63° CONGRESSO NAZIONALE SIGG
GLI ANZIANI:
LE RADICI DA PRESERVARE
ROMA 28 novembre 01 dicembre 2018

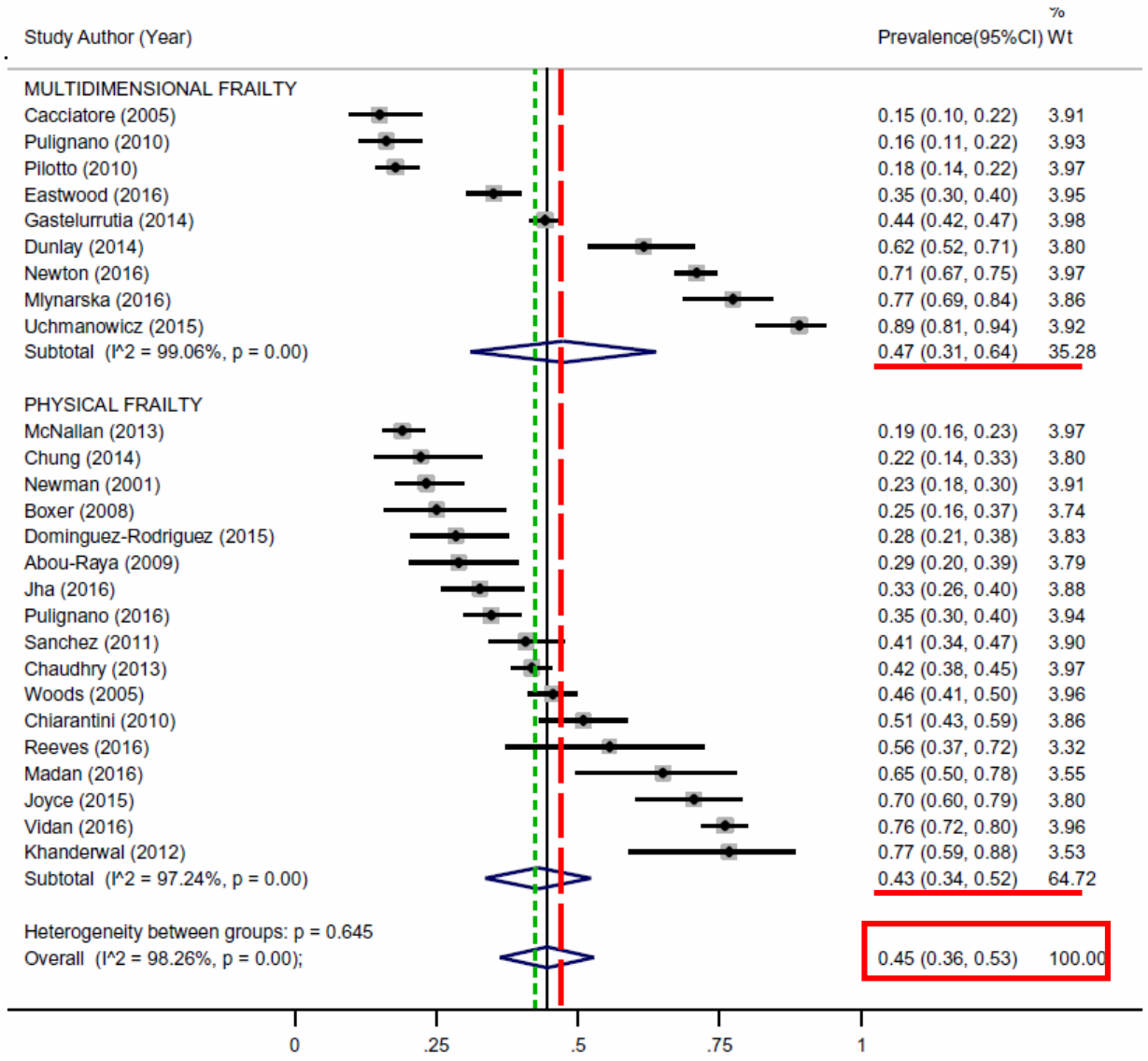
Fragilità, infiammazione e sarcopenia nel paziente Anziano con scompenso cardiaco

Samuele Baldasseroni
Geriatria-UTIG
AOU, Careggi, Firenze

The prevalence of frailty in heart failure: A systematic review and meta-analysis☆,☆☆

Quin E. Denfeld [a,b,*], Kerri Winters-Stone [b,c], James O. Mudd [a], Jill M. Gelow [a], Sawsan Kurdi [d], Christopher S. Lee [a,b]

International Journal of Cardiology 236 (2017) 283–289



Results: A total of 26 studies involving 6896 patientswith HF were included in this meta-analysis. Despite considerable differences across studies, the overall estimated **prevalence of frailty in HF was 44.5%** (95% confidence interval, (36.2%–52.8%; z=10.54; p b 0.001**). The prevalence was slightly lower among studies using Physical Frailty measures (42.9%,** z=9.05; p b 0.001) and **slightly higher among studies using Multidimensional Frailty measures (47.4%, z =5.66; p b 0.001**). There were no significant relationships between study age or functional class and prevalence of frailty.

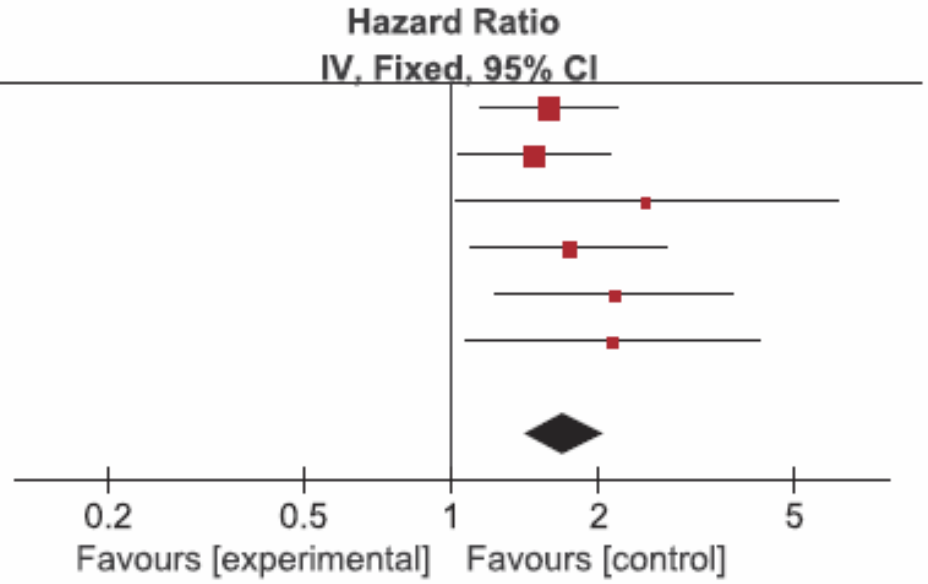
Review Article

Prognostic Value of Frailty for Older Patients with Heart Failure: A Systematic Review and Meta-Analysis of Prospective Studies

Hindawi
BioMed Research International
Volume 2018, Article ID 8739058, 9 pages
https://doi.org/10.1155/2018/8739058

Study or Subgroup	log[Hazard Ratio]	SE	Weight	Hazard Ratio IV, Fixed, 95% CI
Boxer 2010	0.457425	0.161981	33.9%	1.58 [1.15, 2.17]
Cacciatore 2005	0.392042	0.180476	27.3%	1.48 [1.04, 2.11]
Martín-Sánchez 2017	0.916291	0.457081	4.3%	2.50 [1.02, 6.12]
Pulignano 2006	0.553885	0.233748	16.3%	1.74 [1.10, 2.75]
Rodriguez-Pascual 2017	0.765468	0.285052	11.0%	2.15 [1.23, 3.76]
Vidán 2016	0.756122	0.350649	7.2%	2.13 [1.07, 4.23]
Total (95% CI)			**100.0%**	**1.70 [1.41, 2.04]**

Heterogeneity: $Chi^2 = 2.61$, $df = 5$ ($P = 0.76$); $I^2 = 0\%$
Test for overall effect: $Z = 5.62$ ($P < 0.00001$)



The results of the present systematic review and meta-analysis indicate that frailty is more prevalent in older patients with HF and that frailty increases the risk of death by 70%. Therefore, frailty is an effective indicator of the prognostic evaluation of older HF patients and clinical medical staff should attach importance to the role of frailty assessments during HF management.

…..oltre l’ associazione e verso il sinergismo negativo…..

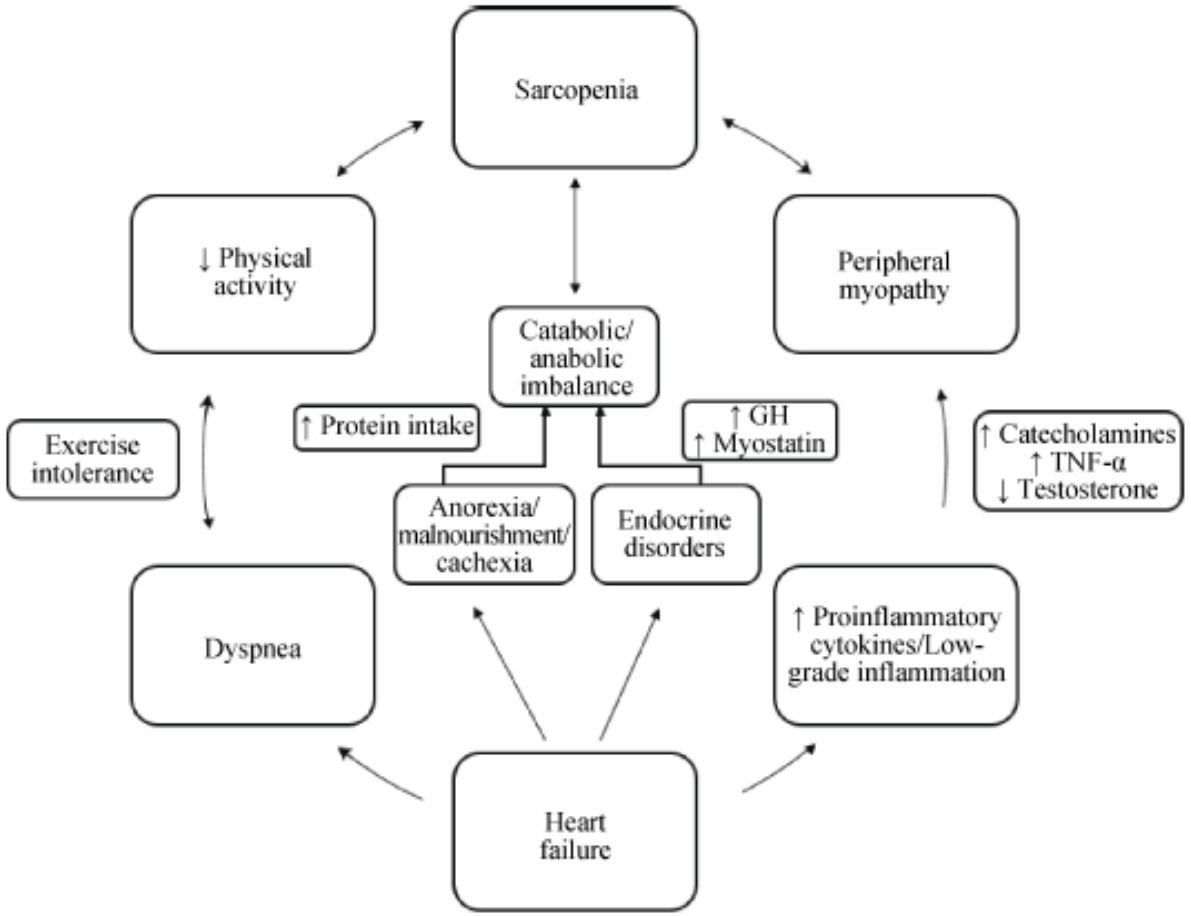
Review · Open Access ·

Sarcopenia in heart failure: mechanisms and therapeutic strategies

Agnese Collamati, Emanuele Marzetti, Riccardo Calvani, Matteo Tosato, Emanuela D’Angelo, Alex N Sisto, Francesco Landi

Center for Geriatric Medicine (CEMI), Institute of Internal Medicine and Geriatrics Catholic, University of the Sacred Heart, Rome, Italy

Journal of Geriatric Cardiology (2016) 13: 615–624



Piano biochimico (intracellulare)

↓

Piano endocrino-metabolico

↓

Piano muscolare-funzionale

↓

Piano clinico-prognostico

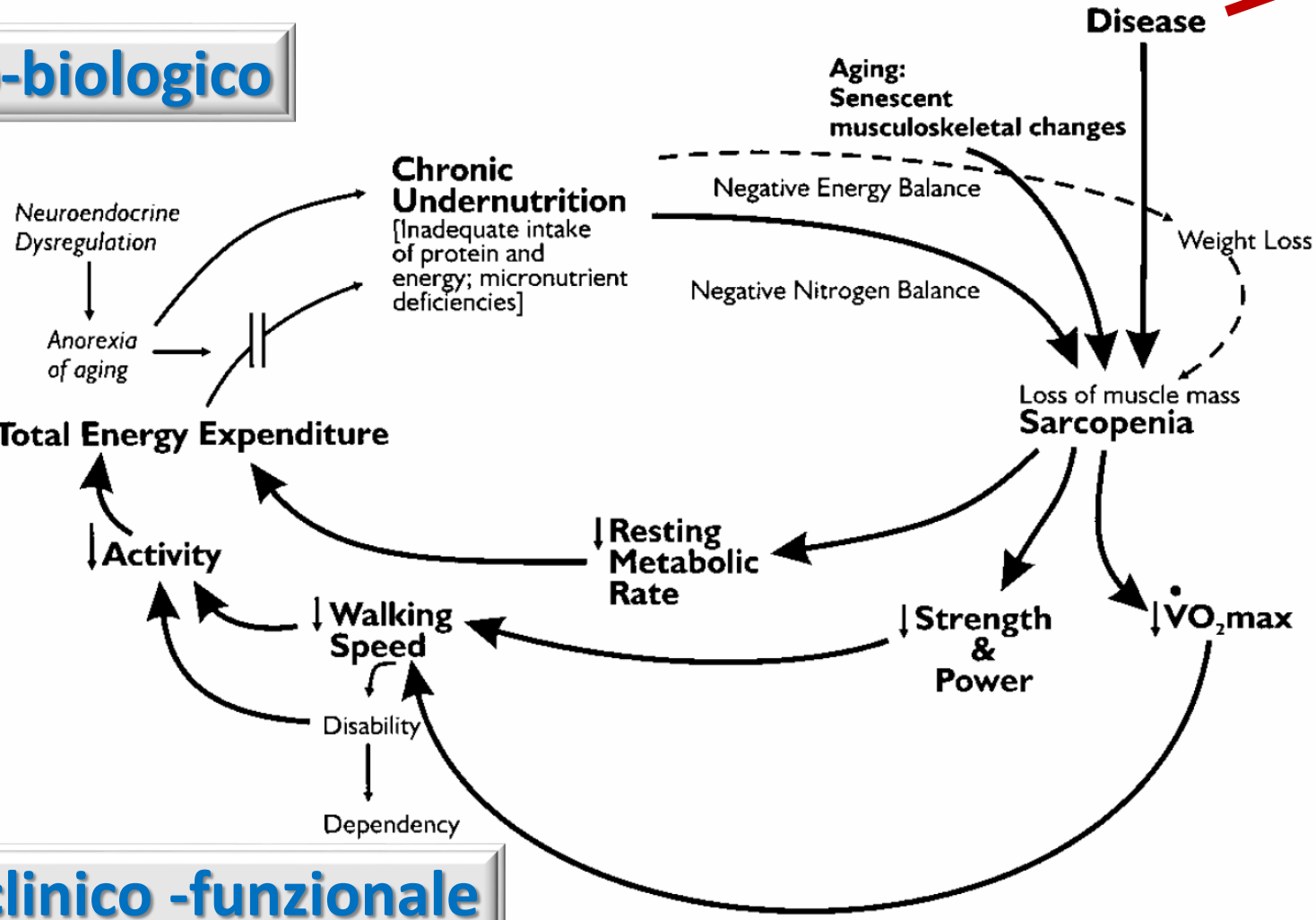
Frailty in Older Adults: Evidence for a Phenotype

Linda P. Fried,[1] Catherine M. Tangen,[2] Jeremy Walston,[1] Anne B. Newman,[3] Calvin Hirsch,[4]
John Gottdiener,[5] Teresa Seeman,[6] Russell Tracy,[7] Willem J. Kop,[8] Gregory Burke,[9]
and Mary Ann McBurnie[2] for the Cardiovascular Health Study
Collaborative Research Group

Heart Failure

Piano-biologico

Chronic inflammation



Sintomi-declino fisico-funzionale

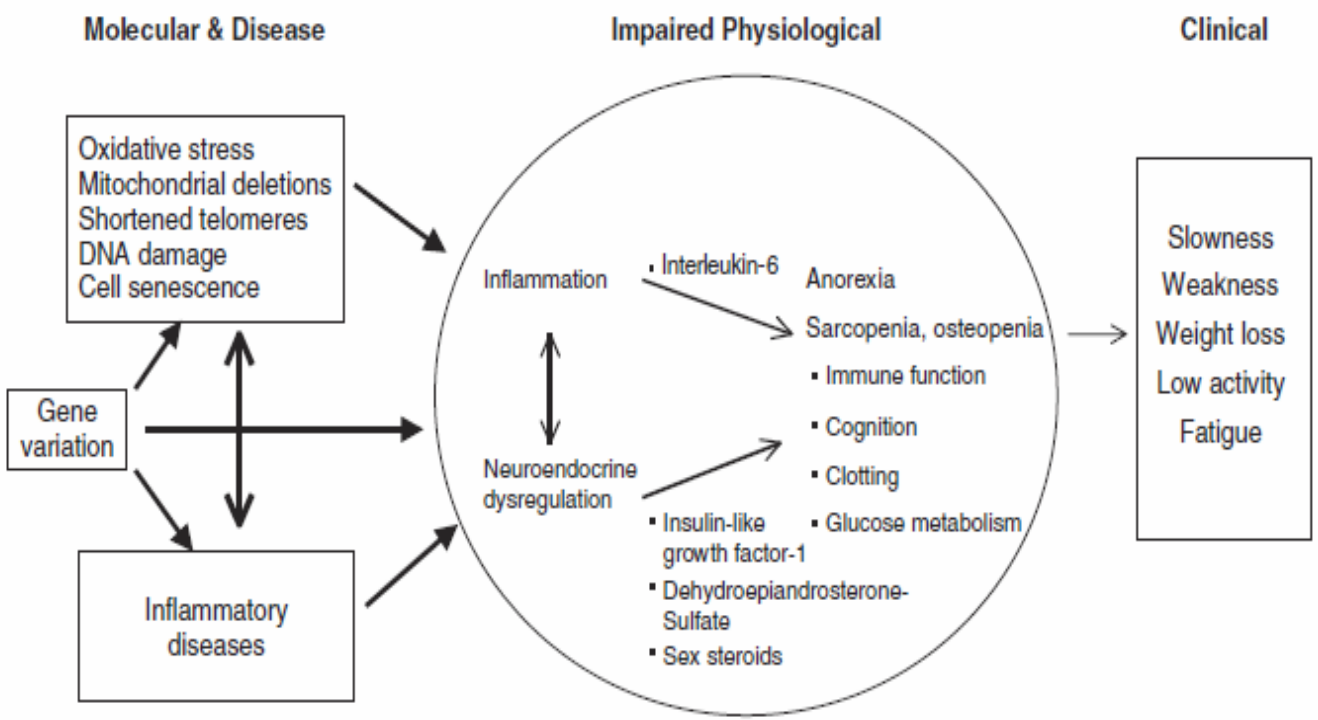
Piano-clinico -funzionale

Journal of Gerontology: MEDICAL SCIENCES
2001, Vol. 56A, No. 3, M146–M156

SPECIAL ARTICLE

Research Agenda for Frailty in Older Adults: Toward a Better Understanding of Physiology and Etiology: Summary from the American Geriatrics Society/National Institute on Aging Research Conference on Frailty in Older Adults

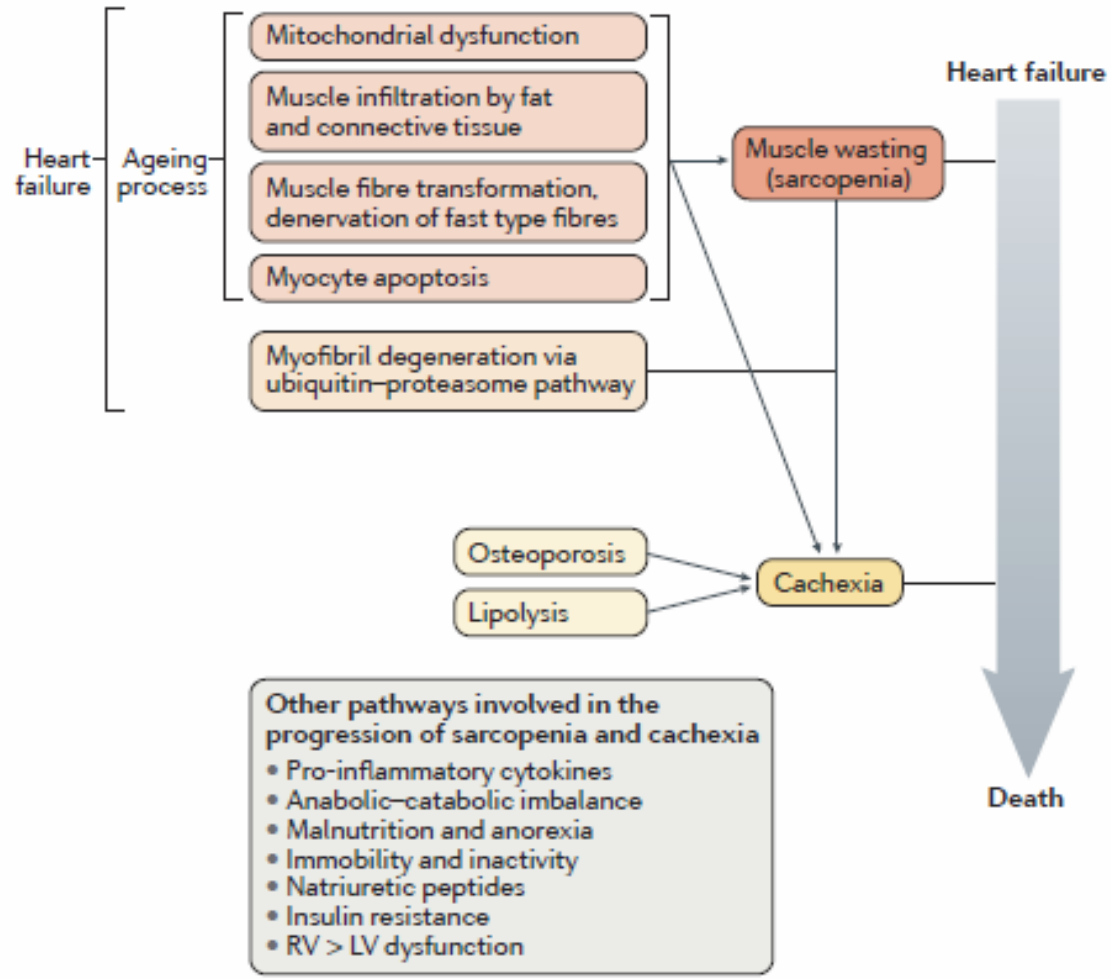
Jeremy Walston, MD, Evan C. Hadley, MD,† Luigi Ferrucci, MD, PhD,† Jack M. Guralnik, MD, PhD,† Anne B. Newman, MD, MPH,‡ Stephanie A. Studenski, MD, MPH,§‖ William B. Ershler, MD,¶ Tamara Harris, MD,† and Linda P. Fried, MD, MPH**



JAGS 54:991–1001, 2006

Muscle wasting and cachexia in heart failure: mechanisms and therapies

Stephan von Haehling[1], Nicole Ebner[1], Marcelo R. dos Santos[1,2], Jochen Springer[1] and Stefan D. Anker[1,3]



Contents lists available at ScienceDirect

Free Radical Biology and Medicine

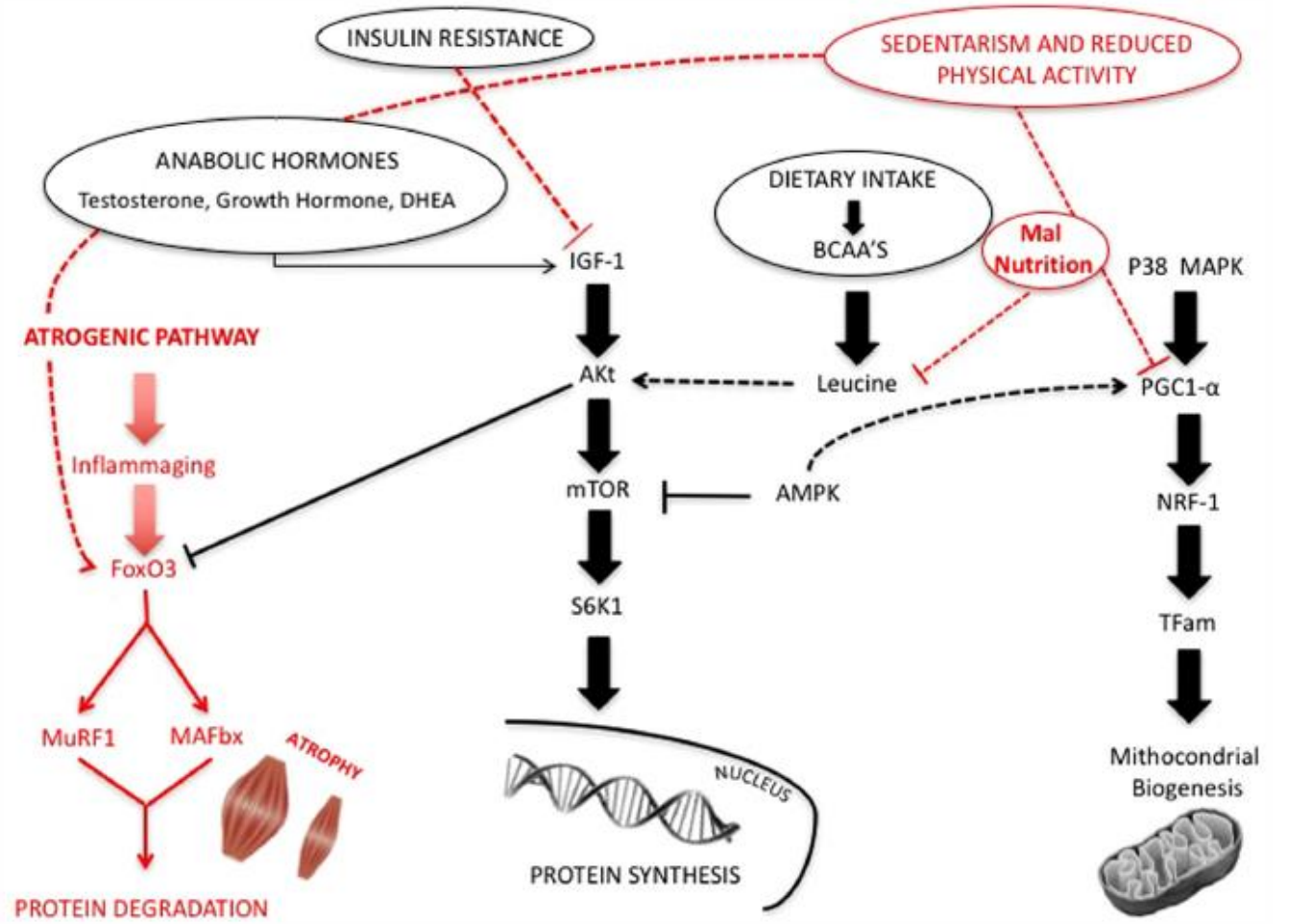
journal homepage: www.elsevier.com/locate/freeradbiomed

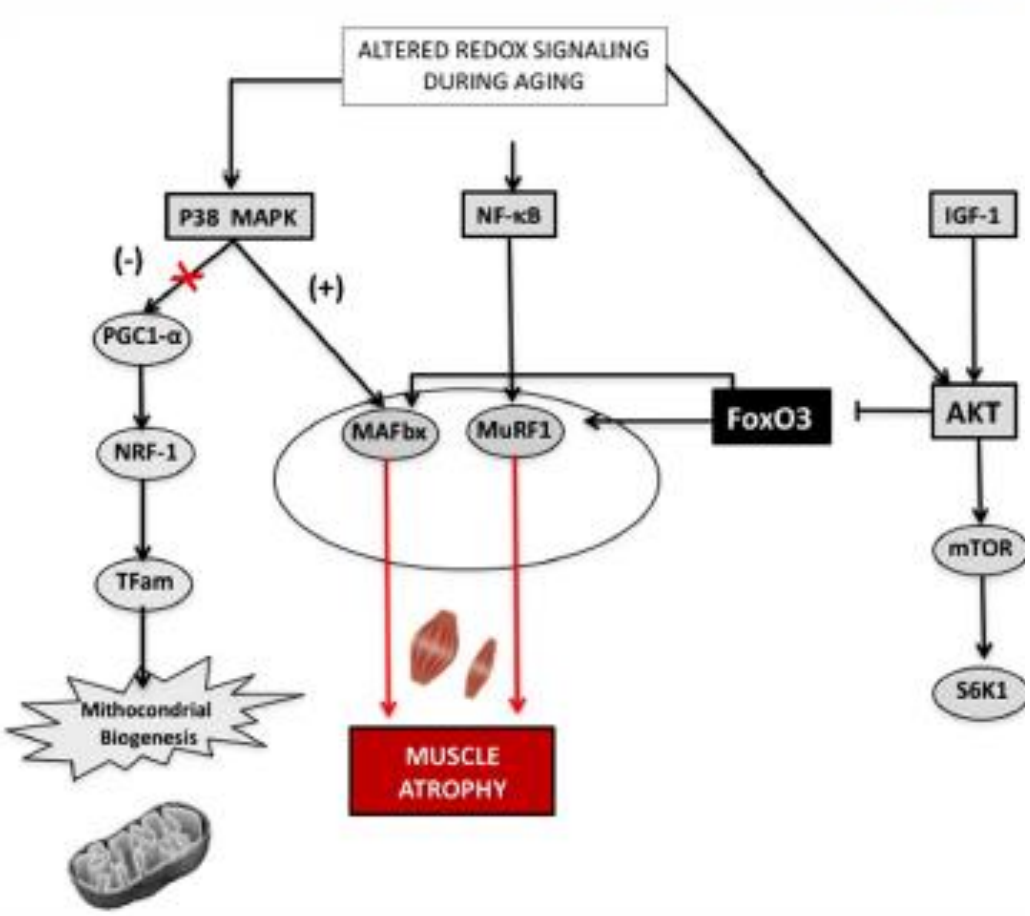
Biology of frailty

Review Article

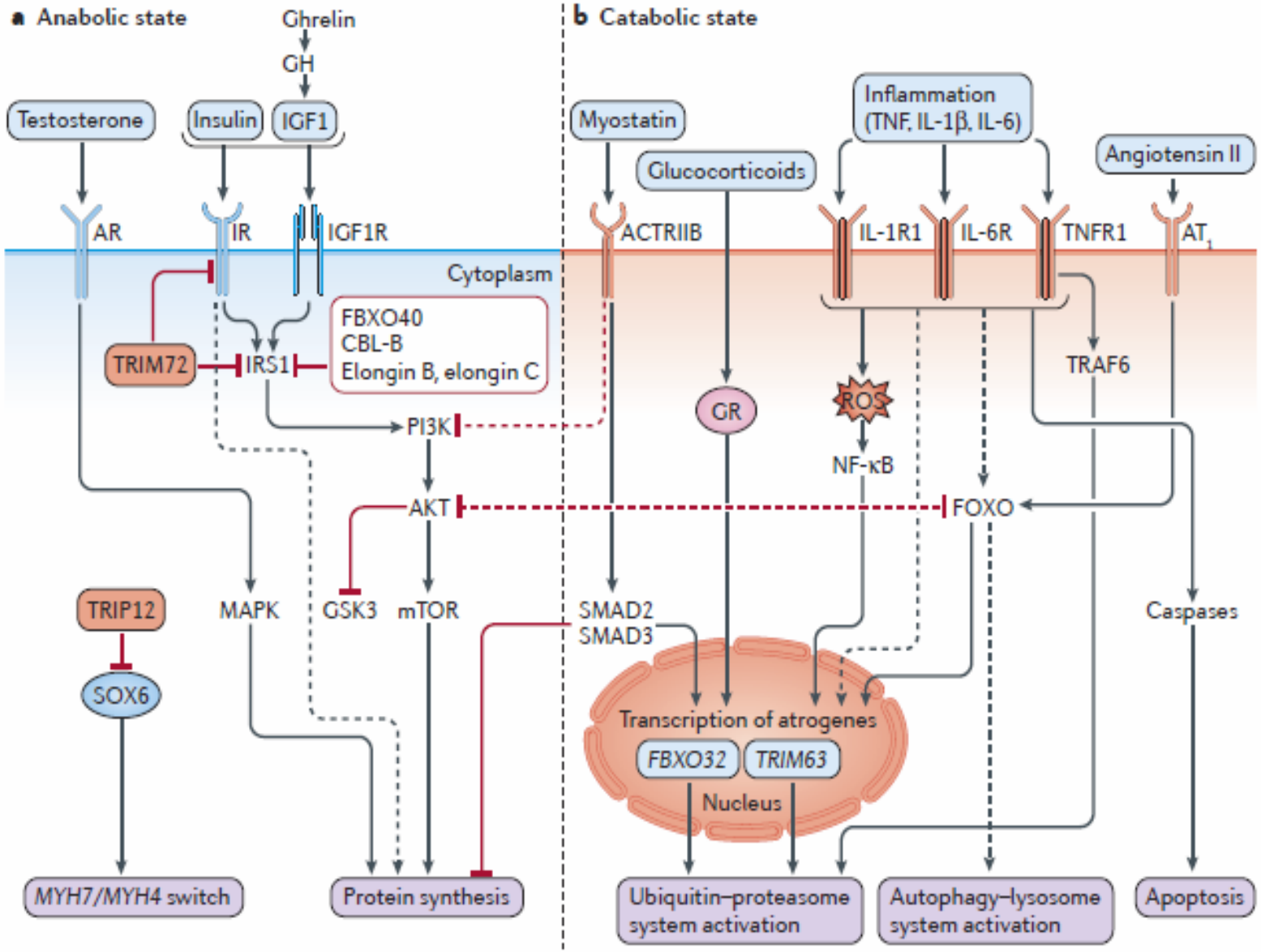
Sarcopenia, frailty and their prevention by exercise

C.M. Nascimento[c], M. Ingles[b], A. Salvador-Pascual[a], M.R. Cominetti[c], M.C. Gomez-Cabrera[a,*], J. Viña[a]



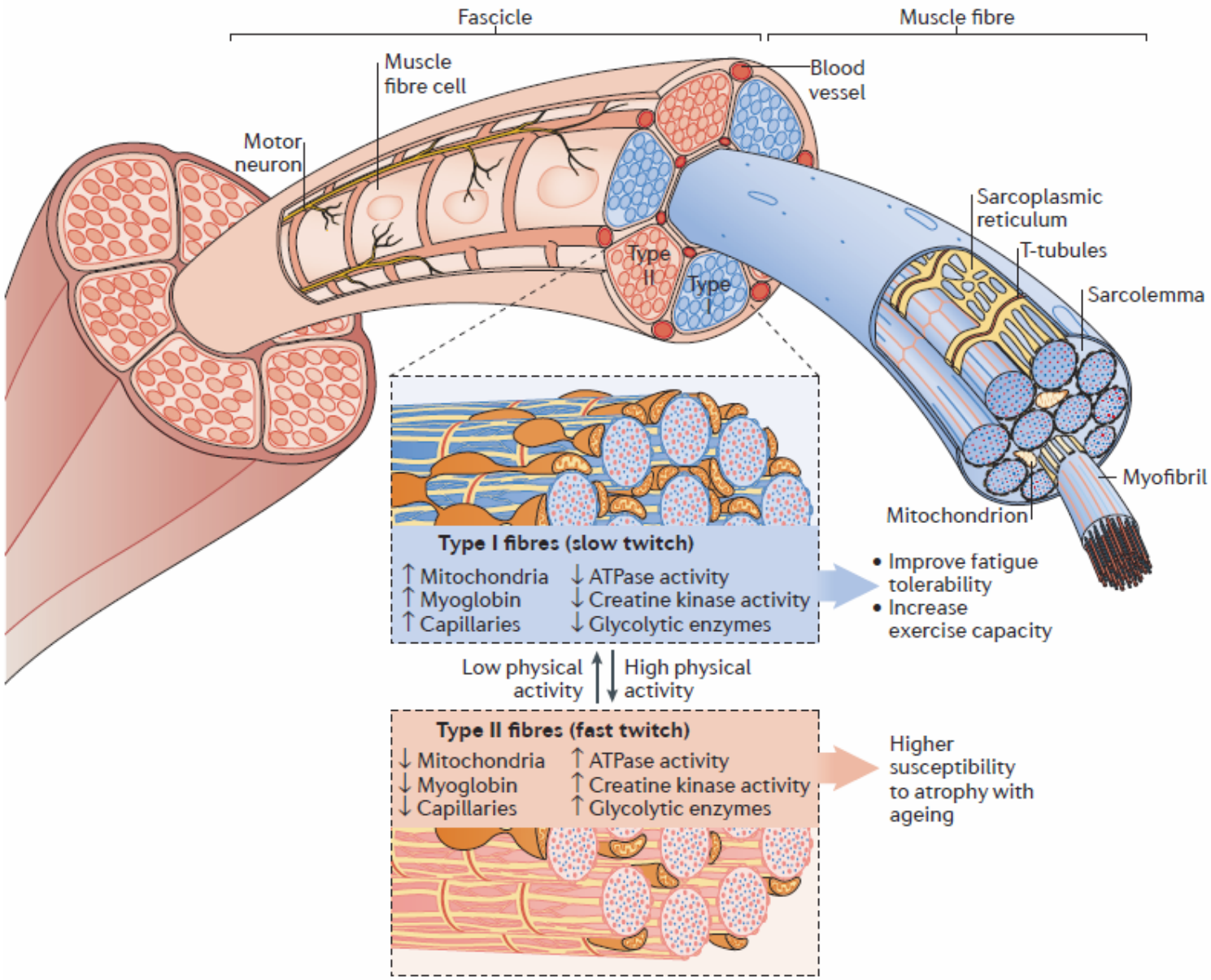


Anabolic/catabolic imbalance in muscle wasting of heart failure



Since skeletal muscle structure is a matter of permanent changes, **an anabolic-/catabolic-imbalance** is required for increased degradation of myofibrils and myocyte apoptosis. Looking at this imbalance, **muscle wasting may be a consequence of reduced muscle anabolism, increased muscle catabolism, or both**. The maintenance of balance depends largely on the balance betweenthe anabolic players growth hormone and insulin-likegrowth factor-1 and the catabolic factors tumor necrosis factor (TNF), interleukin-1 , interferon- , myostatin, and gluco-corticoids

Changes in muscle structure



Physical inactivity

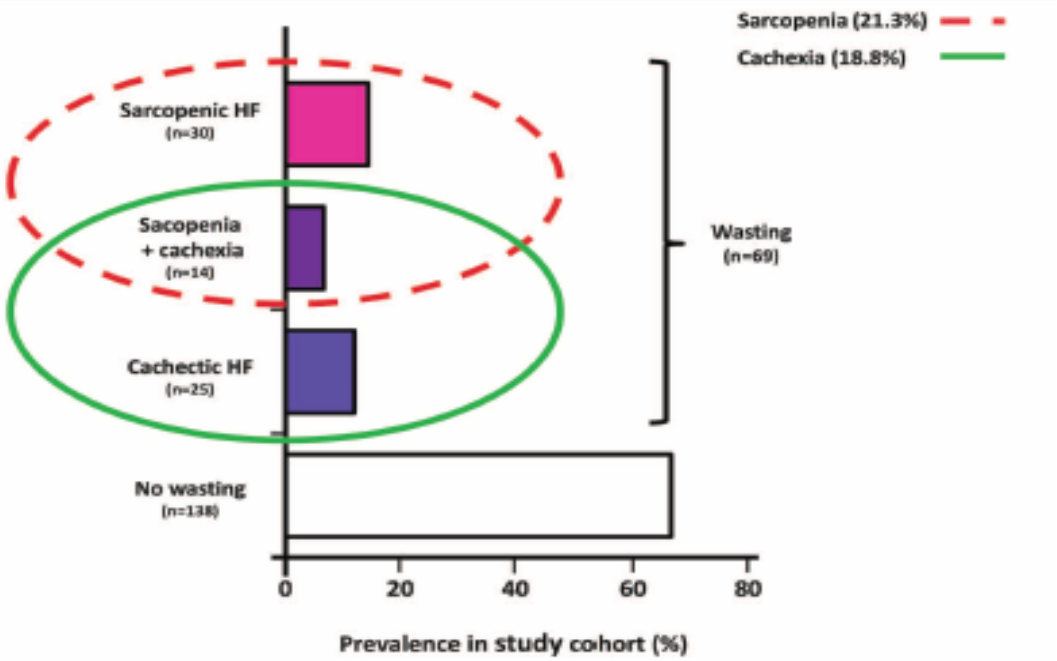
Aging process

Heart Failure

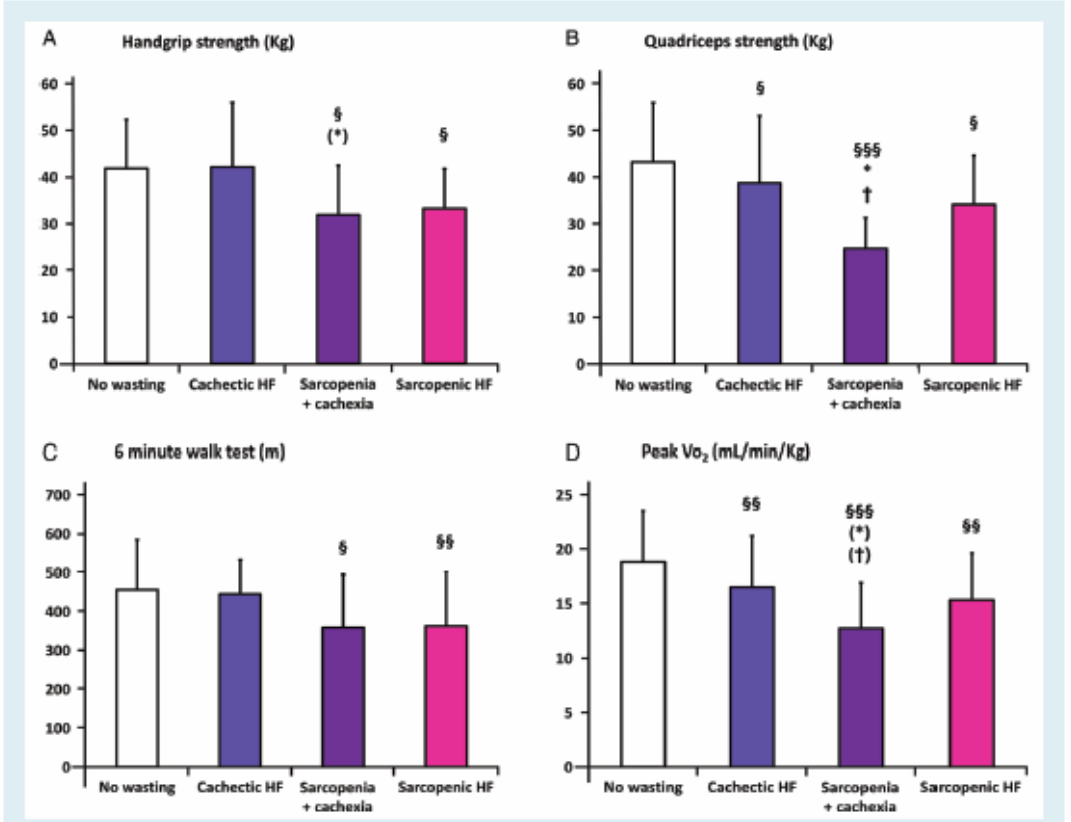
ESC European Society of Cardiology
European Journal of Heart Failure (2018)
doi:10.1002/ejhf.1304

RESEARCH ARTICLE

Comparison of sarcopenia and cachexia in men with chronic heart failure: results from the Studies Investigating Co-morbidities Aggravating Heart Failure (SICA-HF)



	All ($n=207$)	No wasting ($n=138$)	Cachectic HF ($n=25$)	Muscle wasting ($n=44$)	*P*-value
Handgrip strength (kg)	39.8 ± 11.2	41.8 ± 10.5	42.1 ± 13.8	32.8 ± 9.1§(*)	0.009
Quadriceps strength (kg)	39.9 ± 13.3	43.2 ± 12.7	38.7 ± 14.4(§)	31.1 ± 10.4§	0.002
6MWT (m)	438 ± 136	455 ± 129	444 ± 88	360 ± 135§	0.007
Peak VO_2 (mL/min/kg)	17.7 ± 4.9	18.8 ± 4.7	16.5 ± 4.7§	14.4 ± 4.4§	< 0.001
SPPB score	10.5 ± 2.0	10.8 ± 1.7	10.7 ± 1.6	9.3 ± 2.6§(*)	0.009
EQ-5D	0.89 ± 0.09	0.90 ± 0.09	0.91 ± 0.09	0.83 ± 0.09§*	0.04

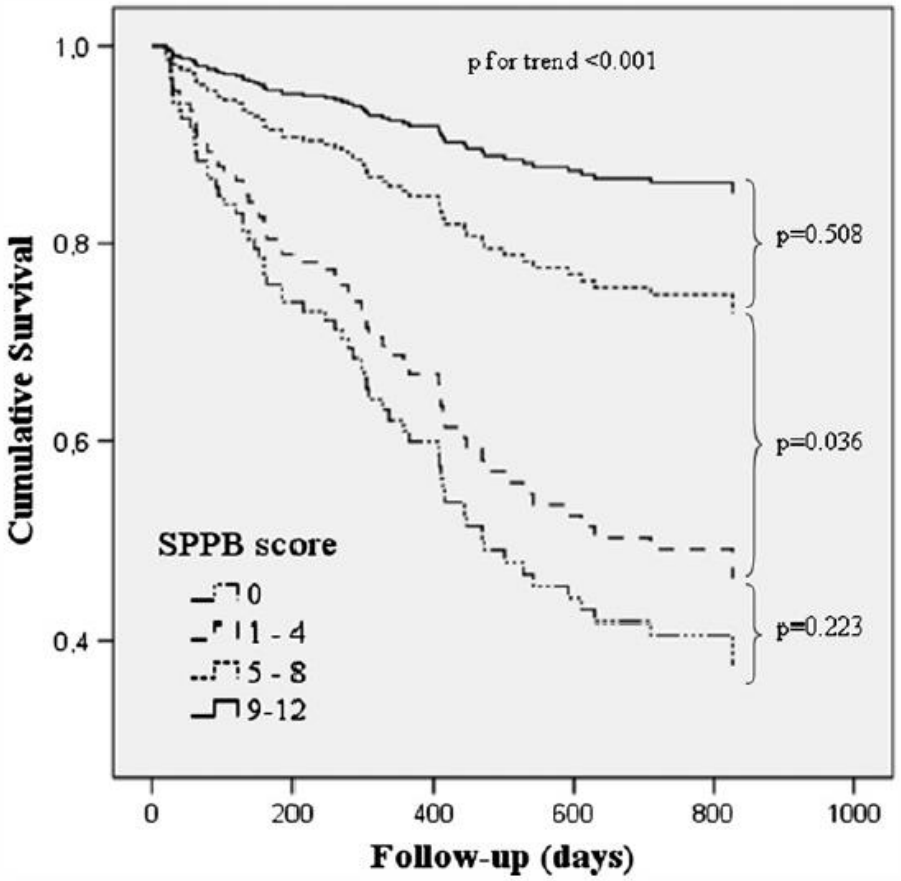


Conclusions

Muscle wasting in elderly subjects has been associated with increasing hospitalization and mortality rates.[28] Our analysis could thus raise a flag that in such a progressive limiting disease like HF, sarcopenia with or without cachexia is associated with poor functional status and QoL. Both cachexia and sarcopenia appear to be valuable targets for the development of therapies in order to improve physical well-being as exemplified by reduced peak VO_2. Increasing muscle mass and muscle strength appear to be most important in this regard.

Lower Extremity Performance Measures Predict Long-Term Prognosis in Older Patients Hospitalized for Heart Failure

DANIELA CHIARANTINI, MD,[1] STEFANO VOLPATO, MD, MPH,[2] FOTINI SIOULIS, MD,[2] FRANCESCA BARTALUCCI, MD,[1] LAURA DEL BIANCO, MD,[1] IRENE MANGANI, MD,[1] GIUSEPPE PEPE, MD,[3] FRANCESCA TARANTINI, MD, PhD,[1] ANDREA BERNI, MD,[4] NICCOLO MARCHIONNI, MD,[1] AND MAURO DI BARI, MD, PhD[1]



Variable	Model 2 HR (95% CI)	*P*
SPPB		.001*
0	6.06 (2.19–16.76)	.001
1–4	4.78 (1.63–14.02)	.004
5–8	1.95 (0.67–5.70)	.223
9–12	Ref.	
Gender	1,16 (0.68–1.99)	.583
Age (y)	0.98 (0.94–1.02)	.355
Site (Ferrara vs. Florence)	1.92 (0.68–5.40)	.216
LVEF (%)	0.97 (0.95–0.99)	.005
CIRS-C	1.50 (1.14–1.98)	.004
NYHA class	1.52 (1.06–2.16)	.022

Conclusions: SPPB is an independent predictor of long-term survival of older subjects hospitalized for decompensated HF. (*J Cardiac Fail 2010;16:390–395*)

Key Words: Short Physical Performance Battery, cardiac failure, elderly, survival.

Incremental Value of Gait Speed in Predicting Prognosis of Older Adults With Heart Failure

Insights From the IMAGE-HF Study

Giovanni Pulignano, MD,[a] Donatella Del Sindaco, MD,[b] Andrea Di Lenarda, MD,[c] Gianfranco Alunni, MD,[d] Michele Senni, MD,[e] Luigi Tarantini, MD,[f] Giovanni Cioffi, MD,[g] Maria Denitza Tinti, MD,[a] Giulia Barbati, PhD,[c] Giovanni Minardi, MD,[a] Massimo Uguccioni, MD,[a] on behalf of the IMAGE-HF Study Investigators

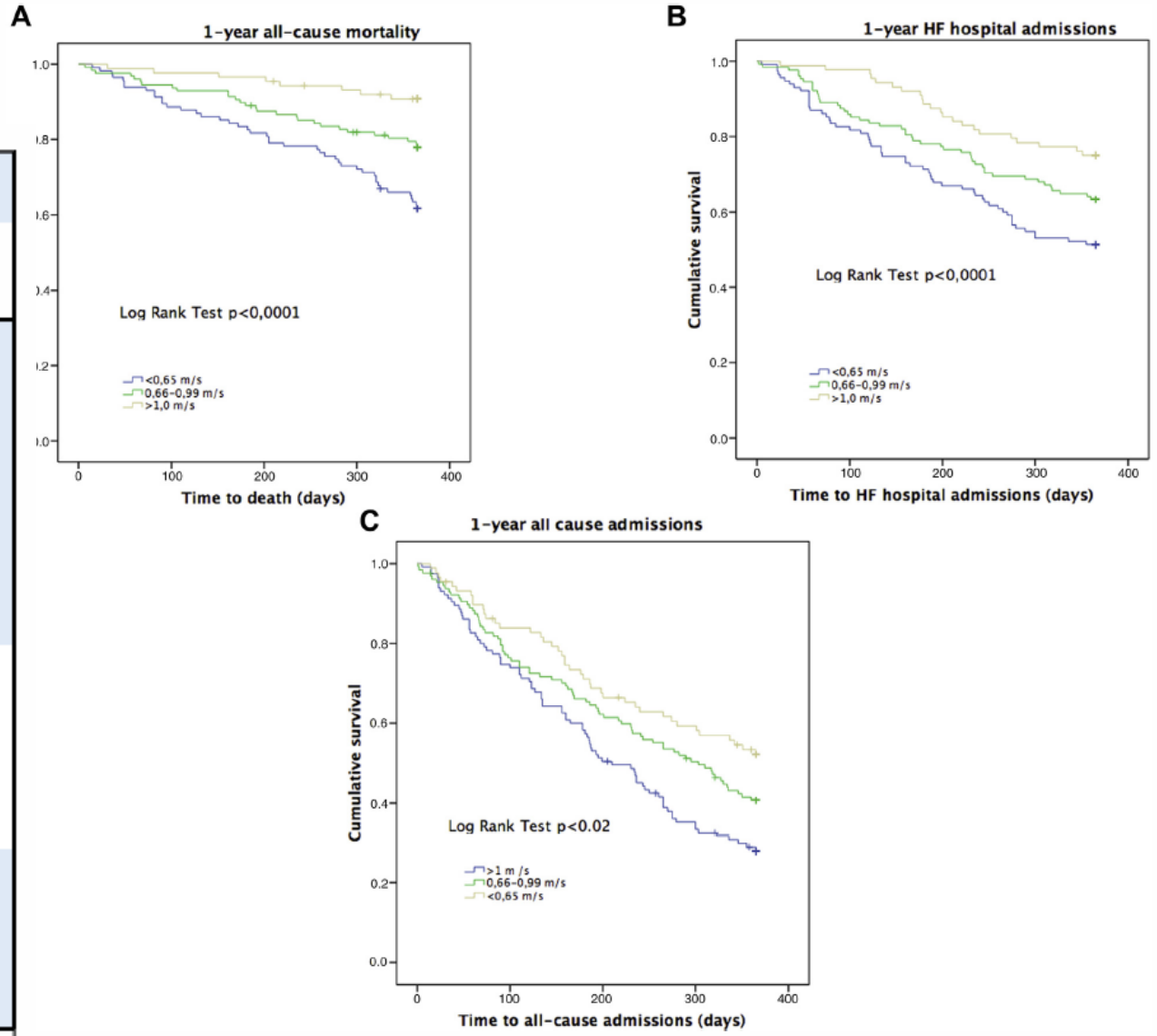
JACC: HEART FAILURE VOL. 4, NO. 4, 2016

ISSN 2213-1779/$36.00

TABLE 4 Multivariable Regression Analyses (Cox Models)

	HR	95% CI Lower	95% CI Upper	p Value
All-cause mortality at 1-yr follow-up				
Age	1.049	1.005	1.095	0.029
SBP	0.980	0.980	0.993	0.020
No beta-blocker therapy	1.992	1.242	3.194	0.004
NYHA class III/IV (yes vs. no)	2.038	1.224	3.393	0.006
LVEF <20% (yes vs. no)	2.419	1.431	4.087	0.001
Gait speed (tertiles)	0.620	0.434	0.884	0.008
Anemia (hemoglobin <12 vs. ≥12 g/dl)	2.359	1.456	3.824	<0.001
Hospital admissions for heart failure at 1-yr follow-up				
No beta-blocker	1.760	1.225	2.530	0.002
NYHA III/IV	2.127	1.455	3.109	<0.001
eGFR <30 ml/min/1.73 m^2	1.605	1.098	2.346	0.015
Gait speed (tertiles)	0.697	0.547	0.899	0.004
All-cause hospital admissions at 1-yr follow-up				
Gait speed (tertiles)	0.741	0.613	0.895	0.002
eGFR <30 ml/min/1.73 m^2	1.455	1.059	1.997	0.021
NYHA class III/IV	1.422	1.067	1.894	0.016

FIGURE 2 Kaplan-Meier Curves for All-Cause Mortality, Heart Failure Hospitalizations, and All-Cause Hospitalizations, According to Gait Speed Tertiles (≤0.65, 0.66 to 0.99, and ≥1.0 m/s)



…..Quali gli effetti della
HF evidence based therapies
su questo
sinergismo NEGATIVO?…

Non selective betablockers

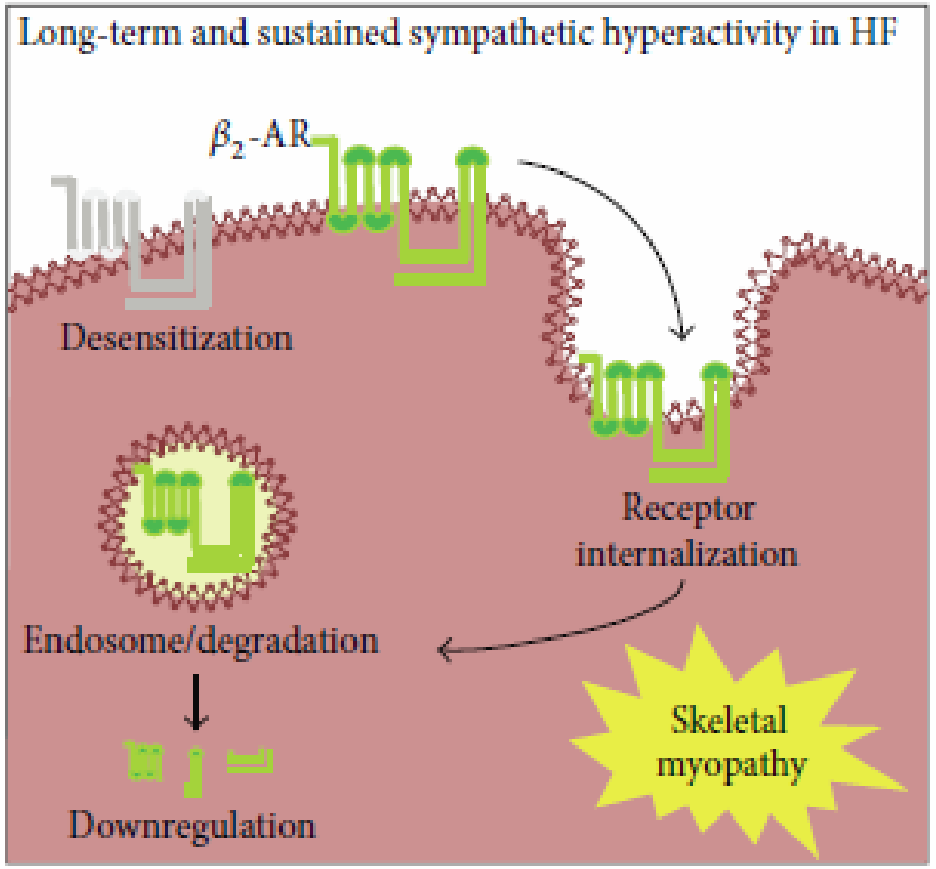
Cardio-Selective Beta-Blocker: Pharmacological Evidence and Their Influence on Exercise Capacity

Dennis Ladage,[1,3] Robert H.G. Schwinger[2] & Klara Brixius[1]

1 Department of Molecular and Cellular Sport Medicine, Institute of Cardiology and Sport Medicine, German Sport University Cologne, Cologne, Germany
2 Clinic II of Internal Medicine and Cardiology, Weiden, Germany
3 Heart Center, Department III of Internal Medicine, University of Cologne, Cologne, Germany

Table 2. Comparison of beta-blockade affecting exercise capacity

Study	Drug	Condition
Dubach 2002	Bisoprolol	Heart failure
Issa 2007	Bisoprolol	Heart failure
Nodari 2003	Atenolol	Heart failure
	Nebivolol	Heart failure
Patrianakos 2005	Nebivolol	DCM
Diehm 2011	Nebivolol	Heart failure
Dalla Libera 2010	Nebivolol	Heart failure
Patrianakos 2005	Nebivolol	Heart failure
	Carvedilol	Heart failure
Suazzi 1999	Carvedilol	Heart failure
Agostini 2002	Carvedilol	Heart failure
Volterrani 2011	Carvedilol	Heart failure
Nessler 2008	Carvedilol	Heart failure
Witte 2005	all	Heart failure
Beloka 2008	Bisoprolol	Healthy
Vankees 2000	Bisoprolol	Healthy
Van Bortel 1992	Nebivolol	Healthy



mitochondrial adaptation
anabolism

vailable online at www.sciencedirect.com
SCIENCE DIRECT
Journal of Molecular and Cellular Cardiology
of Molecular and Cellular Cardiology 38 (2005) 803–807
www.elsevier.com/locate/yjmcc

Rapid communication

ofibrillar protein oxidation in heart failure
protective effect of Carvedilol

arbara Ravara [a], Valerio Gobbo [a], Daniela Danieli Betto [b],
rio [b], Annalisa Angelini [c], Giorgio Vescovo [d]

International Journal of Cardiology
nal Journal of Cardiology 143 (2010) 192–199
www.elsevier.com/locate/ijcard

oxidation in chronic right heart failure in rats:
-blockers prevent it to the same degree?

Luciano Dalla Libera [a], Barbara Ravara [a], Valerio Gobbo [a], Daniela Danieli Betto [b],
Elena Germinario [b], Annalisa Angelini [c], Stefano Evangelista [d], Giorgio Vescovo [e,*]

Clinical Interventions in Aging

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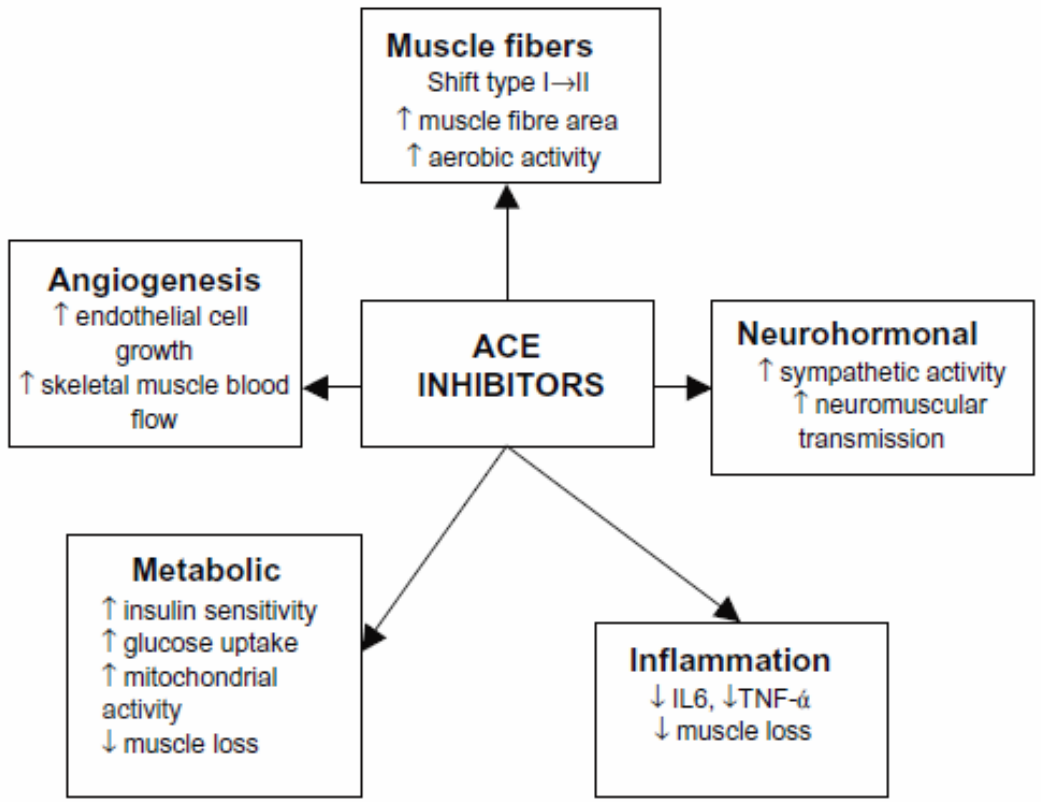
REVIEW

Optimal management of sarcopenia



Clinical Interventions in Aging 2010:5 217–228

ARTICLES

Relation between use of angiotensin-converting enzyme inhibitors and muscle strength and physical function in older women: an observational study

THE LANCET • Vol 359 • March 16, 2002 • www.thelancet.com

Graziano Onder, Brenda W J H Penninx, Rajesh Balkrishnan, Linda P Fried, Paulo H M Chaves, Jeff Williamson, Christy Carter, Mauro Di Bari, Jack M Guralnik, Marco Pahor

Interpretation: ACE inhibitor treatment may halt or slow decline in muscle strength in elderly women with hypertension and without CHF.

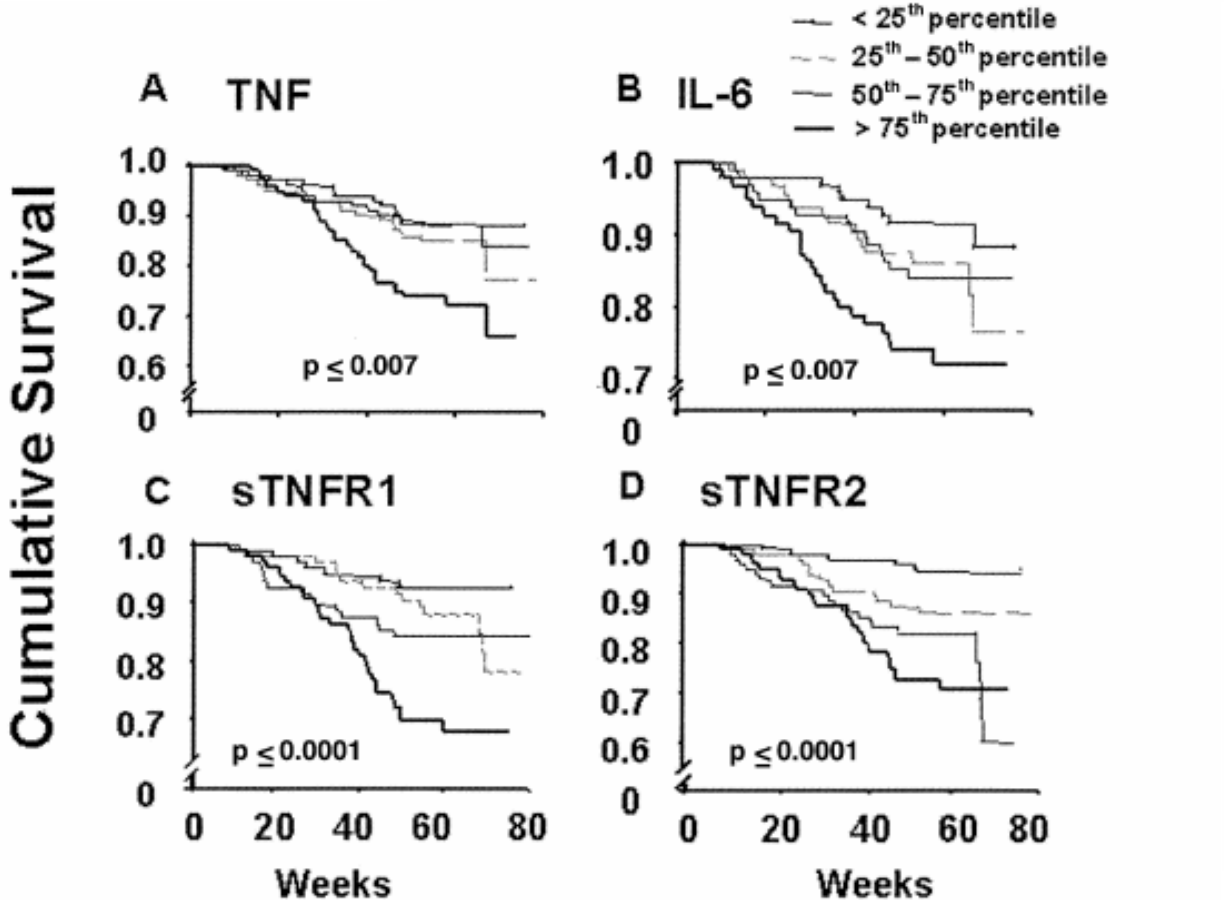
Weight Loss, Muscle Strength, and Angiotensin-Converting Enzyme Inhibitors in Older Adults with Congestive Heart Failure or Hypertension

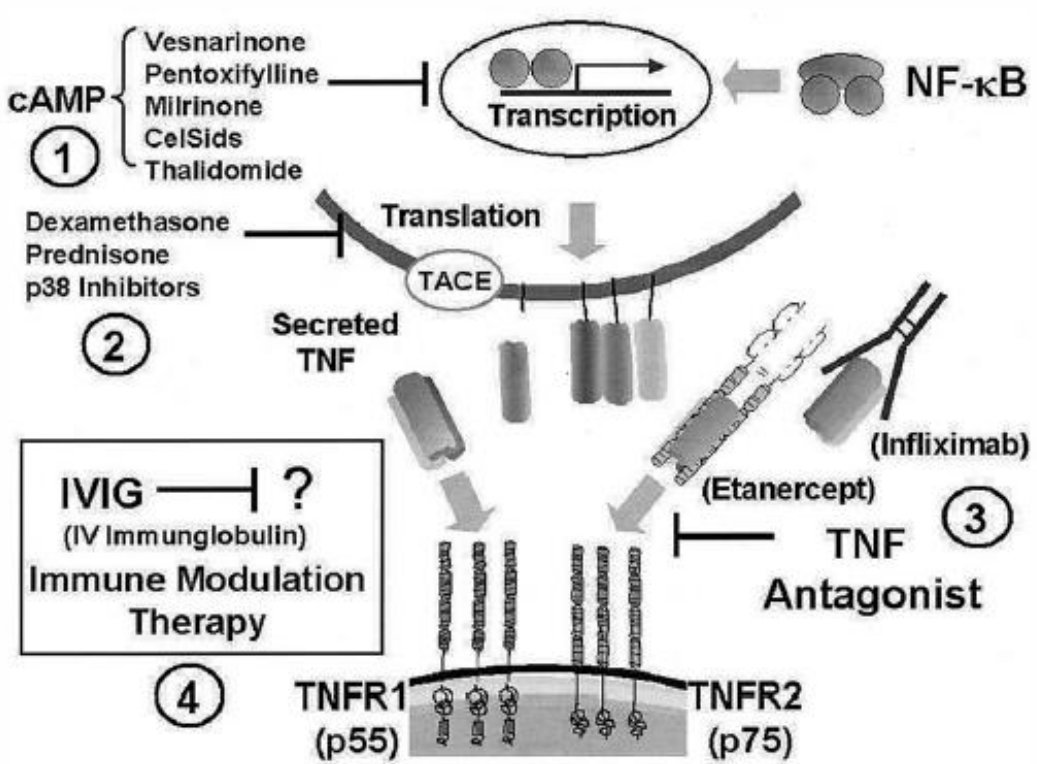
Gina D. Schellenbaum, MPH, Nicholas L. Smith, PhD,* Susan R. Heckbert, MD, PhD,* Thomas Lumley, PhD,† Thomas D. Rea, MD, MPH,‡ Curt D. Furberg, MD, PhD,§ Mary F. Lyles, MD,‖ and Bruce M. Psaty, MD, PhD*‡¶*

In conclusion, ACE inhibitor use was associated with less weight loss in older adults with treated hypertension or CHF, but an association was not found between use of ACE inhibitors and change in grip strength. Some of the benefits older adults with hypertension or CHF receive from ACE inhibitors may be due to weight maintenance.

Targeted Anticytokine Therapy and the Failing Heart

Douglas L. Mann, MD



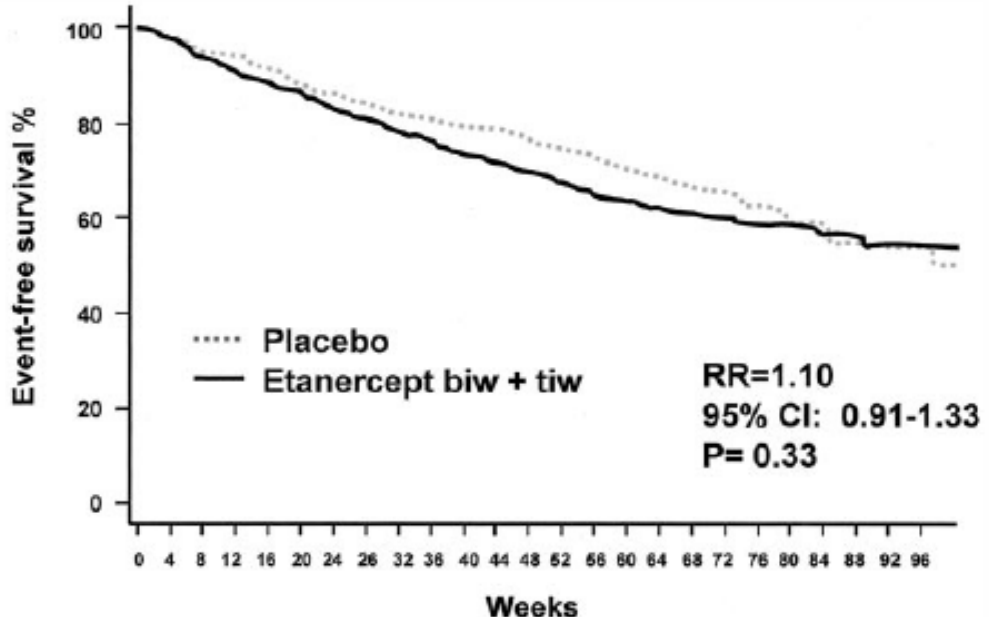


Am J Cardiol 2005;95(suppl):9C–16C

Clinical Investigation and Reports

Targeted Anticytokine Therapy in Patients With Chronic Heart Failure

Results of the Randomized Etanercept Worldwide Evaluation (RENEWAL)

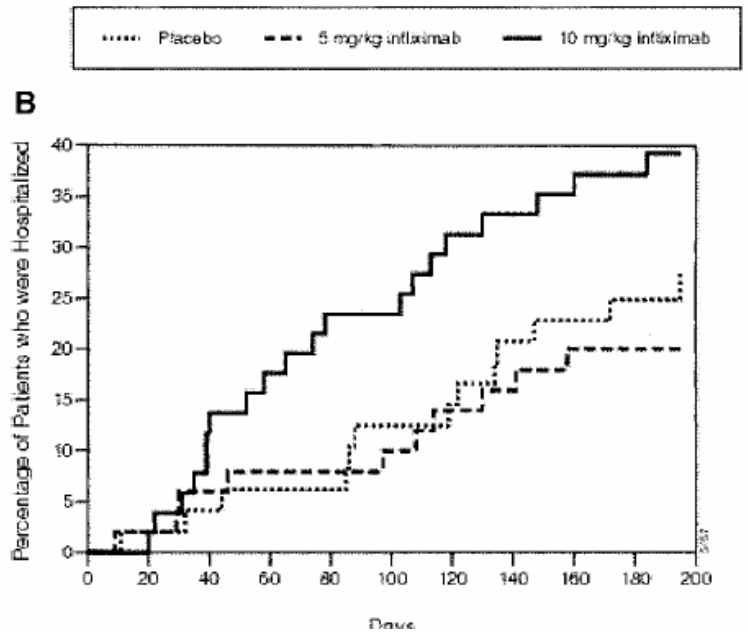


Conclusions—The results of RENEWAL rule out a clinically relevant benefit of etanercept on the rate of death or hospitalization due to chronic heart failure. (*Circulation*. 2004;109:1594-1602.)

(*Circulation*. 2004;109:1594-1602.)

Clinical Investigation and Reports

Randomized, Double-Blind, Placebo-Controlled, Pilot Trial of Infliximab, a Chimeric Monoclonal Antibody to Tumor Necrosis Factor-α, in Patients With Moderate-to-Severe Heart Failure



Conclusions–Short-term TNFα antagonism with infliximab did not improve and high doses (10 mg/kg) adversely affected the clinical condition of patients with moderate-to-severe chronic heart failure. (*Circulation*. 2003;107:3133-3140.)

(*Circulation*. 2003;107:3133-3140.)

Journal of the American College of Cardiology
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ISSN 0735-1097/03/$30.00
doi:10.1016/S0735-1097(03)00848-9

Anti-Inflammatory Effects of Exercise Training in the Skeletal Muscle of Patients With Chronic Heart Failure

Stephan Gielen, MD,* Volker Adams, PHD,* Sven Möbius-Winkler, MD,* Axel Linke, MD,* Sandra Erbs, MD,* Jiangtao Yu, MD,* Werner Kempf, MD,‡ Andreas Schubert, PHD,† Gerhard Schuler, MD,* Rainer Hambrecht, MD*

Leipzig, Germany; and Zürich, Switzerland

Conclusions. In conclusion, a six-month exercise training program in patients with stable CHF is effective in reducing elevated expression of TNF-alpha, IL-6, and IL-1-beta in the skeletal muscle. The reduction of local inflammatory factors is associated with a reduced iNOS expression and intracellular accumulation of nitric oxide.

The present study confirms that training interventions do not only reverse changes associated with disuse but may, in fact, interfere with the inflammation-induced CHF myopathy, that may—in the long run—result in muscle catabolism, wasting, and cardiac cachexia. Thus, regular exercise in CHF patients should be considered not only as a symptomatic intervention aimed at maintaining exercise capacity but also as a therapeutic strategy with local anti-inflammatory effects.

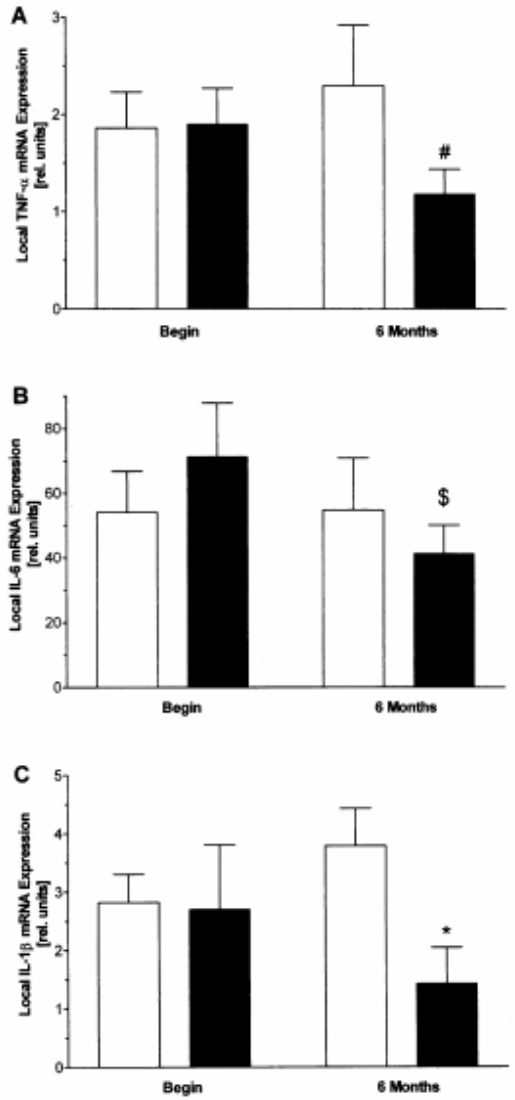


Figure 1. Local expression of tumor necrosis factor (TNF)-alpha **(A)**, interleukin (IL)-6 **(B)**, and IL-1-beta **(C)** in skeletal muscle biopsies of patients in the training group **(black bars)** and the control group **(open bars)** at study baseline and after six months. *$p < 0.05$ versus control group at six months; $p < 0.05$ at six months versus respective baseline; #$p < 0.05$ for change at six months from baseline in training versus control group. mRNA = messenger ribonucleic acid.

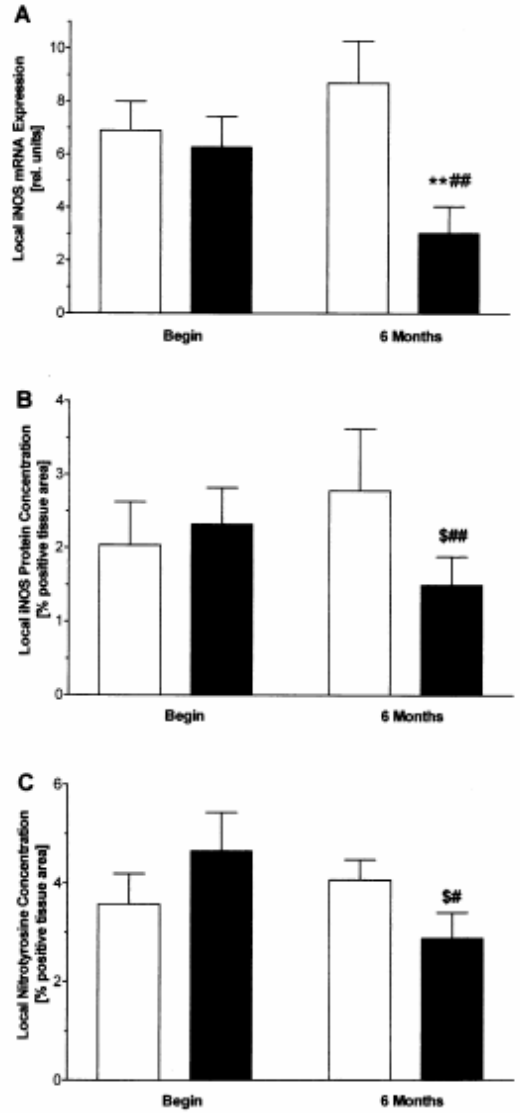
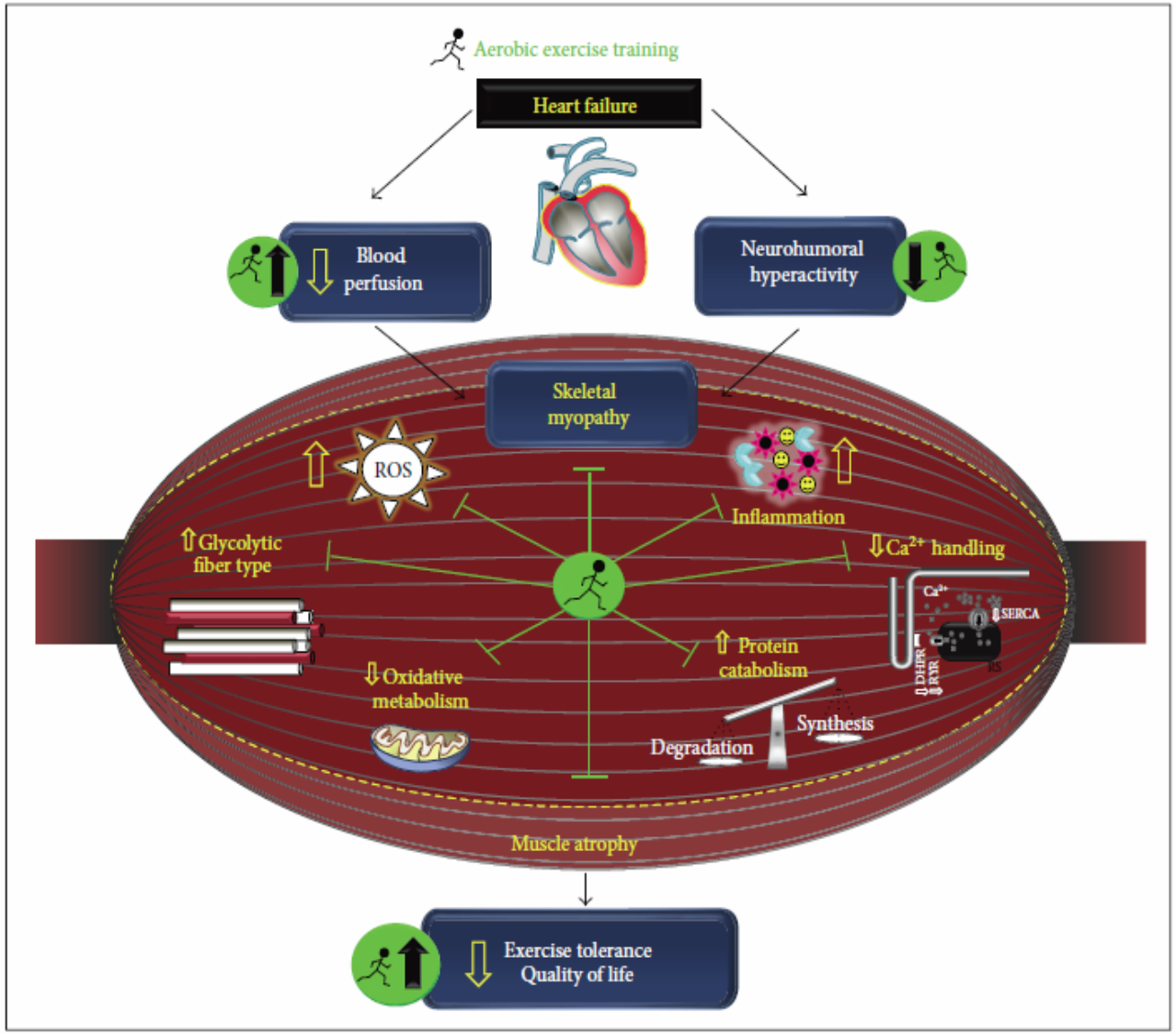


Figure 3. Exercise training **(black bars)** was effective in reducing local inducible nitric oxide synthase (iNOS) messenger ribonucleic acid (mRNA) expression **(A)**, iNOS protein content **(B)**, and nitrotyrosine **(C)** after six months. No change was observed in the control group **(open bars)**. **$p < 0.01$ versus control group at six months; $p < 0.05$ versus respective baseline; #$p < 0.05$; ##$p < 0.01$ for change at six months from baseline in training versus control group.

.. Il ruolo della riabilitazione cardiaca....



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ESC GUIDELINES

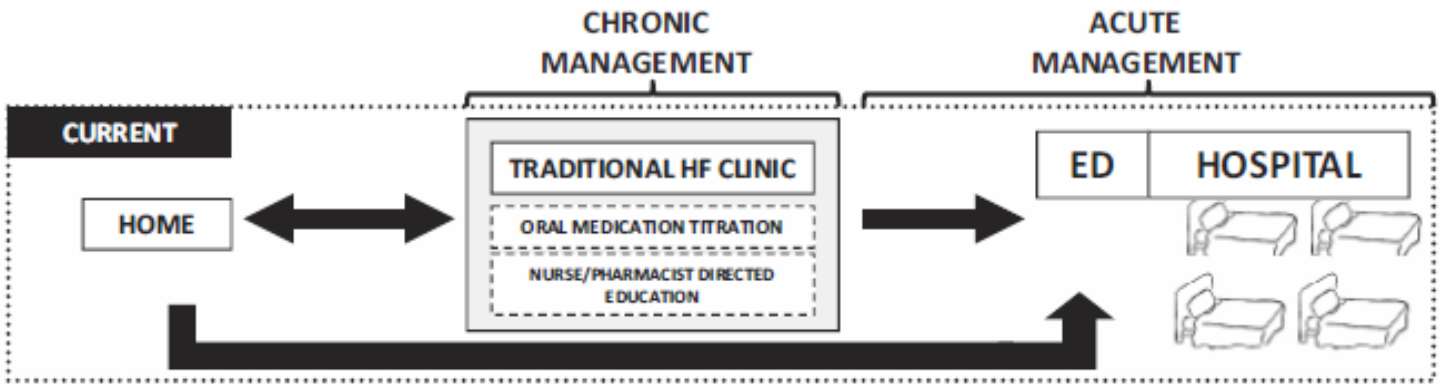
ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2012

The Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2012 of the European Society of Cardiology. Developed in collaboration with the Heart Failure Association (HFA) of the ESC

Recommendations for exercise prescription and multidisciplinary management

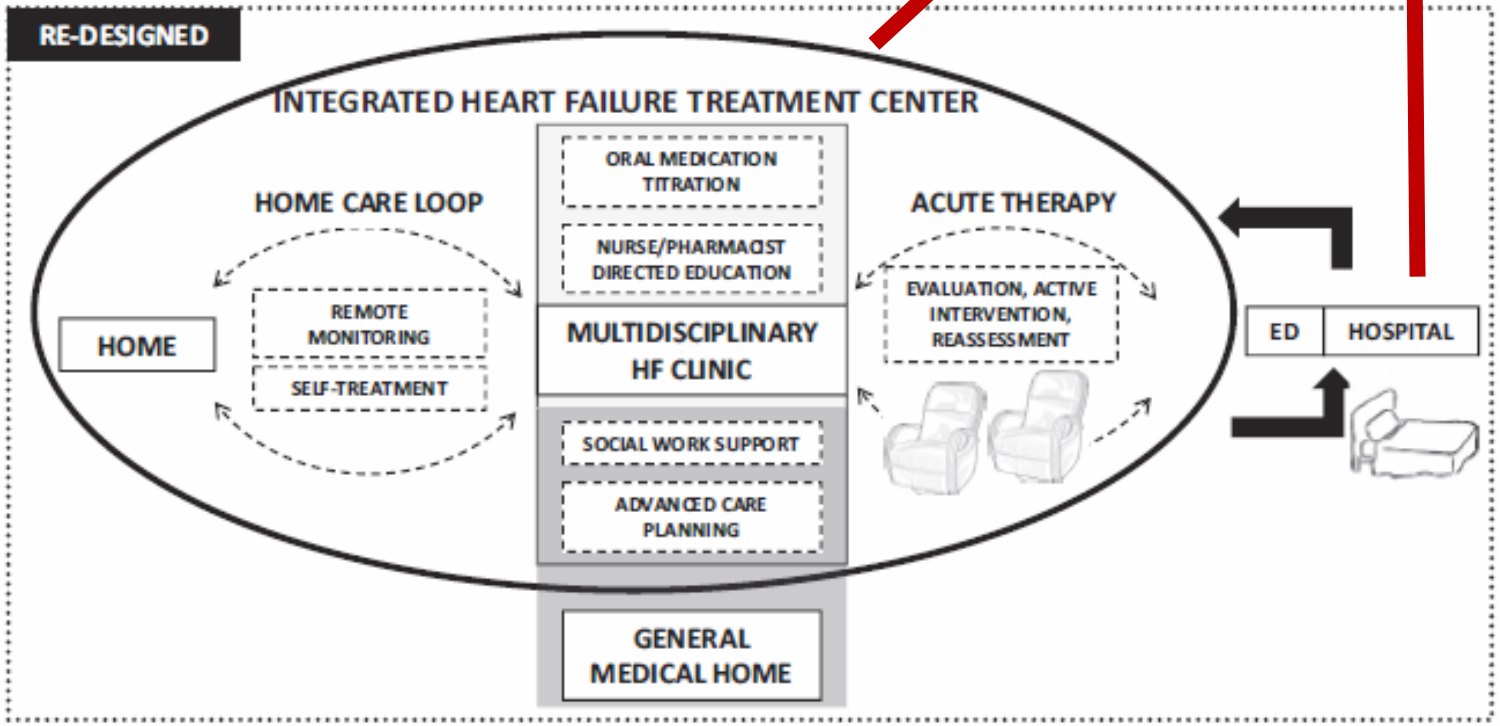
Recommendations	Class[a]	Level[b]	Ref[c]
It is recommended that regular aerobic exercise is encouraged in patients with heart failure to improve functional capacity and symptoms.	I	A	262, 263
It is recommended that patients with heart failure are enrolled in a multidisciplinary-care management programme to reduce the risk of heart failure hospitalization.	I	A	236, 259, 264

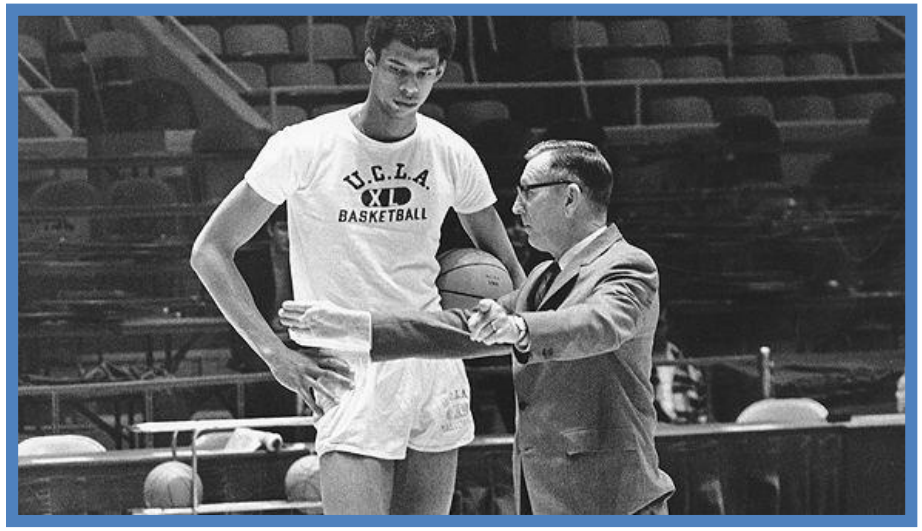
Models of HF care



Cardiac Rehabilitation

Integrate active model for HF management





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