VI CONGRESSO NAZIONALE

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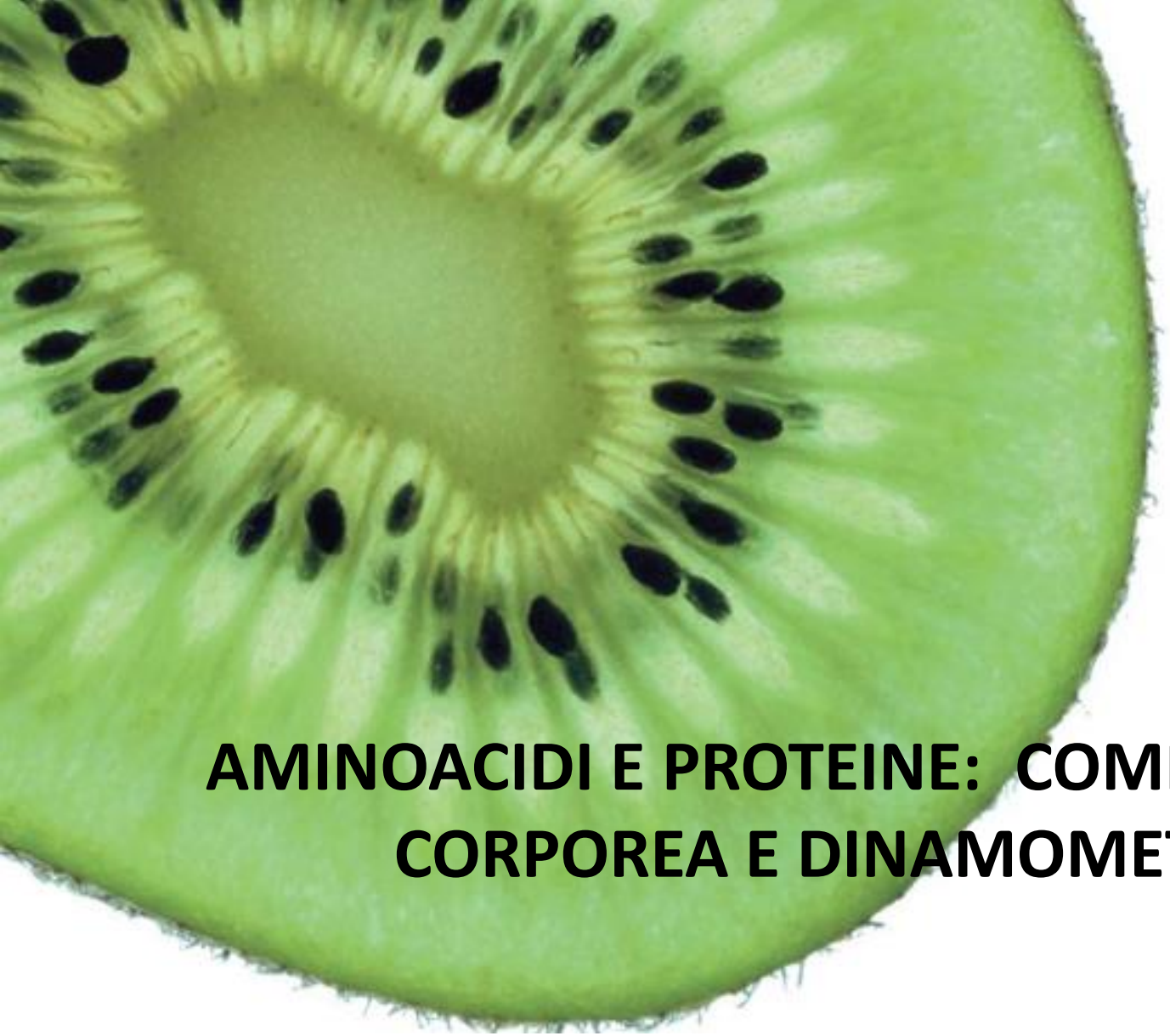


AMINOACIDI E PROTEINE: COMPOSIZIONE CORPOREA E DINAMOMETRIA

Federico Vignati
UOC di Malattie Endocrine e Diabetologia, UOSVD di Nutrizione Clinica ed Obesità

The American Journal of Clinical Nutrition

The underappreciated role of muscle in health and disease[1–3]

Robert R Wolfe

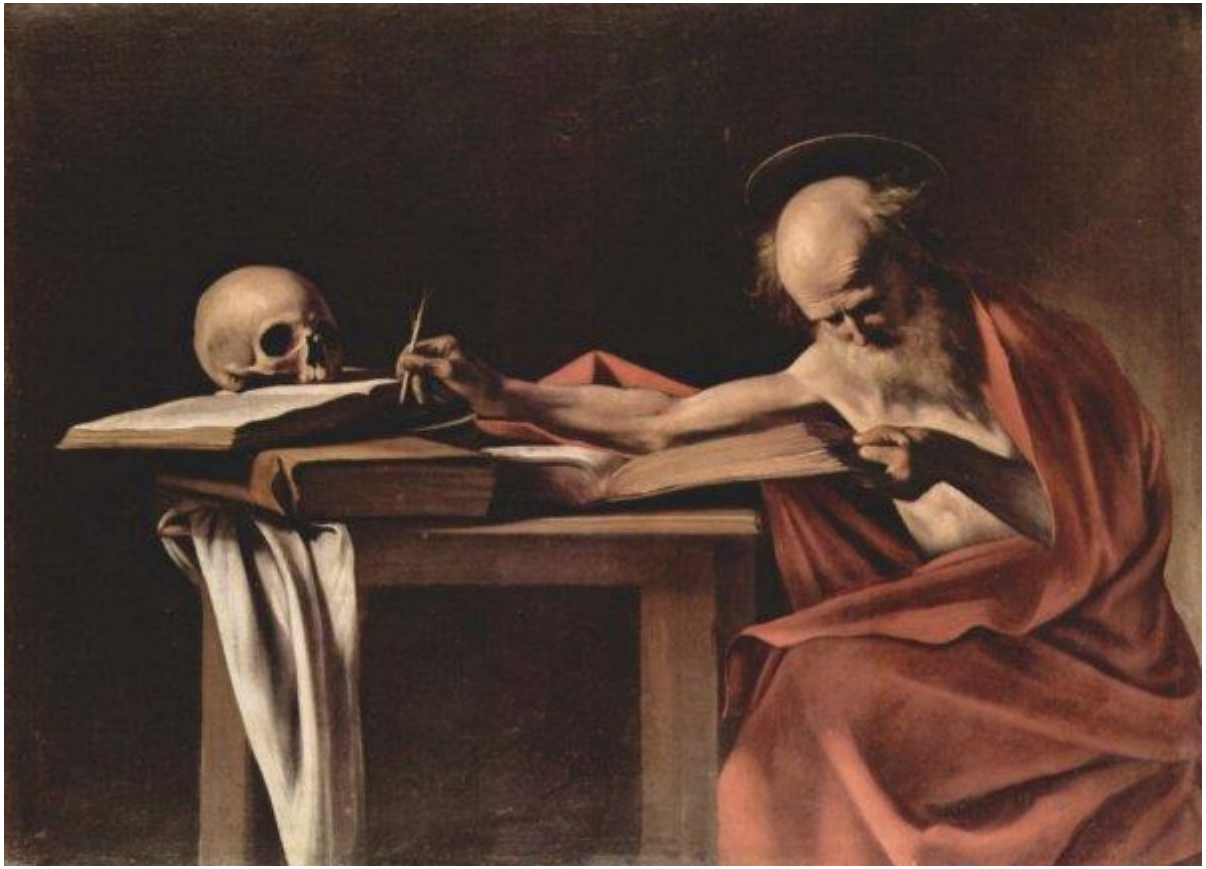
ABSTRACT

Muscle plays a central role in whole-body protein metabolism by serving as the principal reservoir for amino acids to maintain protein synthesis in vital tissues and organs in the absence of amino acid absorption from the gut and by providing hepatic gluconeogenic precursors. Furthermore, altered muscle metabolism plays a key role in the genesis, and therefore the prevention, of many common pathologic conditions and chronic diseases. Nonetheless, the maintenance of adequate muscle mass, strength, and metabolic function has rarely, if ever, been targeted as a relevant endpoint of recommendations for dietary intake. It is therefore imperative that factors directly related to muscle mass, strength, and metabolic function be included in future studies designed to demonstrate optimal lifestyle behaviors throughout the life span, including physical activity and diet. *Am J Clin Nutr* 2006;84:475–82.

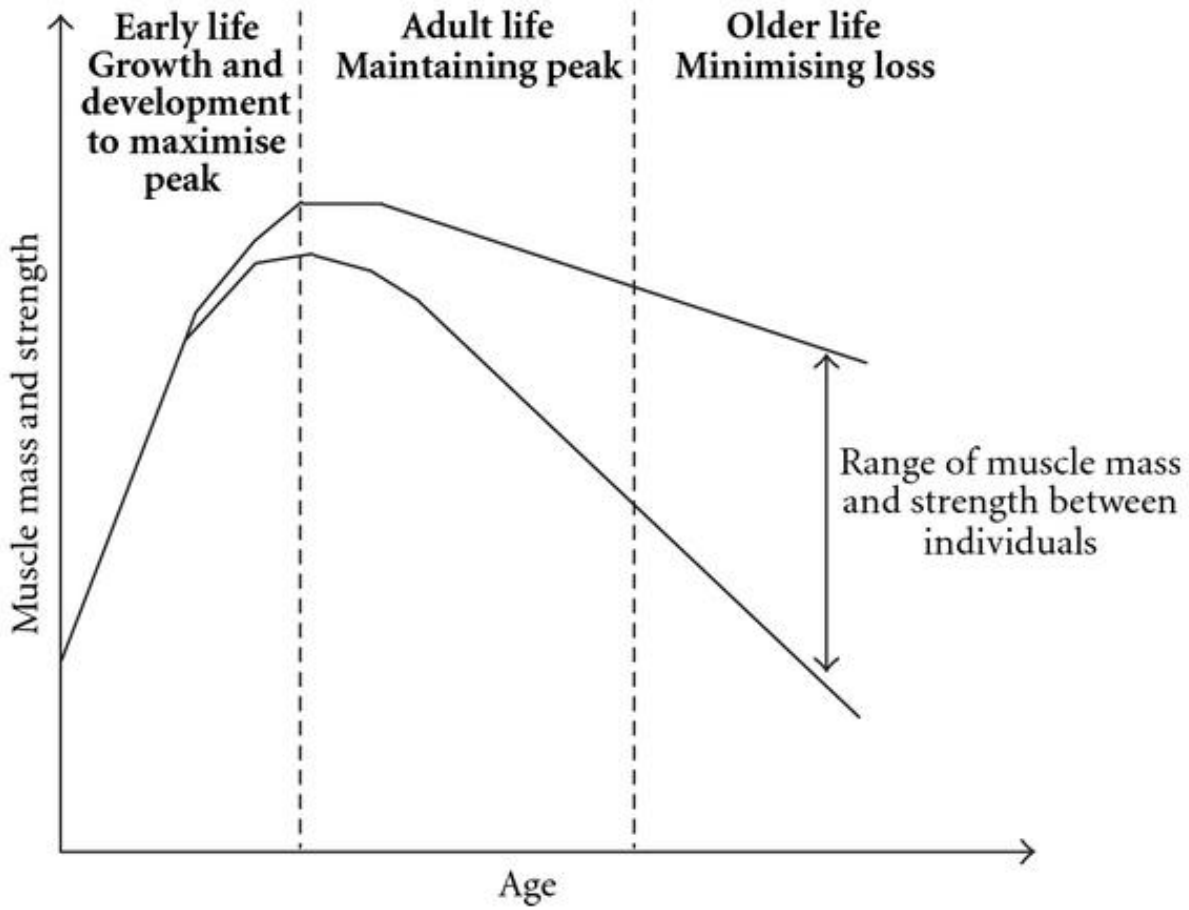
Am J Clin Nutr 2006;84:475–82. Printed in USA. © 2006 American Society for Nutrition

Definizione della sarcopenia

E’ una condizione caratterizzata dalla progressiva perdita di massa e forza muscolare, in parte fisiologica nell’invecchiamento, ma in grado di condizionare negativamente la qualità della vita, la prognosi di altre malattie e la sopravvivenza



Evoluzione della massa magra



Sayer AA et al. J Nutr Health Aging 2008; 12:427-431

Skeletal Muscle and Mortality Results From the InCHIANTI Study

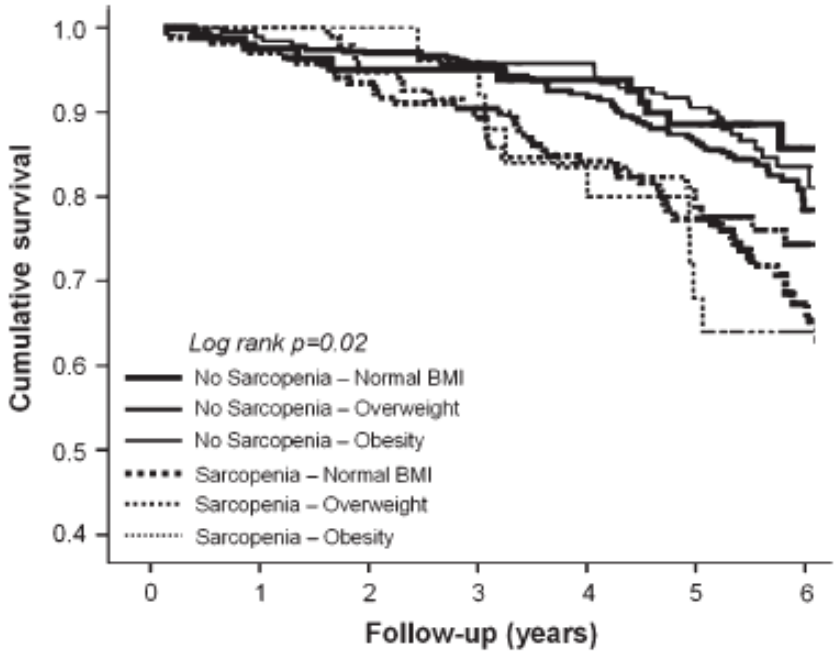


Figure 1. Kaplan-Meier survival curves for mortality according to sarcopenia and body mass index (BMI) groups.

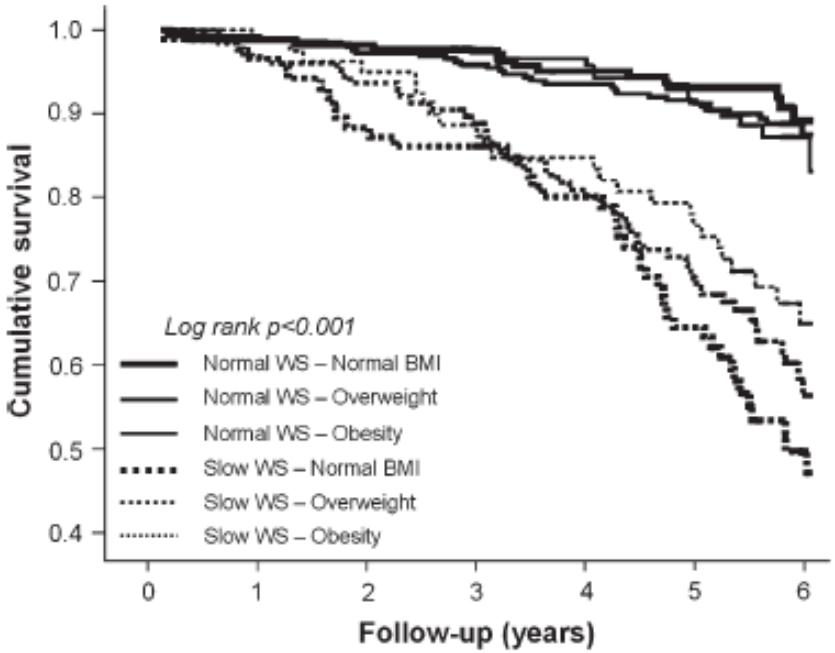


Figure 2. Kaplan-Meier survival curves for mortality according to walking speed (WS) and body mass index (BMI) groups.

Cesari M et al. J Gerontol A Biol Sci Med Sci 2009; 64:377-384

Inquadramento di Sarcopenia

European Working Group on Sarcopenia in Older People[1]

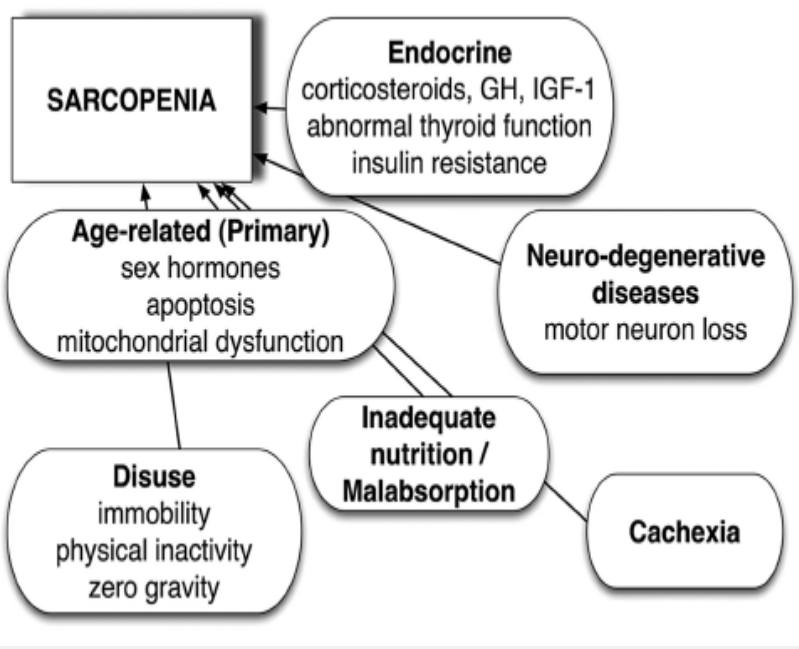


Table 2. Sarcopenia categories by cause

Primary sarcopenia	
Age related sarcopenia	No other cause evident except ageing
Secondary sarcopenia	
Activity related sarcopenia	Can result from bed rest, sedentary lifestyle, deconditioning or zero gravity conditions
Disease related sarcopenia	Associated with advanced organ failure (heart, lung, liver, kidney, brain), inflammatory disease, malignancy or endocrine disease
Nutrition related sarcopenia	Results from inadequate dietary intake of energy and/or protein, as with malabsorption, gastrointestinal disorders or use of medications that cause anorexia

Table 3. EWGSOP conceptual stages of sarcopenia

Stage	Muscle mass	Muscle strength		Performance
Presarcopenia	↓			
Sarcopenia	↓	↓	Or	↓
Severe sarcopenia	↓	↓		↓

A.J. Cruz-Jentoft et al., Age and Ageing 2010; 39: 412–423

HANDGRIP
La forza muscolare è misurabile

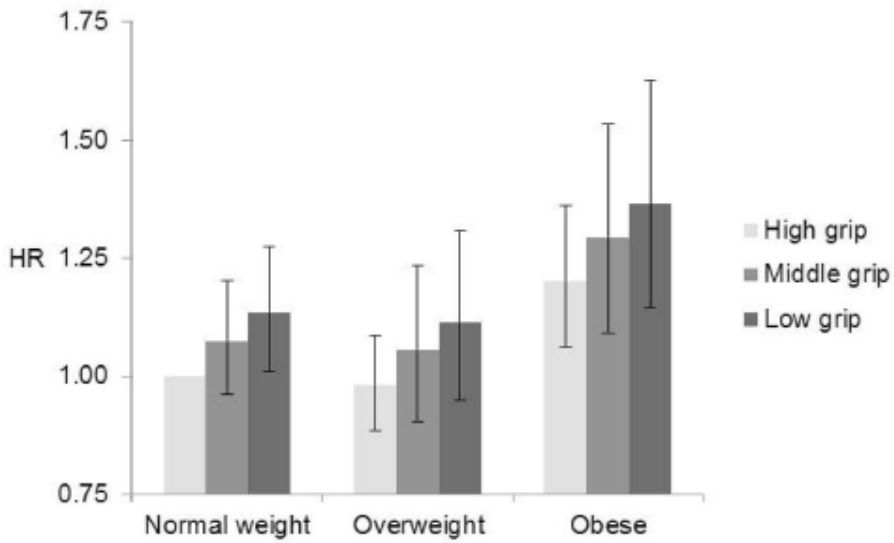
Il dinamometro elettronico è uno strumento professionale, preciso, non invasivo, facile da usare.

Il test di valutazione della forza contrattile dei muscoli flessori della mano mediante handgrip può essere utilizzato:
- per l'impostazione di un trattamento riabilitativo,
- per la valutazione dello stato nutrizionale,
- per stabilire un indice di rischio di mortalità nei pazienti affetti da patologie acute,
- come fattore prognostico nel decorso di malattie ad elevato impatto metabolico
- come indicatore della forza muscolare generale.
- come strumento per scoprire la sarcopenia

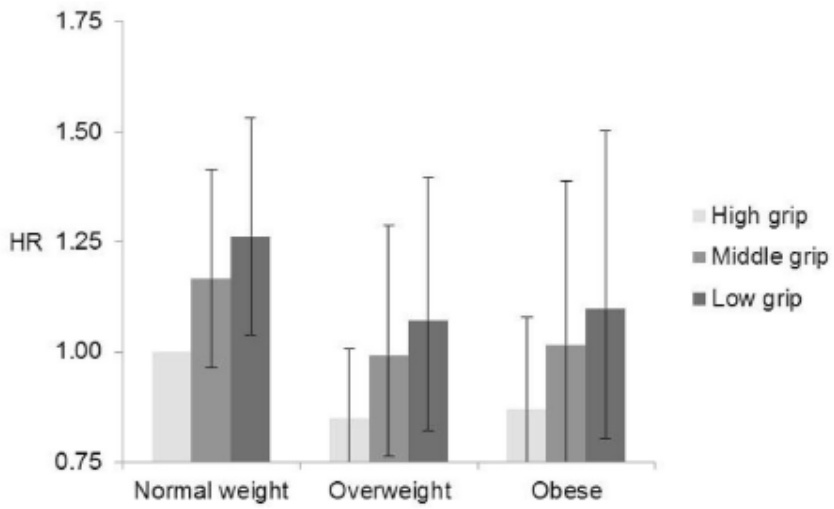
NIH Public Access
Author Manuscript
Int J Obes (Lond). Author manuscript; available in PMC 2015 February 01.

Published in final edited form as:
Int J Obes (Lond). 2014 August ; 38(8): 1126–1132. doi:10.1038/ijo.2013.214.

Obesity and Muscle Strength as Long-term Determinants of All-Cause Mortality – a 33 Year of Follow-up of the Mini-Finland Health Examination Survey

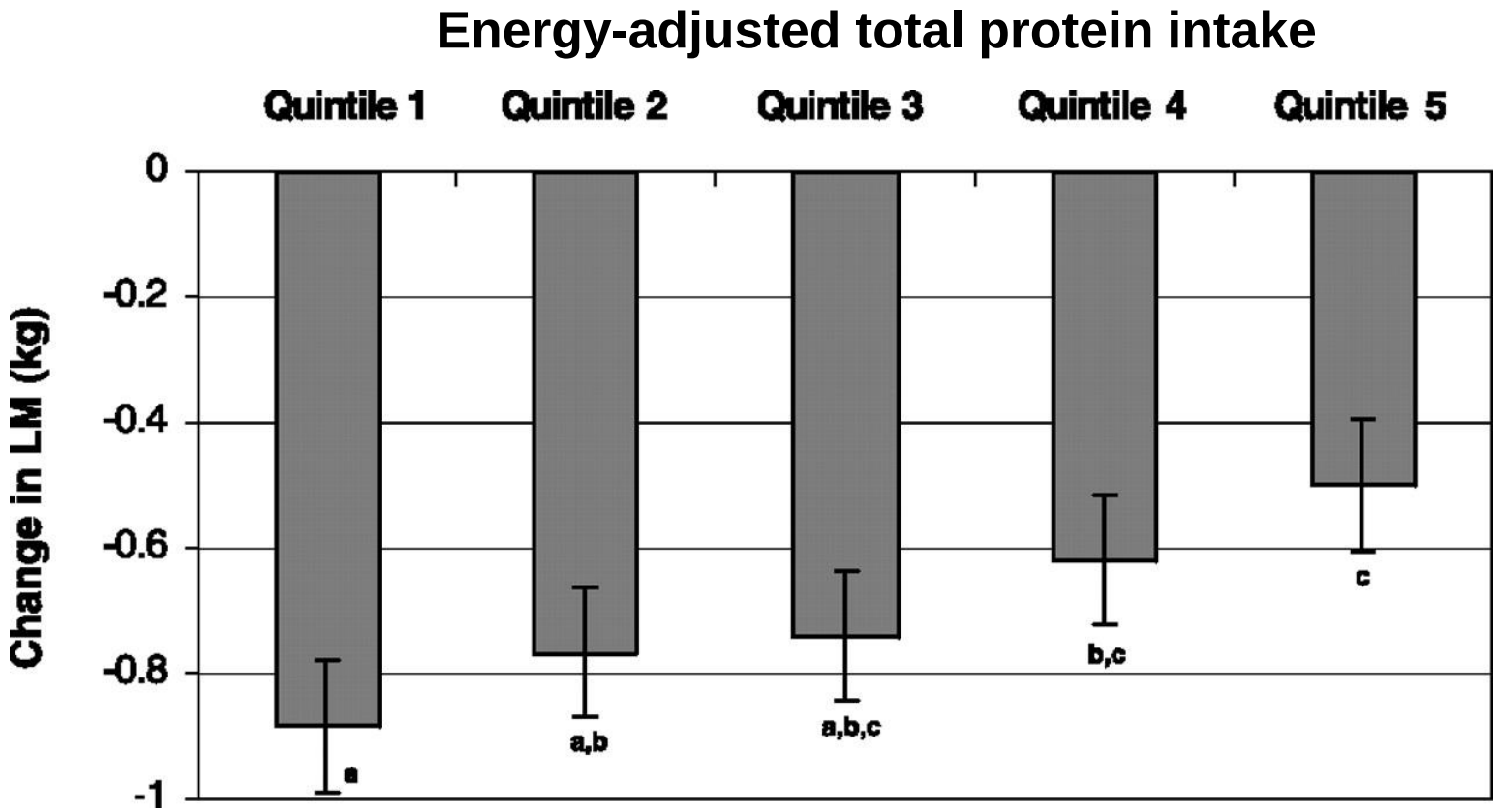


Soggetti 50 – 69 anni



Soggetti > 70 anni

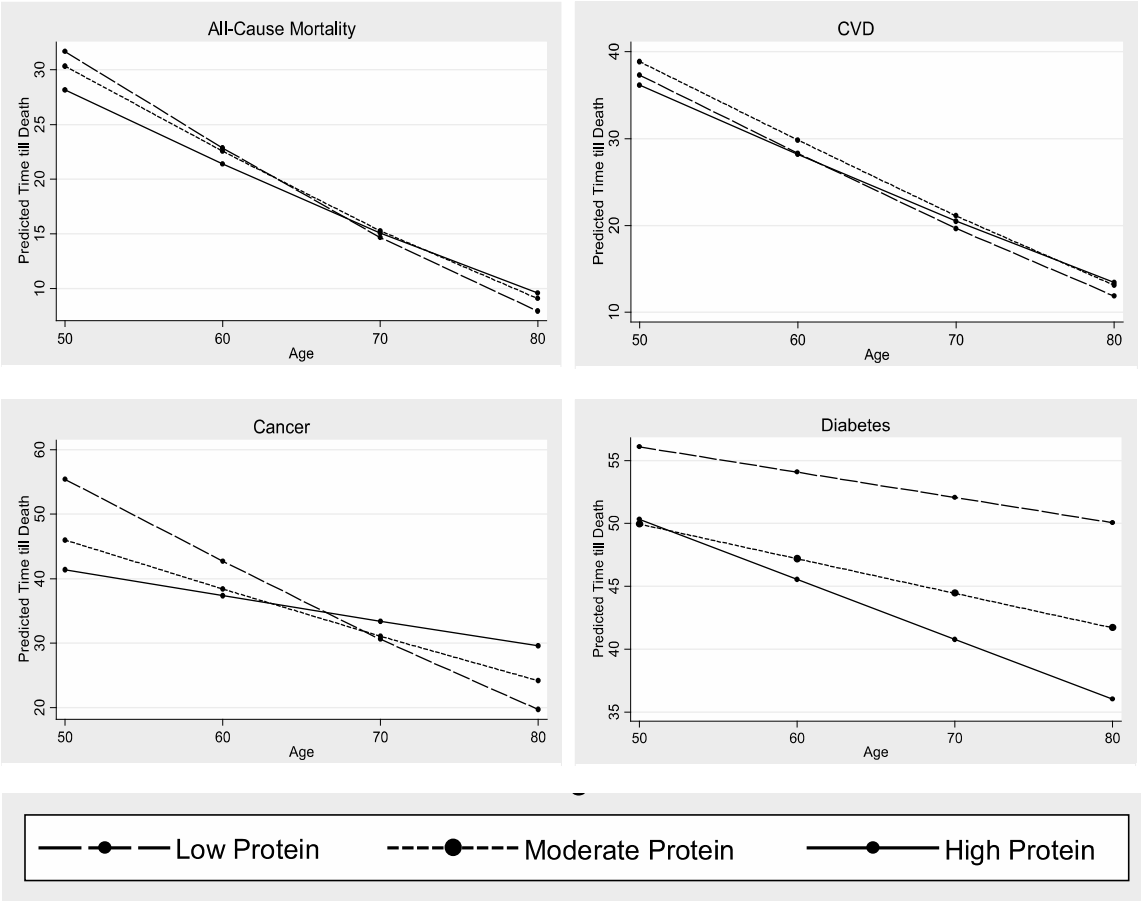
Protein Intake and Muscle Loss with Aging



Unadjusted protein intake	0.8±0.3	0.7±0.3	0.8±0.3	0.9±0.3	1.2±0.4

Houston DK et al. Am J Clin Nutr 2008

Low Protein Intake Is Associated with a Major Reduction in IGF-1, Cancer, and Overall Mortality in the 65 and Younger but Not Older Population



These results suggest that low protein intake during middle age followed by moderate to high protein consumption in old adults may optimize healthspan and longevity.

Levine et al., Cell Metab 19: 407-417, 2014

Cell Metabolism
Article

Low Protein Intake Is Associated with a Major Reduction in IGF-1, Cancer, and Overall Mortality in the 65 and Younger but Not Older Population

50-65 anni (n =3039)	Mortalità CVD	Mortalità All-cause	Mortalità cancer
Low protein (<10%)	HR 1,0	HR 1,0	HR 1,0
Moderate protein (10-19%)	HR 0,79	HR 1,34	HR 3.06
High protein (20 o >%)	HR 1,08	HR 1,74	HR 4,33

Con associazione maggiore se consumo di proteine animali

66 + anni (n =3342)	Mortalità CVD	Mortalità All-cause	Mortalità cancer
Low protein (<10%)	HR 1,0	HR 1,0	HR 1,0
Moderate protein (10-19%)	HR 0,8	HR 0,78	HR 0,67
High protein (20 o >%)	HR 0,78	HR 0,72	HR 0,40

Levine et al., Cell Metab 19: 407-417, 2014

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Levine et al., Cell Metab 19: 407-417, 2014

Supplementazione con Aminoacidi e/o Proteine

Quale è l'apporto proteico ottimale?

Supplementazione nella sarcopenia e nel deficit di forza muscolare

Proteine o aminoacidi?

FABBISOGNO PROTEICO

Fabbisogno medio popolazione adulta	0,7 g/kg/die
Dose raccomandata popolazione adulta	0,9 g/kg/die
Obiettivo nutrizionale per la prevenzione popolazione anziana (>60 anni)	1,1 g/kg/die

Società Italiana di Nutrizione Umana-SINU, 2014

LARN - Livelli di assunzione di riferimento per la popolazione italiana: PROTEINE.

NIH Public Access
Author Manuscript
Curr Opin Clin Nutr Metab Care. Author manuscript; available in PMC 2012 February 9.

Published in final edited form as:
Curr Opin Clin Nutr Metab Care. 2010 January ; 13(1): 34–39. doi:10.1097/MCO.0b013e328333aa66.

Protecting muscle mass and function in older adults during bed rest

Kirk L. English and **Douglas Paddon-Jones**
Department of Physical Therapy, Division of Rehabilitation Sciences. The University of Texas Medical Branch. 301 University Blvd. Galveston, TX 77555-1144

Abstract

Purpose of review—To highlight the losses in muscle mass, strength, power and functional capacity incurred in older adults during bed rest-mediated inactivity and to provide practical recommendations for both the prevention and rehabilitation of these losses.

Recent findings—In addition to sarcopenic muscle loss, older adults lose lean tissue more rapidly than the young during prolonged periods of physical inactivity. Amino acid or protein supplementation has the potential to maintain muscle protein synthesis and may reduce inactivity-induced muscle loss, but should ideally be part of an integrated countermeasure regimen consisting of nutrition, exercise and where appropriate, pharmacologic interventions.

Summary—In accord with recent mechanistic advances we recommend an applied, broad-based 2-phase approach to limit inactivity-mediated losses of muscle mass and function in older adults:

1. Lifestyle: a) consume a moderate amount (25-30 g) of high quality protein with each meal; b) incorporate habitual exercise in close temporal proximity to protein-containing meals.

2. Crises: react aggressively to combat the accelerated loss of muscle mass and function during acute catabolic crises and periods of reduced physical activity. As a base strategy, this should include nutritional support such as targeted protein or amino acid supplementation and integrated physical therapy.

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Curr Opin Clin Nutr Metab Care. Author manuscript; available in PMC 2012 February 9.

Published in final edited form as:
Curr Opin Clin Nutr Metab Care. 2010 January ; 13(1): 34–39. doi:10.1097/MCO.0b013e328333aa66.

Supplementi di AAE o Proteine possono ridurre la perdita muscolare da inattività, ma andrebbero inseriti in un approccio integrato che include
•Nutrizione
•Esercizio
•Intervento farmacologico (se indicato)

Due livelli di intervento: Lifestyle e Crisi

Lifestyle:
a) Consumo di 25 - 30 g di proteine di alto valore biologico ad ogni pasto
b) Esercizio fisico abituale in prossimità temporale con l'assunzione di proteine

Crisi:
a) Reagire in modo tempestivo ed aggressivo per contrastare la perdita di massa e funzione muscolare dovuta a crisi catabolica
b) Come strategia di base ciò dovrebbe includere un supporto nutrizionale con AAE o proteine ed andrebbe associata terapia fisica

Terapia nutrizionale per prevenire la sarcopenia

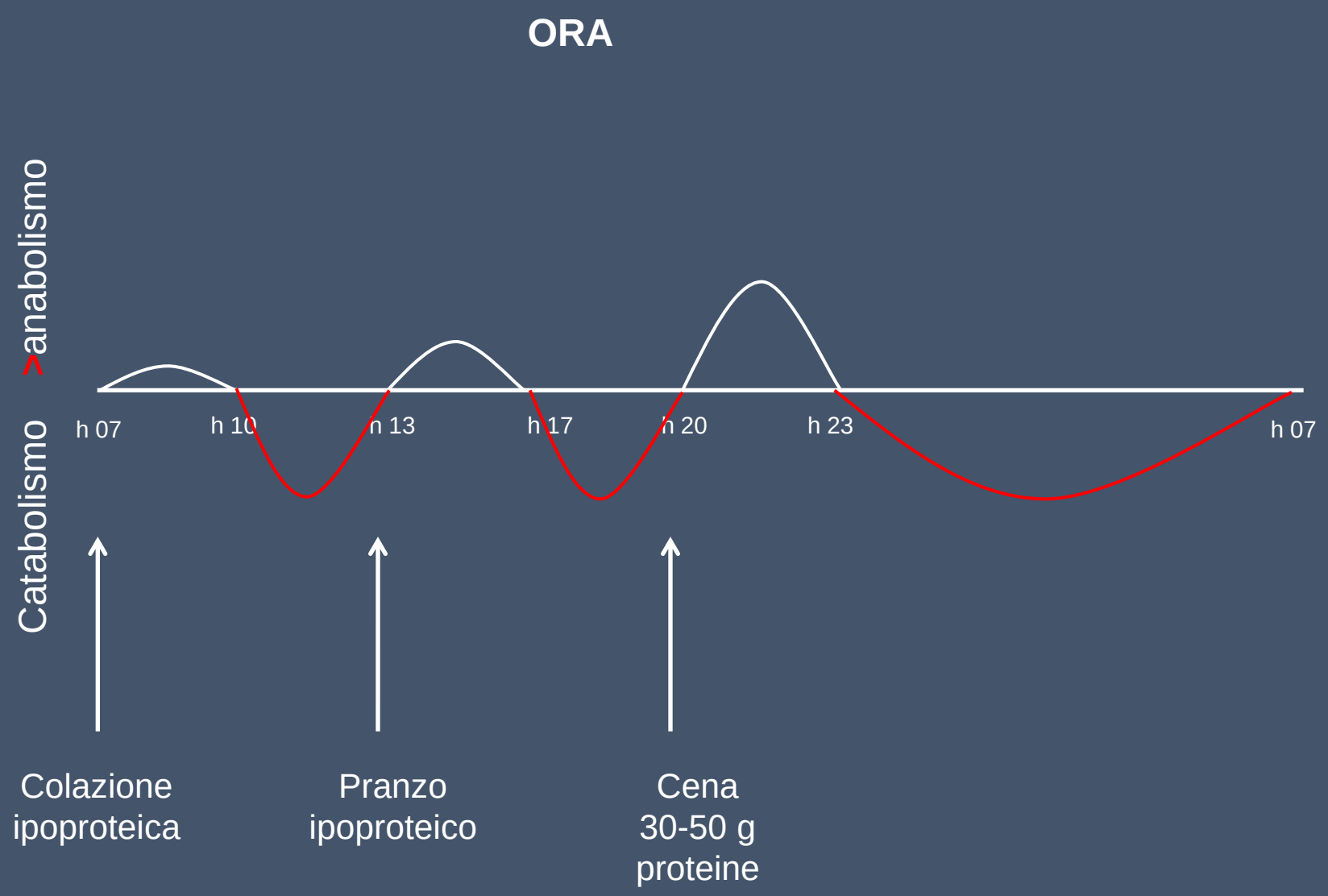
Necessità di ridefinizione del fabbisogno proteico nell'anziano e nelle patologie catabolizzanti

SCOPO

A) Fornire i substrati necessari per contrastare la perdita di massa magra e favorire l'anabolismo in associazione ad attività fisica

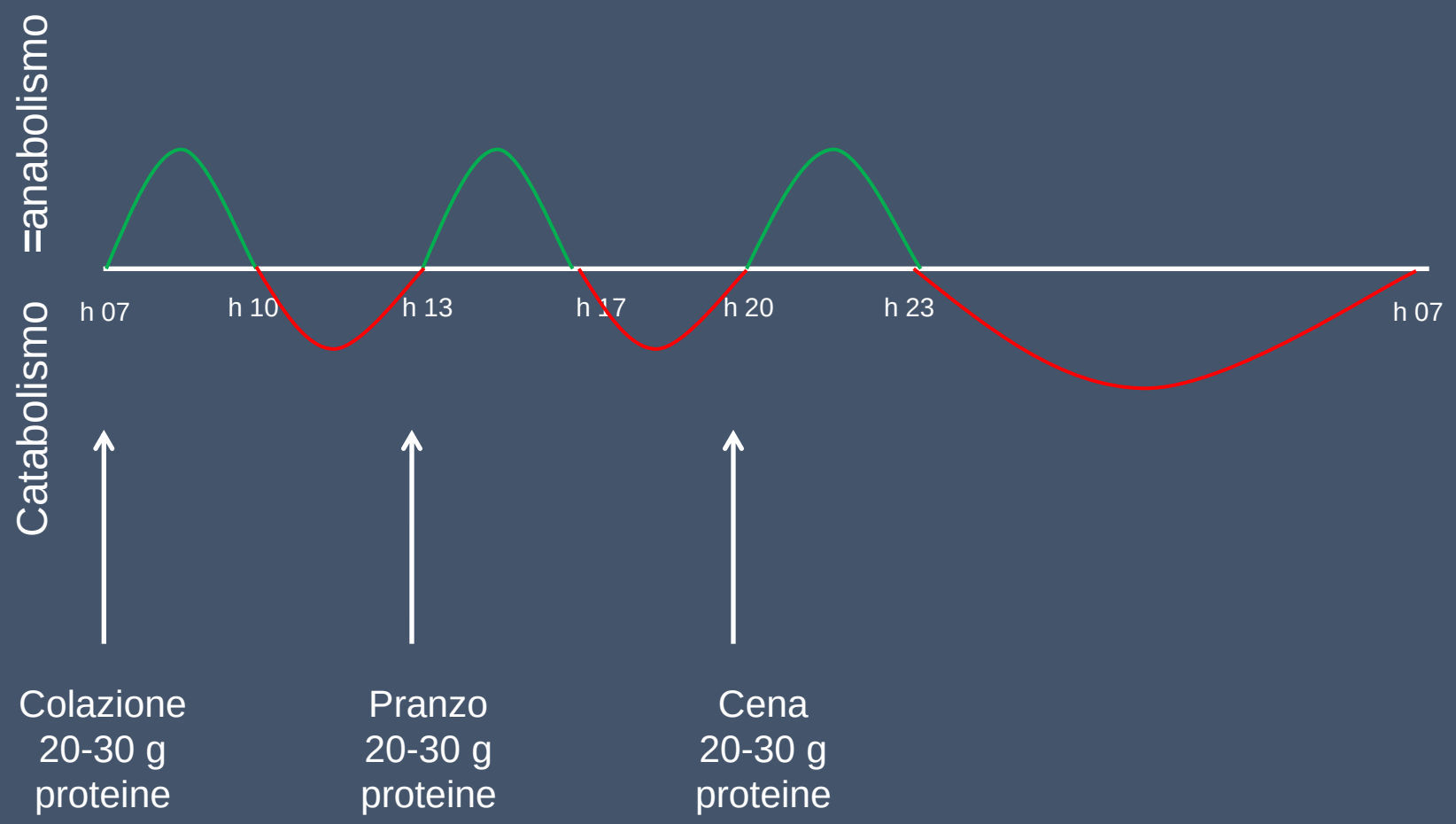
B) Fornire i substrati necessari per contrastare il declino metabolico (deficit mitocondriale) dell'anziano o del malato cronico

UN NUOVO MODELLO DI ALIMENTAZIONE

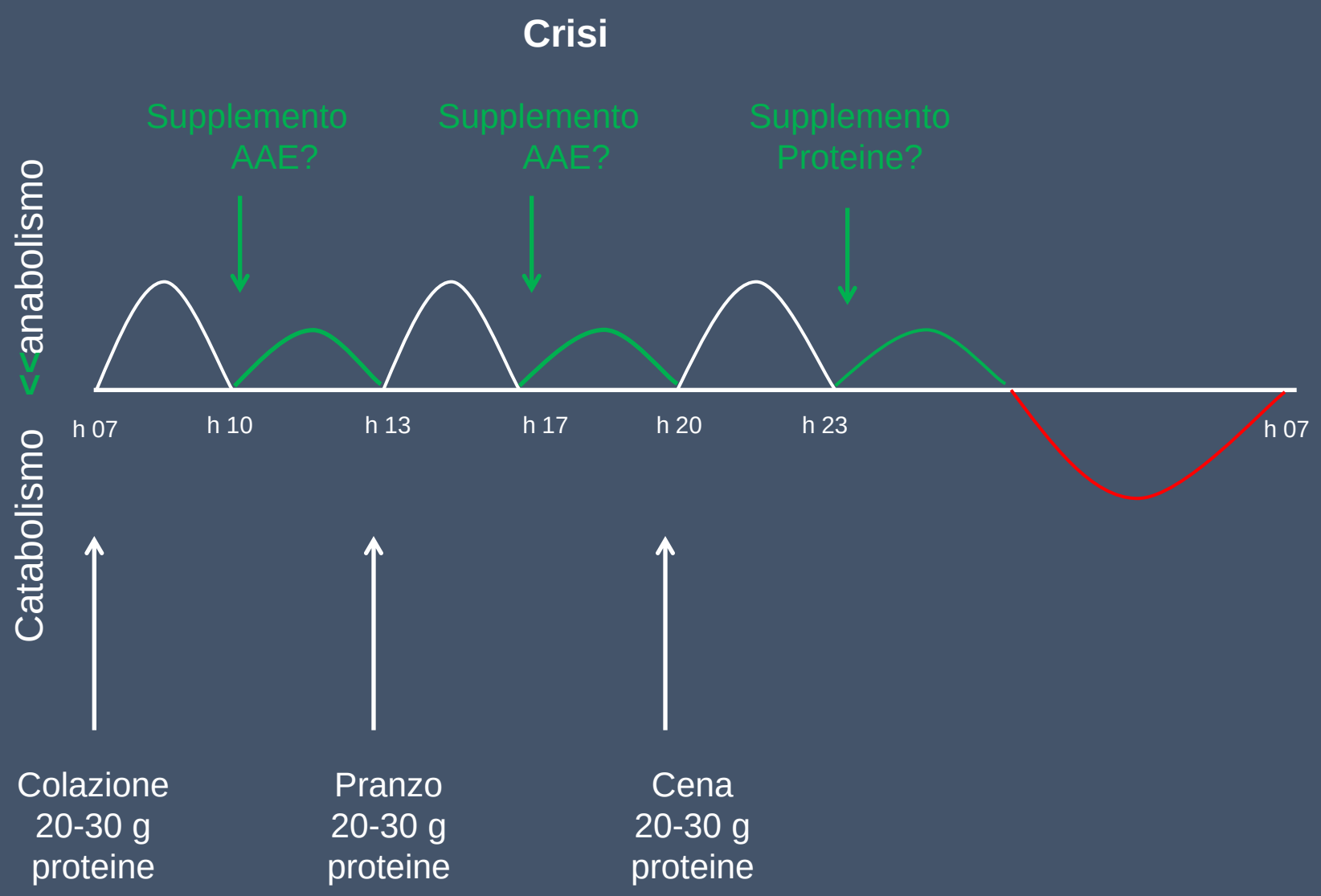


UN NUOVO MODELLO DI ALIMENTAZIONE

Lifestyle



UN NUOVO MODELLO DI ALIMENTAZIONE



CARATTERISTICHE DELLE PROTEINE

Table 1. Protein quality rankings.

Protein Type	Protein Efficiency Ratio	Biological Value	Net Protein Utilization	Protein Digestibility Corrected Amino Acid Score
Beef	2.9	80	73	0.92
Black Beans	0		0	0.75
Casein	2.5	77	76	1.00
Egg	3.9	100	94	1.00
Milk	2.5	91	82	1.00
Peanuts	1.8			0.52
Soy protein	2.2	74	61	1.00
Wheat gluten	0.8	64	67	0.25
Whey protein	3.2	104	92	1.00

Adapted from: U.S Dairy Export Council, Reference Manual for U.S. Whey Products 2nd Edition, 1999 and Sarwar, 1997.

HANNO LO STESSO POTERE ANABOLIZZANTE?

Hoffman JR and Falvo MJ J Sport and Medicine (2004); 3; 118, -130

The Journal of Nutrition. First published ahead of print June 15, 2011 as doi: 10.3945/jn.111.139840.

The Journal of Nutrition
Nutrient Requirements and Optimal Nutrition

Whey Protein but Not Soy Protein Supplementation Alters Body Weight and Composition in Free-Living Overweight and Obese Adults[1,2]

David J. Baer,* Kim S. Stote, David R. Paul, G. Keith Harris, William V. Rumpler, and Beverly A. Clevidence

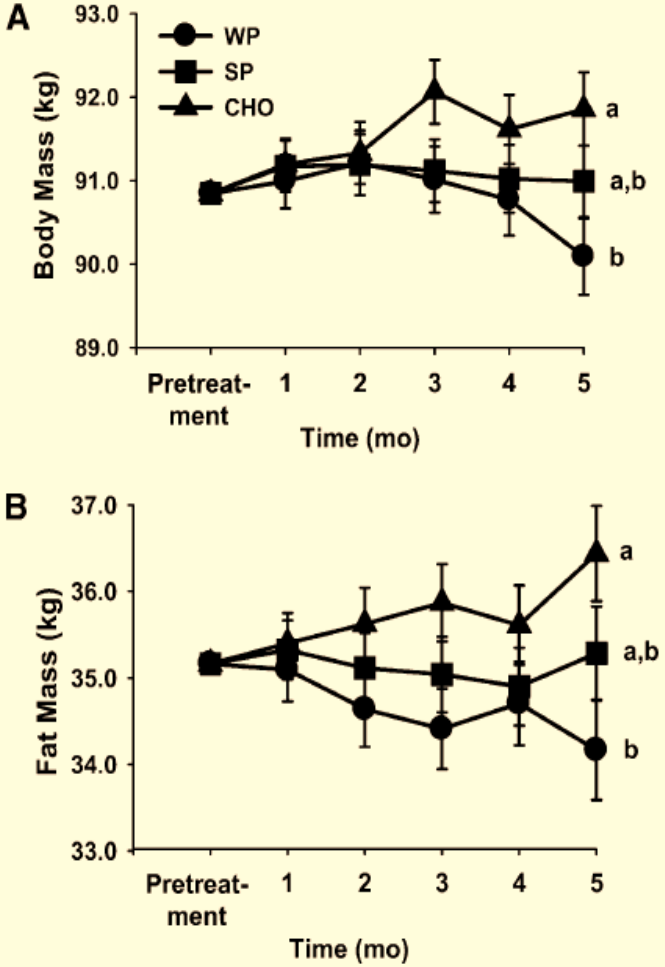
Beltsville Human Nutrition Research Center, Agricultural Research Service, USDA, Beltsville, MD 20705

TABLE 1 Chemical composition of the carbohydrate (CHO), whey protein (WP), and soy protein (SP) treatment supplements[1,2]

	CHO	WP	SP
		g/packet	
Weight	52	51	52
Protein	0.6	27.5	28.1
Moisture	1.7	2.2	1.8
Fat, acid hydrolysis	0.7	1.5	2.0
Ash	1.0	1.4	2.7
Total carbohydrate	48.0	18.4	17.4
Calcium	0.20	0.22	0.25
para-Aminobenzoic acid	0.2	0.2	0.2
		mg/packet	
L-Aspartic acid	36.4	3060	3200
L-Threonine	18.2	1850	945
L-Serine	23.4	1570	1480
L-Glutamic acid	62.4	4860	5340
L-Proline	26.0	1690	1000
L-Glycine	18.2	541	1150
L-Alanine	15.6	1370	1150
L-Cystine	10.4	694	319
L-Valine	20.8	1590	1310
L-Methionine	10.4	592	354
L-Isoleucine	13.0	1730	1310
L-Leucine	26.0	3060	2190
L-Tyrosine	26.0	820	997
L-Phenylalanine	18.2	918	1440
L-Histidine	10.4	530	716
L-Lysine	15.6	2470	1690
L-Arginine	26.0	726	2070
L-Tryptophan	10.4	607	400

[1] Participants consumed 2 treatment packets/d, 1 with breakfast and the evening meal, along with their typical diet.
[2] Chemical composition was determined by Covance Laboratories.

jn.nutrition.org by guest on December 23, 2012



Supplementazione con Whey e leucina

Clinical Nutrition 30 (2011) 759–768

Contents lists available at ScienceDirect

Clinical Nutrition

journal homepage: http://www.elsevier.com/locate/clnu

Original article

Muscle protein synthesis in cancer patients can be stimulated with a specially formulated medical food☆

Nicolaas E.P. Deutz[a], Ahmed Safar[b], Scott Schutzler[a], Robert Memelink[c], Arny Ferrando[a], Horace Spencer[d], Ardy van Helvoort[c], Robert R. Wolfe[a,*]

Composizione proteica :
Caseina 24,2 g,
whey 11,9 g
leucina 4,16 g

3.4. Aim of the study

The objective of the present study was to determine if intake of a specially formulated medical food, high in leucine and protein stimulates muscle protein synthesis acutely in patients with cancer to a greater extent than a conventional medical food. The experi-

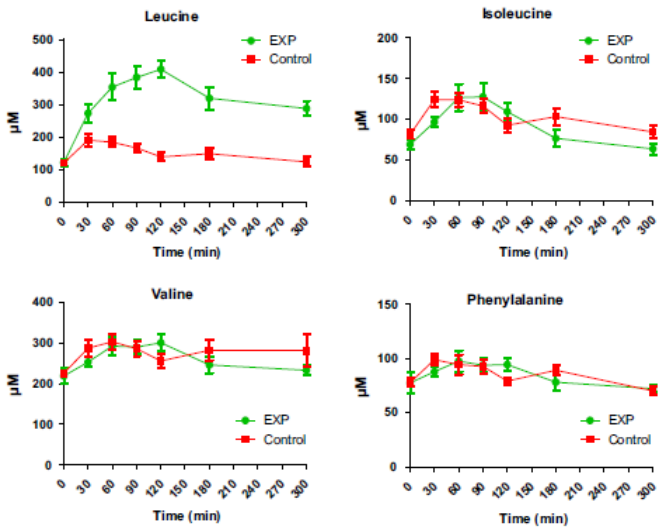
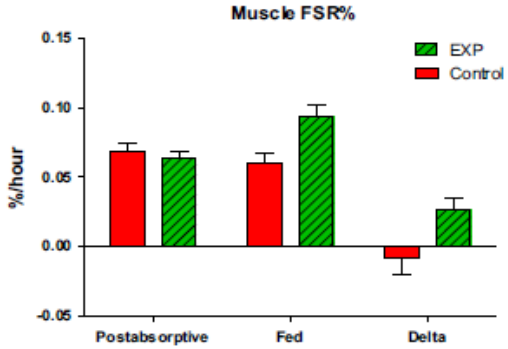


Fig. 2. Plasma leucine, isoleucine, valine and phenylalanine levels after intake of the medical foods. A significant groups effect was observed with respect to leucine ($P < 0.001$), but not for isoleucine, valine or phenylalanine ($P > 0.35$ for all).



Our results demonstrate that it is possible to stimulate muscle protein synthesis in catabolic cancer patients with involuntary weight loss with a specially formulated medical food, rich in leucine and protein. Cachexia is defined as a state in which muscle

Differenze fra proteine ed aminoacidi

PROTEINE

Le proteine devono essere **digerite** per rendere disponibili gli AA

La digestione delle proteine (carne) dipende da una **corretta funzione gastrica e pancreatica** (HCl ed enzimi)

Il pancreas, per produrre gli enzimi digestivi **consuma grandi quantità di energia** e circa il 60% degli AA introdotti con la dieta

Le proteine naturali hanno differente digeribilità e composizione aminoacidica: il potere anabolizzante è molto diverso tra loro

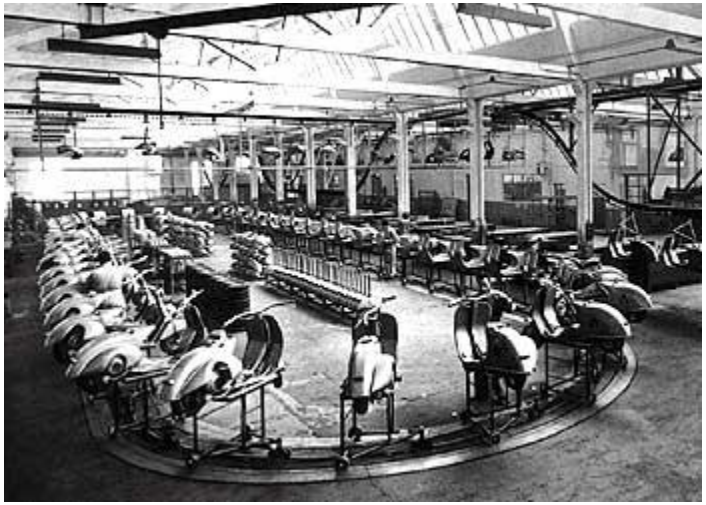
AMINOACIDI

I singoli AA sono rapidamente assimilati dall'apparato digerente **senza consumo di energia (ATP)**

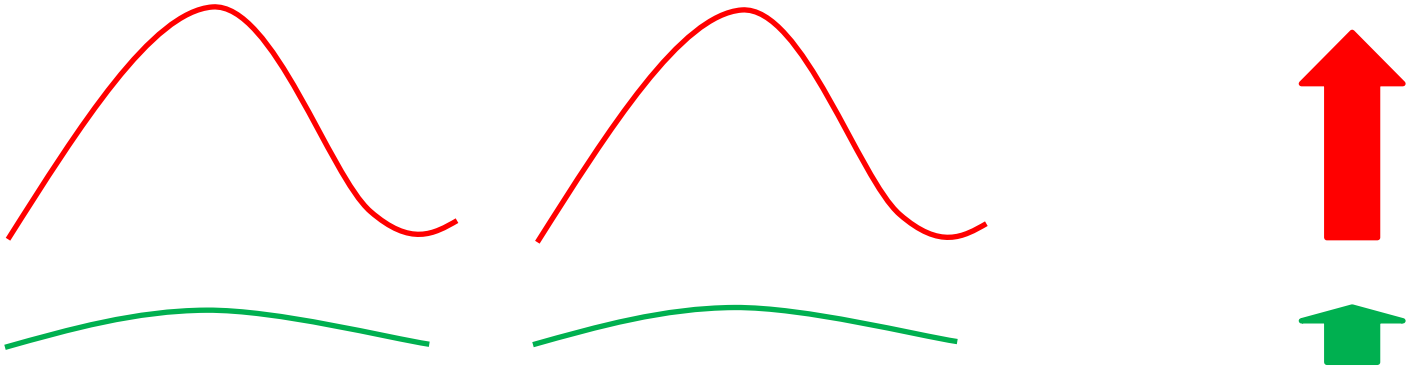
Il trasporto all'interno delle cellule avviene **senza consumo di ATP** ed in funzione del gradiente sangue/citoplasma cellulare

Più è rapido l'incremento della concentrazione nel sangue più è rapida l'entrata nella cellula

Il ruolo centrale degli AAE

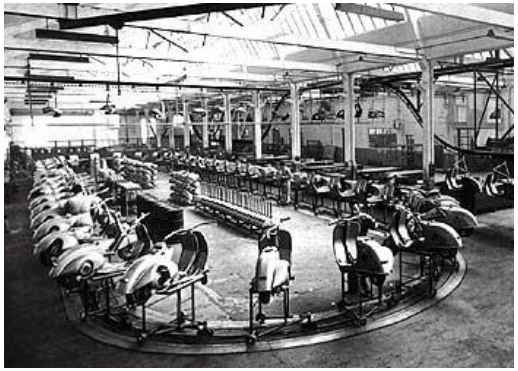
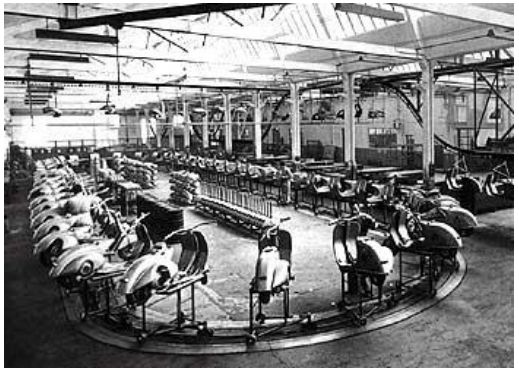
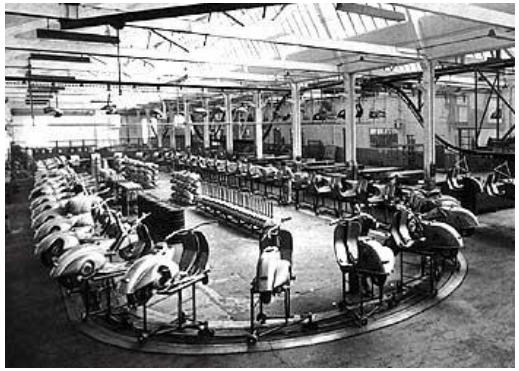


Ciò che fa partire la catena di montaggio è l'aumentata disponibilità cellulare di AA essenziali, indipendentemente dalla concentrazione plasmatica di AAE di partenza



Volpi E, Kobayashi H, Sheffield-Moore M, Mittendorfer B, Wolfe RR. 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(2):250–258.

Il ruolo centrale degli AAE

Per sostenere le sintesi proteiche nel tempo:

Devono essere presenti tutti gli AA essenziali (NON BASTANO I SOLI AA RAMIFICATI o LA SOLA LEUCINA o HMB)

Gli AA essenziali devono rispettare concentrazioni specifiche (ovvero PRECISI RAPPORTI STECHIOMETRICI)

Deve essere somministrato un quantitativo sufficiente a generare un delta di concentrazione plasmatico (ALMENO 4 g di AAE)

Supplementazione con Aminoacidi

Stimolo mitocondriogenesi	Stimolo sintesi proteiche insulino indipendente
Riduzione dello stress ossidativo	

SARCOPENIA =

- DISFUNZIONE MITOCONDRIALE
- INSULINO RESISTENZA
- RIDOTTA CAPACITA' ANTI OSSIDANTE

SONO COME UN FARMACO CHE AGISCE SUI MECCANISMI PATOGENETICI DELLA SARCOPENIA

Aminoacidi e Mitocondri

Cell Metabolism *12*, 362–372, October 6, 2010 ©2010 Elsevier Inc.

Cell Metabolism
Article

Branched-Chain Amino Acid Supplementation Promotes Survival and Supports Cardiac and Skeletal Muscle Mitochondrial Biogenesis in Middle-Aged Mice

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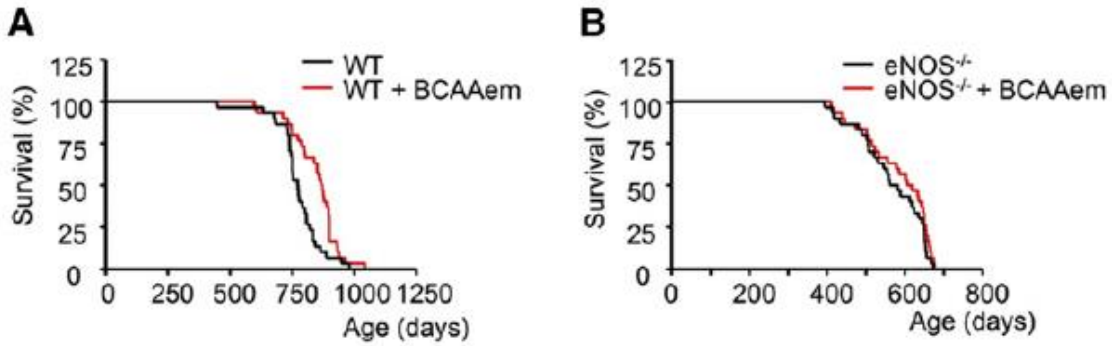


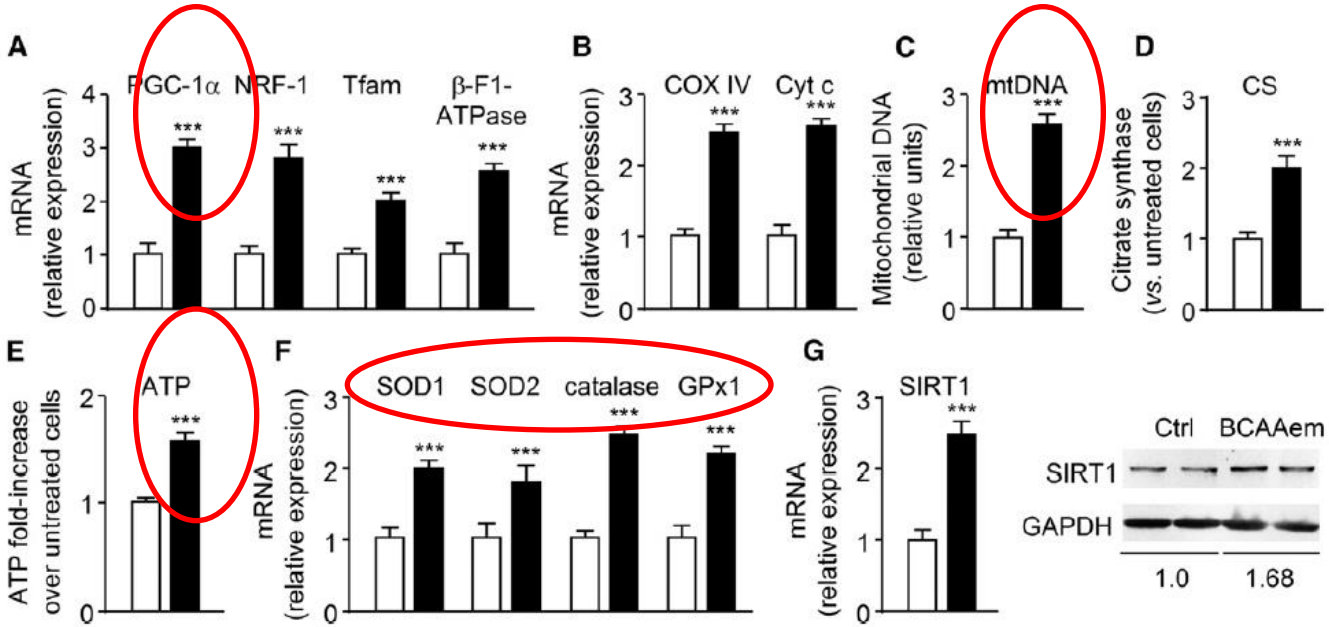
C

	n	mean	median	range	oldest 10%
WT	30	773 ± 17	774	449-979	938 ± 8
WT + BCAAem	30	843 ± 18	869	598-1043	981 ± 10
eNOS $^{-/-}$	30	565 ± 15	572	394-674	666 ± 5
eNOS $^{-/-}$ + BCAAem	30	583 ± 16	612	410-676	673 ± 2

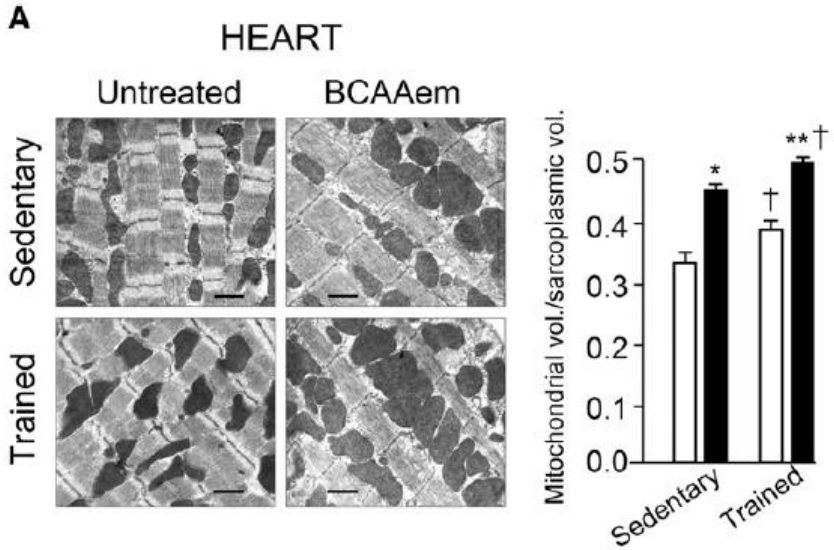
Aminoacidi e Mitocondri

Cell Metabolism

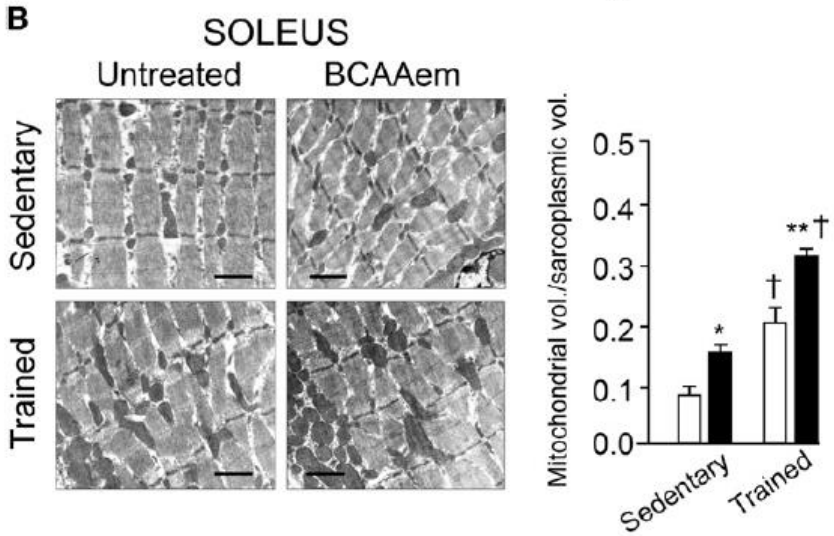
Branched-Chain Amino Acids and Survival



Aminoacidi e Mitocondri

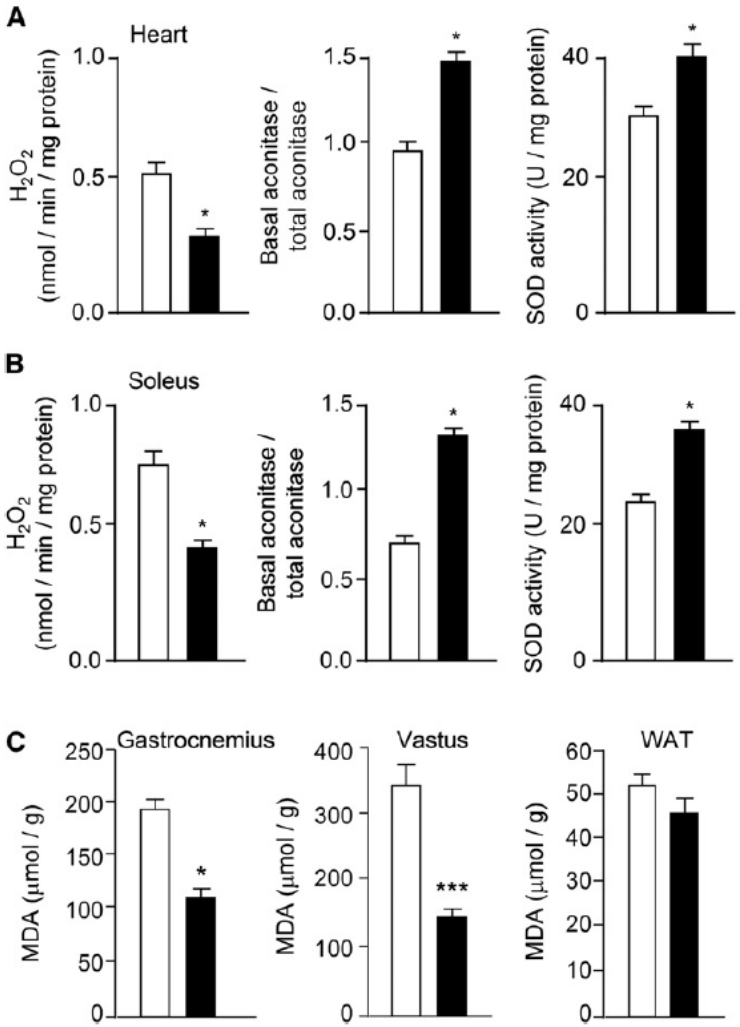


Cuore



Muscolo striato

Aminoacidi e Mitocondri



Gli AAE riducono il danno da stress ossidativo

Figure 6. BCAAem Supplementation Reduces Oxidative Damage in Middle-Aged Mice

(A and B) Mitochondrial H_2O_2 release, basal aconitase/total aconitase ratio, and superoxide dismutase activity (SOD) in heart (A) and soleus muscle (B) from mice supplemented (closed bars) or not (open bars) with BCAAem (*$p < 0.05$ versus untreated mice; n = 10 experiments).

(C) Lipid peroxidation measured as malondialdehyde (MDA) production in skeletal muscles and white adipose tissue (WAT) of BCAAem-treated (closed bars) or not (open bars) animals (n = 5 experiments). All data represent mean ±SEM. See also Figure S5.

Figure 6. BCAAem Supplementation Reduces Oxidative Damage in Middle-Aged Mice

EAAs Stimolano le Sintesi Proteiche in modo Indipendente dall'Insulina

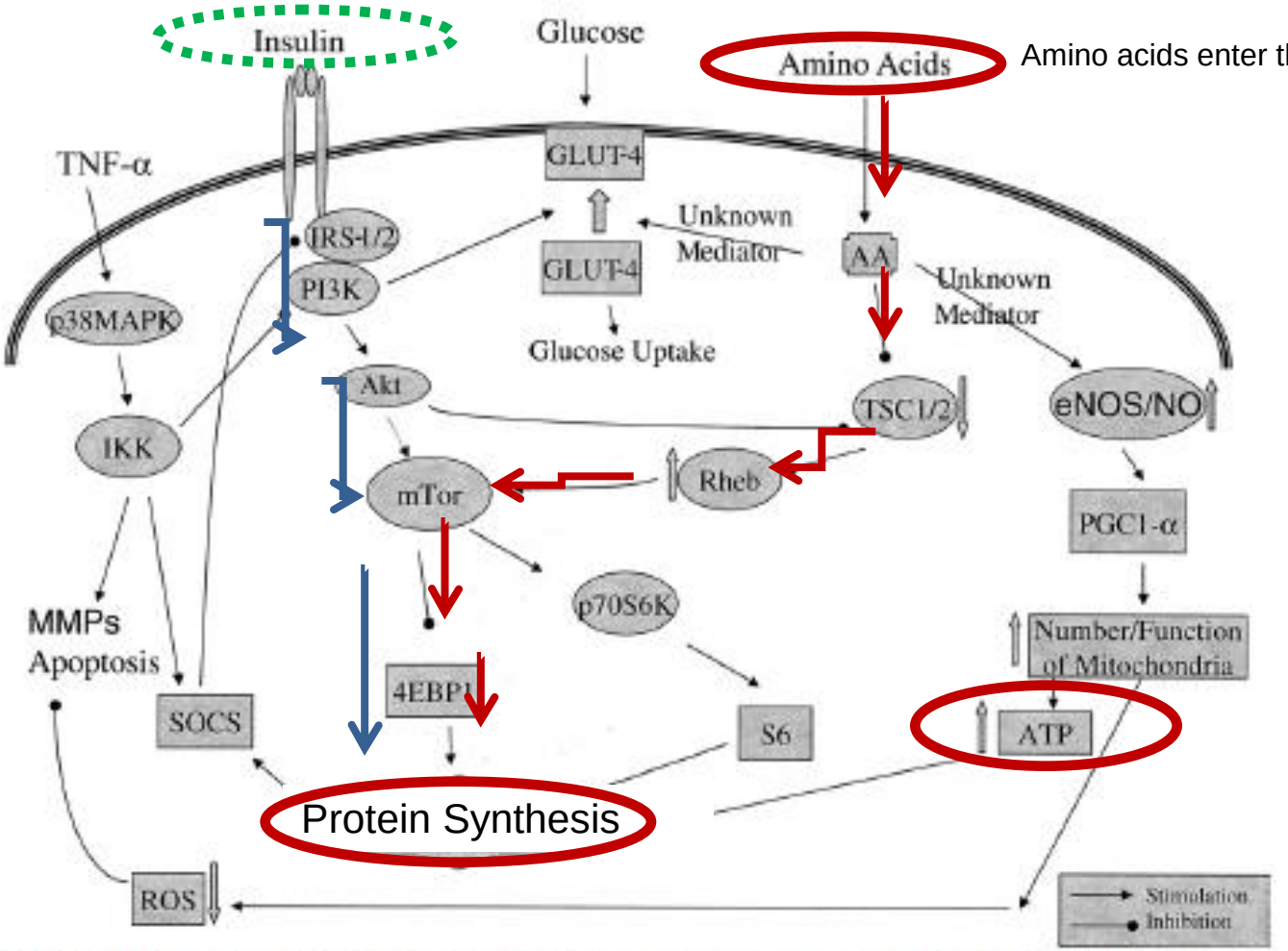


Figure 1. Intracellular regulation of catabolic/anabolic metabolism via mammalian target of rapamycin (mTOR) and other routes. AA = amino acid; Akt = protein kinase B; ATP = adenosine triphosphate; 4EBP1 = eIF4E-binding protein–1; eNOS = endothelial nitric oxide synthase; GLUT-4 = glucose transporter–4; IKK = IκB kinase; IRS = insulin receptor substrates; MAPK = mitogen-activated protein kinase; MMP = matrix metalloproteinase; NO = nitric oxide; p70S6K = p70S6-kinase; PGC1-α = peroxisome proliferator-activated receptor–γ coactivator-1α; P[illegible] *Ras* homolog enriched in brain; ROS = reactive oxygen species; S6 = S6-kinase; SOCS = suppression of cy[illegible] factor–α; TSC1/2 = tuberous sclerosis complex; ↑ = increase; ↓ = decrease.

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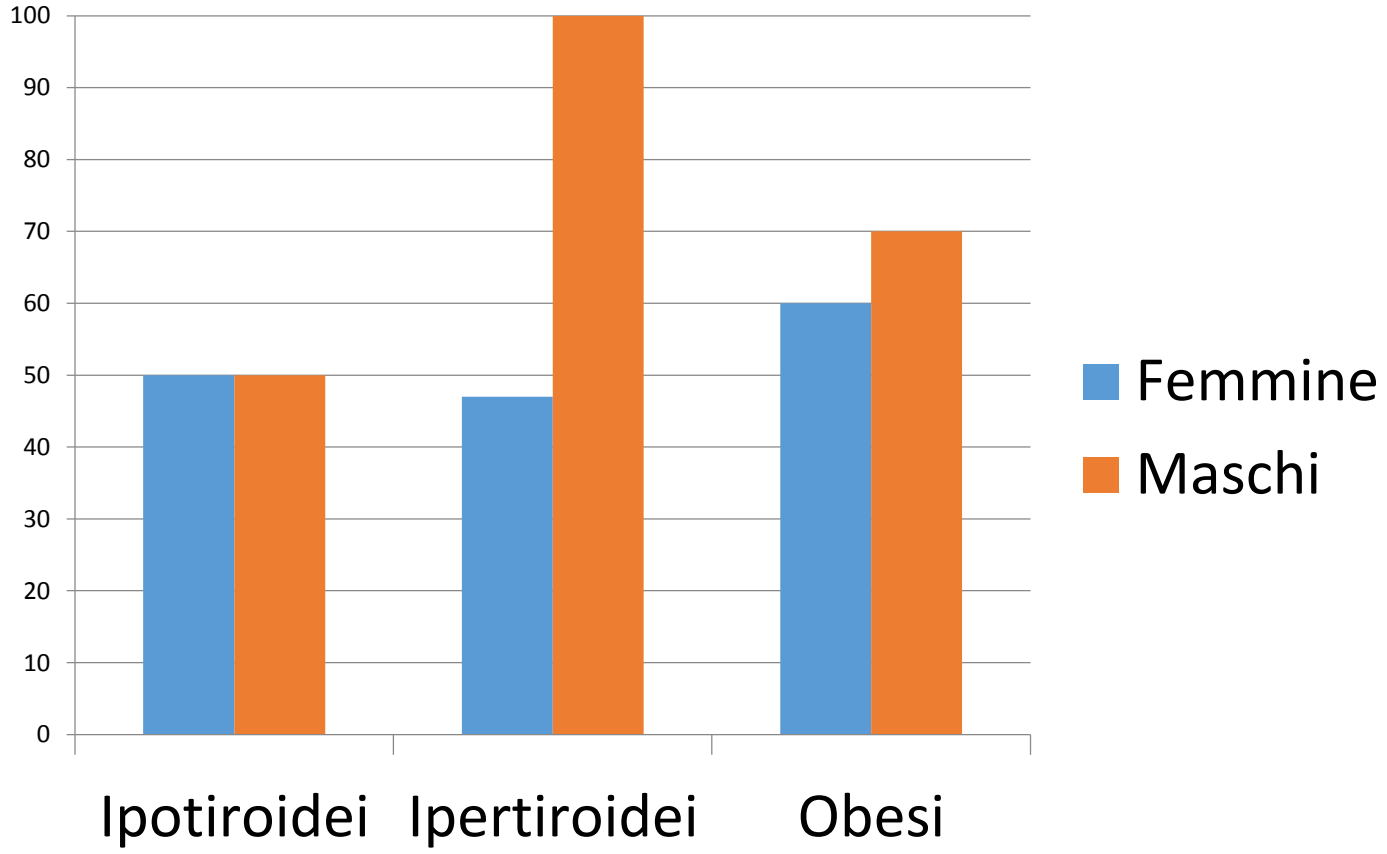
ESPERIENZA PRESSO UOC MALATTIE ENDOCRINE H SANT'ANNA

	BIA	HANDGRIP
IPOTIROIDEI	117 (101F e 16M)	108 (95F e 13M)
IPERTIROIDEI	53 (40F e 13M)	27 (19F e 8M)
OBESI	69 (51F e 18M)	62 (45F e 17M)

CONSIDERATO IL VALORE INDIPENDETE DELLA FORZA MUSCOLARE

Handgrip	Adeguato	Insufficiente
IPOTIROIDEI	47F e 6M	48F e 7M
IPERTIROIDEI	11F e 0M	8F e 8M
OBESI	18F e 5M	27F e 12M

Percentuale di soggetti con deficit di forza muscolare



GRAZIE PER L'ATTENZIONE

SINut

Società Italiana di Nutraceutica

VI CONGRESSO NAZIONALE