



CHANGES IN MUSCULOSKELET AL HEALTH WITH AGING

Module 1

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- Section sub-heading



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SKELETAL MUSCLE

[1.1. Skeletal muscle structure](#)

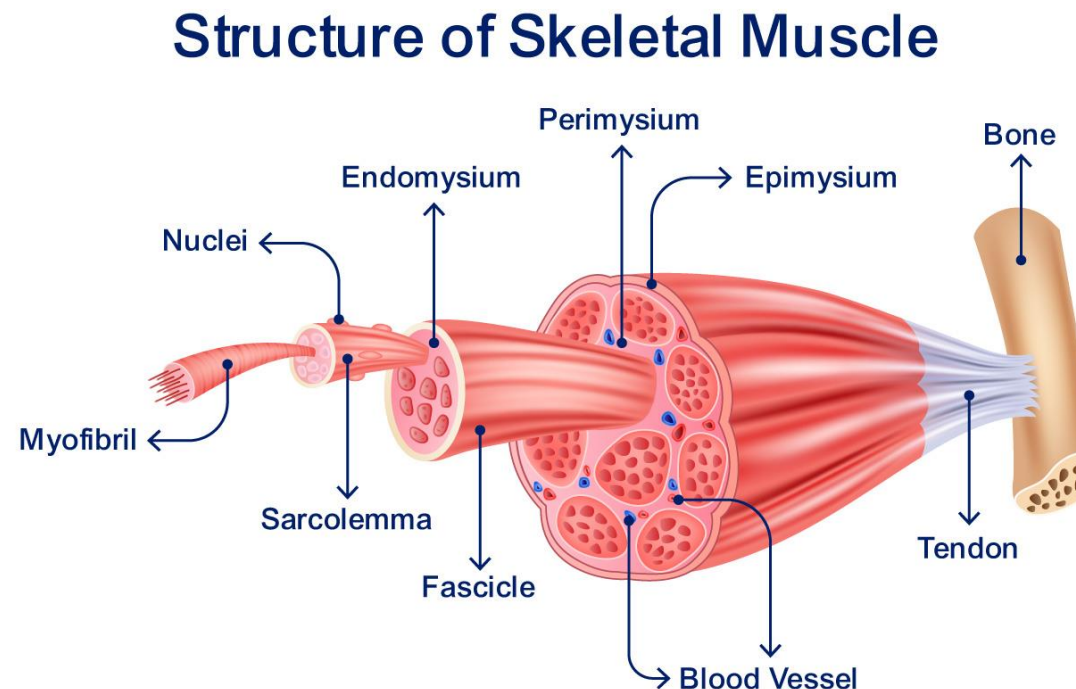
[1.2. Importance of skeletal muscle](#)



SKELETAL MUSCLE

Skeletal muscle structure (1/2)

- Skeletal muscle is made up of muscle fibres (myofibers).
- Each myofiber functions as an individual muscle cell, with multiple nuclei, and contains sarcomeres—the fundamental units of contraction.¹
- Groups of myofibers form fascicles, and multiple fascicles collectively make up the muscle itself.²
- A motor unit consists of a motor neuron and the myofibers it innervates (ranging from 8 [fine movement] to > 1000 [large movement] fibers).³



Schematic representation of skeletal muscle. A: Sarcomere structure is shown in the relaxed state (I) and during contraction (II). Actin (red), Myosin (blue), Titin (Yellow).¹

1. Gotti, et al. Hierarchical fibrous structures for muscle-inspired soft-actuators: A review. Applied Materials Today. 2020;20:100772.

2. McCuller C, et al. Physiology, Skeletal Muscle. 2023 Jul 30. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan--.

3. Gustafsson T, et al. Aging Skeletal Muscles: What Are the Mechanisms of Age-Related Loss of Strength and Muscle Mass, and Can We Impede Its Development and Progression? Int J Mol Sci. 2024 Oct 11;25(20):10932.

SKELETAL MUSCLE

Skeletal muscle structure (2/2)

Features of the different fiber types.

- Myofibers can be classified into three types, with distinct features.¹⁻³
- Type I fibers: slow-twitch,⁴ **resistant to fatigue**, play a key role in maintaining posture.⁵
- Type IIA fibers: fast-twitch, but with an intermediate fatigue, closer to type I fibers in characteristics.⁶
- Type IIX fibers: fast-twitch,⁴ fatigue quickly, responsible for fast movements and lifting heavy loads ‘**high intensity**’ movements.⁷

Characteristic	Type I	Type IIA	Type IIX
Capillarity ¹	High	Intermediate	Low
Main metabolism ^{1,3}	Oxidative (aerobic)	Oxidative/ Glycolytic	Glycolytic (anaerobic)
Fatigue resistance ^{1,2}	High	Intermediate	Low
Contraction speed ^{2,3}	Slow	Fast	Fast
Myosin heavy chain isoform ^{1,2}	MHC-I	MHC-IIA	MHC-IIX
Myofibrillar ATPase activity ¹	Low	Intermediate	High
Mitochondrial density ¹	High	Intermediate	Low



1. Bottinelli R, et al. Human skeletal muscle fibres: molecular and functional diversity. Prog Biophys Mol Biol. 2000;73(2-4):195-262.
2. Mori K. Maintenance of Skeletal Muscle to Counteract Sarcopenia in Patients with Advanced Chronic Kidney Disease and Especially Those Undergoing Hemodialysis. Nutrients. 2021 May 2;13(5):1538.
3. Cicillot S, et al. Muscle type and fiber type specificity in muscle wasting. Int J Biochem Cell Biol. 2013 Oct;45(10):2191-9.
4. Kirk B, Piasecki M. Sarcopenia. 2021;35-43.

5. Coletti C, et al. Exercise-mediated reinnervation of skeletal muscle in elderly people: An update. Eur J Transl Myol. 2022 Feb 28;32(1):10416.
6. Schiaffino S, et al. Fiber types in mammalian skeletal muscles. Physiol Rev. 2011;91(4):1447-1531.
7. Kohn TA, et al. Specific muscle adaptations in type II fibers after high-intensity interval training of well-trained runners. Scand J Med Sci Sports. 2011 Dec;21(6):765-72.

Importance of skeletal muscle



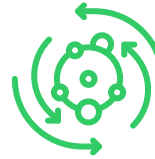
Skeletal muscle overview

- Accounts for ~ 40% of total body weight.¹
- Contains ~60-65% of the body's total protein content.¹ We often think on muscle in terms of movement, but its role goes well beyond that.



Mechanical functions - what we all know

- Generating movement¹
- Maintaining posture¹
- Maintaining balance¹



Metabolic functions - beyond its obvious roles

- Acts as a **reservoir** for essential nutrients (e.g., **amino acids**, **glycogen**)¹
- Large, due to mass, contributor to Resting Metabolic Rate (RMR) – produces heat²
- Plays a key role in glucose and lipid metabolism³ – largest site of post-prandial glucose disposal⁴
- Releasing **myokines** (muscular-derived cytokines with endocrine function) that:⁵
- Modulate low-grade inflammation⁶



1. Frontera WR, et al. Skeletal muscle: a brief review of structure and function. *Calcif Tissue Int.* 2015 Mar;96(3):183-95.
2. Zurlò F, et al. Skeletal muscle metabolism is a major determinant of resting energy expenditure. *J Clin Invest.* 1990;86(5):1423–1427.
3. Kalyani RR, et al. Age-related and disease-related muscle loss: the effect of diabetes, obesity, and other diseases. *Lancet Diabetes Endocrinol.* 2014 Oct;2(10):819-29.

4. DeFronzo RA, et al. The effect of insulin on the disposal of intravenous glucose. Results from indirect calorimetry and hepatic and femoral venous catheterization. *Diabetes.* 1981 Dec;30(12):1000-7.
5. Hoffmann C, et al. Skeletal Muscle as an Endocrine Organ: The Role of Myokines in Exercise Adaptations. *Cold Spring Harb Perspect Med.* 2017 Nov 1;7(11):a029793.
6. Pedersen BK, et al. Muscle as an endocrine organ: focus on muscle-derived interleukin-6. *Physiol Rev.* 2008;88(4):1379–1406.



DECLINE OF PROTEIN SYNTHESIS AND ABSORPTION WITH AGE

[2.1. Muscle protein turnover](#)

[2.2. Anabolic resistance - Muscle gets harder to build with age](#)

[2.3. Factors contributing to anabolic resistance](#)

[2.4. Splanchnic sequestration of protein in older individuals](#)

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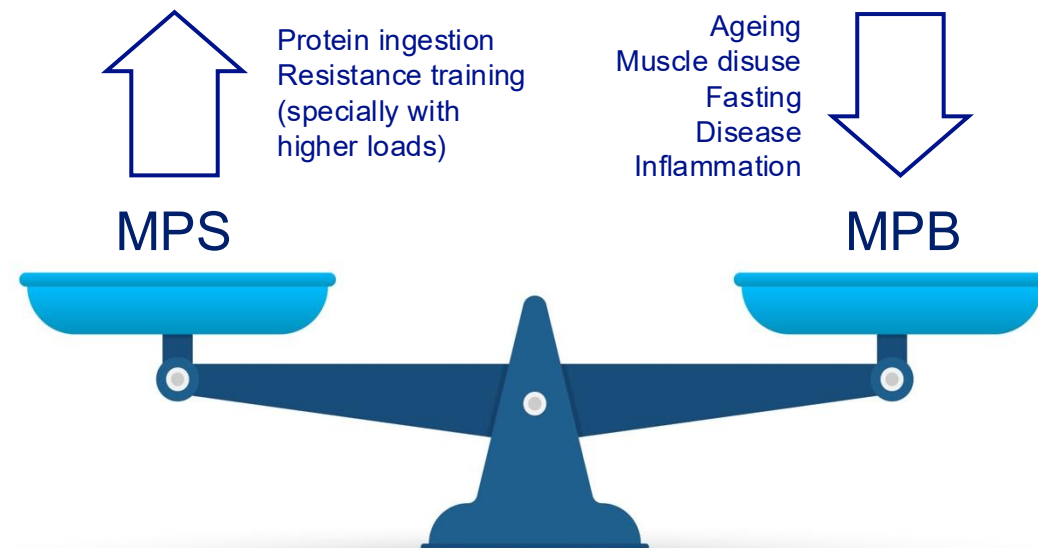
[2.7. Summary](#)



DECLINE OF PROTEIN SYNTHESIS AND ABSORPTION WITH AGE

Muscle protein turnover

- Skeletal muscle is a highly plastic tissue → responds to loading, unloading¹ lack of amino acid (AA) precursors to give up its own reservoir of AA.²
- Muscle proteins have turnover at ~1.5%/ day (~500 g muscle renewed daily).³ – completely ‘new’ muscle in ~67days (likely longer).
- Balance of processes. Muscle protein synthesis (MPS) and muscle protein breakdown (MPB).⁴ **Increasing muscle mass.** Resistance training & protein ingestion enhances mechanical load, stimulating MPS.
- Loss of muscle mass. Muscle disuse, energy deficit (fasting), diseases (cancer, T2D).



Muscle mass balance between muscle protein synthesis (MPS) and muscle protein breakdown (MPB).



1. Schiaffino S, et al. Fiber types in mammalian skeletal muscles. *Physiol Rev* (2011); 91(4): 1447–1531.
 2. Rennie MJ, et al. Rates of protein turnover (synthesis and breakdown) in human muscle: Interactions, measurement, and regulation. *Adv Exp Med Biol*. 1999; 463: 261–274.
 3. Janssen TAH, et al. From molecular to physical function: The aging trajectory. *Curr Res Physiol*. 2024 Dec 16; 8: 100138.
 4. McKendry J, et al. Resistance Exercise, Aging, Disuse, and Muscle Protein Metabolism. *Compr Physiol*. 2021 Jun 30; 11(3):2249-2278.

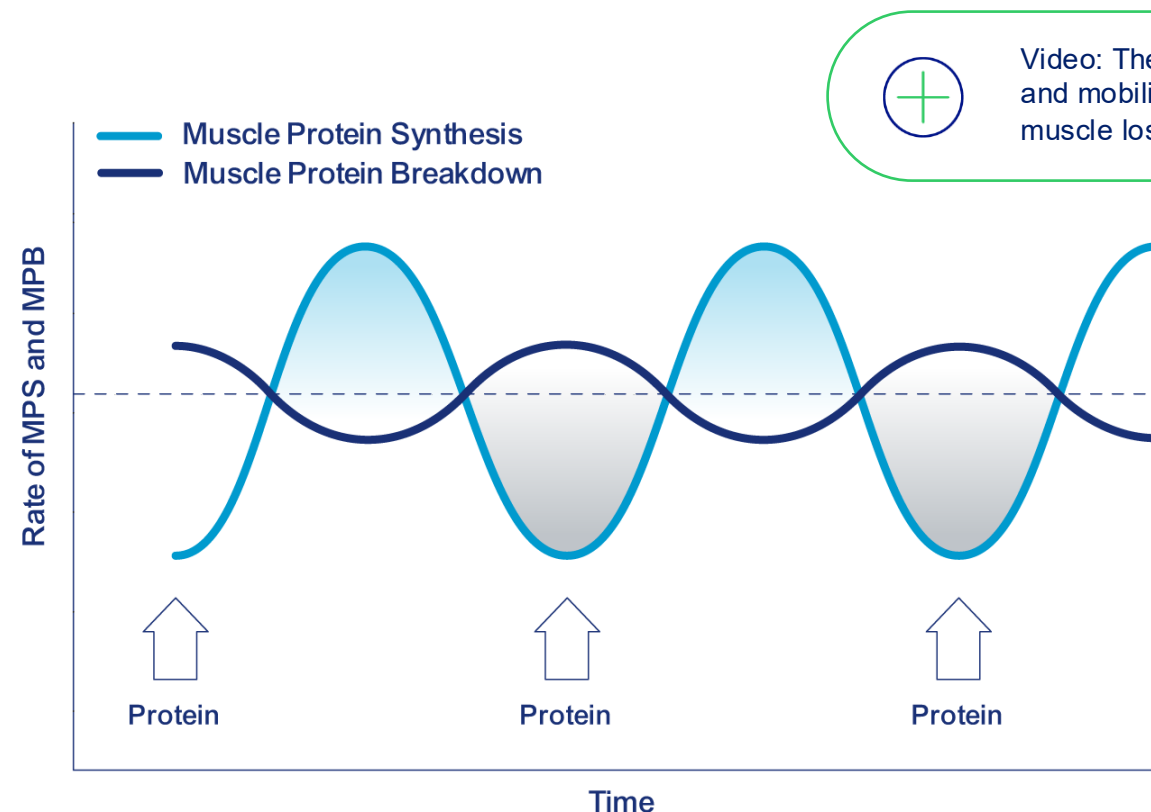
DECLINE OF PROTEIN SYNTHESIS AND ABSORPTION WITH AGE

Anabolic resistance - Muscle gets harder to build with age

- **Anabolic resistance:** Age-related decline in muscle responsiveness to normally robustly anabolic stimuli including protein intake and resistance exercise.¹
- Long periods of muscle disuse (bed rest, immobilization, or pronounced inactivity) also contribute to anabolic resistance.¹
- Older adults experience less muscle protein synthesis and growth from the same amount of protein or exercise compared to younger individuals.²



[Click here for summary](#)



Schematic representation of muscle protein metabolism in response to anabolic stimuli in young and elderly people.² The graph shows the fluctuation in muscle protein synthesis (MPS) and breakdown (MPB) after a “push” to build muscle, like eating protein (arrows). In older adults (thicker black line) the response is blunted.

1. McKendry J, et al. Resistance Exercise, Aging, Disuse, and Muscle Protein Metabolism. Compr Physiol. 2021 Jun 30;11(3):2249-2278.

2. Breen L et al. Skeletal muscle protein metabolism in the elderly: Interventions to counteract the “anabolic resistance” of ageing. Nutr Metab (Lond). 2011;8(1):68.

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Click here for summary

In practice, it implies that, to get the same anabolic effect, older adults need:



More protein per meal¹



Better protein quality – emphasizing the role of leucine²



More targeted resistance training³

1. Moore DR, et al. Protein ingestion to stimulate myofibrillar protein synthesis requires greater relative protein intakes in healthy older versus younger men. *J Gerontol A Biol Sci Med Sci.* 2015;70(1):57–62.
2. Rieu I, et al. Leucine supplementation improves muscle protein synthesis in elderly men independently of hyperaminoacidaemia. *J Physiol.* 2006;575(Pt 1):305–315.
3. McLeod JC, et al. Resistance exercise training as a primary countermeasure to age-related chronic disease. *Front Physiol.* 2019;10:645.



critical role of protein in prevention of aging and illness

Schematic representation of muscle protein metabolism in response to anabolic stimuli in young and elderly people.² The graph shows the fluctuation in muscle protein synthesis (MPS) and breakdown (MPB) after a “push” to build muscle, like eating protein (arrows). In older adults (thicker black line) the response is blunted.

DECLINE OF PROTEIN SYNTHESIS AND ABSORPTION WITH AGE

Factors contributing to anabolic resistance

Protein intake promotes hyperaminoacidemia, which stimulates muscle protein synthesis

Aging introduces factors that impair this process:^{1,2}

- Impaired synthesis¹
- Insulin resistance¹
- Reduced amino acid absorption²
- Increased splanchnic amino acid sequestration²

Reduced
postprandial
amino acid
availability

These impairments contribute to anabolic resistance and muscle mass loss in elderly individuals.²



Click for more information on
Splanchnic aa sequestration

ANABOLIC RESISTANCE



Inactivity or
reduced activity



Low protein
intake



Reduced
absorption



Reduced uptake
in the muscle



Inflammation



Splanchnic
extraction



Vascular
dysfunction



Altered anabolic
pathways

Schematic representation of the factors that contribute to the development of anabolic resistance of protein synthesis with aging. Figure based on concepts described in³

1. Guillet C, et al. Insulin resistance: a contributing factor to age-related muscle mass loss? Diabetes Metab. 2005;31 Spec No 2:S20–S26.
2. Burd NA, et al. Anabolic resistance of muscle protein synthesis with aging. Exerc Sport Sci Rev. 2013 Jul;41(3):169-73.
3. McKendry J, et al. Resistance Exercise, Aging, Disuse, and Muscle Protein Metabolism. Compr Physiol. 2021 Jun 30;11(3):2249-2278.

DECLINE OF PROTEIN SYNTHESIS AND ABSORPTION WITH AGE

Splanchnic sequestration of protein in older individuals

The **splanchnic tissues** (internal organs - intestine, stomach, liver, spleen and pancreas) ¹ absorb dietary amino acids (AA) and distribute them to the body.²

IN OLDER ADULTS



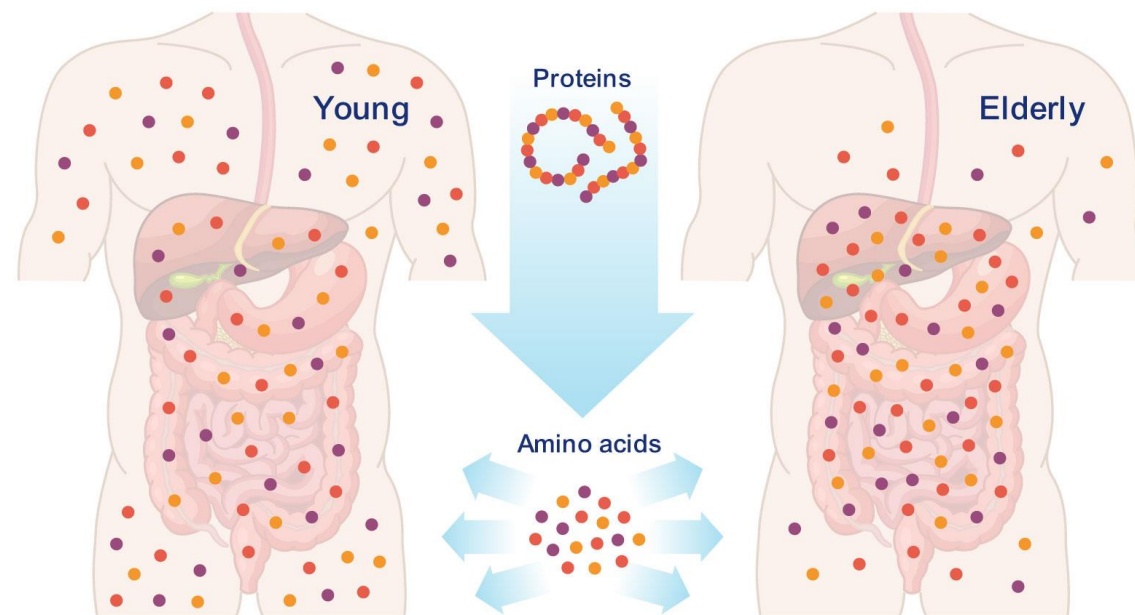
Splanchnic tissues extract more amino acids, (e.g., phenylalanine, leucine)^{2,3}



Reduced amino acid availability for peripheral tissues like muscle



Diminished muscle anabolic response



1. Bruins MJ, et al. Amino Acids, Protein, and the Gastrointestinal Tract. In The Molecular Nutrition of Amino Acids and Protein. Academic Press. 2016;pp. 161-179.
 2. Volpi E, et al. Oral amino acids stimulate muscle protein anabolism in the elderly despite higher first-pass splanchnic extraction. Am J Physiol. 1999 Sep;277(3):E513-20.
 3. Boirie Y, et al. Splanchnic and whole-body leucine kinetics in young and elderly men. Am J Clin Nutr. 1997 Feb;65(2):489-95.

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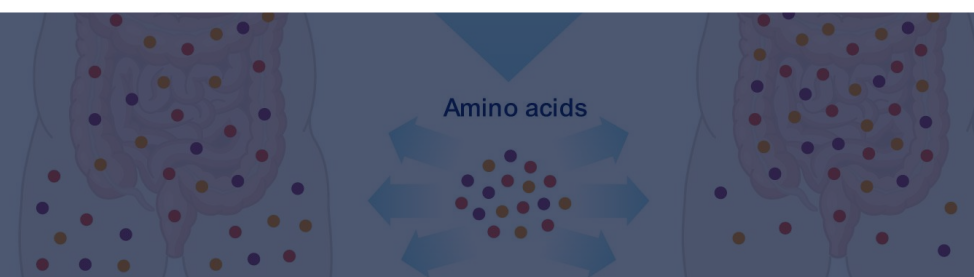


Diminished muscle anabolic response

Older men had significantly greater splanchnic extraction of amino acids, especially branched-chain amino acids (BCAAs) compared to younger men after a protein meal.

Despite similar total leucine absorption, more is retained in the liver and gut in the older group.^{1,2}

1. Volpi E, et al. Oral amino acids stimulate muscle protein anabolism in the elderly despite higher first-pass splanchnic extraction. *Am J Physiol.* 1999 Sep;277(3):E513-20.
2. Boirie Y, et al. Splanchnic and whole-body leucine kinetics in young and elderly men. *Am J Clin Nutr.* 1997 Feb;65(2):489-95.



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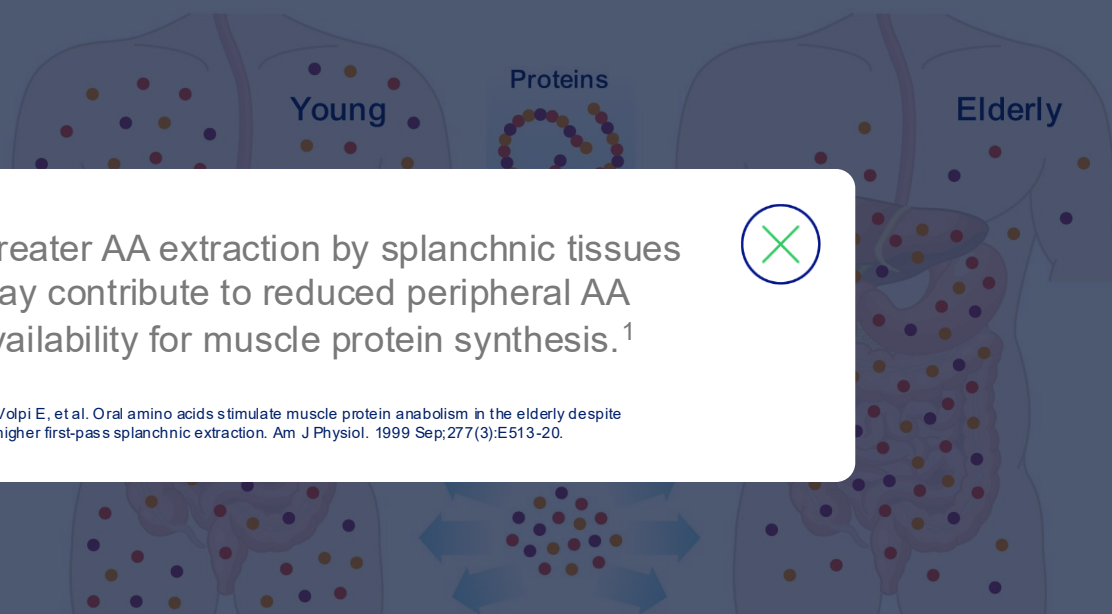
Reduced amino acid availability for peripheral tissues like muscle



Diminished muscle anabolic response

Greater AA extraction by splanchnic tissues may contribute to reduced peripheral AA availability for muscle protein synthesis.¹

1. Volpi E, et al. Oral amino acids stimulate muscle protein anabolism in the elderly despite higher first-pass splanchnic extraction. *Am J Physiol.* 1999 Sep;277(3):E513-20.



1. Bruins MJ, et al. Amino Acids, Protein, and the Gastrointestinal Tract. In *The Molecular Nutrition of Amino Acids and Protein*. Academic Press. 2016;pp. 161-179.
 2. Volpi E, et al. Oral amino acids stimulate muscle protein anabolism in the elderly despite higher first-pass splanchnic extraction. *Am J Physiol.* 1999 Sep;277(3):E513-20.
 3. Boirie Y, et al. Splanchnic and whole-body leucine kinetics in young and elderly men. *Am J Clin Nutr.* 1997 Feb;65(2):489-95.

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IN OLDER ADULTS



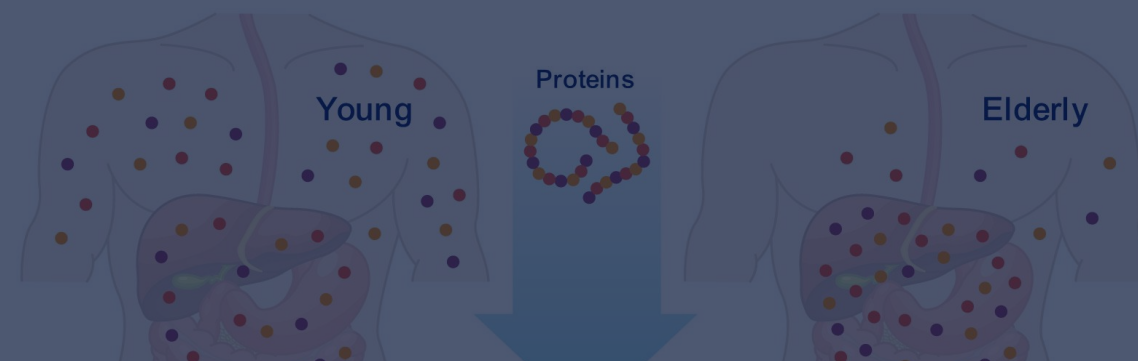
Splanchnic tissues extract more amino acids, (e.g., phenylalanine, leucine)^{2,3}



Reduced amino acid availability for peripheral tissues like muscle



Diminished muscle anabolic response



Despite reduced peripheral AA availability, sufficient EAA intake could still stimulate muscle protein synthesis, albeit to a lesser extent than in younger individuals.¹



1. Volpi E, et al. Oral amino acids stimulate muscle protein anabolism in the elderly despite higher first-pass splanchnic extraction. Am J Physiol. 1999 Sep;277(3):E513-20.

1. Bruins MJ, et al. Amino Acids, Protein, and the Gastrointestinal Tract. In The Molecular Nutrition of Amino Acids and Protein. Academic Press. 2016;pp. 161-179.
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DECLINE OF PROTEIN SYNTHESIS AND ABSORPTION WITH AGE

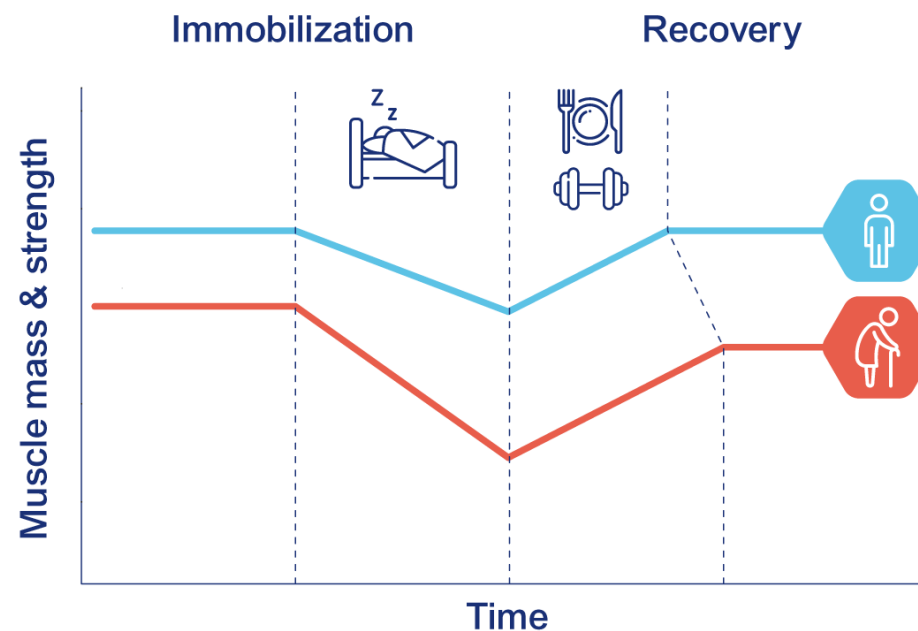
Impact of muscle disuse (1/2)

Inactivity in older adults triggers the onset of muscle wasting.

Inactivity can cause rapid muscle loss:¹

- Bed rest (10–42 days) leads to 0.5–0.6% muscle loss per day.¹
- Strength loss during inactivity ranges from mild (0.3%) to severe (4.2%).¹

Even brief periods of immobilization (<10 days) can cause the quadriceps to shrink by about 1.5%.¹



	Young	Old
Baseline lean muscle mass	↑	↓
Loss during inactivity	↓	↑
Recovery	↑	↓

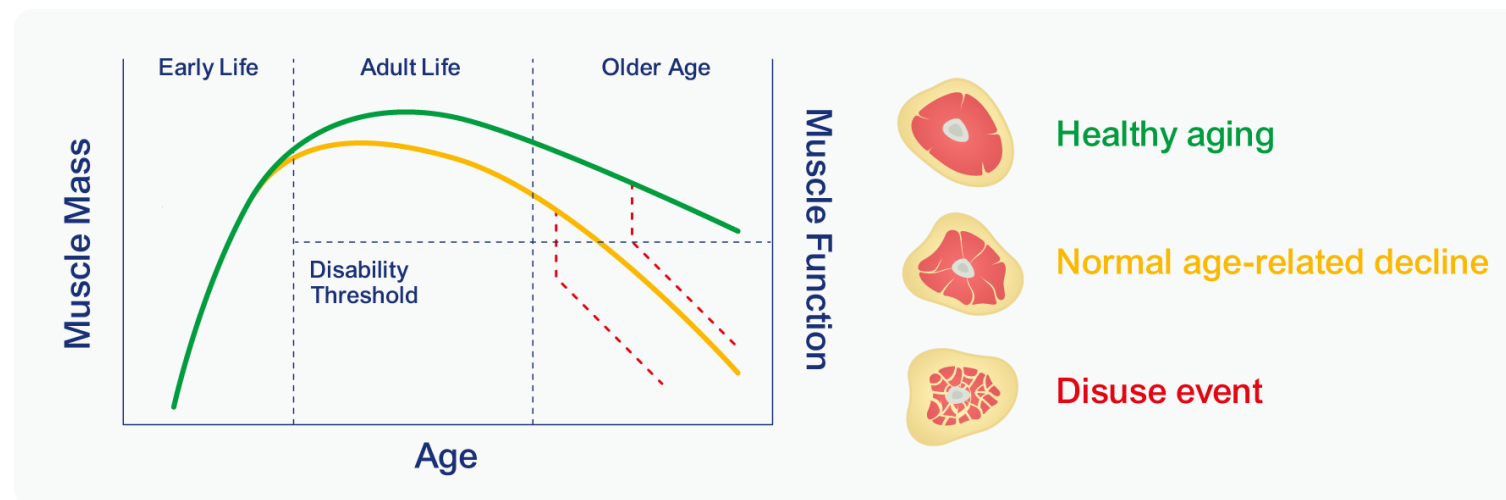
Impact of immobilization on muscle mass and strength in young and older adults.
Figure based on concepts described in^{2,3}

1. Kortebein P, et al. Functional impact of 10 days of bed rest in healthy older adults. J Gerontol A Biol Sci Med Sci. 2008 Oct;63(10):1076-81.
2. Bowden Davies KA, et al. Reduced physical activity in young and older adults: metabolic and musculoskeletal implications. Ther Adv Endocrinol Metab. 2019 Nov 19;10:2042018819888824.
3. Rejc E, et al. Loss of maximal explosive power of lower limbs after 2 weeks of disuse and incomplete recovery after retraining in older adults. J Physiol. 2018 Feb 15;596(4):647-665.

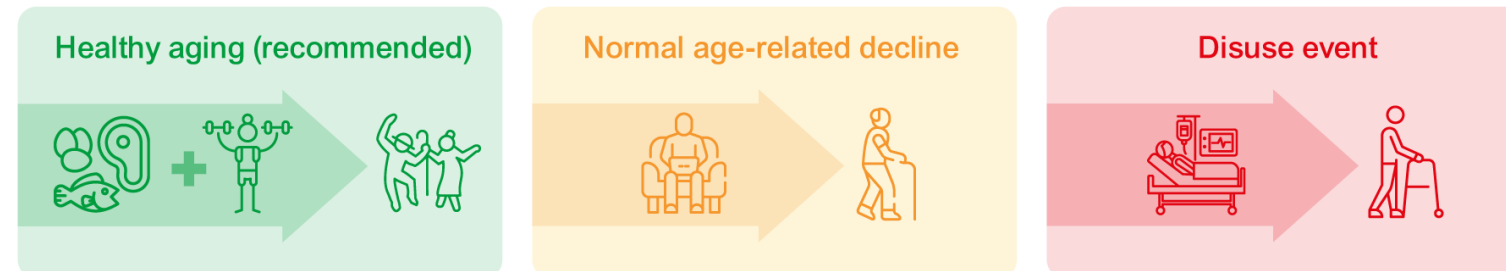
DECLINE OF PROTEIN SYNTHESIS AND ABSORPTION WITH AGE

Impact of muscle disuse (2/2)

- Disuse from immobilization or bed rest leads to rapid and significant declines in MPS, often within days.¹⁻³
- This suppressed basal MPS and anabolic resistance to feeding are key drivers of muscle atrophy in both young and older adults.¹⁻³



Contributing factors to muscle atrophy in older adults. Figure based on concepts. Figure based on concepts described in 4.



1. Glover EI, et al. Immobilization induces anabolic resistance in human myofibrillar protein synthesis with low and high dose amino acid infusion. J Phys. 2008 Dec 15;586(24):6049-61.
2. Kortebein P, et al. Effect of 10 days of bed rest on skeletal muscle in healthy older adults. JAMA. 2007 Apr 25;297(16):1772-4.
3. Wall BT, et al. Short-term muscle disuse lowers myofibrillar protein synthesis rates and induces anabolic resistance to protein ingestion in healthy young men. Am J Physiol Endocrinol Metab 2016 Jan 15;310(2):E137-47.
4. Coletta G, et al. An elusive consensus definition of sarcopenia impedes research and clinical treatment: A narrative review. Ageing Res Rev. 2023 Apr;86:101883.

DECLINE OF PROTEIN SYNTHESIS AND ABSORPTION WITH AGE

Factors impacting on sarcopenia



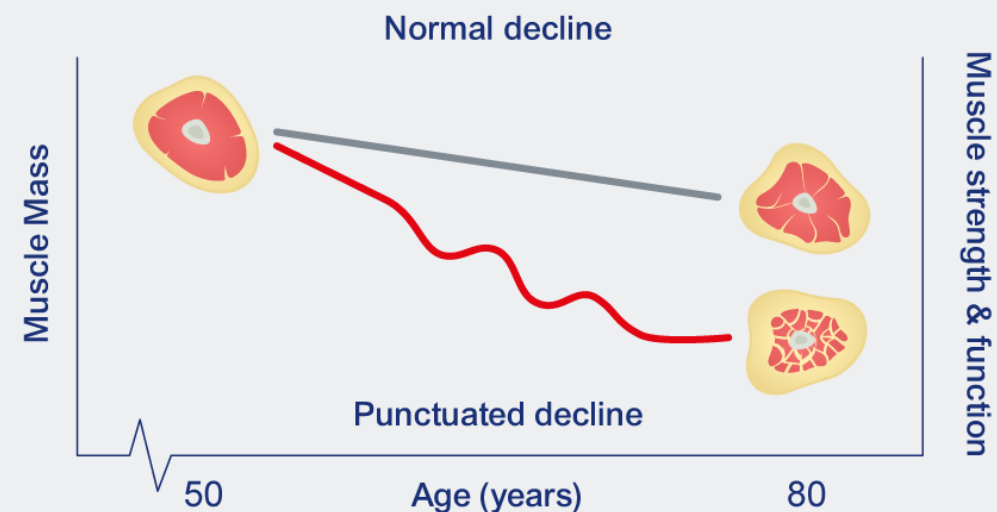
Factors affecting normal muscle decline

- Satellite cell dysfunction
- Anabolic resistance
- Decreased protein synthesis
- Decreased anabolic hormones
- Mitochondrial dysfunction
- Impaired regenerative capacity
- Impaired vascular response

Factors accelerating a punctuated decline

- Insufficient energy
- Illness
- Habitual PA decline
- Insuline resistance
- Protein malnutrition
- Hospitalization
- Increased inflammation

Muscle loss



Summary

- ✓ Skeletal muscle is **highly plastic**, comprising ~40% of body mass.
- ✓ Muscle mass is maintained by balance of synthesis & breakdown; aging disrupts this balance.
- ✓ Resistance exercise stimulates muscle growth, but **aging leads to anabolic resistance**.
- ✓ Older adults more sequestration by splanchnic tissues.
- ✓ Same protein intake & exercise yield less stimulation of MPS and muscle growth in older adults.
- ✓ Periods of **inactivity cause rapid muscle loss**, especially within the first week due to a decline in MPS.





IMPACT OF INFLAMMATION ON MUSCLES

[3.1. “Inflammaging”](#)

[3.2. Impact of inflammation on muscle breakdown](#)

[3.3. Inflammation affects physical performance](#)

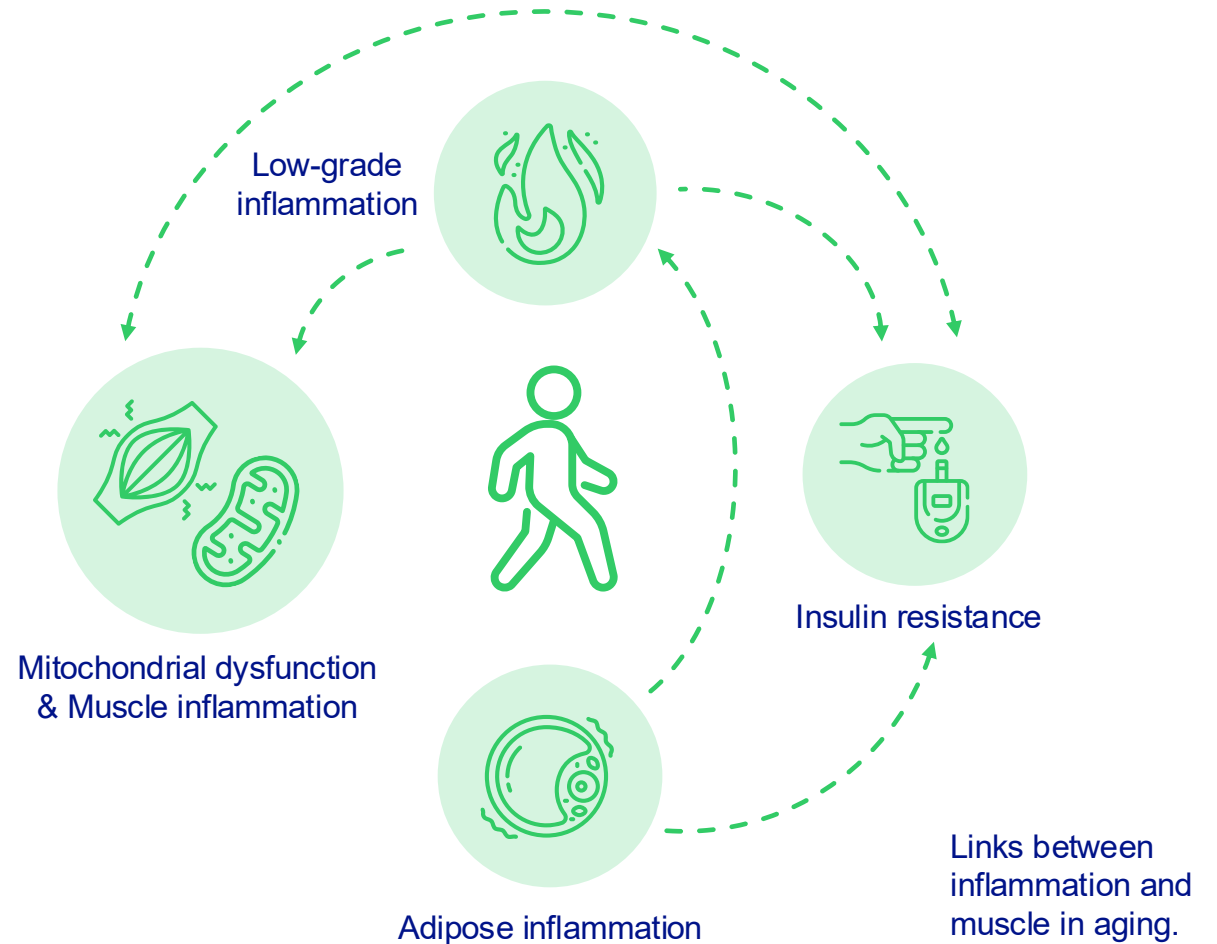
[3.4. Summary](#)



IMPACT OF INFLAMMATION ON MUSCLES

“Inflammaging”

- Precise balance between inflammation and regeneration is essential for effective muscle repair and renewal.¹
- Aging is associated with increased systemic and local muscle inflammation that accelerates age-related muscle loss.¹
- Key factors contributing to systemic inflammation in aging:¹
 - Mitochondrial dysfunction
 - Chronic activation of immune pathways
 - Adipose tissue inflammation and gut dysbiosis
 - Impaired autophagy



IMPACT OF INFLAMMATION ON MUSCLES

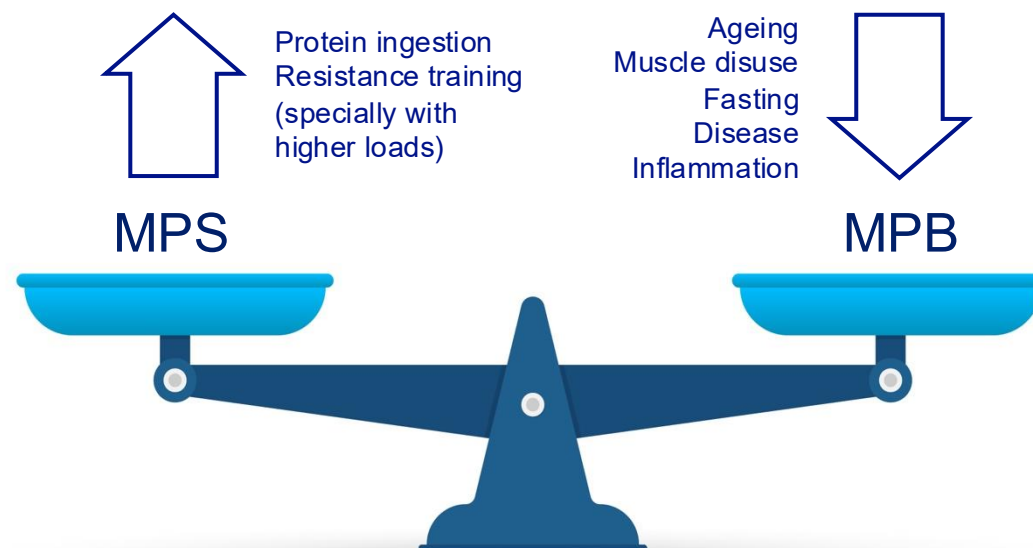
Impact of inflammation on muscle breakdown

Increased proinflammatory cytokines cause body-wide inflammation, which:¹

- Lowers the building of new proteins.
- Increases their breakdown.
- Ultimately leading to muscle shrinking.

Rising inflammation accelerates muscle breakdown and energy demands which:²

- Triggers amino acid release to support gluconeogenesis.
- Fuels acute-phase protein production.



Muscle mass balance

Influence of aging and illness on muscle loss¹



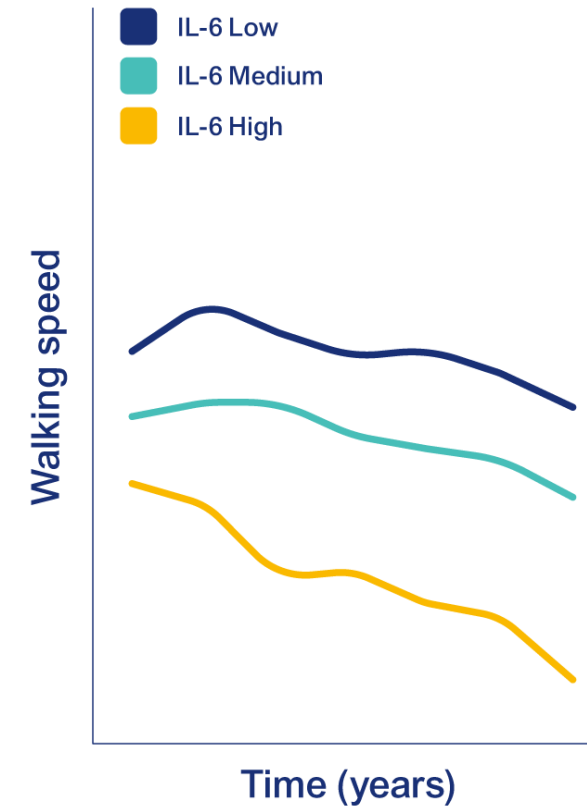
1. Costamagna D, et al. Role of Inflammation in Muscle Homeostasis and Myogenesis. Mediators Inflamm. 2015;2015:805172.
2. Wolfe RR. The underappreciated role of muscle in health and disease. Am J Clin Nutr. 2006 Sep;84(3):475-82.

IMPACT OF INFLAMMATION ON MUSCLES

Inflammation affects physical performance

Higher blood levels of inflammatory markers (e.g., IL-6, TNF- α or IL-1RA) are linked to:

- Greater declines in muscle mass and strength.¹
- Faster deterioration of mobility.²
- Reduced lower-limb function and physical activity.³



Change over the walking speed according to IL-6 levels.
Figure based on concepts described in 1.

1. Ferrucci L, et al. Change in muscle strength explains accelerated decline of physical function in older women with high interleukin-6 serum levels. J Am Geriatr Soc. 2002 Dec;50(12):1947-54.
2. Visser M, et al. Relationship of interleukin-6 and tumor necrosis factor-alpha with muscle mass and muscle strength in elderly men and women: the Health ABC Study. J Gerontol A Biol Sci Med Sci. 2002 May;57(5):M326-32.
3. Cesari M, et al. Inflammatory markers and physical performance in older persons: the InCHIANTI study. J Gerontol A Biol Sci Med Sci. 2004 Mar;59(3):242-8.

Summary

- ✓ **Inflammaging** is a chronic low-grade, non-pathogen-related/'sterile', inflammation associated with aging.
- ✓ Low-grade systemic inflammation in aging is driven by factors such as mitochondrial dysfunction, chronic immune activation, adipose tissue inflammation, gut dysbiosis, and impaired autophagy.
- ✓ Inflammaging **disrupts the balance between muscle regeneration and degradation**, contributing to conditions like sarcopenia, frailty, and insulin resistance.
- ✓ **Increased proinflammatory cytokines** impair muscle health by reducing protein synthesis, increasing protein breakdown, and promoting muscle wasting.
- ✓ **Higher levels of inflammatory markers** are associated with reduced muscle strength, mobility decline, and lower-limb physical function, impacting overall physical performance in older adults.





THE VICIOUS CYCLE BETWEEN MUSCLE LOSS AND DISEASE PROGRESSION

- [4.1. Impact of muscle loss on muscle strength](#)
 - [4.2. Impact of muscle loss on movement and physical function](#)
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Impact of muscle loss on muscle strength (1/2)

- Older adults' muscles weaken due to loss of muscle mass (MM)^{1,2} and reduced neural drive.³

Sex	Median rate of MM loss per year ⁴	Annual MM loss at age 75 ⁴	Annual strength loss at age 75 ⁴
♂	0.47%	0.80-0.98%	3-4%
♀	0.37%	0.64-0.70%	2.5-3%

- Ethnicity affects muscle mass loss mainly by influencing baseline muscle mass and rate of decline.²

1. Stoevers K, et al. Sarcopenia and Predictors of Skeletal Muscle Mass in Elderly Men With and Without Obesity. Gerontology and Geriatric Medicine. 2017;3.

2. Silva AM, et al. Ethnicity-related skeletal muscle differences across the lifespan. Am J Hum Biol. 2010 Jan-Feb;22(1):76-82.

3. Piasecki M, et al. Age-dependent motor unit remodelling in human limb muscles. Biogerontology. 2016 Jun;17(3):485-96Cruz-Jentoft A, et al. Sarcopenia: revised European consensus on definition and diagnosis. Age Ageing. 2019 Jan 1;48(1):16-31. Erratum in: Age Ageing. 2019 Jul 1;48(4):601.

4. Mitchell WK, et al. Sarcopenia, dynapenia, and the impact of advancing age on human skeletal muscle size and strength; a quantitative review. Front Physiol. 2012 Jul 11;3:260.

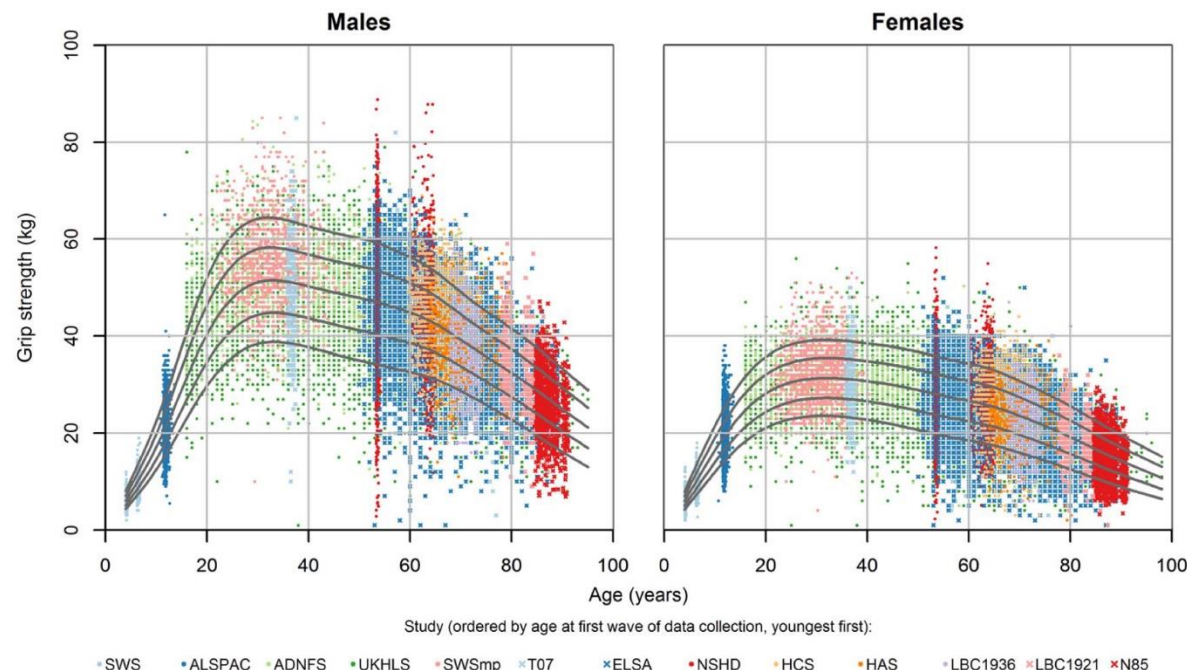


Impact of muscle loss on muscle strength (2/2)

- Muscle strength rises in youth, stabilizes in midlife, and declines progressively with age.¹
- Peak muscle strength occurs at ~40; after 30, muscle mass drops 0.8% yearly, strength declines 1.5–3% yearly.²⁻⁴



Why is hand grip testing so useful?



Normative data for grip strength across the life course in men and women in the UK. Centiles shown are 10th, 25th, 50th, 75th and 90th. Color-coding represents different birth cohorts used for the study.⁴

1. Cruz-Jentoft A. et al. Sarcopenia: revised European consensus on definition and diagnosis. Age Ageing. 2019 Jan 1;48(1):16-31. Erratum in: Age Ageing. 2019 Jul 1;48(4):601.
2. Keller K, et al. Strength and muscle mass loss with aging process. Age and strength loss. Muscles Ligaments Tendons J. 2014 Feb 24;3(4):346-50.
3. Mitchell WK, et al. Sarcopenia, dynapenia, and the impact of advancing age on human skeletal muscle size and strength; a quantitative review. Front Physiol. 2012 Jul 11;3:260.
4. Dodds RM, et al. Grip strength across the life course: normative data from twelve British studies. PLoS One. 2014 Dec 4;9(12):e113637.

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Why is hand grip testing so useful?

Why is hand grip strength (HGS) test important in the measurement of muscle strength?

- Reflects muscle function. HGS reflects muscle mass and strength, serving as a reliable upper body measure. It does not reflect lower limb muscle function.¹
- Practical and non-invasive. HGS is simple, quick, and requires no specialized equipment.²
- Strongly associated with mortality. Low HGS is associated higher mortality, disease, disability, and hospitalization, outperforming traditional measures like blood pressure.²
- Sensitive to sarcopenia and frailty. HGS identifies age-related muscle loss and weakness, sarcopenia, osteoporosis risk, and functional decline.²
- Applicable across Populations. HGS is versatile, useful across ages, populations, ethnicities, and socioeconomic groups.²
- Age-related norms and cutoffs are available.^{3,4}

1. Harris-Love MO, et al. The Influence of Upper and Lower Extremity Strength on Performance-Based Sarcopenia Assessment Tests. J Funct Morphol Kinesiol. 2018 Dec;3(4):53.

2. Vaishya R, et al. Hand grip strength as a proposed new vital sign of health: a narrative review of evidences. J Health Popul Nutr. 2024 Jan 9;43(1):7.

3. Chen LK, et al. Sarcopenia in Asia: consensus report of the Asian Working Group for Sarcopenia. J Am Med Dir Assoc. 2014 Feb;15(2):95-101.

4. Chiles Shaffer N, et al. Agreement and Predictive Validity Using Less-Conservative Foundation for the National Institutes of Health Sarcopenia Project Weakness Cutpoints. J Am Geriatr Soc. 2017 Mar;65(3):574-579.

Impact of muscle loss on movement and physical function

- Older adults with reduced muscle mass face a higher risk of experiencing a decline in physical function (gait speed, short physical performance battery, mobility limitations, Barthel Index) over time.¹
- Walking speed (WS) is significantly associated with cardiovascular risk factors and occurrence of cardiovascular events.²
- Higher WS correlates with lower risk of all-cause mortality.³



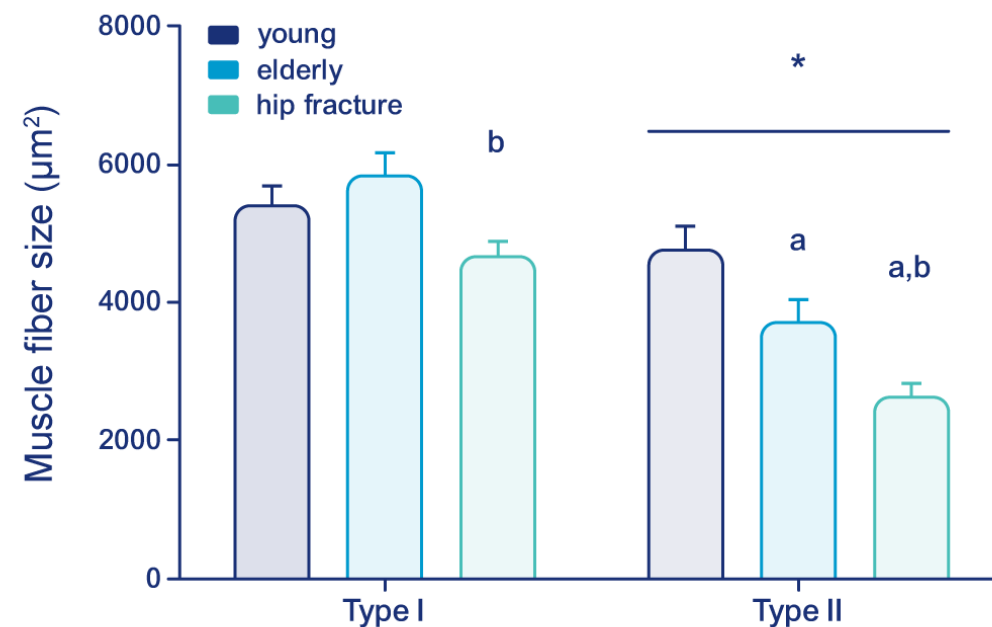
Muscle loss increases the risk of falls

Sarcopenia is strongly linked to more falls and injuries in older adults.¹

Key factor: loss of fast contracting type II muscle fibers.²

Atrophy and loss of type II fibers with age leads to:²

- Poorer balance
- Less ability to react to a loss of balance; requires rapid adjustments
- Higher risk of falls and injuries like hip fractures



Type I and type II muscle fibers size distribution in young, elderly and hip fracture women group. Figure based on concepts described in 2.

Sarcopenia

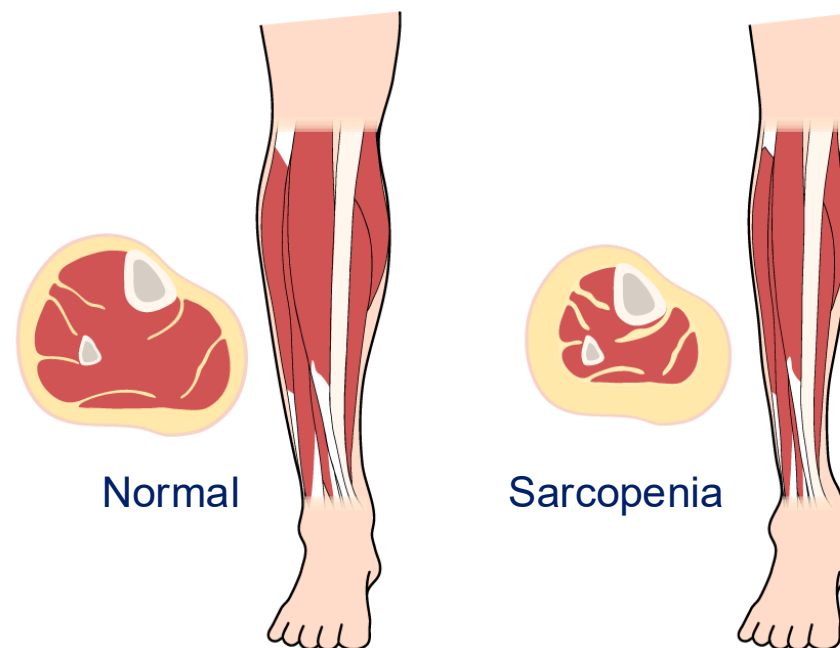
As a pathological progression of muscle loss, sarcopenia is characterized by a generalized and progressive decline in skeletal muscle mass and strength.¹⁻²

Affects 11–20% of healthy older (>60 years) Europeans, with rates rising.³

Sarcopenia develops gradually and is driven by a wide variety range of contributing factors.²



Click for contributing factors in sarcopenia development



Representation of a muscle and muscle section in normal or in sarcopenic conditions



Sarcopenia

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Sarcopenia develops gradually and is driven by a wide variety range of contributing factors.²



Click for contributing factors in sarcopenia development

Contributing factors to sarcopenia



Genetic factors



Insulin resistance



Chronic inflammation



Chronic diseases



Anabolic resistance



Disuse event



Physical inactivity / sedentary behaviour



Unintentional weight loss



Malnutrition

Risks associated with sarcopenia

Sarcopenia increases the risk of:^{1,2}



Physical disability



Falls



Functional decline



Frailty



Death

Affects 11–20% of healthy older (>60 years) Europeans, with rates rising.³



1. Cruz-Jentoft AJ et al. Sarcopenia: revised European consensus on definition and diagnosis. Age Ageing. 2019;48(1):16–31

2. Cruz-Jentoft AJ et al. Sarcopenia. Lancet. 2019;393(10191):2636–46.

3. Ethgen O, et al. The Future Prevalence of Sarcopenia in Europe: A Claim for Public Health Action. Calcif Tissue Int. 2017 Mar;100(3):229–234.

Sarcopenic obesity

Sarcopenic obesity is characterized by:¹

- Excessive fat accumulation
- Loss of skeletal muscle mass and function

Main contributors:¹

- Age
- Sedentary lifestyle
- Poor diet
- Inflammation
- Oxidative stress
- Hormonal changes
- Insulin resistance.

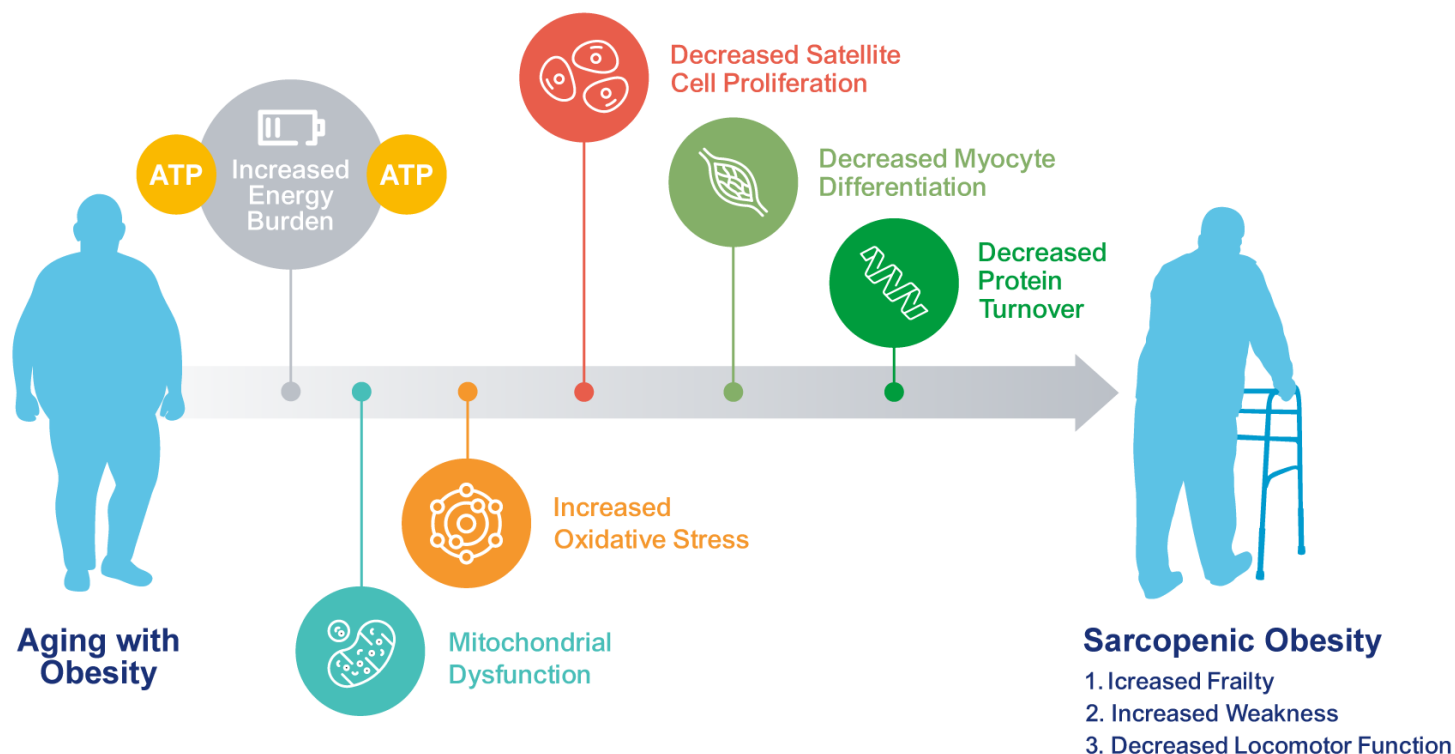


Vicious cycle connecting obesity and muscle wasting.²



Mechanisms of sarcopenic obesity

Mechanism of sarcopenic obesity¹



1. Axelrod CL, et al. Sarcopenic obesity: emerging mechanisms and therapeutic potential. Metabolism. 2023 Sep;146:155639.

2. Wei S, et al. Sarcopenic obesity: epidemiology, pathophysiology, cardiovascular disease, mortality, and management. Front Endocrinol (Lausanne). 2023 Jun 30;14:1185221.

The consequences of muscle loss and sarcopenia

- Loss of muscle mass and strength is key in the decline of physical abilities especially as people get older.^{1,2}
- Muscle loss greatly increases the risk of:¹
 - Physical disability
 - Falls and infections
- Reduced activity due to disease speeds up muscle loss.²
- This creates a **vicious cycle** that leads to higher chances of serious illness and death in older adults.²

Consequences of muscle loss and sarcopenia¹⁻⁶



Shorter survival



Falls and fractures



Wound healing issues



Disease progression/
treatment toxicity (cancer)



Physical impairment
disability



Greater length of
hospital stay



Poor quality of life



Postoperative complications



Need for rehabilitation

1. Cruz-Jentoft AJ, et al Sarcopenia: revised European consensus on definition and diagnosis. Age Ageing. 2019 Jul 1;48(4):601.
2. Janssen TAH, et al From molecular to physical function: The aging trajectory. Curr Res Physiol. 2024 Dec 16;8:100138.
3. Demling RH. Nutrition, anabolism, and the wound healing process: an overview. Eplasty. 2009;9:e9.
4. Prado CM, et al. Sarcopenia as a determinant of chemotherapy toxicity and time to tumor progression in metastatic breast cancer patients receiving capecitabine treatment. Clin Cancer Res. 2009 Apr 15;15(8):2920-6.
5. Friedman J, et al. Implications of sarcopenia in major surgery. Nutr Clin Pract. 2015 Apr;30(2):175-9.
6. Liefers JR, et al. Sarcopenia is associated with postoperative infection and delayed recovery from colorectal cancer resection surgery. Br J Cancer. 2012 Sep 4;107(6):931-6.

Summary

- ✓ Muscle strength peaks at ~40, and muscle mass perhaps earlier (~30) then **declines** impacting mobility and daily activities.
- ✓ Aging reduces walking speed and makes **standing up** more difficult, especially from age 70 onward.
- ✓ Loss of fast-twitch (type II) fibers weakens balance and reflexes, raising the risk of falls and fractures.
- ✓ Sarcopenia is a **progressive loss of muscle** mass and strength, typically beginning after age 30, but manifesting in measurable functional declines at around age 50
- ✓ In **sarcopenic obesity**, muscle loss is worsened by **fat accumulation**, leading to inflammation, insulin resistance, and higher disease risk.
- ✓ Muscle loss is **foundational in a downward spiral**—reduced activity, immune dysfunction, infections, and frailty—leading to greater disability and mortality.





CONCLUSIONS

- ✓ Skeletal muscle accounts for ~40% of body mass and stores over half of total body protein.
- ✓ **Skeletal muscle** not only supports movement but also stores amino acids, is the largest site of blood sugar regulation, is a large contributor to resting metabolic rate, supports immune response, and **aids recovery from illness**.
- ✓ Muscle mass depends on a **balance between synthesis and breakdown**, disrupted by aging.
- ✓ Loss of muscle mass impacts on **muscle strength**, **loss of movement** and increased **risk of falls**.
- ✓ **Sarcopenia** and **sarcopenic obesity** accelerate physical decline and metabolic dysfunction, increasing the risk of disease, frailty, and early death in older adults
- ✓ Loss of muscle mass and function is a major driver of frailty, falls, disability, and poor recovery creating a **vicious cycle** where these issues further accelerate muscle loss, ultimately increasing morbidity and mortality.
- ✓ Resistance exercise and protein intake promote growth but **aging and inactivity lead to anabolic resistance** which subsequently results in muscle loss, and reduced muscle strength.



This training material has been reviewed for scientific accuracy and relevance by Stuart Phillips – McMaster Experts. It is intended for educational purposes only and does not replace clinical judgment or institutional guidelines.



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- **Director** of the physical activity center of excellence (**PACE**) and the Mc Master center for nutrition, exercise and health research
- Leads the exercise metabolism research group.
- His academic work primarily investigates how **nutrition** and **physical activity** influence skeletal muscle in humans.

