Nutrition Interventions for Frailty and Sarcopenia

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Outline

- Frailty and sarcopenia
- Protein intake and mechanisms of sarcopenia
- Importance of protein quantity and intake distribution pattern
- Special considerations for hospitalized older adults
- Vitamin D
- Summary and conclusions
Frailty and Sarcopenia

CYCLE OF FRAILTY

Chronic undernutrition

↓ Energy expenditure

↓ Activity

↓ Walking speed

Disability

Dependency

Death

Sarcopenia

↓ Insulin sensitivity

Osteopenia

↓ VO₂max

↓ Resting metabolic rate

↓ Strength

↓ Power

Immobilization

Falls

Injuries

Impaired balance

Aging

Disease

Medications

Environment

Modified from Fried et al. Sci. Aging Knowl. Environ. 2005
Sarcopenia

Universal, progressive and involuntary decline in lean body mass and function associated with aging, primarily due to loss of skeletal muscle

Roubenoff and Castaneda, JAMA, 2001

Strength and Mortality in Older Adults

Health ABC Study
2,292 healthy older adults, 70-79 yr at enrollment

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Aging Attenuates the Meal Stimulated Increase in Muscle Protein Synthesis

Volpi et al. J Clin Endocrinol Metab, 2000
Muscle Protein Synthesis is Resistant to the Anabolic Effect of Insulin in Older Adults

Rasmussen et al., FASEB J, 2006
Fujita et al. Diabetologia, 2009

Percent per hour

Fasting
Insulin

Young Adults Prandial Dose
Older Adults Prandial Dose
Older Adults High Dose

Rasmussen et al., FASEB J, 2006
Fujita et al. Diabetologia, 2009
Cellular Mechanisms of Resistance to Anabolic Stimulation in Older Adults

- Primary Active Transport
- Secondary Active Transporters (i.e., SNAT2, ASC)
- Tertiary Active Transporters (i.e., LAT1)
- Intracellular Proteins Implicated to Mediate Amino Acid Signal to mTORC1
- mTORC1 Signaling Proteins/Complexes
- Insulin Receptor

Protein Synthesis
- Translation Initiation
- Translation Elongation
Endothelial Dysfunction Contributes to Resistance to Anabolic Stimulation in Elders

Timmerman, et al., J Clin Endocrinol Metab, 2010; and Diabetes, 2010
Pharmacological Vasodilation Restores the Anabolic Response of Muscle to Insulin in Older Adults

Muscle Perfusion (Nutritive Flow)

![Muscle Perfusion Graph](image)

- Older Control
- Older Sodium Nitroprusside

Muscle Protein Synthesis

![Muscle Protein Synthesis Graph](image)

- Fasting
- Insulin

Timmerman, Lee et al., Diabetes, 2010
Aerobic Exercise Restores the Muscle Protein Anabolic Response to a Mixed Meal in Elders

**Muscle Perfusion (Nutritive Flow)**

- Fasting
- Meal

- Control
- Exercise

**Muscle Protein Synthesis**

- Fasting
- Meal

* P<0.05 vs. Basal
† P<0.05 vs. Control

Timmerman et al., FASEB J 2010 (abstract)
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Response of Muscle Protein Synthesis To Essential Amino Acids Depends on Leucine Dose

7 g Essential Amino Acids

- 1.7 g Leucine (~15 g protein) [Katsanos et al, AJP, 2006]

- 2.8 g Leucine (~30 g protein) [*]

18 g Essential Amino Acids

- 3.2 g Leucine (~40 g protein) [*]

Volpi et al, AJCN, 2003

Young adults

Older adults
Muscle Protein Synthesis in Older Adults: Protein Meal

30 g of Protein
4 oz beef patty
(~320 kcal)

90 g of Protein
12 oz beef patty
(~960 kcal)

Fasting Meal

Symons et al. AJCN, 2007

Symons et al. J Am Diet Assoc, 2009
Protein Intake Pattern Across Meals in Adults 70 yr and Older

**Reported Distribution**
- Average reported intake ~1 g/kg
- ~20% for Breakfast (14 g)
- ~23% for Lunch (16 g)
- ~46% for Dinner (32 g)

**Ideal Distribution**
- Max. Muscle Protein Synthesis
- Calculated ideal intake ~1.3 g/kg
- ~33% for Breakfast (30 g)
- ~33% for Lunch (30 g)
- ~33% for Dinner (30 g)

Source: NHANES 2007-2008

Paddon-Jones & Rasmussen, Curr Op Clin Nutr Metab Care 2009
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Patterns of Functional Loss and Disablement
Hospitalized Older Adults Are Very Inactive

Steps per Day

Minutes Active per Day

Fisher et al. JAGS 2011
Total Daily Steps and Early Mobilization Predict Hospital Length of Stay in Older Adults

Number of Steps and LOS

Complete Hospital Days

Early Mobilization and LOS
Step Change from 1\textsuperscript{st} to 2\textsuperscript{nd} Hospital Day

Fisher et al. JAGS 2011
Fisher et al. Arch Int Med 2010
Inactivity Induces Significant Muscle Loss in Older Adults

While consuming the protein RDA

Paddon-Jones et al. J Clin Endocrinol Metab, 2004
Kortebein et al. J Gerontology, 2008
Hospitalized Older Patients May Not Eat Adequate Amounts of Protein

Paddon-Jones, ACE Unit pilot data
Excess Dietary Amino Acids Can Prevent Inactivity-Induced Reductions in Muscle Protein Synthesis

Normal diet protein content: 0.8 g/kg/day

Ferrando et al. Clin Nutr 2010
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Summary

In older adults:

• Total daily protein intake is a predictor of sarcopenia
• Response of muscle protein synthesis to amino acids is impaired at lower intakes
• Maximal stimulation of muscle protein synthesis is achieved at intakes of ~3 g of leucine corresponding to ~30 g of whole protein
• Immobilization reduces appetite, protein/energy intake and the response of muscle to anabolic stimulation by nutrients
• Supplementation with amino acids can improve muscle metabolism during immobilization
• Low vitamin D status is associated with reduced physical functioning
• Vitamin D supplementation may reduce the risk of falls
Conclusions and Research Needs

• Adequate protein intake is essential for muscle mass and function in older adults

• Protein is the only macronutrient that has no inactive reservoir (i.e. it is stored in active tissues, mainly muscle, or converted to energy)
  – Is the current protein DRI adequate to maintain function in seniors?
  – Aside from total intake, should we also consider daily intake distribution?

• Protein intake should be adjusted according to health status and activity level
  – What is the optimal protein intake for hospitalized/inactive seniors?
  – What is the optimal protein intake for active seniors?

• Vitamin D intake may be another key nutrient for the reduction of the risk of falls and frailty in older adults
  – Is the current RDA for Vit. D optimal to maintain physical functioning?
Grow old along with me! The best is yet to be, the last of life, for which the first was made

Robert Browning

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