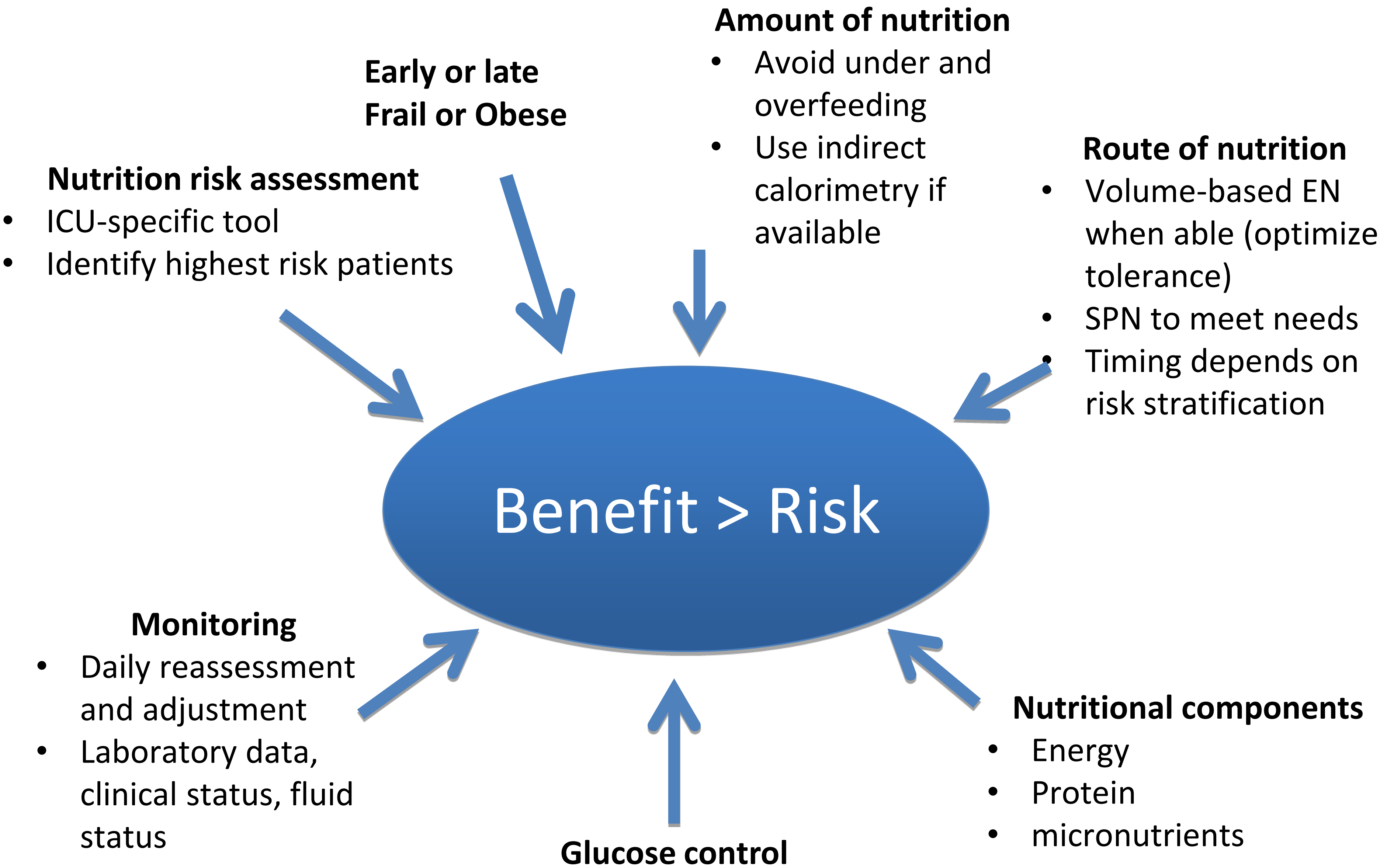
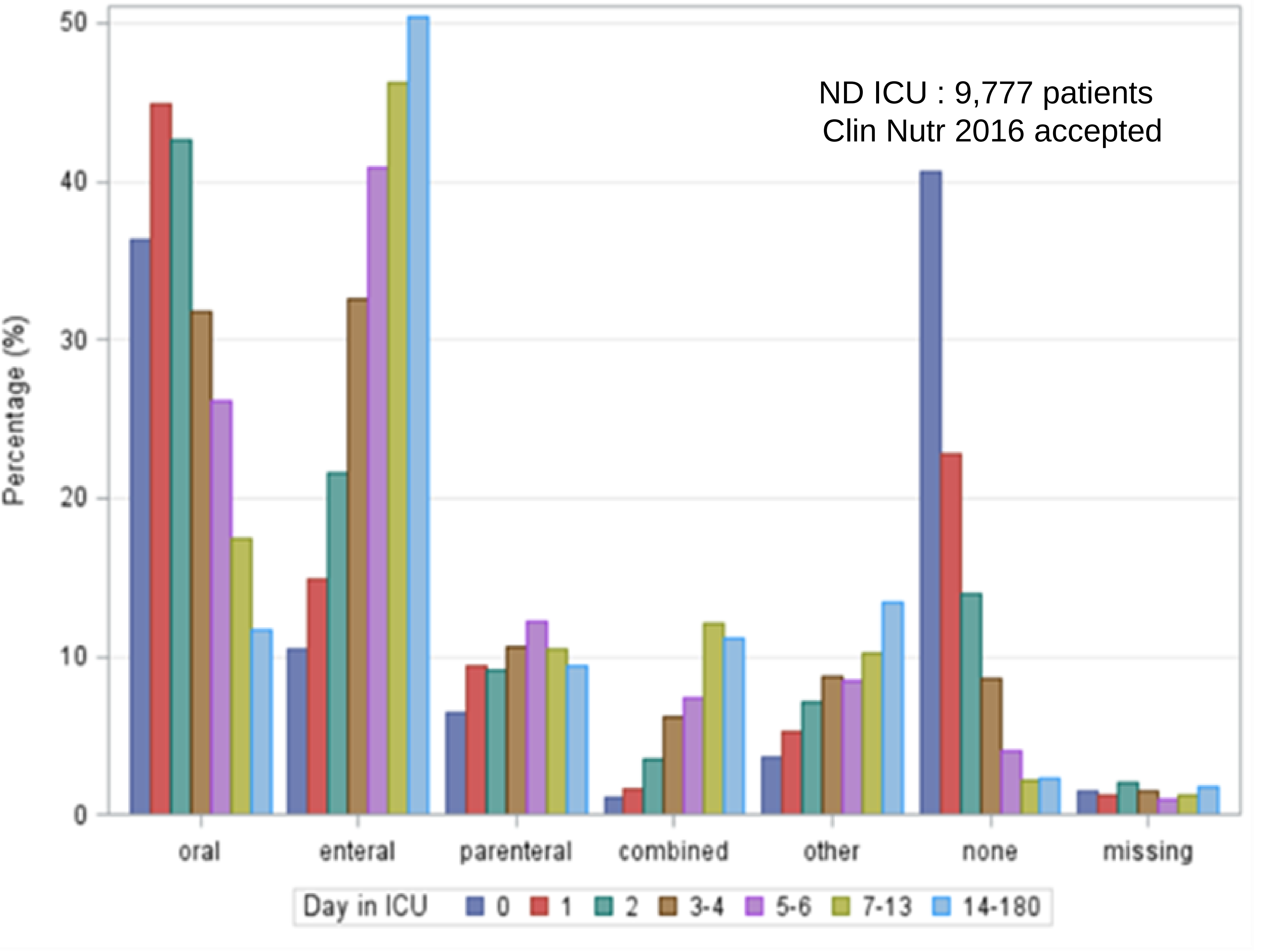
How much protein in the critical illness

Pierre Singer, MD
Institute for Nutrition Research and Critical Care Department
Rabin Medical Center
Tel Aviv University
Israel

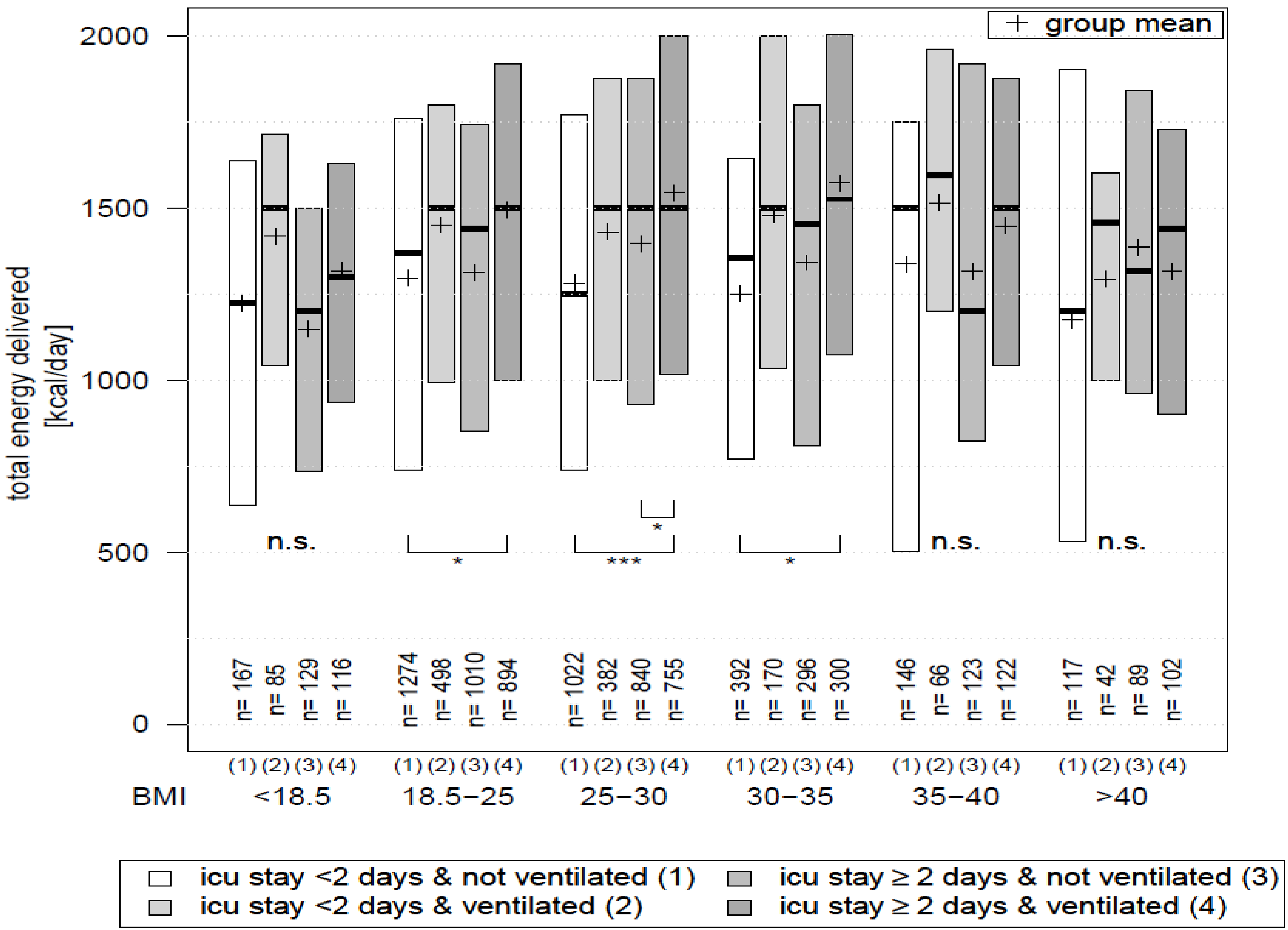


From Singer P: Nutrition in the ICU: beyond physiology. Karger Publisher


ND ICU : 9,777 patients
Clin Nutr 2016 accepted
Percentage (%)
50
40
30
20
10
0
oral
enteral
parenteral
combined
other
none
missing
Day in ICU
0
1
2
3-4
5-6
7-13
14-180

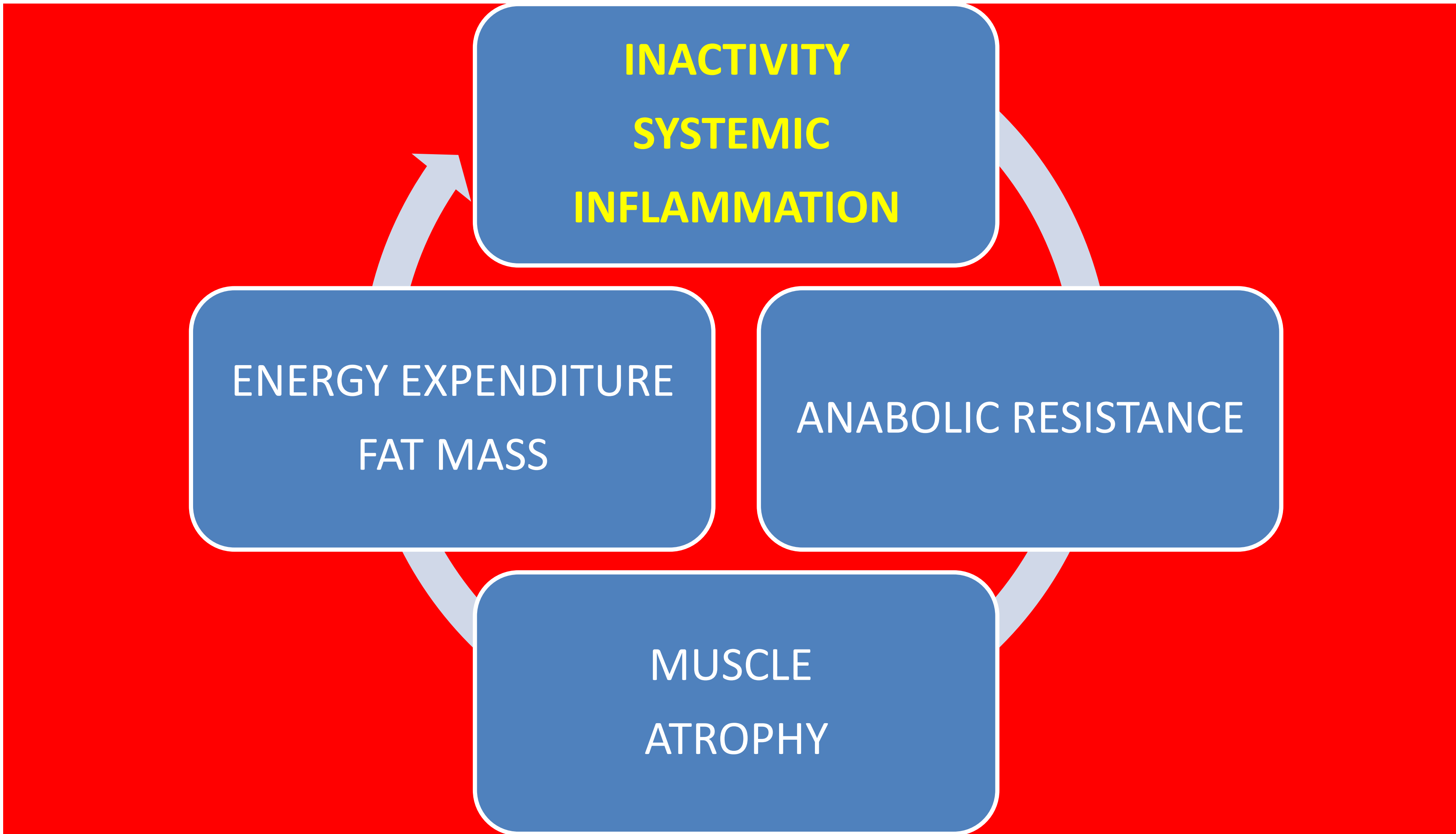
Energy and protein administered in Nutrition Day study

- From 4,125 patients:
- **Protein given 60 ± 31 g/d**
- Lipid given 53 ± 31 g/day
- Carbohydrates 176 ± 87 g/d
- Total median calories: 1,500 kcal/d



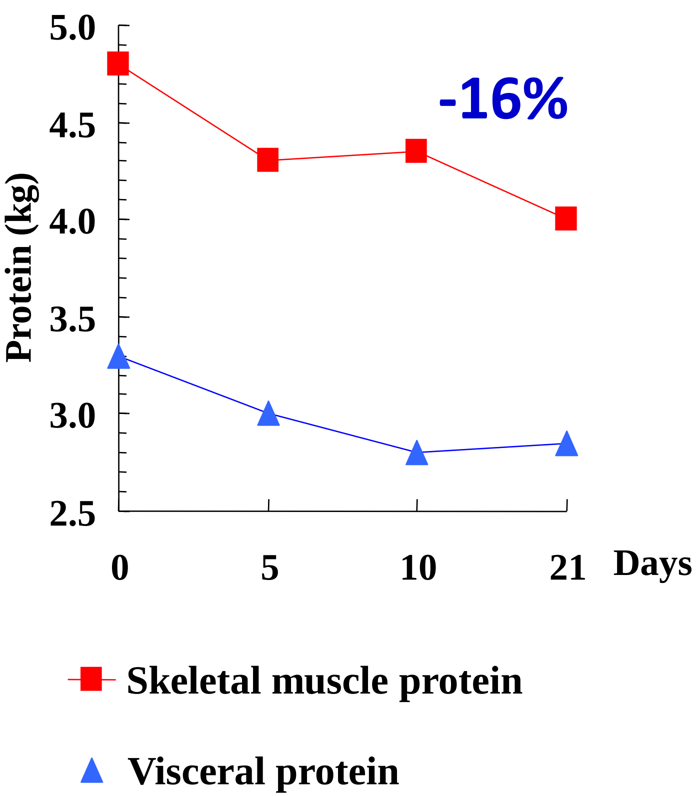
group mean
total energy delivered [kcal/day]
2000
1500
1000
500
0
n.s.
*
***
*
*
n.s.
n.s.
n= 167
n= 85
n= 129
n= 116
n= 1274
n= 498
n= 1010
n= 894
n= 1022
n= 382
n= 840
n= 755
n= 392
n= 170
n= 296
n= 300
n= 146
n= 66
n= 123
n= 122
n= 117
n= 42
n= 89
n= 102
(1) (2) (3) (4)
BMI
<18.5
18.5−25
25−30
30−35
35−40
>40
icu stay <2 days & not ventilated (1)
icu stay <2 days & ventilated (2)
icu stay ≥ 2 days & not ventilated (3)
icu stay ≥ 2 days & ventilated (4)

Message: Give enough protein to fight anabolism resistance



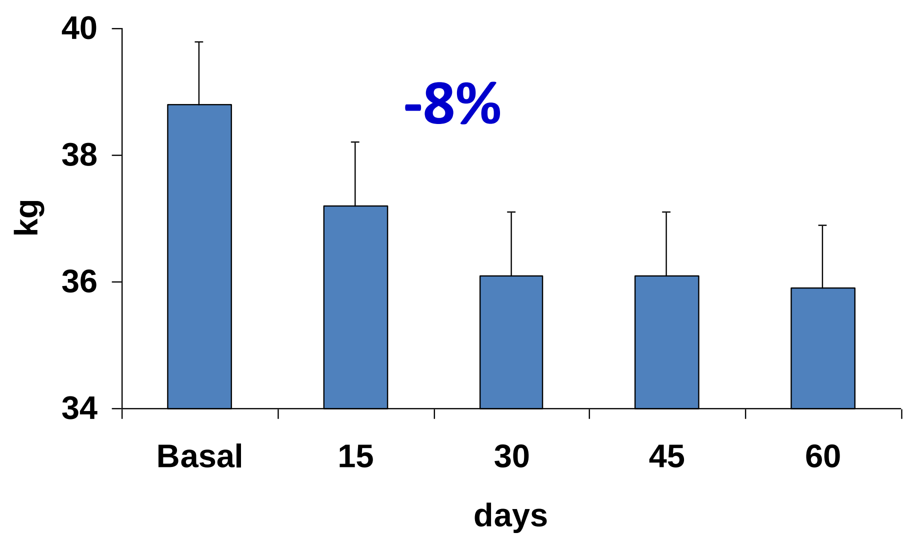
The effects of bed rest
INACTIVITY

CHANGES OF MUSCLE AND VISCERAL PROTEIN CONTENT IN SEVERELY SEPTIC PATIENTS DURING THE FIRST DAYS AFTER THE ONSET OF PERITONITIS



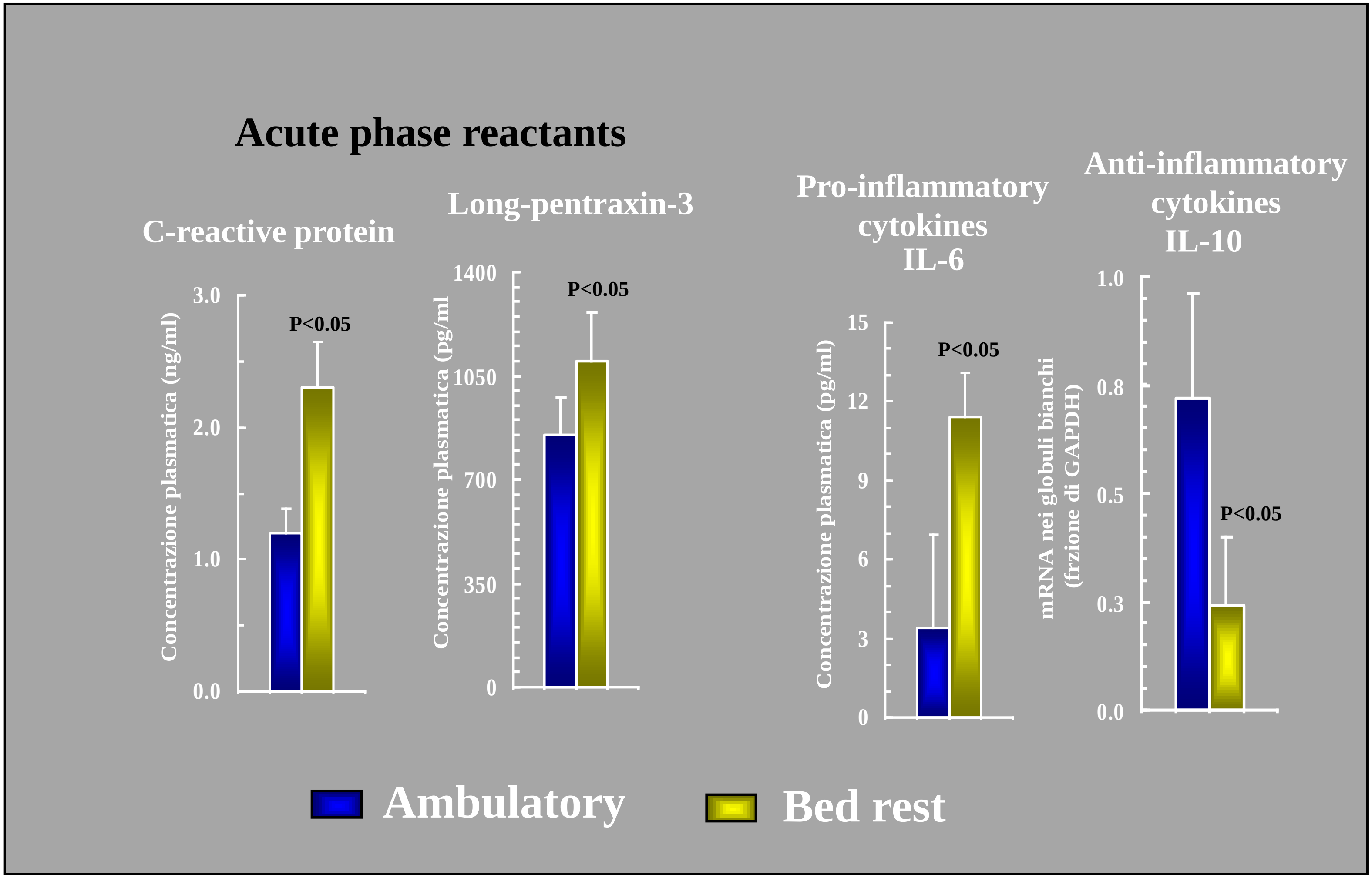
Plank et al, Ann Surg 1998

CHANGES IN LEAN BODY MASS (DXA) DURING TWO-MONTH EXPERIMENTAL BED REST IN WOMEN



ESA/NASA/CNES WISE-study

EFFECTS OF 2-WEEK BED REST ON INFLAMMATORY MEDIATORS IN HEALTHY YOUNG VOLUNTEERS



J Clin Endocrinol Metab 2008

OPEN ACCESS Freely available online PLoS one

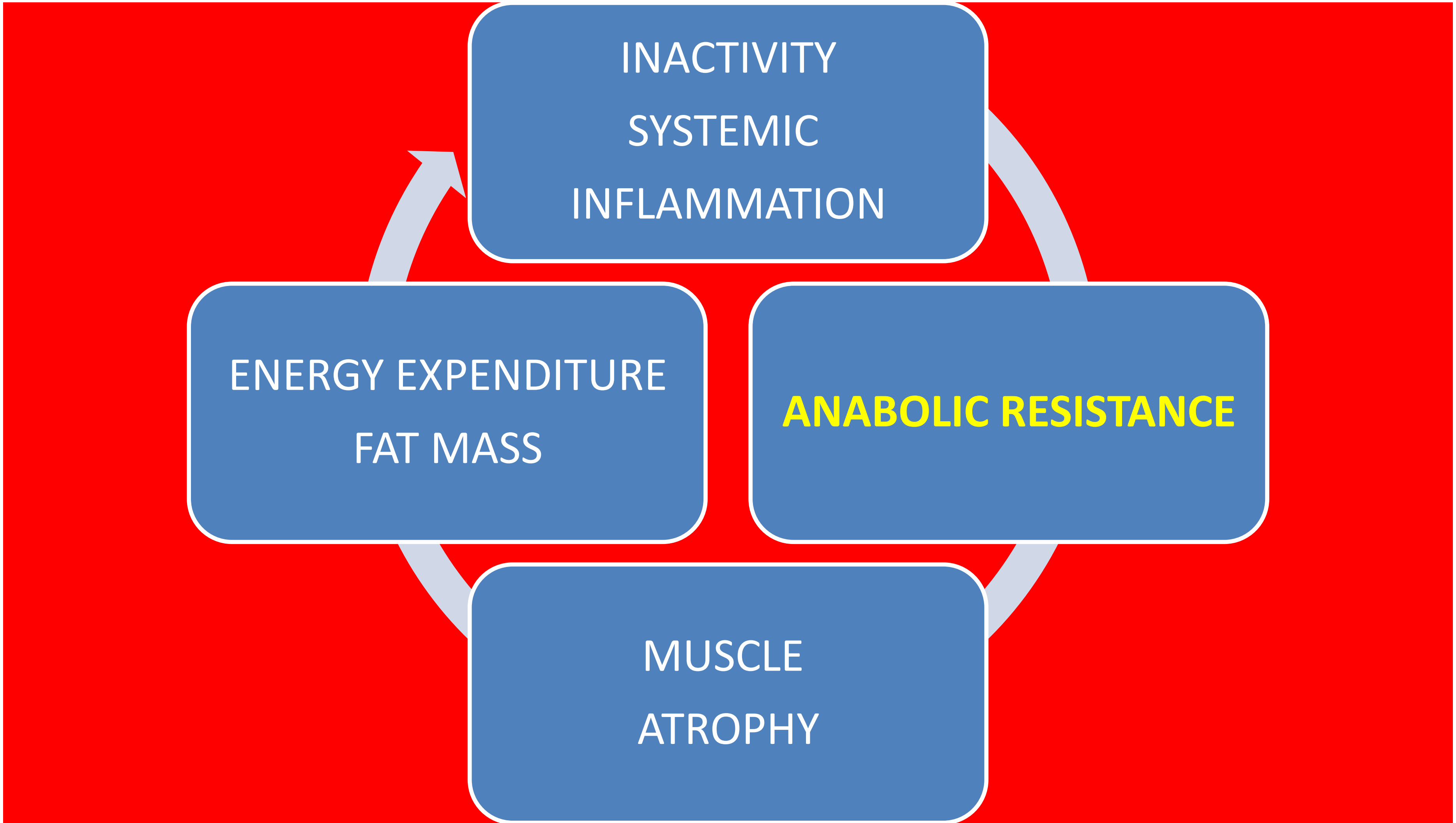
Activated Protein Synthesis and Suppressed Protein Breakdown Signaling in Skeletal Muscle of Critically Ill Patients

Jakob G. Jespersen[1]*, Anders Nedergaard[1], Søren Reitelseder[1], Ulla R. Mikkelsen[1], Kasper J. Dideriksen[1], Jakob Agergaard[1], Frederik Kreiner[2], Frank C. Pott[3], Peter Schjerling[1], Michael Kjaer[1]

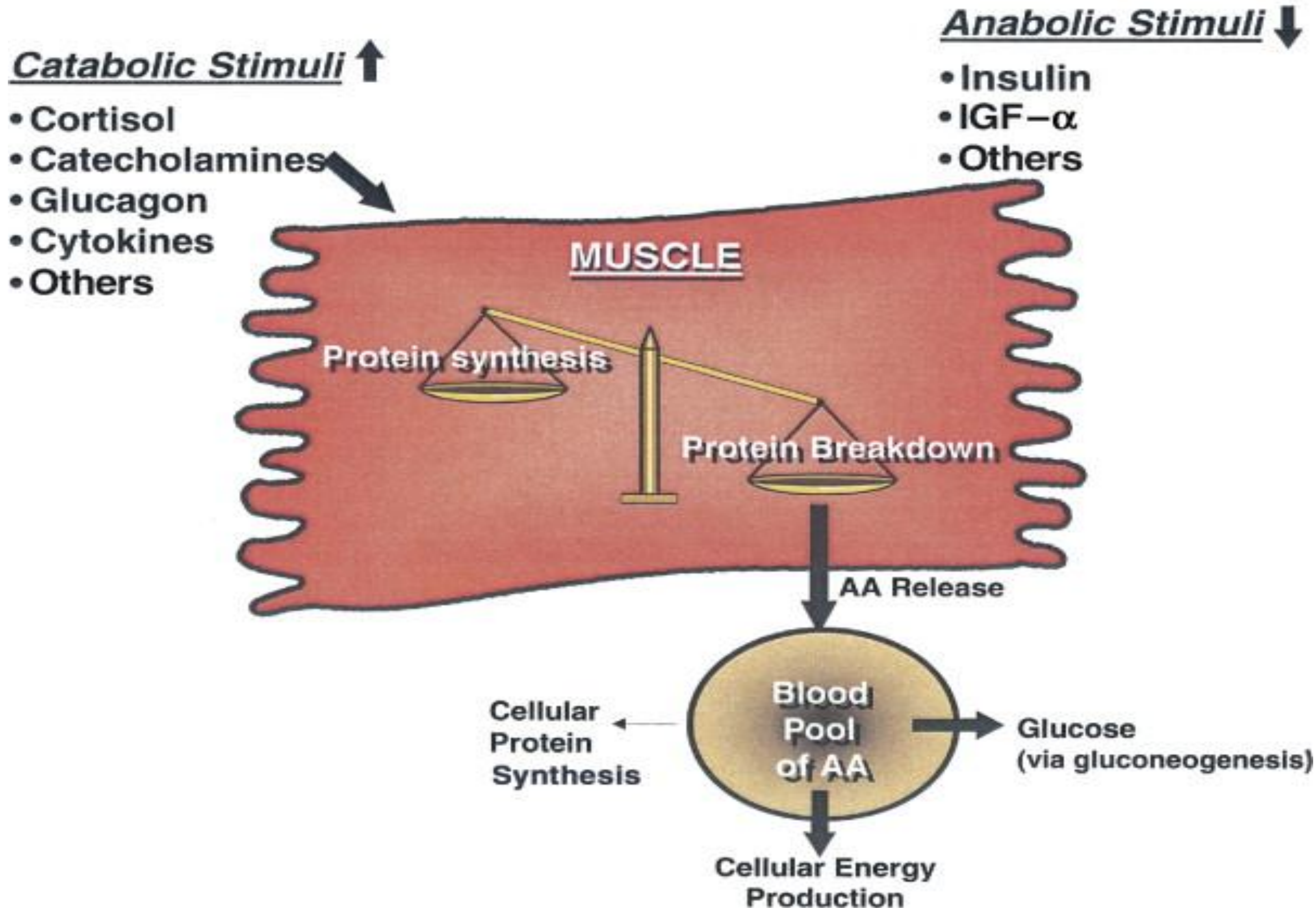
Table 3. Circulating IGF-1, markers of systemic inflammation, proteins and metabolites.

Variable	Control subjects (n = 12)	ICU patients (n = 12)	% Difference
IGF-1, µg/l	132±14	76±14†	−43
Inflammatory markers			
Leukocytes, 10^9/l	ND, nomal range: 3.0–9.0	16.3±3.3	
CRP, mg/l	ND, nomal <10	134±28	
TNF-α, pg/ml	3.9±0.5	27.3±8.4*	+605
IL-6, pg/ml	6.3±1.5	1096±366*	+17371
IL-8, pg/ml	3.8±0.5	201±91[1]	+5246
IL-10, pg/ml	13.9±2.7	607±262*	+4258
MCP-1, pg/ml	266±28	1438±213‡	+440
Proteins and metabolites			
Serum albumin, g/l	ND, nomal range: 34–48	21.1±1.6	
Urea, mmol/l	ND, nomal range: 3.1–8.1	16.9±4.3	
Creatinine, µmol/l	ND, nomal range: 45–105	160±33	

Message: Give enough protein to fight anabolic resistance

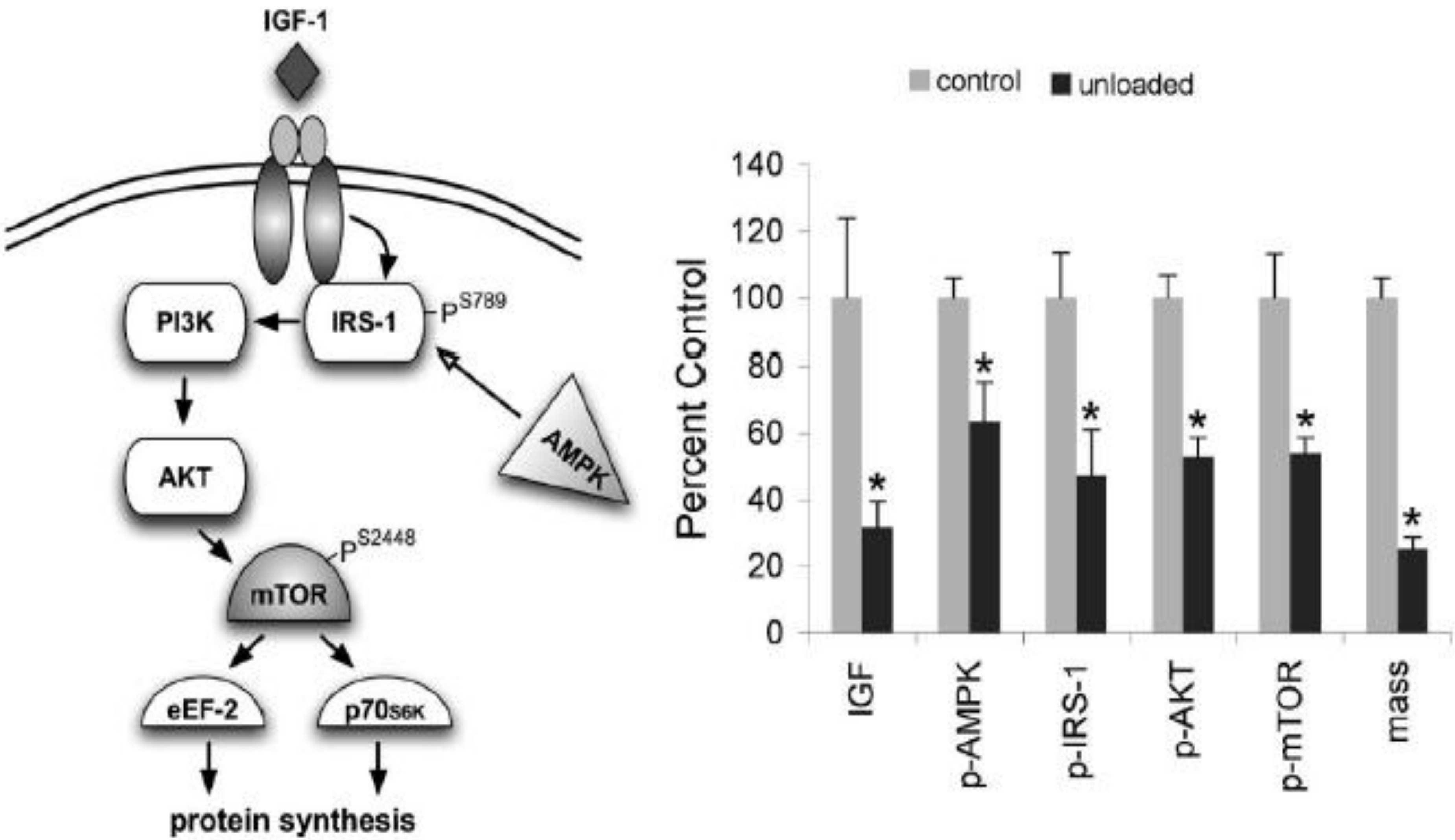


Hypercatabolic Syndrome / Insulin Resistance



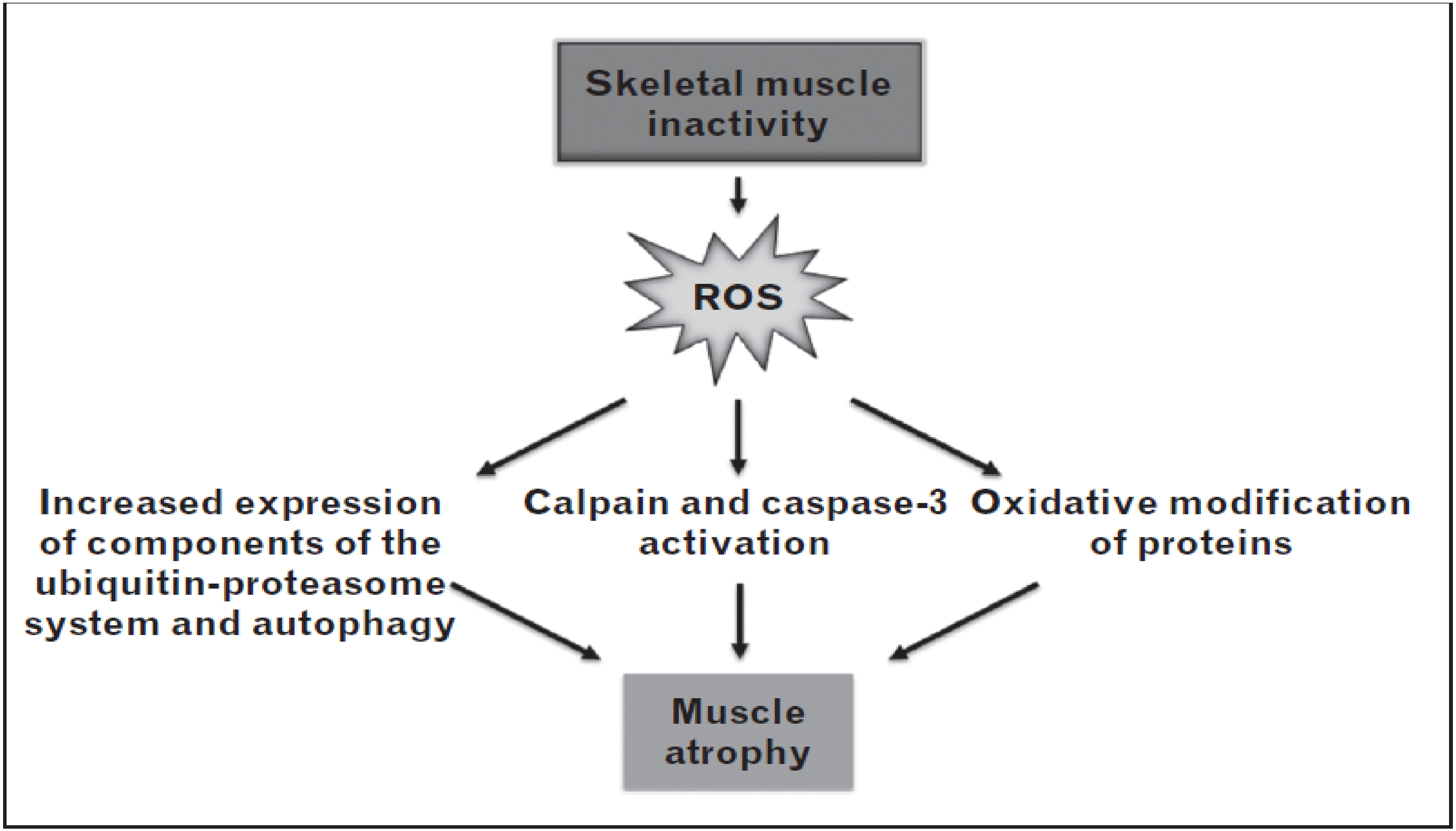
Physical inactivity and muscle weakness in the critically ill

Melissa A. Chambers, PhD; Jennifer S. Moylan, PhD; Michael B. Reid, PhD



Oxidative stress and disuse muscle atrophy: cause or consequence?

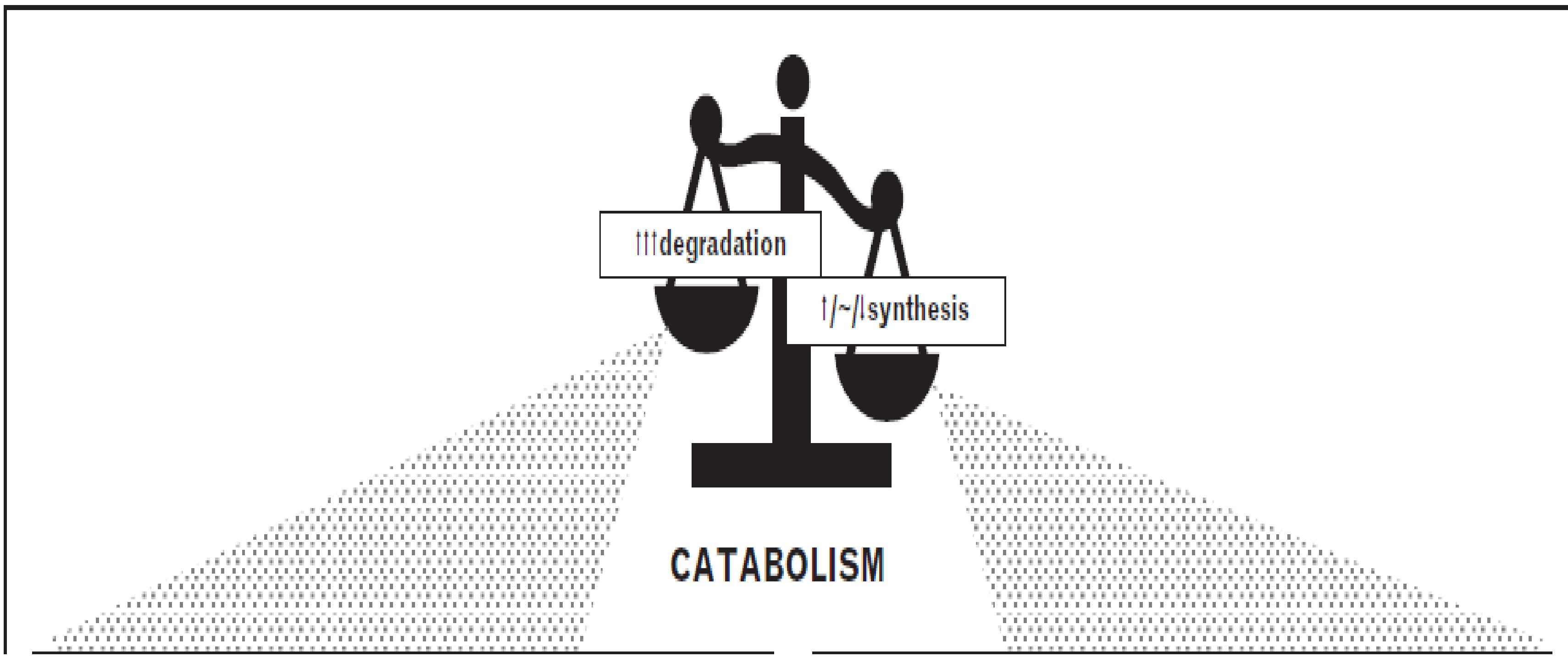
Scott K. Powers[a], Ashley J. Smuder[a], and Andrew R. Judge[b]

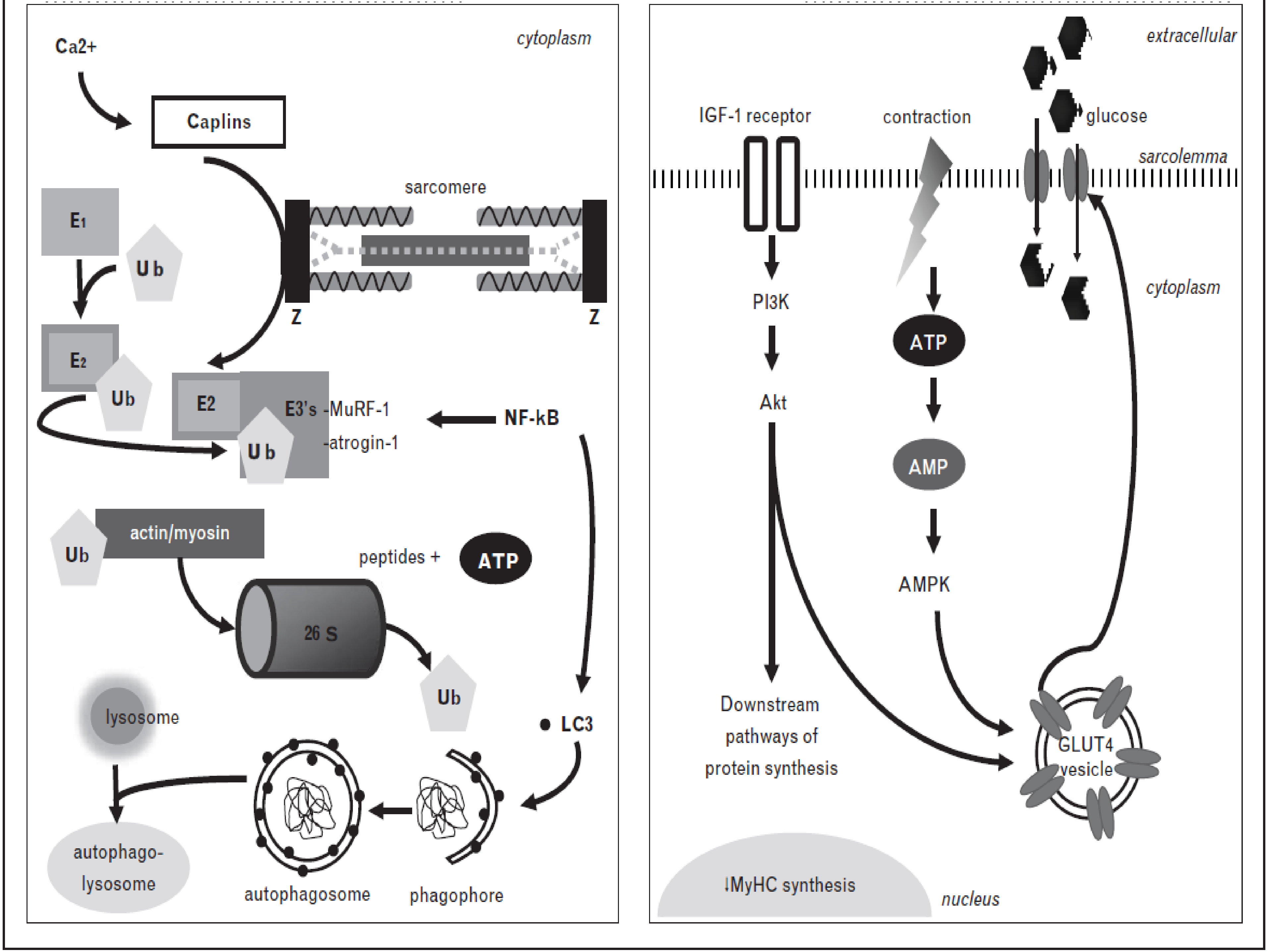


CURRENT OPINION

Myopathic characteristics in septic mechanically ventilated patients

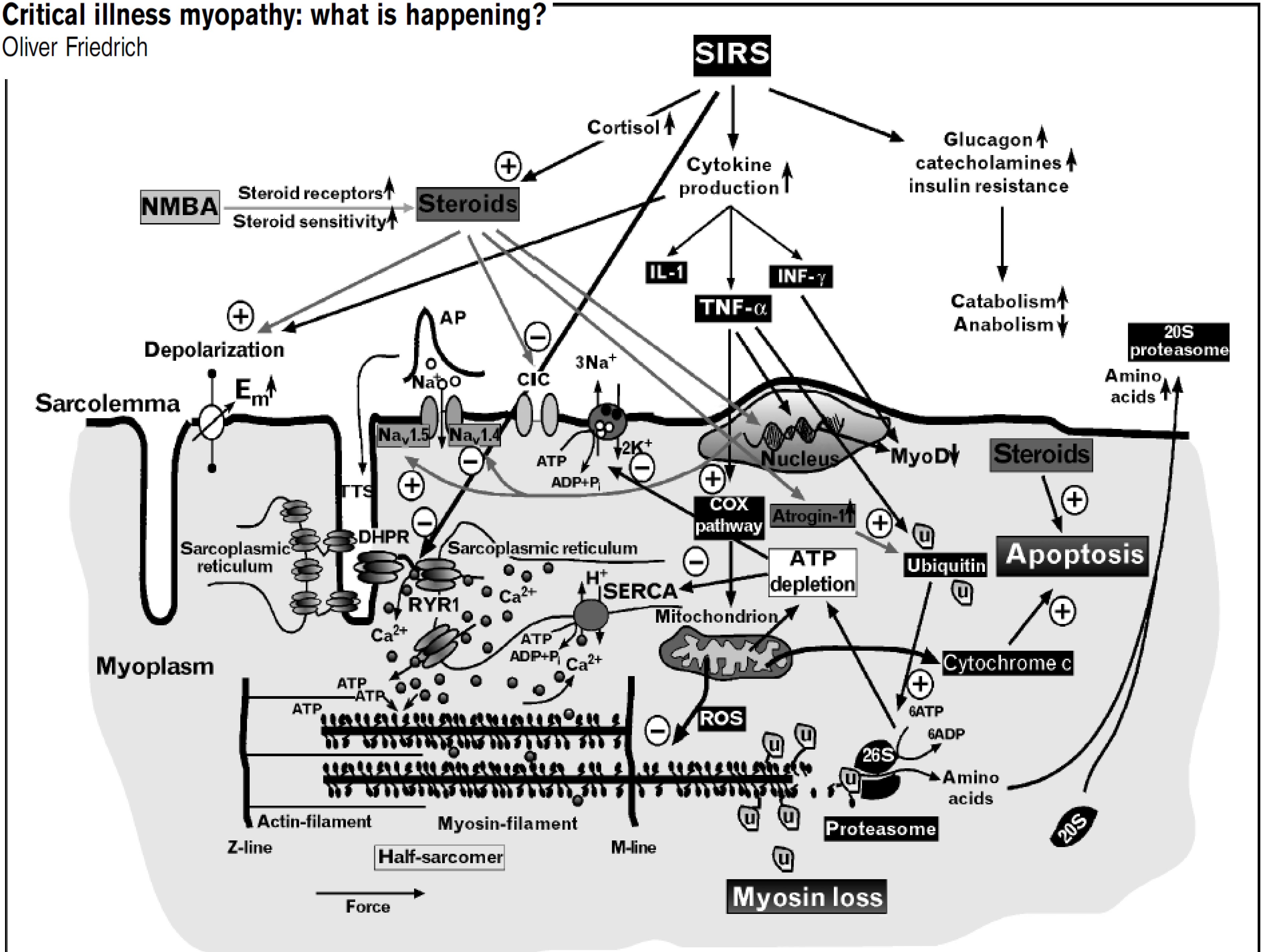
Claire E. Baldwin[a,b] and Andrew D. Bersten[c,d]




cytoplasm
Ca2+
Caplins
sarcomere
Z
Z
E1
Ub
E2
Ub
E2
E3's -MuRF-1
-atrogin-1
Ub
NF-kB
actin/myosin
Ub
peptides +
ATP
26 S
Ub
lysosome
LC3
autophago-
lysosome
autophagosome
phagophore
extracellular
IGF-1 receptor
contraction
glucose
sarcolemma
cytoplasm
PI3K
ATP
Akt
AMP
AMPK
Downstream
pathways of
protein synthesis
GLUT4
vesicle
↓MyHC synthesis
nucleus

Critical illness myopathy: what is happening?

Oliver Friedrich



Hyperglycemia exacerbates muscle protein catabolism in burn-injured patients

Dennis C. Gore, MD; David L. Chinkes, PhD; David W. Hart, MD; Steven E. Wolf, MD; David N. Herndon, MD; Arthur P. Sanford, MD

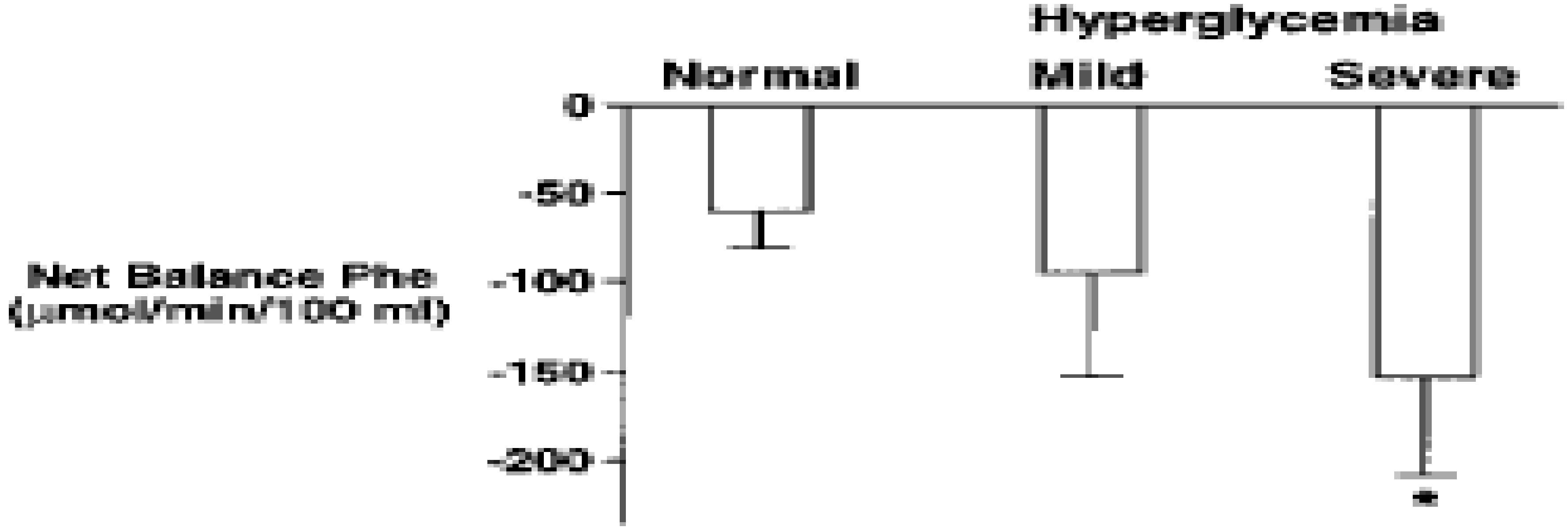


Figure 1. Negative net balance reflects net catabolism. *Phe*, phenylalanine; mean ± SD; $^{*}p < .05$ in comparison with normal.

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

J Clin Endocrinol Metab, July 2002, 87(7):3378–3384

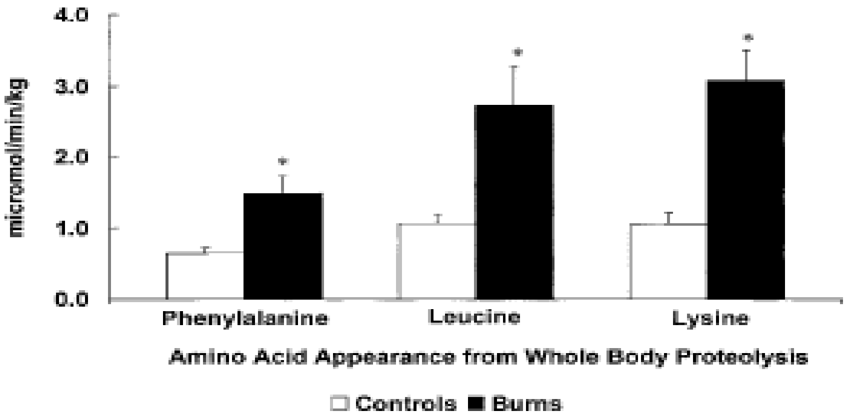
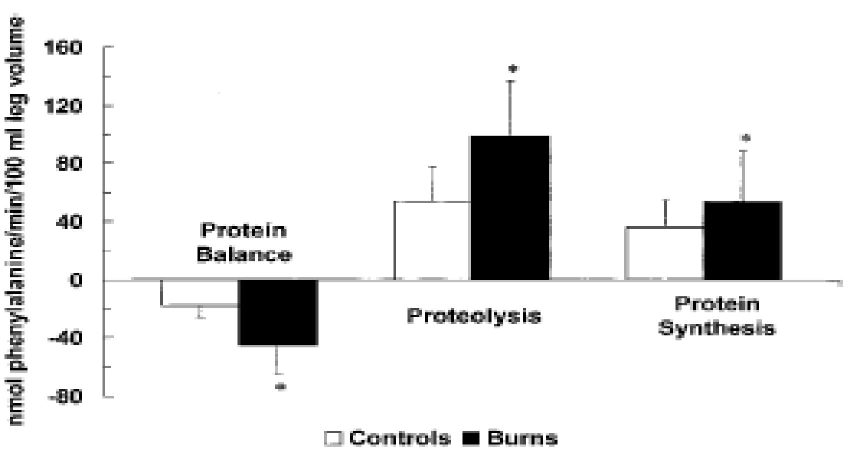
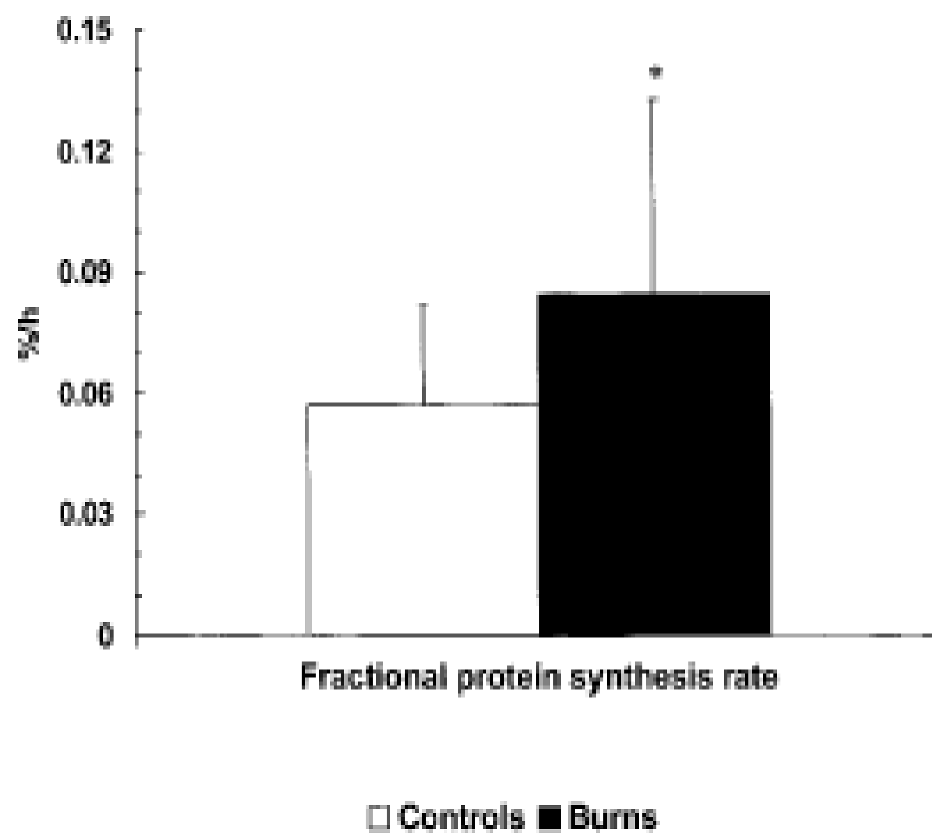


FIG. 1. Amino acid rates of appearance from whole-body proteolysis. *, $P < 0.05$ burn patients *vs.* controls.





Immobilization induces anabolic resistance in human myofibrillar protein synthesis with low and high dose amino acid infusion

Elisa I. Glover[1], Stuart M. Phillips[1], Bryan R. Oates[1], Jason E. Tang[1], Mark A. Tarnopolsky[2], Anna Selby[3], Kenneth Smith[3] and Michael J. Rennie[3]

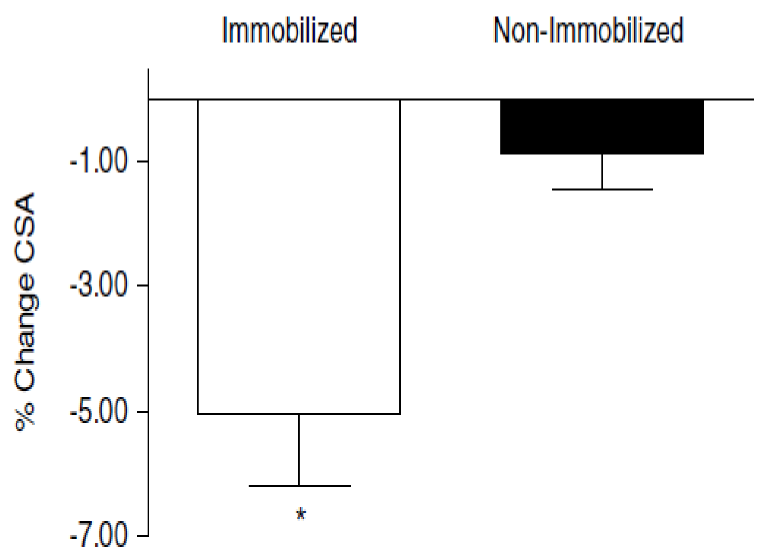


Figure 2. Quadriceps femoris cross-sectional area

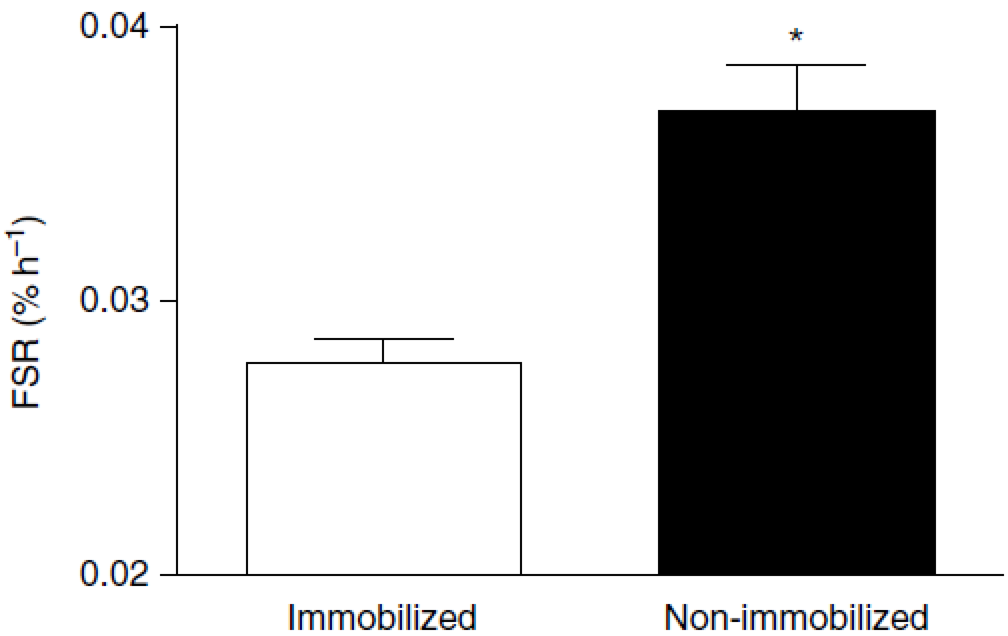
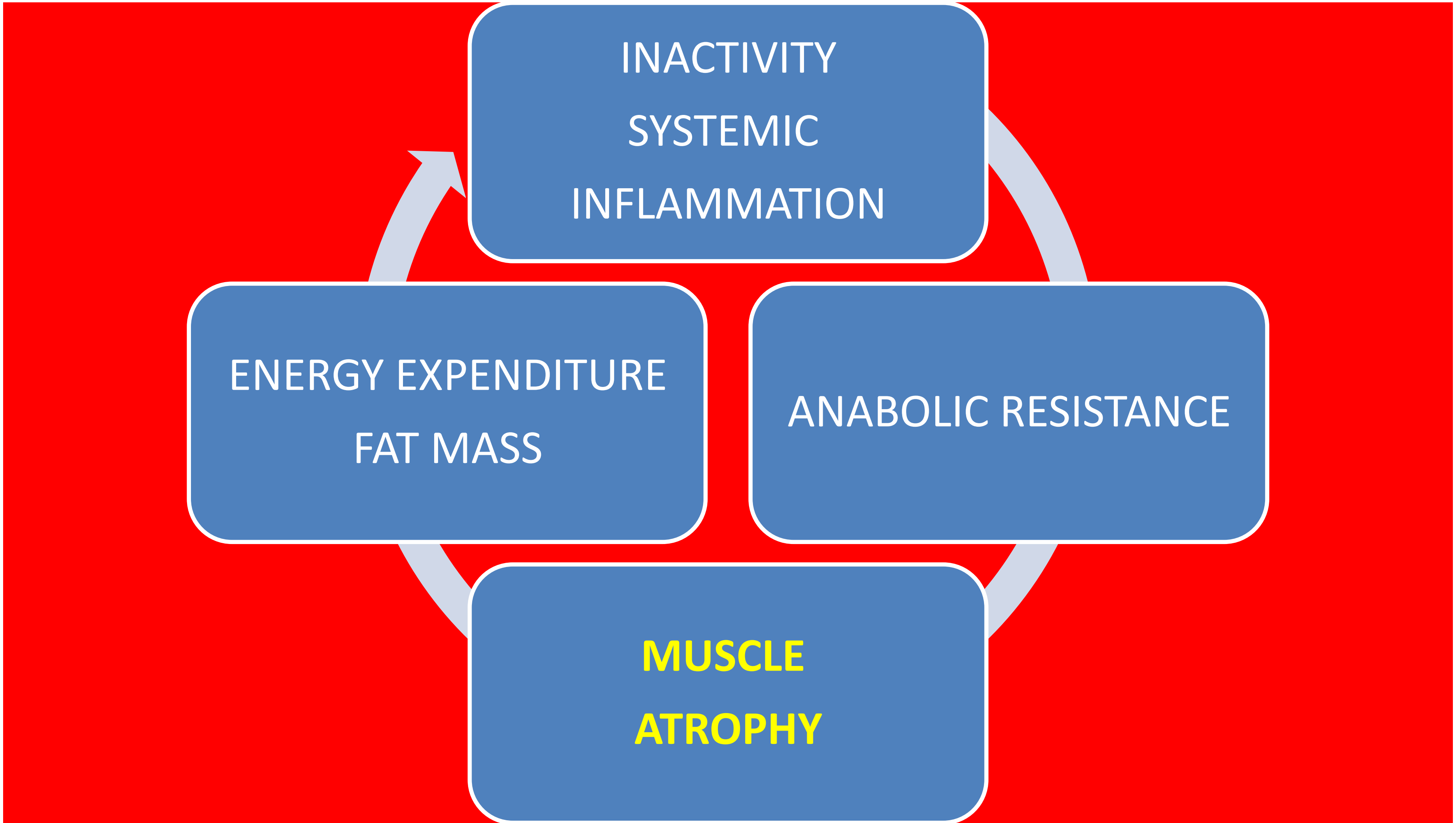


Figure 4. Pooled (from both low and high infused groups) resting fasted myofibrillar protein fractional synthetic rate (FSR)

Message: Give enough protein to fight anabolism resistance



Loss of muscle mass in ICU patients

Daily UL measurement of upper arm, forearm and thigh for a median of 7 days (N=50).

Admission APACHE II score: 17. Mortality: 28%

Reid et al. 2004; Clin Nutr 23: 273-280

Muscle thickness decreased by an average of 1.6% per day

With 6 kg metabolizable protein in lean body mass:
≈ 100g/day

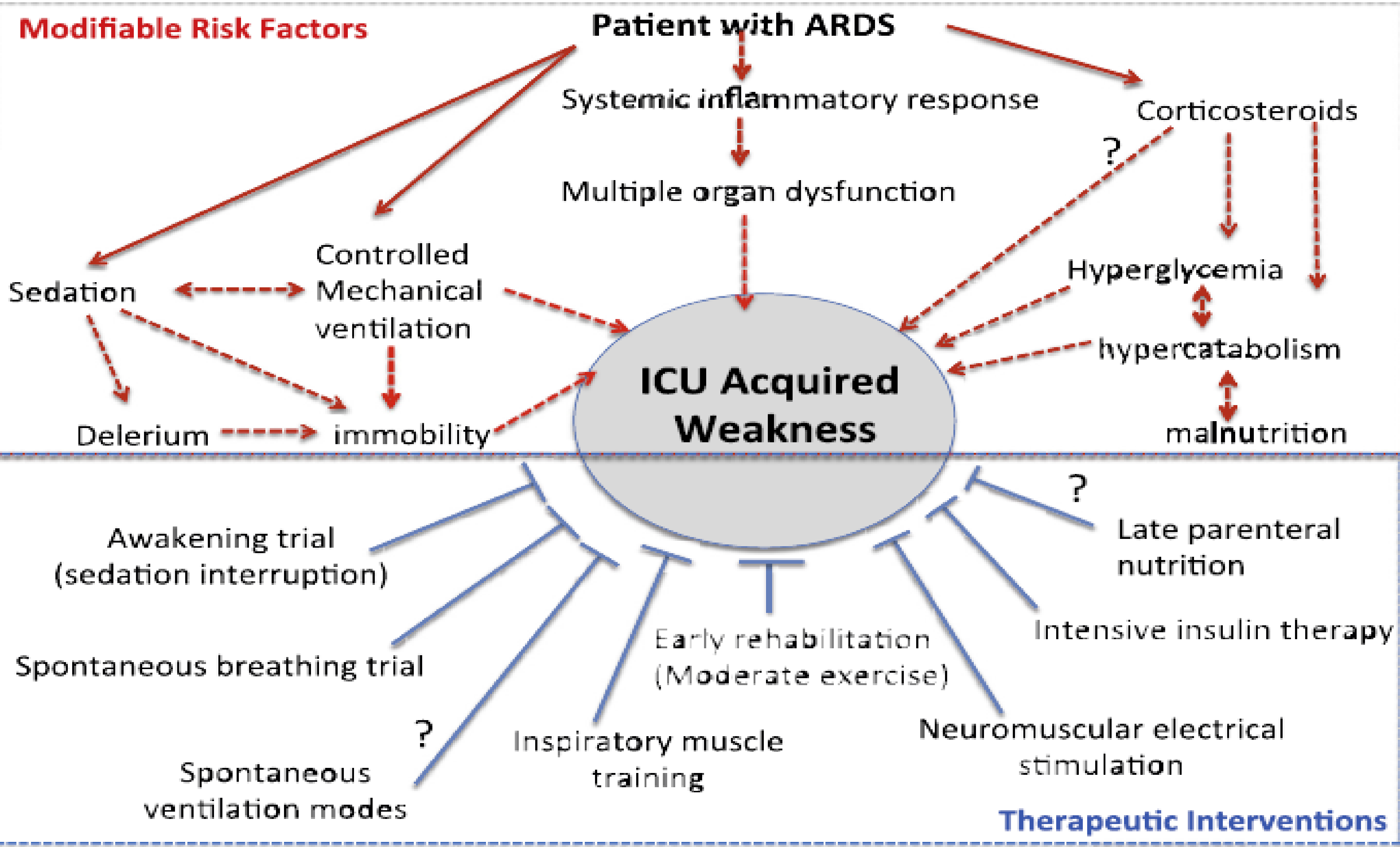
After 10 days: 16% muscle loss
≈ 1000 g protein ≈ 5 kg lean body mass

REE in 24 patients:
10 patients in positive energy balance: 1.1 % per day
14 patients in negative energy balance: 1.3 % per day

Muscle Wasting and Early Mobilization in Acute Respiratory Distress Syndrome

Christopher J. Walsh, MD, FRCPC[a], Jane Batt, MD, FRCPC, PhD[a],
Margaret S. Herridge, MD, FRCPC, MPH[b],
Claudia C. Dos Santos, MD, FRCPC, MSc[a,*]

Clin Chest Med 35 (2014) 811–826



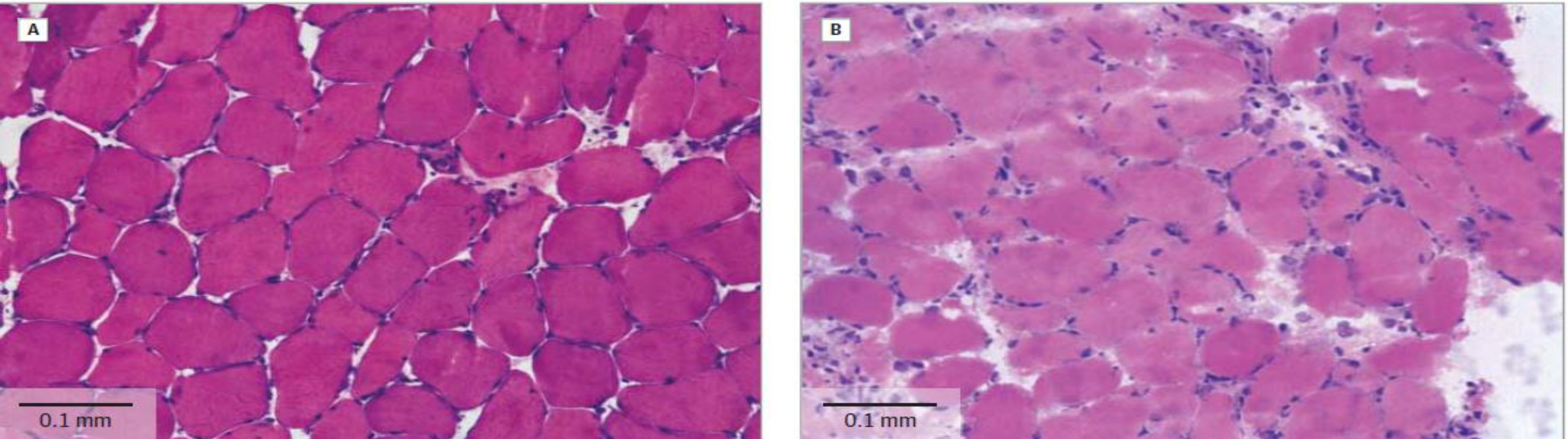
Acute Skeletal Muscle Wasting in Critical Illness

Zudin A. Puthucheary, MRCP; Jaikitry Rawal, MRCS; Mark McPhail, PhD; Bronwen Connolly, BSc; Gamunu Ratnayake, MRCP; Pearl Chan, MBBS; Nicholas S. Hopkinson, PhD; Rahul Padhke, PhD; Tracy Dew, MSc; Paul S. Sidhu, PhD; Cristiana Velloso, PhD; John Seymour, PhD; Chibeza C. Agley, MSc; Anna Selby, PhD; Marie Limb, PhD; Lindsay M. Edwards, PhD; Kenneth Smith, PhD; Anthea Rowlerson, PhD; Michael John Rennie, PhD; John Moxham, PhD; Stephen D. R. Harridge, PhD; Nicholas Hart, PhD; Hugh E. Montgomery, MD

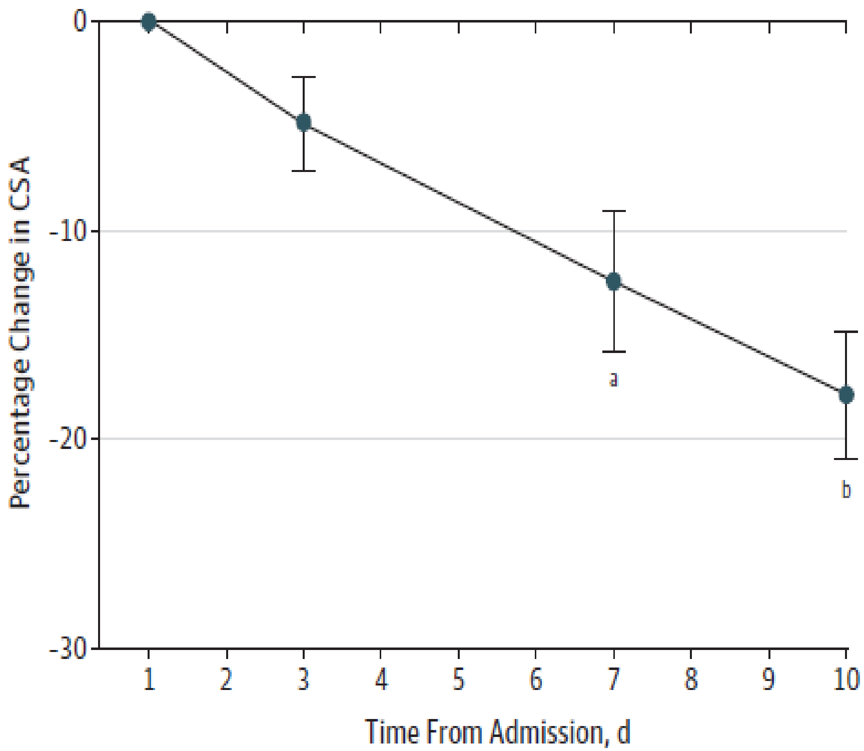
JAMA. 2013;310(15):1591-1600.

Table. Baseline Characteristics of Patients

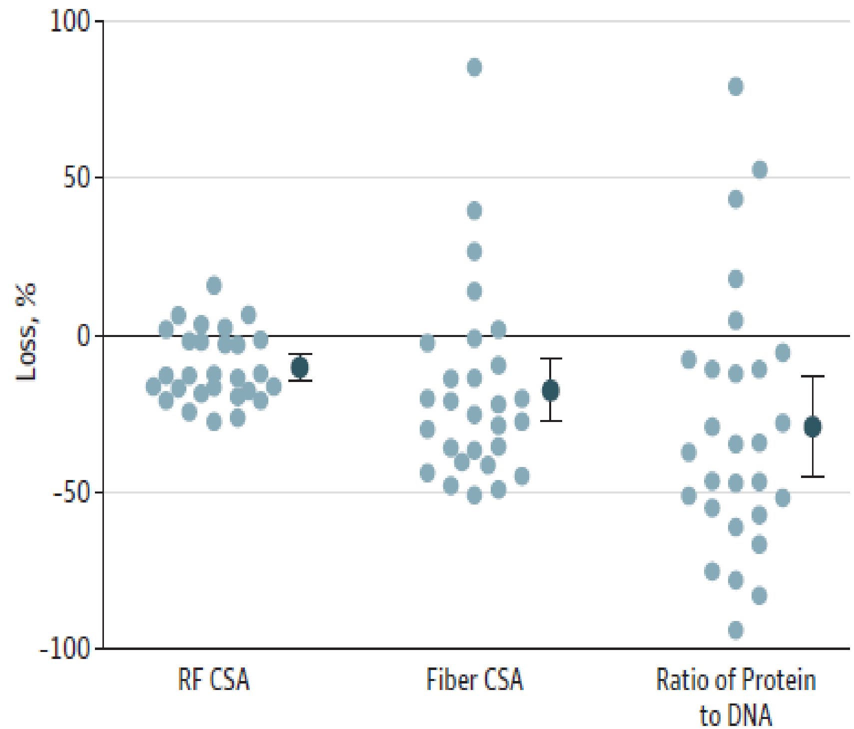
	All Patients (N = 63)	Serial Muscle Biopsies and Ultrasound (n = 42)	Muscle Ultrasound Alone (n = 21)	Stable Isotope Incorporation (n = 11)
Age, mean (95% CI), y	54.5 (50.0-59.1)	55.3 (49.4-61.1)	53.1 (45.4-60.1)	62.7 (50.1-75.4)
Male sex, No. (%)	37 (58.7)	30 (71.4)[a]	7 (31.3)	9 (81.8)[a]
Hospital length of stay prior to ICU admission, median (range), d	1 (1-45)	1 (1-6)	1 (1-45)	1 (1-6)
Period ventilated, median (range), d	10 (2-62)	8.5 (2-62)	10 (4-24)	12 (2-62)
ICU length of stay, median (range), d	16 (7-80)	15.5 (7-80)	17 (7-73)	18 (8-80)
Hospital length of stay, median (range), d	30 (11-334)	29.5 (11-212)	33 (13-334)	50 (17-212)
APACHE II score, mean (95% CI)	23.5 (21.9-25.2)	23.3 (21.3-25.3)	24 (20.1-27.2)	27 (22.9-31.3)
SAPS II score, mean (95% CI)	45.5 (41.8-49.3)	43.4 (39.2-47.6)	49.7 (42.0-57.4)	47 (39.6-54.4)
Survival, No. (%)				
ICU	61 (97)	40 (95)	21 (100)	10 (91)
Hospital	56 (89)	37 (88)	19 (90)	9 (82)
Renal replacement therapy, No. (%)	19 (30.2)	13 (31.0)	6 (29.0)	4 (36.4)
Use of neuromuscular blocking agents, median (range), d	0 (0-6)	0 (0-6)	0 (0-5)	0 (0-6)
Hydrocortisone dose, median (range), mg[b]				
Day 1	0 (0-800)	0 (0-800)	0 (0-400)	200 (0-800)
Total by day 10	0 (0-4533)	0 (0-4533)	0 (0-3360)	450 (0-4533)

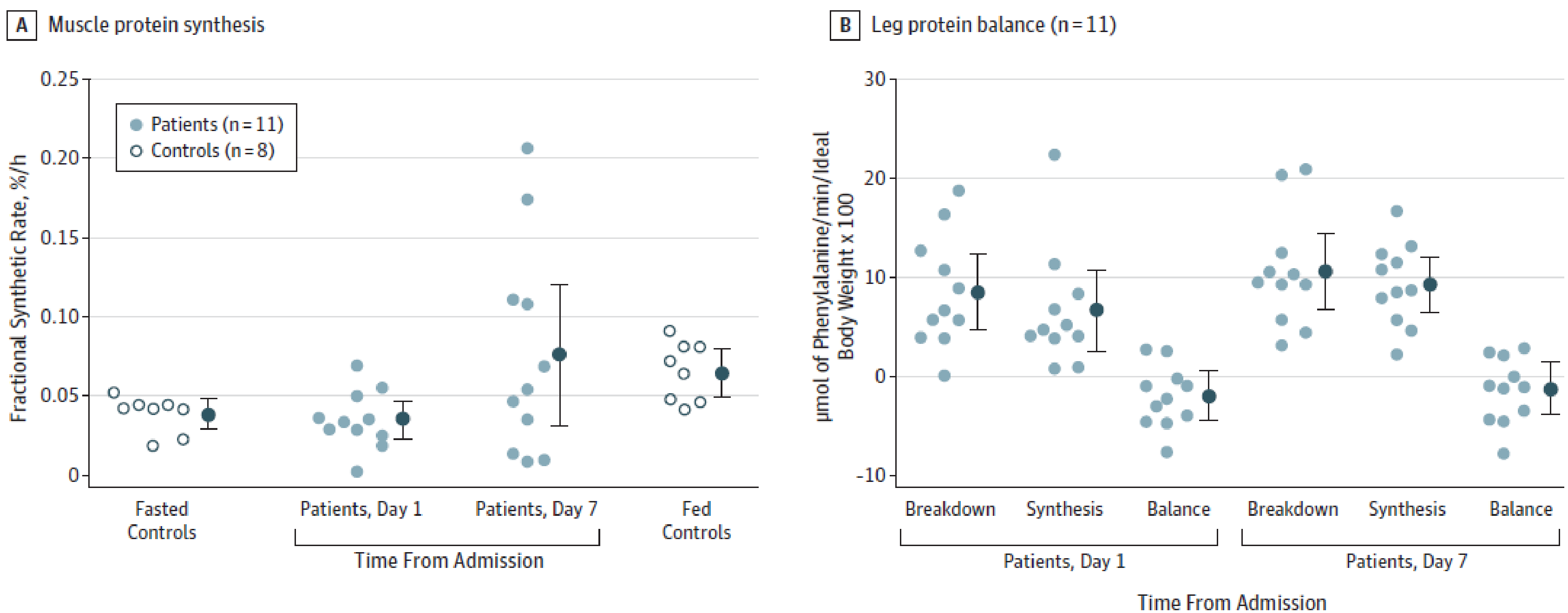


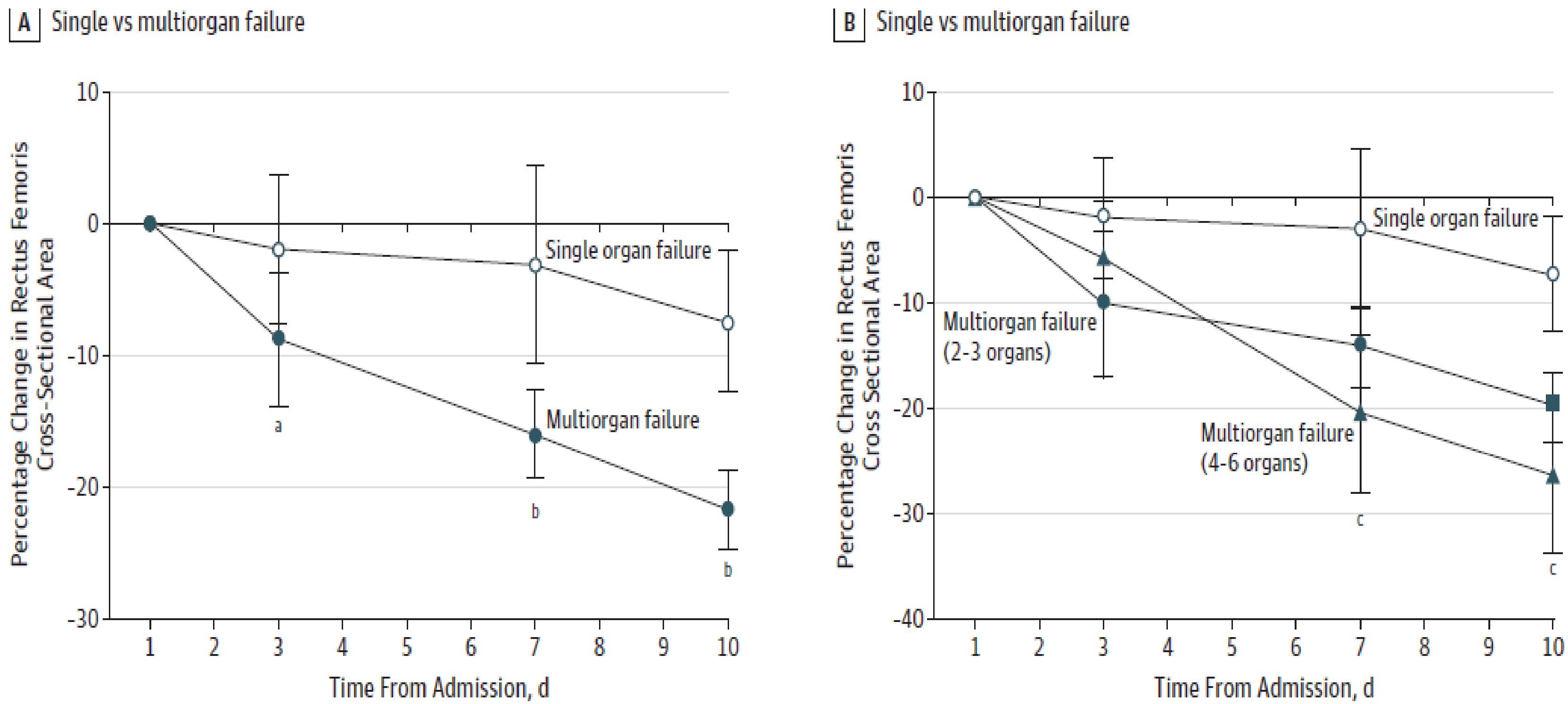
A Change in rectus femoris (RF) cross-sectional area (CSA) over 10 d



B Measures of muscle wasting in patients assessed by all 3 measures on both day 1 and day 7 (n = 28)



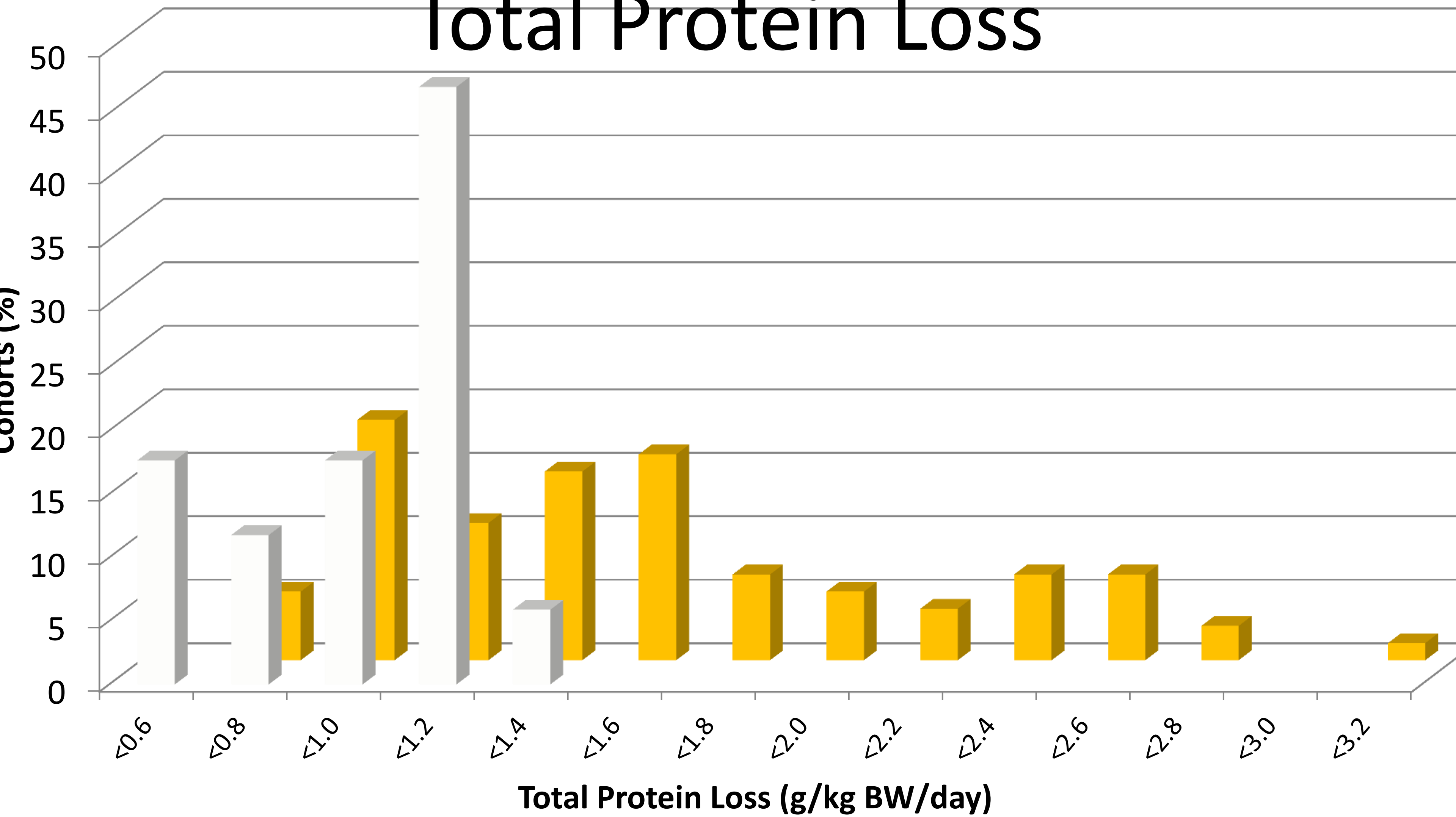

A Muscle protein synthesis
Patients (n = 11)
Controls (n = 8)
Fractional Synthetic Rate, %/h
0.25
0.20
0.15
0.10
0.05
0
Fasted Controls
Patients, Day 1
Patients, Day 7
Fed Controls
Time From Admission
B Leg protein balance (n = 11)
μmol of Phenylalanine/min/Ideal Body Weight x 100
30
20
10
0
-10
Breakdown
Synthesis
Balance
Breakdown
Synthesis
Balance
Patients, Day 1
Patients, Day 7
Time From Admission



No. of patients				
Single organ failure	15	14	15	15
Multiorgan failure	47	43	45	47

No. of patients				
Single organ failure	15	14	15	15
Multiorgan failure				
2-3 Organs	33	31	32	33
4-6 Organs	14	12	13	14

Total Protein Loss

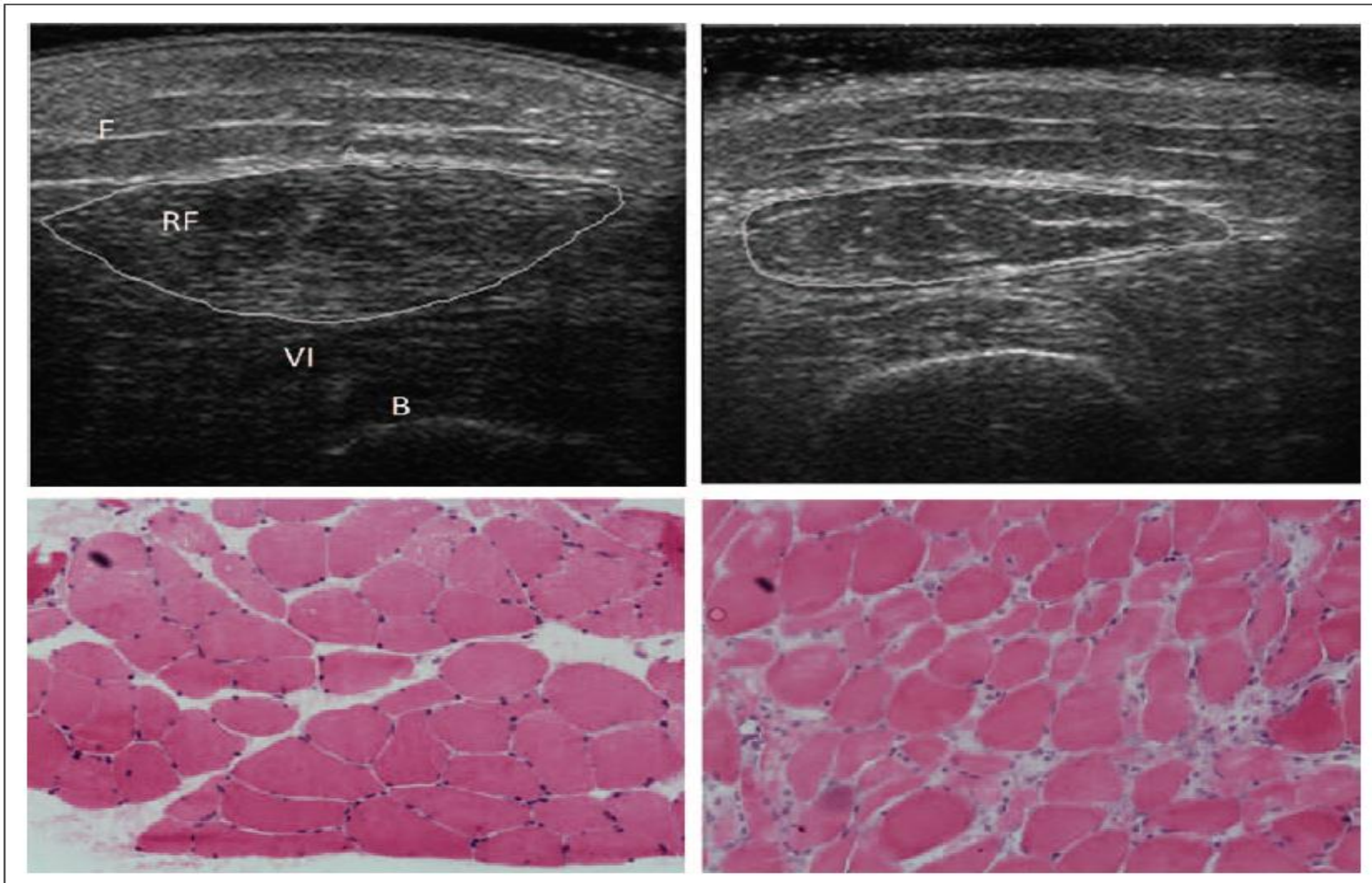


From Kreyman et al Clin Nutr 2013

Qualitative Ultrasound in Acute Critical Illness Muscle Wasting

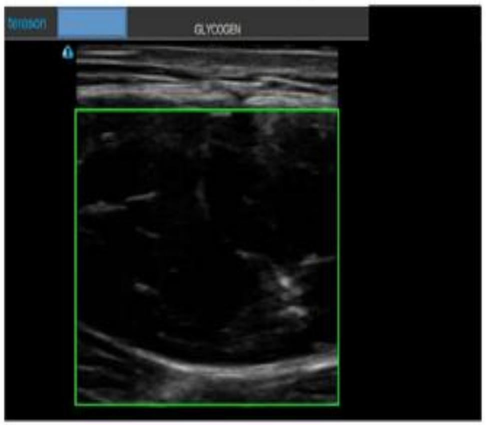
CCM 2015

Zudin A. Puthucheary, PhD[1,2,3]; Rahul Phadke, FRCPath[4]; Jaikitry Rawal, MRCS[1]; Mark J. W. McPhail, PhD[5,6]; Paul S. Sidhu, FRCR[7]; Anthea Rowlerson, PhD[2]; John Moxham, MD[8]; Stephen Harridge, PhD[2]; Nicholas Hart, PhD[9]; Hugh E. Montgomery, MD[1]

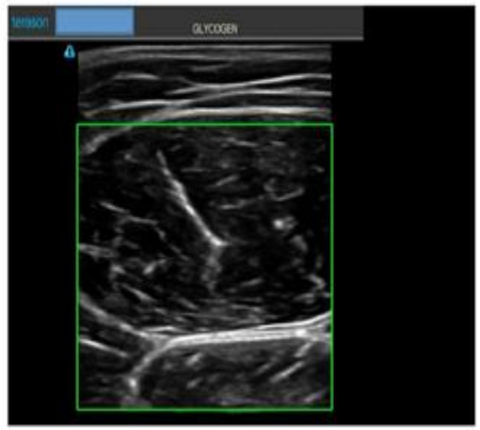


Skeletal Muscle Glycogen Content Score Via U/S

Athlete Before Competition= 90



Moderately Active at Rest= 65



Critically Ill Patient= 0

Scale: 0-90

Muscle Glycogen Scores Via U/S

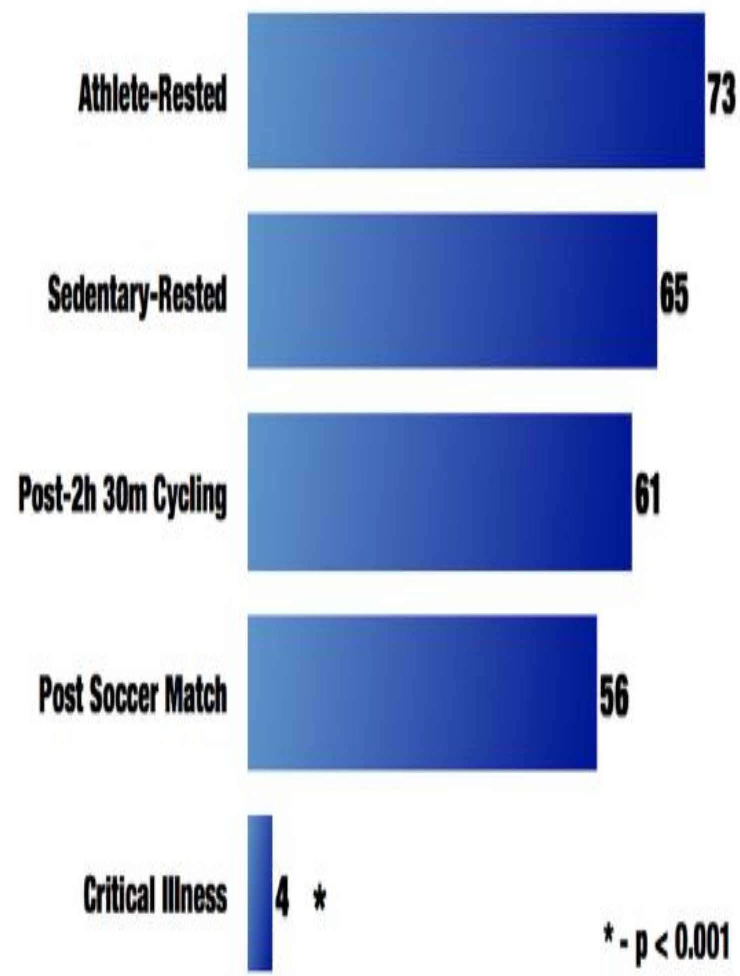
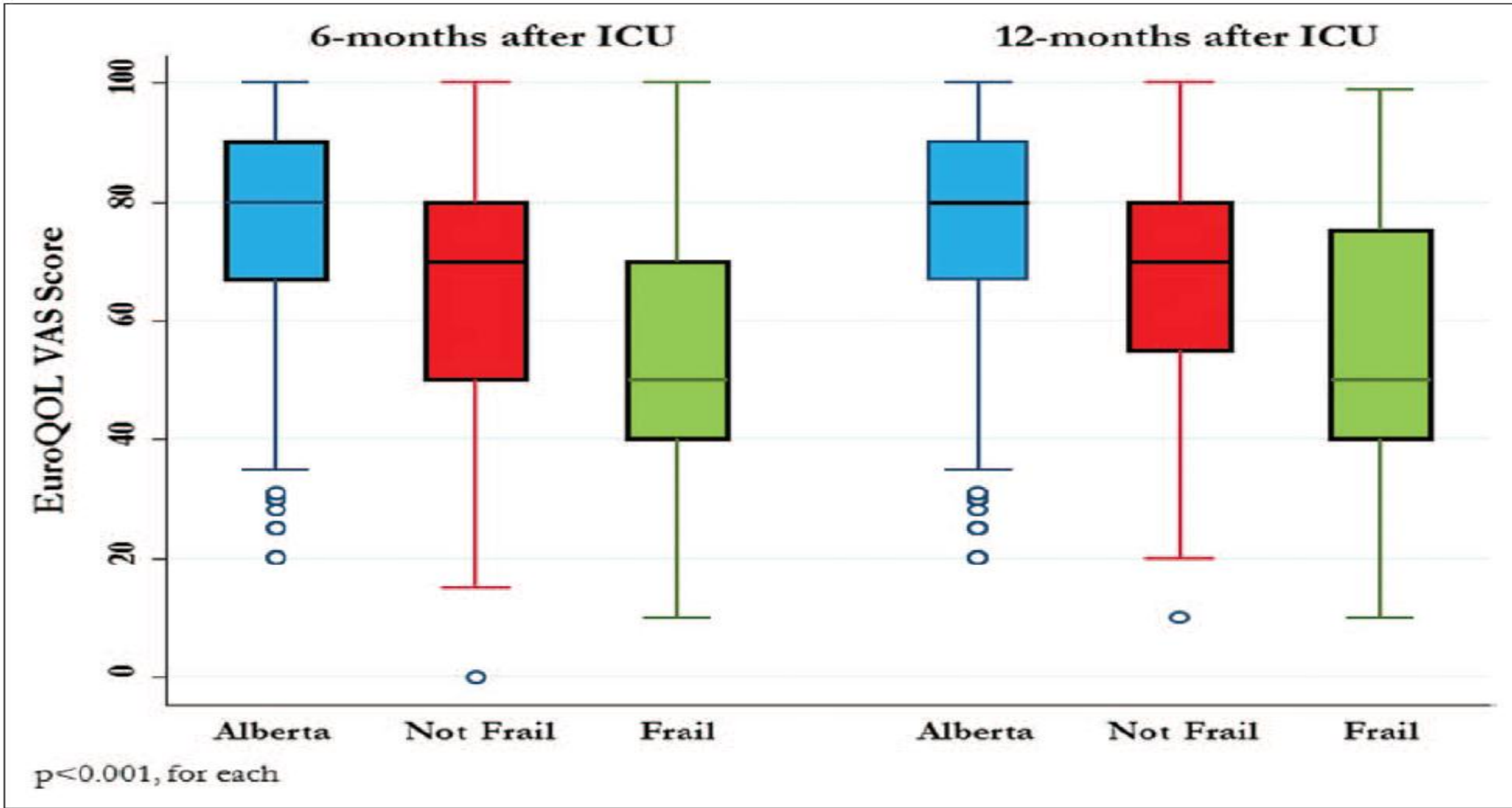


Figure 2 Muscle glycogen scores via ultrasound.

Long-Term Association Between Frailty and Health-Related Quality-of-Life Among Survivors of Critical Illness: A Prospective Multicenter Cohort Study

Critical Care Medicine2015

Sean M. Bagshaw, MD, MSc[1]; H. Thomas Stelfox, MD, PhD[2]; Jeffrey A. Johnson, PhD[3]; Robert C. McDermid, MD[1]; Darryl B. Rolfson, MD[4]; Ross T. Tsuyuki, PharmD, MSc[5,6]; Ouazi Ibrahim, MSc[6]; Sumit R. Majumdar, MD, MPH[5]



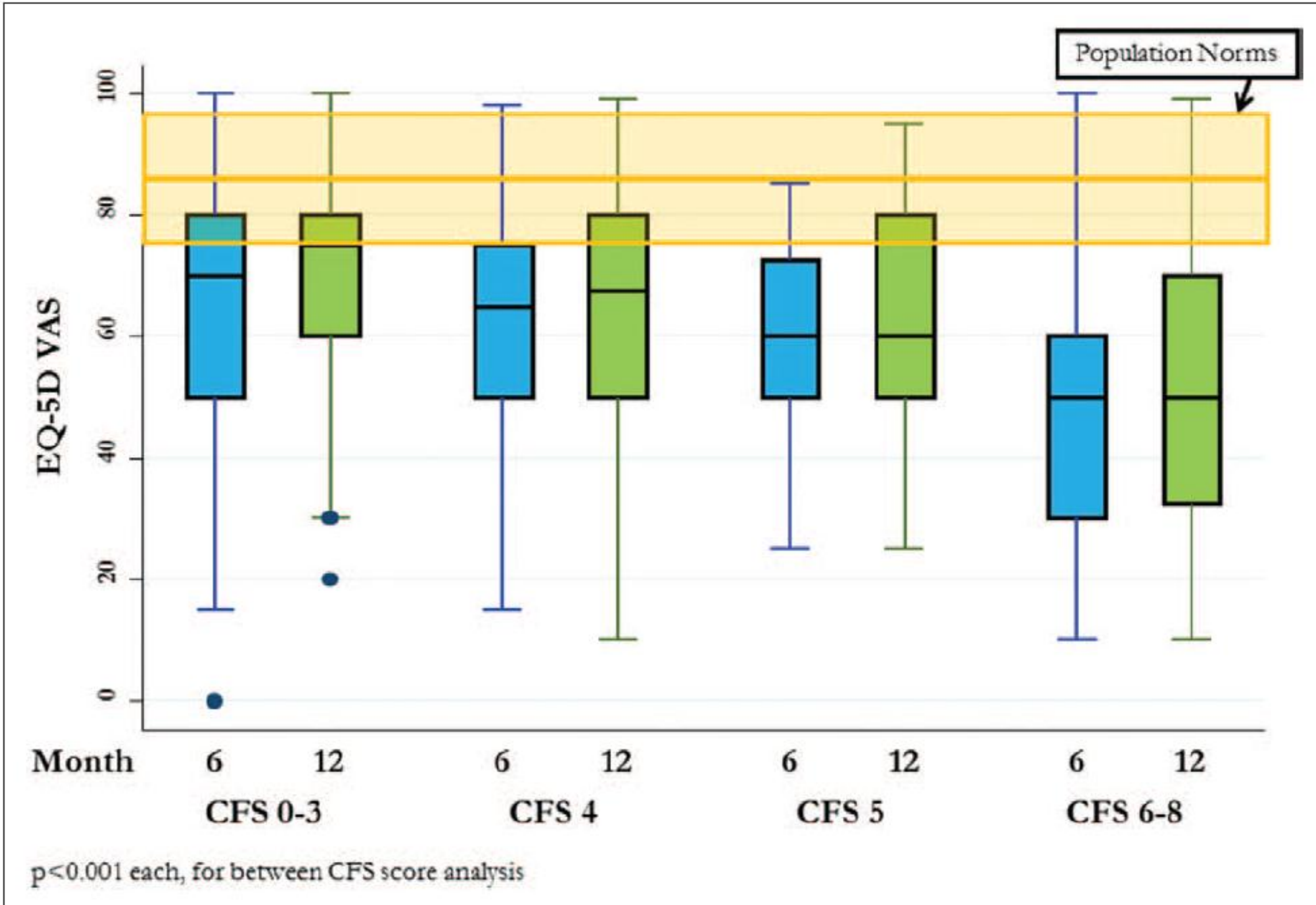


Figure 3. Health-related quality-of-life assessed by the EuroQol (EQ)-visual analogue scale (VAS) at 6 and 12 mo stratified by Clinical Frailty Scale score (CFS).

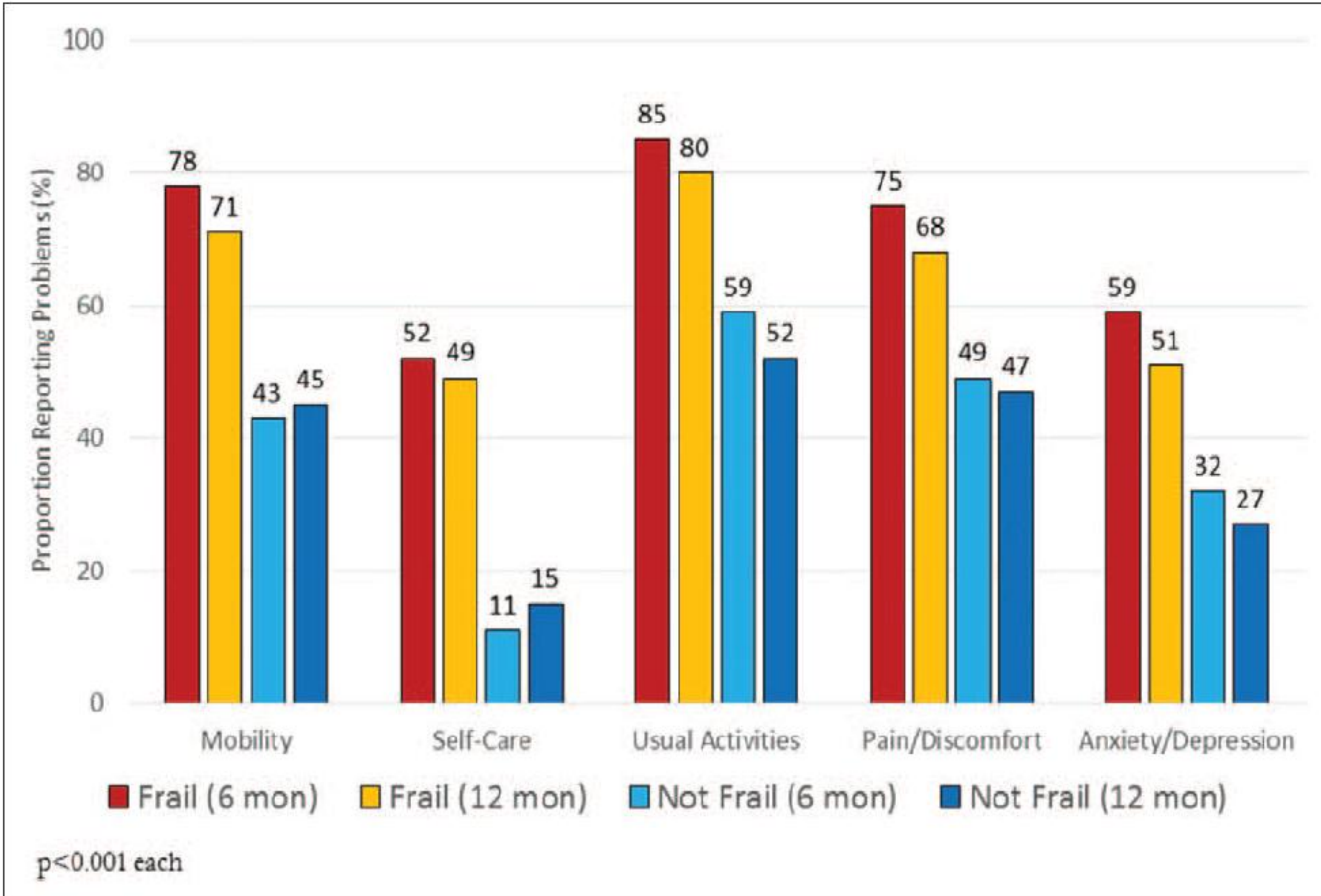
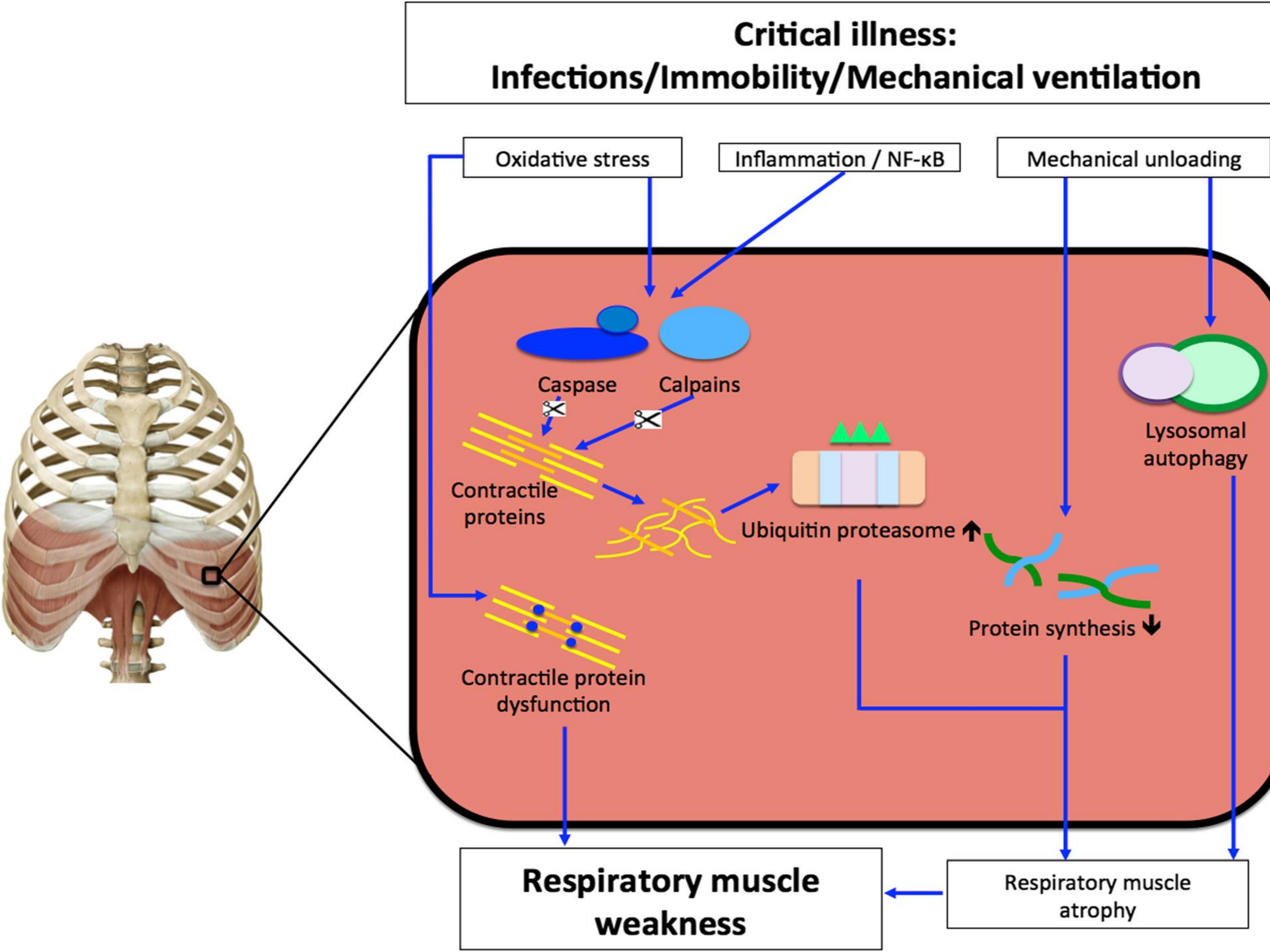
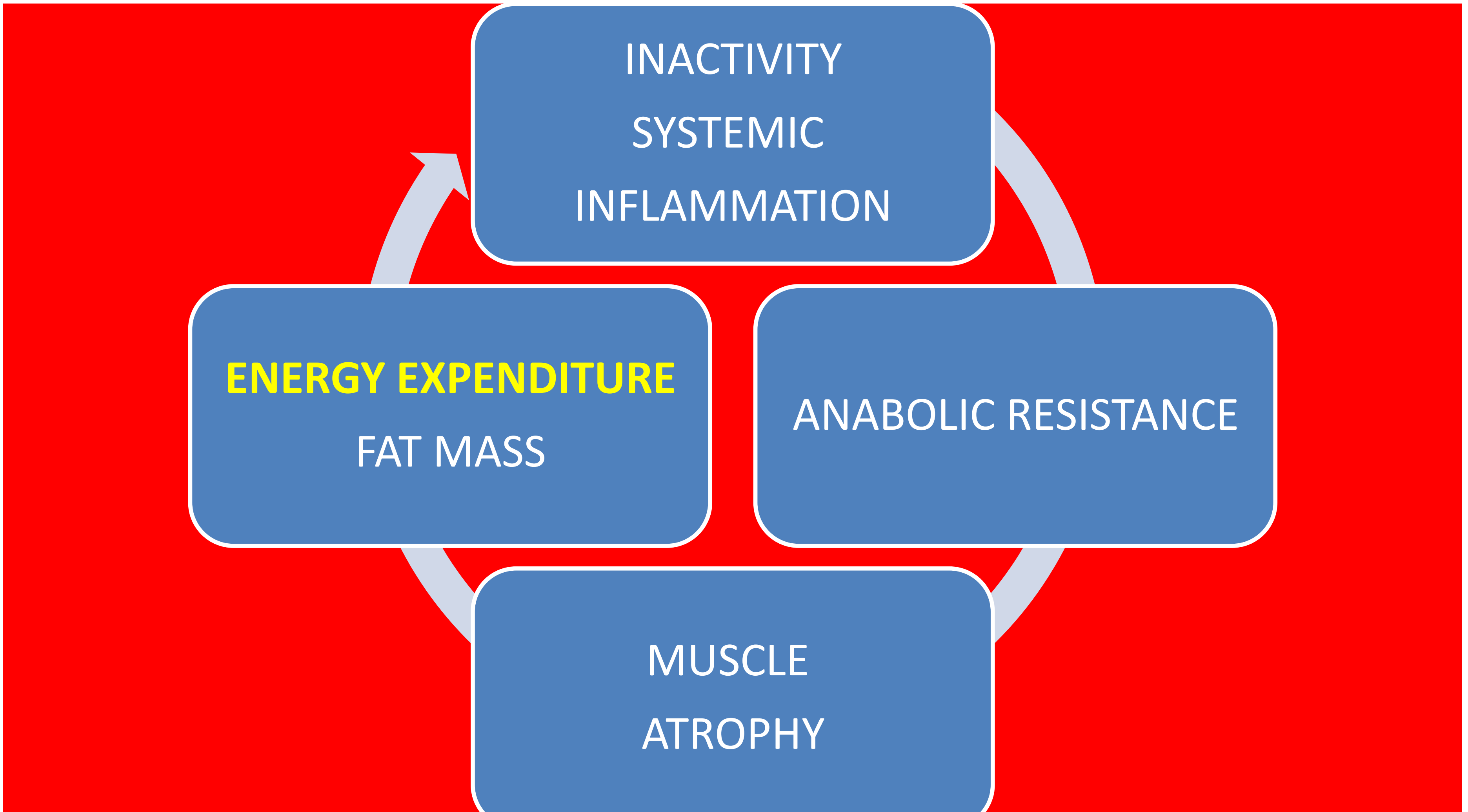


Figure 4. Summary of problems, assessed by the EuroQol-5Q, reported by survivors at 6 and 12 mo stratified by frailty status.

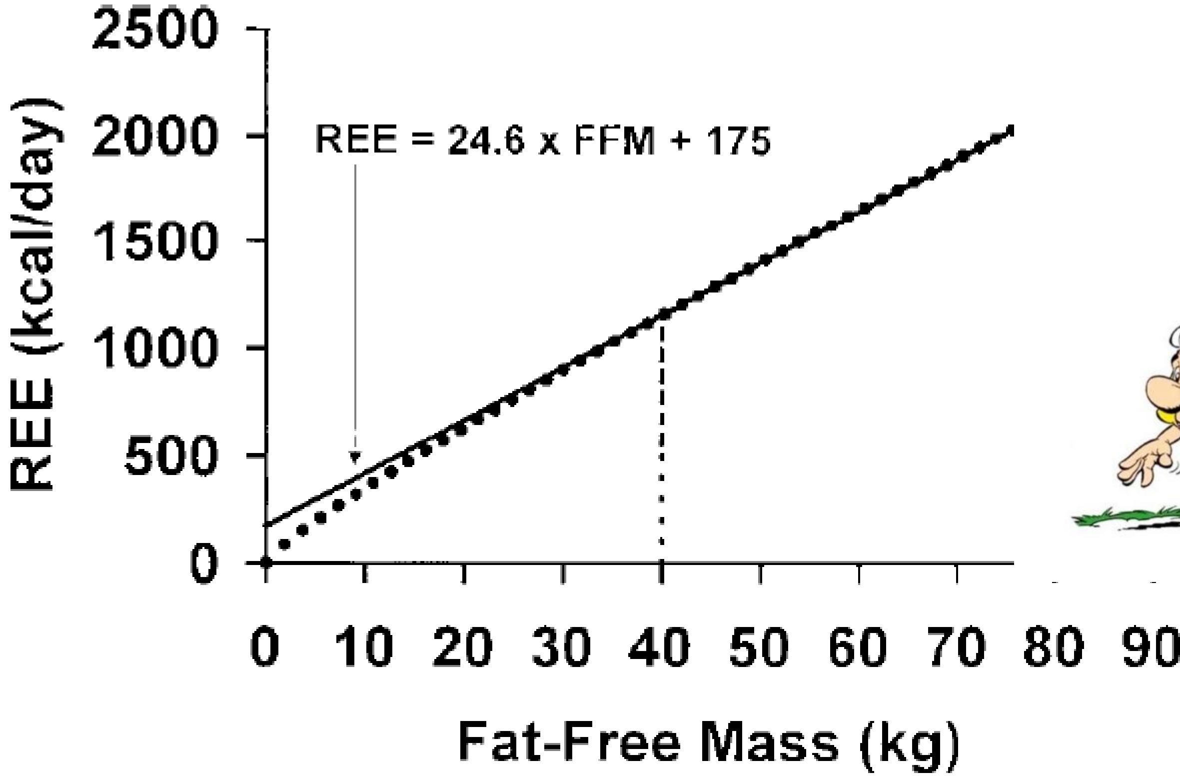

Critical illness:
Infections/Immobility/Mechanical ventilation
Oxidative stress
Inflammation / NF-κB
Mechanical unloading
Caspase
Calpains
Lysosomal autophagy
Contractile proteins
Ubiquitin proteasome ↑
Protein synthesis ↓
Contractile protein dysfunction
Respiratory muscle weakness
Respiratory muscle atrophy

Message: Give enough protein to fight anabolism resistance



FFM & Energy requirements

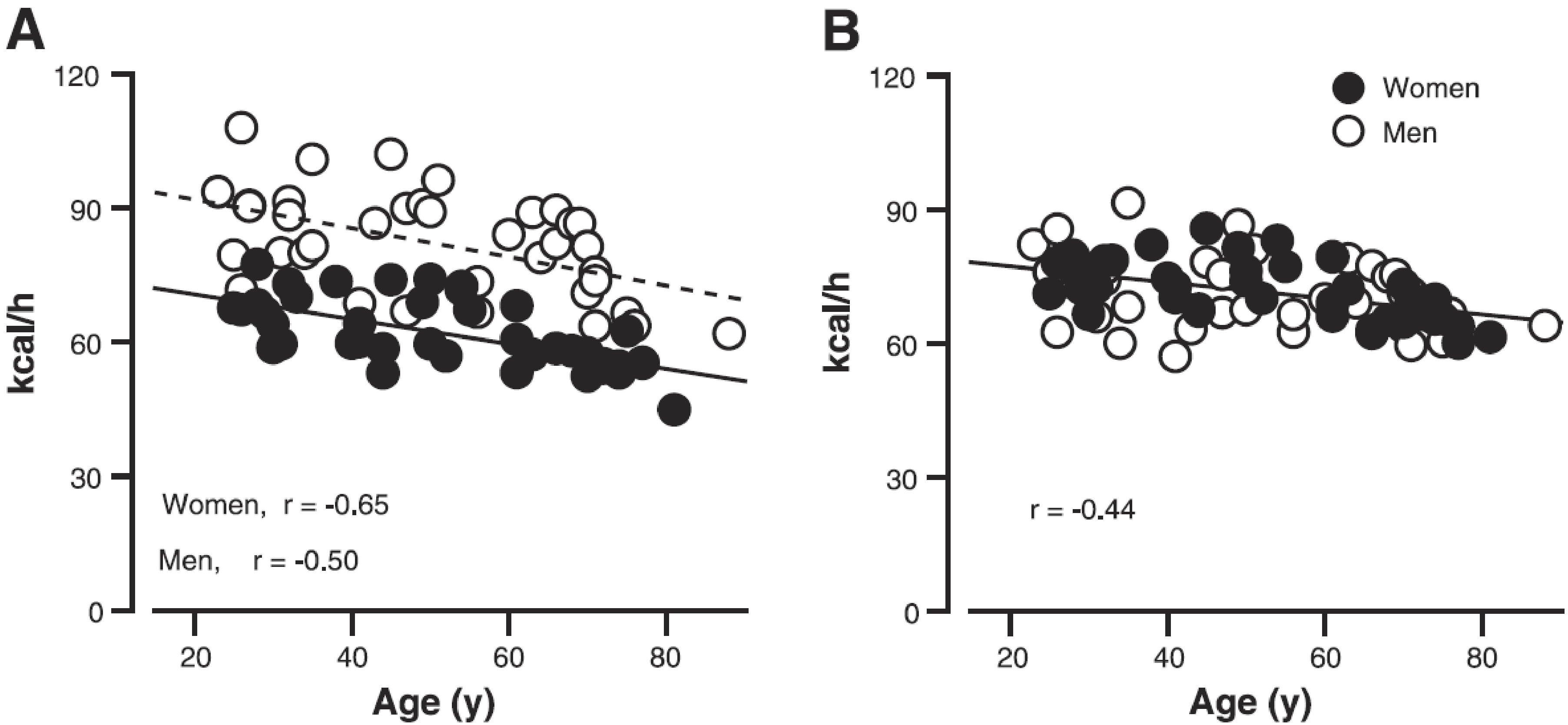
Wang et al. Am J Physiol Endocrinol Metab 2000; 279: E539-E545



$$
\begin{aligned}
\mathrm{REE} &= k_1 \times \mathrm{liver} + k_2 \times \mathrm{kidney} + k_3 \times \mathrm{brain} + k_4 \times \mathrm{heart} + k_5 \times \mathrm{SM} + k_6 \times \mathrm{AT} + K_7 \\
&\quad \times (\mathrm{lung} + \mathrm{thyroid} + \mathrm{adrenal} + \mathrm{spleen} + \mathrm{gut} + \mathrm{skin} + \mathrm{blood} + \mathrm{skeleton}) \\
&= 200 \times (0.0491 \times \mathrm{BM}^{0.70}) + 440 \times (0.0089 \times \mathrm{BM}^{0.71}) + 240 \times (0.1025 \times \mathrm{BM}^{0.71}) \\
&\quad + 440 \times (0.006 \times \mathrm{BM}^{0.98}) + 13 \times (0.468 \times \mathrm{BM}^{0.99}) + 4.5 \times (0.075 \times \mathrm{BM}^{1.19}) \\
&\quad + 12 \times (0.0092 \times \mathrm{BM}^{0.92} + 0.0001 \times \mathrm{BM}^{0.92} + 0.0003 \times \mathrm{BM}^{0.80} + 0.003 \times \mathrm{BM}^{1.02} \\
&\quad + 0.075 \times \mathrm{BM}^{0.94} + 0.106 \times \mathrm{BM}^{0.94} + 0.069 \times \mathrm{BM}^{1.02} + 0.061 \times \mathrm{BM}^{1.09})
\end{aligned} \qquad (10)
$$

Metabolism & Age & Gender

Adjusted for FFM %



Short et al. Am J Physiol Endocrinol Metab 2004; 286: E92-E101

Exploitation of Diagnostic Computed Tomography Scans to Assess the Impact of Nutrition Support on Body Composition Changes in Respiratory Failure Patients

Carol A. Braunschweig, PhD, RD[1]; Patricia M. Sheean, PhD, RD[2]; Sarah J. Peterson, MS, RD[3]; Sandra Gomez Perez, MS, RD[2]; Sally Freels, PhD[4]; Karen L. Troy, PhD[5]; Folabomi C. Ajanaku, BS[6]; Ankur Patel, MD[7]; Joy S. Sclamberg, MD[7]; and Zebin Wang, PhD[8]

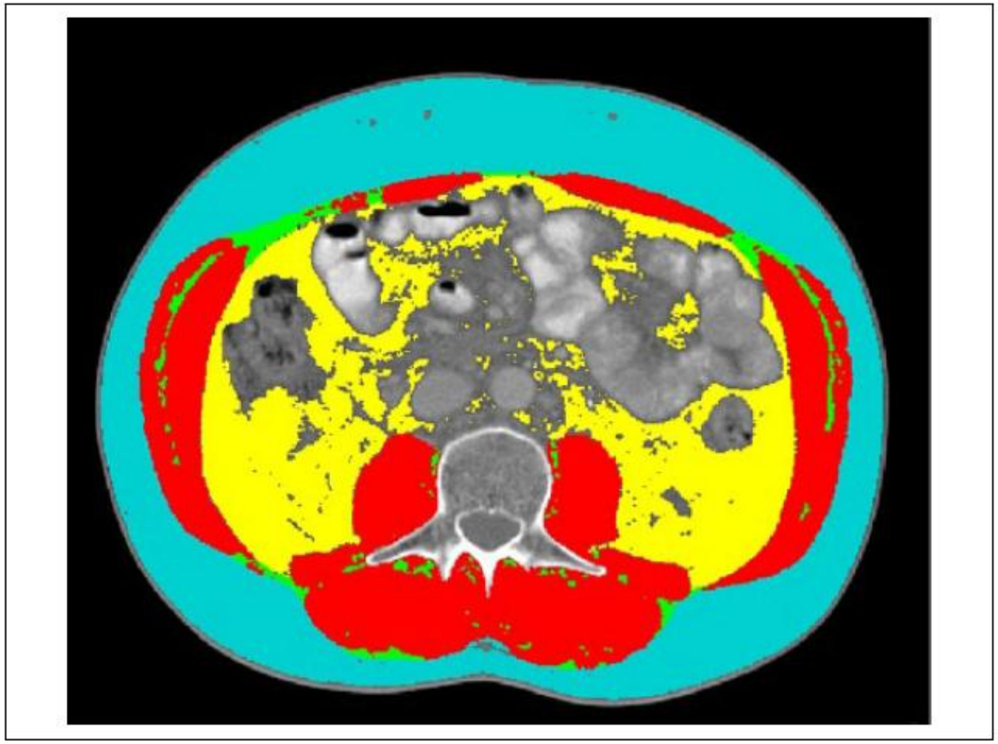


Figure 1. Representative patient showing transverse computed tomography image at the 3rd lumbar vertebrae demonstrating subcutaneous adipose tissue (light blue), abdominal skeletal muscle (red), intermuscular fat (green) and visceral fat (yellow).

Weight loss and loss of function

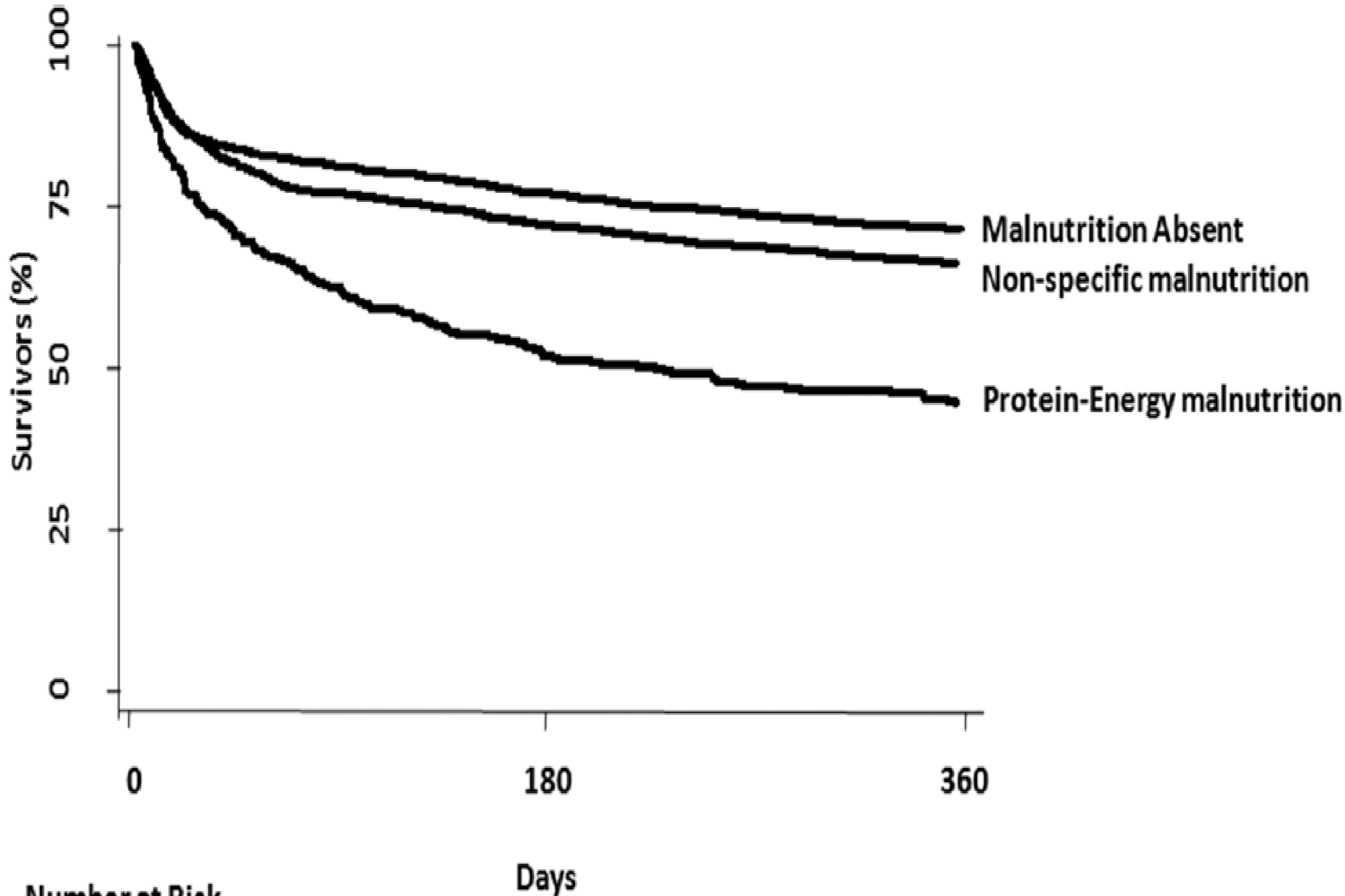
≈ 20 % loss of body protein related to	
Intracell K^+, mmol/l	133 (vs. 152 ; P=0.05)
Grip strength, %	65
Resp muscle strength, %	79
Type 1 muscle fibers (hi ox, lo glyc), area	41 (vs. 73 ; P<0.001)
Type 2 muscle fibers (lo ox, hi glyc), area	28 (vs. 73 ; P<0.001)

Hill et al. 1992; JPEN 16: 197-218

Nutritional Status and Mortality in the Critically Ill*

Kris M. Mogensen, MS, RD, LDN, CNSC[1]; Malcolm K. Robinson, MD[2]; Jonathan D. Casey, MD[3];
Nicole S. Gunasekera, BA[4]; Takuhiro Moromizato, MD[5]; James D. Rawn, MD[2];

Characteristics	Total	*n* (%) Alive at 30 D	*n* (%) Expired at 30 D	*p*	Unadjusted OR (95% CI) for 30-D Mortality
Nutrition status				< 0.001	
Malnutrition absent, *n* (%)	2,123 (32.6)	1,809 (34.3)	314 (25.2)		1.00 (Referent)
Malnutrition absent	47 (0.7)				
At risk for malnutrition	2,076 (31.9)				
Nonspecific malnutrition, *n* (%)	3,641 (55.9)	2,931 (55.6)	710 (57.0)		1.40 (1.21–1.61)
Nonspecific protein-energy malnutrition	3,641 (55.9)				
Protein-energy malnutrition, *n* (%)	754 (11.6)	533 (10.1)	221 (17.8)		2.39 (1.96–2.91)
Mild protein-energy malnutrition	324 (5.0)				
Moderate protein-energy malnutrition	152 (2.3)				
Severe protein-energy malnutrition	33 (0.5)				



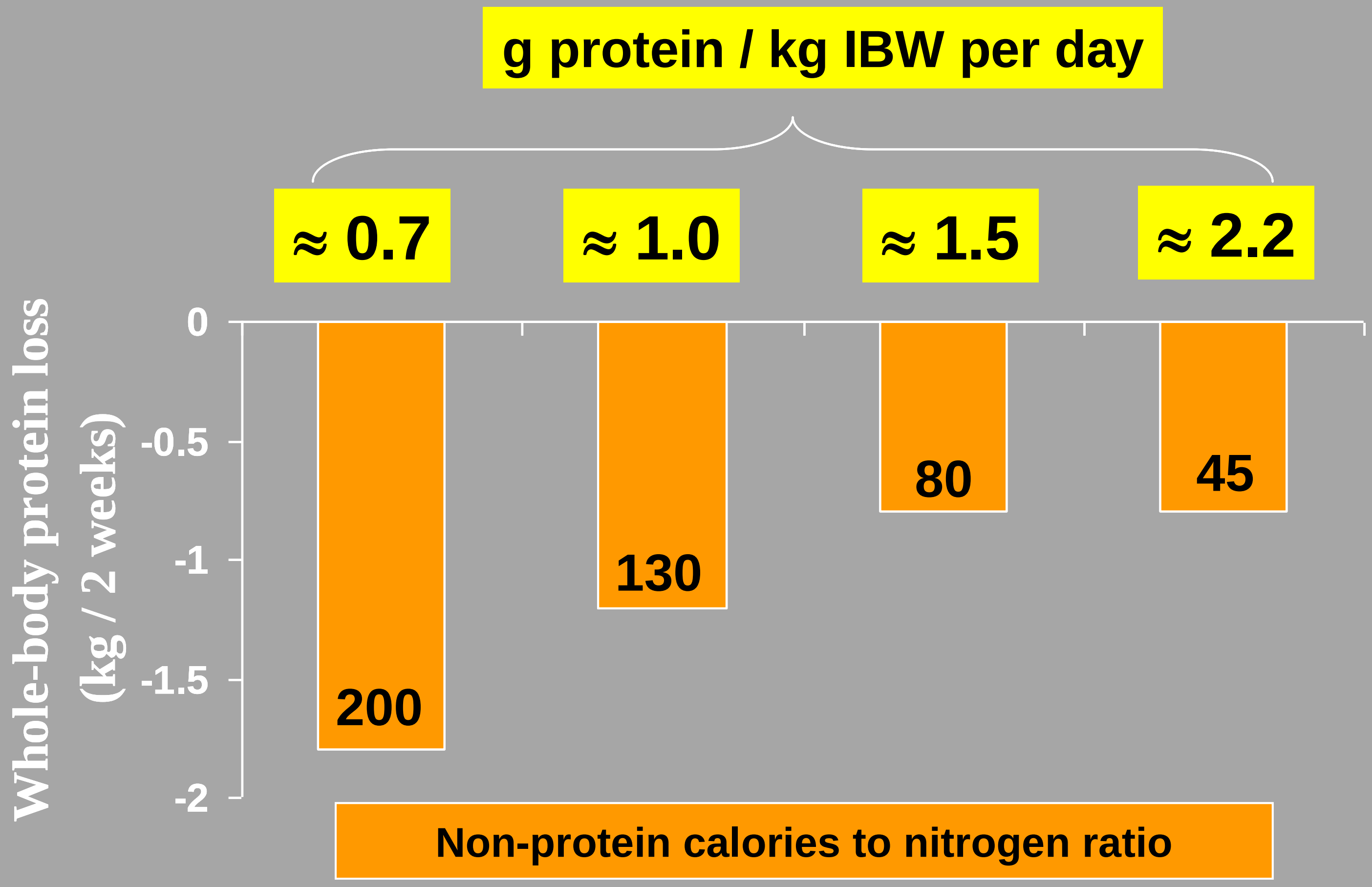
Number at Risk

2052	1514	1291	Malnutrition Absent
1705	1154	966	Non-specific malnutrition
347	170	132	Protein-Energy malnutrition

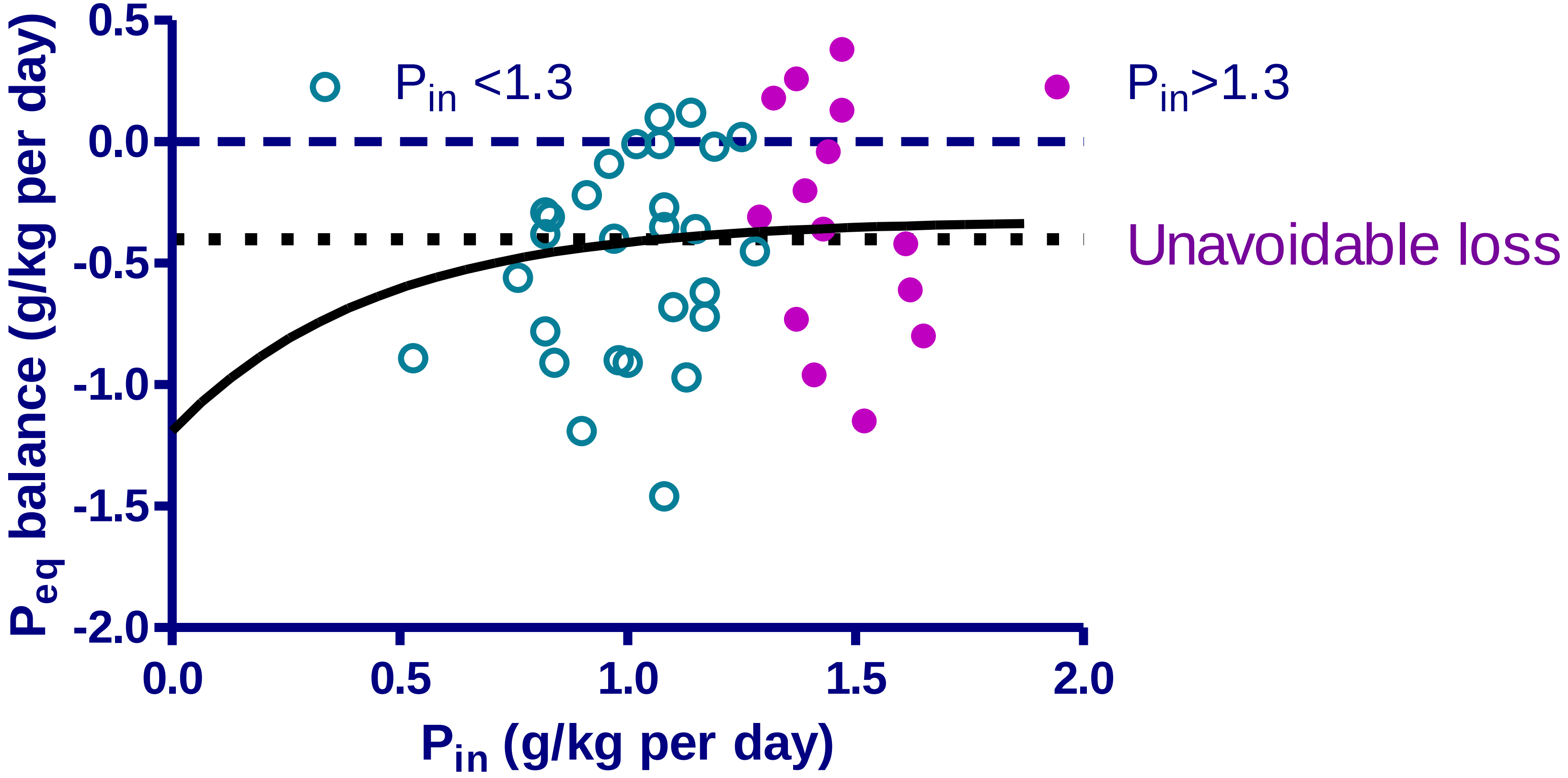
How much protein should we administer?

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



Protein$_{eq}$ balance according to < or >1.3g/kg given



Many patients with unacceptable loss

Balance not related to P_{in}

How much protein?

When PN is indicated, a balanced amino acid mixture should be infused at approximately 1.3 – 1.5 g/kg ideal body weight per day in conjunction with an adequate energy supply.

(Grade B)

- Balanced amino acids mixture is similar to essential amino acid requirements in healthy subjects
- Lean tissue loss is unavoidable in patients with severe trauma or sepsis
- The loss is minimized with 1.3 – 1.5 g/kg per day

ESPEN Guidelines on parenteral nutrition Clin Nutr 2009; 28: 387-400

CURRENT OPINION

Does feeding induce maximal stimulation of protein balance?

Felix Liebau, Åke Norberg, and Olav Rooyackers

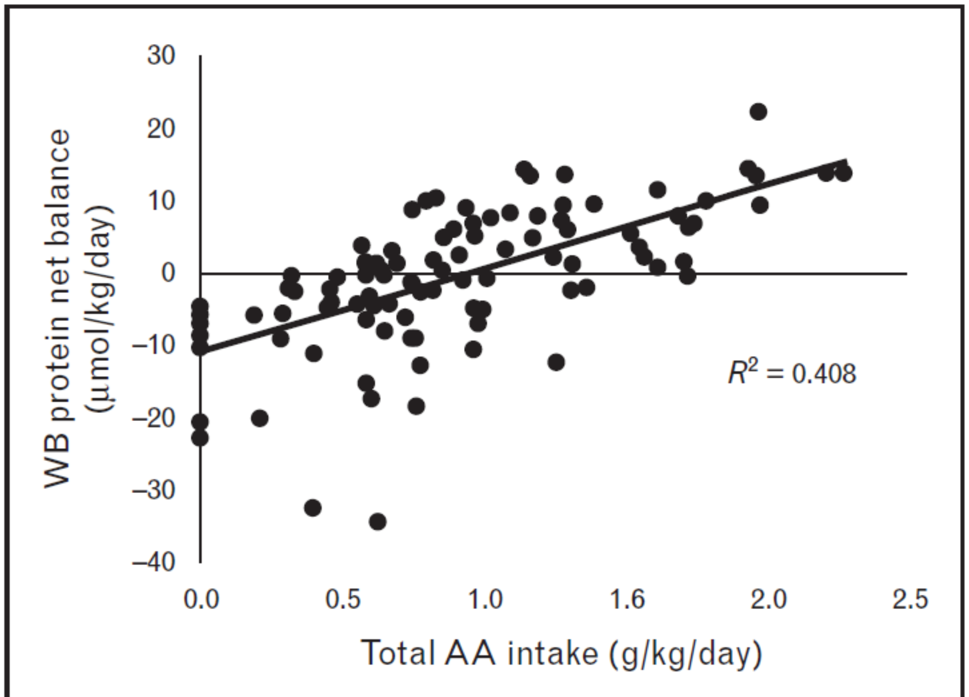
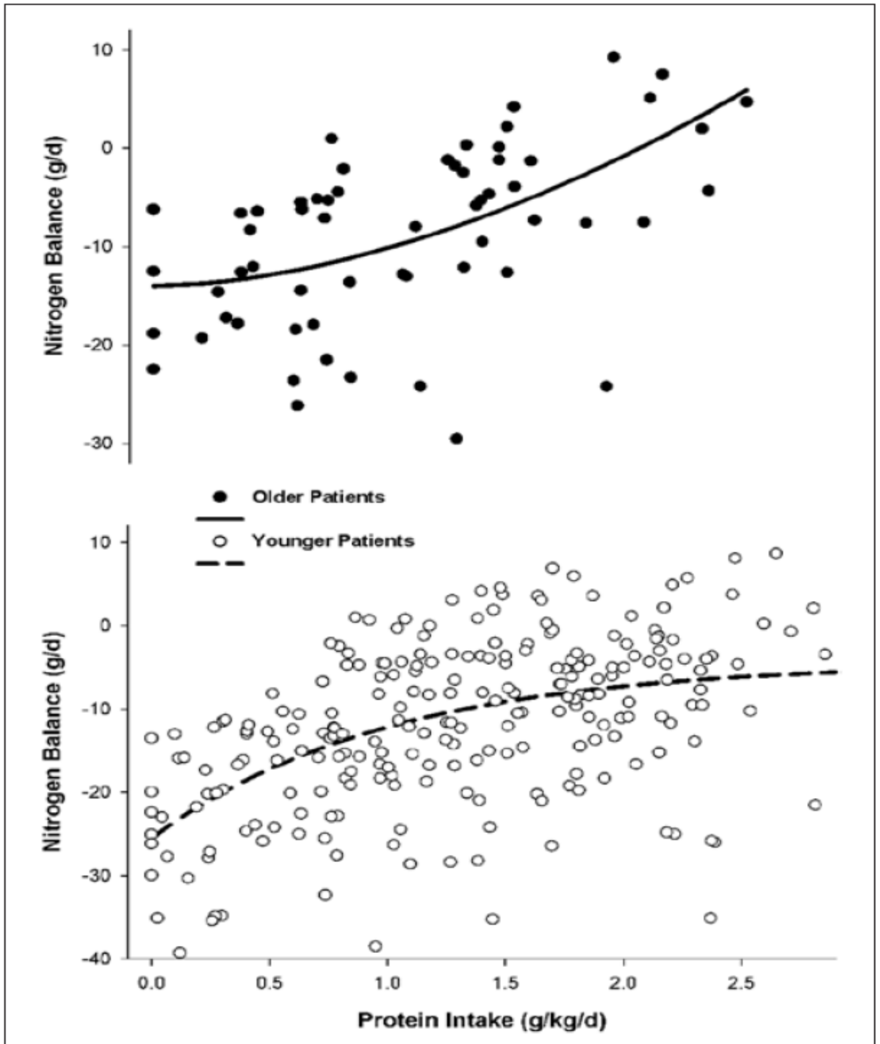
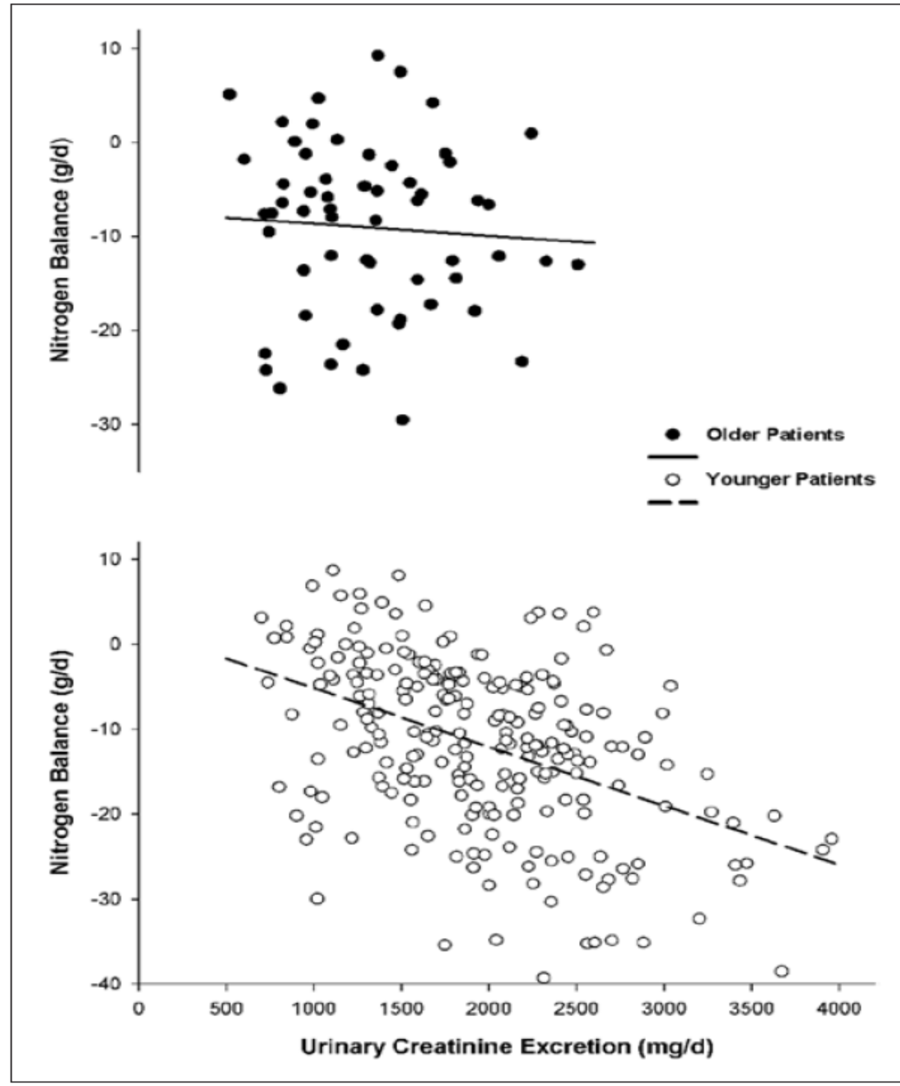


FIGURE 1. Protein balance in relation to amino acid intake in critically ill patients treated in the ICU from four different studies. Whole-body protein balance was measured using isotopically labeled phenylalanine. (Reproduced with

Influence of Aging on Nitrogen Accretion During Critical Illness

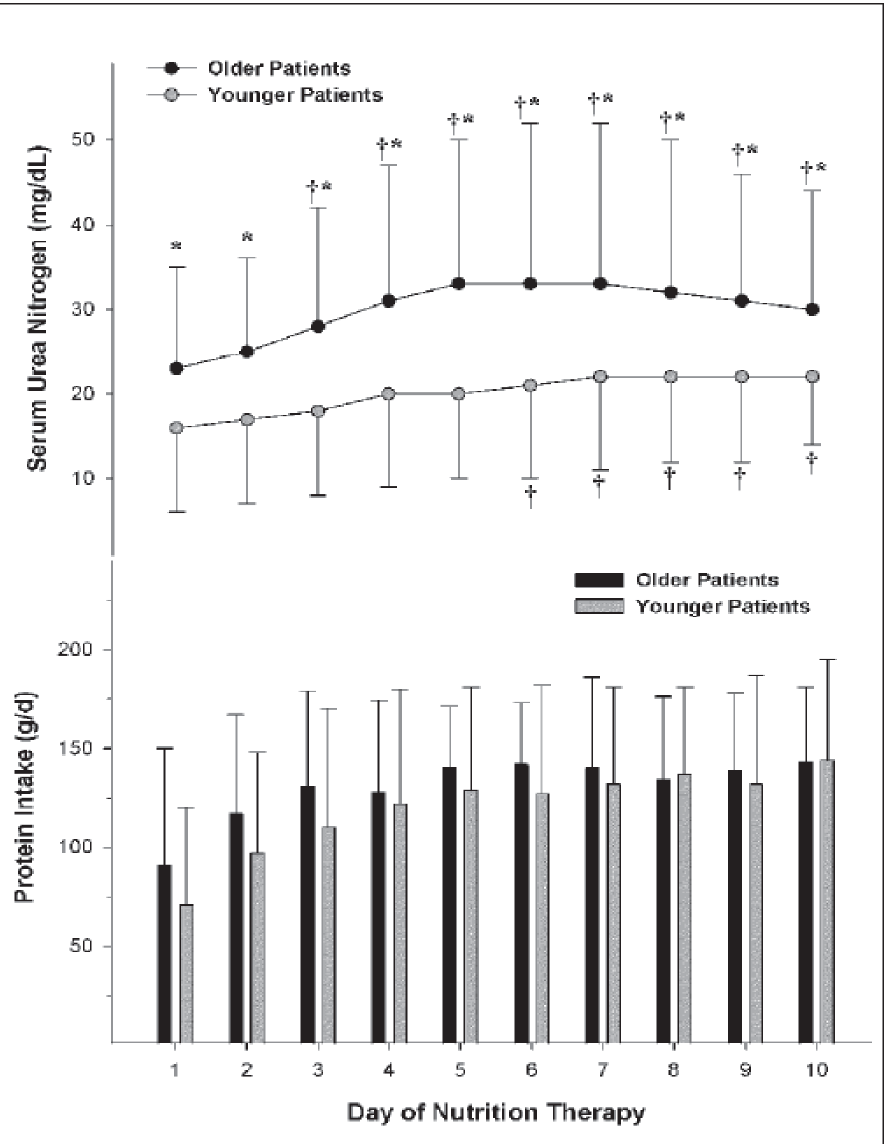
Roland N. Dickerson, PharmD[1]; George O. Maish III, MD[2]; Martin A. Croce, MD[2]; Gayle Minard, MD[2]; and Rex O. Brown, PharmD[1]

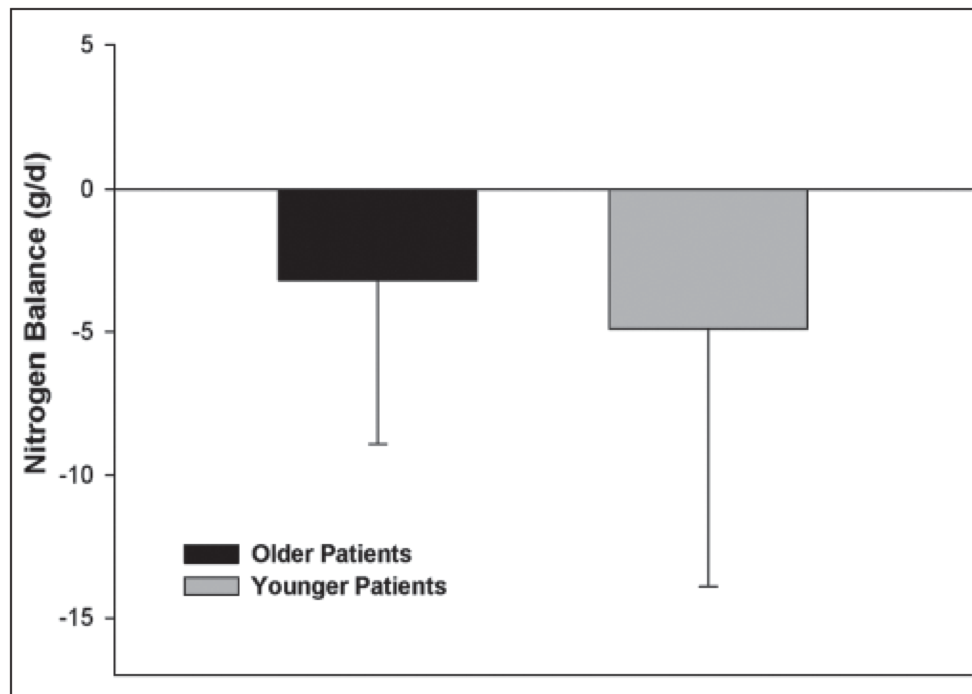




Hypocaloric, High-Protein Nutrition Therapy in Older vs Younger Critically Ill Patients With Obesity

Roland N. Dickerson, PharmD[1]; Theresa L. Medling, PharmD[1]; Ashley C. Smith[1]; George O. Maish III, MD[2]; Martin A. Croce, MD[2]; Gayle Minard, MD[2]; and Rex O. Brown, PharmD[1]





Close to recommended caloric and protein intake by enteral nutrition is associated with better clinical outcome of critically ill septic patients: secondary analysis of a large international nutrition database

CRITICAL CARE

Gunnar Elke[1], Miao Wang[2], Norbert Weiler[1], Andrew G Day[2] and Daren K Heyland[2*]

Table 3 Relationship between enteral nutrition and 60-day mortality

	Unadjusted			Adjusted		
	Odds ratio	95% CI	*P* value	Odds ratio	95% CI	*P* value
A: Total study population (n = 2,270)						
Energy intake						
Per 1,000 kcal	0.51	(0.41-0.64)	<0.001	0.61	(0.48-0.77)	<0.001
Protein intake						
Per 30 gram	0.70	(0.61-0.80)	<0.001	0.76	(0.65-0.87)	<0.001
B: Sensitivity analysis (n = 1,560)						
Energy intake						
Per 1,000 kcal	0.56	(0.44-0.71)	<0.001	0.61	(0.48-0.79)	<0.001
Protein intake						
Per 30 gram	0.72	(0.62-0.83)	<0.001	0.75	(0.64-0.87)	<0.001

M.J. Allingstrup et al. /
Clin Nutr. 2012 Aug;31(4):462-8

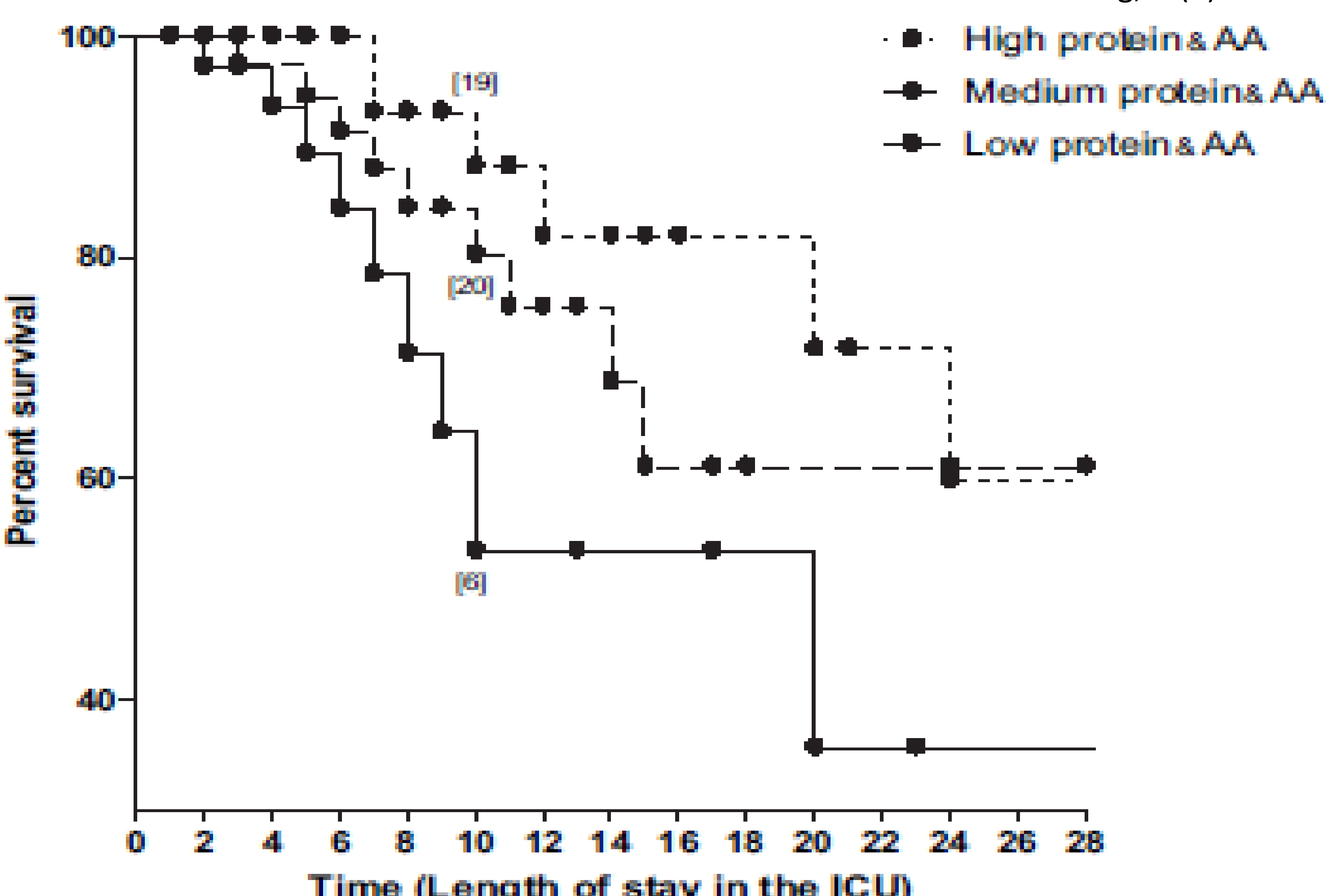
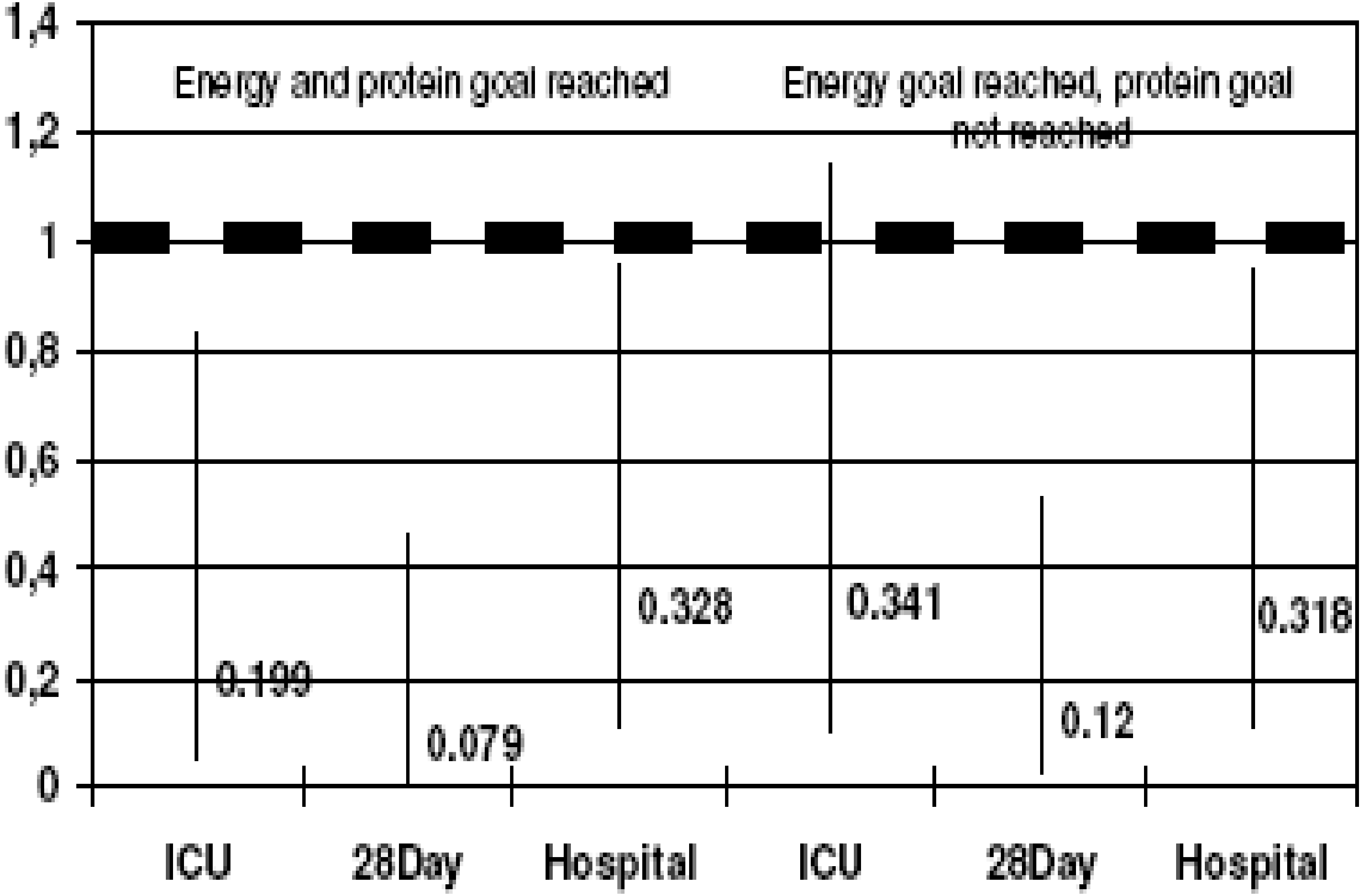


Figure 1. Hazard ratios for women according to energy goal reached and protein goal reached or not.



RetroTICACOS

6 patients incomplete background data
243 not full filling length of stay follow up criteria

Retro TICACOS: 1062 PATIENTS MEASURED

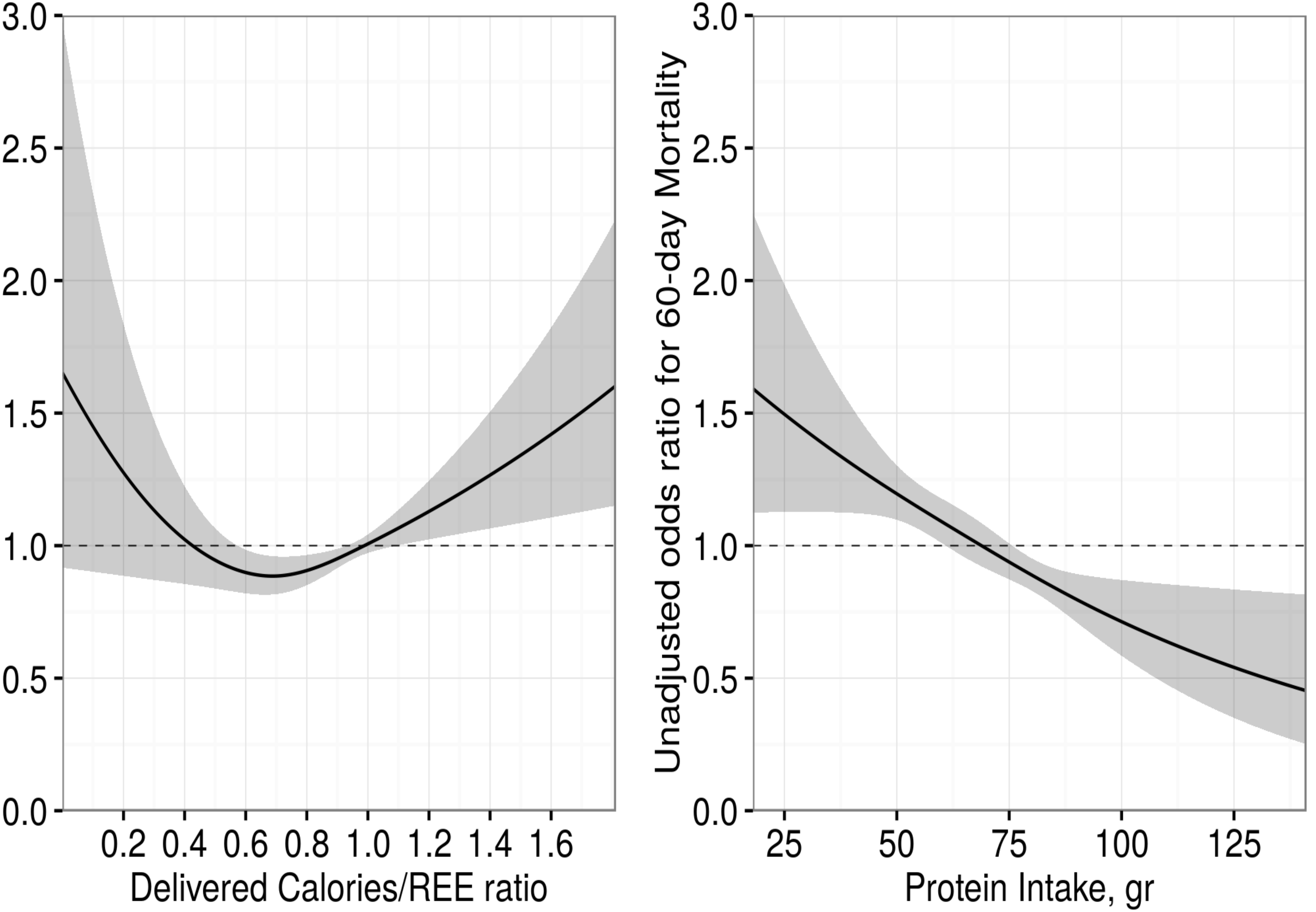
Parameter	Underfed (N=587) Mean	SD	Tight (n=475) Mean	SD	P value
Age (years)	56.1	18.7	59.3	18.8	0.007
Gender M(%)	398 (69.0%)		287 (59.2%)		0.001
Weight (kg)	82.8	22.9	78.3	18.8	0.001
Height (m)	1.71	0.1	1.69	0.09	<0.001
HB in kcal/d					
APACHE II	22.5	7.2	22.8	7.4	0.65
SOFA	8.1	3.8	8.0	3.2	0.71

60 days mortality
Better survival in the tight group

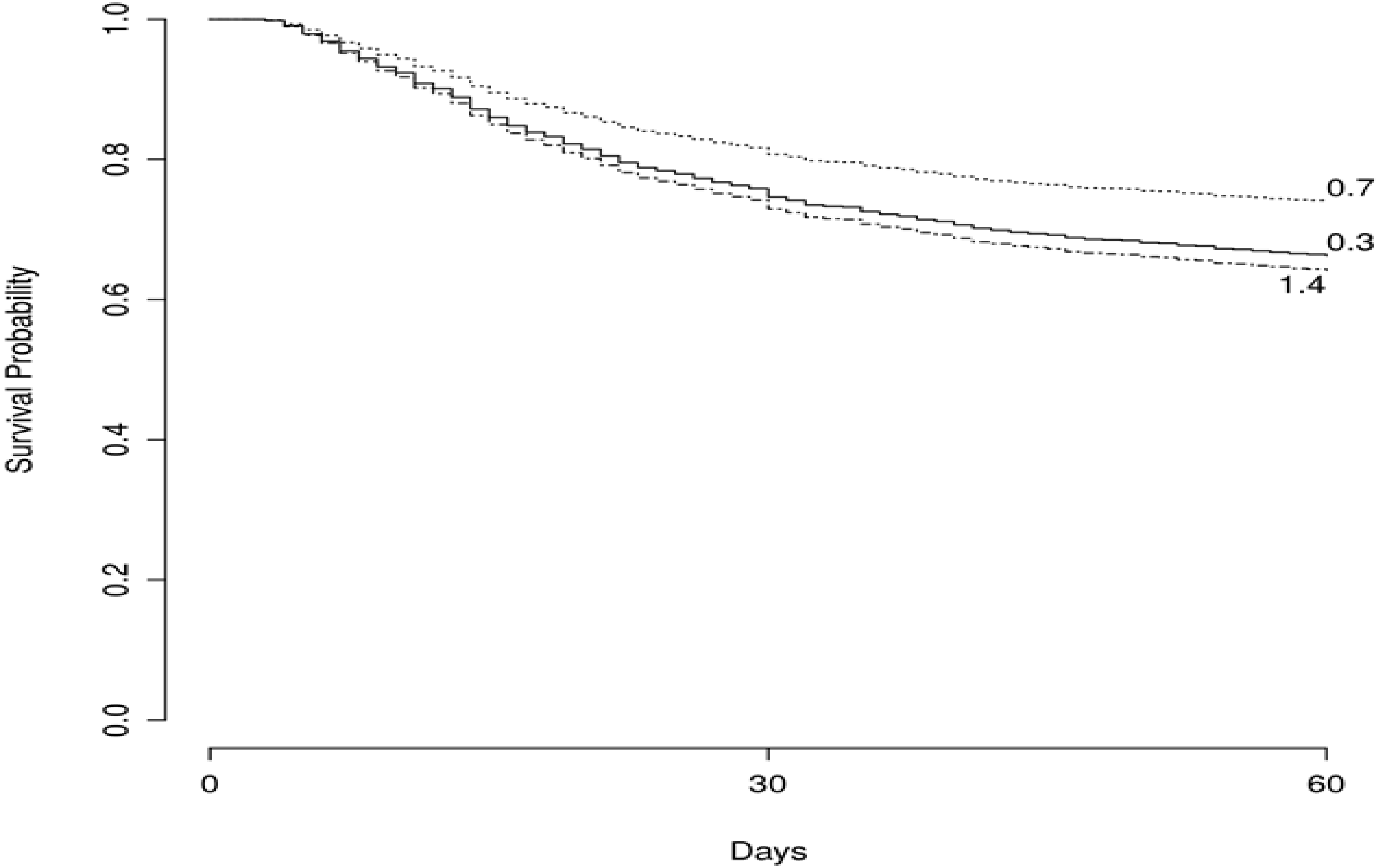
- OR of 0.73 [95% CI 0.55-0.97], p=0.03
- cox regression, survival analysis had an

  OR of 0.75 [95% CI 0.58-0.94]. P=

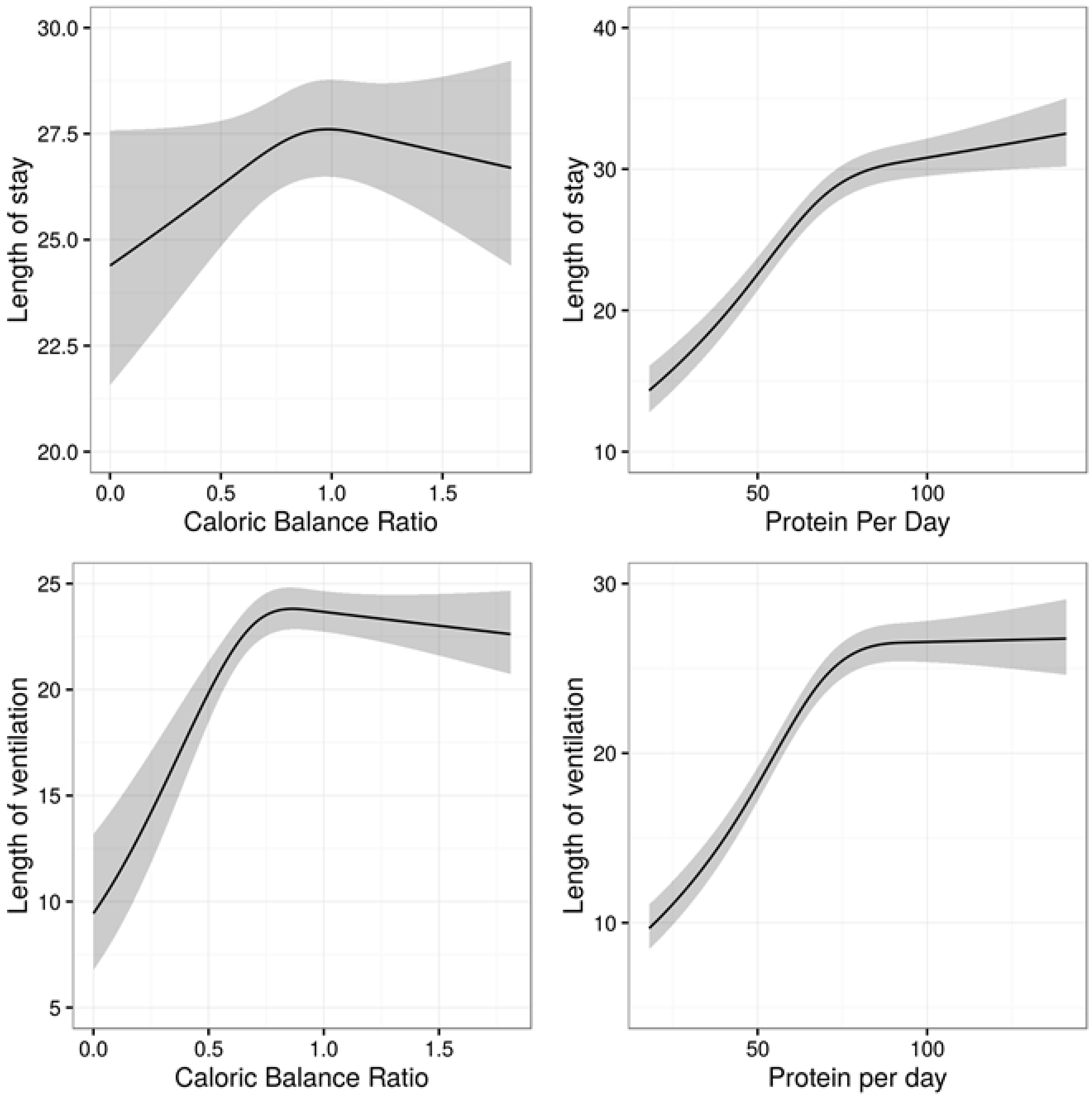
- The other parameters with a strong correlation with mortality were albumin and SOFA score (0.77 and 1.14 respectively)



3.0
2.5
2.0
1.5
1.0
0.5
0.0
0.2 0.4 0.6 0.8 1.0 1.2 1.4 1.6
Delivered Calories/REE ratio
Unadjusted odds ratio for 60-day Mortality
25 50 75 100 125
Protein Intake, gr



Survival Probability
1.0
0.8
0.6
0.4
0.2
0.0
0.7
0.3
1.4
0
30
60
Days



30.0
27.5
25.0
22.5
20.0
Length of stay
0.0
0.5
1.0
1.5
Caloric Balance Ratio
40
30
20
10
Length of stay
50
100
Protein Per Day
25
20
15
10
5
Length of ventilation
0.0
0.5
1.0
1.5
Caloric Balance Ratio
30
20
10
Length of ventilation
50
100
Protein per day

ONLINE FIRST

JAMA. 2013 May 22;309(20):2130-8.

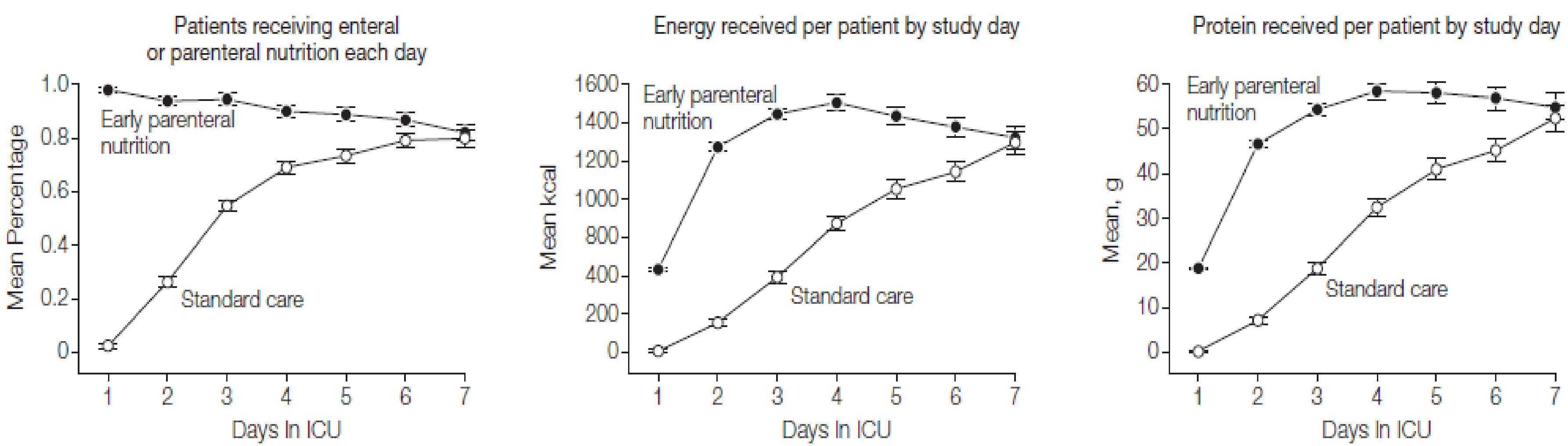
Early Parenteral Nutrition in Critically Ill Patients With Short-term Relative Contraindications to Early Enteral Nutrition

A Randomized Controlled Trial

Gordon S. Doig, PhD

Importance Systematic reviews suggest adult patients in intensive care units (ICUs)

Figure 2. Enteral and Parenteral Nutrition Delivery Process Measures for Patients Remaining in the Study ICU



No. of patients																					
Early parenteral nutrition	681	676	611	518	435	376	313	681	676	611	518	435	376	313	681	676	611	518	435	376	313
Standard care	682	675	599	480	410	353	301	682	675	599	480	410	353	301	682	675	599	480	410	353	301

Table 2. Mortality, Quality of Life, and Length of Stay

	Standard Care (n = 680)[a]	Early PN (n = 678)[a]	Risk Difference, % (95% CI)	Odds Ratio (95% CI)	*P* Value
Deaths before study day 60, No. (%)	155 (22.8)	146 (21.5)	−1.26 (−6.6 to 4.1)	0.93 (0.71 to 1.21)	.60
Covariate-adjusted deaths before study day 60[b]			0.04 (−4.2 to 4.3)	1.00 (0.76 to 1.31)	>.99
Quality of life and physical function, mean (SD)[c]	(n = 525)	(n = 532)	Difference (95% CI)		
RAND-36 general health status[d]	45.5 (26.8) (n = 516)	49.8 (27.6) (n = 525)	4.3 (0.95 to 7.58)		.01
ECOG performance status[e]	1.53 (1.1) (n = 516)	1.51 (1.1) (n = 525)	−0.02 (−0.15 to 0.11)		.70
RAND-36 physical function[f]	40.7 (29.6) (n = 513)	42.5 (30.8) (n = 524)	1.8 (−1.85 to 5.52)		.33
Discharge status and length of stay	(n = 682)	(n = 681)	Difference (95% CI)		
ICU stay, mean (95% CI), d	9.3 (8.9 to 9.7)	8.6 (8.2 to 9.0)	−0.75 (−1.47 to 0.04)		.06
Deaths before ICU discharge, No. (%)	100 (14.66)	81 (11.89)	−2.77% (−8.08% to 2.52%)		.15
Hospital stay, mean (95% CI), d	24.7 (23.7 to 25.8)	25.4 (24.4 to 26.6)	0.7 (−1.4 to 3.1)		.50
Deaths before hospital discharge, No. (%)	151 (22.1)	140 (20.6)	−1.58% (−6.91% to 3.69%)		.51

The Association Between Nutritional Adequacy and Long-Term Outcomes in Critically Ill Patients Requiring Prolonged Mechanical Ventilation: A Multicenter Cohort Study*

Xuejiao Wei, MSc[1]; Andrew G. Day, MSc[1,2]; Hélène Ouellette-Kuntz, PhD[1]; Daren K. Heyland, MD, MSc[2,3]

TABLE 1. (*Continued*). Patient Baseline Characteristics and Short-Term Clinical Outcomes

Variable	Overall	Nutritional Adequacy[a]			p[b]
		Low (0% and ≤ 50%)	Moderate (≥ 50% and < 80%)	High (≥ 80%)	
Short-term clinical outcomes					
ICU length of stay					
Median (interquartile range)	18 (13–29)	18 (13–28)	19 (13–31)	18 (12–29)	
Mechanical ventilation duration					
Median (interquartile range)	15 (11–25)	15 (10–23)	15 (11–25)	15 (11–25)	
ICU mortality[c] (%)	123 (26)	47 (26)	62 (27)	14 (23)	0.63
Hospital mortality (%)	151 (32)	58 (32)	75 (32)	18 (29)	0.85

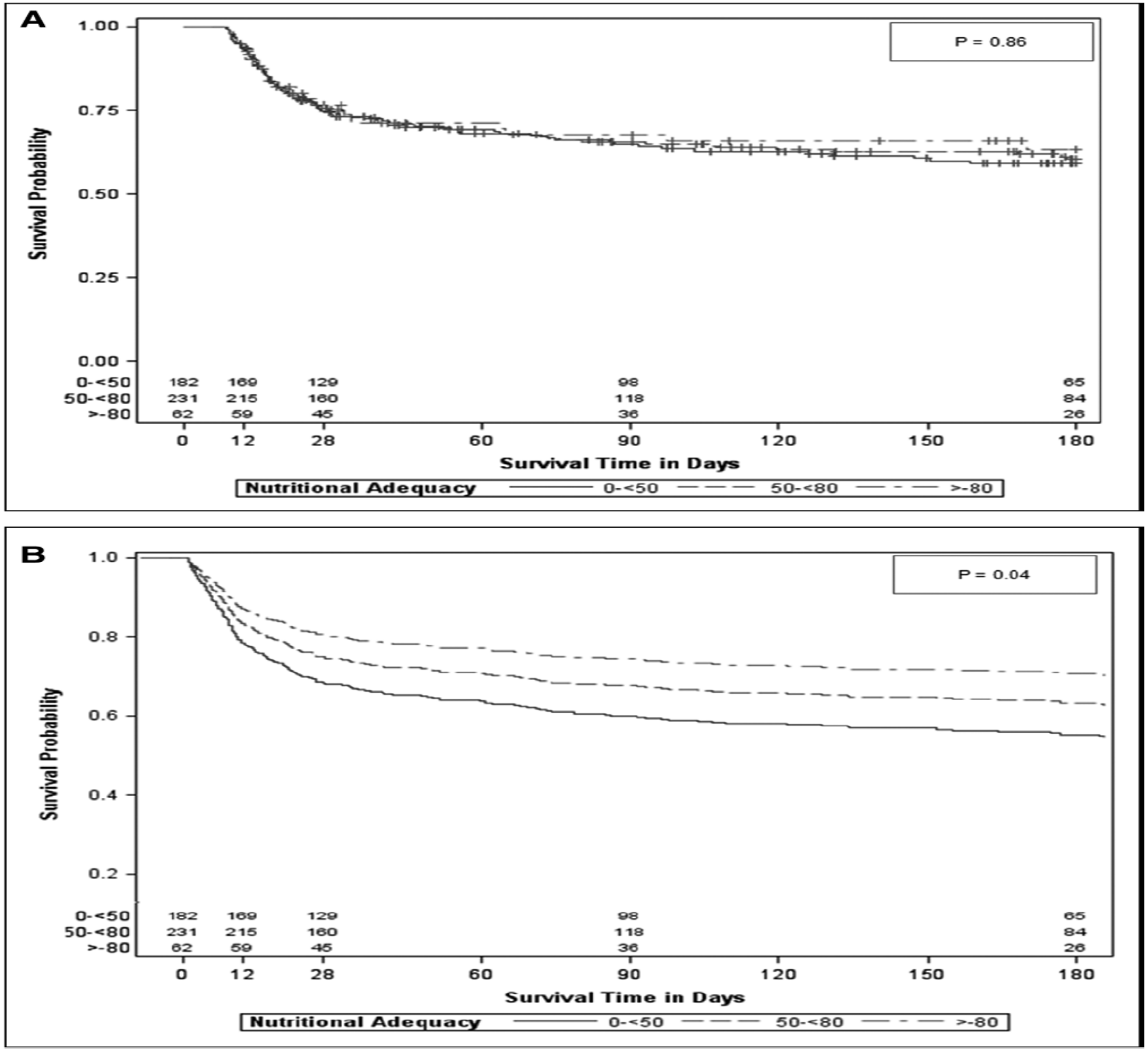
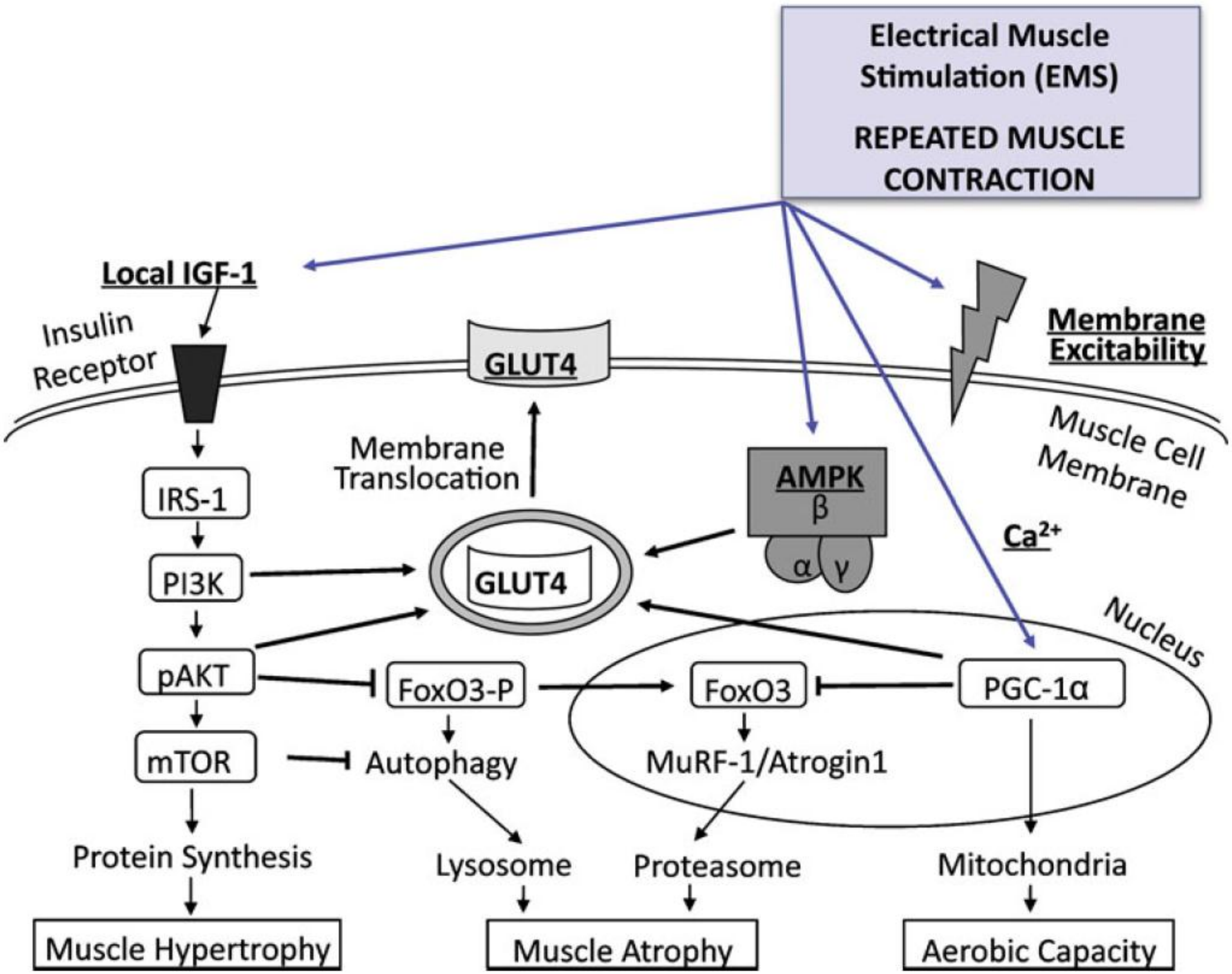


Figure 2. Crude (**A**) and adjusted (**B**) survival curves stratified by nutritional adequacy groups in 475 patients who were mechanically ventilated in the ICU for more than 8 days. Adjusted covariates include age, Acute Physiology and Chronic Health Evaluation II score, baseline Sequential Organ Failure Assessment, Charlson Comorbidity Index, admission category, primary ICU diagnosis, body mass index, and region.

TABLE 4. Estimates of the Effect of Nutritional Adequacy on 36-Item Short-Form Health Survey Scores

36-Item Short-Form Health Survey	Nutritional Adequacy[a] per 25% Increase			
	Crude Estimate[b] (95% CI)	*p*	Adjusted Estimate[b,c] (95% CI)	*p*
Physical Functioning				
3 mo ($n = 179$)[d]	7.7 (2.3–13.1)	0.006	7.3 (1.4–13.2)	0.02
6 mo ($n = 202$)[d]	5.3 (0.0–10.5)	0.05	4.2 (−1.3 to 9.6)	0.14
Role Physical				
3 mo ($n = 178$)[d]	8.3 (3.0–13.5)	0.002	8.3 (2.7–14.0)	0.004
6 mo ($n = 202$)[d]	5.0 (−0.2 to 10.2)	0.06	3.2 (−2.3 to 8.5)	0.25
Physical Component Scale				
3 mo ($n = 175$)[d]	1.8 (−0.1 to 3.7)	0.06	1.8 (−0.2 to 3.8)	0.07
6 mo ($n = 200$)[d]	1.8 (−0.2 to 3.7)	0.07	1.3 (−0.7 to 3.3)	0.19



Electrical Muscle Stimulation (EMS)
REPEATED MUSCLE CONTRACTION
Local IGF-1
Insulin Receptor
GLUT4
Membrane Excitability
Muscle Cell Membrane
Membrane Translocation
AMPK
β
α
γ
IRS-1
PI3K
GLUT4
Ca2+
Nucleus
pAKT
FoxO3-P
FoxO3
PGC-1α
mTOR
Autophagy
MuRF-1/Atrogin1
Protein Synthesis
Lysosome
Proteasome
Mitochondria
Muscle Hypertrophy
Muscle Atrophy
Aerobic Capacity

Exercise to fight anabolic resistance

Table 2
Specific treatment modalities for early rehabilitation in the ICU studied in positive prospective trials

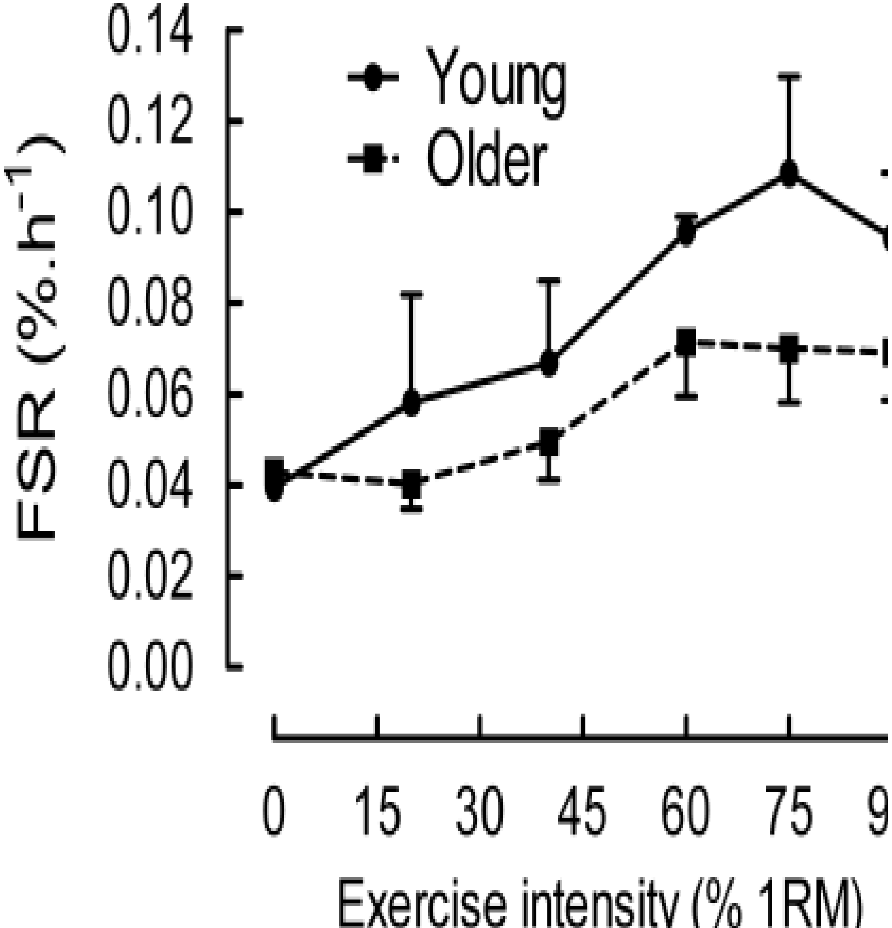
Treatment Modality/Intervention	Study/Study Design	Patient Population	Primary Outcome/Results
UE/LE exercise	Schweickert et al,[89] 2009 RCT N = 104	Sedated adult ICU patients on MV <72 h	Significantly higher rate of return to independent functional status at hospital discharge (59% in treatment group vs. 35%; *P*<.02)
Bed exercises and mobilization	Malkoc et al,[120] 2009 N = 510 Prospective intervention group Retrospective case group	Multidisciplinary internal medicine ICU: 51% of patients required MV	Decreased length of MV and ICU stay in intervention group vs controls
Early activity protocol (sitting on chair or edge of bed; ambulation with walker)	Thomsen et al,[79] 2008 Before-after cohort study N = 104	Patients in RICU requiring >4 d of MV	Significant increase in rate of ambulation in patient cohort transferred to an RICU implementing early activity protocol vs pretransfer levels
Cycle ergometry (passive or active) combined with UE/LE exercise	Burtin et al,[83] 2009 RCT N = 67	Single-center surgical and medical ICU patients with expected prolonged stay (at least 12 d after admission to ICU)	Significantly increased 6MWD, quadriceps force, and physical functioning at hospital discharge in treatment group vs controls
IMT with threshold inspiratory device	Martin et al,[97] 2011 RCT N = 69	Single-center medical and surgical ICU patients with failure to wean from MV with usual care	IMT significantly improved MIP and weaning outcome compared with sham treatment
NMES	Routsi et al,[85] 2010 RCT N = 52	Patients in the ICU with APACHE score ≥13 capable of assessment with MRC	MRC score was significantly higher in patients with NMES compared with patients who received sham treatment

Abbreviations: 6MWD, 6MW distance; APACHE, acute physiology and chronic health evaluation; IMT, inspiratory muscle training; LE, lower extremity; MIP, maximal inspiratory pressure; RICU, respiratory ICU; UE, upper extremity.

Age-related differences in the dose–response relationship of muscle protein synthesis to resistance exercise in young and old men

Vinod Kumar[1], Anna Selby[1], Debbie Rankin[1], Rekha Patel[1], Philip Atherton[1], Wulf Hildebrandt[1], John Williams[2], Kenneth Smith[1], Olivier Seynnes[3], Natalie Hiscock[4] and Michael J. Rennie[1]

J Physiol 587.1 (2009) pp 211–217



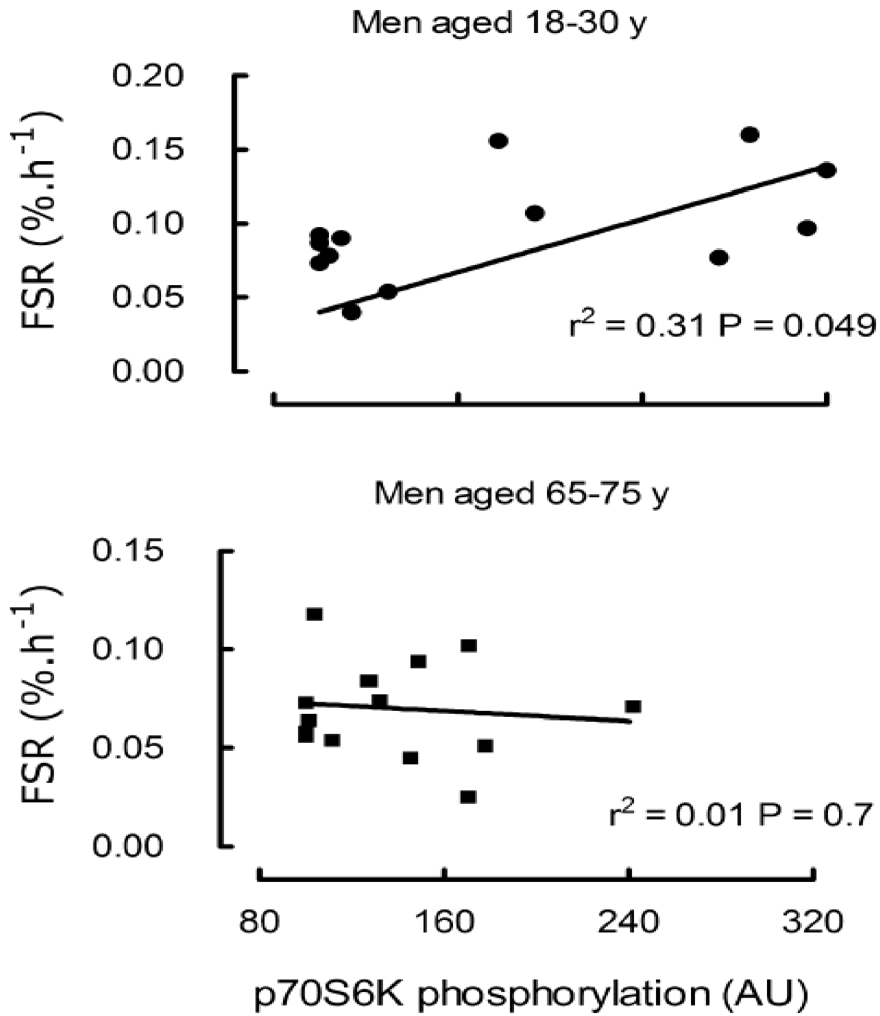


FIGURE 3. Effect of protein delivery on mortality

M Davies et al ICM submitted

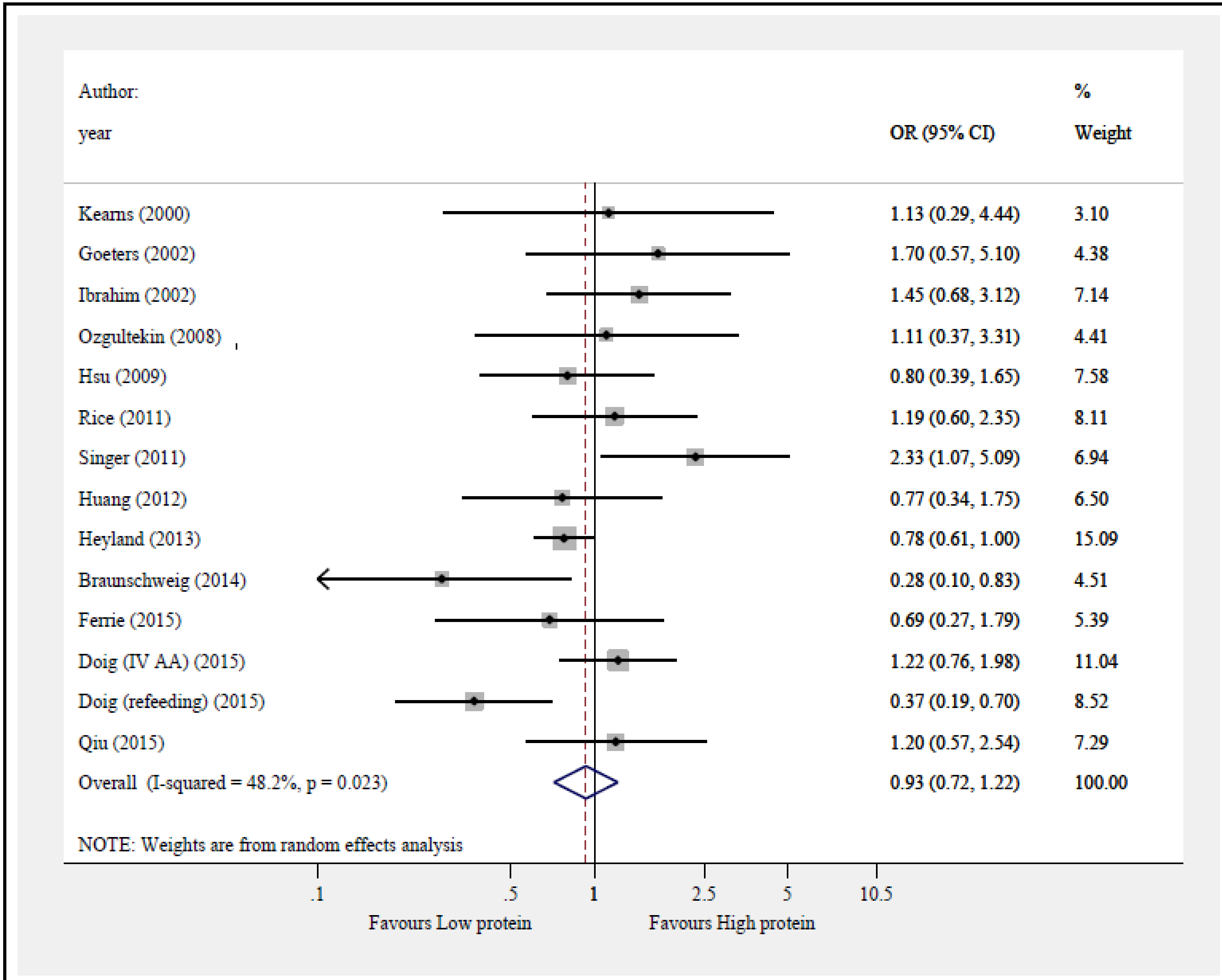
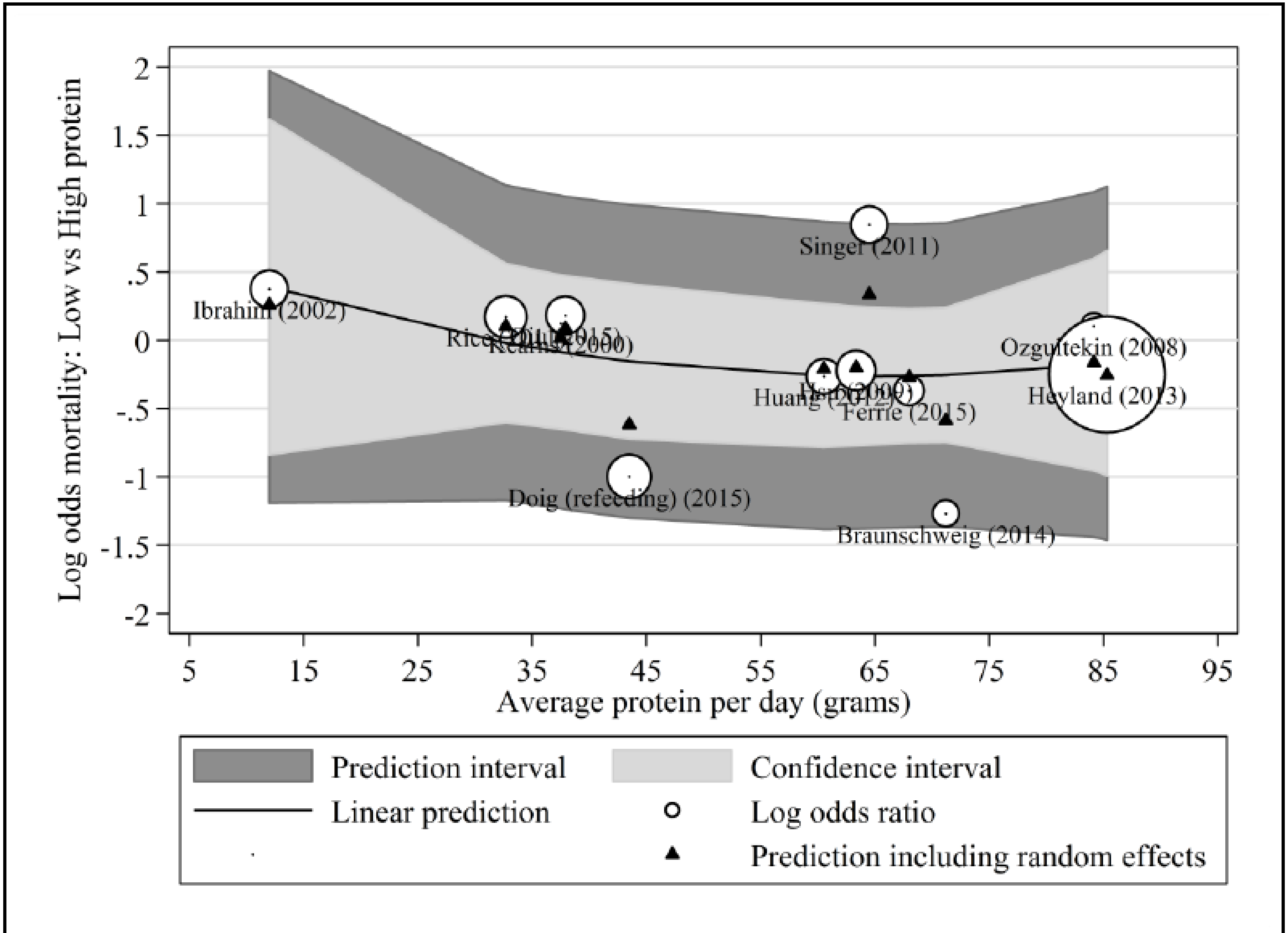


FIGURE 5. Meta-regression analysis of effect of average protein delivery on mortality



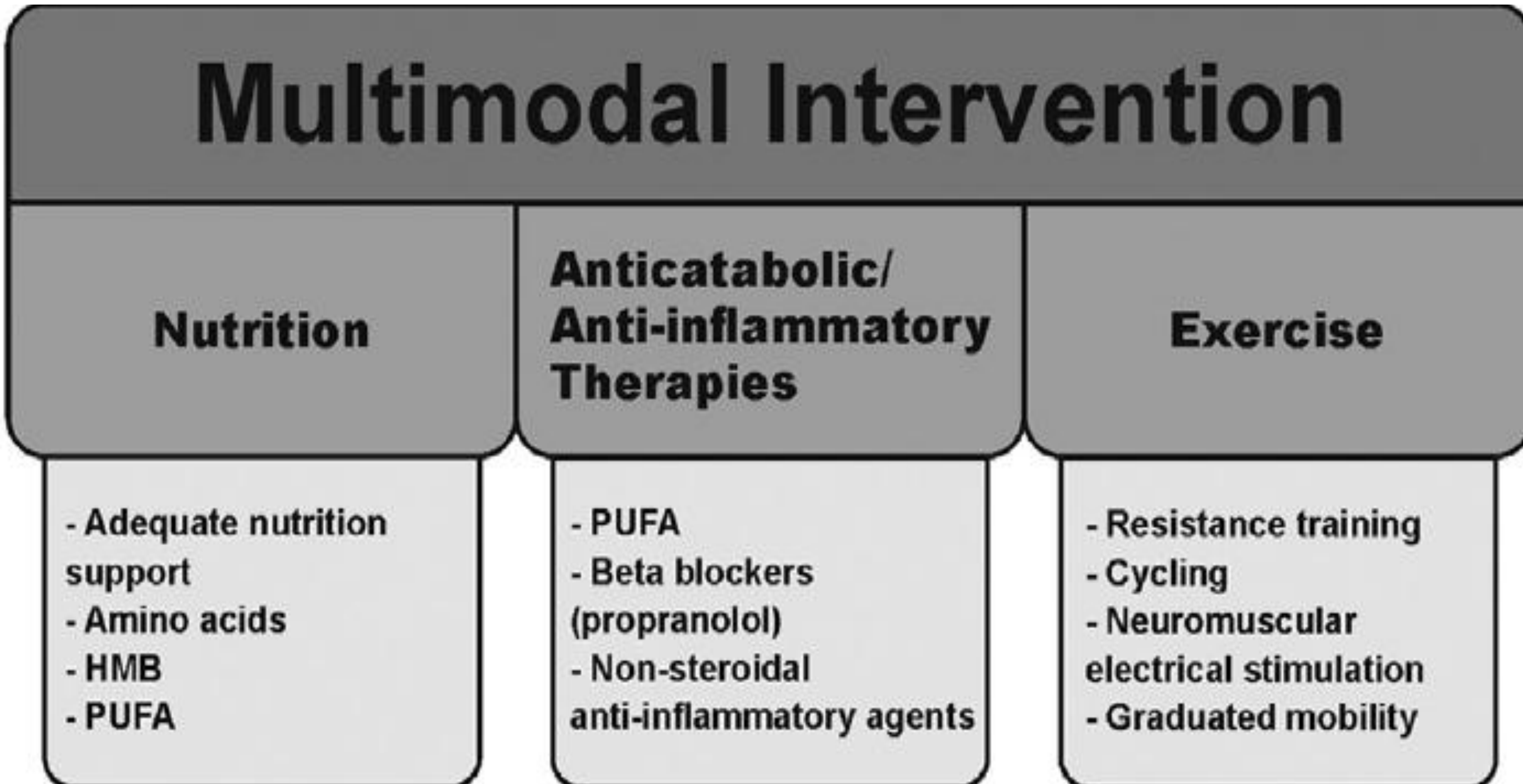
??? ????? ?????.mp4

Patient Story Timothee_Mpeg4 H264_8894.mp4

Opinion paper

Combining nutrition and exercise to optimize survival and recovery from critical illness: Conceptual and methodological issues

Daren K. Heyland [a, *], Renee D. Stapleton [b], Marina Mourtzakis [c], Catherine L. Hough [d], Peter Morris [e], Nicolaas E. Deutz [f], Elizabeth Colantuoni [g], Andrew Day [a], Carla M. Prado [h], Dale M. Needham [i]



Winning the war against ICU-acquired weakness: new innovations in nutrition and exercise physiology

Paul E Wischmeyer[1*] and Inigo San-Millan[2]

Ensuring Optimal Survival and Post-ICU Quality of Life in High-Risk ICU Patients: Permissive Underfeeding Is Not Safe!*

Paul E. Wischmeyer, MD

Critical Care Medicine August 2015 • Volume 43 • Number 8

TABLE 1. Recent Trials in ICU Nutrition Delivery

Study Outcomes	Trials Not Supporting Goal (> 80% kcal/d) Nutritional Delivery in ICU			
	Early versus Late Parenteral Nutrition in Critically Ill Adults (6)	EDEN Trial (Pilot) (4)	EDEN Trial (Full Randomized Controlled Trial) (3)	Arabi Trial (2)
Age (mean)	64	53	52	51
ICU LOS	3.5			13.1
Hospital LOS	15			
Mechanical ventilation days	2	5.6	5	11.9
Mortality, %				
ICU	6.2			19.6
Hospital	10.65	21		36
Postdischarge	11.2		22.7	38.6
Primary outcomes	Significant reduced LOS in ICU for late PN (median, 3 d) vs early PN (median, 4 d)	No outcome changes in trophic vs full feeding groups for ventilation days, mortality, or infection	No outcome changes in trophic vs full feeding groups for ventilation days, mortality, or infection	Nonsignificant trend to lower 28-d mortality for trophic (18.3%) compared with target feeding (23.3%) ($p < 0.07$)
Secondary outcomes	Significant higher infectious complications, duration of MV, and hospital LOS for early PN	Full feeding group more likely to be discharged home then rehabilitation unit ($p < 0.04$)	No change in HRQoL at 12 mo	No difference in LOS or duration of MV
Limitations	> 50% of patients with short stays (< 3 d) and with no indication for nutrition	Primarily young, obese patients with short duration of stay	Primarily young, obese patients with short duration of stay	Very small difference in caloric intake between trophic and full feeding group (~10% difference: 1,067 ± 306 vs 1,252 ± 432 kcal/d)
	Potential for overfeeding with glucose infusions in early PN group	Low protein delivery (0.8 g/kg/d) in both groups (including full feed group)	Low protein delivery (0.6–0.8 g/kg/d) in both groups (including full feed group)	Low protein intake (0.6 g/kg/d in all patients)
	Low protein intake (0.8 g/kg/d in all patients)			

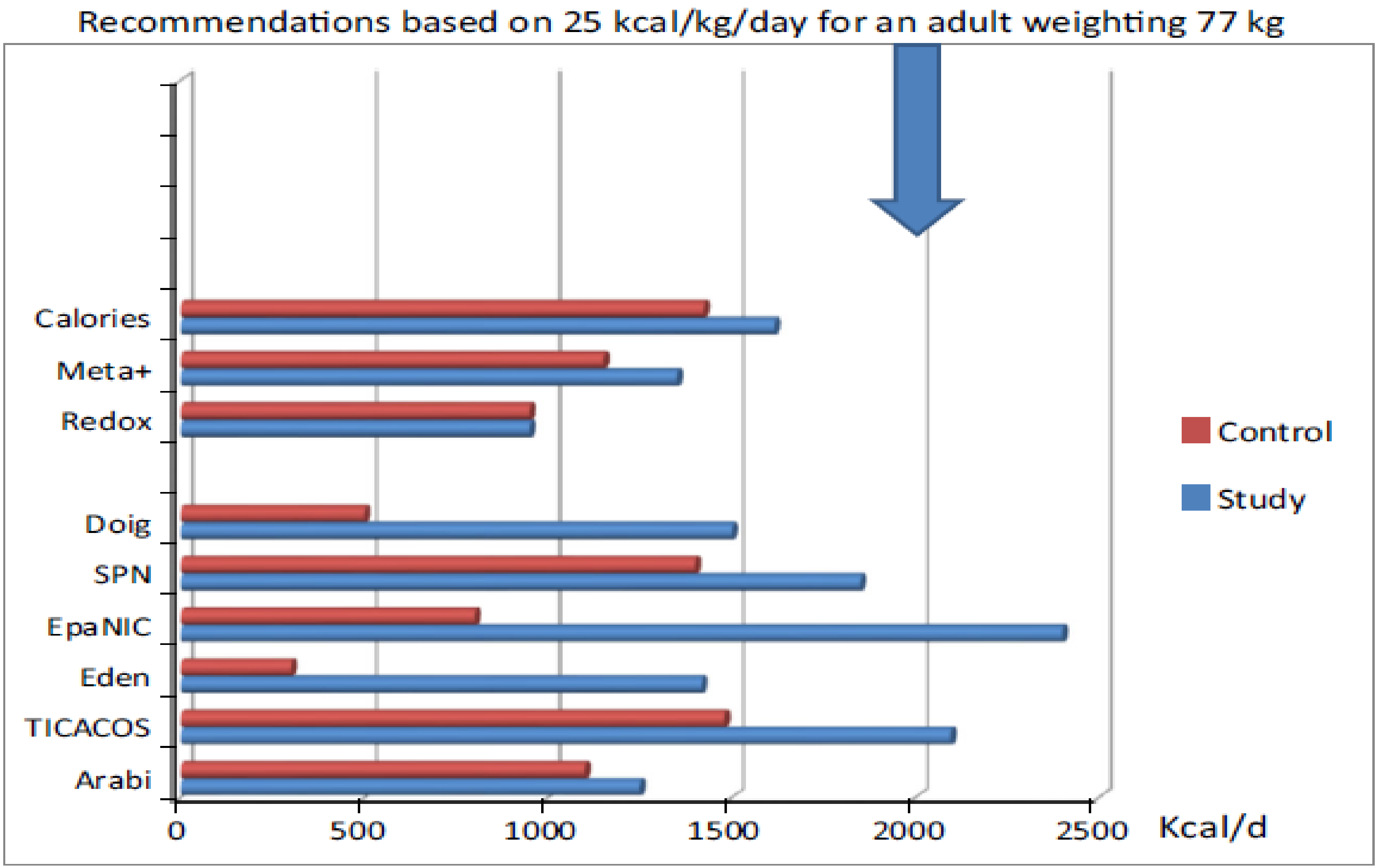
Trials Supporting Goal (> 80% kcal/d) Nutritional Delivery in ICU			
Early PN (7)	The Tight Calorie Control Trial (9)	SPN (8)	Wei et al (5)
69	61	61	62
9	12	13	18
25	25	31.5	
6.9	10.75	6.64	15
	25.4	10	26
21	38.3	24	32
	47	23	
No significant change in crude day 60 mortality (standard care [22.8%] vs early PN [21.5%])	Significant lower hospital mortality for goal calorie group (28.5%) vs underfed control group (48.2)	Significant reduced nosocomial infections for EN + SPN (27%) vs EN (38%) after day 9	Significant improved survival and 3 mo HRQoL with improved nutrition delivery
Significant shorter duration of MV Improved HRQoL for early PN group No change in infection in PN vs EN	Longer duration of MV and ICU LOS, and higher infection rate for goal calorie study group	No significant difference in the ICU LOS, hospital LOS, or mortality	Significant improvement in HRQol in medical ICU patients at 3 and 6 mo with improved nutrition delivery
Many gastrointestinal surgical patients	Did not account for nonnutrition energy delivery	No difference in infections over entire study period	Observational trial
	Metabolic cart energy goals (may not be widely applicable currently)	Metabolic cart energy goals (may not be widely applicable currently)	Protein intake not able to be quantified

Intensive Care Med (2015) 41:154–156
DOI 10.1007/s00134-014-3537-8

EDITORIAL

Pierre Singer
Jonathan Cohen

Nutrition in the ICU: proof of the pudding is in the tasting



To Implement Guidelines: The (Bad) Example of Protein Administration in the ICU

Journal of Parenteral and Enteral Nutrition
Volume XX Number X
Month 2013 1-3

DOI: 10.1177/0148607113481063
jpen.sagepub.com
hosted at

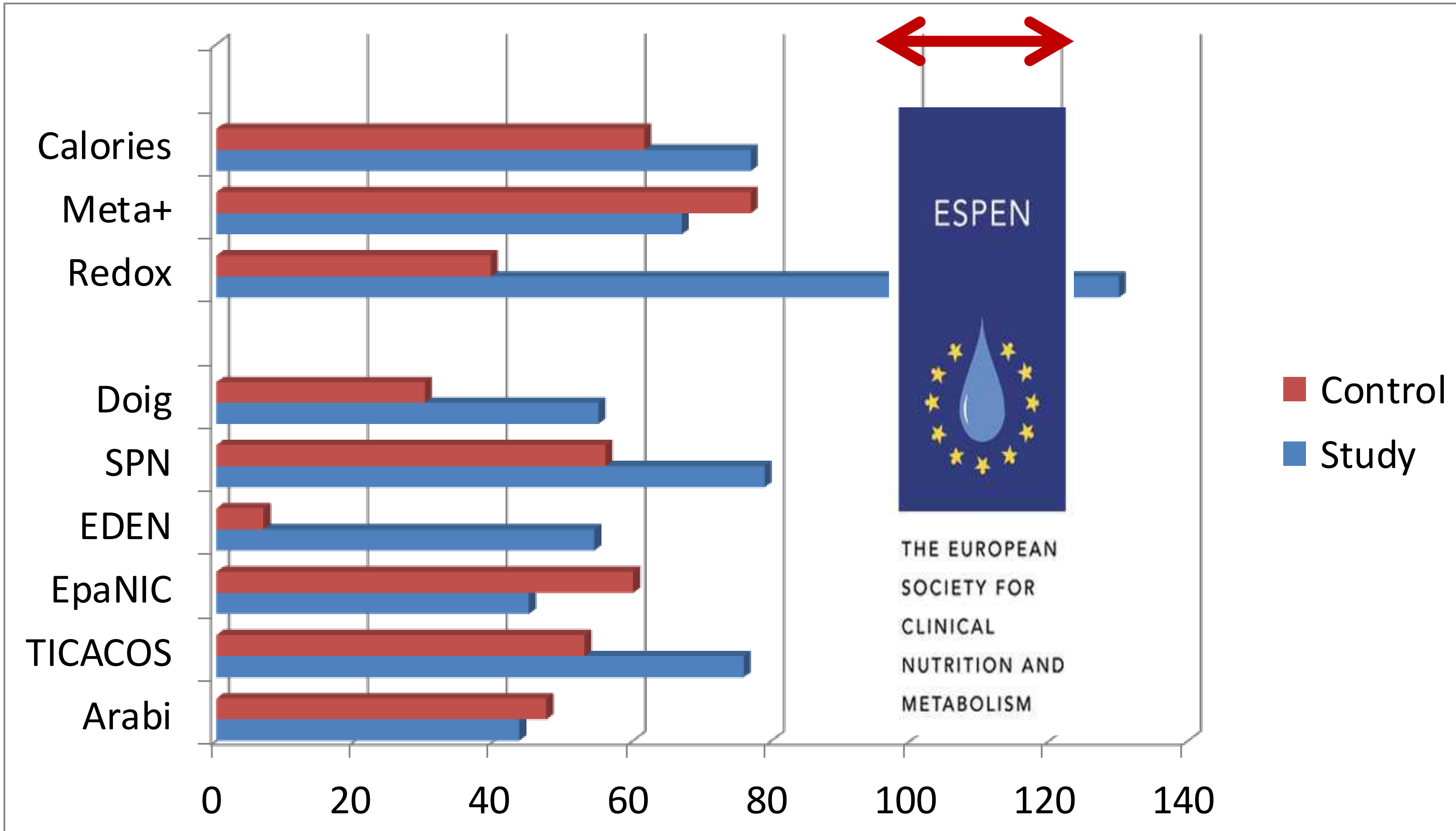
Pierre Singer, MD; and Jonathan D. Cohen, MD

Table 1. Protein Intake Inspired by Recent Prospective Nutrition Studies in the Intensive Care Unit.

Studies	Protein Intake in Control Group	Protein Intake in Study Group
Van den Berghe et al,[9] g/kd/d	0.85	0.80
Rice et al,[10] g/d	11	54
Arabi et al,[11] g/d	47.5	43.6
Singer et al,[12] g/d (g/kg/d)	53 (0.68)	76 (1)
Heidegger et al,[13] g/d	56	79
Casaer et al,[14] g/d	<60	<60
Weijs et al,[8] g/d	67	89

Adapted from Singer and Pichard.[25]

Protein intake observed vs GL



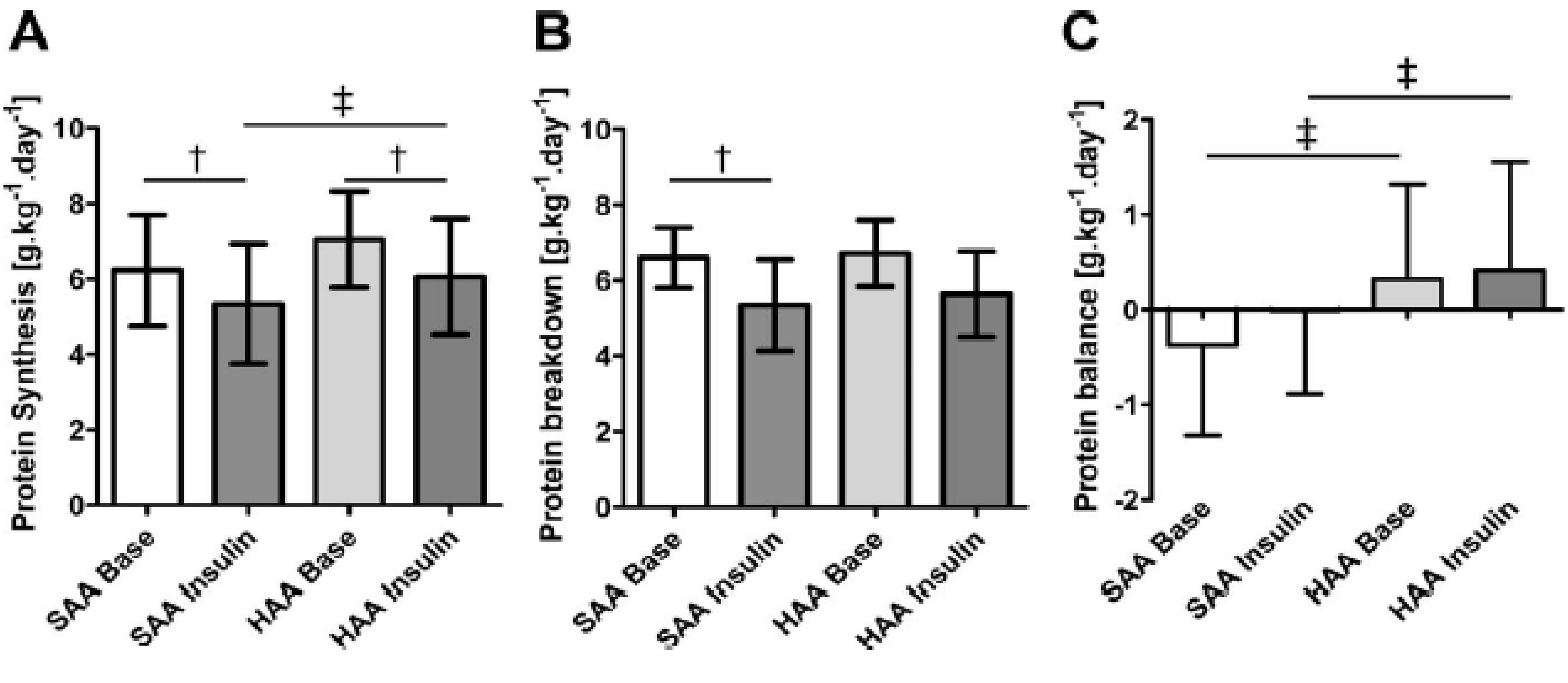
1.2 g/kg/d 77kg

How to improve?

- Increase quantity
- Improve quality
- Better glucose control
- Exercise

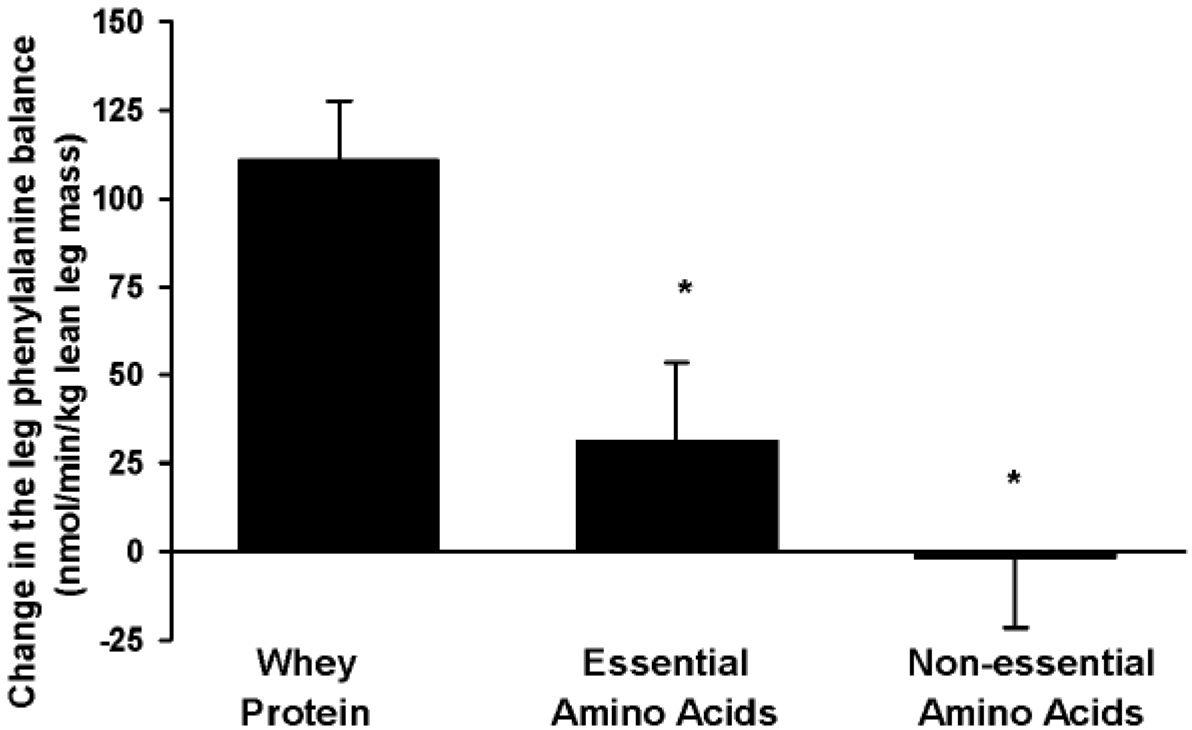
Current recommended parenteral protein intakes do not support protein synthesis in critically ill septic, insulin-resistant adolescents with tight glucose control

Sascha C. A. T. Verbruggen, MD, PhD; Jorge Coss-Bu, MD; Manhong Wu, PhD; Henk Schierbeek, PhD; Koen F. M. Joosten, MD, PhD; Archana Dhar, MD; Johannes B. van Goudoever, MD, PhD; Leticia Castillo, MD, FCCM



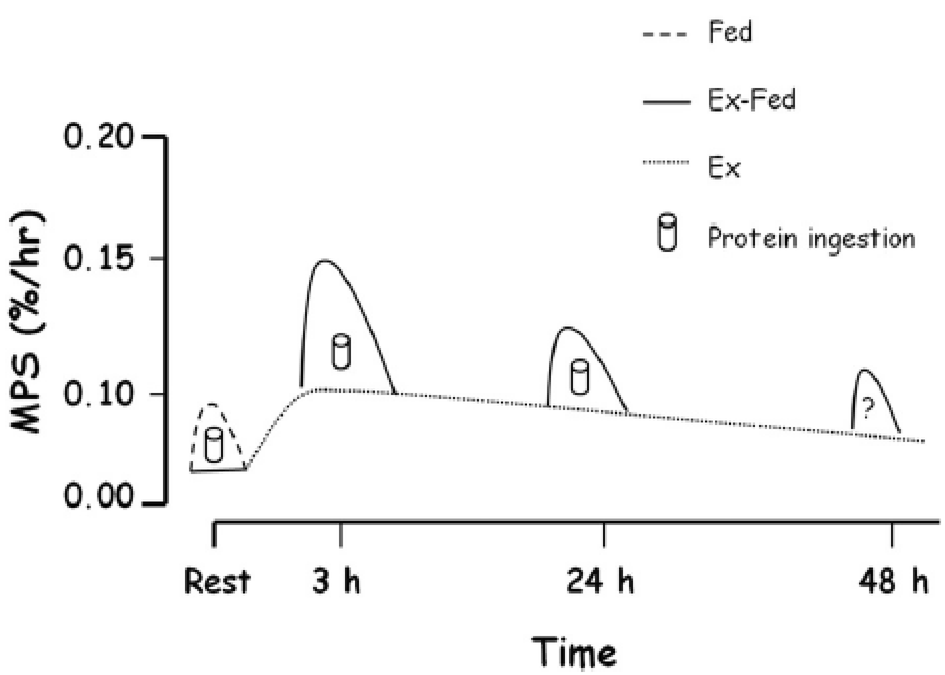
Whey protein ingestion in elderly results in greater muscle protein accrual than ingestion of its constituent essential amino acid content

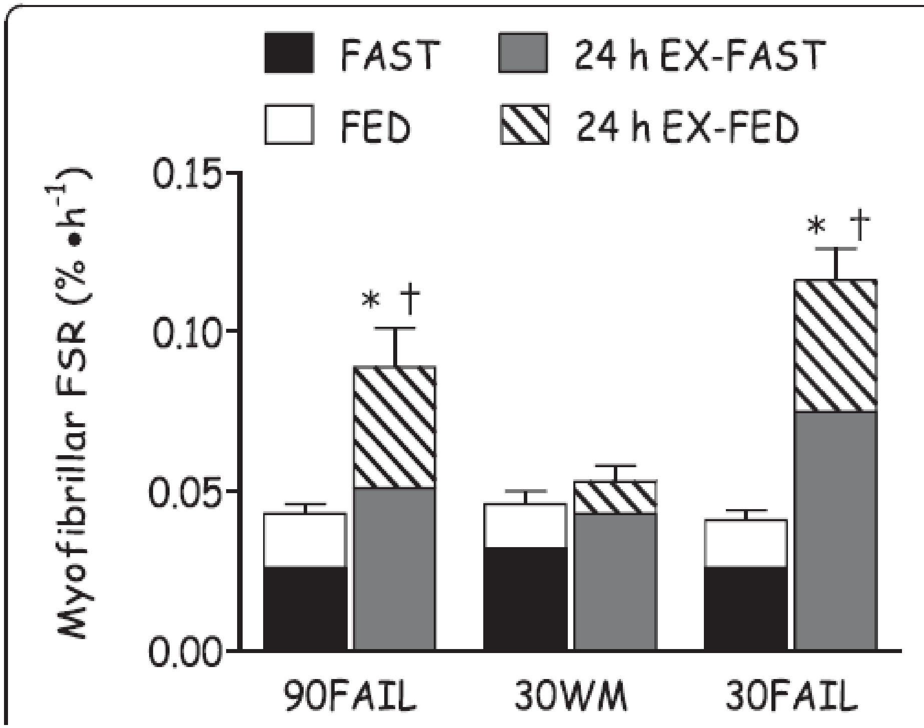
Christos S. Katsanos[a,*], David L. Chinkes[b], Douglas Paddon-Jones[c], Xiao-jun Zhang[b], Asle Aarsland[d], and Robert R. Wolfe[e]



Nutritional regulation of muscle protein synthesis with resistance exercise: strategies to enhance anabolism

Tyler A Churchward-Venne, Nicholas A Burd and Stuart M Phillips*





Exercise

Conclusions

- Muscle atrophy is linked to anabolism resistance
- High amount of protein is needed (>1.5 g/d) and some patients need more
- Requirements adapted to weight, age, metabolic status: not a unique recommendation!
- Exercise may decrease protein catabolism and improve anabolic resistance.