Regulación neuroendócrina y Sarcopenia

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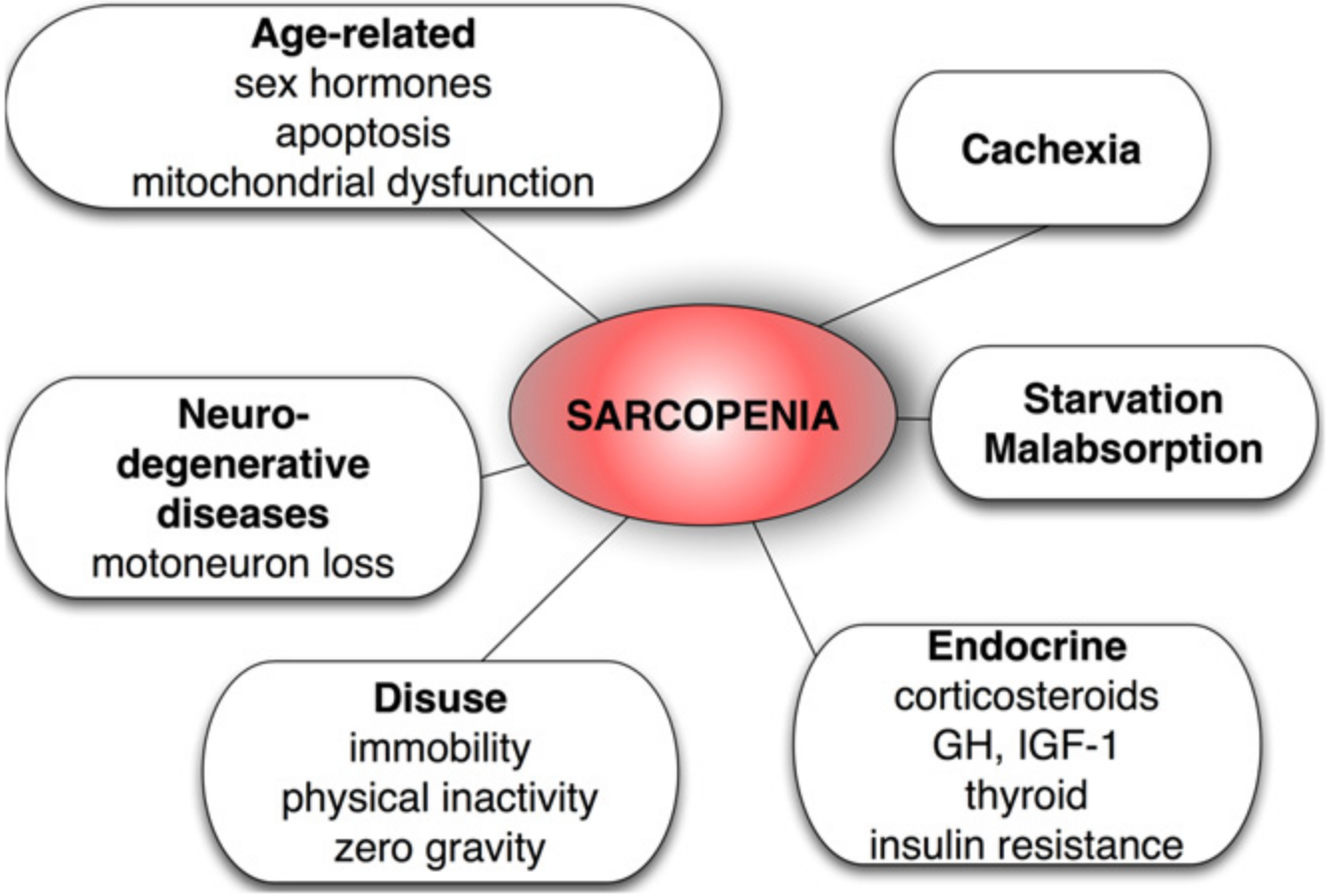
Regulación neuroendócrina y Sarcopenia

- Edad disminuyen una serie de hormonas
- Esta disminucion esta directamente relacionada con las alteraciones que se observan en diversos procesos fisiologicos

- La eclosión de la sarcopenia: Informe preliminar del Observatorio de la Sarcopenia de la Sociedad Española de Geriatría y Gerontología. Rev Esp Geriatr Gerontol. 2011;46:100-10. - vol.46 num 02



Conditions potentially leading to sarcopenia. Muscaritoli M, et al., Consensus definition of sarcopenia, cachexia and pre-cachexia: Joint document aborated. Clinical Nutrition (2010), doi:10.1016/j.clnu.2009.12.004

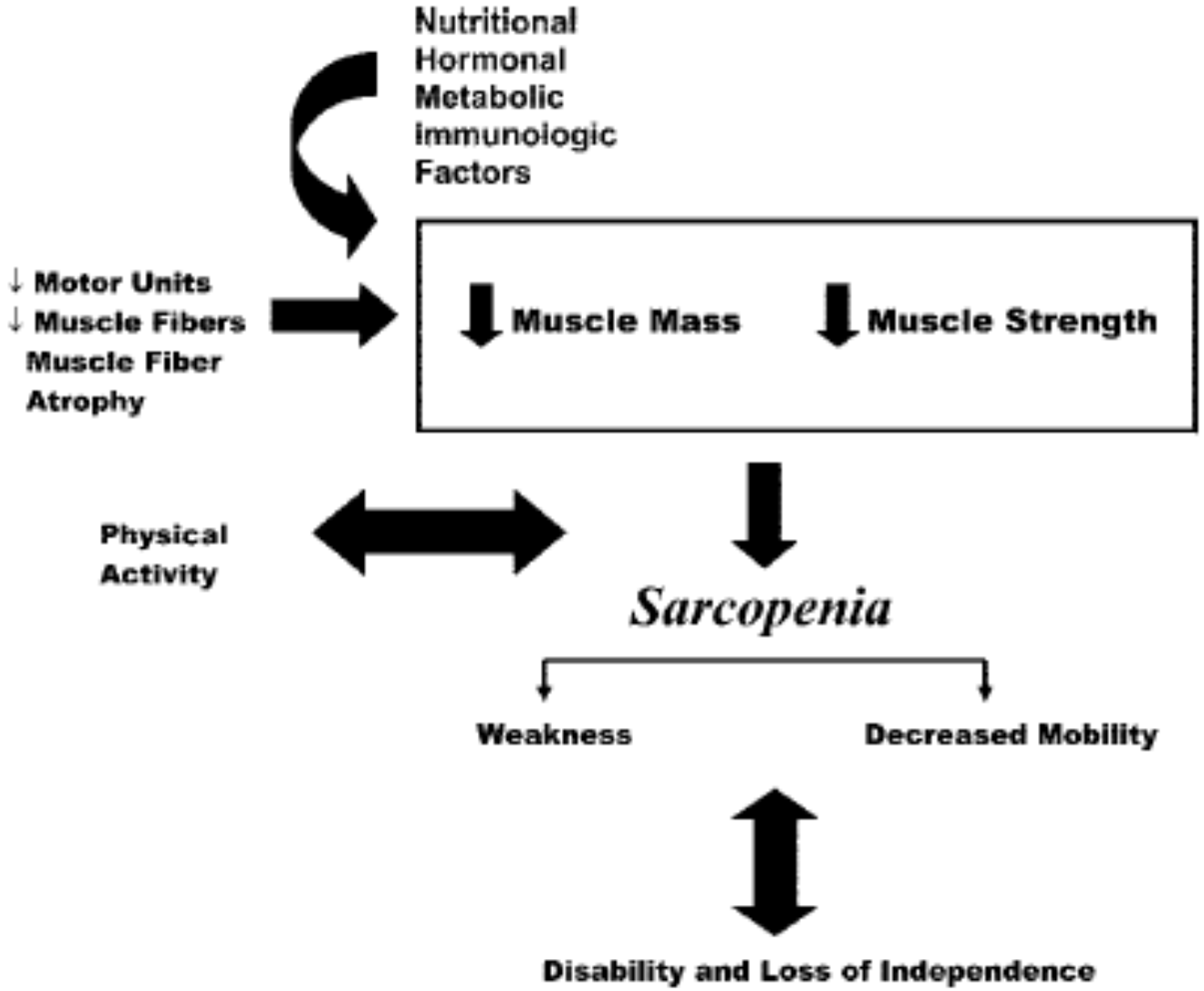


Fig. 1. Factors contributing to sarcopenia. This figure summarizes the influence of multiple factors that lead to age-associated declines in muscle mass and strength and the subsequent impact on disability and loss of independence.

J Appl Physiol 95:1717-1727, 2003.

Table 1 Risk factors of sarcopenia

Factors	Ageing process	Chronic health conditions
Constitutional		
Female sex	Increased muscle turnover	Cognitive impairment
Low birth weight	↑ Catabolic stimuli	Mood disturbances
Genetic susceptibility	↑ Protein degradation	Diabetes mellitus
	Low-grade inflammation	Heart failure
Lifestyle	↓ Anabolic stimuli	Liver failure
Malnutrition	↓ Protein synthesis	Renal failure
Low protein intake		Respiratory failure
Alcohol abuse	Reduced number of muscle cells	Osteoarthritis
Smoking	↑ Myostatin (↓ recruitment)	Chronic pain
Physical inactivity	↑ Apoptosis	
		Obesity
Living conditions	Hormonal deregulation	
Starvation	↓ Testosterone, DHEA production	Catabolic effects of drugs
Bed rest, immobility, deconditioning	↓ Oestrogen production	
Weightlessness	↓ 1–25 (OH)2 vitamin D	
	↑ Thyroid function	
	↓ Growth hormone, IGF-1	
	↑ Insulin resistance	
	Changes in neuromuscular system	
	↓ CNS input (loss of α-motor neurons)	
	Neuromuscular disjunction	*Cancer?*
	↓ Ciliary neurotrophic factor (CNTF)	*Chronic inflammatory disease?*
	↓ Motor unit firing rate	
	Mitochondrial dysfunction	
	↓ Peripheral vascular flow	

Curr Opin Clin Nutr Metab Care 13:1–7; 2010

Factores humorales

- Descenso los niveles de hormonas anabolizantes
  - Hormona de crecimiento humana
  - *Dehidroepiandrosterona*
    - Testosterona
  - Estrogenos
  - Función tiroidea
- ↓ de efecto trofico → atrofia muscular

Hormona de crecimiento humana

- Su producion pituitaria ↓ mayores 30 ↑ efeito inibitorio somatostatina
  ↓ síntesis proteica

Se ha implicado en la pérdida de masa magra corporal

R. Burgos Peláez . Enfoque terapéutico global de la sarcopenia *Nutr Hosp 2006, 21:51-60)*

Hazzard Geriatric Medicine and Gerontology. *Sixth Edition*
Aging of the Endocrine System and Selected Endocrine Disorders

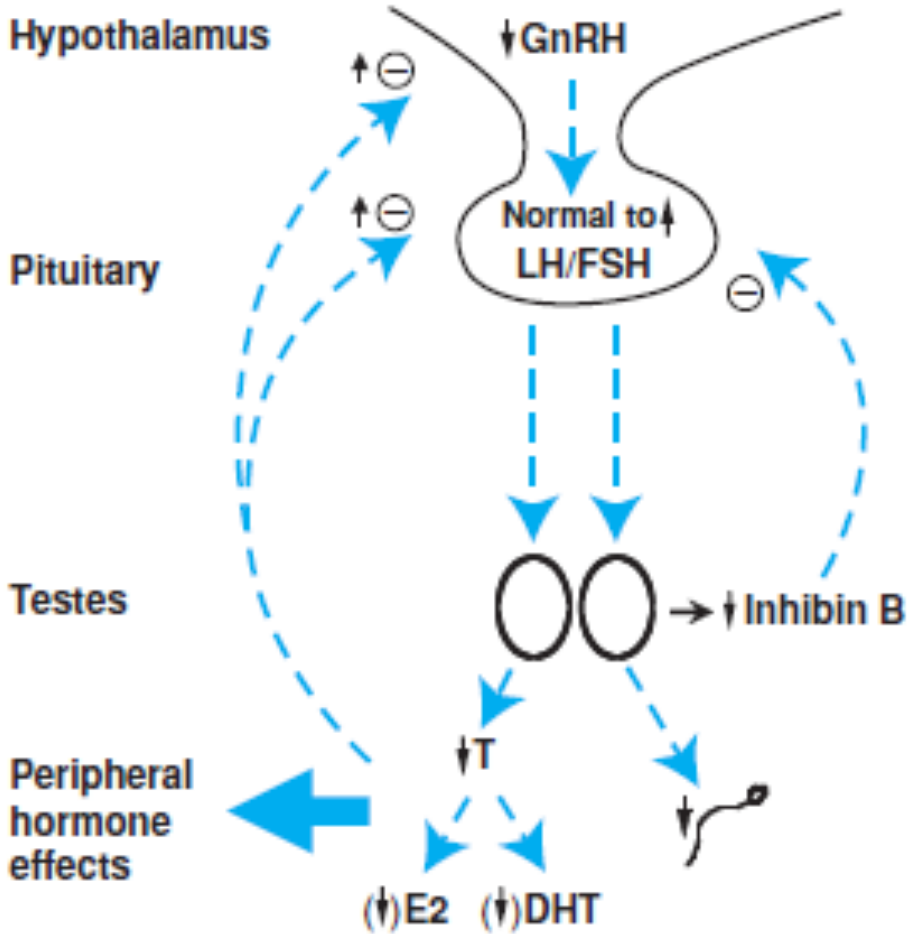


FIGURE 107-4. Age-related changes in male hypothalamic–pituitary–gonadal axis function. GnRH, gonadotropin-releasing hormone; LH, luteinizing hormone; FSH, follicle-stimulating hormone; E2, estradiol; DHT, dihy-

Dehidroepiandrosterona

- DHEA se produce en el córtex adrenal y sirve como precursor de diversos esteroides sexuales →potente efecto anabólico
- Las concentraciones ↓ progresivamente con la edad a partir de la tercera década de la vida

  ↓ síntesis proteica

  ↓la fuerza muscular

- Valenti, G., Denti, L., Maggio, M., Ceda, G., Volpato, S., Bandinelli, S., Ceresini, G., Cappola,A., Guralnik, J. M., and Ferrucci, L. (2004). Effect of DHEAs on skeletal muscle over the life span: The InCHIANTI study. J. Gerontol. A. Biol. Sci. Med. Sci. 59, 466–472.

Effect of Dehydroepiandrosterone on Muscle Strength and Physical Function in Older Adults: A Systematic Review

J Am Geriatr Soc 59:997–1002, 2011

155 eligible studies (5661 participants)

CONCLUSION:

- The benefit of DHEA on muscle strength and physical function in older adults remains inconclusive.
- Some measures of muscle strength may improve,

although consensus was not reached.

- DHEA does not appear to routinely benefit measures of physical function or performance.

Testosterona

↓ con el envejecimiento gran impacto negativo en el trofismo tanto del músculo como del hueso

- ↓ síntesis proteica ↓ masa muscular e la fuerza muscular → menor masa muscular esquelética apendicular

↑ mRNA y IGF-1 intramuscular

- Wolfe, R., Ferrando, A., SheYeld-Moore, M., and Urban, R. (2000). Testosterone and muscle protein metabolism. Mayo Clin. Proc. 75(Suppl.), S55–S59.

Estrogenos

- Durante la menopausia se ha observado una disminucion en la fuerza muscular →rapida disminucion en la produccion hormonal.

- Menopausia ↓ en la masa magra y en la densidad mineral ósea, relacionados con la deprivación estrogénica.
- Baumgartner, R. N., Waters, D. L., Gallagher, D., Morley, J. E., and Garry, P. J. (1999). Predictors of skeletal muscle mass in elderly men and women. Mech. Ageing Dev. 107, 123–136

Estrogenos

- Su disminucion con la edad supondria de forma indirecta un aumento del catabolismo y degradacion de proteinas → inhibir la produccion de Interleukin
  - IL-1 e IL-6 y factor de necrosis tumoral α

- La eclosión de la sarcopenia: Informe preliminar del Observatorio de la Sarcopenia de la Sociedad Española de Geriatría y Gerontología. Rev Esp Geriatr Gerontol. 2011;46:100-10. - vol.46 num 02

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Estrogenos

- Mujeres con osteoporosis tienen una menor masa muscular esquelética apendicular en comparación con controles sin osteoporosis.
  - Walsh y cols. demostraran que la sarcopenia es más prevalente en mujeres con osteopenia (25%) y osteoporosis (50%) que en mujeres con densidad mineral ósea normal (0,8%)

Walsh M, Hunter GR, Livingstone MB: Sarcopenia in premenopausaland postmenopausal women with osteopenia, osteoporosis and normal bone mineral density. *Osteoporos Int* 2006; 17:61-7.

Vitamina D

- Investigaciones involucrado en la aparicion de sarcopenia con niveles sericos bajos de 25 hidroxivitamina D
  - y niveles elevados de parathormona
- ↓ vitamina D
  - puede estar relacionado con la perdida de masa y de fuerza muscular

Visser M, Deeg DJ, Lips P. Low vitamin D and high parathyroid hormonelevels as determinants of loss of muscle strength and muscle. Fielding et al JAMDA – May 2011 sarcopenia: The Longitudinal Aging Study Amsterdam. J Clin Endocrinol Metab 2003;88:5766–5772.

Insulina

- ↑progresivo en la grasa muscular
  - Aumento en la incidencia de resistencia a la insulina

  ↓ efecto anabolico da insulina

- Insulina estimula mitochondria muscular

  ↑ sintese proteica

Roubenoff R and Hughes VA. Sarcopenia: current concepts. *J Gerontol A Biol Sci Med Sci 55: M716–M724, 2000.*

Sarcopenia Exacerbates Obesity-Associated Insulin Resistance and Dysglycemia: Findings from the National Health and Nutrition Examination Survey III; 2010

- Conclusions:
  - Sarcopenia, independent of obesity, is associated with adverse glucose metabolism, and the association is strongest in individuals under 60 years of age, which suggests that low muscle mass may be an early predictor of diabetes susceptibility

Srikanthan P, Hevener AL, Karlamangla AS (2010) Sarcopenia Exacerbates Obesity-Associated Insulin Resistance and Dysglycemia: Findings from the National Health and Nutrition Examination Survey III. PLoS ONE 5(5): e10805. doi:10.1371/journal.pone.0010805

Insulin-like growth factor-1

- Las concentraciones de IGF-1 en ancianos predicen la presencia de sarcopenia de una manera inversa, actuando como un factor protector en hombres

- Payette H, Roubenoff R, Jacques PF, Dinarello CA, Wilson PW, Abad LW y cols.: Insulin-like growth factor-1 and interleukin 6 predict sarcopenia in very old community-living men and women: the Framingham Heart Study. *J Am Geriatr Soc* 2003; 51:1237-43.

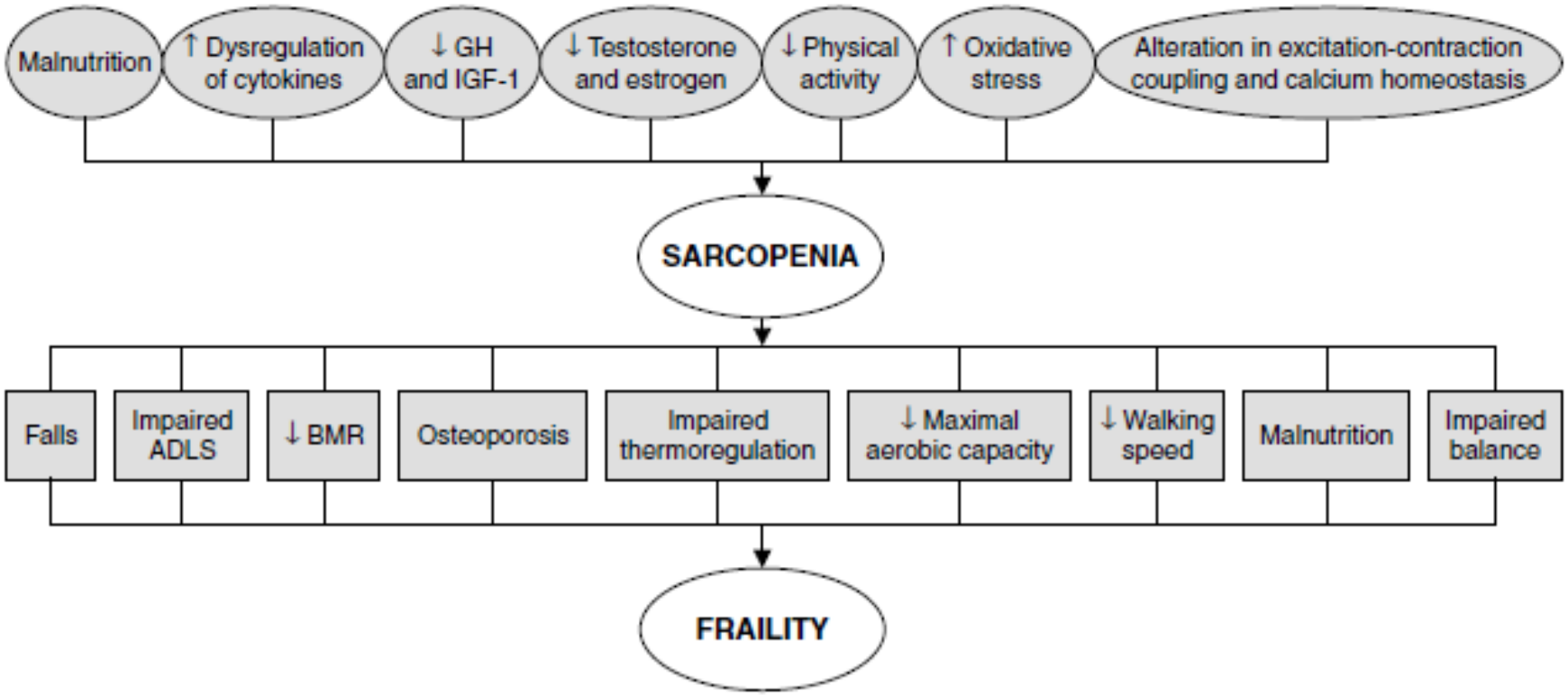

Fig. 1. Pathogenesis and functional and metabolic consequences of sarcopenia. **ADLS** = activities of daily living score; **BMR** = basal metabolic rate; **GH** = growth hormone; **IGF-1** = insulin-like growth factor-1.

Role of Hormones in the Pathogenesis and Management of Sarcopenia. Drugs Aging 2002; 19 (11): 865-877

Table 2 Summary of treatment options

Intervention	Effect	Comments
Exercise	Increased cardiovascular fitness with increased endurance	Pros: overall beneficial effects
Aerobic	Increases mitochondrial volume and activity	of exercise to individual
Resistance	Increased muscle mass and strength	Cons: motivation
	Increased skeletal muscle protein synthesis and muscle fiber size	to exercise remains low
	Improvement in physical performance	
Nutritional supplement	Varying evidence of increased muscle mass and strength	Pros: ensures good protein intake
		Cons: may reduce natural food intake
Hormone therapy	Varying evidence of increased muscle mass and strength	Cons: masculinization of women;
Testosterone		increased risk of prostatic cancer in men
Estrogen	Poor evidence of increased muscle mass but not function	Cons: risk of breast cancer
Growth hormone	Some evidence for increased muscle mass. Varying evidence	Cons: side effects including fluid
	for increased muscle strength	retention, orthostatic hypotension
Vitamin D	Variable evidence for increased muscle	Pros: fracture reduction; possible
	strength	cardiovascular benefits
	Reduced falls in nursing home residents	
ACE inhibitors	Some evidence for increased exercise capacity	Pros: other cardiovascular benefits
		Cons: renal function needs monitoring
Creatine	Variable evidence of increased muscle strength	Cons: reports of nephritis
	and endurance especially when combined with exercise	
Potential new treatments		
Myostatin antagonists	No trials in older people	
PPAR [δ] agonist	No human trials	
AICAR	No human trials	

Abbreviations: PPAR-δ, peroxisome-proliferator-activated receptor-δ; AICAR, 5-aminoimidazole-4-carboxamide-1-beta-4-ribofuranoside; ACE, angiotensin-converting enzyme.

Muito obrigada