

17-20
Dicembre
2025
Napoli

70^o C O N G R E S S O
N A Z I O N A L E
SIGG
LIBERI E LONGEVI

Università degli
Studi di Napoli
Federico II
Polo Didattico
di **SCAMPIA**



L-Arginina e vitamina C liposomiale nel paziente sarcopenico

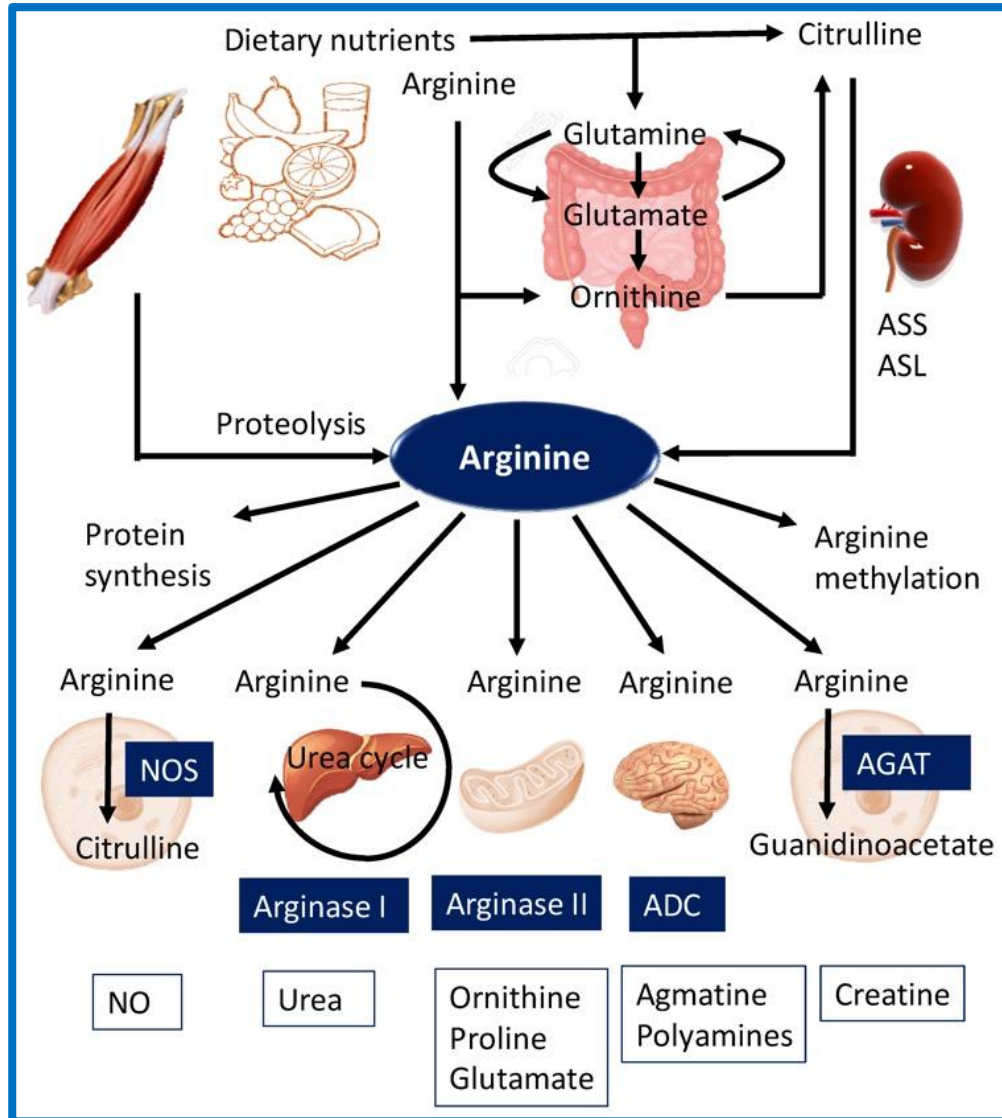
Prof. Francesco Landi

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Fondazione Policlinico Universitario Agostino Gemelli IRCCS

Università Cattolica del Sacro Cuore

Arginina



Etimologia

“ἀργυρος” (argyros) = argento

Amminoacido essenziale in certe condizioni (es. bambini in fase di accrescimento, traumi, ustioni, ulcere da pressione)

Principali fonti di arginina nella dieta:

- frutta secca
- legumi
- carne
- pesce

ASS = argininosuccinate synthetase;

ASL = argininosuccinate lyase;

NO—nitric oxide;

NOS—nitric oxide synthase;

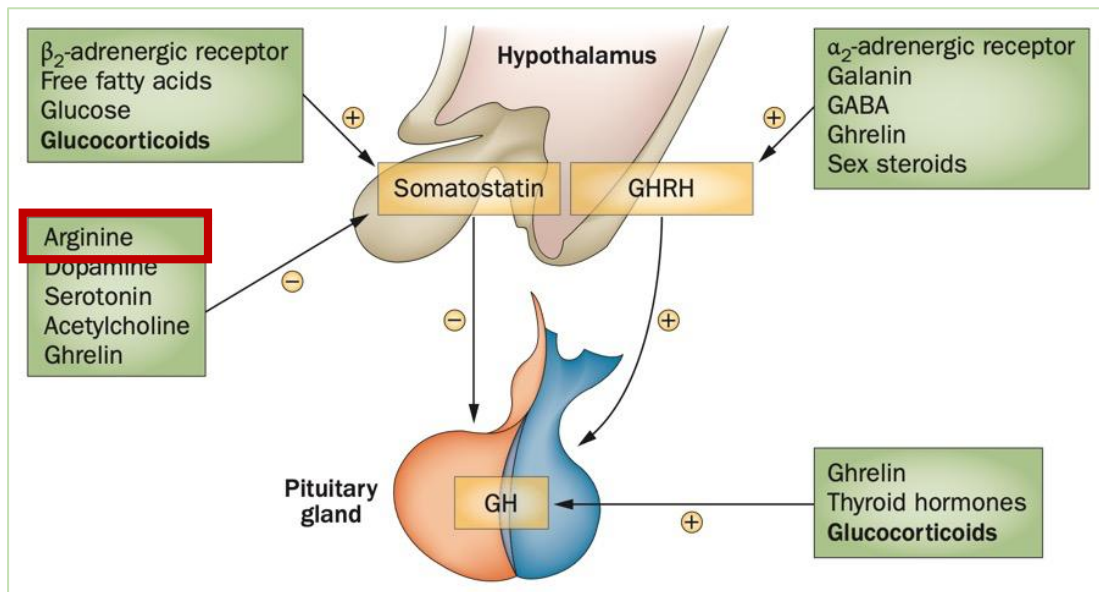
ADC—arginine decarboxylase;

AGAT—arginine:glycine amidinotransferase.

Arginina

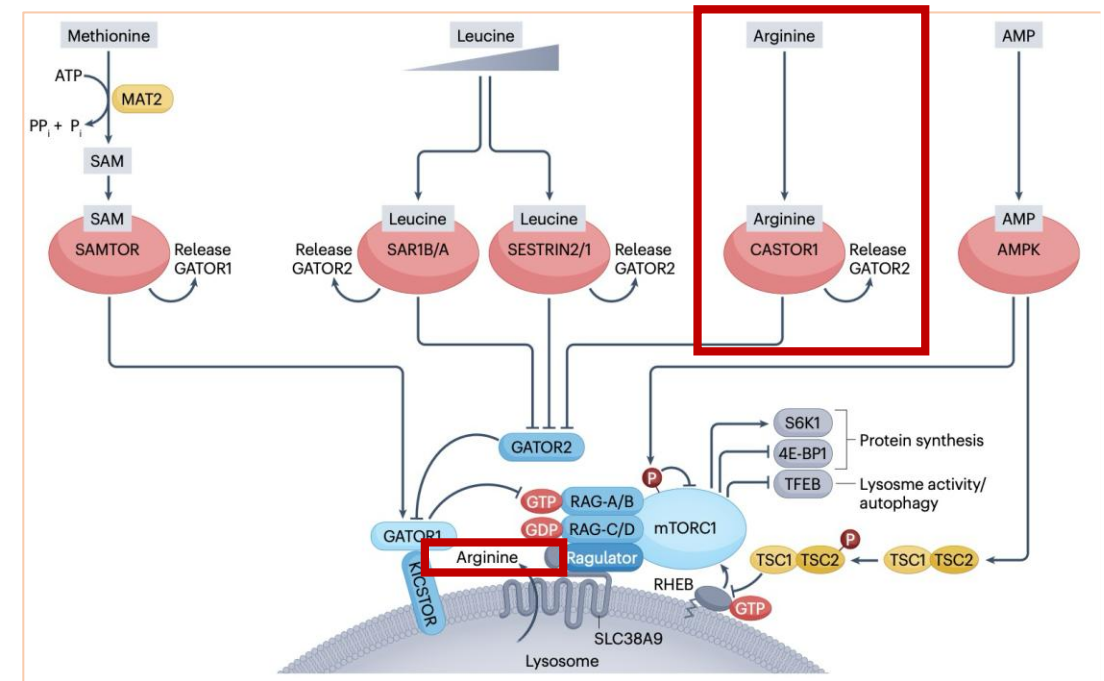
Arginina e anabolismo muscolare: meccanismi

Stimolazione secrezione GH



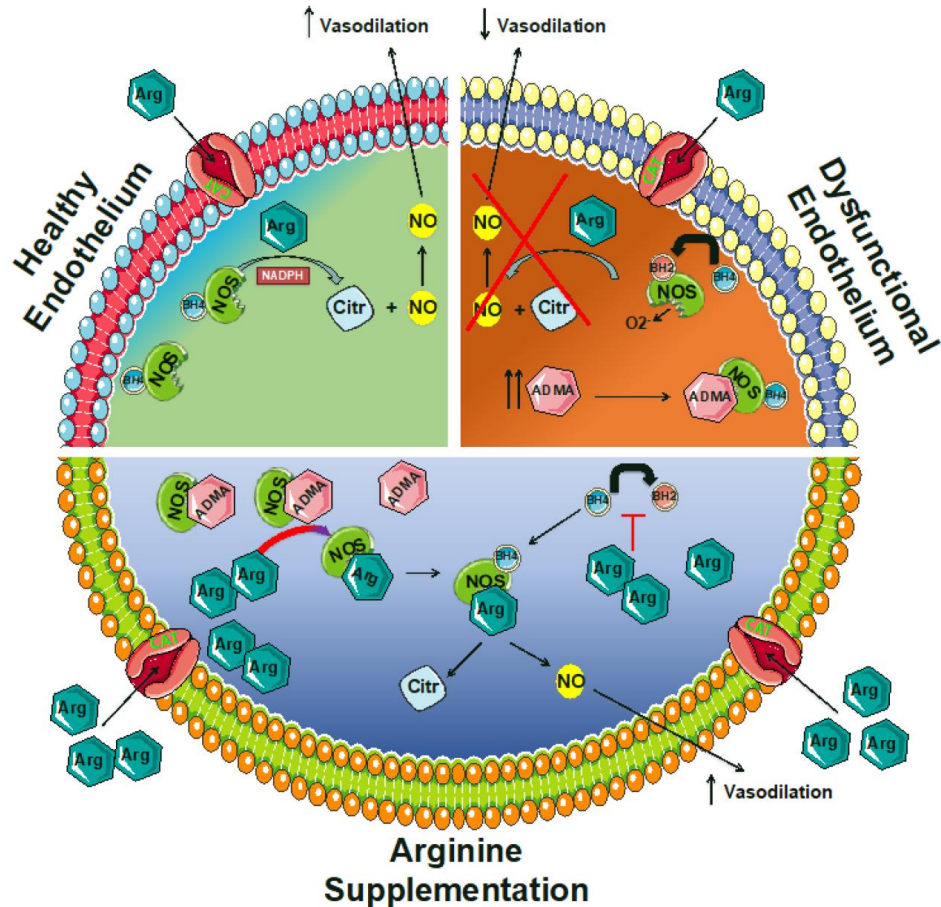
Nat. Rev. Endocrinol. 9, 265–276 (2013)

Attivazione segnali anabolici



Nature Reviews Molecular Cell Biology | Volume 24 | May 2023 | 355–374

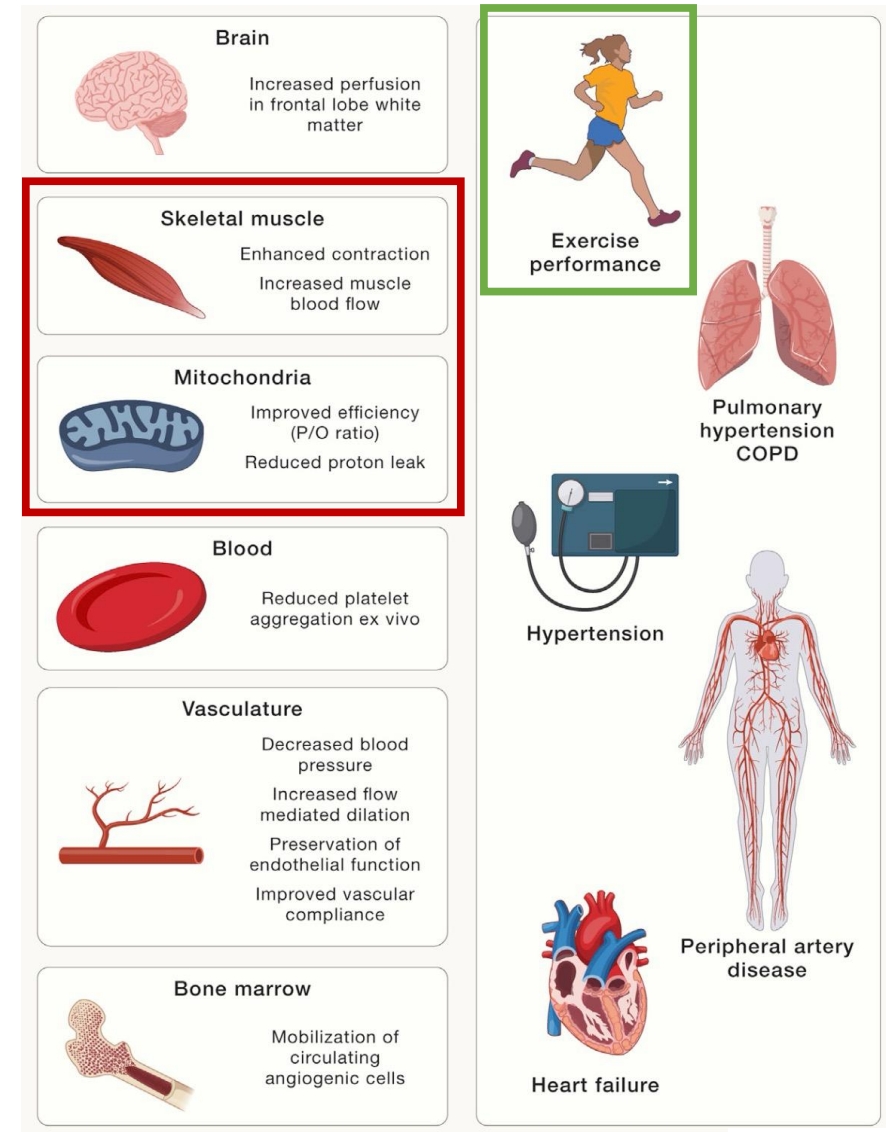
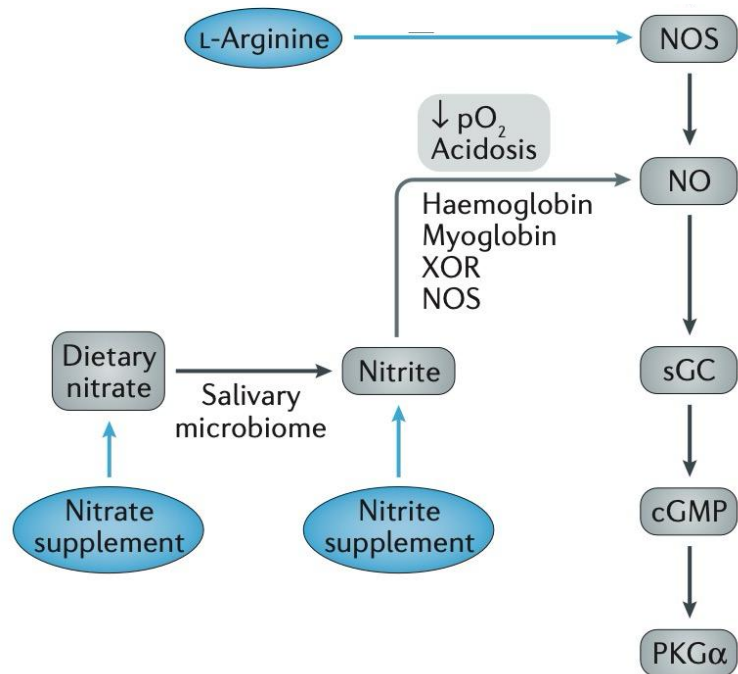
Arginina



- Amminoacido che svolge un ruolo chiave nella produzione di **ossido nitrico**
- Esistono due principali vie metaboliche:
 - produzione di ossido nitrico (NO) attraverso l'attività della ossido nitrico sintasi (NOS)
 - produzione di **ornitina** attraverso l'attività dell'arginasi
- La ossido nitrico sintasi (NOS) e l'arginasi regolano la biodisponibilità dell'ossido nitrico.
- Alcuni derivati della L-arginina possono modulare la biodisponibilità dell'ossido nitrico. Ad esempio, la dimetilarginina asimmetrica (**ADMA**) inibisce l'enzima NOS, riducendo la produzione di NO.

Arginina

Ossido nitrico e performance fisica



doi:10.1038/nrcardio.2017.224

Cell 185, August 4, 2022

Arginina

DIETARY NITRIC OXIDE PRECURSORS AND EXERCISE PERFORMANCE

Sports Science Exchange (2016) Vol. 29, No. 156, 1-6

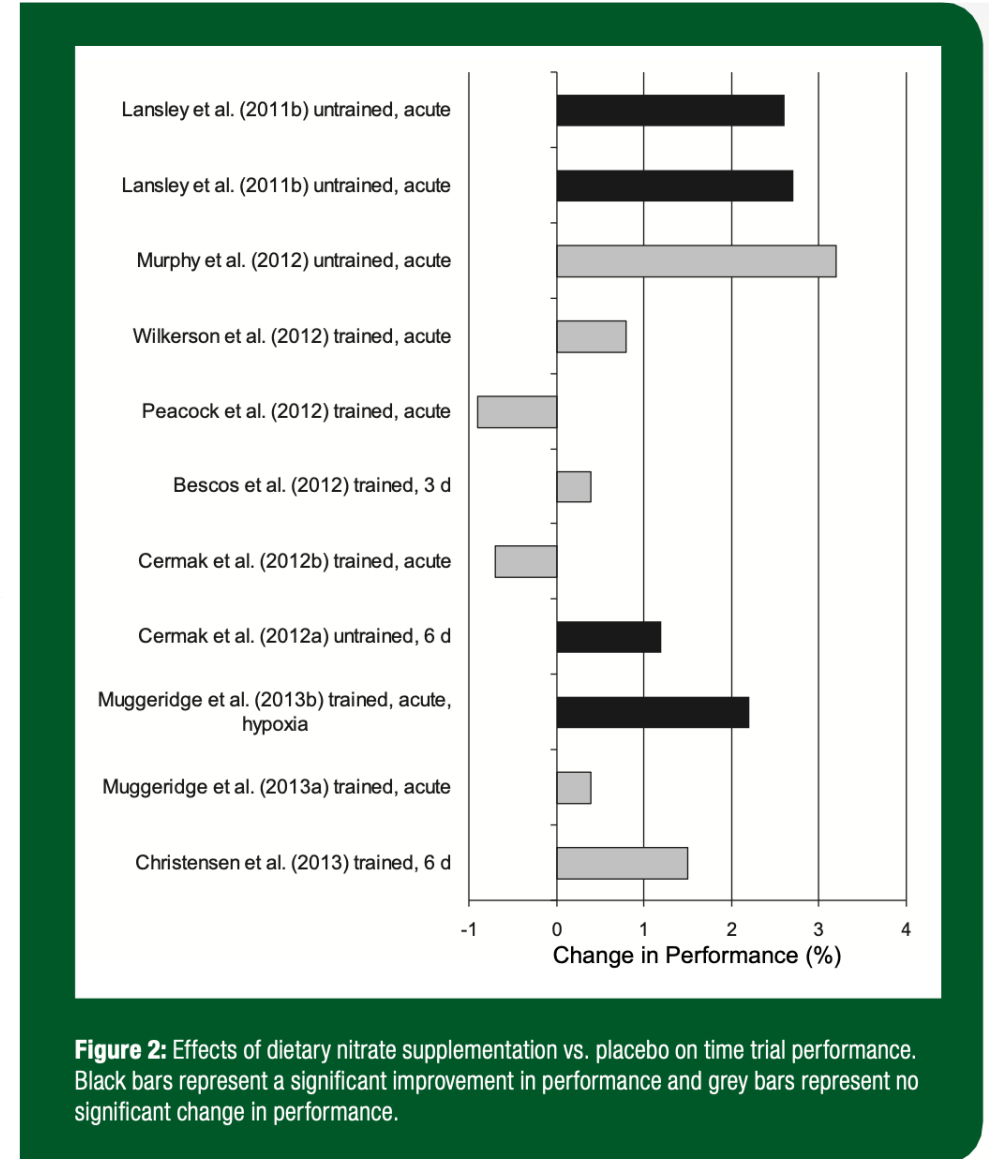
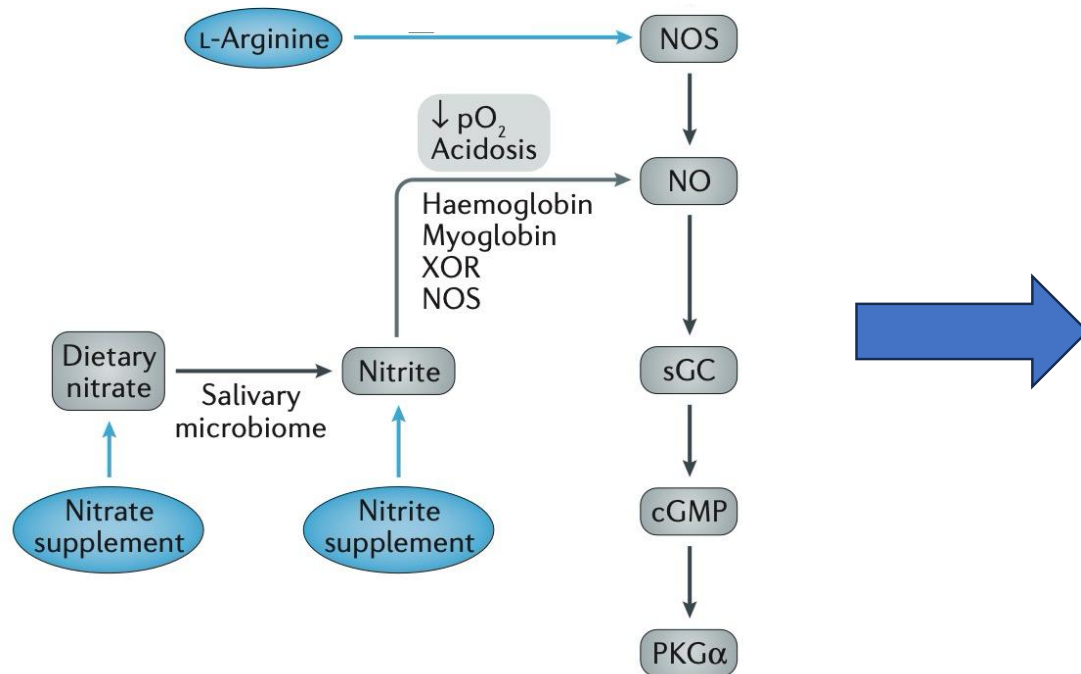


Figure 2: Effects of dietary nitrate supplementation vs. placebo on time trial performance. Black bars represent a significant improvement in performance and grey bars represent no significant change in performance.

Arginina

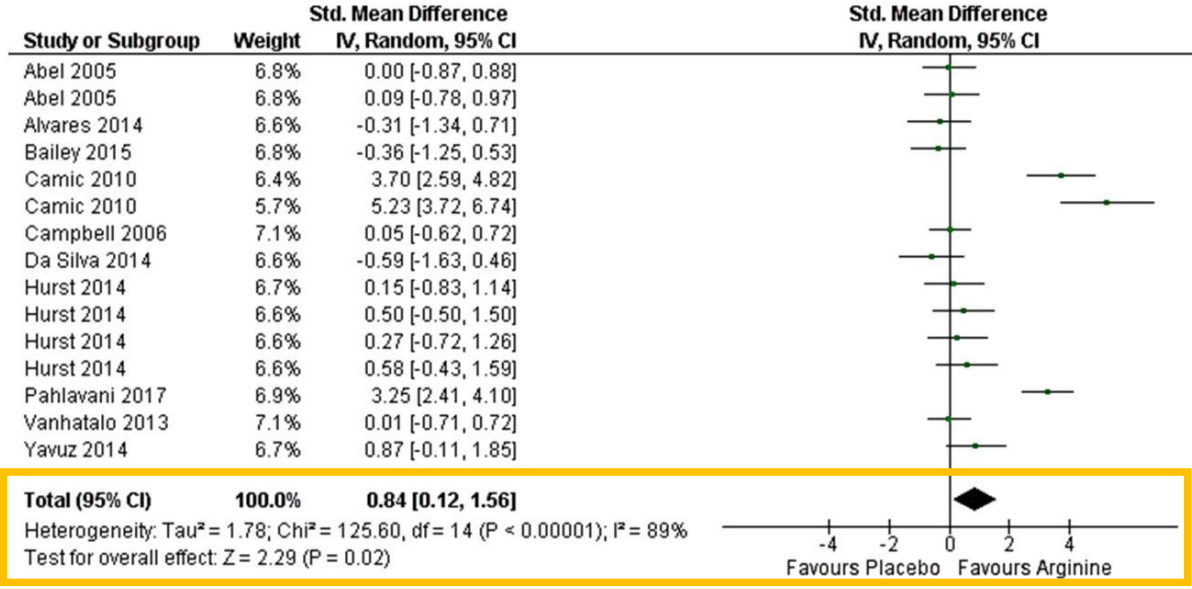
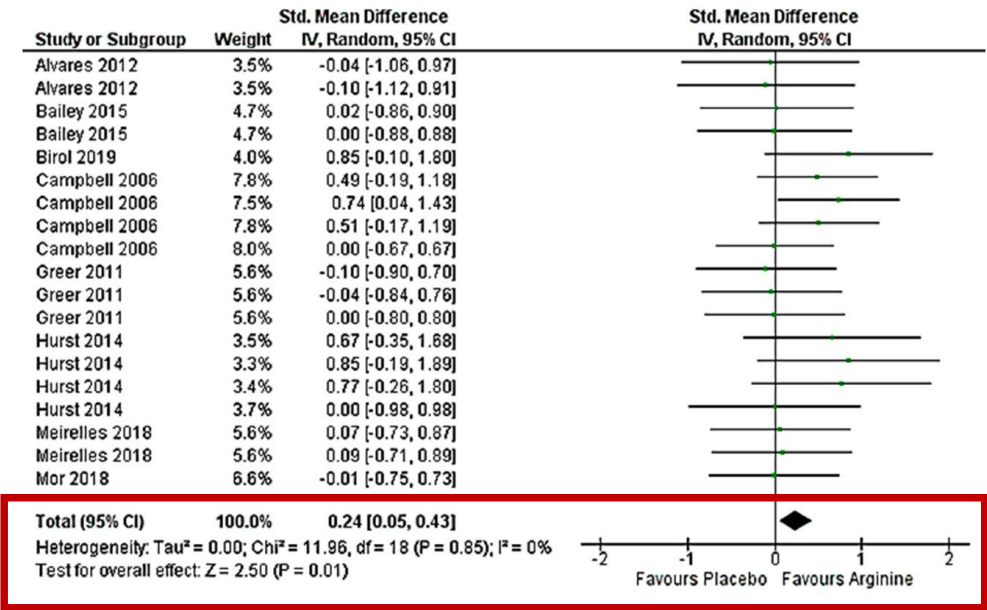
Effects of Arginine Supplementation on Athletic Performance Based on Energy Metabolism: A Systematic Review and Meta-Analysis



Anaerobic performance (>VO₂max)

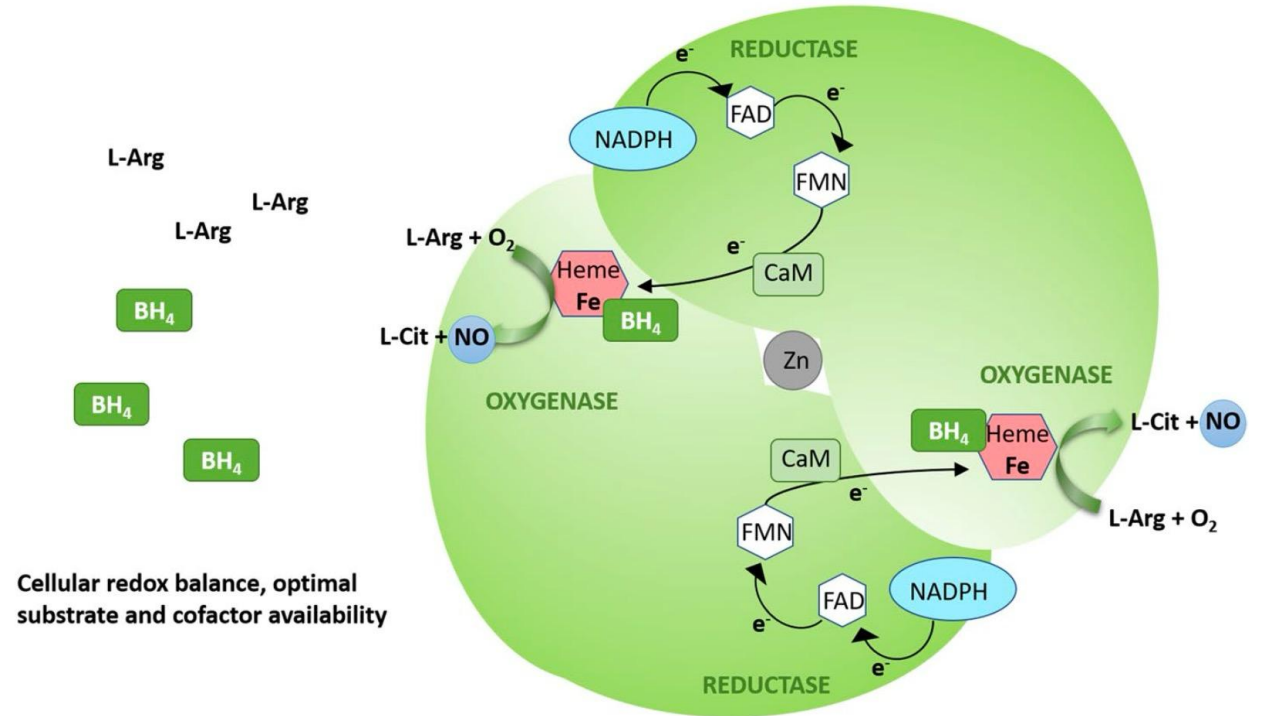
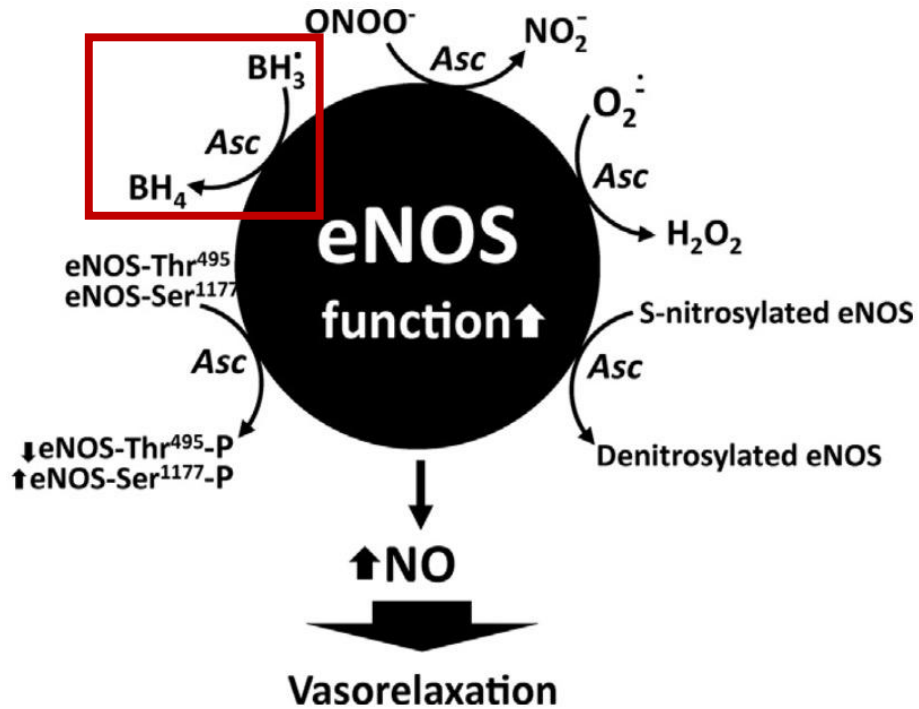


Aerobic performance (≤VO₂max)



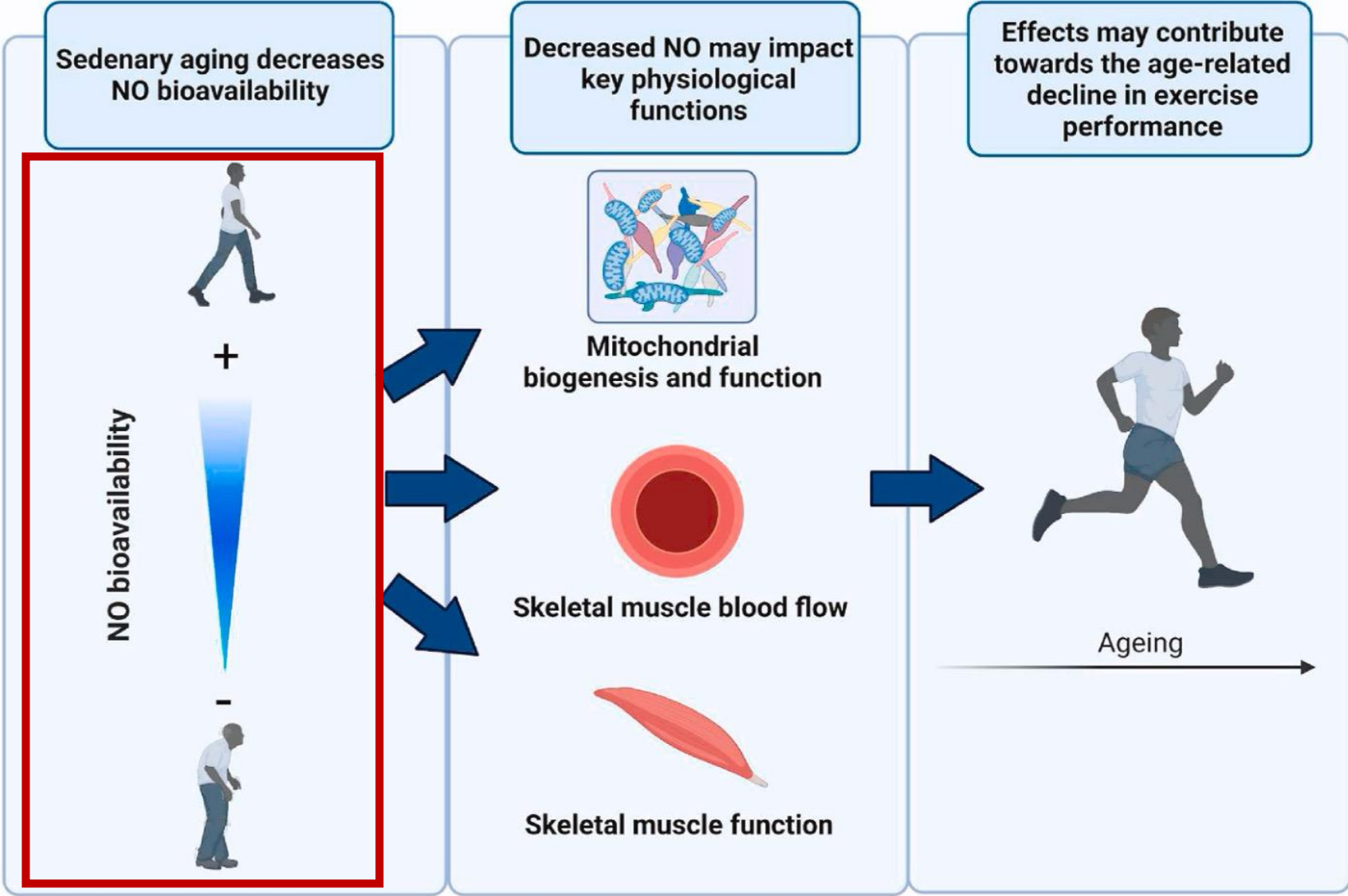
Arginina – Vitamina C

Bioarginina = L-arginina (1.66g) + vitamina C (500mg)

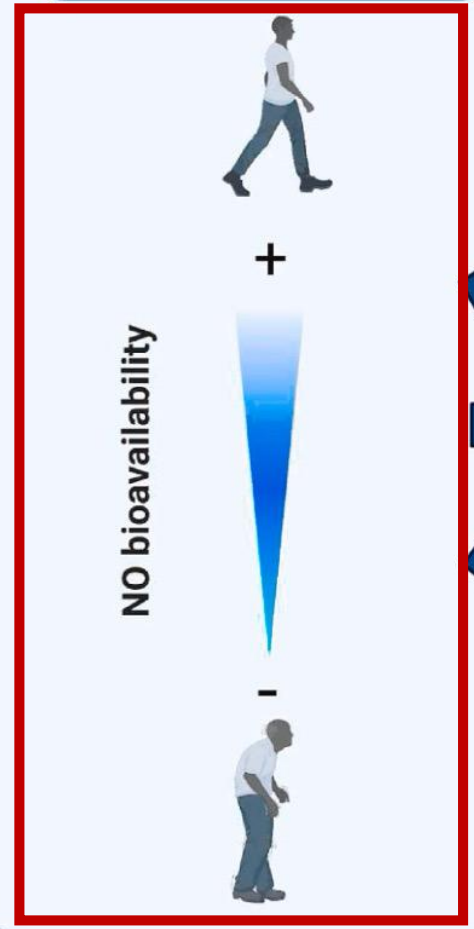


BH4 = tetraidrobiopterina

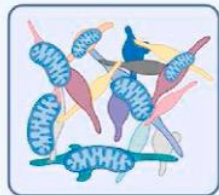
Perché supplementare Arginina – Vitamina C



Sedentary aging decreases NO bioavailability



Decreased NO may impact key physiological functions



Mitochondrial biogenesis and function



Skeletal muscle blood flow

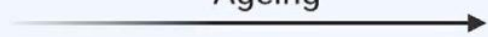


Skeletal muscle function

Effects may contribute towards the age-related decline in exercise performance



Ageing



Disfunzione endoteliale

Article

Impaired Endothelial Function in Convalescent Phase of COVID-19: A 3 Month Follow Up Observational Prospective Study




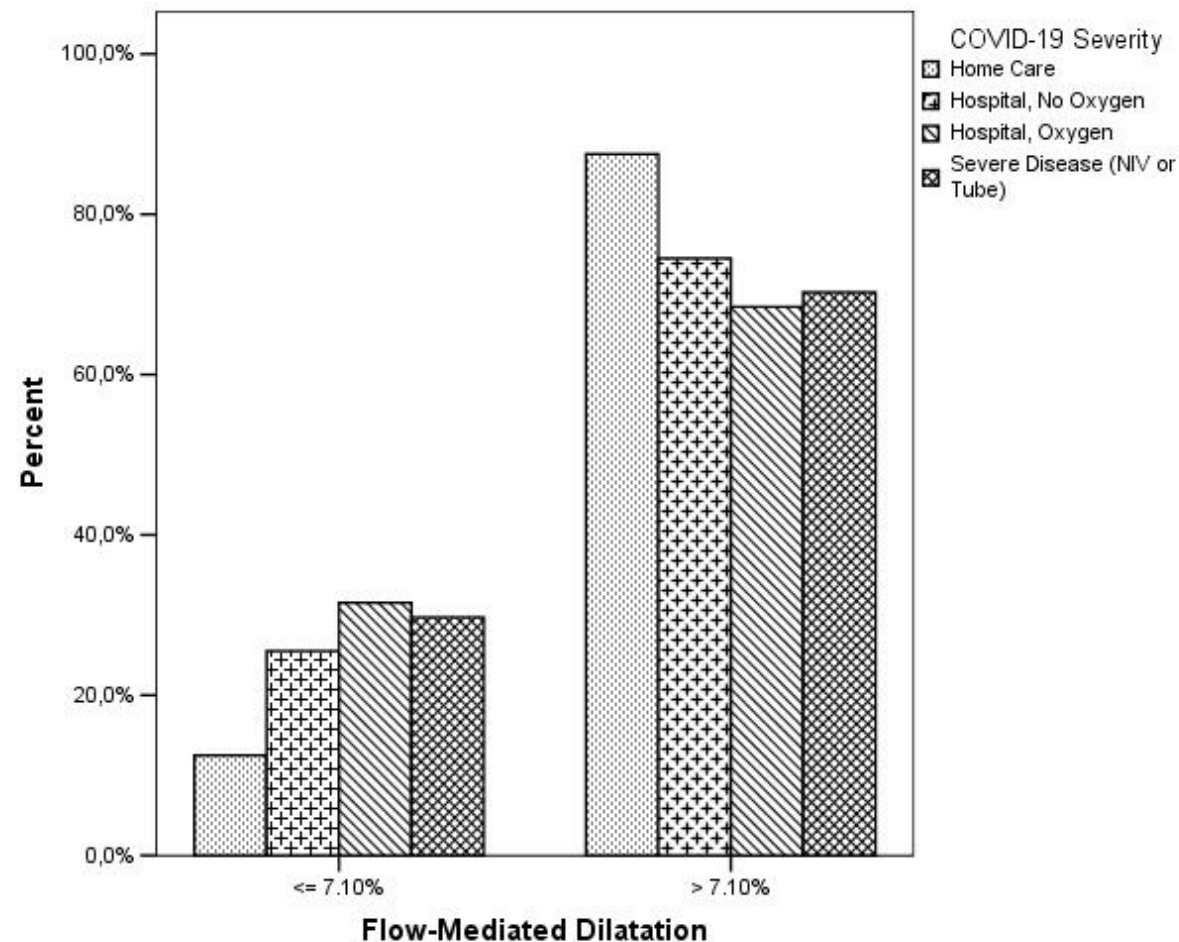
Luca Santoro ^{1,†}, Lorenzo Falsetti ^{2,†} , Vincenzo Zaccone ^{2,*}, Antonio Nesci ¹, Matteo Tosato ³ , Bianca Giupponi ⁴, Maria Cristina Savastano ⁵ , Gianluca Moroncini ⁶, Antonio Gasbarrini ^{7,8}, Francesco Landi ^{3,8}, Angelo Santoliquido ^{1,8} and on behalf of Gemelli against COVID-19 Post-Acute Care Study Group [‡]

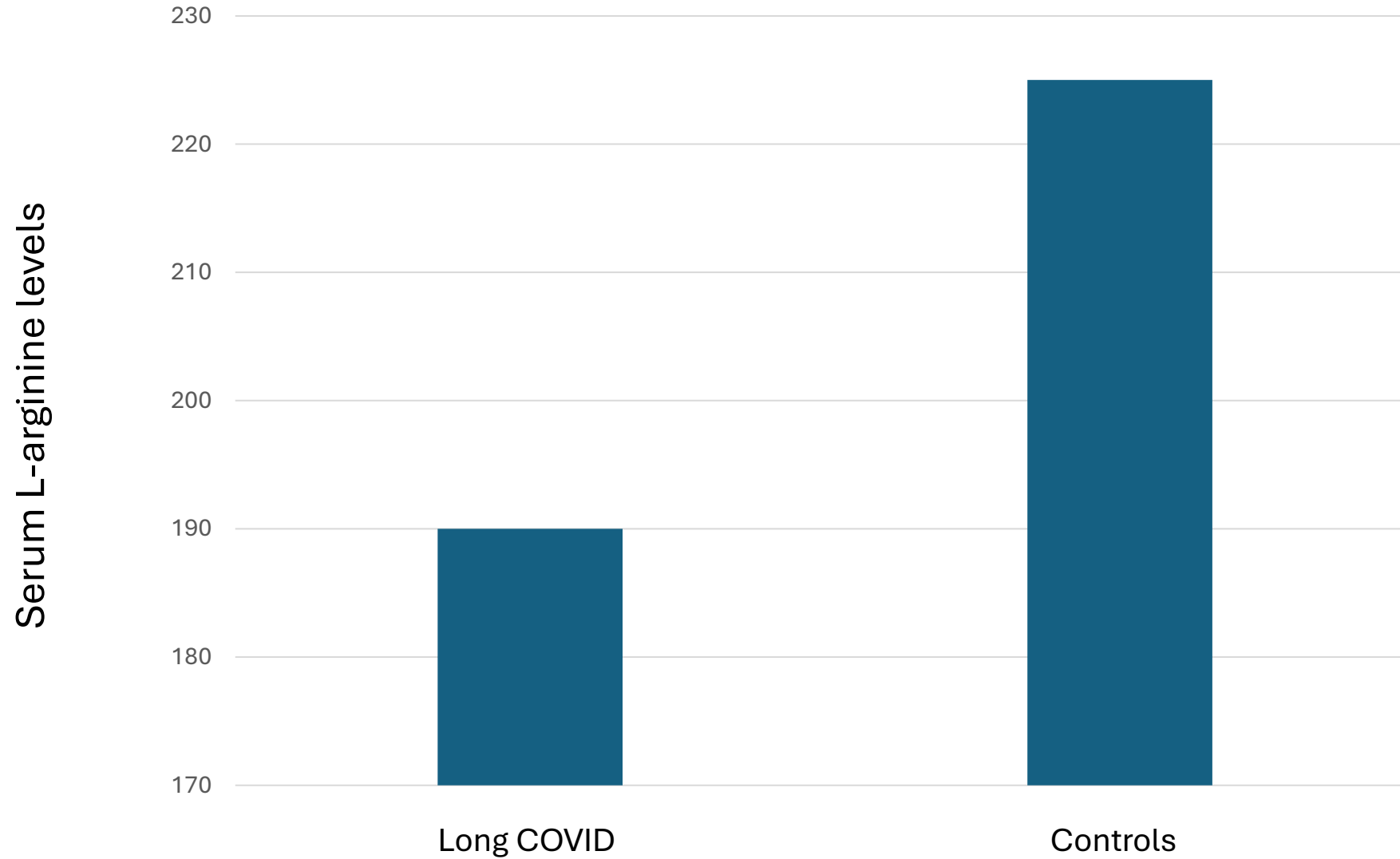
Table 5. Multinomial regression analysis (reference category: not hospitalized).

Severity		p	OR	95% CI	
				Lower	Upper
Hospital, no oxygen	FMD ≤ 7.10%	0.005	2.39	1.29	4.42
Hospital, oxygen	FMD ≤ 7.10%	0.0001	3.22	1.88	5.51
Hospital, NIV, or ICU	FMD ≤ 7.10%	0.0009	2.96	1.55	5.65

Legend: CI = confidence interval; FMD = flow-mediated dilation; NIV = non-invasive ventilation; OR= odds ratio.



Biodisponibilità arginina



Arginina – Vitamina C nel Long-COVID19

Effects of L-Arginine Plus Vitamin C Supplementation on Physical Performance, Endothelial Function, and Persistent Fatigue in Adults with Long COVID: A Single-Blind Randomized Controlled Trial

Matteo Tosato ¹, Riccardo Calvani ^{1,*}, Anna Picca ^{1,2}, Francesca Ciciarello ¹, Vincenzo Galluzzo ¹, Hélio José Coelho-Júnior ^{1,3}, Angela Di Giorgio ¹, Clara Di Mario ⁴, Jacopo Gervasoni ¹, Elisa Gremese ^{1,3,4}, Paolo Maria Leone ¹, Antonio Nesci ¹, Anna Maria Paglionico ¹, Angelo Santoliquido ^{1,5}, Luca Santoro ¹, Lavinia Santucci ⁶, Barbara Tolusso ⁴, Andrea Urbani ^{1,7}, Federico Marini ⁸, Emanuele Marzetti ^{1,3} and Francesco Landi ^{1,3} on behalf of the Gemelli against COVID-19 Post-Acute Care Team

Inclusion Criteria

- A
- I
- S
- a



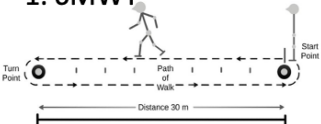
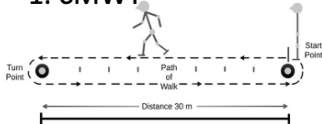
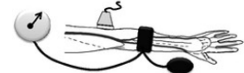
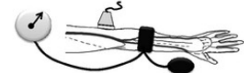
Treatment Group:
1 bottle twice per day orally containing:
L-arginine 1,66 g
Vitamin C 500 mg

Placebo Group:
1 bottle twice per day orally containing:
placebo (solution with same colour and flavour)

Exclusion Criteria

- H
- P
- (
- R

Outcomes:
Fatigue persistence, changes in handgrip strength, distance covered at 6MWT and FMD

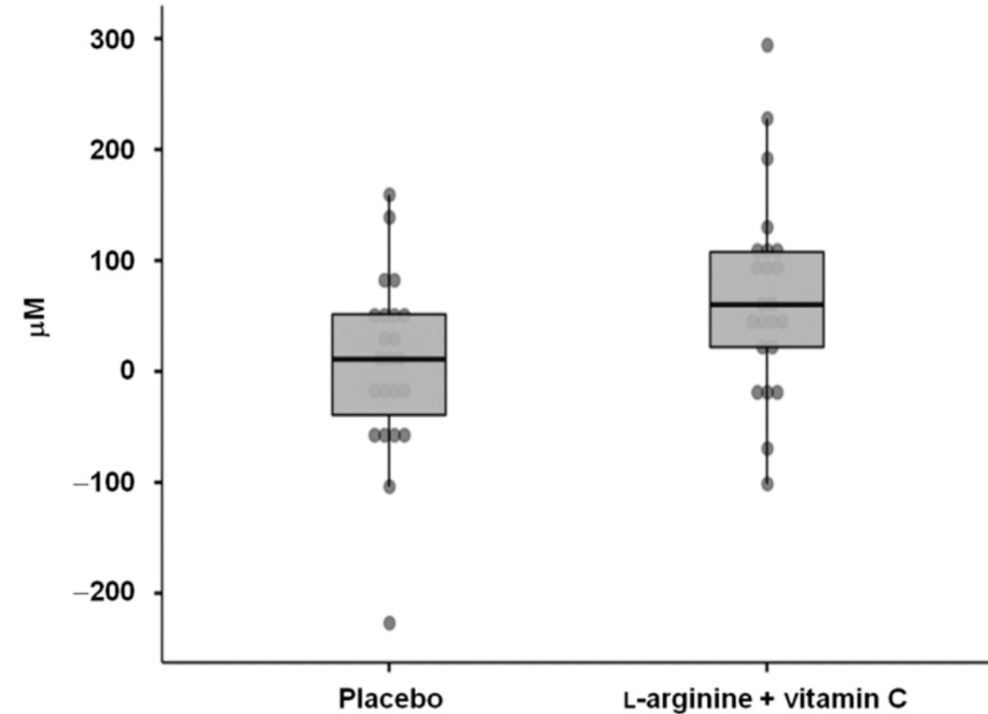
Visit 1 (T ₀)	Visit 2 (T ₁) – 28 days
 <p>Blood collection for metabolic markers and immune cells characterization (phenotype and activity)</p>	 <p>Blood collection for metabolic markers and immune cells characterization (phenotype and activity)</p>
<p>Assessment of physical performance and fatigue</p> <p>1. 6MWT</p>  <p>2. Borg rating perceived exertion scale</p>	<p>Assessment of physical performance and fatigue</p> <p>1. 6MWT</p>  <p>2. Borg rating perceived exertion scale</p>
<p>Handgrip Exhaustion time</p>	<p>Handgrip Exhaustion time</p>
<p>Flow-mediated dilation test</p> 	<p>Flow-mediated dilation test</p> 

Arginina – Vitamina C nel Long-COVID19

Effects of L-Arginine Plus Vitamin C Supplementation on Physical Performance, Endothelial Function, and Persistent Fatigue in Adults with Long COVID: A Single-Blind Randomized Controlled Trial

Matteo Tosato ¹, Riccardo Calvani ^{1,*}, Anna Picca ^{1,2}, Francesca Ciciarello ¹, Vincenzo Galluzzo ¹, Hélio José Coelho-Júnior ^{1,3}, Angela Di Giorgio ¹, Clara Di Mario ⁴, Jacopo Gervasoni ¹, Elisa Gremese ^{1,3,4}, Paolo Maria Leone ¹, Antonio Nesci ¹, Anna Maria Paglionico ¹, Angelo Santoliquido ^{1,5}, Luca Santoro ¹, Lavinia Santucci ⁶, Barbara Tolusso ⁴, Andrea Urbani ^{1,7}, Federico Marini ⁸, Emanuele Marzetti ^{1,3} and Francesco Landi ^{1,3} on behalf of the Gemelli against COVID-19 Post-Acute Care Team

Δ [L-Arg] sierica dopo trattamento



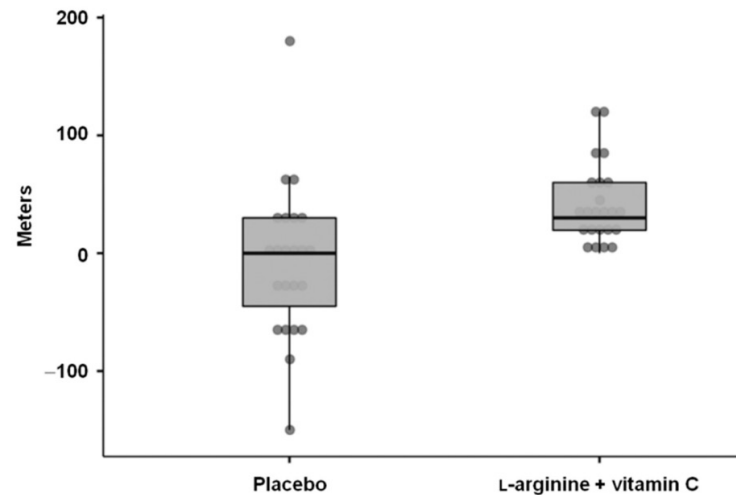
Differenza media Bioarg vs. placebo= 62.4 μM;
effect size = 0.72; $p = 0.02$

Arginina – Vitamina C nel Long-COVID19

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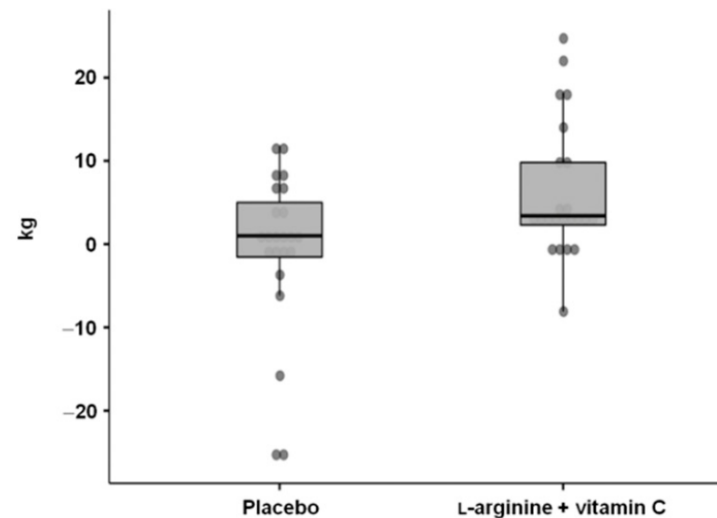
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Δ distanza test 6 minuti



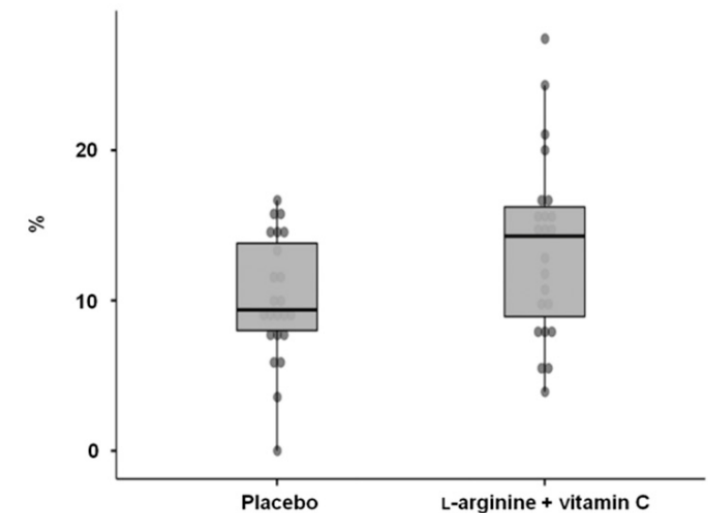
Differenza media Bioarg vs placebo= 50m;
effect size = 0.56; $p = 0.001$

Δ Handgrip



Differenza media Bioarg vs placebo= 3.4Kg;
effect size = 0.37; $p = 0.03$

Δ FMD



Differenza media Bioarg vs placebo= 3.4%;
effect size = 0.66; $p = 0.03$

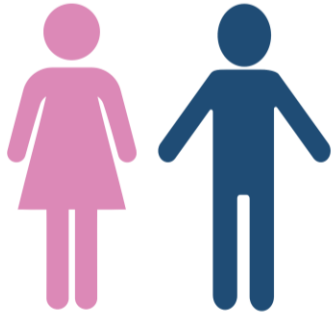
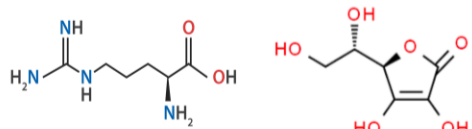
Arginina – Vitamina C nel Long-COVID19

Effects of L-Arginine Plus Vitamin C Supplementation on Physical Performance, Endothelial Function, and Persistent Fatigue in Adults with Long COVID: A Single-Blind Randomized Controlled Trial

Matteo Tosato ¹, Riccardo Calvani ^{1,*}, Anna Picca ^{1,2}, Francesca Ciciarello ¹, Vincenzo Galluzzo ¹, Hélio José Coelho-Júnior ^{1,3}, Angela Di Giorgio ¹, Clara Di Mario ⁴, Jacopo Gervasoni ¹, Elisa Gremese ^{1,3,4}, Paolo Maria Leone ¹, Antonio Nesci ¹, Anna Maria Paglionico ¹, Angelo Santoliquido ^{1,5}, Luca Santoro ¹, Lavinia Santucci ⁶, Barbara Tolusso ⁴, Andrea Urbani ^{1,7}, Federico Marini ⁸, Emanuele Marzetti ^{1,3} and Francesco Landi ^{1,3} on behalf of the Gemelli against COVID-19 Post-Acute Care Team

L-arginine (1.66 g) + vitamin C (500 mg) b.i.d.

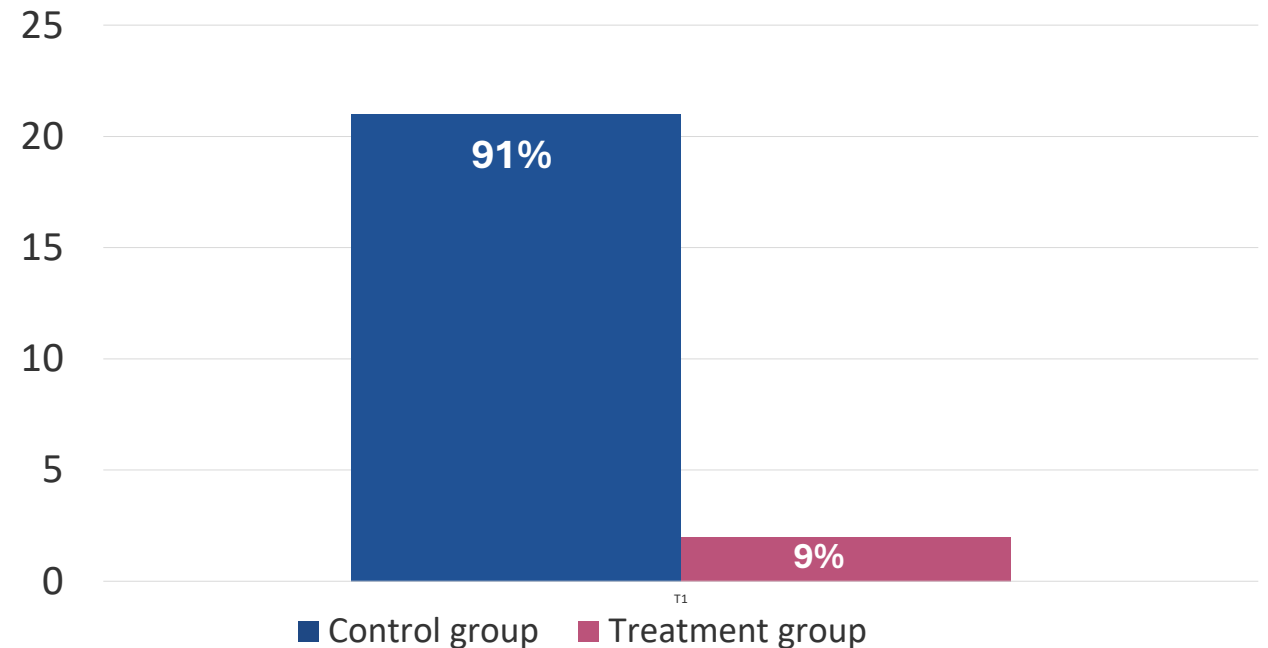
28 day-intervention/Placebo-controlled



20-60 year-old
Long COVID (persistent fatigue)

- + Serum L-arginine
- + 6-minute walk distance
- + Handgrip strength
- + Flow-mediated dilation
- Fatigue

Prevalence of fatigue after 28-day



Effects of L-Arginine Plus Vitamin C Supplementation on L-Arginine Metabolism in Adults with Long COVID: Secondary Analysis of a Randomized Clinical Trial

Characteristic	Long COVID		Healthy Controls (n = 11)
	L-Arginine + Vitamin C (n = 23)	Placebo (n = 23)	
Age, years	47.3 ± 10.7	48.4 ± 8.0	48.8 ± 11.1
Women, n (%)	15 (65.2)	15 (65.2)	6 (55.5)
BMI, kg/m ²	25.6 ± 5.6	25.6 ± 4.0	25.8 ± 4.7
Glucose, mmol/L	4.8 ± 0.6	4.8 ± 0.6	5.0 ± 0.3
Total Cholesterol, mmol/L	5.4 ± 1.1	5.3 ± 1.1	4.6 ± 0.5
Albumin, mmol/L	0.66 ± 0.05	0.65 ± 0.04	0.67 ± 0.05
Creatinine, μmol/L	69.7 ± 16.4	68.2 ± 14.9	64.0 ± 11.7
CRP, nmol/L, median (IQR)	33.3 (80.9)	33.3 (22.9)	33.1 (18.4)
Hemoglobin, g/L	14.3 ± 1.5	14.2 ± 1.4	14.3 ± 1.2
White Blood Cells, 10 ⁹ L	5.6 ± 2.0	6.1 ± 1.8	5.8 ± 2.0
L-arginine, μM	192.7 ± 74.1	196.6 ± 80.6	221.6 ± 31.3
Citrulline, μM	41.4 ± 13.2	41.6 ± 11.9	30.1 ± 7.5
Ornithine, μM	122.5 ± 43.6	124.9 ± 56.6	82.9 ± 12.5
ADMA, μM	0.60 ± 0.14	0.64 ± 0.19	0.48 ± 0.02
MMA, μM	0.13 ± 0.05	0.14 ± 0.06	0.10 ± 0.02
SDMA, μM	0.71 ± 0.15	0.77 ± 0.25	0.53 ± 0.11
Arginine/ADMA	320.9 ± 97.0	316.5 ± 103.2	462.8 ± 31.3
Arginine/ornithine	1.8 ± 1.0	1.8 ± 0.9	2.7 ± 0.4
GABR	1.3 ± 0.6	1.3 ± 0.6	2.0 ± 0.3

Long COVID
ADMA = 125 ng/mL
SDMA = 150 ng/mL

 **ClevelandHeartLab**[®]
Know your risk.

RELATIVE RISK

ADMA
(ng/mL)



REFERENCE RANGE

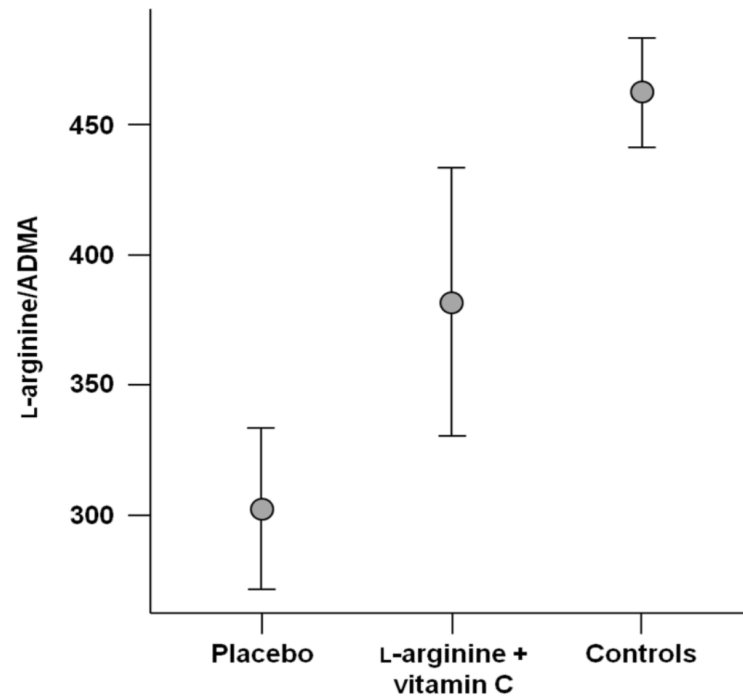
SDMA
(ng/mL)



Effects of L-Arginine Plus Vitamin C Supplementation on L-Arginine Metabolism in Adults with Long COVID: Secondary Analysis of a Randomized Clinical Trial

Intervento: 2 flaconi/d Bioarginina vs. placebo per 28 giorni

L-Arg/ADMA dopo trattamento



Studio ARGO



Effetto della supplementazione di L-Arginina e Vitamina C in anziani con sarcopenia probabile

- RCT contro placebo
- uomini e donne; età ≥ 70 anni con sarcopenia probabile
- Supplementazione con 2 flaconi/die di L-arginina (1.66g) + Vitamina C liposomiale (500mg) o placebo per 8 settimane

Endpoint primario: Δ distanza percorsa nel six minute walking test (6MWT)

Endpoint secondari: Δ Handgrip strength, Chair stand test, Flow mediated dilation

Studio ARGO – *Caratteristiche popolazione*



	Totale	Bioarginina	Placebo
N	86	43	43
Età	75.8 (3.4)	74.8 (4.4)	76.5 (2.6)
Sesso, F (%)	53%	53%	53%
BMI (m/kg²)	24.1 (2.4)	24.0 (2.0)	24.2 (2.6)
6MWT, m	407.2 (126.2)	408.3 (128.8)	405.3 (119.2)
STS, s	10.7 (3.3)	10.5 (2.3)	11.0 (3.6)
Handgrip, kg			
F	14.5 (2.5)	14.7 (2.7)	14.3 (2.4)
M	23.0 (3.2)	22.8 (3.0)	22.7 (3.4)
ALM, kg			
F	15.2 (3.2)	15.0 (3.4)	15.2 (2.8)
M	18.2 (3.9)	18.4 (4.3)	17.8 (3.7)

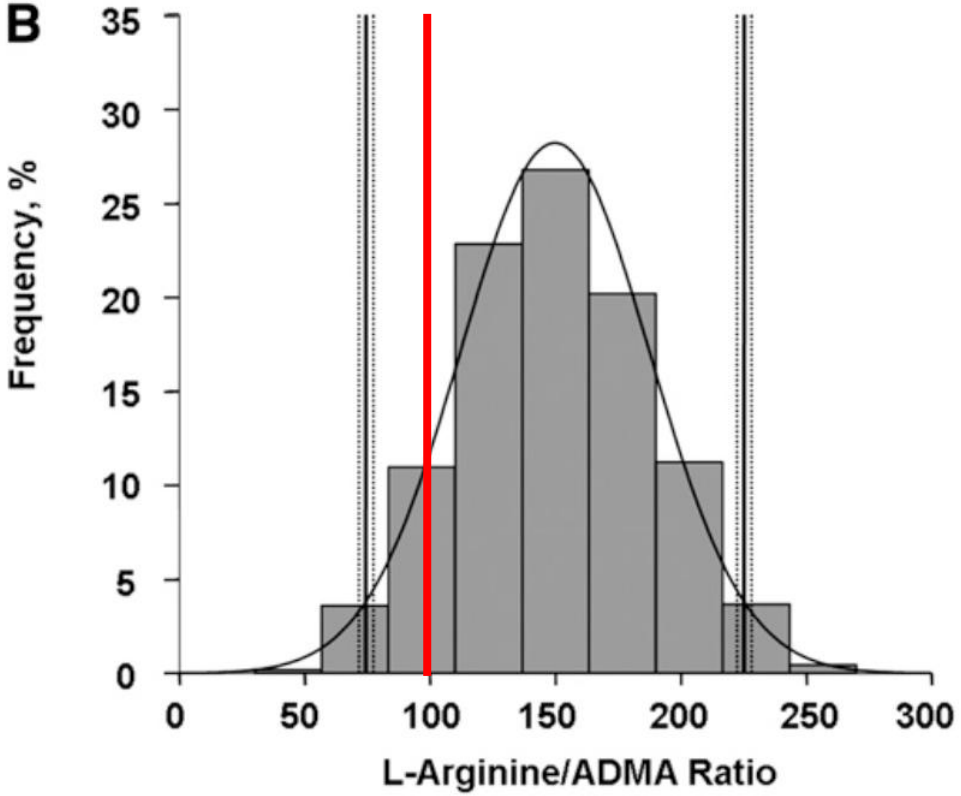
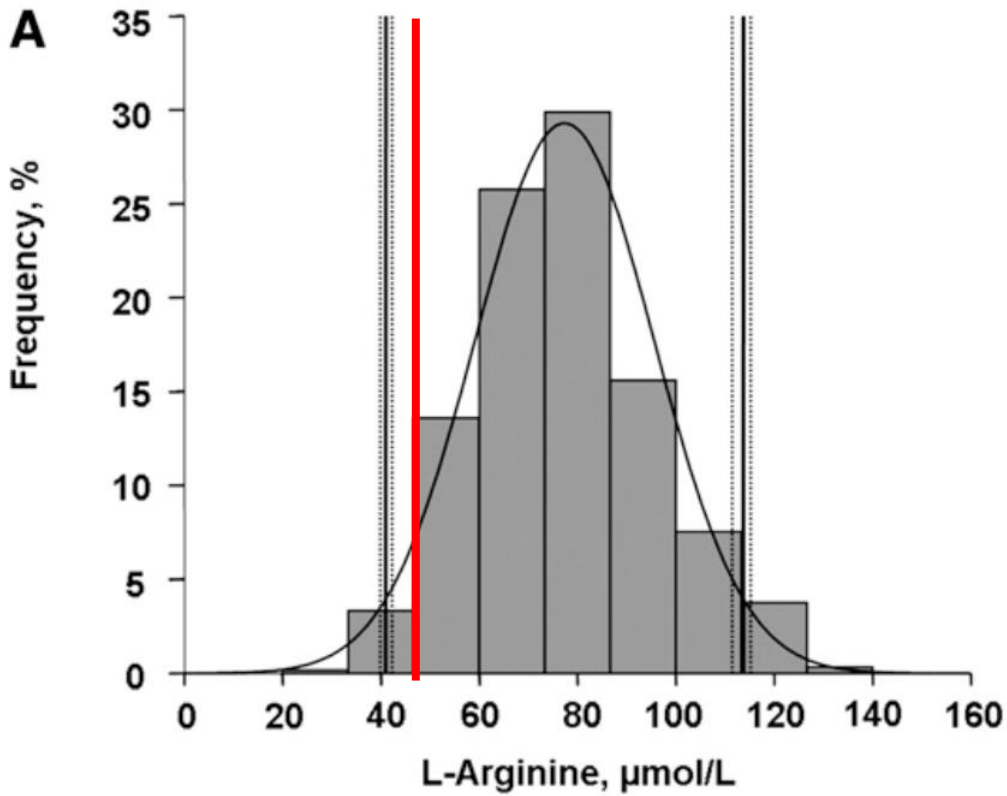


Studio ARGO – Caratteristiche popolazione

Reference Intervals for Plasma L-Arginine and the L-Arginine:Asymmetric Dimethylarginine Ratio in the Framingham Offspring Cohort¹⁻³

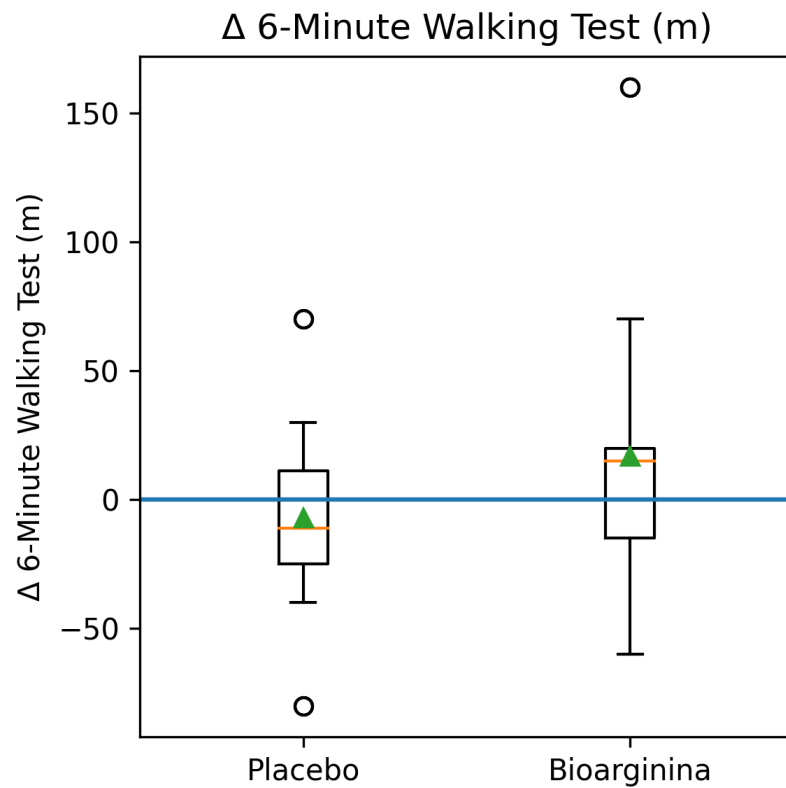
Nicole Lüneburg,^{4*} Vanessa Xanthakis,^{5,8,9} Edzard Schwedhelm,⁴ Lisa M. Sullivan,⁵ Renke Maas,⁶ Maike Anderssohn,⁴ Ulrich Riederer,⁷ Nicole L. Glazer,⁹ Ramachandran S. Vasani,⁸⁻¹⁰ and Rainer H. Böger⁴

— 25° percentile popolazione ARGO



Studio ARGO – *Risultati*

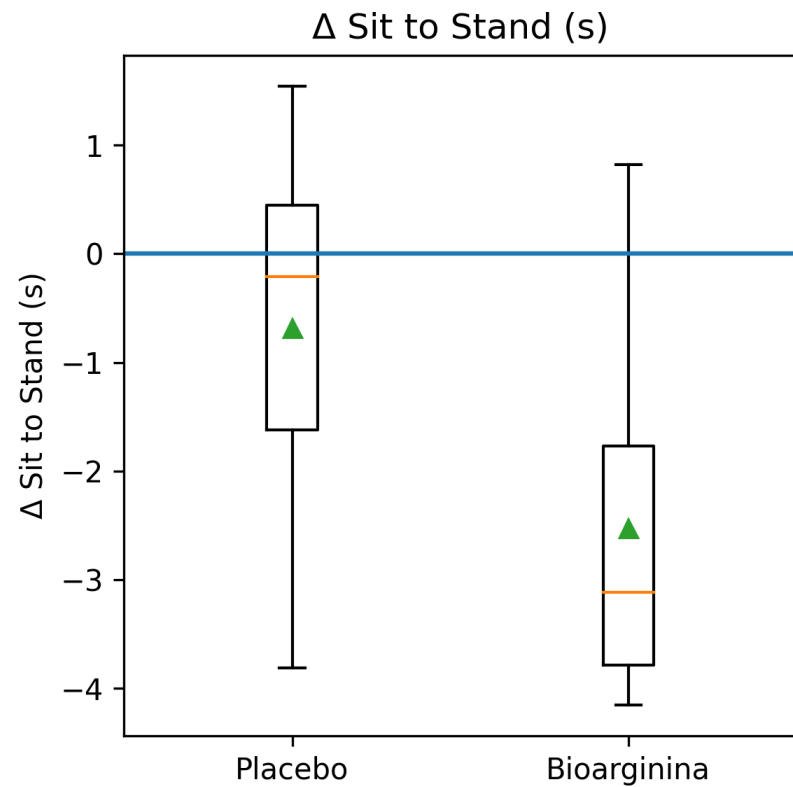
Variazione distanza percorsa al 6mwt



Differenza media tra gruppi (Bioarginina – Placebo): +23.9 m
p = 0.048

Studio ARGO – Risultati

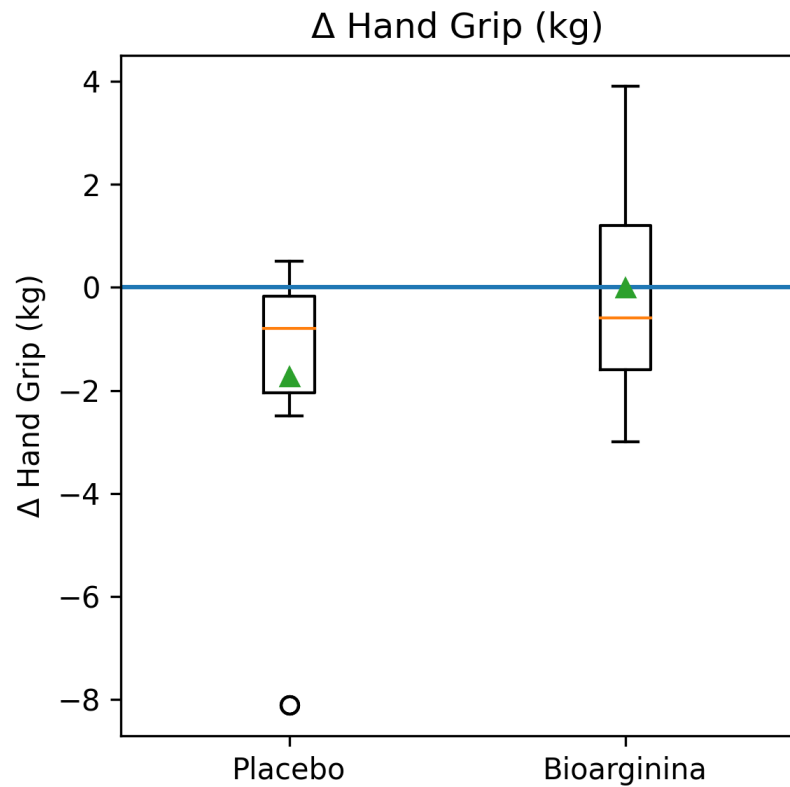
Variazione tempo del test della sedia



Differenza media tra gruppi (Bioarginina – Placebo): -1.84 s
p = 0.06

Studio ARGO – Risultati

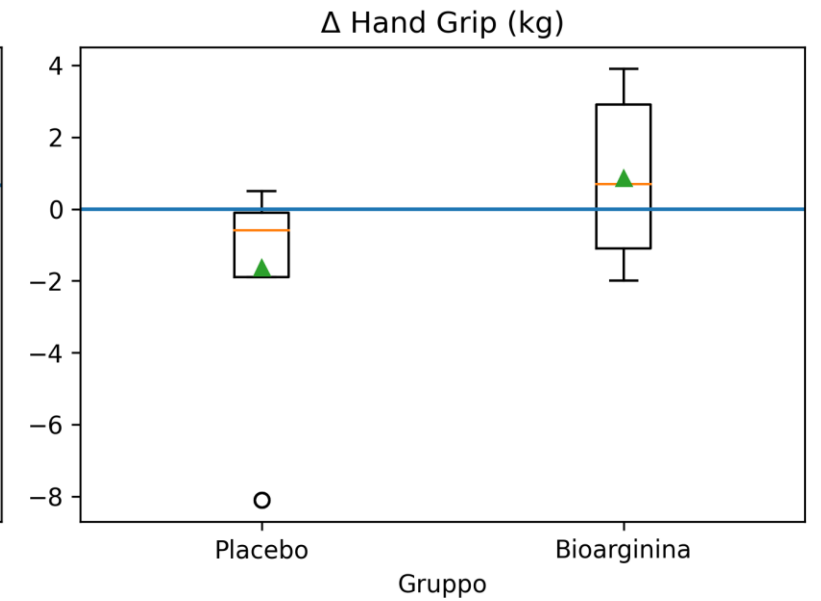
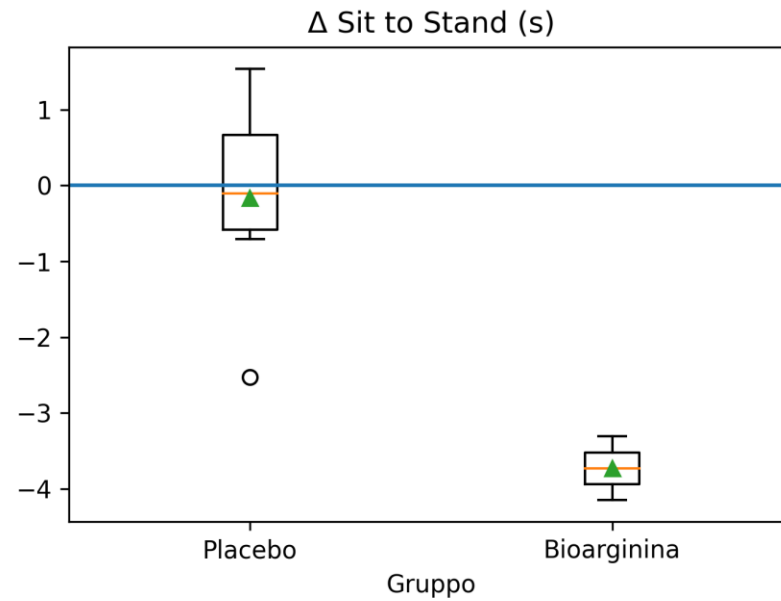
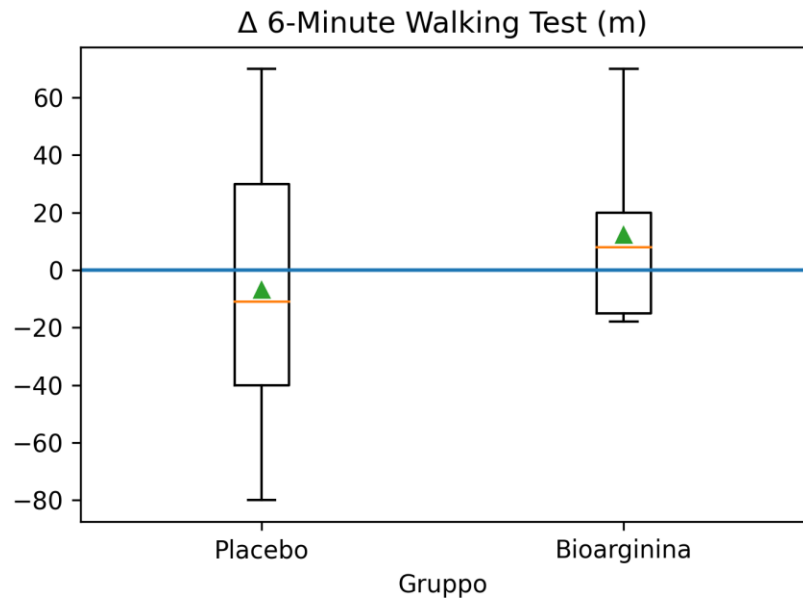
Variazione forza prensione mano (handgrip)



Differenza media tra gruppi (Bioarginina – Placebo): +1.73 kg
p = 0.009

Studio ARGO – Risultati

Donne - Variazione T2 – T0



p < 0.05

Partecipanti di sesso femminile

CONCLUSIONI

- **L'arginina svolge un ruolo chiave nella produzione di ossido nitrico, a sua volta fondamentale per la performance muscolare**
- **La supplementazione di l-arginina e vitamina C liposomiale ha dimostrato di migliorare gli outcomes funzionali in una coorte di pazienti anziani con sarcopenia probabile come test del cammino di 6 minuti, test della sedia ed handgrip strength**
- **Tali risultati sono particolarmente evidenti nelle donne**