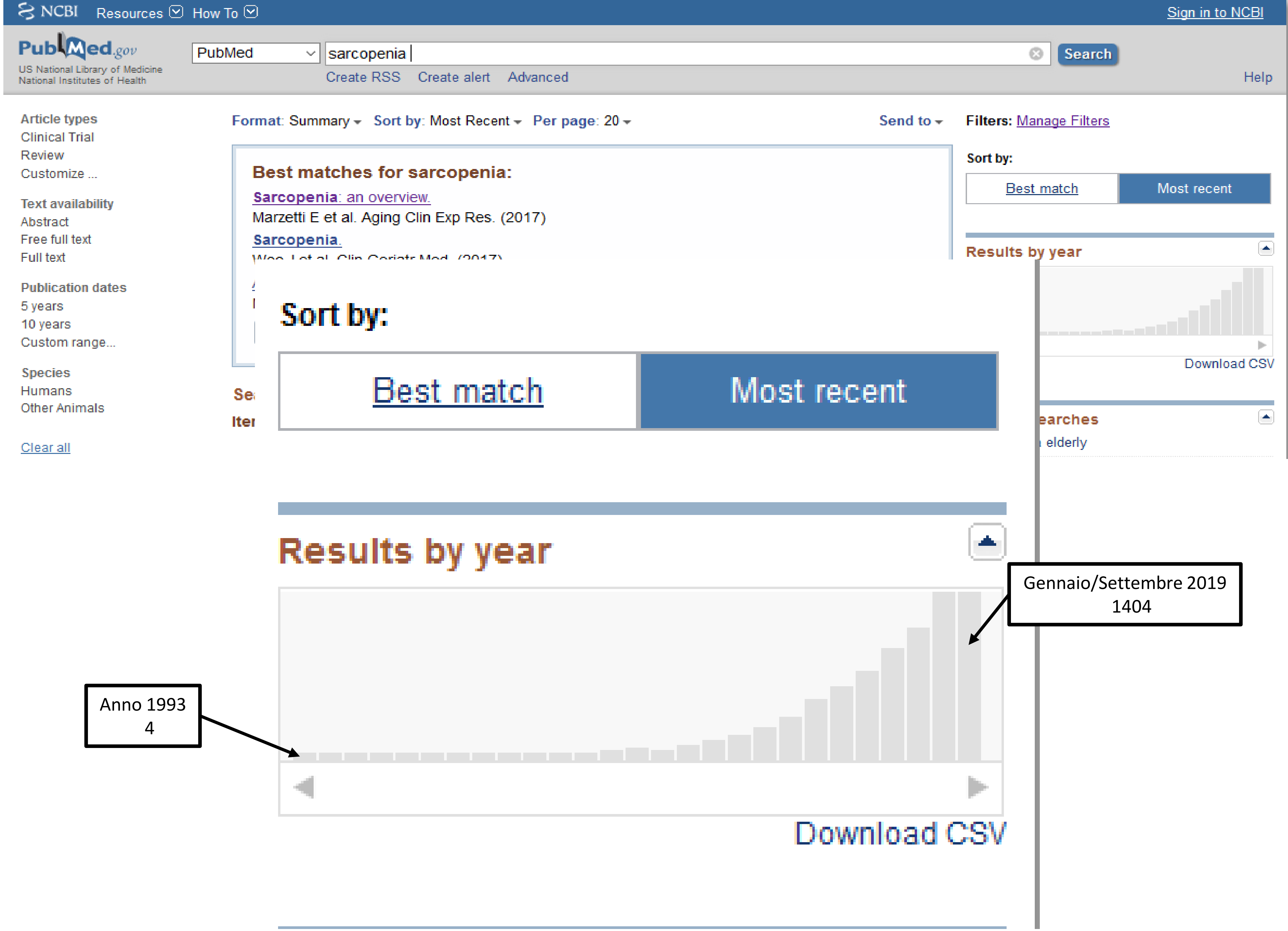
Sarcopenia
(approccio nutrizionale)

Federico Vignati

UOC Malattie Endocrine e Diabetologia
AO Sant'Anna Como
ASST lariana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Best matches for sarcopenia:
Sarcopenia: an overview.
Marzetti E et al. Aging Clin Exp Res. (2017)
Sarcopenia.
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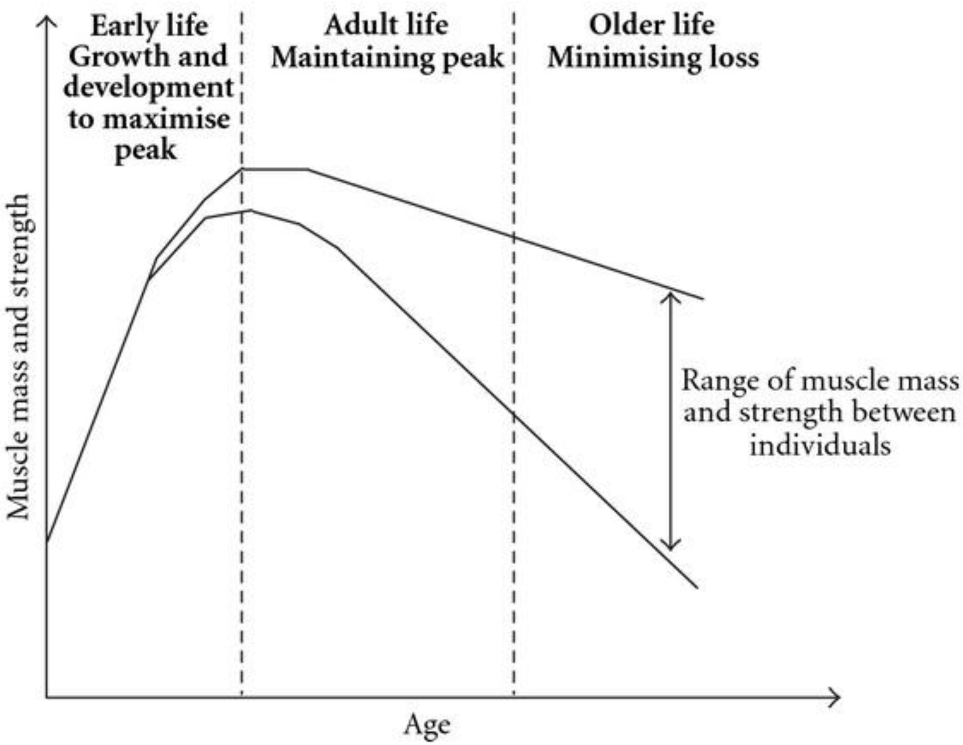
Modificazioni della massa muscolare con l'età



Ciò che caratterizza la popolazione anziana sia sana che, a maggior ragione, malata, è il progressivo declino della massa e della funzione muscolare

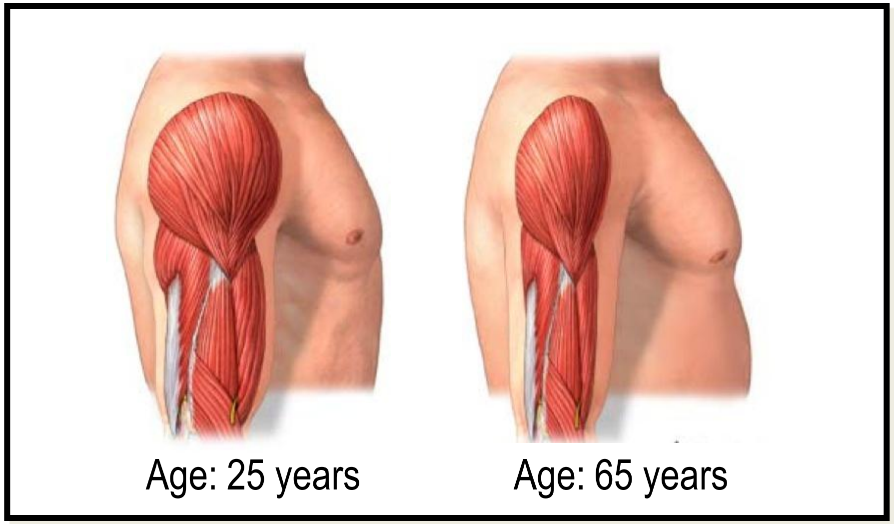
i.e.

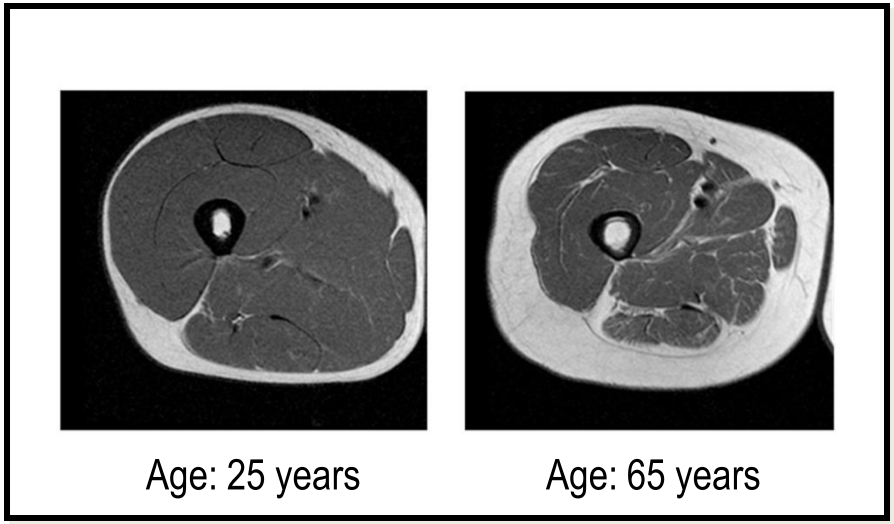
SARCOPENIA

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

What Is Sarcopenia?

Sarcopenia is defined as age-associated loss of muscle mass, strength, and function (Evans et al. 2004)

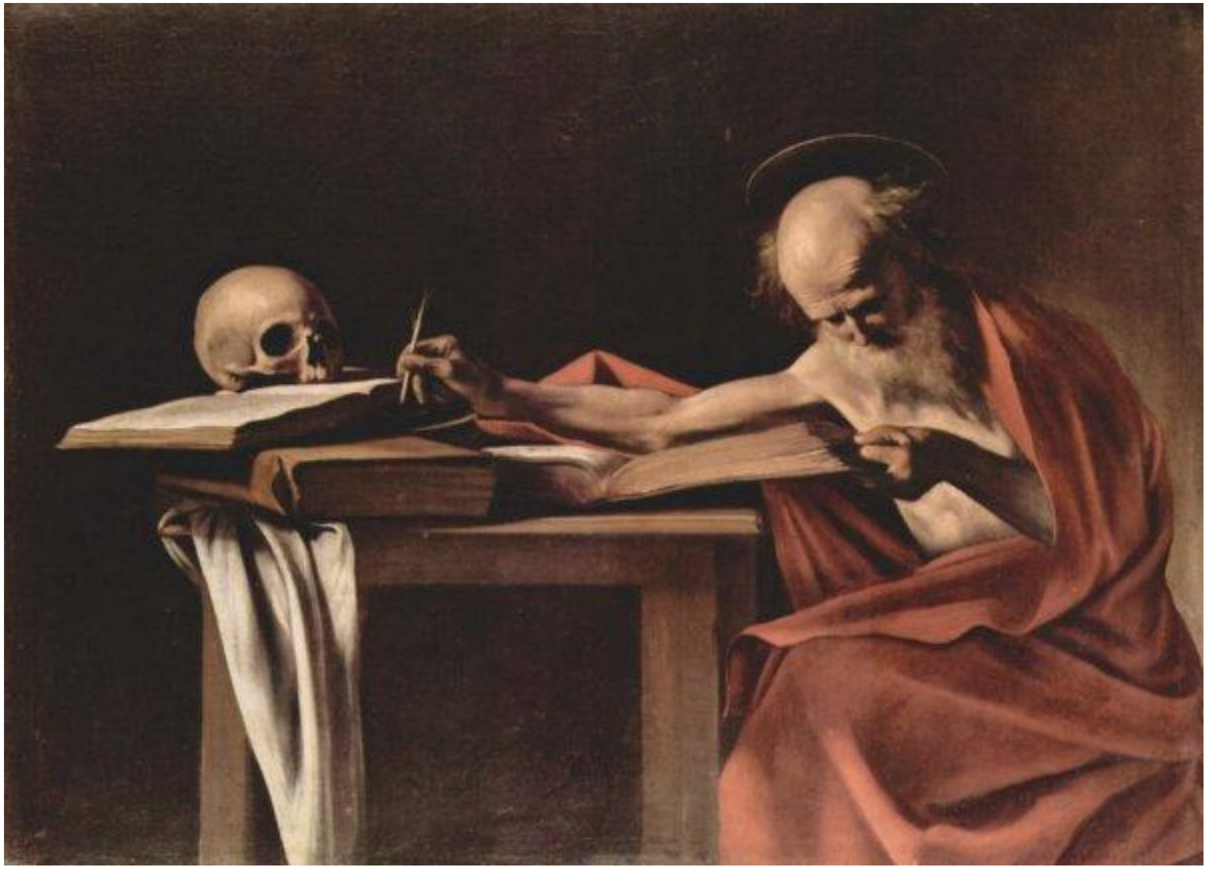




Muscle mass: decrease in muscle fibers
Muscle quality: remaining fibers becoming atrophic

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



Definizione della sarcopenia

La sarcopenia è la perdita associata all'età di massa e funzione muscolare. Le cause della sarcopenia sono multifattoriali e possono includere malattie, modificazioni della funzione endocrina, malattie croniche, infiammazione, insulino resistenza e deficit nutrizionali. Sebbene la cachessia possa essere una componente della sarcopenia, le due condizioni non sono la stessa cosa. La diagnosi di sarcopenia dovrebbe essere considerata in tutti i pazienti anziani in cui si osservi un declino della funzione fisica, della forza o dello stato generale di salute. La sarcopenia dovrebbe essere specificamente considerata in pazienti allettati, che non siano in grado di alzarsi da una sedia o che abbiano una camminata con velocità inferiore ad 1 metro al secondo ed in quelli con un rapporto massa magra/massa grassa appendicolare < di 2 DS rispetto alla popolazione giovane.

European Working Group on Sarcopenia in Older People

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

Inquadramento di Sarcopenia

European Working Group on Sarcopenia in Older People[1]

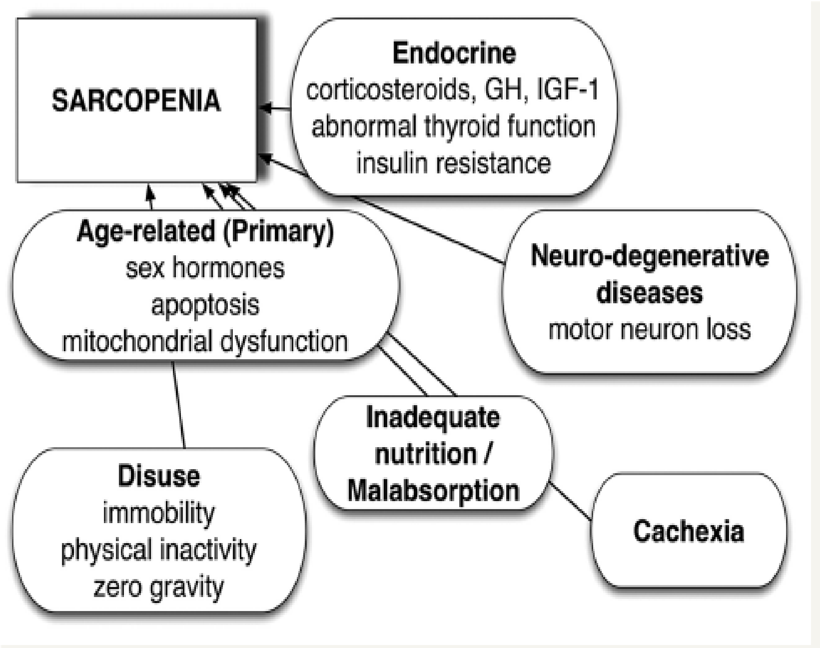


Table 2. Sarcopenia categories by cause

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

L'esercizio fisico: una via fondamentale non sempre percorribile

L'esercizio fisico è fondamentale per il mantenimento e l'accrescimento della massa e della forza muscolare[1,2]

In molti soggetti anziani la possibilità di praticare esercizio è compromessa da disabilità, fragilità o malattie (*ie* allettamento) [3]

In questo contesto il controllo dell'intake proteico e aminoacidico rappresenta una delle poche alternative per prevenire/rallentare il catabolismo muscolare [4]

1) Dela F and Kjaer M. Resistance training, insulin sensitivity and muscle function in the elderly. Essays Biochem. (2006) **42**, (75–88)
2) Taaffe DR. Sarcopenia--exercise as a treatment strategy. Aust Fam Physician. 2006 Mar;35(3):130-4.
3) Kortebein P, Ferrando A, Lombeida J, Wolfe R, Evans WJ. Effect of 10 Days of Bed Rest on Skeletal Muscle in Healthy Older Adults. JAMA. 2007;297(16):1769-1774.
4) Paddon-Jones D et al. Essential amino acid and carbohydrate supplementation ameliorates muscle protein loss in humans during 28 days bedrest . J Clin Endocrinol Metab. 2004 Sep;89(9):4351-8.

La linea di intervento nutrizionale: il «cuore» del problema

Molti anziani non consumano un sufficiente quantitativo di proteine e ciò provoca una riduzione della massa magra e a un deterioramento funzionale[1]

L'apporto proteico raccomandato di proteine è di 0.8 g/kg/die e circa il 40% degli ultrasettantenni non raggiunge questo quantitativo[2]

Anche i soggetti anziani che hanno un apporto proteico entro le dosi raccomandate, possono avere un bilancio azotato negativo e potrebbero necessitare di un apporto proteico maggiore rispetto a quanto raccomandato per mantenere il tessuto muscolare [3]

1) Bartali B et al. Low nutrient intake is an essential component of frailty in older persons. J Gerontol A Biol Sci Med Sci. 2006;61:589–593.
2) Houston DK et al. Dietary intake is associated with lean mass change in older community-dwelling adults: the health aging and body composition (The Health ABC Study) study. Am J Clin Nutr. 2008;87:150–155
3) Campbell WW, Trappe TA, Wolfe RR, Evans WJ. The recommended dietary allowance for protein may not be adequate for older people to maintain skeletal muscle. J Gerontol A Biol Sci Med Sci. 2001;56:M373–M380

Approccio nutrizionale nella sarcopenia

Quale è l’apporto proteico ottimale?

Supplementazione nella sarcopenia

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.

PERCHE' LA POPOLAZIONE ANZIANA NECESSITA DI UN MAGGIOR APPORTO PROTEICO PER OTTENERE LO STESSO EFFETTO ANABOLICO DEL GIOVANE?

Skeletal muscle protein metabolism in the elderly: Interventions to counteract the 'anabolic resistance' of ageing

Leigh Breen and Stuart M Phillips*

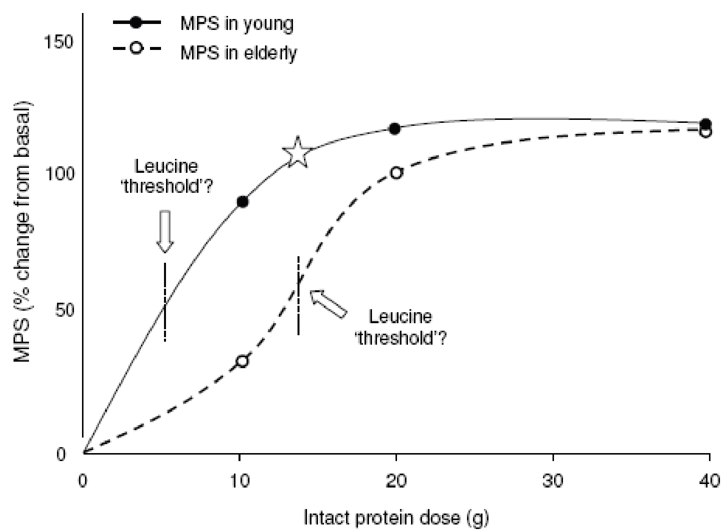


Figure 2 Dose response curve of MPS in elderly and young muscle with protein ingestion at rest. MPS in the young is stimulated above basal with ~2.5 g of crystalline EAA (found in ~5 g of intact protein) before reaching a plateau at ~10 g of crystalline EAA (found in ~20 g of intact protein). In the elderly, MPS is increased above rest after ingestion of 20 g of whey protein and, like younger adults, the response plateaus thereafter. Star indicates MPS in both young and elderly after 6.7 g of EAA (typically found in 15 g of whey protein) enriched with leucine (41% or ~2.8 g) [36]. Finely dashed lines indicate the hypothesized leucine 'threshold' which must be surpassed in order to stimulate a robust increase in rates of MPS. The threshold may be considerably lower in the young (<1 g leucine in 2.5 g of crystalline EAA's) compared with the elderly (~1.5-2 g of leucine contained in 15-20 g of whey protein).

Nutr Metab 2011; 8:68

Raccomandazioni nutrizionali sarcopenia

JAMDA 14 (2013) 542–559

ELSEVIER

JAMDA

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Special Article

Evidence-Based Recommendations for Optimal Dietary Protein Intake in Older People: A Position Paper From the PROT-AGE Study Group

Jürgen Bauer MD [a,*], Gianni Biolo MD, PhD [b], Tommy Cederholm MD, PhD [c], Matteo Cesari MD, PhD [d],

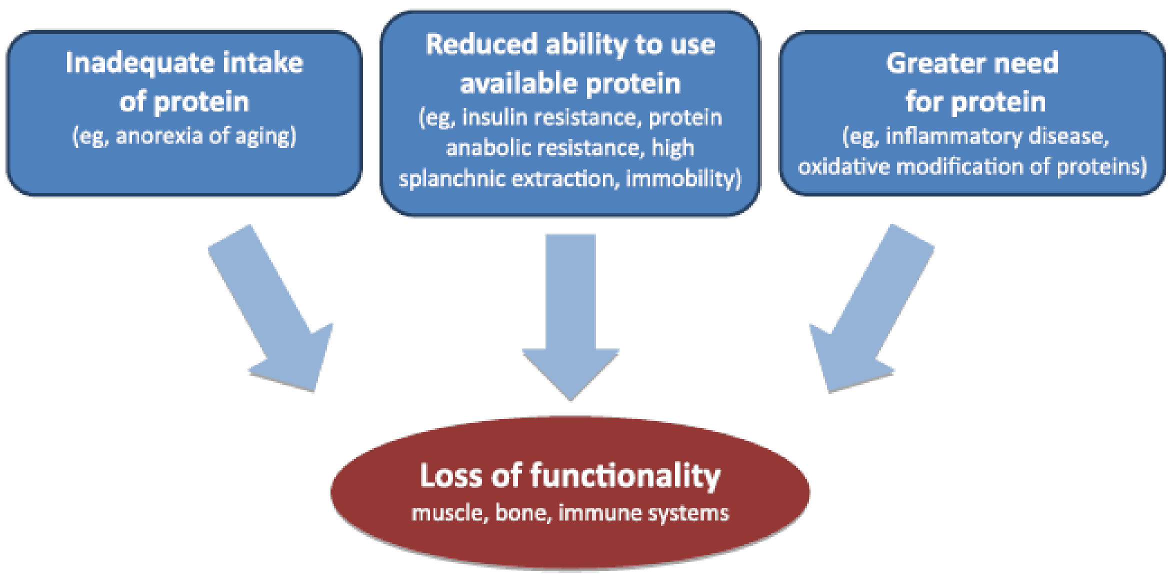

Fig. 1. Aging-related causes of protein shortfall. Such protein deficits have adverse consequences, including impairment of muscular, skeletal, and immune function.

JAMDA 14 (2013) 542–559

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Speci

Evic
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Peter
Yves

Recommended Protein Intake for Healthy Older People: Current Recommendations and Evolving Evidence

ANZIANI SANI

PROT-AGE recommendations for dietary protein intake in *healthy* older adults

- To maintain and regain muscle, older people need more dietary protein than do younger people; older people should consume an average daily intake in the range of 1.0 to 1.2 g/kg BW/d.
- The per-meal anabolic threshold of dietary protein/amino acid intake is higher in older individuals (ie, 25 to 30 g protein per meal, containing about 2.5 to 2.8 g leucine) in comparison with young adults.
- Protein source, timing of intake, and amino acid supplementation may be considered when making recommendations for dietary protein intake by older adults.
- More research studies with better methodologies are desired to fine tune protein needs in older adults.

JAMDA 14 (2013) 542–559

JAMDA

journal homepage: www.jamda.com

Special Article

Evidence-Based Recommendations for Optimal Dietary Protein Intake in Older People: A Position Paper From the PROT-AGE Study Group

Jürgen Ba
Alfonso J.
Peter Steh
Yves Boiri

PhD[d],
hD[h],
, PhD[l],

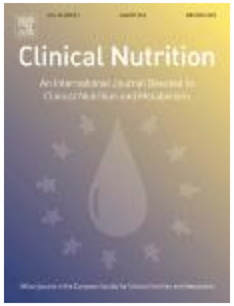
Protein Recommendations in Acute and Chronic Diseases

ANZIANI con PATOLOGIE ACUTE o CRONICHE

PROT-AGE recommendations for protein levels in geriatric patients with specific acute or chronic diseases

- The amount of additional dietary protein or supplemental protein needed depends on the disease, its severity, the patient's nutritional status prior to disease, as well as the disease impact on the patient's nutritional status.
- Most older adults who have an acute or chronic disease need more dietary protein (ie, 1.2–1.5 g/kg BW/d); people with severe illness or injury or with marked malnutrition may need as much as 2.0 g/kg BW/d.
- Older people with severe kidney disease (ie, estimated glomerular filtration rate [GFR] < 30 mL/min/1.73m^2) who are not on dialysis are an exception to the high-protein rule; these individuals need to limit protein intake.

Protein intake and exercise for optimal muscle function with aging: Recommendations from the ESPEN Expert Group



- Nicolaas E.P. Deutz[a], Jürgen M. Bauer[b],Rocco Barazzoni[c], Gianni Biolo[c], Yves Boirie[d], Anja Bosy-Westphal[e],
- Tommy Cederholm[f, g], Alfonso Cruz-Jentoft[h], Zeljko Krznariç[i], K. Sreekumaran Nair[j],Pierre Singer[k], Daniel Teta[l], Kevin Tipton[m], Philip C. Calder[n, o]

Soggetti anziani sani	**1,0 – 1,2 g/kg /die**
Soggetti anziani malnutriti o a rischio di malnutrizione per la presenza di malattie acute o croniche	**1,2 – 1,5 g/kg /die**
Soggetti anziani con malattie gravi o ferite/ustioni	**> 1,5 g/kg /die**

Tutte le persone anziane dovrebbero fare:
Attività fisica giornaliera o esercizio fisico (aerobico o di resistenza) il più a lungo possibile

Clinical Nutrition 24 April 2014

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.

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.

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)

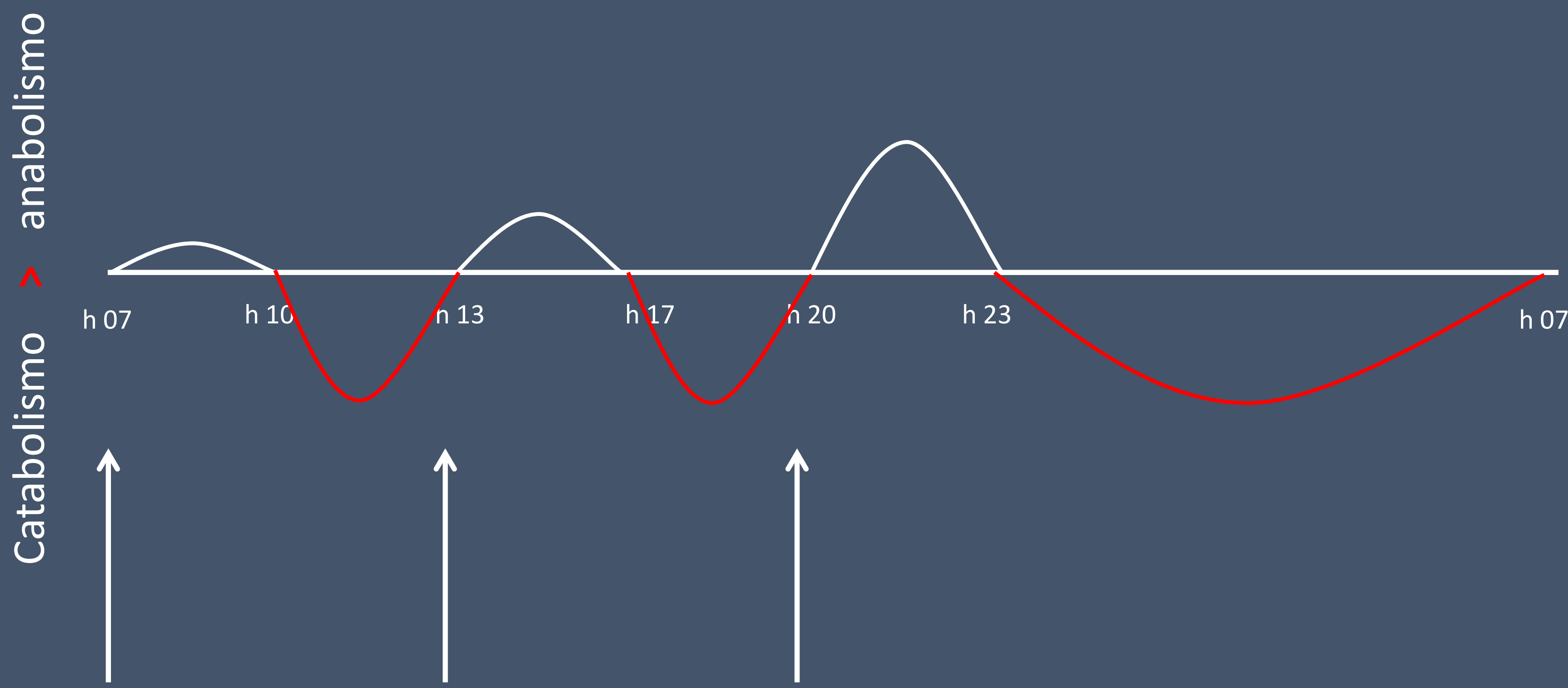
Due livelli di intervento: Lifestyle e Crisi

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

UN NUOVO MODELLO DI ALIMENTAZIONE

ORA

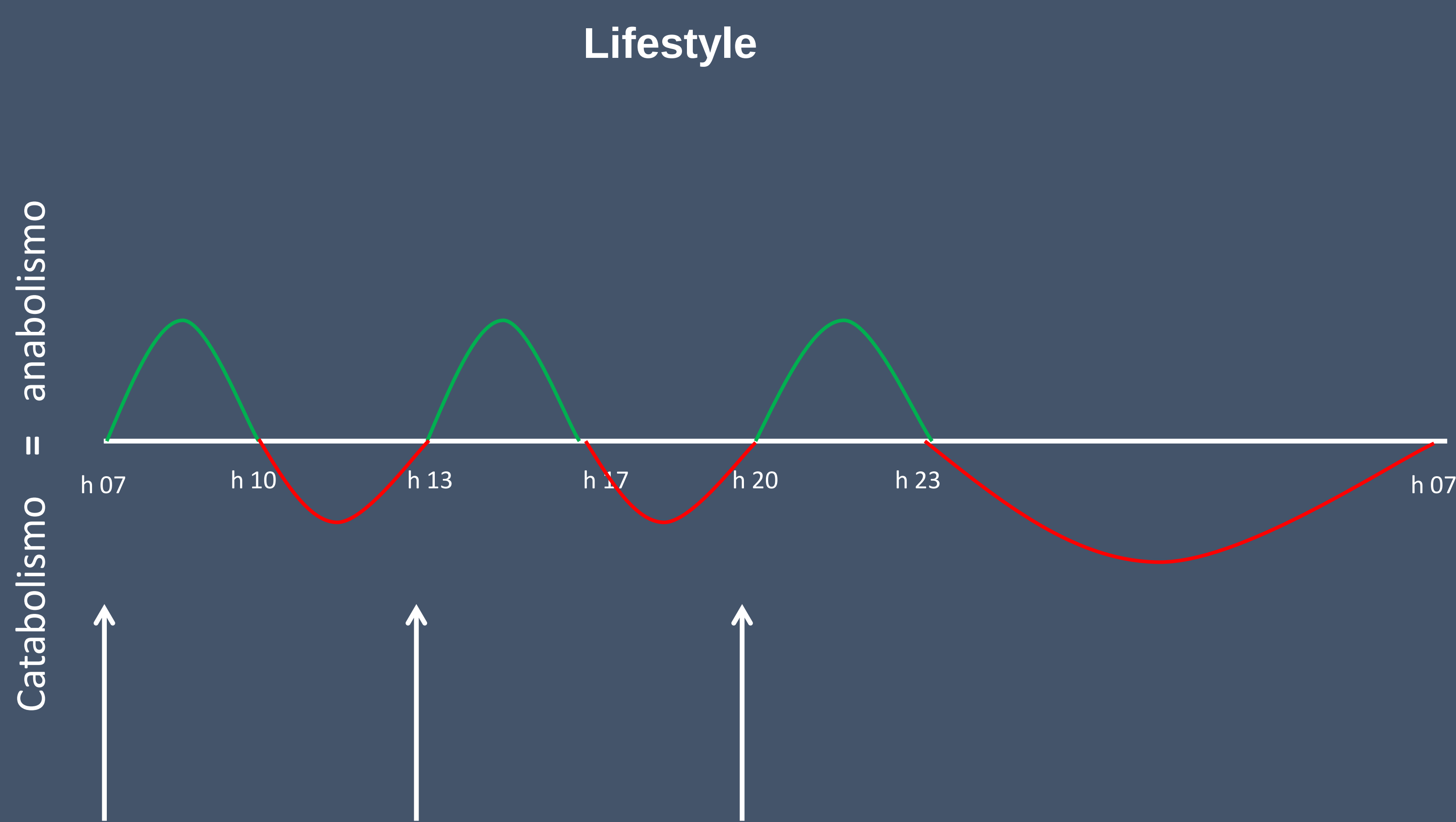


Colazione
ipoproteica

Pranzo
ipoproteico

Cena
30-50 g
proteine

UN NUOVO MODELLO DI ALIMENTAZIONE

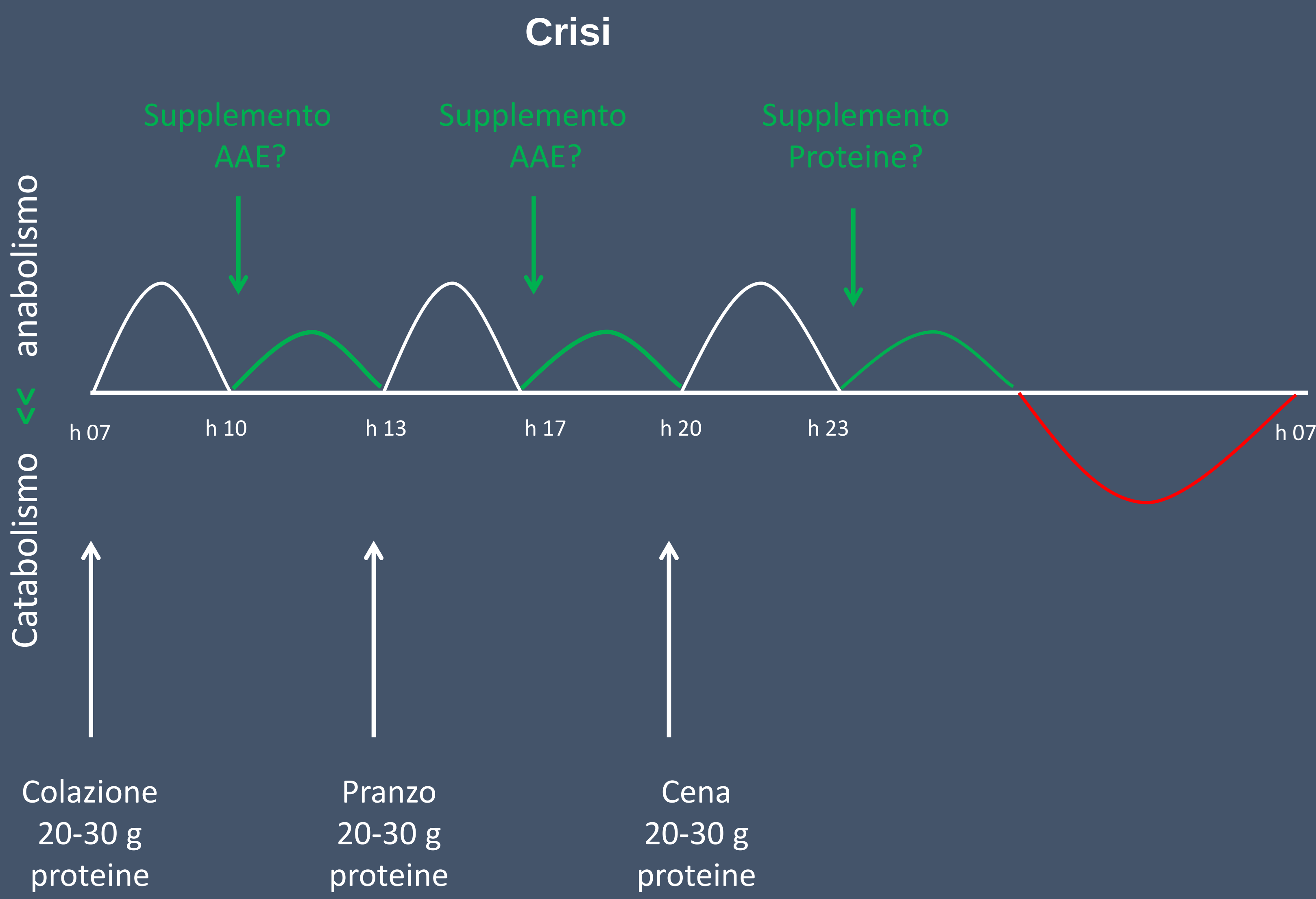


Colazione
20-30 g
proteine

Pranzo
20-30 g
proteine

Cena
20-30 g
proteine

UN NUOVO MODELLO DI ALIMENTAZIONE



Cell Metabolism
Article

Cell PRESS

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

Cell Metabolism
Article

Cell PRESS

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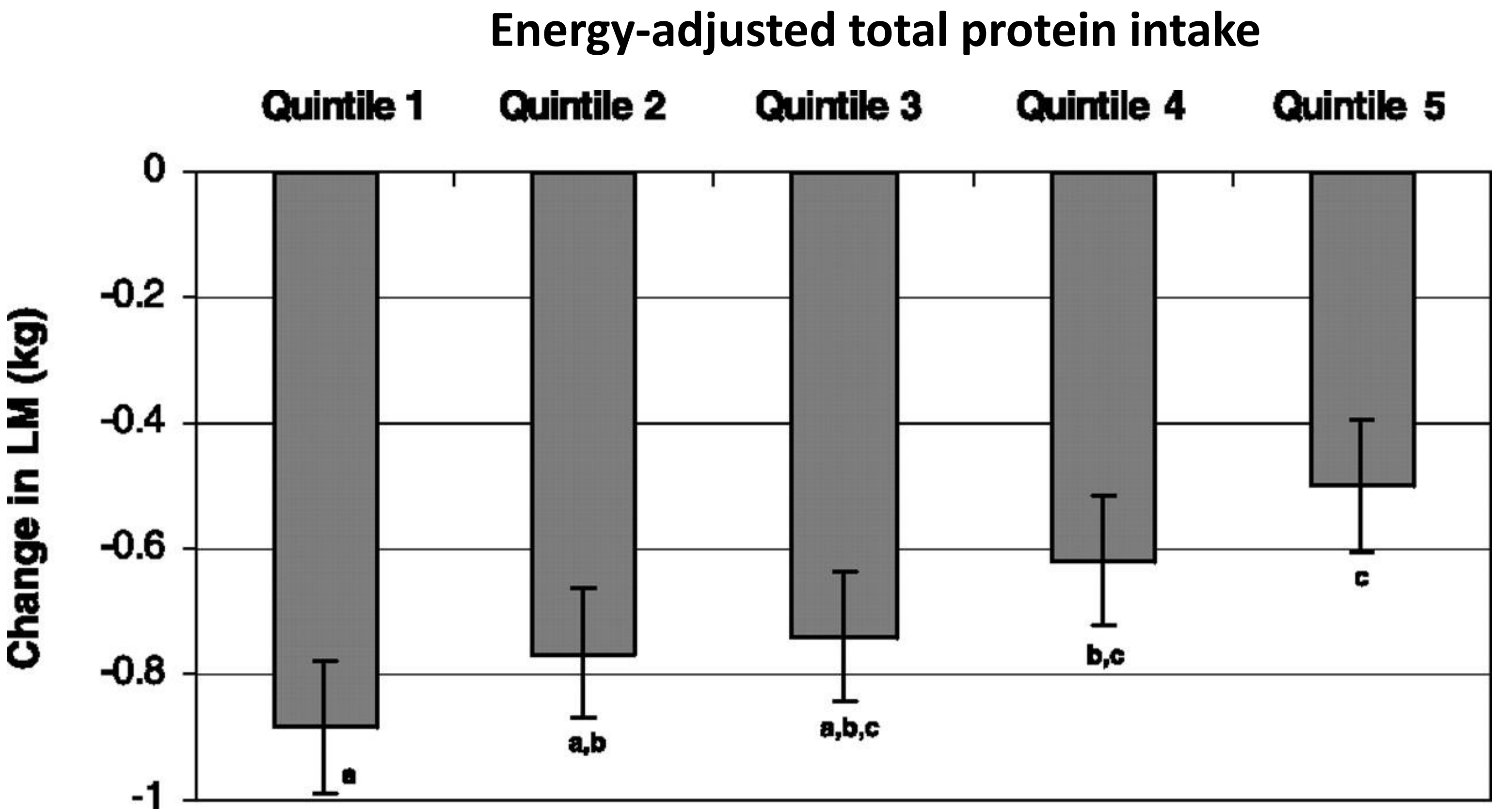
Levine et al., Cell Metab 19: 407-417, 2014

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

Razionale della Supplementazione con Proteine

Ruolo delle proteine alimentari

The role of dietary protein in optimizing muscle mass, function and health outcomes in older individuals

Robert R. Wolfe*

La disponibilità di **aminoacidi essenziali** regola la sintesi proteica muscolare

Una sintesi proteica stimolata si traduce in un incremento della massa, della forza e della funzione muscolare

Maggiore massa e forza muscolare e migliore funzione sono correlate ad un miglioramento della salute

Whereas that cause-effect relationship between muscle mass, strength and function and health outcomes is subject to debate, it is clear that increased muscle mass and function in the elderly translates to an improved ability to perform activities of daily living and therefore quality of life. Improved quality of life is sufficient reason to increase dietary protein intake. Since there is no evidence that a reasonable increase in dietary intake adversely affects health outcomes, and deductive reasoning suggests beneficial effects of a higher protein intake, it is logical to recommend that the optimal dietary protein intake for older individuals is greater than the recommend dietary allowance of 0·8 g protein/kg/day.

British Journal of Nutrition (2012), **108**, S88–S93

Quando pensate alla supplementazione con proteine cosa vi viene in mente?

- Proteine vegetali (soia, pisello, ecc.)
- Caseina
- Proteine del siero del latte (Whey)
- Collagene
- Whey + leucina
- Whey + caseina
- Whey + beta-IDROSSIMETILBUTIRRATO
  (β-HMB)

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 LOSTESSO 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.

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

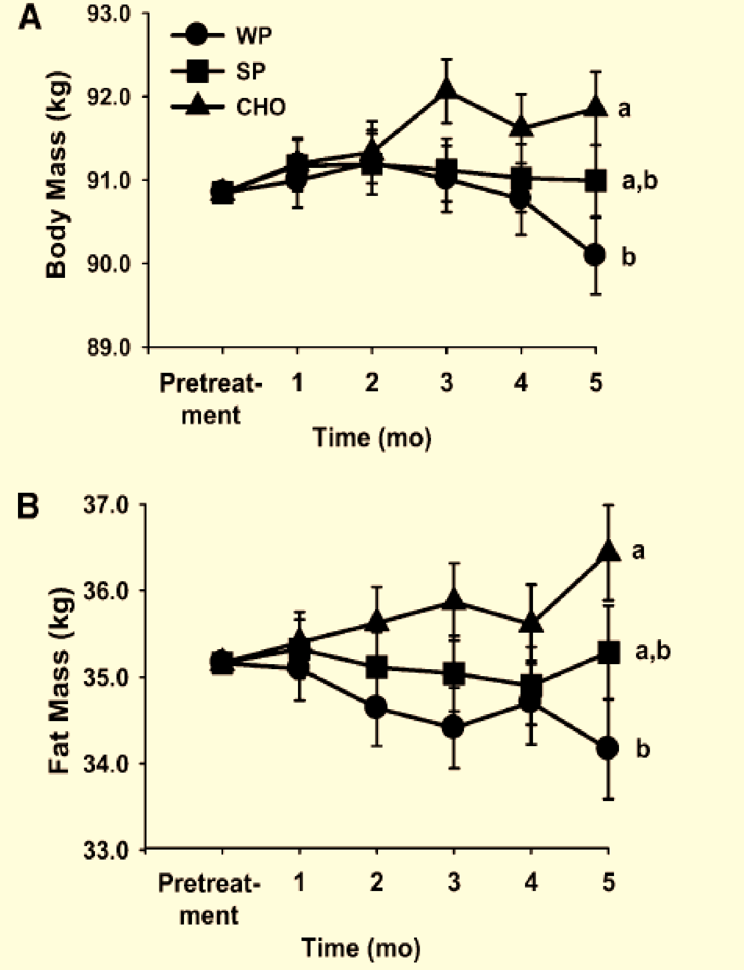
David J. Baer,* Kim S. Stote, David R. Paul, G. Keith Harris, William V. Rumpler, and Beverly A. Clevidence

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]

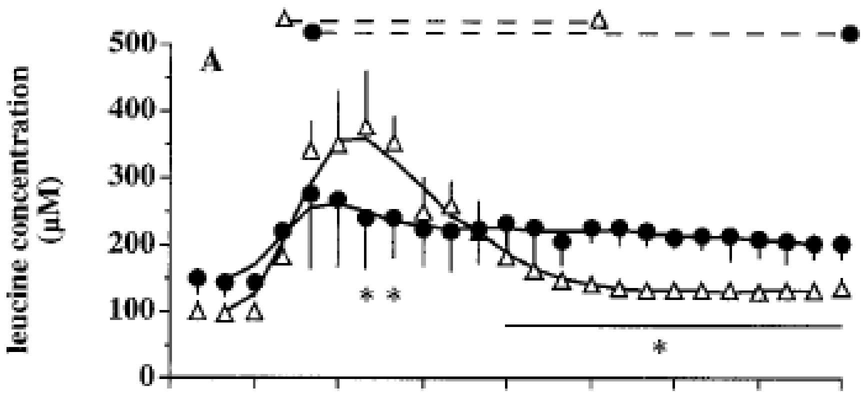
	CHO	WP	SP
		g/packet	
Weight	52	51	52
Protein	0.6	27.5	28.1
Moisture	1.7	2.2	1.8
Fat, acid hydrolysis	0.7	1.5	2.0
Ash	1.0	1.4	2.7
Total carbohydrate	48.0	18.4	17.4
Calcium	0.20	0.22	0.25
para-Aminobenzoic acid	0.2	0.2	0.2
		mg/packet	
L-Aspartic acid	36.4	3060	3200
L-Threonine	18.2	1850	945
L-Serine	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	1600
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.



CARATTERISTICHE DELLE PROTEINE

La velocità di digestione come fattore condizionante il meccanismo d’azione



A, B, C	● ^{13}C-CAS	△ ^{13}C-WP

FIG. 2. (*A*) Plasma leucine concentrations, (*B*) enrichments of the i.v. infused $^2H_3$ tracer, and (*C*) enrichments of the orally administered ^{13}C tracer, after a labeled WP meal (^{13}C-WP study) and a CAS meal (^{13}C-CAS study). *, Statistical differences between the two protein meals ($P < 0.05$). The dashed lines at the top of each panel indicate a significant difference from baseline ($P < 0.05$) within each study.

Boire Y et al Proc Natl Acad Sci 23, 1997 vol. 94 no. 26

CARATTERISTICHE DELLE PROTEINE

Incrememento degli aminoacidi plasmatici dopo pasto con caseina o sieroproteine di latte dopo 100 e 300 min nell'uomo

Table 2. Amino acid intake, baseline plasma amino acid concentrations, and relative increase (%) above baseline of amino acid concentrations after 100 and 300 min

	Amino acid intake, μmol/kg			100 min, increase above baseline, %		300 min, increase above baseline, %	
Amino acid	CAS	WP	Baseline amino acid concentration, μM	CAS	WP	CAS	WP
Asp	509	202	7 ± 2	44 ± 93	113 ± 58*	6 ± 41	−6 ± 25
Thr	242	126	114 ± 21	44 ± 15*	110 ± 25*†	27 ± 18*	6 ± 12
Ser	247	156	104 ± 17	18 ± 12*	48 ± 17*	11 ± 17	−4 ± 6†
Asn	—	—	65 ± 19	32 ± 22*	71 ± 25*†	18 ± 22	−26 ± 25
Glu	773	670	110 ± 43	14 ± 11*	46 ± 16*	12 ± 12*	−10 ± 7*†
Gln	—	—	513 ± 87	5 ± 10	21 ± 7*	7 ± 17	−1 ± 9
Pro	304	398	175 ± 31	97 ± 34*	68 ± 31*	67 ± 23*	−5 ± 15†
Gly	128	87	190 ± 29	−1 ± 7	−2 ± 11*	−4 ± 10	−21 ± 11*
Ala	328	128	291 ± 83	10 ± 12	45 ± 28*	−7 ± 13	−24 ± 14*
Val	251	203	226 ± 39	54 ± 9*	97 ± 15*	48 ± 17*	13 ± 6†
Met	82	73	20 ± 5	81 ± 38*	172 ± 75*	34 ± 21*	2 ± 41†
Ile	222	135	60 ± 13	90 ± 26*	274 ± 64*†	62 ± 43*	11 ± 14†
Leu	382	380	132 ± 25	77 ± 24*	236 ± 56*†	61 ± 30*	29 ± 11*†
Tyr	119	114	58 ± 18	75 ± 41*	86 ± 28*	40 ± 22*	−8 ± 14†
Phe	126	119	49 ± 10	34 ± 17*	46 ± 21*	19 ± 12*	−12 ± 11†
Lys	379	183	174 ± 53	104 ± 124*	140 ± 54*†	78 ± 131*	8 ± 11
His	68	68	90 ± 12	16 ± 18	32 ± 19*†	14 ± 10*	6 ± 10
Arg	89	67	69 ± 19	48 ± 22*	78 ± 30*	17 ± 22	−7 ± 16

*P < 0.05 vs. baseline; †P < 0.05 CAS vs. WP.

Supplementazione con Whey Protein

Stimulation of net muscle protein synthesis by whey protein ingestion before and after exercise

Kevin D. Tipton,[1] Tabatha A. Elliott,[2,3] Melanie G. Cree,[2,3]
Asle A. Aarsland,[2,4] Arthur P. Sanford,[2,3] and Robert R. Wolfe[2,3]

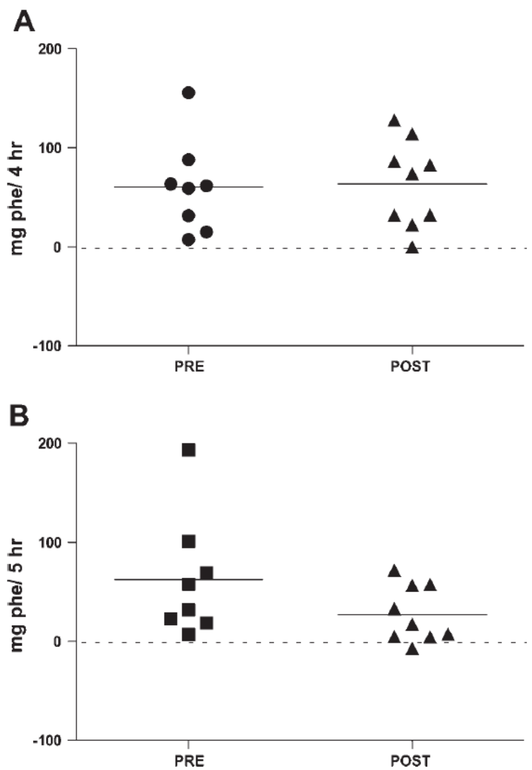


Fig. 5. Individual and mean values for phenylalanine uptake (area under the curve for net balance) across the leg for 4 h following ingestion of 20 g of whey protein immediately preceding exercise or following exercise (*A*) and during and for 5 h following resistance exercise with ingestion of 20 g of whey protein immediately preceding exercise or following exercise (*B*). All values are means ± SE.

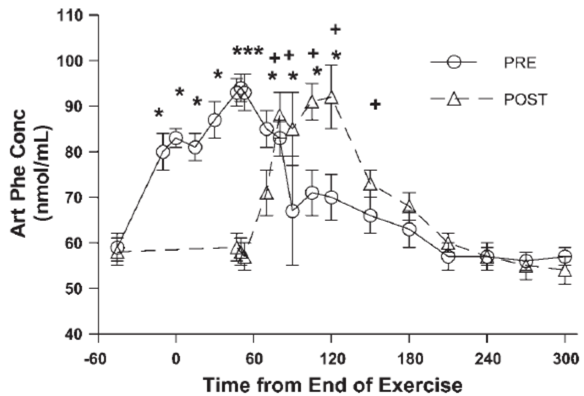


Fig. 3. Arterial phenylalanine concentration at rest and for 5 h following resistance exercise during ingestion of 20 g of whey protein immediately preceding exercise or following exercise. All values are means ± SE. *Significantly different from resting values for PRE. +Significantly different from resting values for POST.

Le Whey Protein sono in grado di indurre la sintesi proteica muscolare sia se somministrate prima che dopo una sessione di esercizio fisico

Am J Physiol Endocrinol Metab 292: E71–E76, 2007.

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-

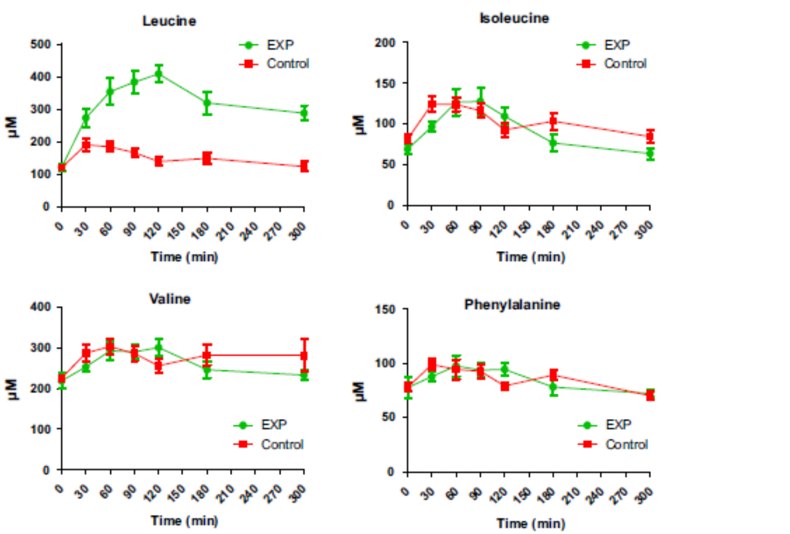
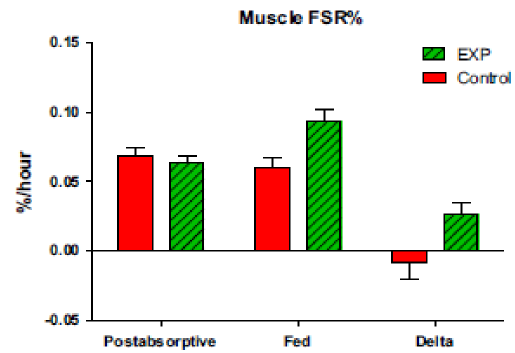


Fig. 2. Plasma leucine, isoleucine, valine and phenylalanine levels after intake of the medical foods. A significant groups effect was observed with respect to leucine ($P < 0.001$), but not for isoleucine, valine or phenylalanine ($P > 0.35$ for all).



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

Quando pensate alla supplementazione con aminoacidi cosa vi viene in mente?

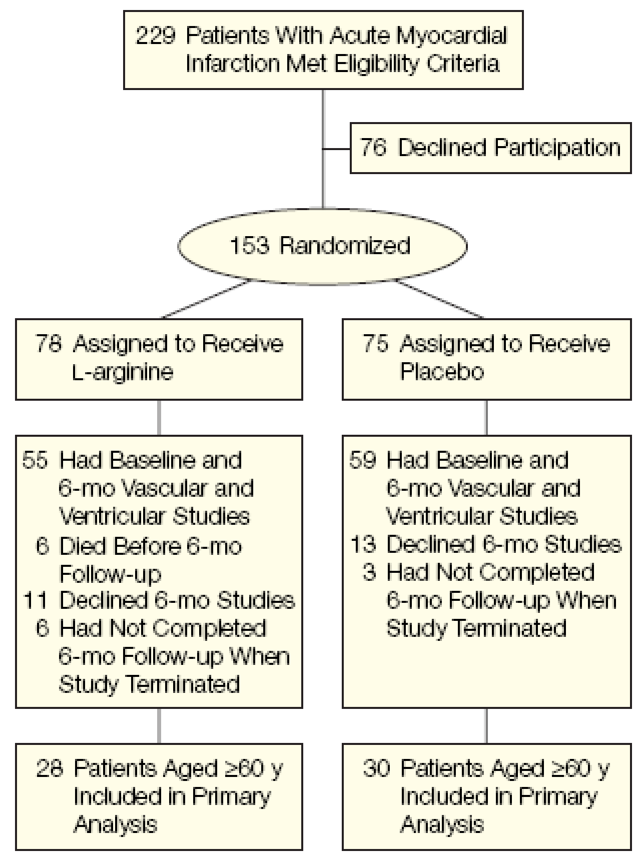
- Arginina
- Glutammina
- Leucina
- Aminoacidi ramificati (BCAA)
- Aminoacidi essenziali (EAA)
- Beta-HMB
- Altro…

Supplementazione con Arginina ad alte dosi

L-Arginine Therapy in Acute Myocardial Infarction
The Vascular Interaction With Age in Myocardial Infarction (VINTAGE MI) Randomized Clinical Trial

L Arginina 6 – 9 g/die x 6 mesi

Figure. Patient Flow Through the Study



JAMA, January 4, 2006—Vol 295, No. 1 (Reprinted)

Razionale della Supplementazione con Aminoacidi Essenziali

nutrients

Article

Influence of Diets with Varying Essential/Nonessential Amino Acid Ratios on Mouse Lifespan

Claudia Romano [1,†], Giovanni Corsetti [1,*,†], Vincenzo Flati [2,†], Evasio Pasini [3], Anna Picca [4,5], Riccardo Calvani [4,5], Emanuele Marzetti [4] and Francesco Saverio Dioguardi [6,*]

STUDI SULLA SOPRAVVIVENZA (TOPO adulto) CON DIETE «*ISONITROGEN*»

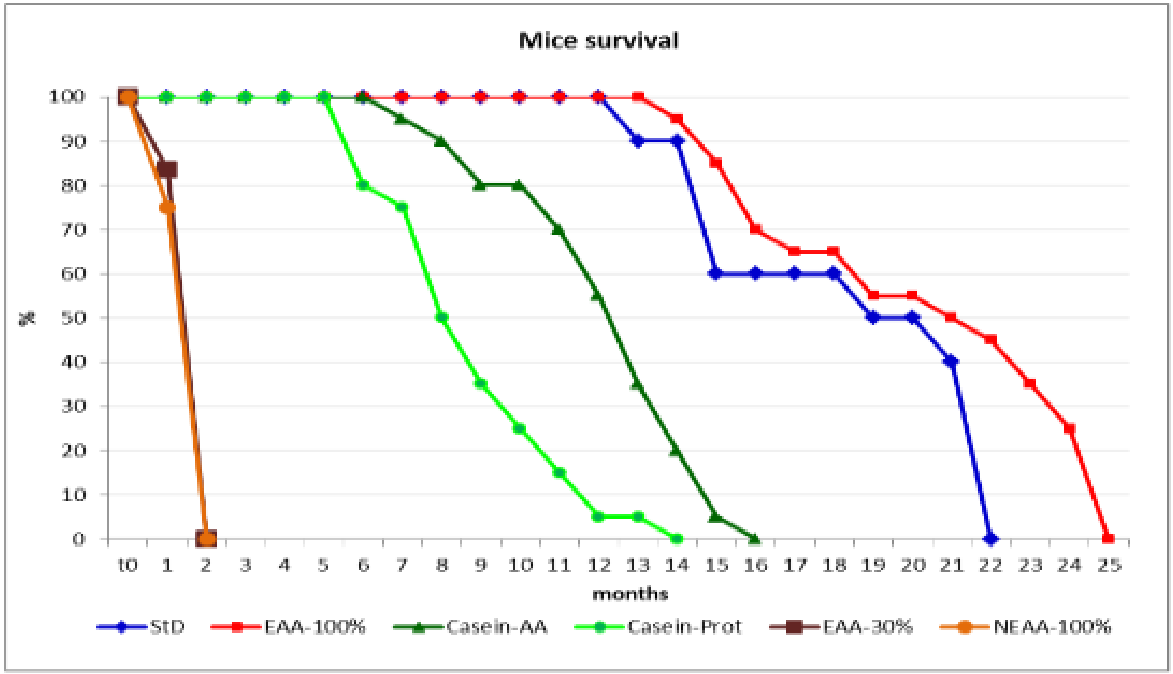


Figure 1. Percentage of mice's survival according to diet. Animals fed with NEAA-100% and EAA-30% diets (orange and brown lines) had shorter lifespans when compared to StD (blue line). It is interesting to observe the different survival curves between the animals fed with the diet containing casein whole protein (light-green line) and those fed with free AAs of casein (dark-green line). In addition, note the longest survival of the mice fed with EAA-100% diet (red line). Mantel–Cox test: Casein-AA vs. Casein-Prot, $z = 3.95$, $p < 0.001$; Casein-AA vs. StD, $z = 5.17$, $p < 0.001$; EAA-100% vs. StD, $z = 2.28$, $p = 0.0226$; EAA-30% vs. NEAA-100%, $z = 0.21$, $p = 0.83$.

Nutrients **2019**, *11*, 1367; doi:10.3390/nu11061367 www.mdpi.com/journal/nutrients

STUDI SULLA SOPRAVVIVENZA (TOPO) CON DIETE «*ISONITROGEN*»

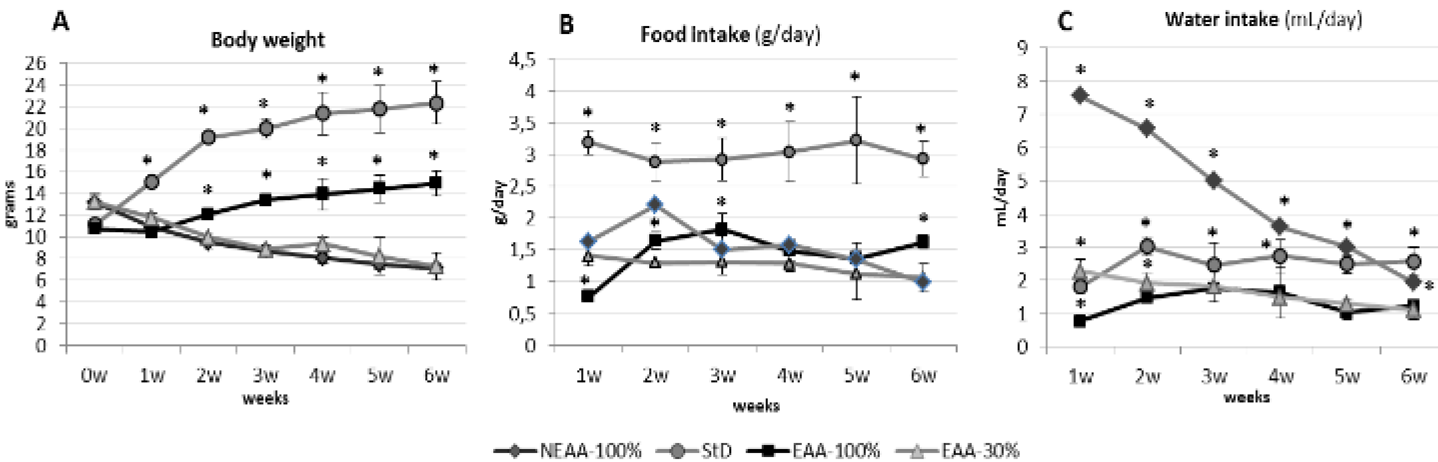


Figure 2. Comparison between BW (**A**), food (g/day) (**B**), and water (mL/day) consumption (**C**) (mean ± sd) of animals fed with NEAA-100% and EAA-30% diets, StD and EAA-100% diet after 6 weeks. NEAA-100% and EAA-30% diets drive rapid BW decrease, whereas EAA-100% diet slowly increases BW compared to StD (**A**). Note that EAA-100% diet was consumed in the same amount as NEAA-100% and EAA-30% diets (**B**). NEAA-100%-fed animals showed a higher water intake compared to StD, whereas EAA-30% and EAA-100%-fed animals had a lower water consumption than StD (**C**). Black square, EAA-100%; gray rhombus, NEAA-100%; gray triangle, EAA-30%; gray circle, StD. ANOVA and Bonferroni t-test, * $p < 0.05$ vs. all diets.

Nutrients **2019**, *11*, 1367; doi:10.3390/nu11061367 www.mdpi.com/journal/nutrients

Supplementazione con Aminoacidi

Stimolo mitocondriogenesi	Stimolo sintesi proteiche insulino indipendente

Riduzione dello stress ossidativo

SARCOPENIA =

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

SONO COME UN FARMACO CHE AGISCE SUI MECCANISMI PATOGENETICI DELLA SARCOPENIA

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

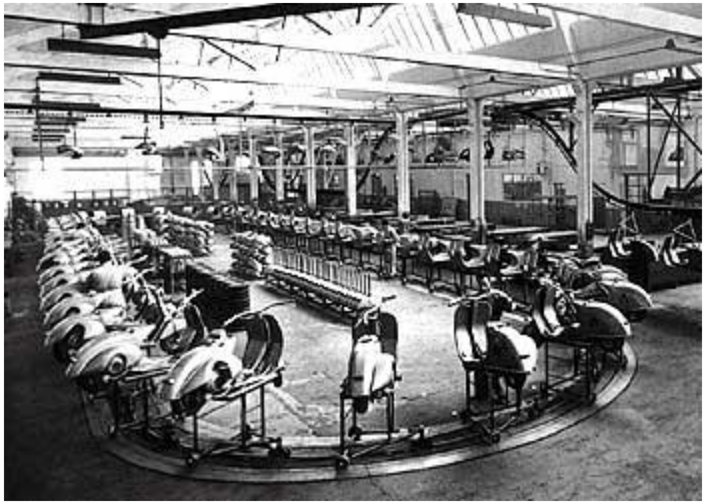
AMINOACIDI

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

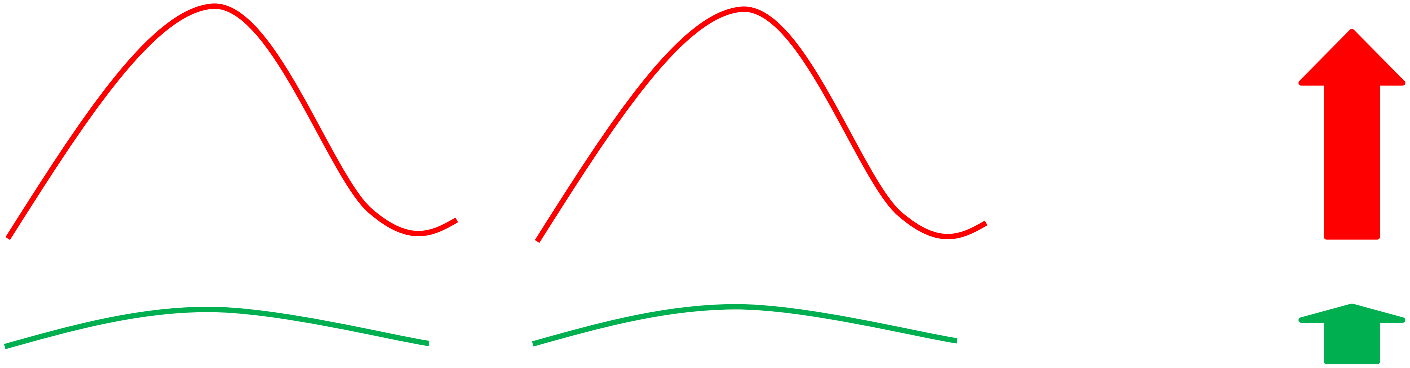
Il trasporto all'interno delle cellule avviene **senza consumo di ATP** ed in funzione del gradiente sangue/citoplasma cellulare

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

Il ruolo centrale degli AAE

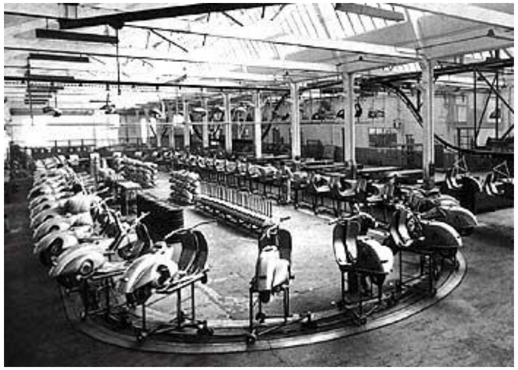
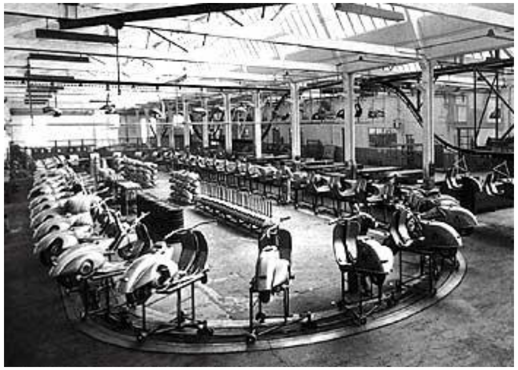
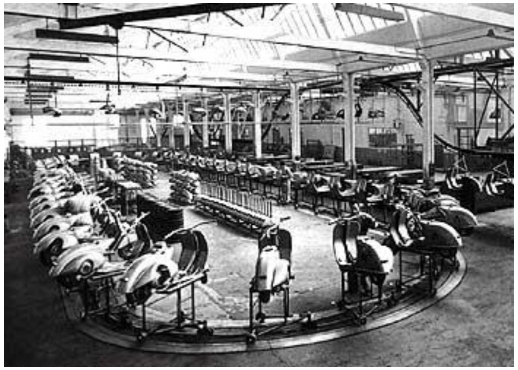


Ciò che fa partire la catena di montaggio è l'aumentata disponibilità cellulare di AA essenziali, indipendentemente dalla concentrazione plasmatica di AAE di partenza



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)

Modificazioni Mitocondriali Associate all'Età

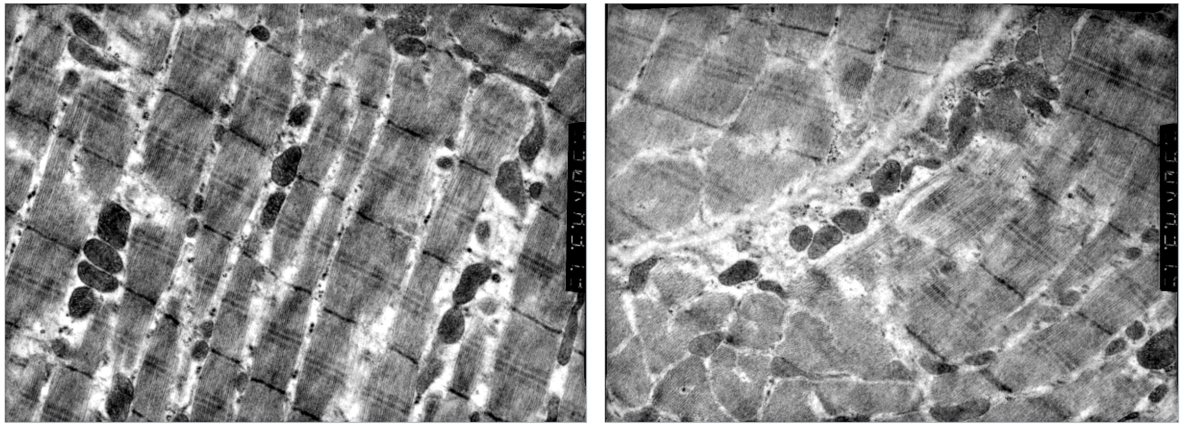
- Le modificazioni mitocondriali dovute all'invecchiamento sono un fattore cruciale nella perdita di funzionalità muscolare del muscolo dell'anziano
- *Age-related decline in mitochondrial function in healthy exercising elderly*

Figueiredo et al. ***Biogerontology***. 2008

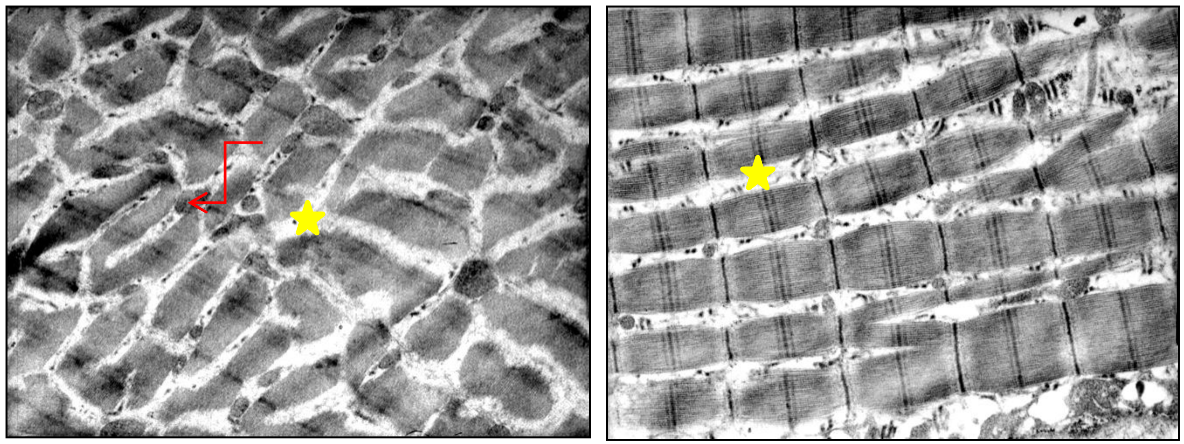
Animal-Groups	**Number of Mitochondria / 100µm³**	
	Skeletal muscle	Cardiac muscle
Young Control	154.71 ± 72.07	141.40 ± 26.02
Old Control	53.93 ± 50.01	93.79 ± 25.91*
Old EAA-supplemented	167.27 ± 111.02	129.33 ± 34.90**

Corsetti et al. ***Am J Cardio*** 2008.

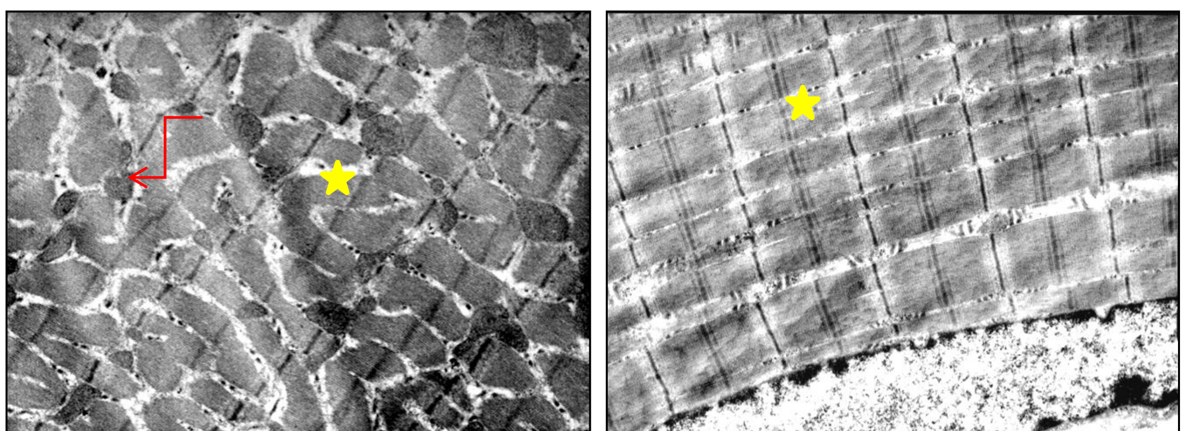
Ratti giovani



Ratti anziani

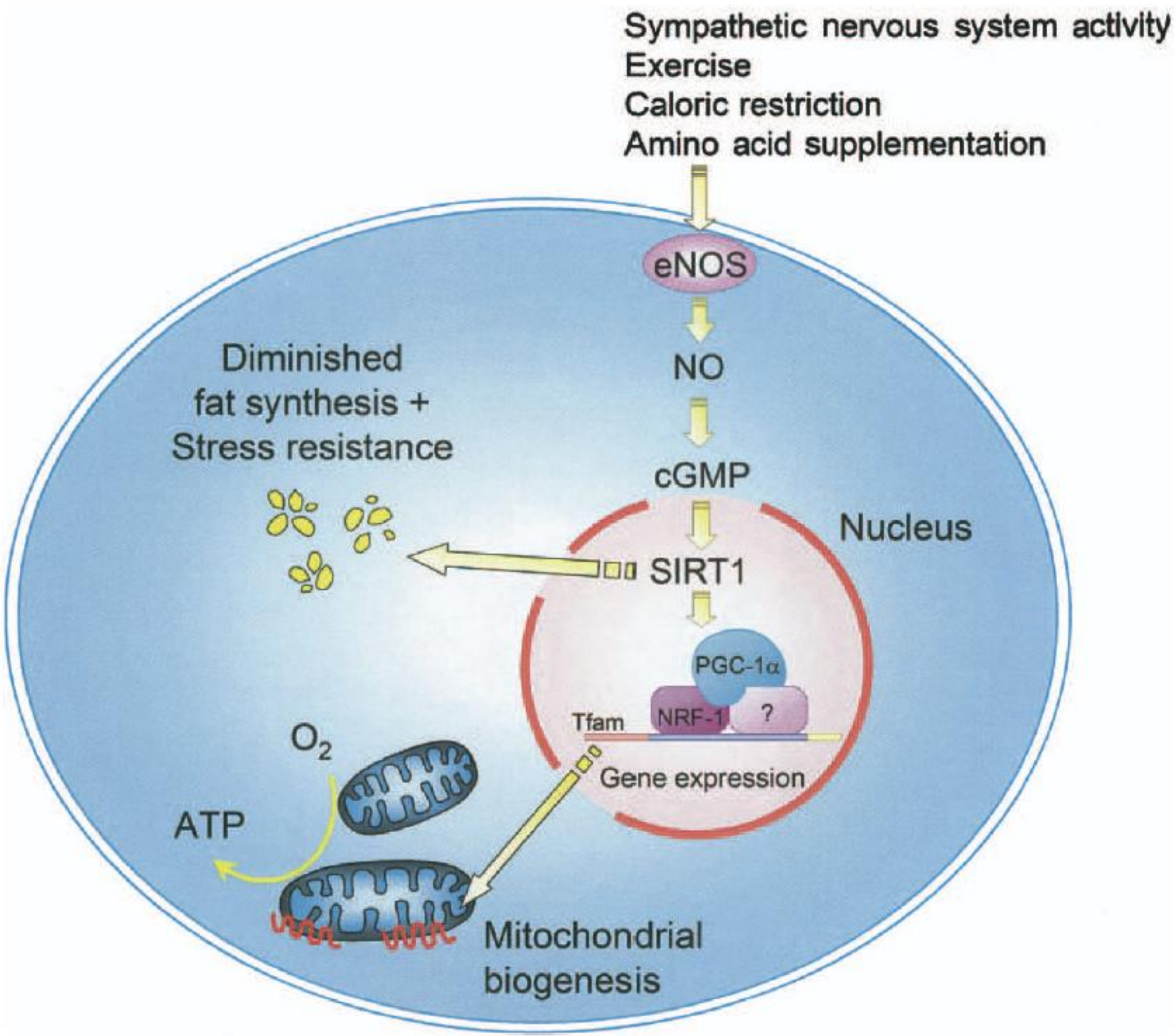


Ratti anziani trattati con AA



Muscoli scheletrici a ME 8900x

Essential Amino Acids and Mitochondrial Biogenesis



Impairment of mitochondrial function associated with:

- neurodegenerative diseases,
- neuromuscular disorders
- liver and heart failure
- type 2 diabetes
- sarcopenia

"EAAs may improve mitochondrial biogenesis and energy production"

Nisoli et al. ***Am J Cardiol*** 2008.

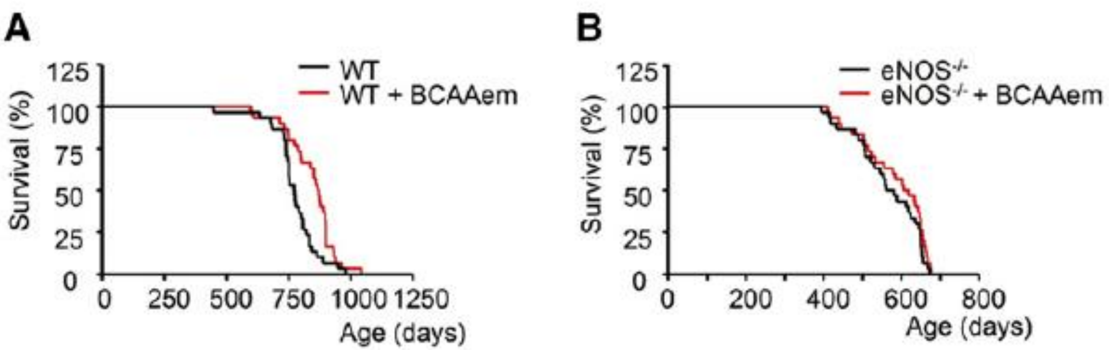
Aminoacidi e Mitocondri

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

Giuseppe D'Antona,[1,2] Maurizio Ragni,[3] Annalisa Cardile,[3] Laura Tedesco,[3,4] Marta Dossena,[3,5] Flavia Bruttini,[1,2] Francesca Caliaro,[1,2] Giovanni Corsetti,[6] Roberto Bottinelli,[1,2] Michele O. Carruba,[3,4] Alessandra Valerio,[3,5] and Enzo Nisoli[3,4,*]



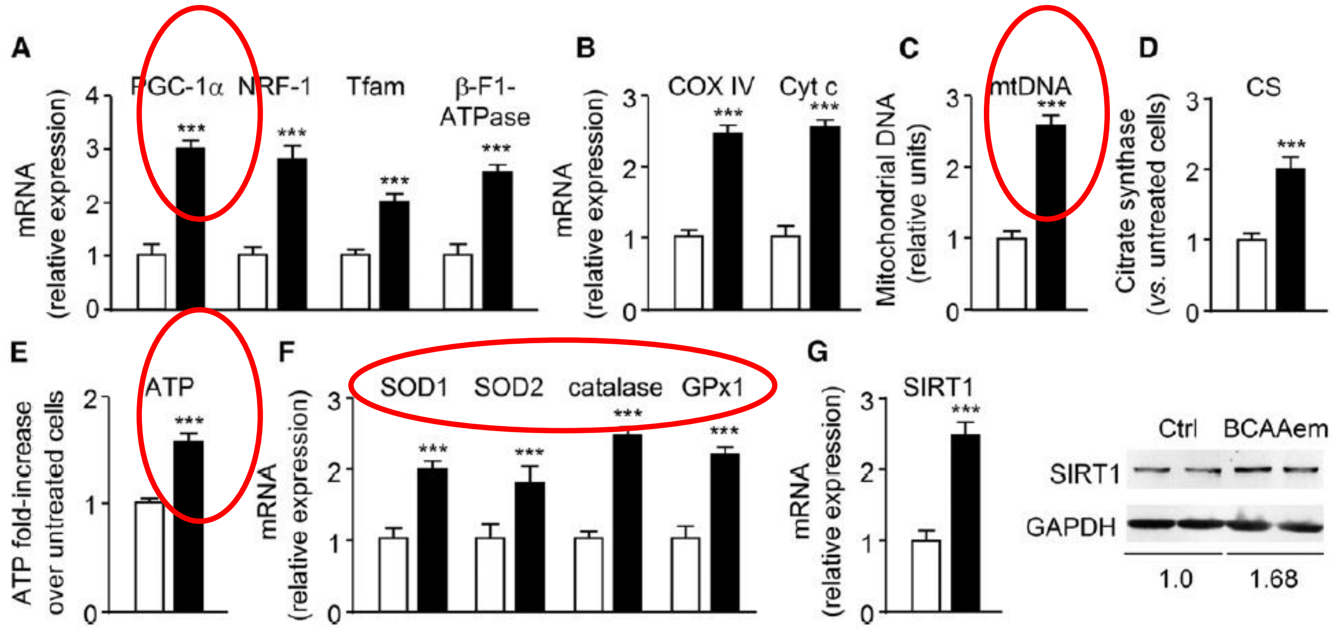
C

	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

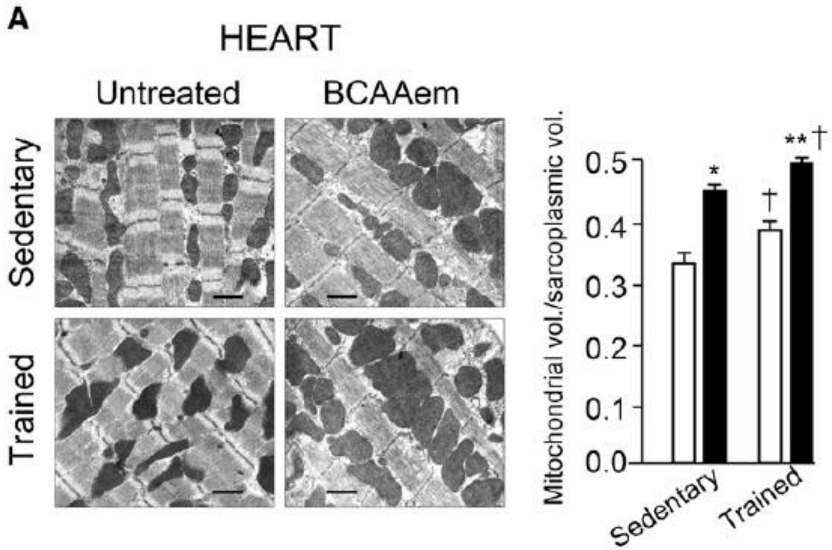
Aminoacidi e Mitocondri

Cell Metabolism

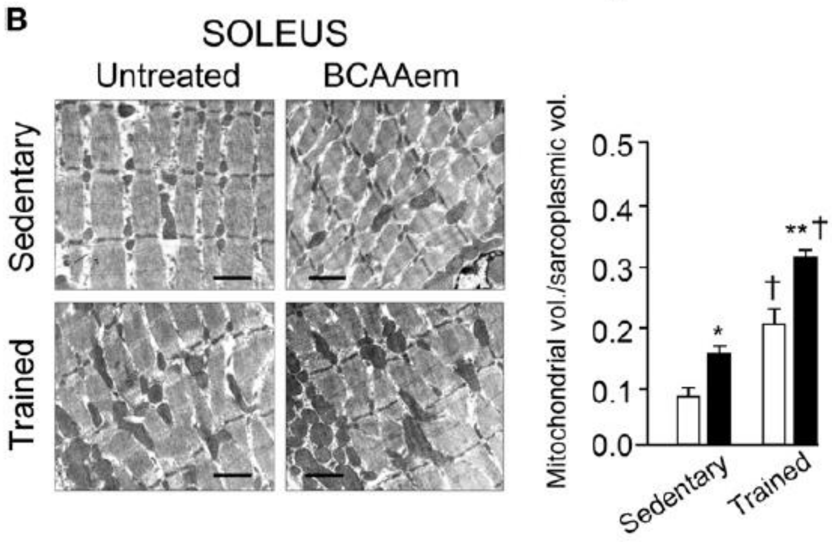
Branched-Chain Amino Acids and Survival



Aminoacidi e Mitocondri



Cuore



Muscolo striato

Aminoacidi e Mitocondri

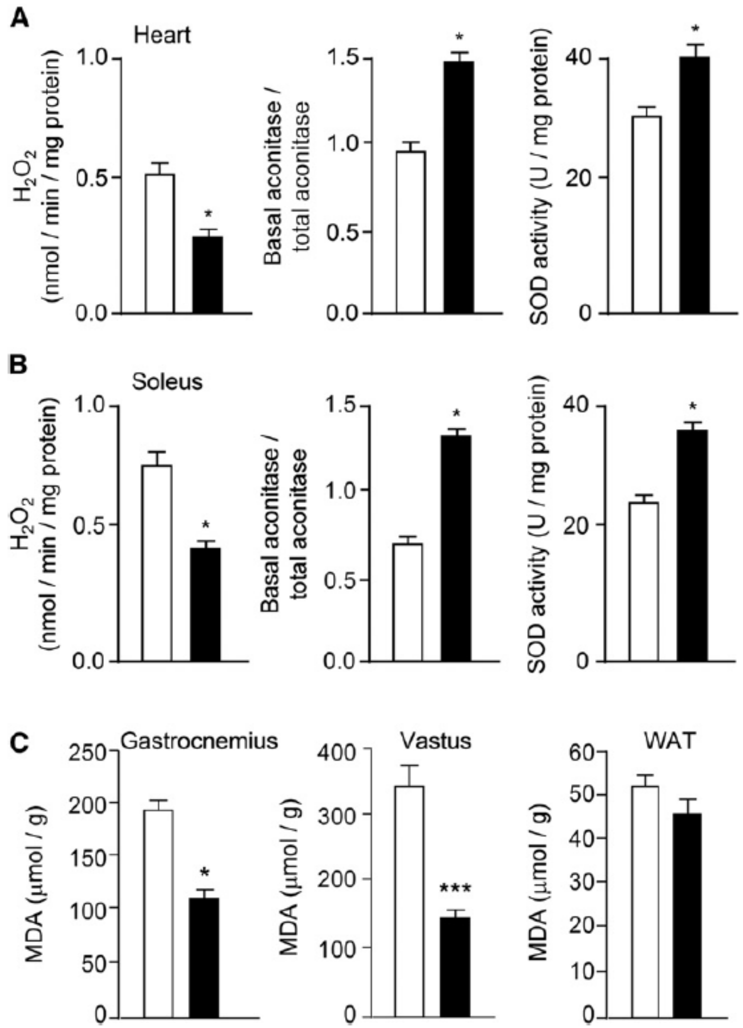


Figure 6. BCAAem Supplementation Reduces Oxidative Damage in Middle-Aged Mice

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.

EAAs Stimolano le Sintesi Proteiche in modo Indipendente dall’Insulina

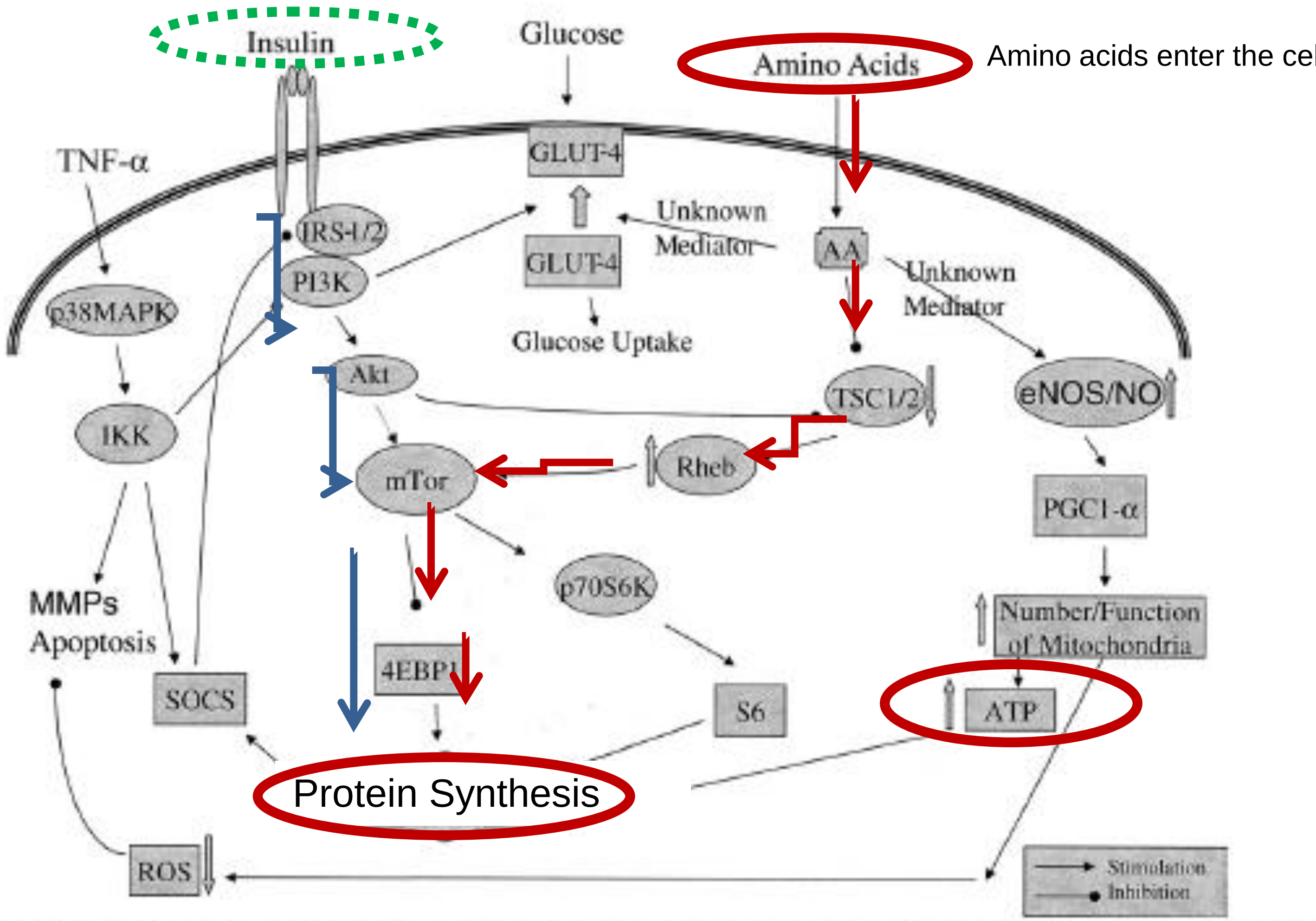
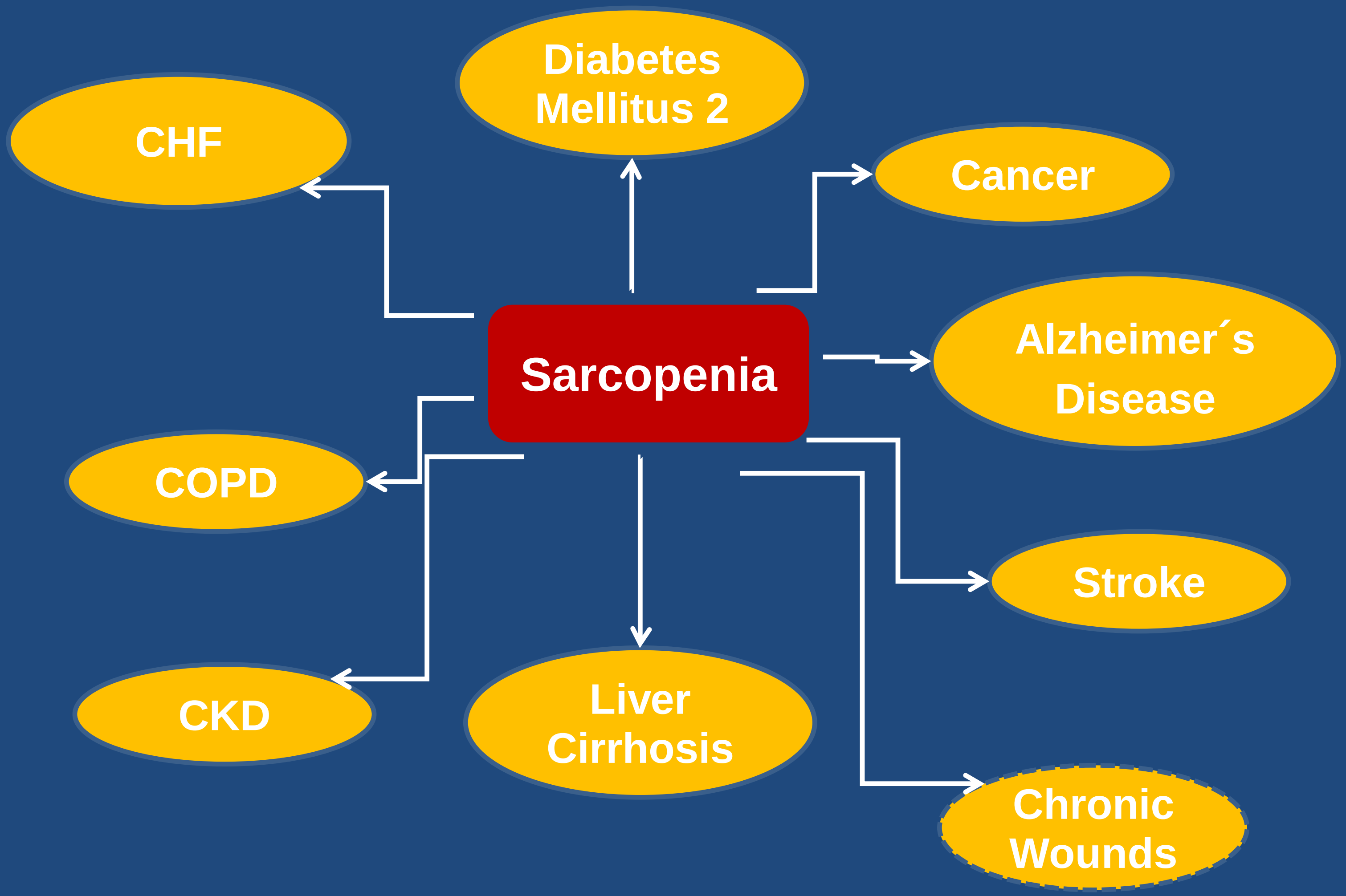


Figure 1. Intracellular regulation of catabolic/anabolic metabolism via mammalian target of rapamycin (mTOR) and other routes. AA – amino acid; Akt – protein kinase B; ATP – adenosine triphosphate; 4EBP1 – eIF4E-binding protein–1; eNOS – endothelial nitric oxide synthase; GLUT-4 – glucose transporter–4; 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; PI3K ... *Ras* homolog enriched in brain; ROS – reactive oxygen species; S6 – S6-kinase; SOCS – suppression of cy... factor–α; TSC1/2 – tuberous sclerosis complex; ↑ – increase; ↓ – decrease.

Flati et al. ***Am J Cardiol*** 2008.

Studi con EAA
in soggetti anziani

Studi con EAA in soggetti anziani



Grazie per l’attenzione