







VI Congresso Nazionale BaM Nutrizione e Neurodegenerazione

SESSIONE IV: RELATORI



Ruolo della Nutrizione nella Riabilitazione

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Ruolo della nutrizione nella riabilitazione



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<u>DEFINIZIONE:</u> Il complesso delle misure mediche, fisioterapiche, psicologiche e di addestramento funzionale intese a migliorare o ripristinare l'efficienza psicofisica di soggetti portatori di minorazioni congenite o acquisite

Nei casi di seria menomazione psicofisica, rappresenta essenzialmente una misura ergoterapica

Rappresenta la terza fase dell'intervento medico, successiva e complementare a quelle di ordine preventivo e diagnostico-curativo (evento acuto).

Qual è il paziente candidato ad un trattamento riabilitativo?







Declino strutturale e funzionale

Con l'avanzare dell'età si riscontra un deterioramento strutturale e funzionale in gran parte dei sistemi fisiologici...

Sarcopenia: European consensus on definition and diagnosis

Report of the European Working Group on Sarcopenia in Older People

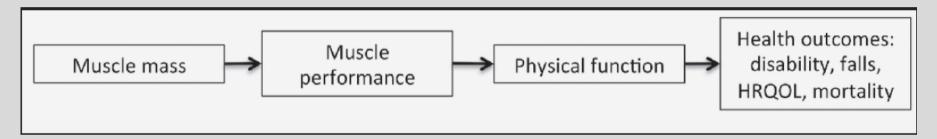


The presence of both

- low muscle mass
- low muscle function (strength or performance)

SARCOPENIA TRIALS IN SPECIFIC DISEASES: REPORT BY THE INTERNATIONAL CONFERENCE ON FRAILTY AND SARCOPENIA RESEARCH TASK FORCE

B. VELLAS^{1,2}, R. FIELDING³, S. BHASIN⁴, F. CERRETA⁵, B. GOODPASTER⁶, J.M. GURALNIK⁷, S. KRITCHEVSKY⁸, V. LEGRAND⁹, C. FORKIN¹⁰, J. MAGAZINER¹¹, J.E. MORLEY¹², L. RODRIGUEZ-MANAS¹³, R. ROUBENOFF¹⁴, S. STUDENSKI¹⁵, D.T. VILLAREAL¹⁶, M. CESARI^{1,2}, ON BEHALF OF THE INTERNATIONAL CONFERENCE ON FRAILTY AND SARCOPENIA RESEARCH TASK FORCE



Abstract: Muscle atrophy occurs as a consequence of a number of conditions, including cancer, chronic obstructive pulmonary disease (COPD), diabetes mellitus, heart failure, and other chronic diseases, where it is generally a predictor of poor survival. It also occurs as a consequence of disuse and an age-related loss of muscle mass and strength (sarcopenia). The aims of the 2016, International Conference on Frailty and Sarcopenia Research (ICFSR) Task Force were to examine how these specific chronic conditions have been employed in treatment trials thus far and how future trials using these patient groups might be designed for efficient identification of effective sarcopenia interventions. Functional limitations assessed as gait speed, distance walked over a set time period, or other attributes of physical performance have been suggested as outcome measures in sarcopenia trials. Indeed, such measures have already been used successfully in a number of trials aimed at preventing disability in older adults.

Jeruity Aging, 2016;5(4):194-200

Trattamento:

Components of training

The physical activity program includes aerobic, strength, flexibility, and balance training.

Intensity of training

Participants are introduced to the physical activity program in a structured way such that they begin with lighter intensity and gradually increase intensity over time

Frequency and duration of training

The program consists of physical activity at least 5 times per week (up to 7). Sessions should be of 30-60 minutes each

EXERCISE TRAINING AND NUTRITIONAL SUPPLEMENTATION FOR PHYSICAL FRAILTY IN VERY ELDERLY PEOPLE

MARIA A. FIATARONE, M.D., EVELYN F. O'NEILL, C.T.R.S., NANCY DOYLE RYAN, D.T., KAREN M. CLEMENTS, M.P.H., GUIDO R. SOLARES, Ph.D., MIRIAM E. NELSON, Ph.D., SUSAN B. ROBERTS, Ph.D., JOSEPH J. KEHAYIAS, Ph.D., LEWIS A. LIPSITZ, M.D., AND WILLIAM J. EVANS, Ph.D.

OUTCOME VARIABLE	No. of Subjects†		Stui	DY GROUP			P Value	
		EXERCISE	EXERCISE PLUS SUPPLEMENT	SUPPLEMENT	CONTROL	EFFECT OF EXERCISE	EFFECT OF SUPPLEMENT	INTERACTION
				change (perce	nt change)		1	
Muscle strength and mobility								
Right knee (kg)	89	4.9±0.6	5.0±0.5	-0.8 ± 0.6	0.1 ± 0.6	< 0.001	0.45	0.41
		(156.1 ± 29.3)	(215.7 ± 28.3)	(-24.6 ± 32.1)	(18.3 ± 29.1)	(<0.001)	(0.79)	(0.10)
Left knee (kg)	87	5.2±0.6	5.0±0.6	-1.1 ± 0.6	-0.3±0.6	<0.001	0.41	0.69
· •		(178.8 ± 29.1)	(204.2 ± 28.5)	(-24.4 ± 32.7)	(13.8 ± 28.8)	(<0.001)	(0.84)	(0.31)
Right hip (kg)	48	8.8±1.2	6.3±1.0	0.7±1.0	1.3±1.0	< 0.001	0.84	0.63
		(81.4 ± 16.4)	(90.3 ± 14.5)	(4.3 ± 14.3)	(19.6 ± 14.0)	(<0.001)	(0.51)	(0.20)
Left hip (kg)	48	8.1 ± 1.0	6.8±0.9	0.6 ± 0.9	0.7±0.8	<0.001	0.72	0.70
• · · • ·		(75.3 ± 16.2)	(100.2 ± 14.3)	(4.9 ± 14.7)	(14.0 ± 13.7)	(<0.001)	(0.41)	(0.22)
Right leg press (kg)	38	8.3±2.9	14.9 ± 3.0	0.6 ± 3.7	1.8±3.3	0.007	0.40	0.23
		(26.1 ± 14.4)	(82.1 ± 15.0)	(6.3 ± 18.5)	(6.1 ± 16.7)	(0.012)	(0.09)	(0.09)
Left leg press (kg)	39	9.3 ± 2.1	12.9±2.4	1.4±2.9	-1.1±2.6	< 0.001	0.24	0.82
		(33.3 ± 9.2)	(67.6 ± 10.3)	(7.2 ± 12.5)	(-3.5 ± 11.2)	(<0.001)	(0.05)	(0.28)
Gait (m/sec)	90	0.04 ± 0.02	0.06 ± 0.02	0.00 ± 0.02	-0.02 ± 0.02	0.009	0.31	0.97
		(8.6 ± 5.5)	(14.9 ± 5.7)	(5.2 ± 5.6)	(-7.2 ± 5.4)	(0.02)	(0.11)	(0.60)
Stair-climbing power (W)	83	11.1 ± 2.5	7.9±2.7	4.2±2.7	-2.5 ± 2.7	0.001	0.53	0.08
		(33.8 ± 9.3)	(23.0 ± 10.0)	(12.5 ± 10.0)	(-5.2 ± 9.8)	(0.01)	(0.74)	(0.17)
Physical activity (counts/day)	45	3412±1700	553±1751	142±1600	-1230 ± 1670	0.12	0.68	0.24
		(51.0 ± 18.4)	(17.6 ± 18.9)	(-6.7 ± 17.3)	(-2.6 ± 18.1)	(0.03)	(0.34)	(0.46)
Body composition					,	` ,		(/
Weight (kg)	88	0.2 ± 0.4	1.0 ± 0.4	0.8 ± 0.4	-0.5 ± 0.4	0.19	0.01	0.48
		(0.4 ± 0.6)	(1.8 ± 0.6)	(1.5 ± 0.7)	(-0.8 ± 0.6)	(0.21)	(0.01)	(0.48)
Whole-body potassium (g)	75	0.4 ± 1.5	1.5 ± 1.4	1.0±1.6	0.2±1.4	0.79	0.53	0.91
		(0.4 ± 1.9)	(2.2 ± 1.9)	(1.1 ± 2.0)	(0.9 ± 1.9)	(0.86)	(0.62)	(0.71)
Thigh-muscle area (cm ²)	61	0.9 ± 1.7	1.7±1.7	-2.7 ± 2.1	-0.4 ± 1.9	0.14	0.69	0.43
		(2.0 ± 2.5)	(3.4 ± 2.6)	(-2.8 ± 3.1)	(-0.9 ± 2.9)	(0.11)	(0.93)	(0.56)

"Oral nutritional support with or without exercise in the management of malnutrition in nutritionally vulnerable older people: a systematic review and meta-analysis"

Exercise combined with ONS was associated with significantly higher improvements in limb strength

Nutritional support improved fat-free mass but the addition of exercise had no significant effect physical activity level and timed upand-go test

Conclusion: Combining exercise with ONS may provide additional improvements to muscle strength but had no effect on other measures of physical functioning, nutritional status or morbidity in nutritionally vulnerable older adults.

Quale supporto nutrizionale?

Gli studi suggeriscono che il supporto nutrizionale è importante nella gestione del soggetto fragile/malnutrito al fine di migliorare il peso corporeo ma, per quel che concerne il ripristino della massa muscolare e l'impatto che questo può avere sullo stato funzionale, anche la qualità del supporto gioca un ruolo altrettanto importante.

Vitamin D and Its Role in Skeletal Muscle

Lisa Ceglia · Susan S. Harris

Calcif Tissue Int (2013) 92:151-162

There is accumulating evidence that 25-hydroxyvitamin D (25-(OH)D) is **not only involved in bone health**, but may also play a role in non-skeletal systems via the vitamin D receptor (VDR).

Vitamin D via intranuclear VDR activates gene transcription which results in the synthesis of specific proteins believed to influence muscle calcium handling, phosphate transport across the cell membrane, and muscle cell differentiation and proliferation.

The Effects of Vitamin D on Skeletal Muscle Strength, Muscle Mass, and Muscle Power: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

Objective: The aim was to summarize with a meta-analysis, the effects of vitamin D supplementation on muscle function.

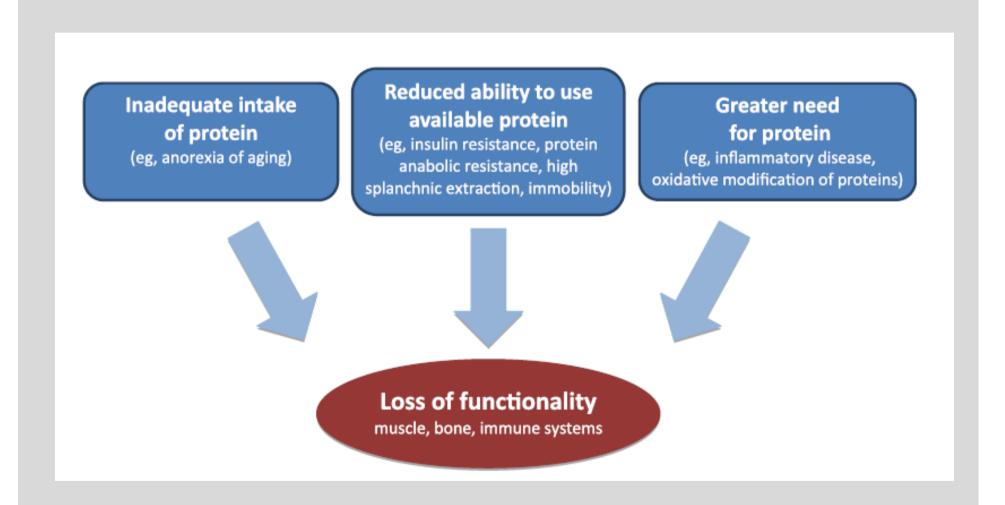
Data Sources: A systematic research of randomized controlled trials, performed between 1966 and January 2014 has been conducted on Medline, Cochrane Database of Systematics Reviews, Cochrane Central Register of Controlled and completed by a manual review of the literature and congressional abstracts.

Data Synthesis: Results revealed a small but significant positive effect of vitamin D supplementation on global muscle strength with a standardized mean difference (SMD) of 0.17 (P = .02). No significant effect was found on muscle mass (SMD 0.058; P = .52) or muscle power (SMD 0.057; P = .657). Results on muscle strength were significantly more important with people who presented a 25-hydroxyvitamin D level <30 nmol/L. Supplementation seems also more effective on people aged 65 years or older compared to younger subjects (SMD 0.25; 95% CI 0.01 to 0.48 vs SMD 0.03; 95% CI -0.08 to 0.14).

[In assenza di attività fisica]

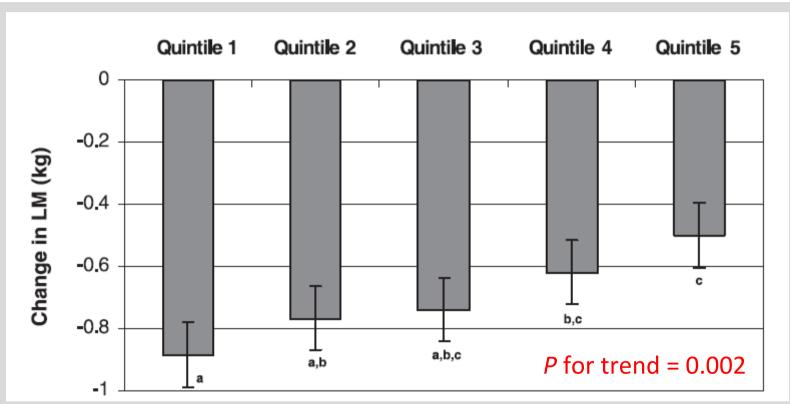
(J Clin Endocrinol Metab 99: 4336-4345, 2014)

Optimal muscle protein metabolism, is highly dependent upon an adequate intake of dietary proteins and amino acids



Dietary protein intake is associated with lean mass change in older, community-dwelling adults: the Health, Aging, and Body Composition (Health ABC) Study^{1–3}

Am J Clin Nutr 2008;87:150–5.



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, Alfonso J. Cruz-Jentoft MD^e, John E. Morley MB, BCh^f, Stuart Phillips PhD^g, Cornel Sieber MD, PhD^h, Peter Stehle MD, PhDⁱ, Daniel Teta MD, PhD^j, Renuka Visvanathan MBBS, PhD^k, Elena Volpi MD, PhD^l, Yves Boirie MD, PhD^m

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

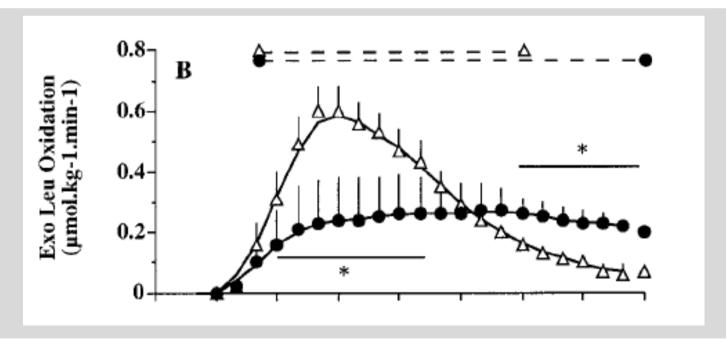
The absorption kinetics and the amino acid composition of dietary proteins are also important factors to be taken into account. Indeed, the speed of absorption of dietary amino acids by the gut affects postprandial protein synthesis, breakdown, and deposition.

Slow and fast dietary proteins differently modulate postprandial protein accretion

Proc. Natl. Acad. Sci. USA 94 (1997)

(amino acid turnover/postprandial protein anabolism/milk protein/stable isotopes)

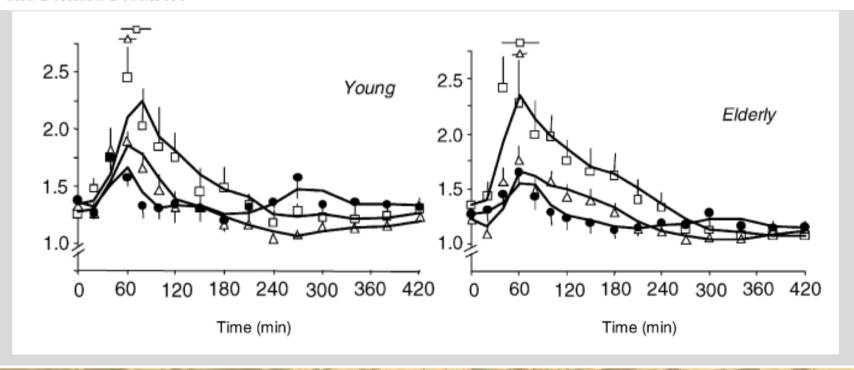
YVES BOIRIE*, MARTIAL DANGIN*†, PIERRE GACHON*, MARIE-PAULE VASSON‡, JEAN-LOUIS MAUBOIS\$, AND BERNARD BEAUFRÈRE*¶



In young adults, slowly digested proteins (casein) induce greater protein retention than those that are rapidly digested (e.g., whey). An opposite pattern has been detected in elderly individuals

The rate of protein digestion affects protein gain differently during aging in humans

Martial Dangin*†, Christelle Guillet*, Clara Garcia-Rodenas†, Pierre Gachon*, Corinne Bouteloup-Demange*, Kristel Reiffers-Magnani†, Jacques Fauquant‡, Olivier Ballèvre† and Bernard Beaufrère*

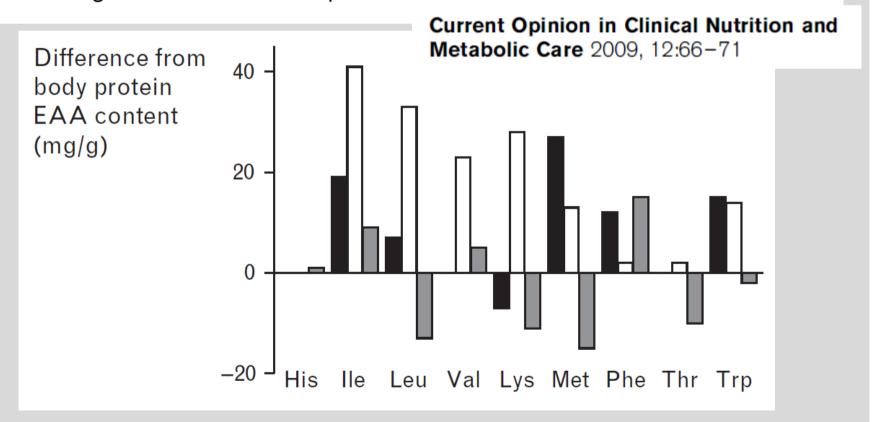


The amino acid composition of dietary proteins has a great impact on their muscle anabolic potency. Essential amino acids (EAAs) are the primary stimulus for protein

synthesis

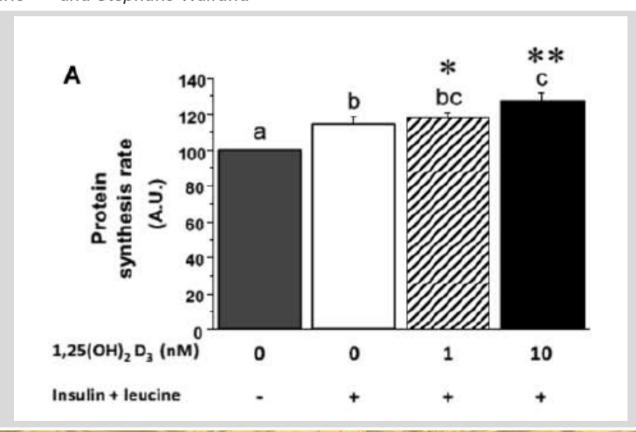
Maximizing muscle protein anabolism: the role of protein quality

Jason E. Tang and Stuart M. Phillips



1,25(OH)₂-vitamin D₃ enhances the stimulating effect of leucine and insulin on protein synthesis rate through Akt/PKB and mTOR mediated pathways in murine C2C12 skeletal myotubes Mol. Nutr. Food Res. 2013, 57, 2137-2146

Jérôme Salles^{1,2}, Audrey Chanet^{1,2}, Christophe Giraudet^{1,2}, Véronique Patrac^{1,2}, Philippe Pierre^{3,4,5}, Marion Jourdan⁶, Yvette C. Luiking⁶, Sjors Verlaan⁶, Carole Migné^{1,2}, Yves Boirie^{1,2,7} and Stéphane Walrand^{1,2}



Effects of a Vitamin D and Leucine-Enriched Whey Protein Nutritional Supplement on Measures of Sarcopenia in Older Adults, the PROVIDE Study: A Randomized, Double-Blind, Placebo-Controlled Trial

JAMDA 16 (2015) 740-747

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บ	ı	p = 0.045	Control (n=125)

	Mean (SD)	Change From Baseline	e, Mean (SD)	Estimated Between-Group	P*
	Baseline	Week 7	Week 13	DifferenceMean (95% CI)Active — Control	
Handgrip strengtl	h, kg		,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,		
Active†	20.9 (7.9)	0.20 (3.2)	0.79 (3.6)	0.30 (-0.46-1.05)	.44
Control	20.6 (7.5)	0.34(2.8)	0.54 (3.2)	3.554FT74V3F13V9 - 375-4,47595 - 7535EPF04V	
SPPB					
Active ¹	7.5 (1.9)	0.50 (1.26)	0.86 (1.38)**	0.11 (-0.21-0.42)	.51
Control ^{††}	7.5 (2.0)	0.51 (1.21)	0.77 (1.45)**	1 80 X 10 X 10 X	
Chair-stand time,		89878 (SEVAGN 8410)			
Active ^{§§}	17.1 (15.2, 21.2)	-1.4(-3.3-0.4)	-2.5 (-4.2 to -0.6)**	-1.01^{\S} (-1.77 to -0.19)	.018
Control	17.6 (14.6, 20.6)	-1.0(-3.0-1.1)	-1.2 (-3.3-0.8)**		
Balance test 11	N 10 100		N. 50		
Active [¶]	3.0 (2.0, 4.0)	0.0 (0.0-0.0)	0.0(0.0-1.0)	N.A.	.89
Control ^{††}	3.0 (2.0, 4.0)	0.0 (0.0-1.0)	0.0 (0.0-1.0)		
Gait speed, m/s	and the second s	0.0000000000000000000000000000000000000	7. 100.00		
Active ¹	0.8 (0.2)	0.03 (0.11)	0.07 (0.12)**	0.01^{\S} (-0.02-0.04)	.46
Control***	0.8 (0.2)	0.03 (0.10)	0.05 (0.12)**	10.800 S 100 NOTE	

Whey protein, amino acids, and vitamin D supplementation with physical activity increases fat-free mass and strength, functionality, and quality of life and decreases inflammation in sarcopenic elderly^{1,2}

Mariangela Rondanelli, 3* Catherine Klersy, 6 Gilles Terracol, 7 Jacopo Talluri, 8 Roberto Maugeri, 7 Davide Guido, 4 Milena A Faliva, 3 Bruno S Solerte, 5 Marisa Fioravanti, 5 Henry Lukaski, 9 and Simone Perna 3

Effects of supplementation compared	wastate.	-1	a commendate and the state of	-1.111-1
Effects of supplementation compared	wiin	DIacedo II	n exercise-trained	elderly beoble
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	Dietary supplement group $(n = 69)$		Placebo group $(n = 61)$		Treatment effect	
Variable	Mean change (95% CI)	Intragroup P ²	Mean change (95% CI)	Intragroup P^2	Mean difference (95% CI)	P^3
Fat-free mass, 4 g	1382 (847, 1918)	< 0.001	-312 (-930, 307)	0.316	1695 (892, 2498)	< 0.001
Fat mass, g	-345 (-747 , 57.18)	0.092	-484 (-1049, 81.74)	0.092	-114 (-786, 559)	0.689
Gynoid, %	-1.39 (-2.22 , -0.56)	0.001	-0.92 (-1.83, -0.02)	0.046	0.54 (-0.67, 1.75)	0.451
Android, %	-2.03(-2.99, -1.06)	0.001	-0.26 (-1.43, 0.92)	0.66	1.80 (0.30, 3.29)	0.021
RSMM, kg/m ²	0.21 (0.07, 0.35)	0.004	-0.06 (-0.21, 0.90)	0.42	0.27 (0.07, 0.47)	0.009
MNA score	1.76 (1.23, 2.28)	< 0.001	0.24 (-0.63, 1.11)	0.585	1.52 (0.51, 2.52)	0.003
Weight, kg	1.12 (0.37, 1.87)	0.004	-0.89 (-1.62, -0.15)	0.019	2.00 (0.97, 3.04)	< 0.001
BMI, kg/m ²	0.42 (0.11, 0.72)	0.008	-0.42 (-0.70, -0.14)	0.004	0.84 (0.43, -1.25)	< 0.001
Waist circumference, cm	4.93 (-0.86, 10.72)	0.094	2.27 (-1.72, 6.25)	0.259	2.67 (-4.29, 9.62)	0.449
ADL score	0.54 (0.39, 0.68)	< 0.001	-0.61 (-0.79, -0.42)	< 0.001	1.14 (0.91, 1.38)	< 0.001
SF-36 MCS score	4.50 (2.68, 6.32)	< 0.001	2.48 (0.21, 4.75)	0.033	2.02 (-0.85, 4.89)	0.166
SF-36 PCS score	1.32 (-0.05, 2.68)	0.059	-0.77 (-2.10 , 0.58)	0.249	2.09 (0.21, 3.97)	0.030
CRP, mg/dL	-0.19 (-0.57 , 0.19)	0.329	0.44 (-0.02, 0.90)	0.061	0.63 (0.04, 1.22)	0.038
IGF-I, ng/mL	20.7 (11.0, 30.4)	< 0.001	1.8 (-4.2, 7.8)	0.541	19.7 (7.1, 32.3)	0.002
Handgrip, kg	3.20 (2.23, 4.18)	< 0.001	-0.47 (-1.07 , 0.12)	0.117	3.68 (2.55, 4.81)	< 0.001

ClinicalTrials.gov Protocol Registration and Results System (PRS) Receipt Release Date: April 26, 2017

Protocol Registration and Results System

ClinicalTrials.gov ID: NCT03124277

Brief Title: Nutritional Support for Rehabilitation In Parkinsonism

Official Title: A Whey Protein-based Nutritional Supplement Enriched in Vitamin D, Leucine

and Calcium for Patients With Parkinsonism Undergoing Rehabilitation

Treatment: a Randomized Trial

This randomized, trial will tested the hypothesis that nutritional supplementation with whey protein, essential amino acids - mainly leucine - vitamin D and calcium would increase the efficacy of physical rehabilitation in old adults suffering from Parkinson's disease o parkinsonism

Experimental group:

Best local diet + two servings (40 grams each) of powder containing 20 g whey protein, 3 g total leucine, 800 IU vitamin D, and 500 mg calcium.

Control group:

Best local diet

Study enpoints:

Primary Outcome Measure:

Distance walked during the six minutes walking test

Secondary Outcome Measures:

- ➤ Timed up and go test
- ➤ Berg balance scale
- ➤ Handgrip strength
- Gait speed (4 minutes walking test)
- Self-perceived functional status (SPDDS)
- ➤ Body weight
- ➤ Muscle mass
- >Adverse events
- Treatment continuation



Tale studio potrebbe chiarire in parte anche il ruolo di un supporto nutrizionale specifico nel percorso riabilitativo di pazienti affetti da disabilità ma non sarcopenici.

Sarcopenia and Dynapenia in Patients With Parkinsonism

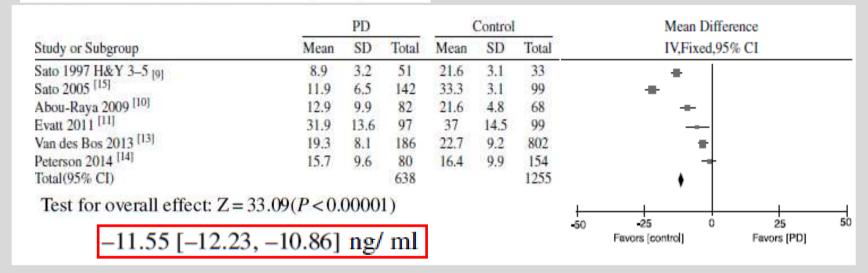
Michela Barichella MD^a, Giovanna Pinelli MD, PhD^{a,b}, Laura Iorio MD^a, Erica Cassani MD^a, Angela Valentino BioD^a, Chiara Pusani RD^a, Valentina Ferri MD^a, Carlotta Bolliri BioD^a, Marianna Pasqua BioD^a, Gianni Pezzoli MD^a Giuseppe Frazzitta MD^b, Emanuele Cereda MD, PhD^{c,*}

Participants: Consecutive patients (n = 364) aged 65 years or older, affected by parkinsonian syndromes. Measurements: Skeletal muscle mass (SMM), as well as strength and gait speed (GS) were assessed by bioimpedence analysis, handgrip dynamometry, and the 4-meter walking test, respectively. Based on these assessments, sarcopenia was diagnosed using the European Working Group on Sarcopenia in Older People criteria. Dynapenia was defined as handgrip strength less than 30 kg in men and less than 20 kg in women.

Results: In total, 235 patients (64.6%) had a diagnosis of idiopathic PD. Low SMM index was recorded in 27 patients. Due to gait disturbances and postural instability, GS could not be measured in 98 patients and was found to be reduced in 61.3% of those assessed. Prevalence of sarcopenia and dynapenia was 6.6% (95% confidence interval [CI] 4.3—9.7) and 75.5% (95% CI 70.8—79.9), respectively. Sarcopenia tended to be higher in patients unable to perform GS assessment and was unrelated to the type of parkinsonian syndrome. It was associated with older age, longer disease duration, more severe disease, and higher disability in activities of daily living, as assessed by disease-specific clinical rating scale. Dynapenia was directly associated with parkinsonism other than PD, older age, and disability, whereas regular physical therapy appeared to be a preventive factor. However, it was unrelated to disease duration and severity. Finally, the disability score of activities of daily living was inversely correlated with handgrip strength and GS, whereas no association was found with SMM index.

Systematic Review of the Relationship between Vitamin D and Parkinson's Disease

Journal of Parkinson's Disease 6 (2016) 29-37



Dietary habits and neurological features of Parkinson's disease patients: Implications for practice

Michela Barichella ^a, Emanuele Cereda ^{b, *}, Erica Cassani ^a, Giovanna Pinelli ^a, Laura Iorio ^a, Valentina Ferri ^a, Giulia Privitera ^a, Marianna Pasqua ^a, Angela Valentino ^a, Fatemeh Monajemi ^a, Serena Caronni ^a, Caterina Lignola ^a, Chiara Pusani ^a, Carlotta Bolliri ^a, Samanta A. Faierman ^a, Alessandro Lubisco ^c, Giuseppe Frazzitta ^d, Maria L. Petroni ^e, Gianni Pezzoli ^a



Randomized, double-blind, placebo-controlled trial of vitamin D supplementation in Parkinson disease^{1–4}

Masahiko Suzuki, Masayuki Yoshioka, Masaya Hashimoto, Maiko Murakami, Miki Noya, Daisuke Takahashi, and Mitsuyoshi Urashima

			Difference between groups		
Outcome	Vitamin D_3 $(n = 55)$	Placebo $(n = 57)$	RR (95% CI); RD (95% CI)	P (95% CI) or P	
HY stage (stages 1–5)					
Change (after - before)	0.02 ± 0.62^2	0.33 ± 0.70		$0.005 (0.003, 0.006)^3$	
Within-group P	0.79	0.0006		1000 1000 1000	
Not worsened or improved $[n (\%)]$	16 (29.1)	7 (12.3)	2.37 (1.06, 5.31); 0.17 (0.02, 0.32)	0.028⁴	
UPDRS total (0-195)					
Change (after – before)	-0.87 ± 12.8	4.20 ± 14.5		$0.11 (0.10, 0.11)^3$	
Within-group P	0.85	0.05			
Not worsened or improved $[n (\%)]$	21 (38.2)	22 (38.6)	$0.99 \ (0.62, 1.58); -0.00 \ (-0.18, 0.18)$	0.96^{4}	
UPDRS part I (0-16)					
Change (after – before)	0.11 ± 1.30	0.49 ± 1.63		$0.28 (0.27, 0.29)^3$	
Within-group P	0.66	0.06			
Not worsened or improved $[n \ (\%)]$	12 (21.8)	12 (21.1)	1.04 (0.51, 2.11); 0.01 (-0.14, 0.16)	0.924	
UPDRS part II (0-48)					
Change (after – before)	-0.87 ± 12.8	4.37 ± 14.6		$0.004 (0.003, 0.006)^3$	
Within-group P	0.32	0.004	_		
Not worsened or improved $[n \ (\%)]$	26 (47.3)	16 (28.1)	1.68 (1.02, 2.78); 0.19 (0.02, 0.37)	0.036⁴	
UPDRS part III (0-108)					
Change (after – before)	-1.05 ± 10.0	1.05 ± 9.09		$0.26 (0.25, 0.27)^3$	
Within-group P	0.37	0.58			
Not worsened or improved $[n \ (\%)]$	27 (49.1)	27 (47.4)	1.04 (0.71, 1.52); 0.02 (-0.17, 0.20)	0.86^{4}	

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