

Conclusion: WY ingestion improves skeletal muscle protein accrual through mechanisms that are beyond those attributed to its EAA content.

4. Volpi E, et al. Essential amino acids are primarily responsible for the amino acid stimulation of muscle protein anabolism in healthy elderly adults. *Am J Clin Nutr.*2003;78:250-8. [pubmed](#)

Background: Nutritional supplementation may be used to treat muscle loss with aging (sarcopenia). However, if physical activity does not increase, the elderly tend to compensate for the increased energy delivered by the supplements with reduced food intake, which results in a calorie substitution rather than supplementation. Thus, an effective supplement should stimulate muscle anabolism more efficiently than food or common protein supplements. We have shown that balanced amino acids stimulate muscle protein anabolism in the elderly, but it is unknown whether all amino acids are necessary to achieve this effect.

Objective: We assessed whether nonessential amino acids are required in a nutritional supplement to stimulate muscle protein anabolism in the elderly.

Design: We compared [total $n = 14$] the response of muscle protein metabolism to either 18 g essential amino acids (EAA group; $n = 6$, age 69 ± 2 y) or 40 g balanced amino acids (18 g essential amino acids + 22 g nonessential amino acids, BAA group; $n = 8$, age 71 ± 2 y) given orally in small boluses every 10 min for 3 h to healthy elderly volunteers. Muscle protein metabolism was measured in the basal state and during amino acid administration via L- phenylalanine infusion, femoral arterial and venous catheterization, and muscle biopsies.

Results: Phenylalanine net balance increased from the basal state ($P < 0.01$), with no differences between groups (BAA: from -16 ± 5 to 16 ± 4 ; EAA: from -18 ± 5 to 14 ± 13) because of an increase ($P < 0.01$) in muscle protein synthesis and no change in breakdown.

Conclusion: Essential amino acids are primarily responsible for the amino acid-induced stimulation of muscle protein anabolism in the elderly.

5. Symons, TB, et al. A moderate serving of high-quality protein maximally stimulates skeletal muscle protein synthesis in young and elderly subjects. *JADA*. 2009;109(9):1582-6. [pubmed](#)

Background: Ingestion of sufficient dietary protein is a fundamental prerequisite for muscle protein synthesis and maintenance of muscle mass and function. Elderly people are often at increased risk for protein-energy malnutrition, sarcopenia, and a diminished quality of life.

Methods: This study sought to compare changes in muscle protein synthesis and anabolic efficiency in response to a single moderate serving (220 kcal; 30 g protein) or large serving (660 kcal; 90 g protein) of 90% lean beef. Venous blood and vastus lateralis muscle biopsy samples were obtained during a primed, constant infusion of L-phenylalanine in healthy young (n=17; 34±3 years) and elderly (n=17; 68 ±2 years) individuals (total n= 34). Mixed muscle fractional synthesis rate was calculated during a 3-hour postabsorptive period and for 5 hours after meal ingestion. Data were analyzed using a two-way repeated measures analysis of variance with Tukey's pairwise comparisons.

Results: A 30g protein (moderate) serving of lean beef increased muscle protein synthesis by approximately 50% in both young and older volunteers. Despite a threefold increase in protein and energy content, there was no further increase in protein synthesis after ingestion of 90 g of protein lean beef in either age group.

Conclusion: Ingestion of more than 30 g protein in a single meal does not further enhance the stimulation of muscle protein synthesis in young and elderly.

6. McClave, S. et al. Guidelines for the Provision and Assessment of Nutrition Support Therapy in the Adult Critically Ill Patient: Society of Critical Care Medicine (SCCM) and American Society for Parenteral and Enteral Nutrition (ASPEN). *JPEN*.2009;33:277. [pubmed](#)

7. Hoffer, J. & Bistran, B. Appropriate protein provision in critical illness: a systematic and narrative review. *Am J Clin Nutr*.2012;96:591-600. [pubmed](#)

Background: Widely varying recommendations have been published with regard to the appropriate amount of protein or amino acids to provide in critical illness.

Objective: We carried out a systematic review of clinical trials that compared the metabolic or clinical effects of different protein intakes in adult critical illness and comprehensively reviewed all of the available evidence pertinent to the safe upper limit of protein provision in this setting.

Design: MEDLINE was searched for clinical trials published in English between 1948 and 2012 that provided original data comparing the effects of different levels of protein intake on clinically relevant outcomes and evidence pertinent to the safe upper limit of protein provision to critically ill adults.

Results: The limited amount and poor quality of the evidence preclude conclusions or clinical recommendations but strongly suggest that 2.0–2.5 g protein substrate • kg normal body weight/d is safe and could be optimum for most critically ill patients. At the present time, most critically ill adults receive less than half of the most common current recommendation, 1.5 g protein/kg/d, for the first week or longer of their stay in an intensive care unit.

Conclusion: There is an urgent need for well-designed clinical trials to identify the appropriate level of protein provision in critical illness.

8. Koopman, R., et al. Ingestion of a protein hydrolysate is accompanied by an accelerated in vivo digestion and absorption rate when compared with its intact protein. *Am J Clin Nutr.*2009;90:1-10. [pubmed](#)

Background: It has been suggested that a protein hydrolysate, as opposed to its intact protein, is more easily digested and absorbed from the gut, which results in greater plasma amino acid availability and a greater muscle protein synthetic response.

Objective: We aimed to compare dietary protein digestion and absorption kinetics and the subsequent muscle protein synthetic response to the ingestion of a single bolus of protein hydrolysate compared with its intact protein in vivo in humans.

Design: Ten elderly men (mean age: 64 ± 1 y) were randomly assigned to a crossover experiment that involved 2 treatments in which the subjects consumed a 35-g bolus of specifically produced L-phenylalanine-labeled intact casein (CAS) or hydrolyzed casein (CASH). Blood and muscle-tissue samples were collected to assess the appearance rate of dietary protein-derived phenylalanine in the circulation and subsequent muscle protein fractional synthetic rate over a 6-h postprandial period.

Results: The mean exogenous phenylalanine appearance rate was $27 \pm 6\%$ higher after ingestion of CASH when compared with CAS ($P < 0.001$). Splanchnic extraction was significantly lower in CASH compared with CAS treatment ($P < 0.01$). Plasma amino acid concentrations increased to a greater extent (25–50%) after the ingestion of CASH than with CAS ($P < 0.01$). Muscle protein synthesis rates averaged $0.054 \pm 0.004\%$ and $0.068 \pm 0.006\%/h$ in the CAS and CASH treatments, respectively ($P = 0.10$).

Conclusions: Ingestion of a protein hydrolysate, as opposed to its intact protein, accelerates protein digestion and absorption from the gut, augments postprandial amino acid availability, and tends to increase the incorporation rate of dietary amino acids into skeletal muscle protein.

9. Tang E., et al. Ingestion of whey hydrolysate, casein, or soy protein isolate: effects on mixed muscle protein synthesis at rest and following resistance exercise in young men. *J Appl Physiol.*2009;107:987-992. [pubmed](#)

Background: This study was designed to compare the acute response of mixed muscle protein synthesis (MPS) to rapidly (i.e., whey hydrolysate and soy) and slowly (i.e., micellar casein) digested proteins both at rest and after resistance exercise.

Methods: Three groups of healthy young men ($n = 6$ per group, total $n = 18$) performed a bout of unilateral leg resistance exercise followed by the consumption of a drink containing an equivalent content of essential amino acids (10 g) as either whey hydrolysate, micellar casein, or soy protein isolate. Mixed MPS was determined by a primed constant infusion of L-phenylalanine.

Results: Ingestion of whey protein resulted in a larger increase in blood essential amino acid, branched-chain amino acid, and leucine concentrations than either casein or soy ($P < 0.05$). Mixed MPS at rest (determined in the nonexercised leg) was higher with ingestion of faster proteins (whey = 0.091 ± 0.015 , soy = 0.078 ± 0.014 , casein = $0.047 \pm 0.008\%/h$); MPS after consumption of whey was ~93% greater than casein ($P < 0.01$) and ~18% greater than soy ($P = 0.067$). A similar result was observed after exercise (whey > soy > casein); MPS following whey consumption was ~122% greater than casein ($P < 0.01$) and 31% greater than soy ($P < 0.05$). MPS was also greater with soy consumption at rest (64%) and following resistance exercise (69%) compared with casein (both $P < 0.01$).

Conclusion: We conclude that the feeding-induced stimulation of MPS in young men is greater after whey hydrolysate or soy protein consumption than casein both at rest and after resistance exercise; moreover, despite both being fast proteins,

whey hydrolysate stimulated MPS to a greater degree than soy after resistance exercise. These differences may be related to how quickly the proteins are digested (i.e., fast vs. slow) or possibly to small differences in leucine content of each protein.

10. Tappenden, K, et al. Critical Role of Nutrition in Improving Quality of Care: An Interdisciplinary Call to Action to Address Adult Hospital Malnutrition. *JPEN*.2013;37:482-497. [pubmed](#)

The current era of healthcare delivery, with its focus on providing high-quality, affordable care, presents many challenges to hospital-based health professionals. The prevention and treatment of hospital malnutrition offer a tremendous opportunity to optimize the overall quality of patient care, improve clinical outcomes, and reduce costs. Unfortunately, malnutrition continues to go unrecognized and untreated in many hospitalized patients. This article represents a call to action from the interdisciplinary Alliance to Advance Patient Nutrition to highlight the critical role of nutrition intervention in clinical care and to suggest practical ways to promptly diagnose and treat malnourished patients and those at risk for malnutrition. We underscore the importance of an interdisciplinary approach to addressing malnutrition both in the hospital and in the acute posthospital phase. It is well recognized that malnutrition is associated with adverse clinical outcomes. Although data vary across studies, available evidence shows that early nutrition intervention can reduce complication rates, length of hospital stay, readmission rates, mortality, and cost of care. The key is to systematically identify patients who are malnourished or at risk and to promptly intervene. We present a novel care model to drive improvement, emphasizing the following 6 principles: (1) create an institutional culture where all stakeholders value nutrition, (2) redefine clinicians' roles to include nutrition care, (3) recognize and diagnose all malnourished patients and those at risk, (4) rapidly implement comprehensive nutrition interventions and continued monitoring, (5) communicate nutrition care plans, and (6) develop a comprehensive discharge nutrition care and education plan.