The Danish Society of Clinical Nutrition
Annual Clinical Nutrition Meeting 2012
Copenhagen, Denmark – 8 June 2012

Anabolic resistance: a road map to malnutrition

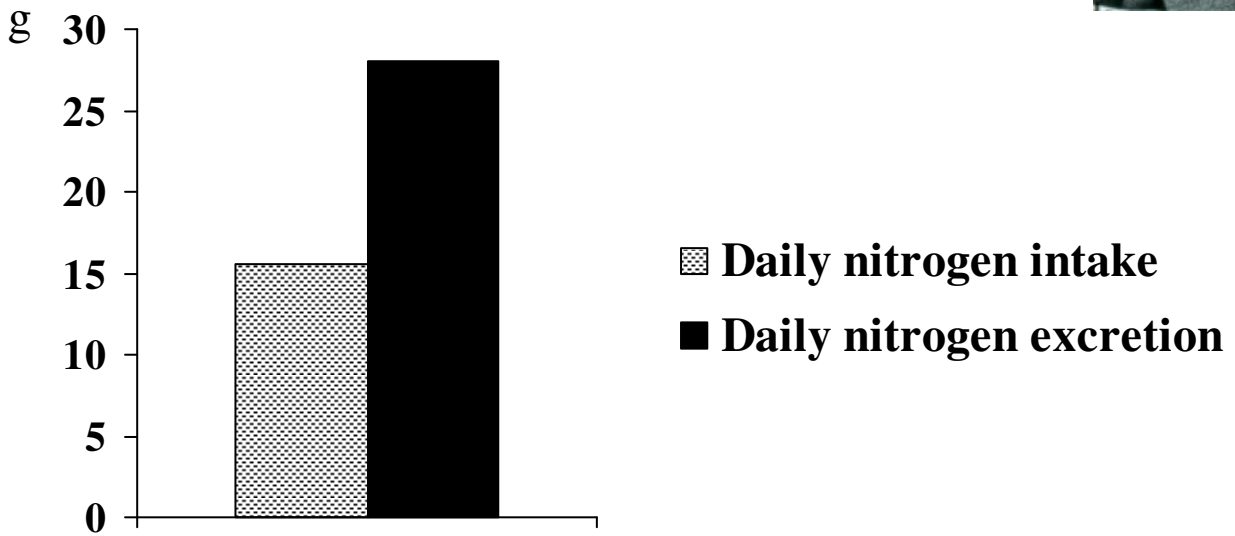
Gianni Biolo

Department of Medical Science - University of Trieste
Department of Internal Medicine - AOUTS
Trieste - Italy

NUTRITION: RESISTANCE AND REACTION TO TRAUMA

D. P. Cuthbertson, *C.B.E.*, D.SC., M.D., LL.D., F.R.S.E.
(*Director Rowett Research Institute, Aberdeen*)

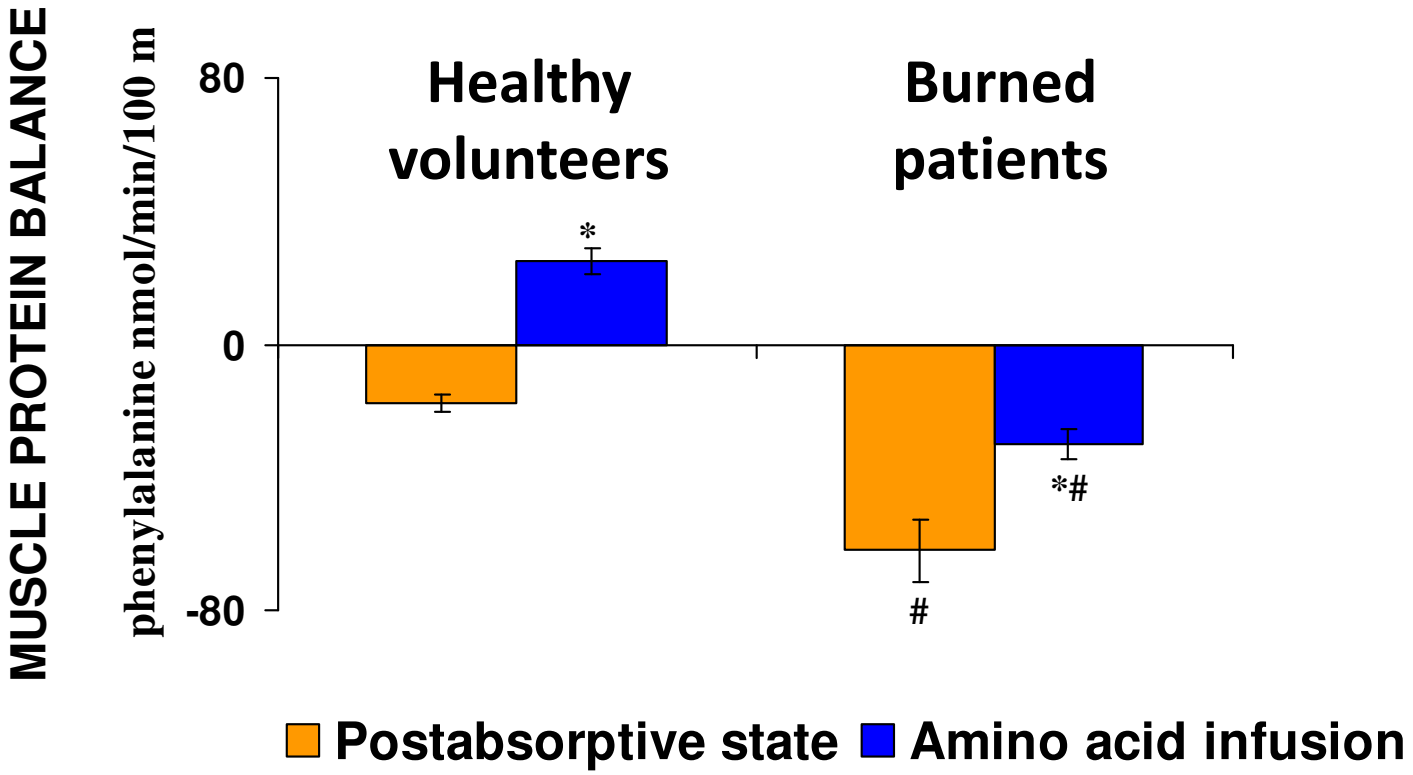
J Coll Gen Pract. 1963



Nitrogen balance of a fractured patient of 34 years receiving 1.5 g protein/kg/day
(*The Disturbance of Metabolism Produced by Bony and non-Bony Injury. Biochem J. 1930*)

EFFECTS OF AMINO ACID INFUSION ON SKELETAL MUSCLE PROTEIN BALANCE IN SEVERELY BURNED PATIENTS

Biolo & Wolfe, Clinical Nutrition (abstract) 2001



*, P<0.05 vs. postabsorptive state #, P<0.05 vs. healthy volunteers

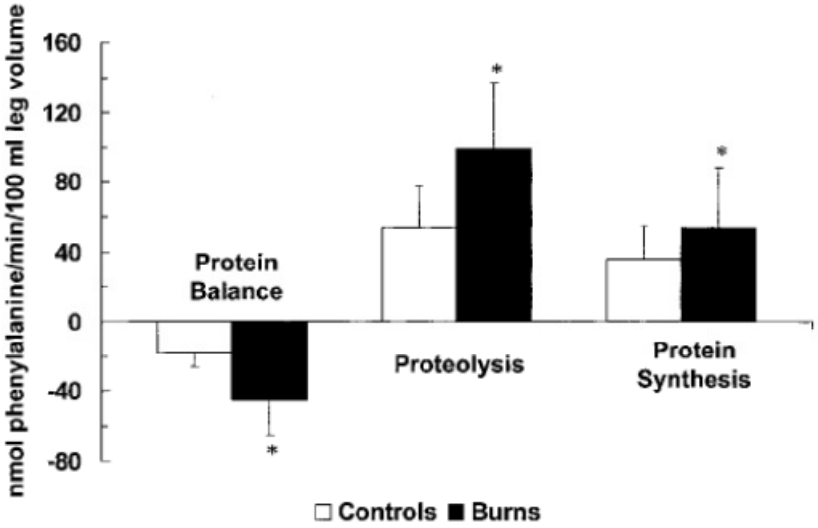
0015-7227/02/$15.00/0
Printed in U.S.A.

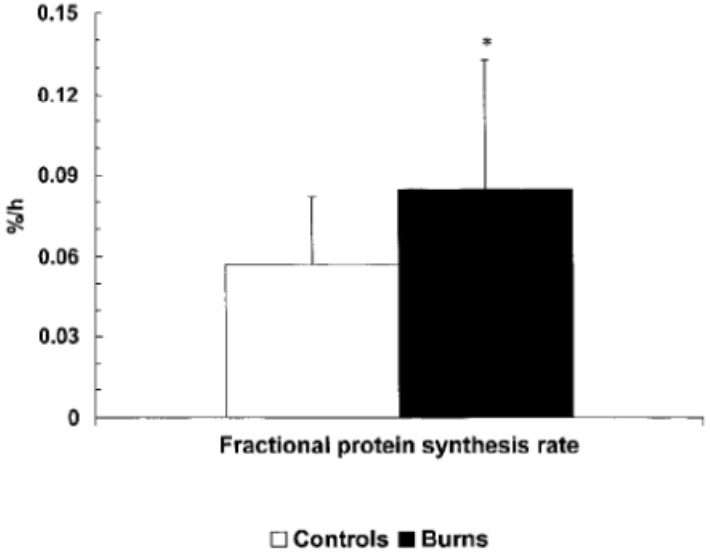
The Journal of Clinical Endocrinology & Metabolism 87(7):3378–3384

Inverse Regulation of Protein Turnover and Amino Acid Transport in Skeletal Muscle of Hypercatabolic Patients

GIANNI BIOLO, R. Y. DECLAN FLEMING, SERGIO P. MAGGI, THUAN T. NGUYEN, DAVID N. HERNDON, AND ROBERT R. WOLFE

Shriners Burns Hospital and University of Texas Medical Branch, Galveston, Texas 77550





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The Journal of Clinical Endocrinology & Metabolism 87(7):3378–3384

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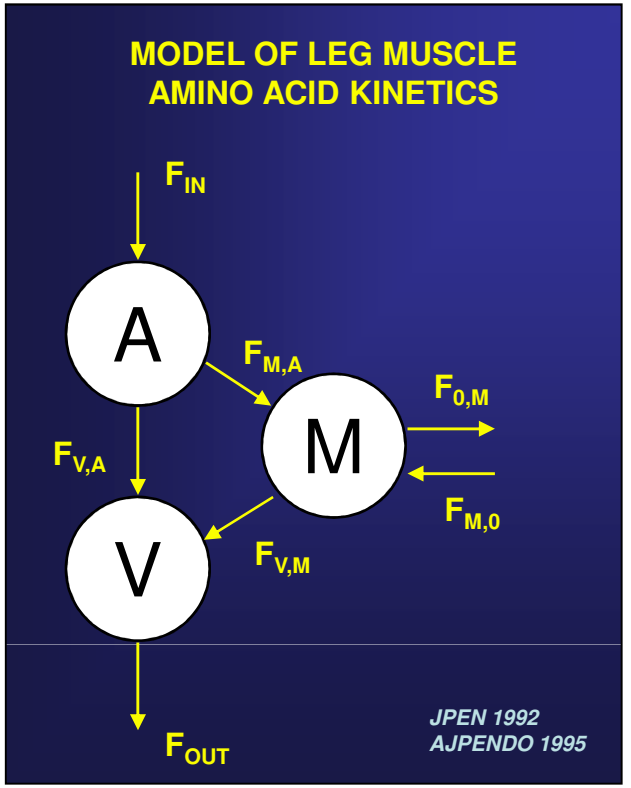

THE ROLE OF TRANSMEMBRANE AMINO ACID TRANSPORT KINETICS IN ANABOLIC RESISTANCE

0015-7227/02/$15.00/0
Printed in U.S.A.

The Journal of Clinical Endocrinology & Metabolism 87(7):3378–3384

Inverse Regulation of Protein Turnover and Amino Acid Transport in Skeletal Muscle of Hypercatabolic Patients

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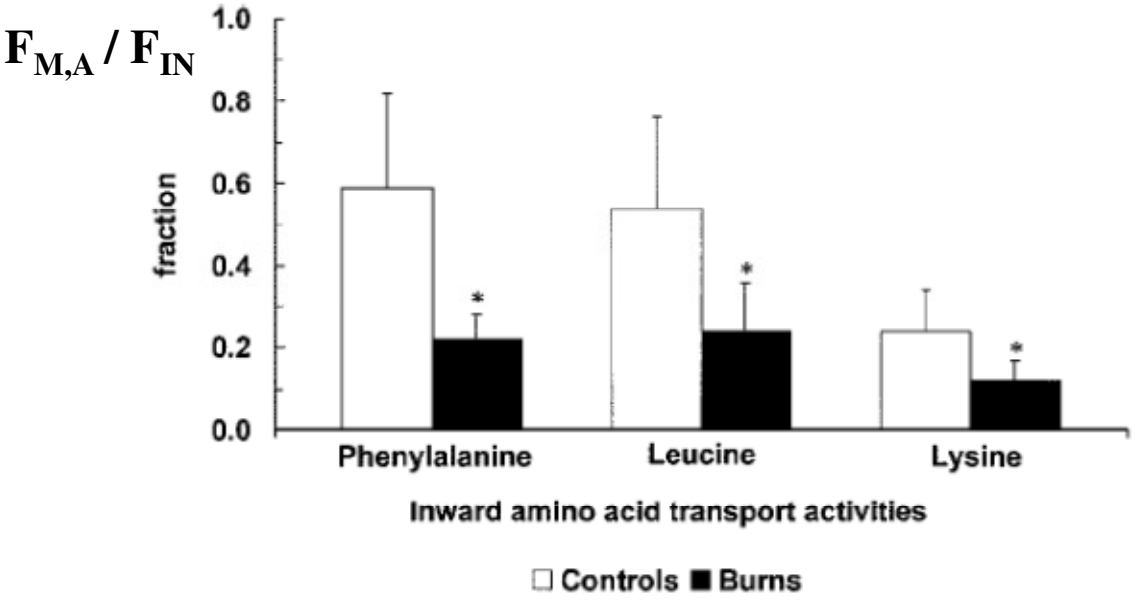
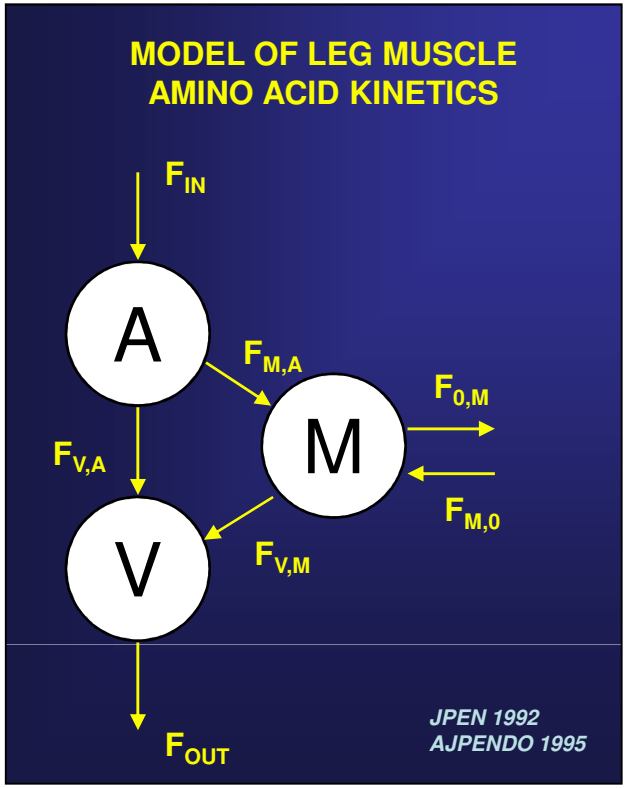


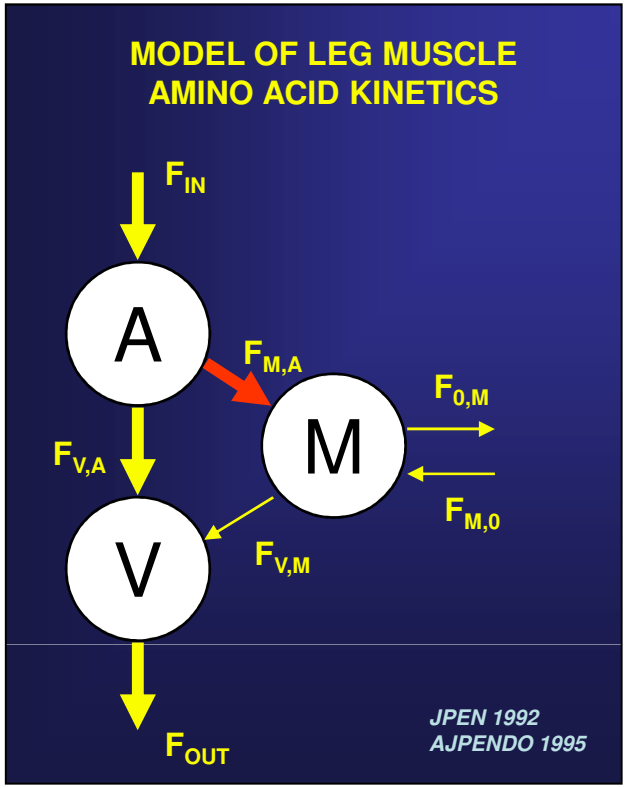


impaired ability of transport systems
and
increased shunting of leg blood flow from artery to vein through non-nutritive routes

Anabolic resistance in critically ill patients

Michael J. Rennie, BSc, MSc, PhD, FRSE

Crit Care Med 2009 Vol. 37, No. 10 (Suppl.)



"Strategies to decrease anabolic resistance should include attempts to increase microvascular, nutritive muscle blood flow."

Physiologic Hyperinsulinemia Stimulates Protein Synthesis and Enhances Transport of Selected Amino Acids in Human Skeletal Muscle

Gianni Biolo,*[1] R. Y. Declan Fleming,[‡] and Robert R. Wolfe[‡§1]

*Departments of *Internal Medicine, [‡]Surgery, and [§]Anesthesiology, The University of Texas Medical Branch; and the [1]Shriners Burns Institute, Galveston, Texas 77550*

J. Clin. Invest. 95:811-819, 1995

MUSCLE PROTEIN SYNTHESIS

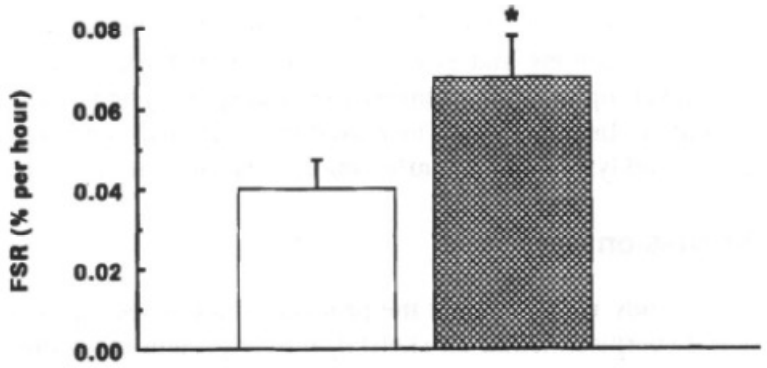
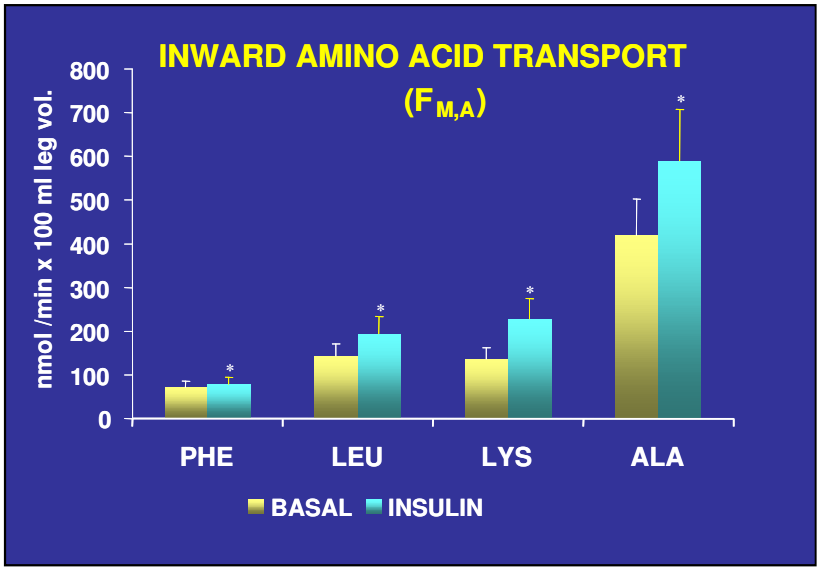
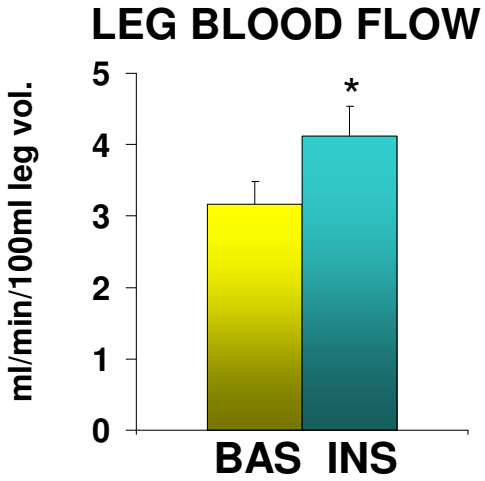


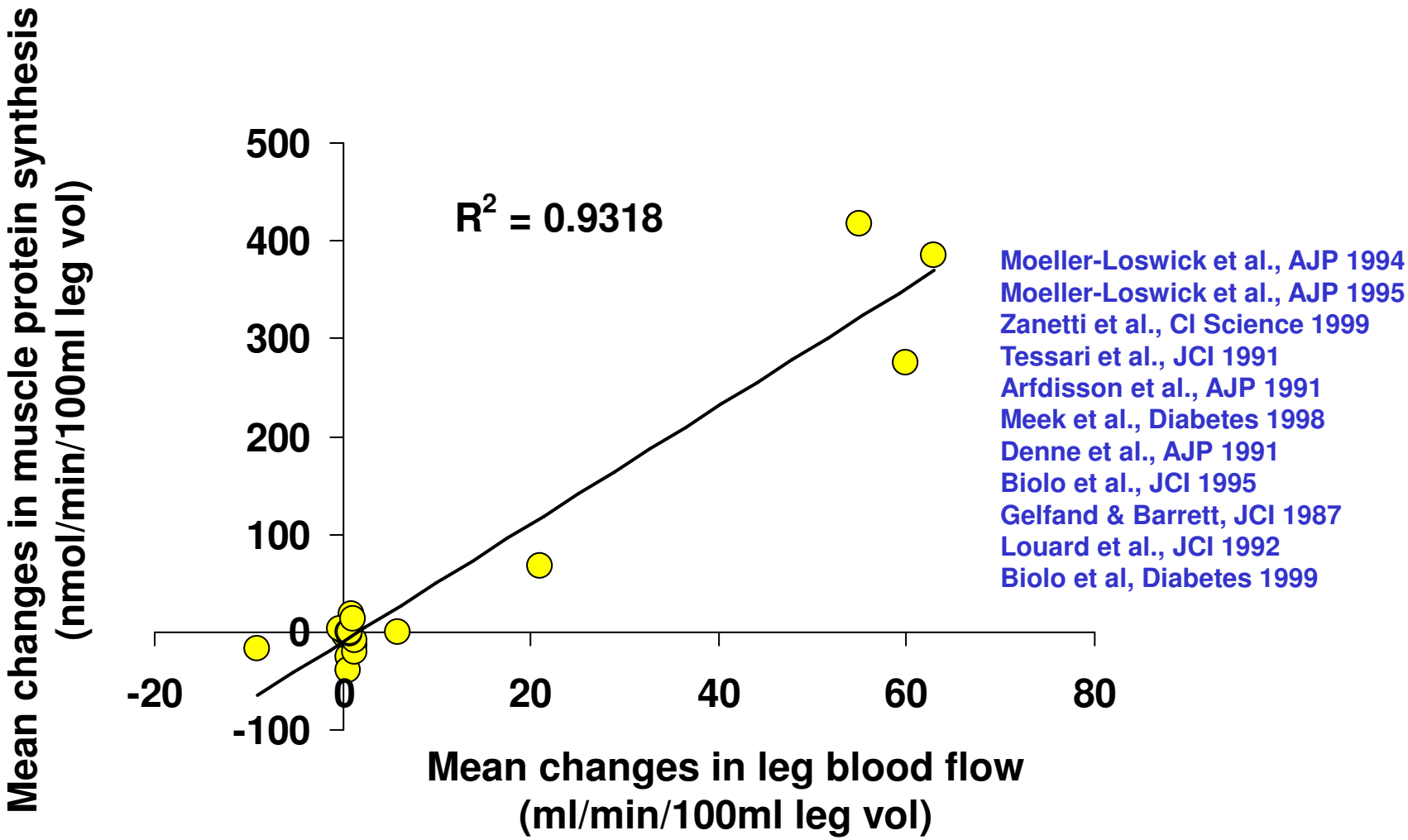
Figure 4. Insulin effects on FSR of muscle protein. *$P < 0.05$ insulin vs basal (paired t test). ▭, basal; ■, insulin.

	Basal Period	Insulin Period
Insulin concentration in femoral vein, μIU/ml	10±2	77±9*
Leg blood flow, ml·min^{-1}·100 ml leg volume^{-1}	3.16±0.39	4.12±0.48*





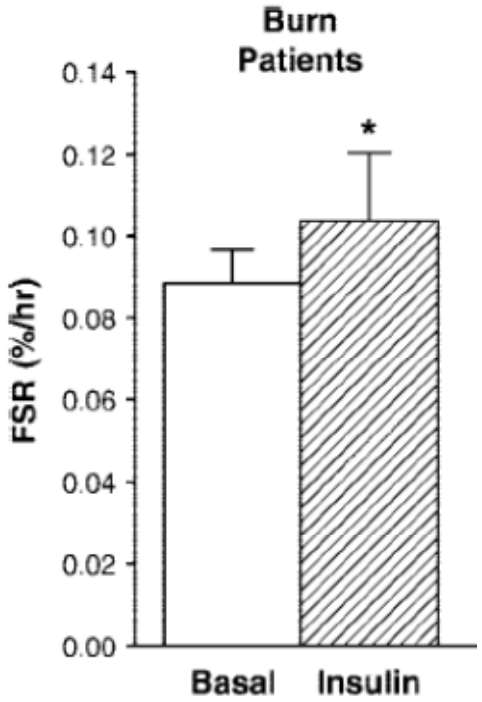
RELATIONSHIPS BETWEEN INSULIN-MEDIATED STIMULATION OF MUSCLE BLOOD FLOW AND PROTEIN SYNTHESIS
(leg or forearm A-V balance technique combined with stable isotopes)



Am J Physiol Endocrinol Metab 286: E529–E534, 2004.
First published December 9, 2003; 10.1152/ajpendo.00258.2003.

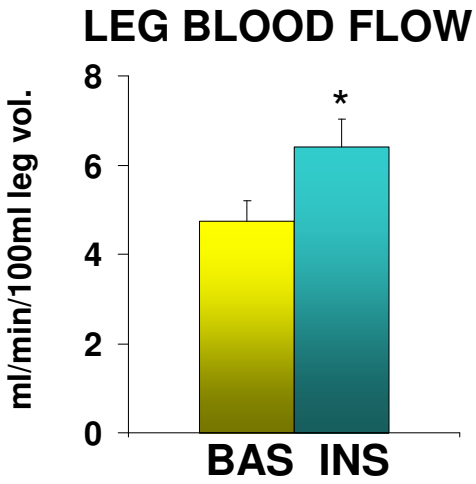
Extremity hyperinsulinemia stimulates muscle protein synthesis in severely injured patients

Dennis C. Gore, Steven E. Wolf, Arthur P. Sanford, David N. Herndon, and Robert R. Wolfe
Department of Surgery, The University of Texas Medical Branch, Galveston, Texas 77555



MUSCLE PROTEIN SYNTHESIS

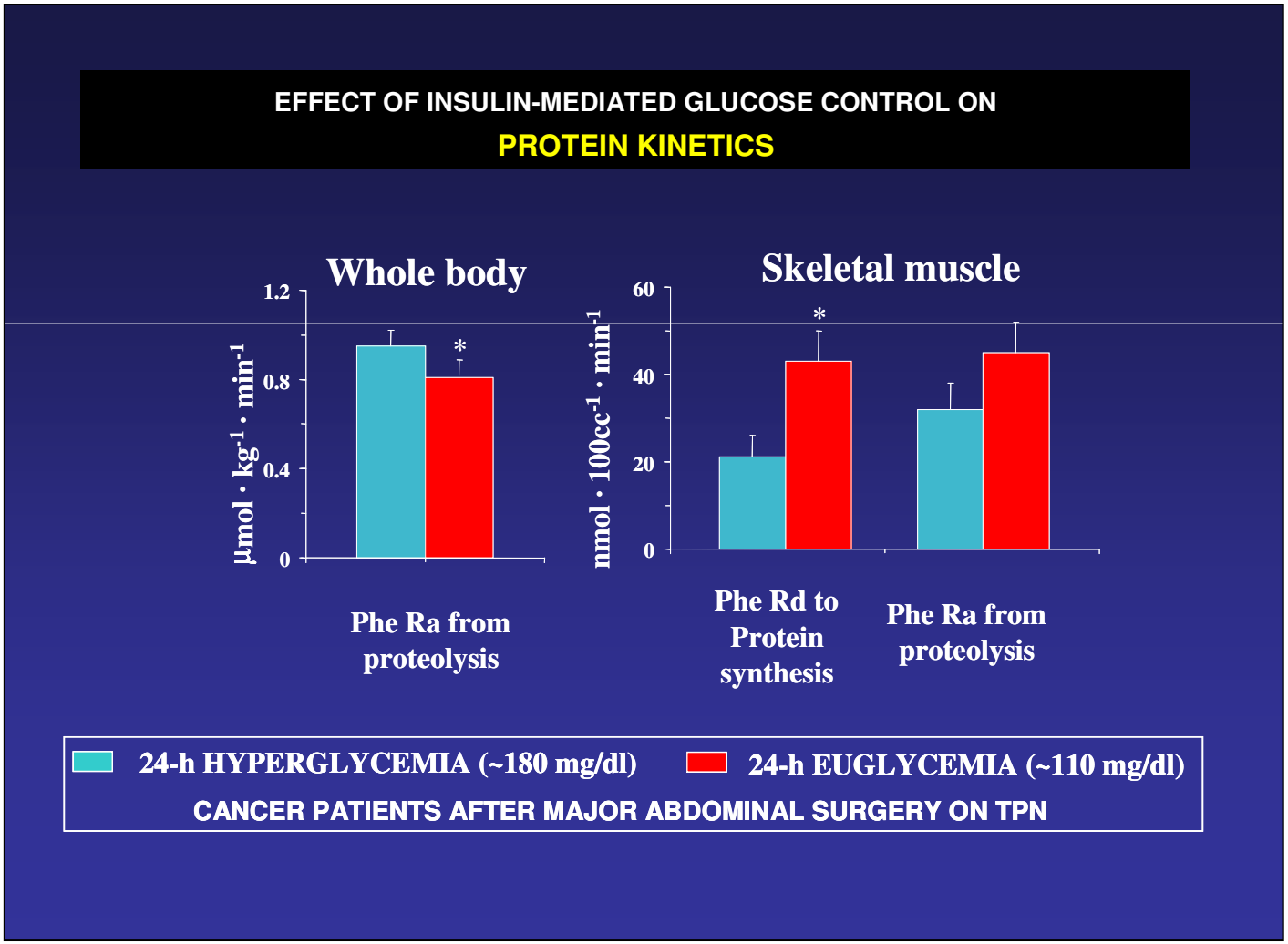
	Basal Period	Insulin Period
Insulin concentration in femoral vein, μIU/ml	50.5±5.9	128.3±10.4*†
Leg blood flow, ml·min^{-1}·100 ml leg volume^{-1}	4.73±0.57	6.40±1.39*



Treating hyperglycemia improves skeletal muscle protein metabolism in cancer patients after major surgery

Crit Care Med 2008 Vol. 36, No. 6

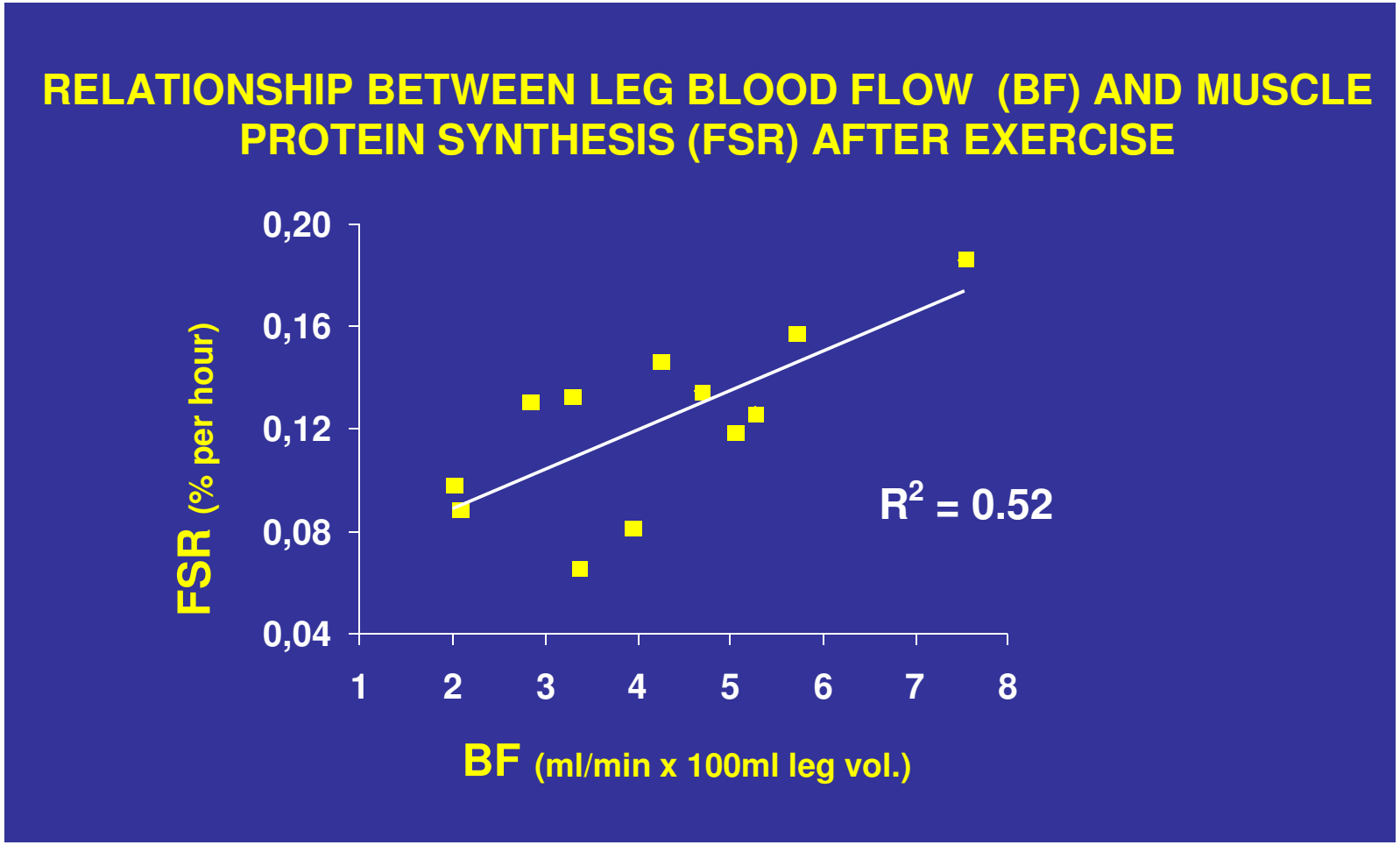
Gianni Biolo, MD, PhD; Marcello De Cicco, MD; Stefania Lorenzon, MD; Viviana Dal Mas, MD; Dario Fantin, MD; Rita Paroni, MD; Rocco Barazzoni, MD; Michela Zanetti, MD; Gaetano Iapichino, MD; Gianfranco Guarnieri, MD



Am J Physiol. 1995 Mar;268(3 Pt 1):E514-20.

Increased rates of muscle protein turnover and amino acid transport after resistance exercise in humans.

Biolo G, Maggi SP, Williams BD, Tipton KD, Wolfe RR.
Department of Internal Medicine, University of Texas Medical Branch, Galveston.

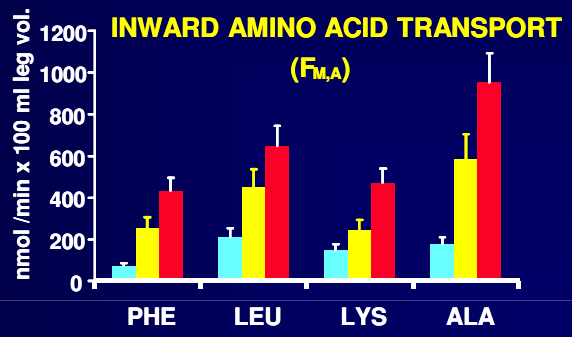


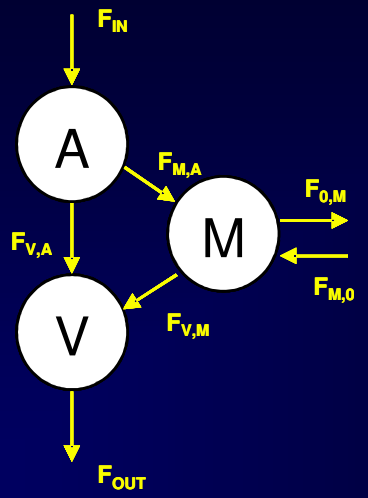
Exercise increases microvascular, nutritive muscle blood flow

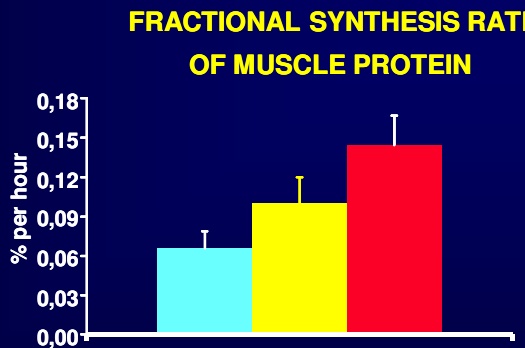
An abundant supply of amino acids enhances the metabolic effect of exercise on muscle protein

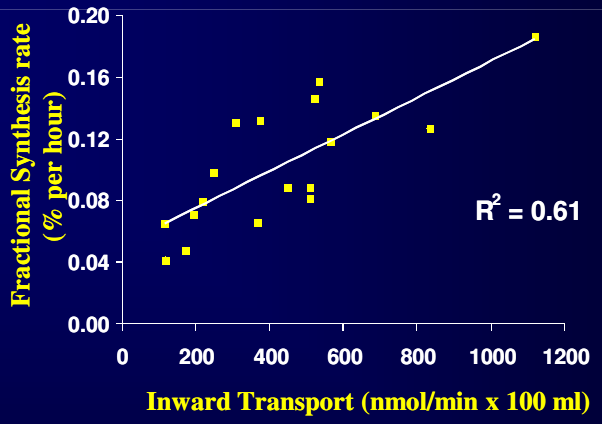
AJPENDO 1997

GIANNI BIOLO, KEVIN D. TIPTON, SAMUEL KLEIN, AND ROBERT R. WOLFE
Department of Metabolism, Shriners Burns Institute
and The University of Texas Medical Branch, Galveston, Texas 77550







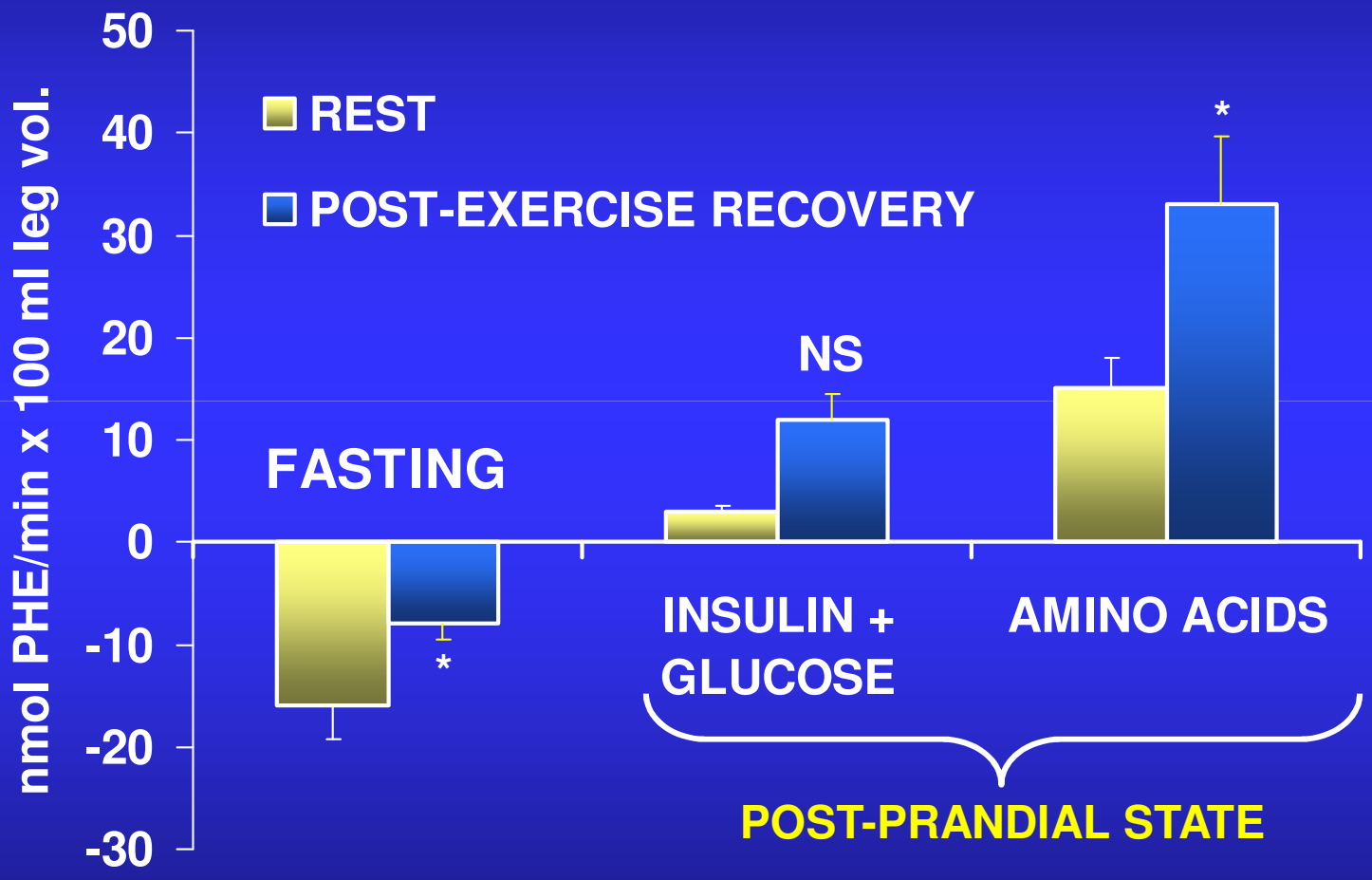


BASAL

HYPERAMINOACIDEMIA AT REST

HYPERAMINOACIDEMIA AFTER EXERCISE

Regulation of muscle protein balace in the fasting and postprandial states at rest and after exercise



*: P<0.05 RECOVERY VS. REST

AJPENDO 1995
AJPENDO 1997
Diabetes 1999

Resistance training to counteract the catabolism of a low-protein diet and reduce the malnutrition-inflammation complex syndrome of chronic kidney disease

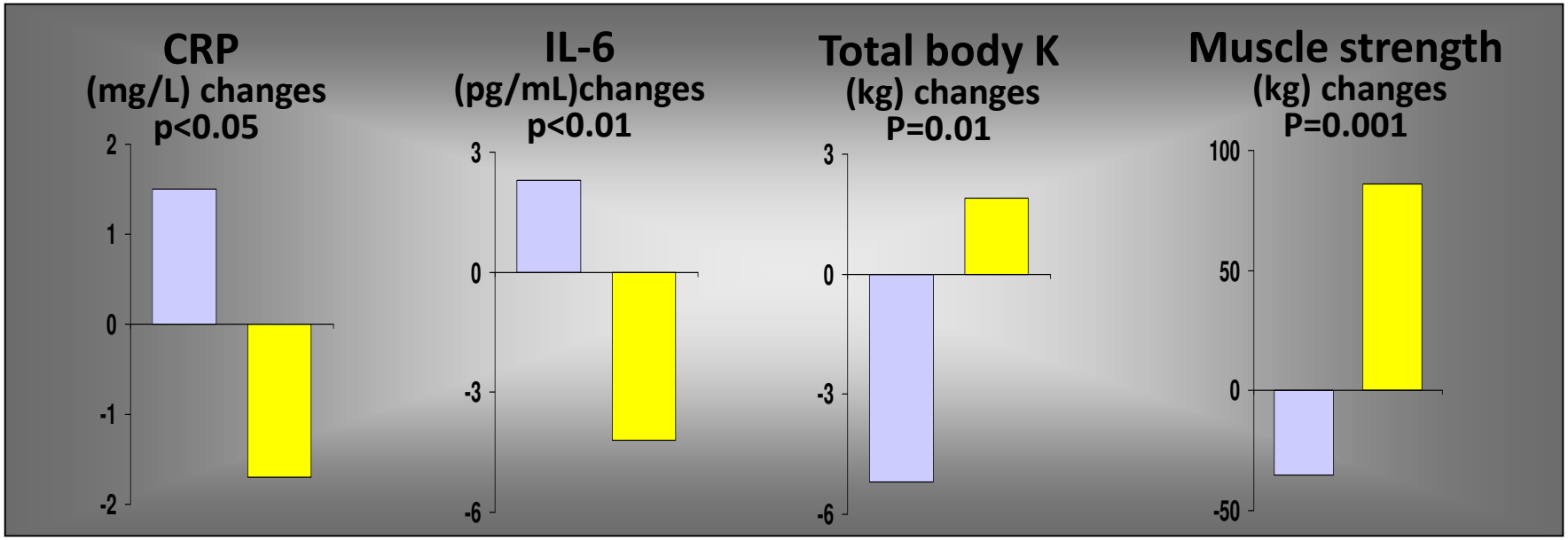
Castaneda et al. Ann Int Med 2001; Am J Kidney Dis 2004

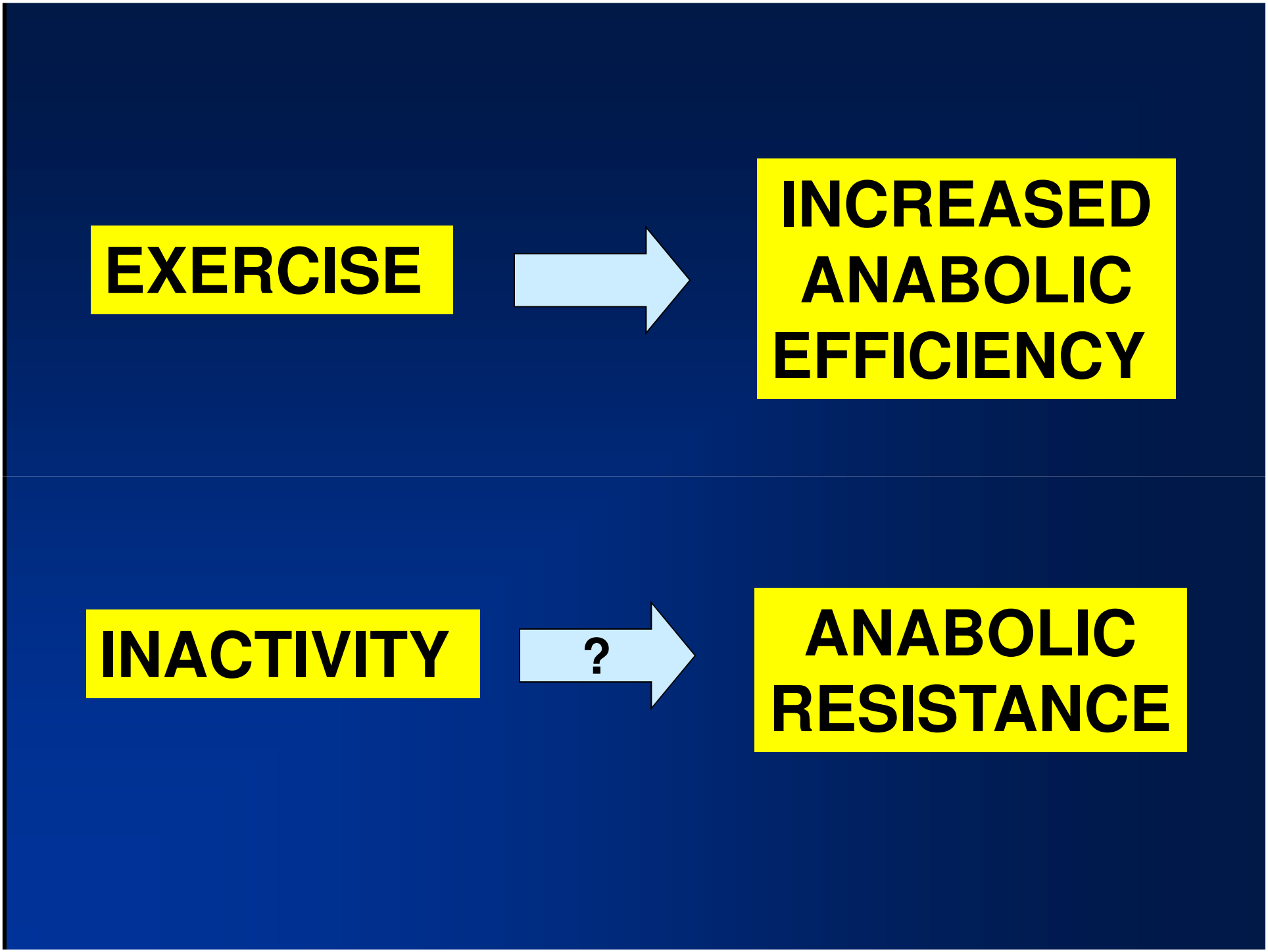
Patients with chronic kidney disease, not on dialysis therapy
n = 26
Randomized, Controlled Trial

12 weeks

low-protein diet (0.6 g/kg/d)

low-protein diet (0.6 g/kg/d)
+
resistance exercise training




EXERCISE
INCREASED ANABOLIC EFFICIENCY
INACTIVITY
?
ANABOLIC RESISTANCE

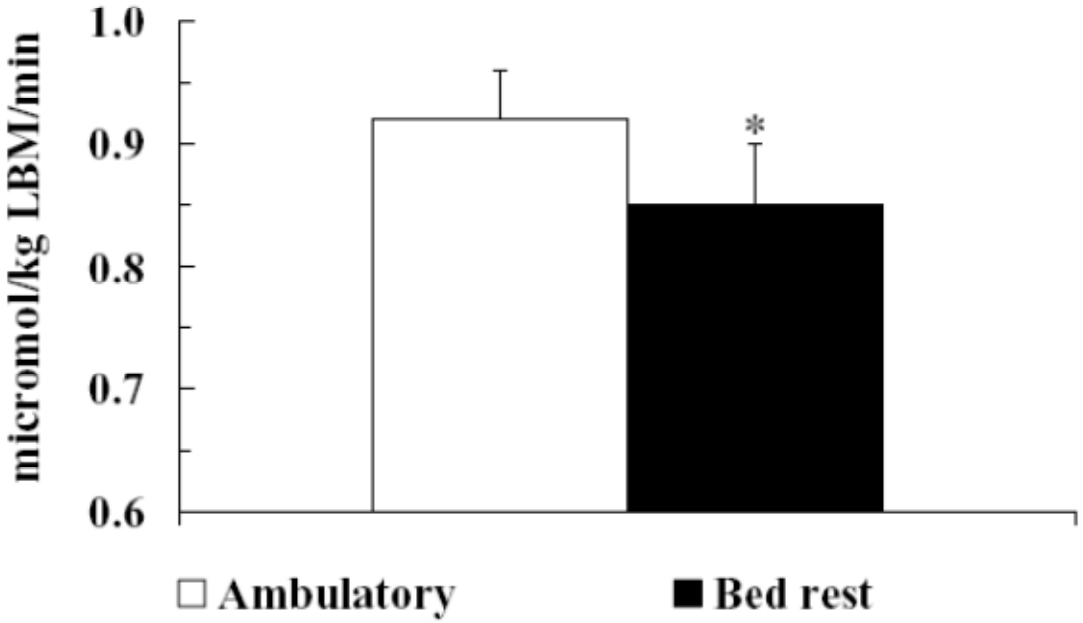
J Physiol 558.2 (2004) pp 381–388

RAPID REPORT

Short-term bed rest impairs amino acid-induced protein anabolism in humans

Gianni Biolo[1], Beniamino Ciocchi[1], Marion Lebenstedt[2], Rocco Barazzoni[1], Michela Zanetti[1], Petra Platen[2], Martina Heer[3] and Gianfranco Guarnieri[1]

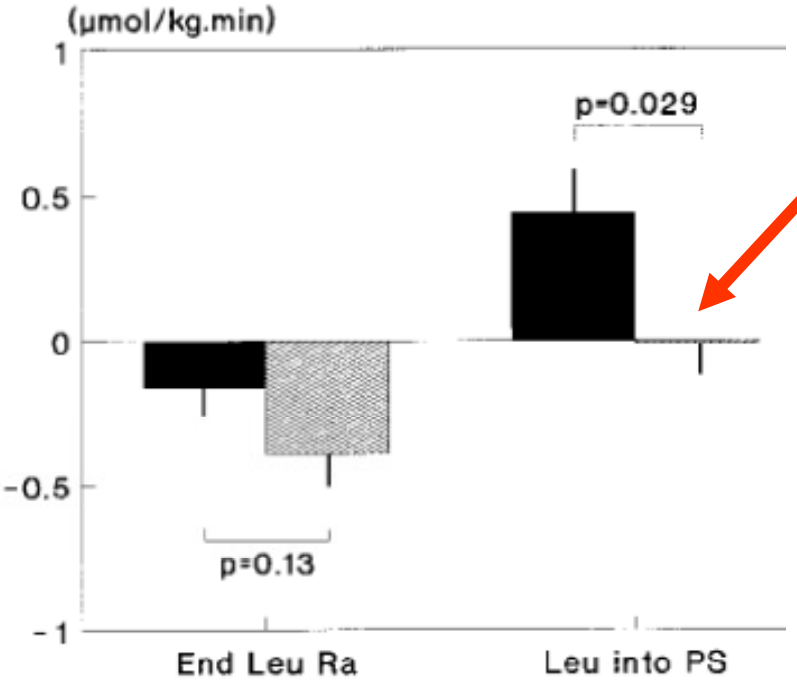
[1]*Department of Clinical, Technological and Morphological Sciences, Division of Internal Medicine, University of Trieste, Italy*
[2]*Institute of Cardiology and Sports Medicine, German Sport University, Cologne, Germany*
[3]*DLR-Institute of Aerospace Medicine, Cologne, Germany*



GASTROENTEROLOGY 1996;111:127–137

Response of Phenylalanine and Leucine Kinetics to Branched Chain–Enriched Amino Acids and Insulin in Patients With Cirrhosis

PAOLO TESSARI,* MICHELA ZANETTI,* ROCCO BARAZZONI,* GIANNI BIOLO,* ROCCO ORLANDO,† MONICA VETTORE,* SANDRO INCHIOSTRO,* PAOLA PERINI,† and ANTONIO TIENGO*
Departments of *Metabolic Diseases and †Internal Medicine, University of Padova, Padova, Italy



anabolic resistance

CONTROLS
CIRRHOTIC PATIENTS

CHANGES VERSUS BASELINE
AFTER INSULIN, GLUCOSE AND AMINO ACID INFUSION

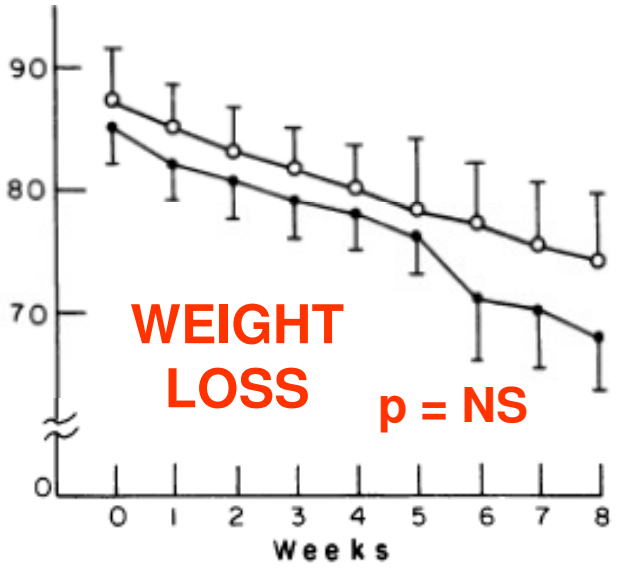
Metabolic Effects of Very Low Calorie Weight Reduction Diets

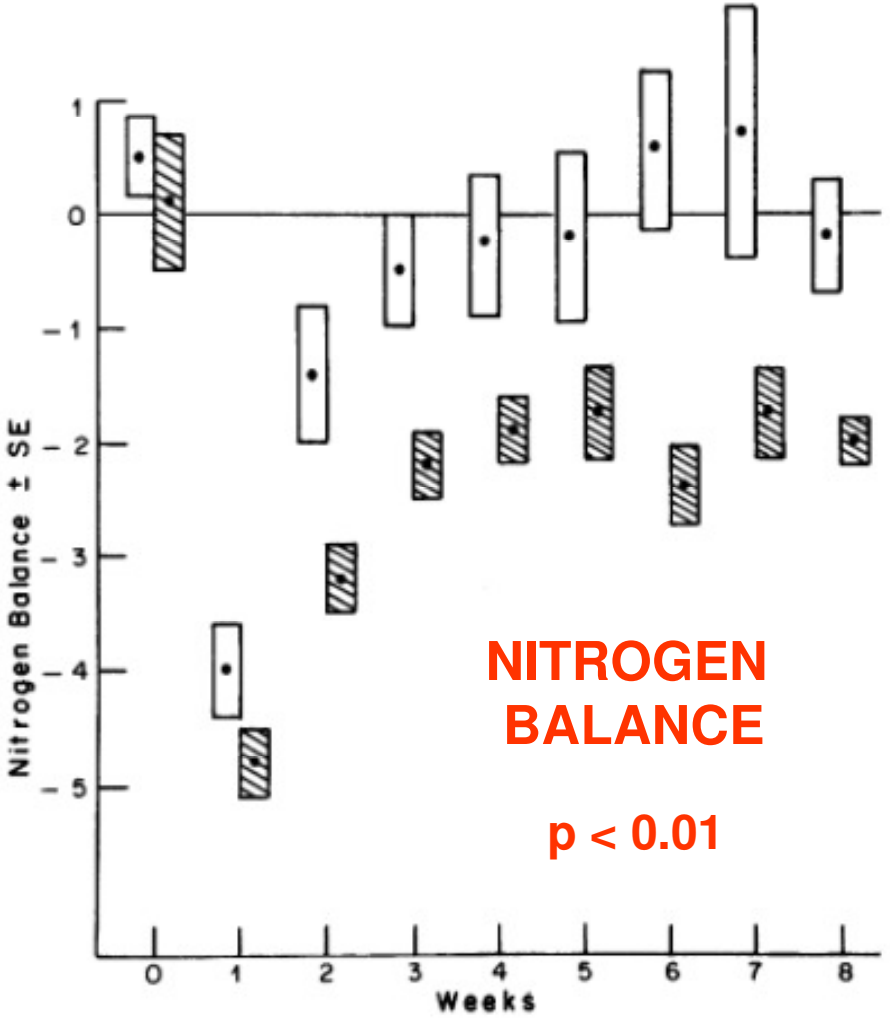
L.J. Hoffer, B.R. Bistrian, V.R. Young, G.L. Blackburn, and D.E. Matthews

J Clin Invest 1984

501 ± 39 kcal
0.8 g protein/kg ideal BW

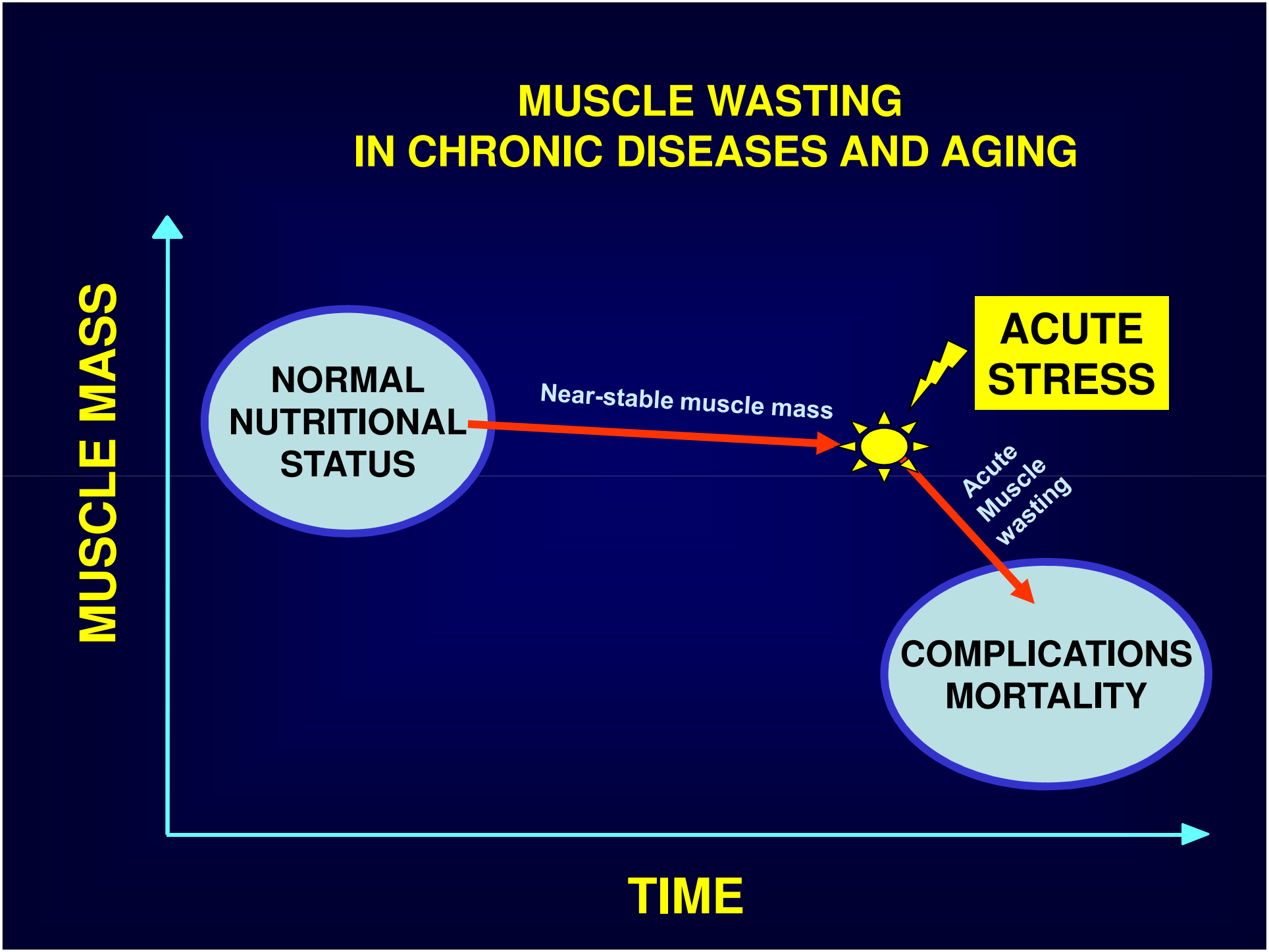
559 ± 79 kcal
1.5 g protein/kg ideal BW





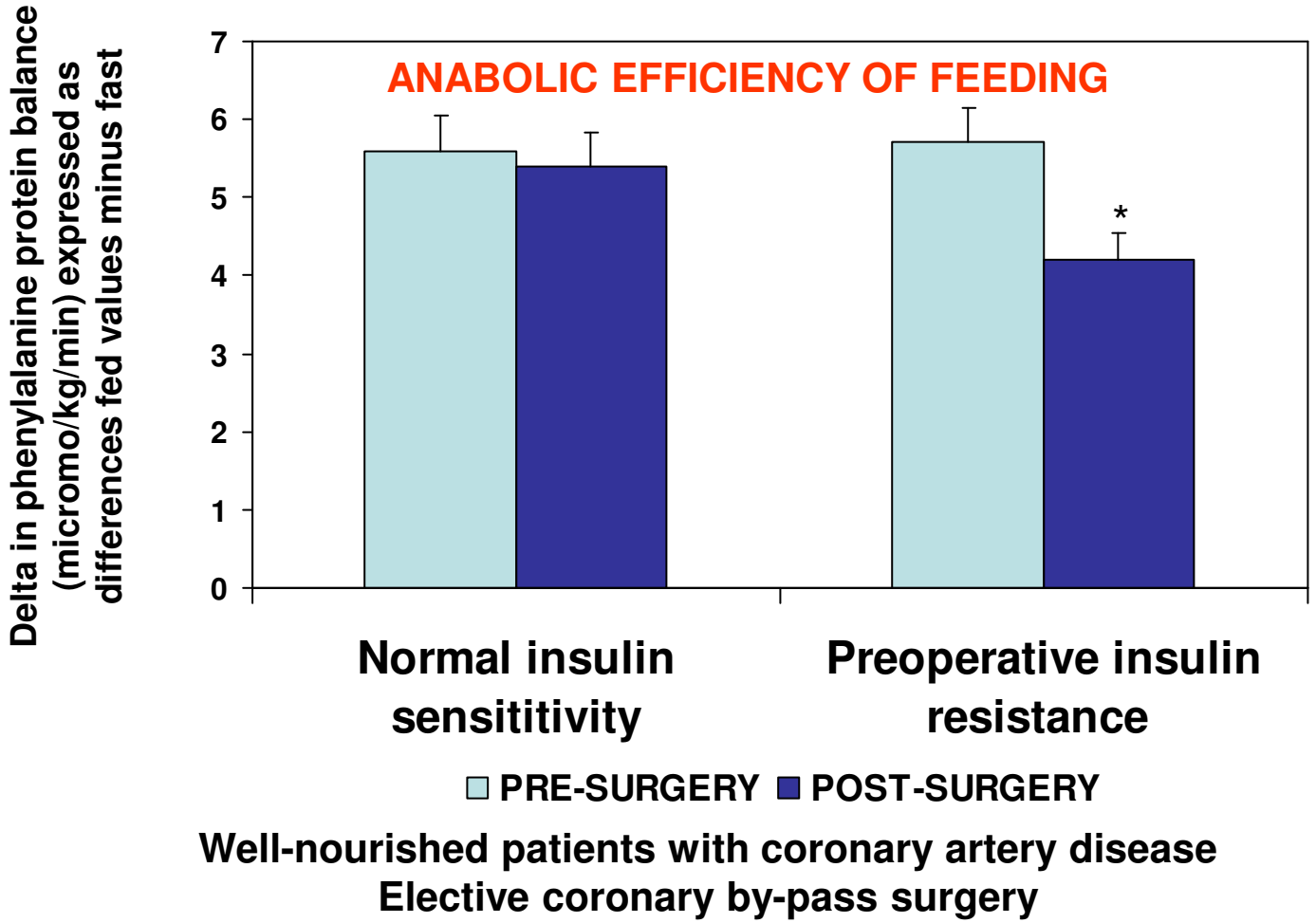
CHRONIC CONDITIONS WITH ANABOLIC RESISTANCE

- Sarcopenia of aging
- Cancer cachexia
- Chronic renal failure
- Rheumatoid arthritis
- Osteoarthritis
- HIV/AIDS
- COPD
- Anorexia
- Male hypogonadism
- Obesity (weight loss)
- Corticosteroid administration (transplant, autoimmune disease)
- Coronary artery disease
- Congestive heart failure
- Liver Cirrhosis
- Type 1 and 2 diebetes mellitus
- Hip fracture
- Disuse atrophy (spinal cord injury, bed rest, microgravity)

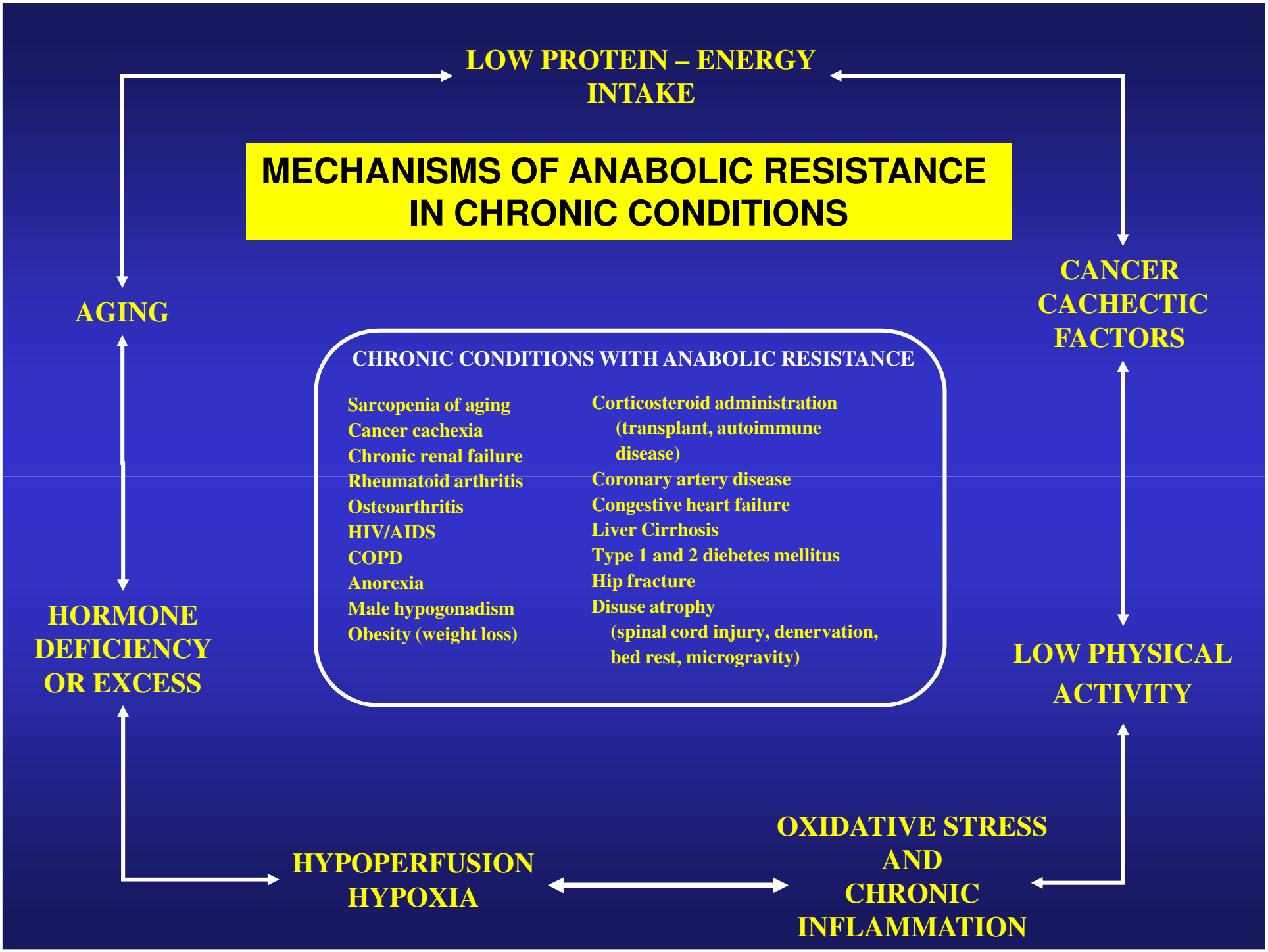

MUSCLE WASTING
IN CHRONIC DISEASES AND AGING
MUSCLE MASS
NORMAL NUTRITIONAL STATUS
Near-stable muscle mass
ACUTE STRESS
Acute Muscle wasting
COMPLICATIONS MORTALITY
TIME

PREOPERATIVE INSULIN RESISTANCE AND THE IMPACT OF FEEDING ON POSTOPERATIVE PROTEIN BALANCE. A STABLE ISOTOPE STUDY

Francesco Donatelli, Davide Corbella, Marta Di Nicola, Franco Carli, Luca Lorini, Roberto Fumagalli, Gianni Biolo.
Ospedali Riuniti di Bergamo, Italy; McGill University Health Centre, Montreal, Quebec, Canada; University of Trieste, Italy
J Clin Endocrinol Metab 2011

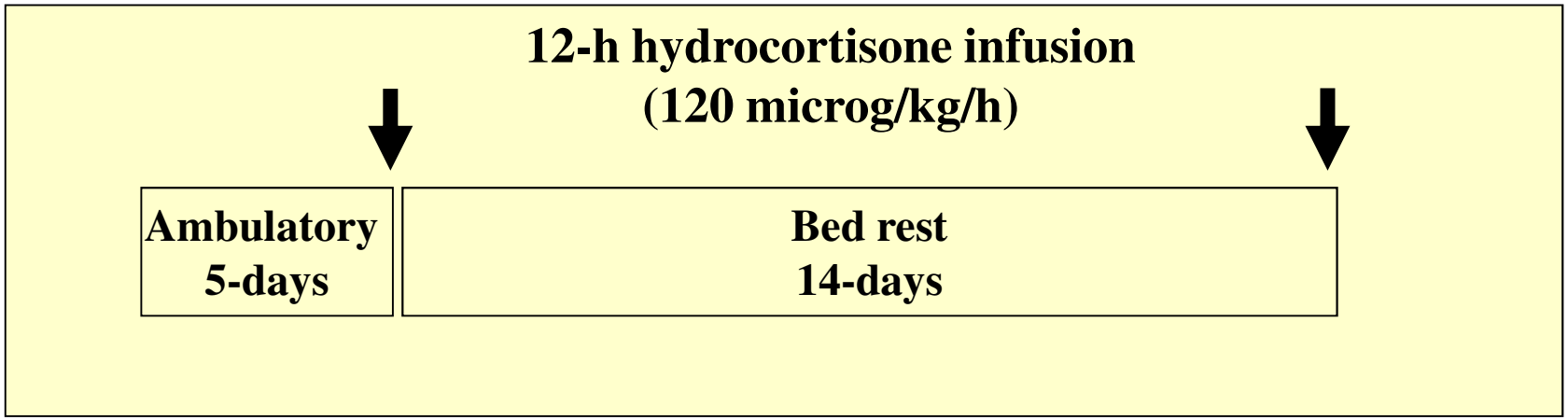


*, p=0.04, surgery effect of; p=0.002, group effect; p<0.001 group x surgery interaction

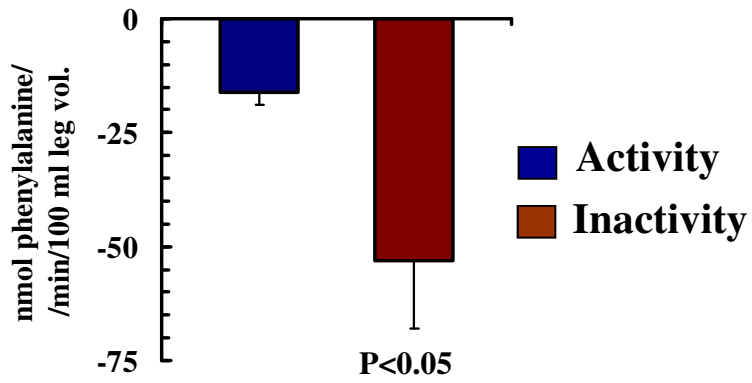

LOW PROTEIN – ENERGY INTAKE
MECHANISMS OF ANABOLIC RESISTANCE IN CHRONIC CONDITIONS
AGING
CANCER CACHECTIC FACTORS
CHRONIC CONDITIONS WITH ANABOLIC RESISTANCE
Sarcopenia of aging
Cancer cachexia
Chronic renal failure
Rheumatoid arthritis
Osteoarthritis
HIV/AIDS
COPD
Anorexia
Male hypogonadism
Obesity (weight loss)
Corticosteroid administration (transplant, autoimmune disease)
Coronary artery disease
Congestive heart failure
Liver Cirrhosis
Type 1 and 2 diebetes mellitus
Hip fracture
Disuse atrophy (spinal cord injury, denervation, bed rest, microgravity)
HORMONE DEFICIENCY OR EXCESS
LOW PHYSICAL ACTIVITY
HYPOPERFUSION HYPOXIA
OXIDATIVE STRESS AND CHRONIC INFLAMMATION

Inactivity Amplifies the Catabolic Response of Skeletal Muscle to Cortisol

Ferrando et al., J Clin Endocrinol & Metab, 1999



MUSCLE PROTEIN BALANCE

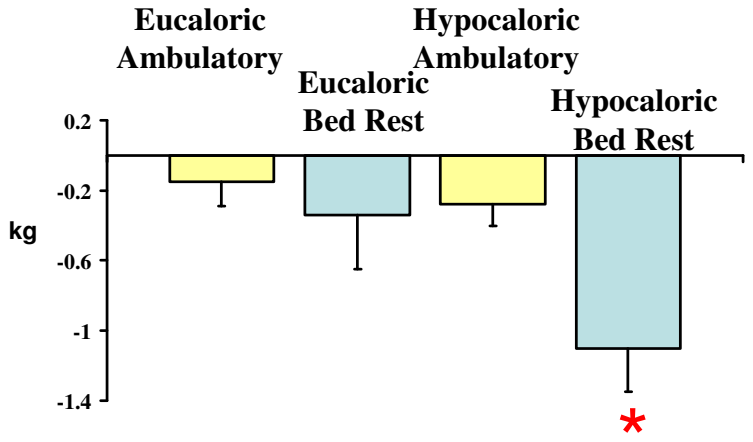


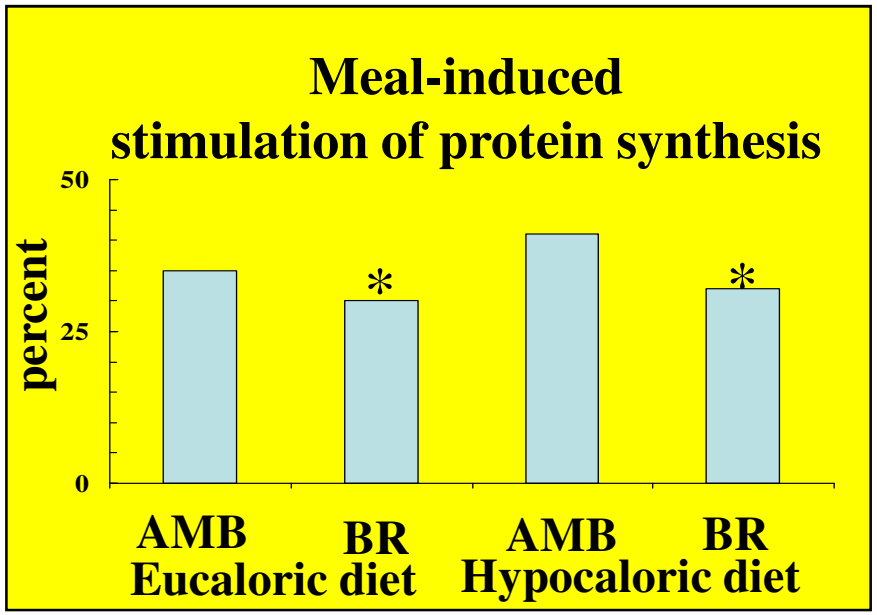
Calorie restriction accelerates the catabolism of lean body mass during 2 wk of bed rest[1–3]

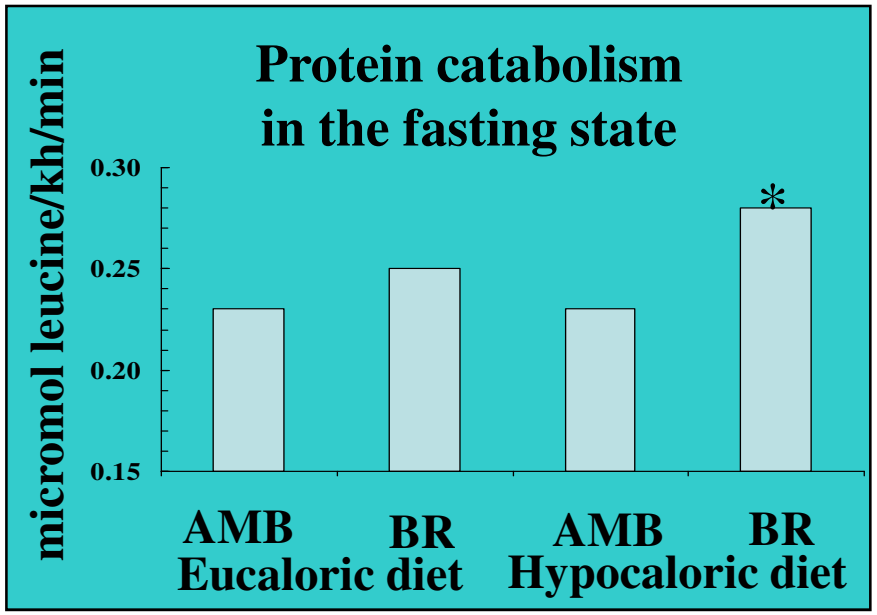
Gianni Biolo, Beniamino Ciocchi, Manuela Stulle, Alessandra Bosutti, Rocco Barazzoni, Michela Zanetti, Raffaella Antonione, Marion Lebenstedt, Petra Platen, Martina Heer, and Gianfranco Guarnieri

Am J Clin Nutr 2007;86:366–72.

CHANGES IN LEAN MASS (DEXA)



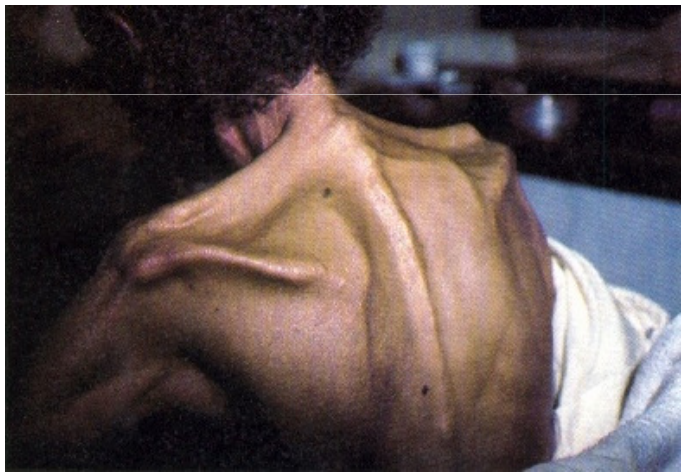




MALNUTRITION IN PATIENTS WITH CANCER OR CHRONIC DISEASES

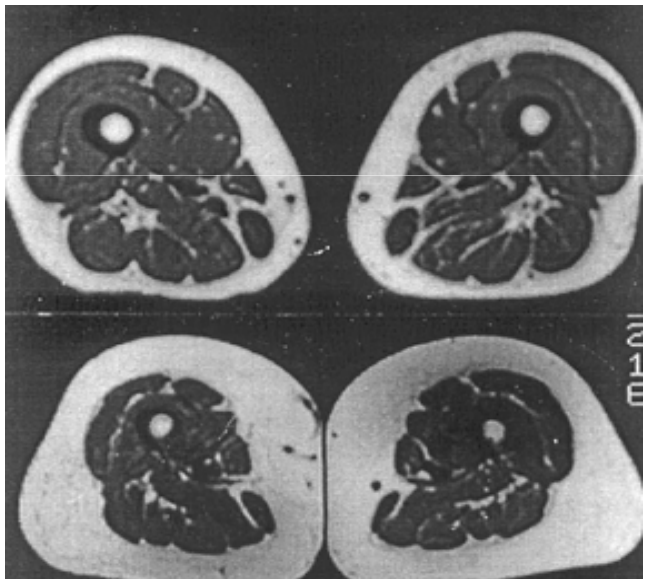
Anabolic resistance → muscle atrophy

CACHEXIA



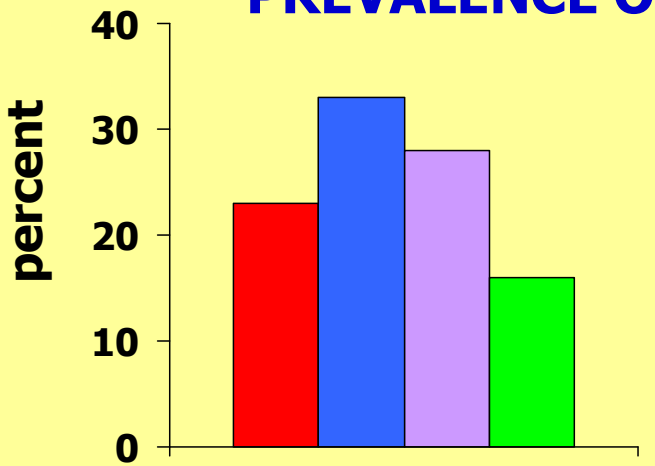
ANOREXIA

SARCOPENIC OBESITY



ADEQUATE OR INCREASED NUTRIENT INTAKE

PREVALENCE OF OBESITY IN COPD PATIENTS



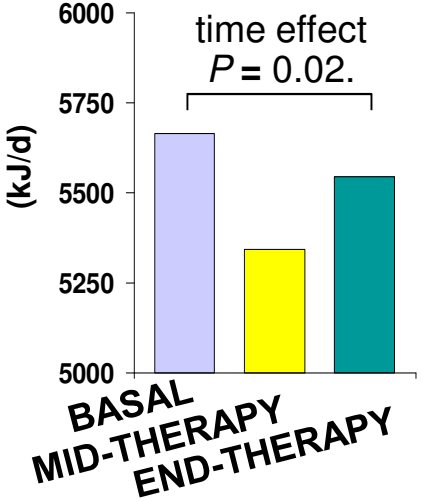
Body Mass Index (kg/m^2) (BMI)

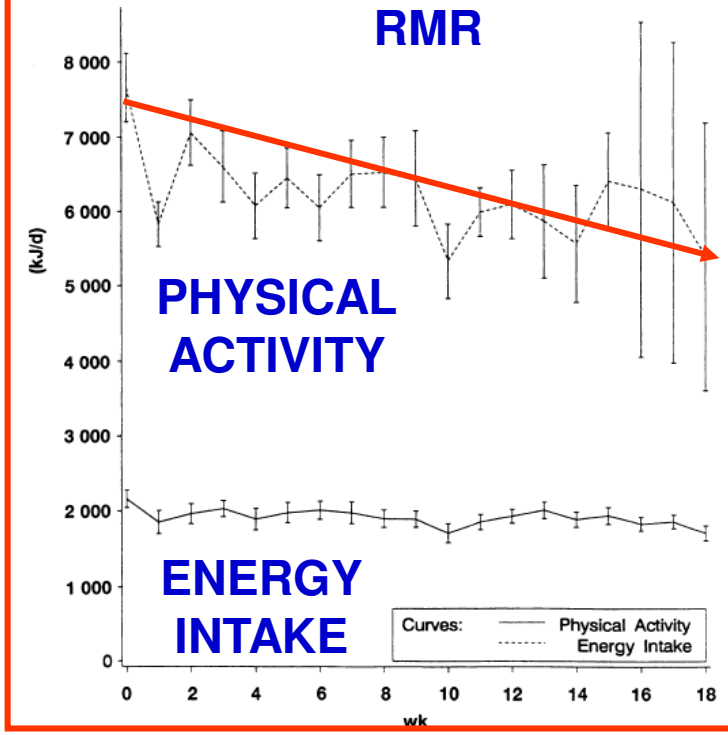
- Low (<21)
- Normal (21-25)
- High (25-30)
- Obese (>30)

628 elderly patients with moderate to severe COPD (61% male)

Breyer et al., Clin Nutr 2009

Reduced rates of metabolism and decreased physical activity in breast cancer patients receiving adjuvant chemotherapy[1–3] *Am J Clin Nutr* 1997;65:1495–501

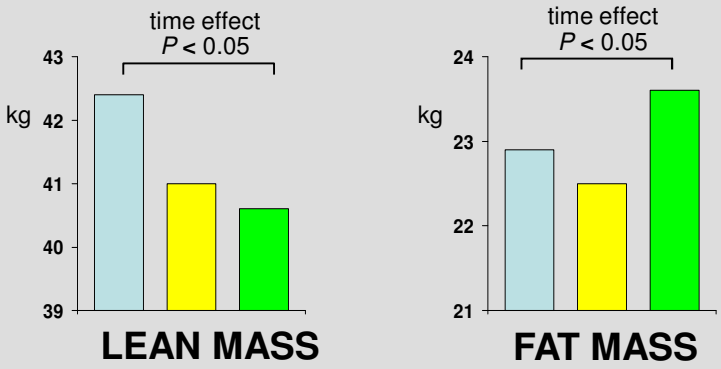




REDUCED ENERGY REQUIREMENT IN CANCER PATIENTS

Weight and Body Composition Changes during and after Adjuvant Chemotherapy in Women with Breast Cancer

***J Clin Endocrinol Metab* 2004**

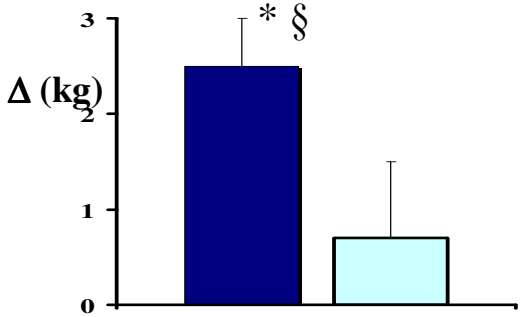


Positive energy balance is associated with accelerated muscle atrophy and increased erythrocyte glutathione turnover during 5 wk of bed rest[1–3]

Gianni Biolo, Francesco Agostini, Bostjan Simunic, Mariella Sturma, Lucio Torelli, Jean Charles Preiser, Ginette Deby-Dupont, Paolo Magni, Felice Strollo, Pietro di Prampero, Gianfranco Guarnieri, Igor B Mekjavic, Rado Pišot, and Marco V Narici

Am J Clin Nutr 2008;88:950–8.

Changes in fat mass (bioimpedence)



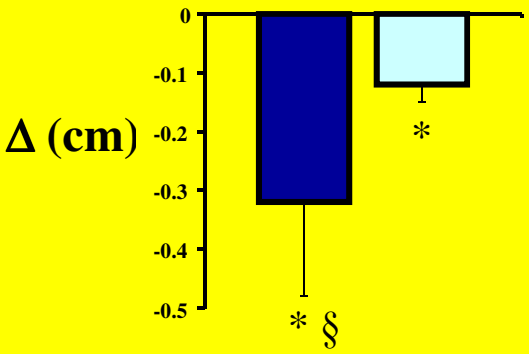
Positive Energy Balance

Near-neutral Energy Balance

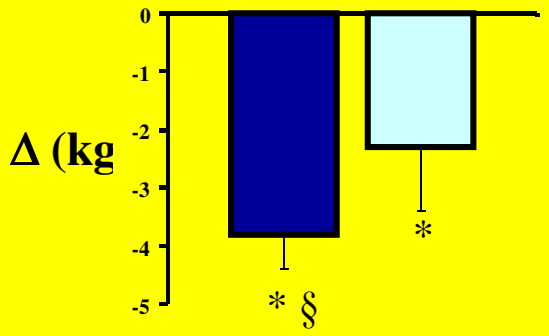
***, p<0.05 significant different from zero;**
§, p<0.05 versus near-neutral energy balance

EFFECTS OF POSITIVE ENERGY BALANCE ON BED REST-MEDIATED MUSCLE ATROPHY

Changes in vastus lateralis thickness (ultrasounds)

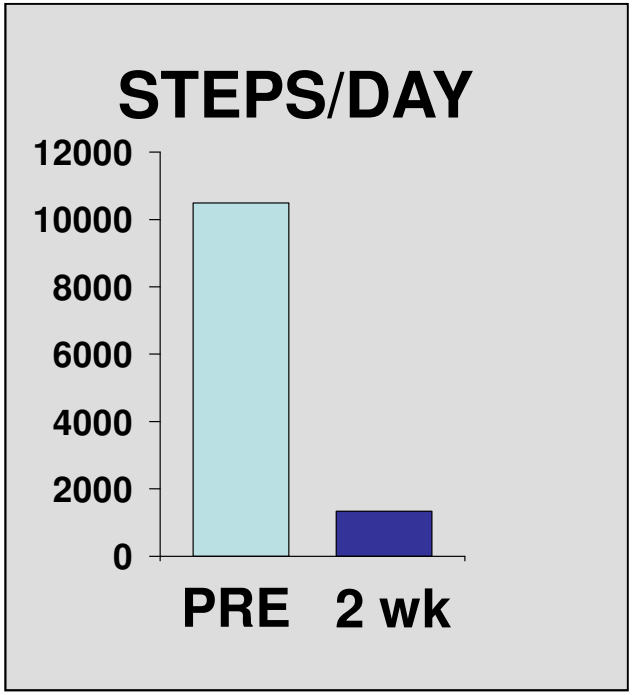


Changes in fat-free mass (bioimpedence)

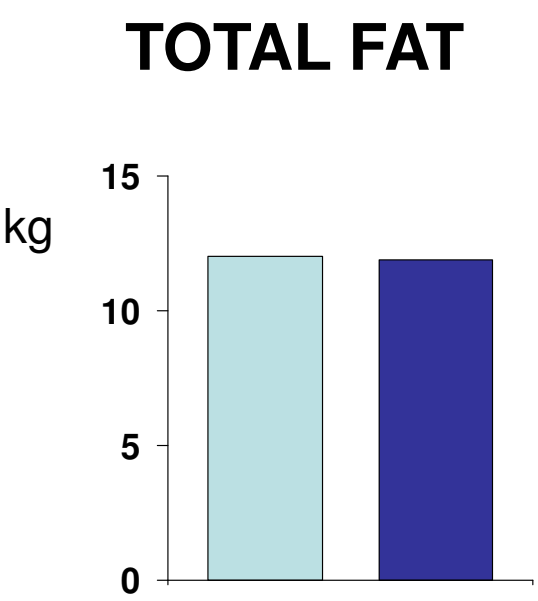


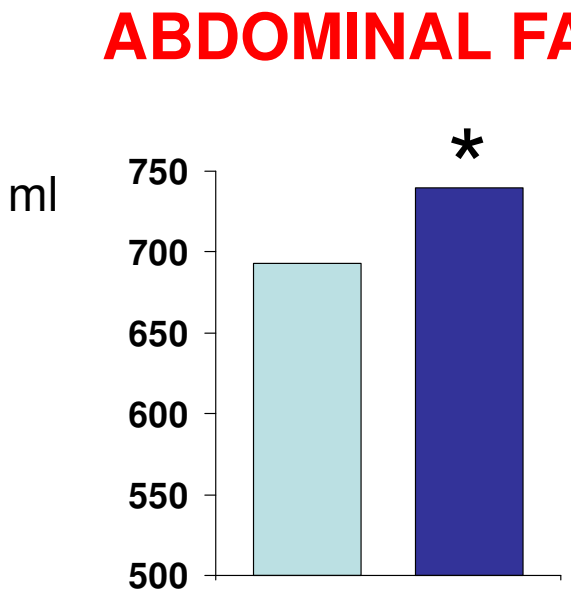
Metabolic Responses to Reduced Daily Steps in Healthy Nonexercising Men

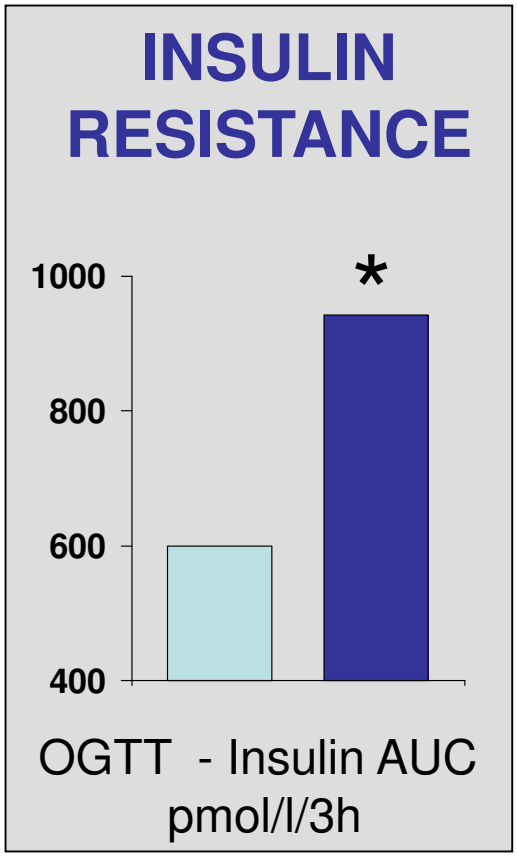
JAMA 2008



*, P<0.05







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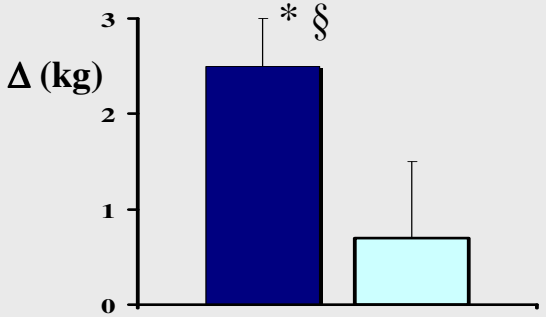
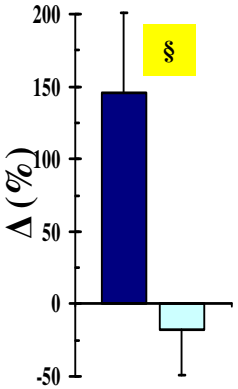


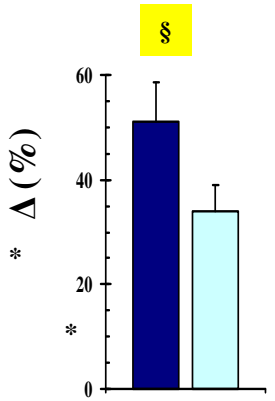
Positive Energy Balance

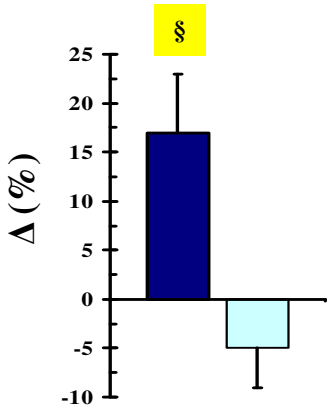
Near-neutral Energy Balance

CRP

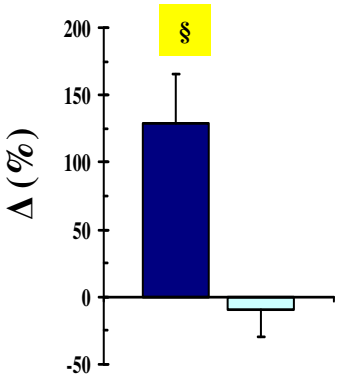


LEPTIN





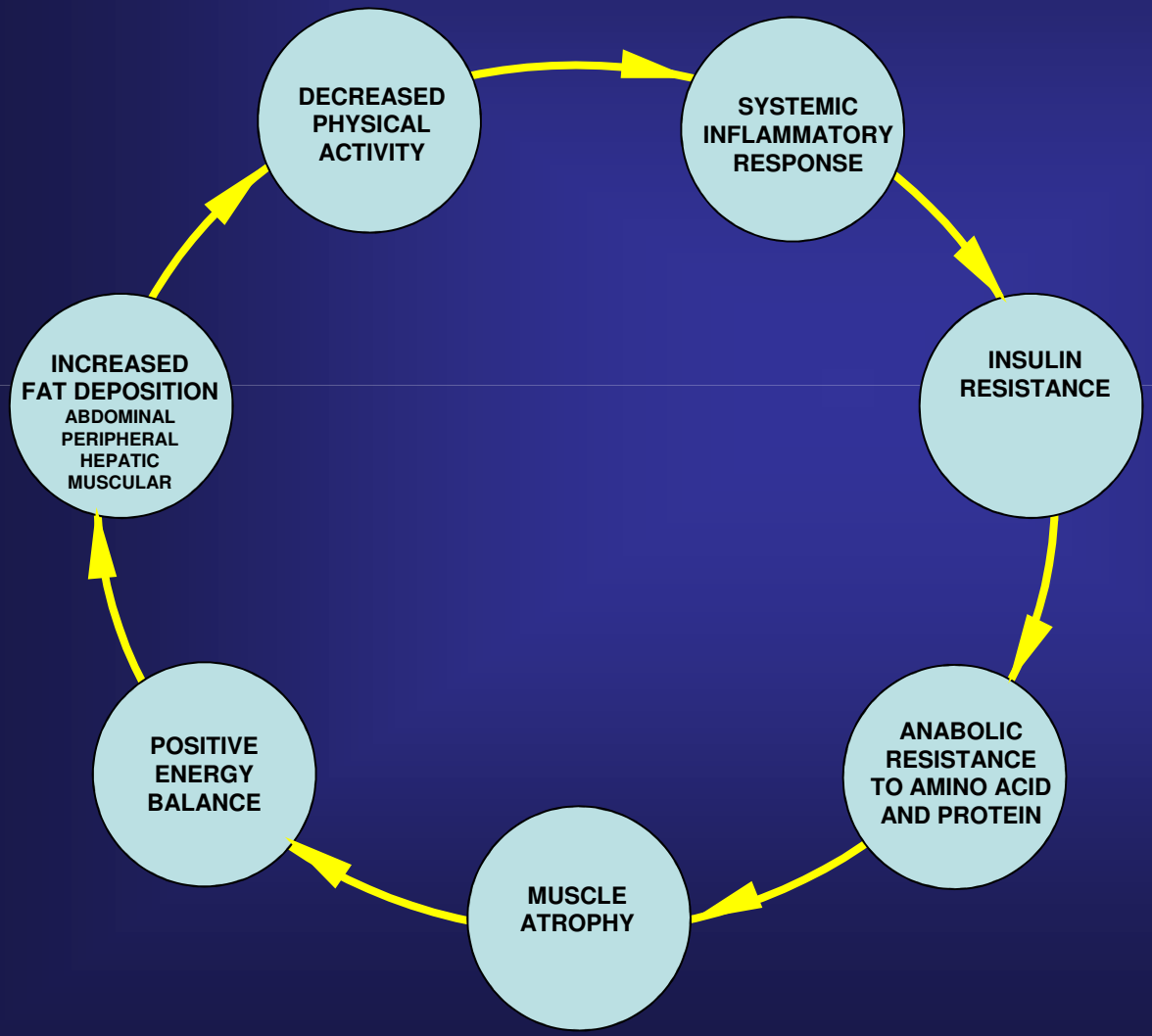
ERYTHOCYTE GLUTATHIONE SYNTHESIS RATE



PLASMA MYELOPEROXIDASE

*, p<0.05 significant different from zero;
§, p<0.05 versus lower energy balance

THE VICIOUS CYCLE OF SARCOPENIC OBESITY



Prevalence and clinical implications of sarcopenic obesity in patients with solid tumours of the respiratory and gastrointestinal tracts: a population-based study

Carla M M Prado, Jessica R Lieffers, Linda J McCargar, Tony Reiman, Michael B Sawyer, Lisa Martin, Vickie E Baracos

Lancet Oncol 2008; 9: 629–35

2115 cancer patients

↓

15% obesity

↓

15% sarcopenic obesity

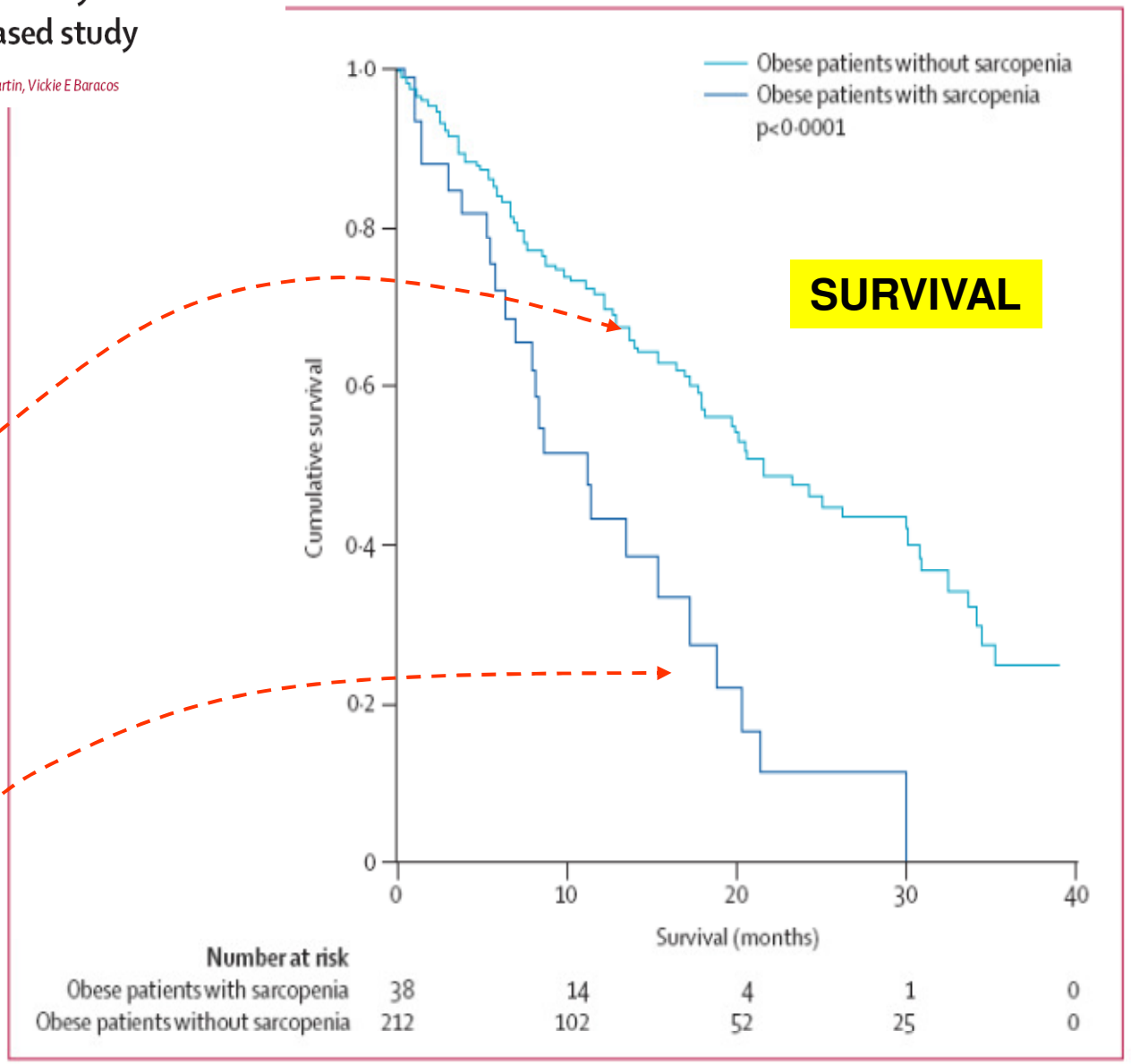
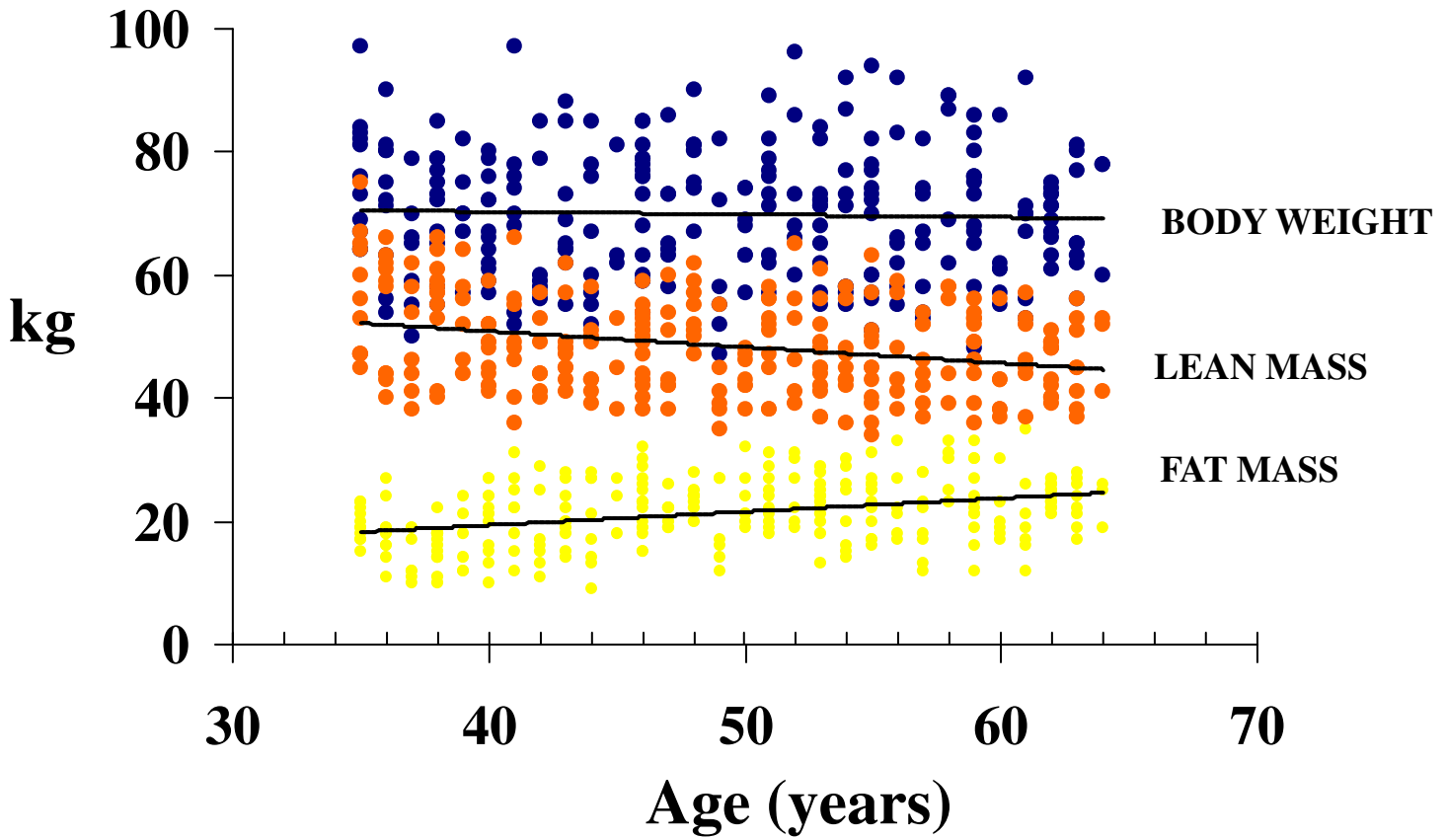


Figure 3: Survival of obese patients who had sarcopenia and obese patients who did not have sarcopenia

CROSS-SECTIONAL STUDY
252 healthy subjects with normal body mass index, 35 to 65 years

BODY WEIGHT AND COMPOSITION IN AGING



Aging is associated with diminished accretion of muscle proteins after the ingestion of a small bolus of essential amino acids[1–3]

Christos S Katsanos, Hisamine Kobayashi, Melinda Sheffield-Moore, Asle Aarsland, and Robert R Wolfe

Am J Clin Nutr 2005;82:1065–73.

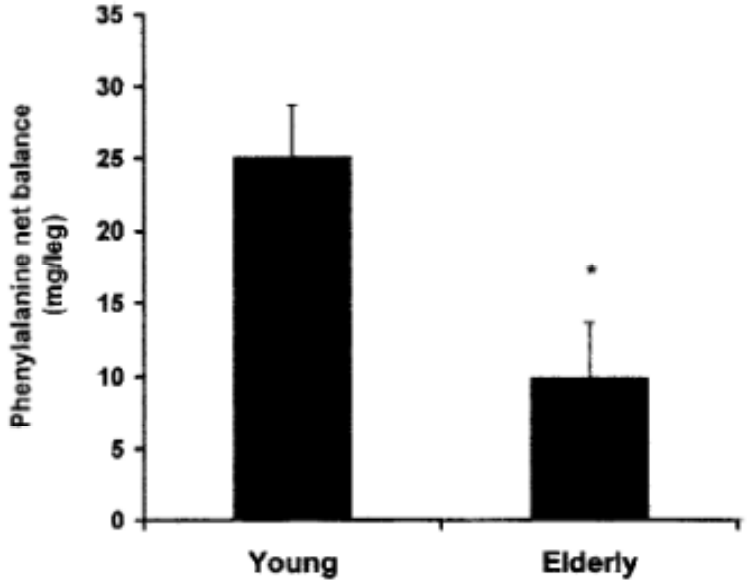


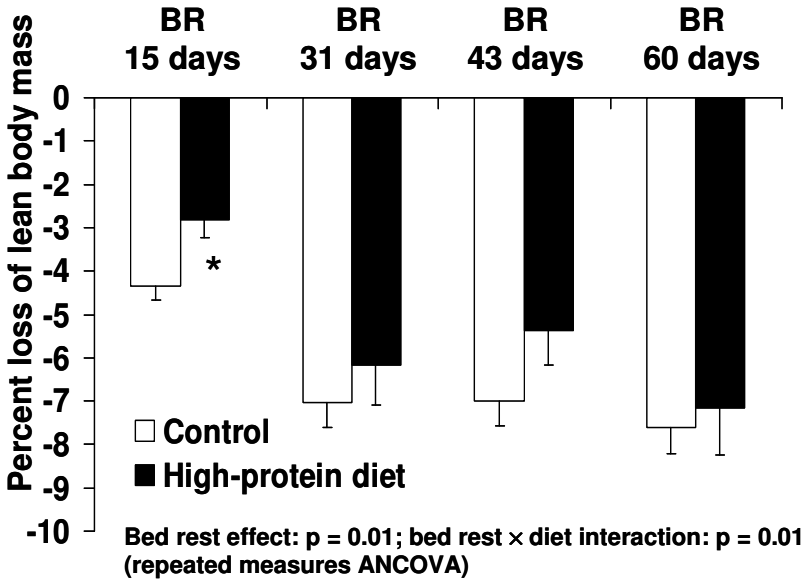
FIGURE 5. Mean (±SEM) leg phenylalanine net balance 3.5 h after the ingestion of essential amino acids calculated by measuring the area under the phenylalanine net balance response curve (in the calculations, basal net balance was taken as zero) in the elderly ($n = 11$) and the young ($n = 8$). Data were analyzed with a t test. *Significantly different from the young, $P = 0.010$.

Long-term bed-rest (60 days) in healthy female volunteers

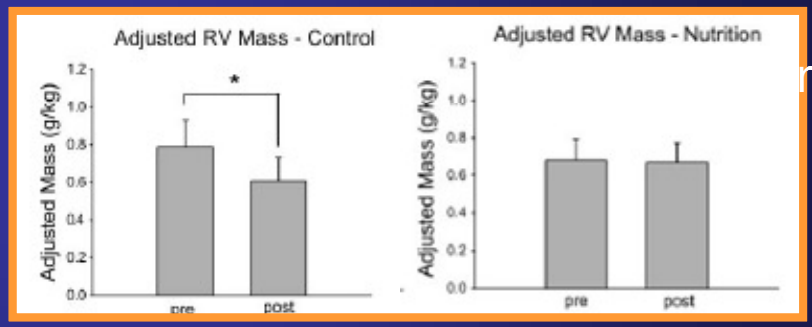
WISE 2005 (Women International Space Simulation for Exploration)

ESA/CNES/NASA/CSA

	ADAPTATION (20 days)	EXPERIMENTAL PERIOD (60 days)	REABILITATION (20 days)
N = 8	Ambulatory conditions	"Bed Rest"- Eucaloric diet 1 g protein / (kg · day) non-protein calories to nitrogen ratio 134±3 kcal/g	Ambulatory conditions
N = 6	Ambulatory conditions	"Bed Rest"- Eucaloric diet 1.4 g protein / (kg · day) 0.16 g BCAA / (kg · day) non-protein calories to nitrogen ratio 86±2 kcal/g	Ambulatory conditions



SKELETAL MUSCLE ATROPHY (DEXA)



CARDIAC ATROPHY (MRI)

Dorfman et al., J Appl Physiol 2007

Protein-containing nutrient supplementation following strength training enhances the effect on muscle mass, strength, and bone formation in postmenopausal women

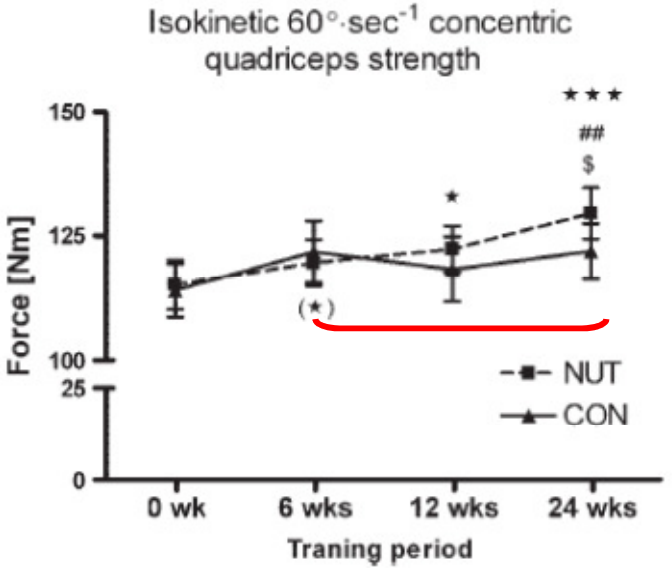
J Appl Physiol 105: 274–281, 2008.

Table 4. *Bone mineral density*

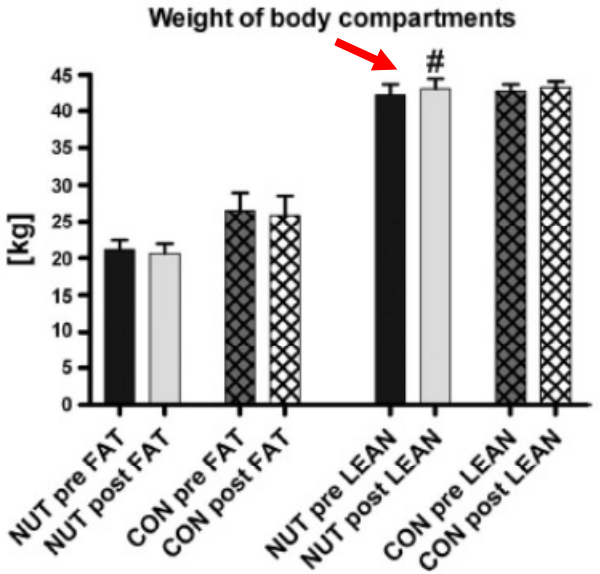
	Control Group	Nutrient Group
Total BMD, g/mm³		
0 wk	1.117±0.022	1.113±0.027
24 wk	1.122±0.023	1.116±0.027
Femoral neck BMD, g/mm³		
0 wk	0.943±0.028	0.953±0.051
24 wk	0.930±0.024	0.978±0.043
L2–L4 BMD, g/mm³		
0 wk	1.043±0.032	1.084±0.053
24 wk	1.068±0.038*	1.108±0.049*

Values are means ± SE of bone mineral density (BMD) at whole body, femoral neck, and lumbar spine (L2–L4). *$P < 0.05$ compared with 0 wk.

Adjusting for covariates (age at inclusion, BMI at inclusion, and BMD of the femoral neck at inclusion) a significant ($P < 0.05$) difference was seen in the response to training of bone mineral density between the two groups.



Strength improvements from 6 to 24 wk, a significant difference was apparent between groups: nutrient group, 9±3% vs. control, 1±2% ($P < 0.05$).



Clinical Nutrition (2006) **25**, 330–360

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ESPEN GUIDELINES

ESPEN Guidelines on Enteral Nutrition: Geriatrics ☆

The majority of sick elderly patients require at least 1 g protein/kg/day and around 30 kcal/kg/day of energy, depending on their activity.

Clinical Nutrition 28 (2009) 461–466

Contents lists available at ScienceDirect

Clinical Nutrition

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

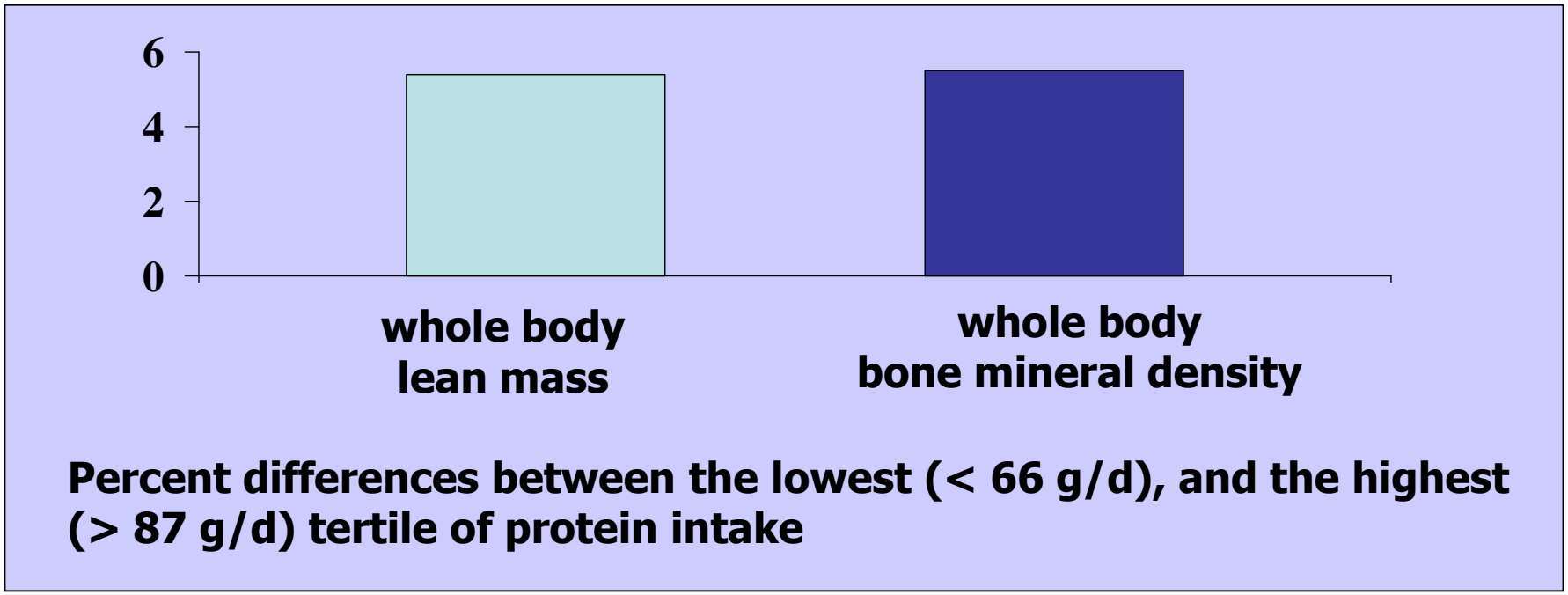
ESPEN Guidelines on Parenteral Nutrition: Geriatrics

In designing the programme, it should be remembered that the majority of sick elderly patients require at least 1.0–1.2 g protein/kg per day and 20–30 kcal/kg per day of non-protein energy,[4,5] depending on the severity of the disease, the degree of current inflammation/catabolism, the physical activity level and the need and time course of rehabilitation.

4. Wolfe RR, Miller SL, Miller KB. Optimal protein intake in the elderly. *Clin Nutr* 2008;**27**:675–84.
5. Alix E, Berrut G, Boré M, Bouthier-Quintard F, Buia JM, Chlala A, et al. Energy requirements in hospitalized elderly people. *JAGS* 2007;**55**:1085–9.

A 5-Year Cohort Study of the Effects of High Protein Intake on Lean Mass and Bone Mineral Content in Elderly Postmenopausal Women
J Bone Miner Res. 2009

- relationship between baseline protein intake and lean mass and bone mineral content (DEXA)
- 862 elderly postmenopausal women (mean age: 75 yrs)
- 5 years follow-up

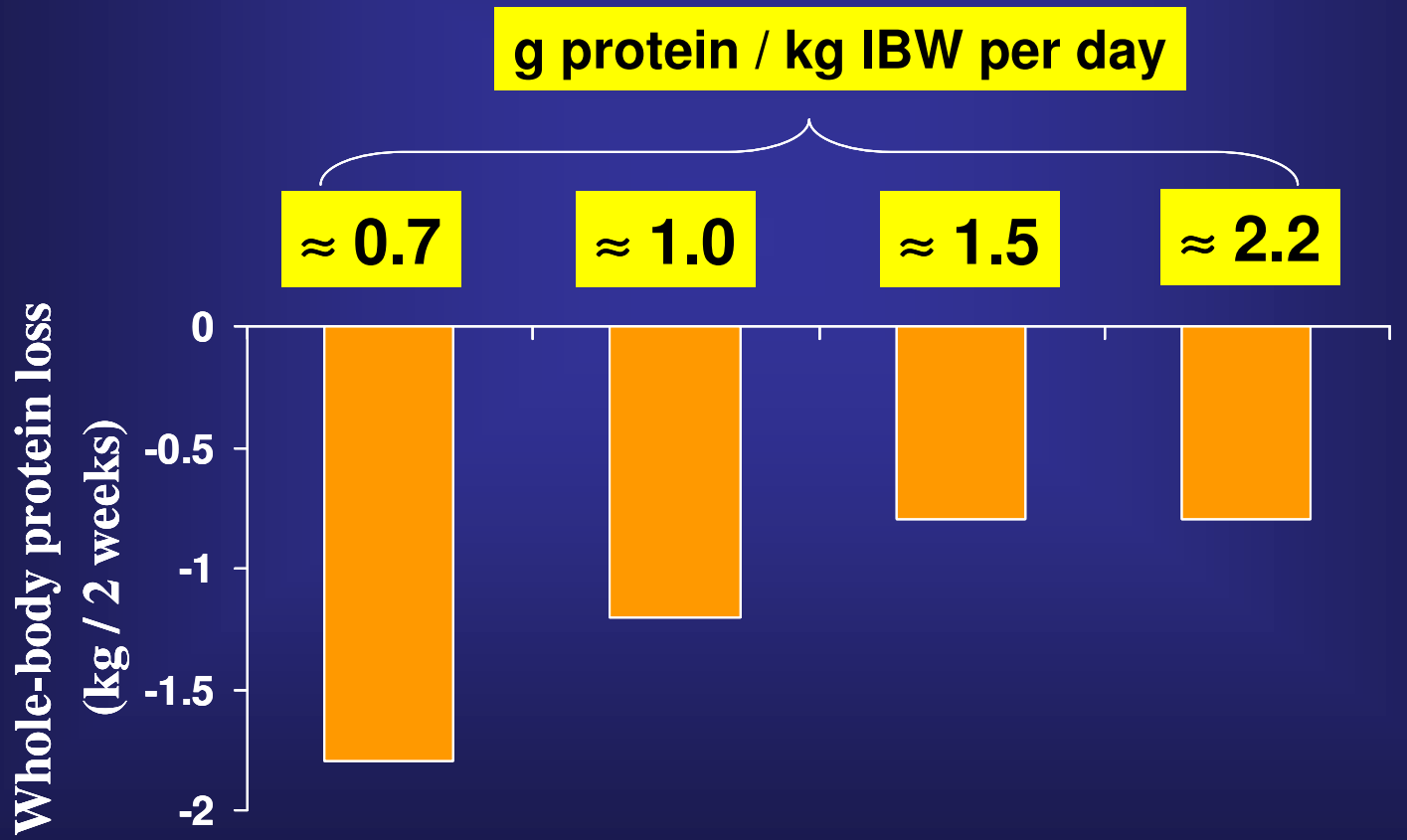


Percent differences between the lowest (< 66 g/d), and the highest (> 87 g/d) tertile of protein intake

A higher protein intake is associated with long term beneficial effects on muscle mass and size and bone mass in elderly women

PROTEIN REQUIREMENT IN CRITICAL ILLNESS AT ADEQUATE ENERGY INTAKE

Wolfe et al., Ann Surg 1983; *Ishibashi et al., Crit Care Med 1998*
Hoffer Am J Clin Nutr 2003



ESPEN

THE EUROPEAN SOCIETY FOR CLINICAL NUTRITION AND METABOLISM

Protein/amino acid requirement

"1.3–1.5 g/kg ideal body weight per day in conjunction with an adequate energy supply"

(Grade B)

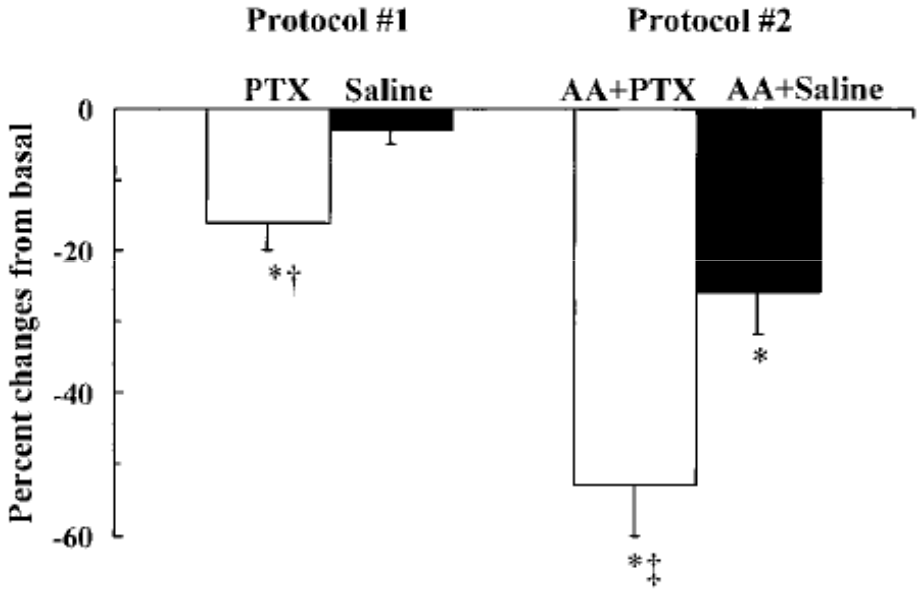
2009 ESPEN Guidelines

Medications and nutraceuticals to counteract anabolic resistance

Pentoxifylline Acutely Reduces Protein Catabolism in Chronically Uremic Patients

Gianni Biolo, MD, PhD, Beniamino Ciocchi, MD, Alessandra Bosutti, MSc, Roberta Situlin, MD, Gabriele Toigo, MD, and Gianfranco Guarnieri, MD

American Journal of Kidney Diseases, Vol 40, No 6 (December), 2002: pp 1162-1172



Percentage of changes from basal in whole-body proteolysis during pentoxifylline (PTX) or saline infusion in the postabsorptive state (protocol 1) and during amino acid infusion alone (AA) or in combination with pentoxifylline (AA + PTX; protocol 2). *Significantly different from basal. †$P < 0.05$, PTX versus saline. ‡$P < 0.05$, PTX + AA versus AA.

Dietary omega-3 fatty acid supplementation increases the rate of muscle protein synthesis in older adults: a randomized controlled trial[1–3]

Gordon I Smith, Philip Atherton, Dominic N Reeds, B Selma Mohammed, Debbie Rankin, Michael J Rennie, and Bettina Mittendorfer

Am J Clin Nutr 2011;93:402–12.

8 weeks supplementation

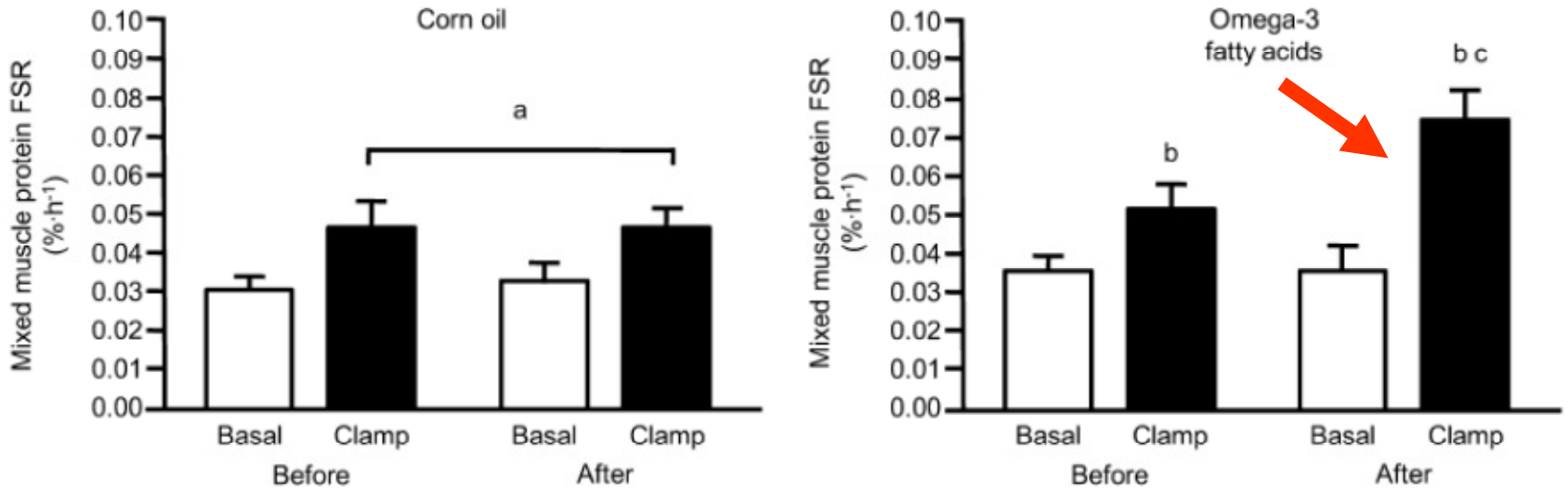


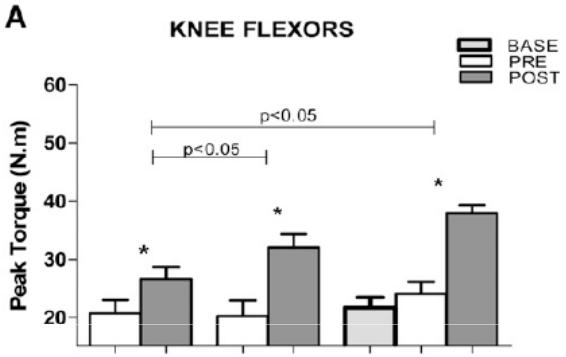
FIGURE 1. Mean (±SEM) mixed skeletal muscle protein fractional synthesis rate (FSR), calculated by using the average plasma free phenylalanine he precursor pool enrichment, during basal, postabsorptive conditions and during the hyperaminoacidemic-hyperinsulinemic clamp before and after 8 wk of supplementation with either corn oil ($n = 7$) or omega-3 fatty acids ($n = 8$). There was no difference in the muscle protein FSR between the omega-3 fatty acid and corn oil groups before the intervention [ANOVA showed a significant effect of clamp ($P < 0.001$), no significant effect of group ($P = 0.47$), and no interaction ($P = 0.60$)]. [a]In the corn oil group, ANOVA showed a significant main effect of clamp ($P < 0.01$). In the omega-3 fatty acid group, ANOVA showed a significant effect of clamp ($P < 0.01$) and an interaction ($P < 0.001$), which was followed by Tukey's post hoc analysis. [b]Significantly different from the corresponding basal value, $P < 0.01$. [c]Significantly different from the corresponding value before omega-3 fatty acid supplementation, $P < 0.01$. Furthermore, the before-after intervention change in the anabolic response (increase in the muscle protein FSR from basal values) was significantly greater in the omega-3 fatty acid group than in the corn oil group ($P = 0.01$, Student's t test for independent samples).

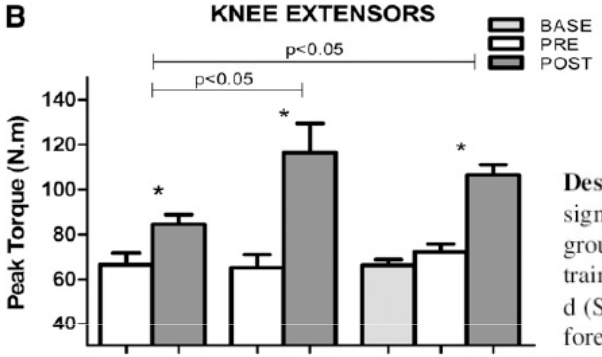
CLAMP = INSULIN+GLUCOSE+AMINO ACID INFUSION

Fish-oil supplementation enhances the effects of strength training in elderly women[1–3]

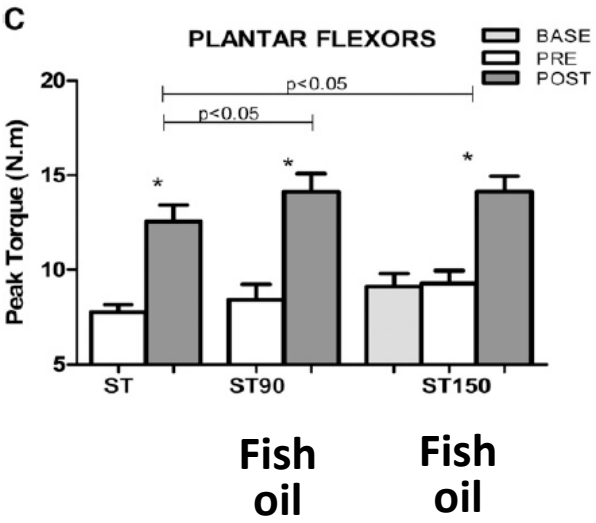
Am J Clin Nutr 2012;95:428–36.

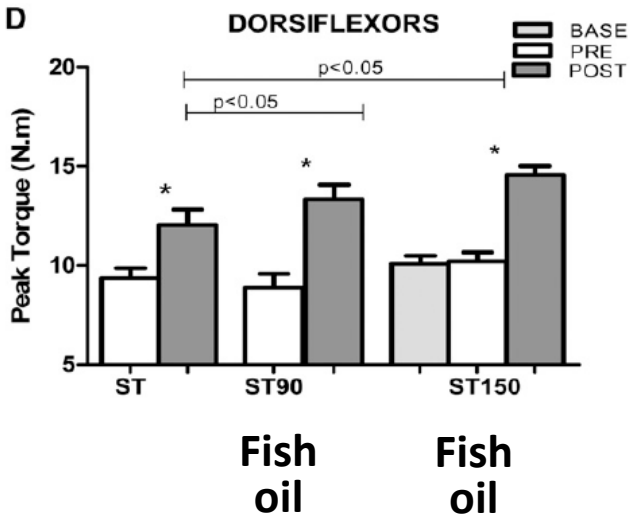
90-day strength training increased muscle strength in elderly women. The inclusion of fish oil supplementation caused greater improvements in muscle strength and functional capacity.





Design: Forty-five women (aged 64 ± 1.4 y) were randomly assigned to 3 groups. One group performed strength training only (ST group) for 90 d, whereas the others performed the same strength-training program and received FO supplementation (2 g/d) for 90 d (ST90 group) or for 150 d (ST150 group; supplemented 60 d before training). Muscle strength and functional capacity were assessed before and after the training period.



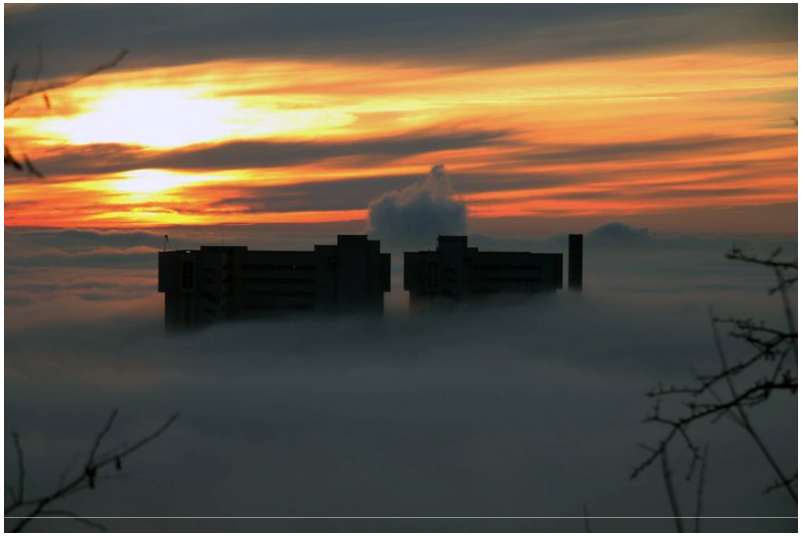


ANABOLIC RESISTANCE

- Critical illness
- Chronic diseases
- Aging
- Inactivity

COUNTERACTING ANABOLIC RESISTANCE

- Increase microvascular, nutritive muscle blood flow (exercise)
- Definition of optimal protein intake in each condition
- Control of energy balance and fat mass
- Medications and nutraceuticals (?)



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