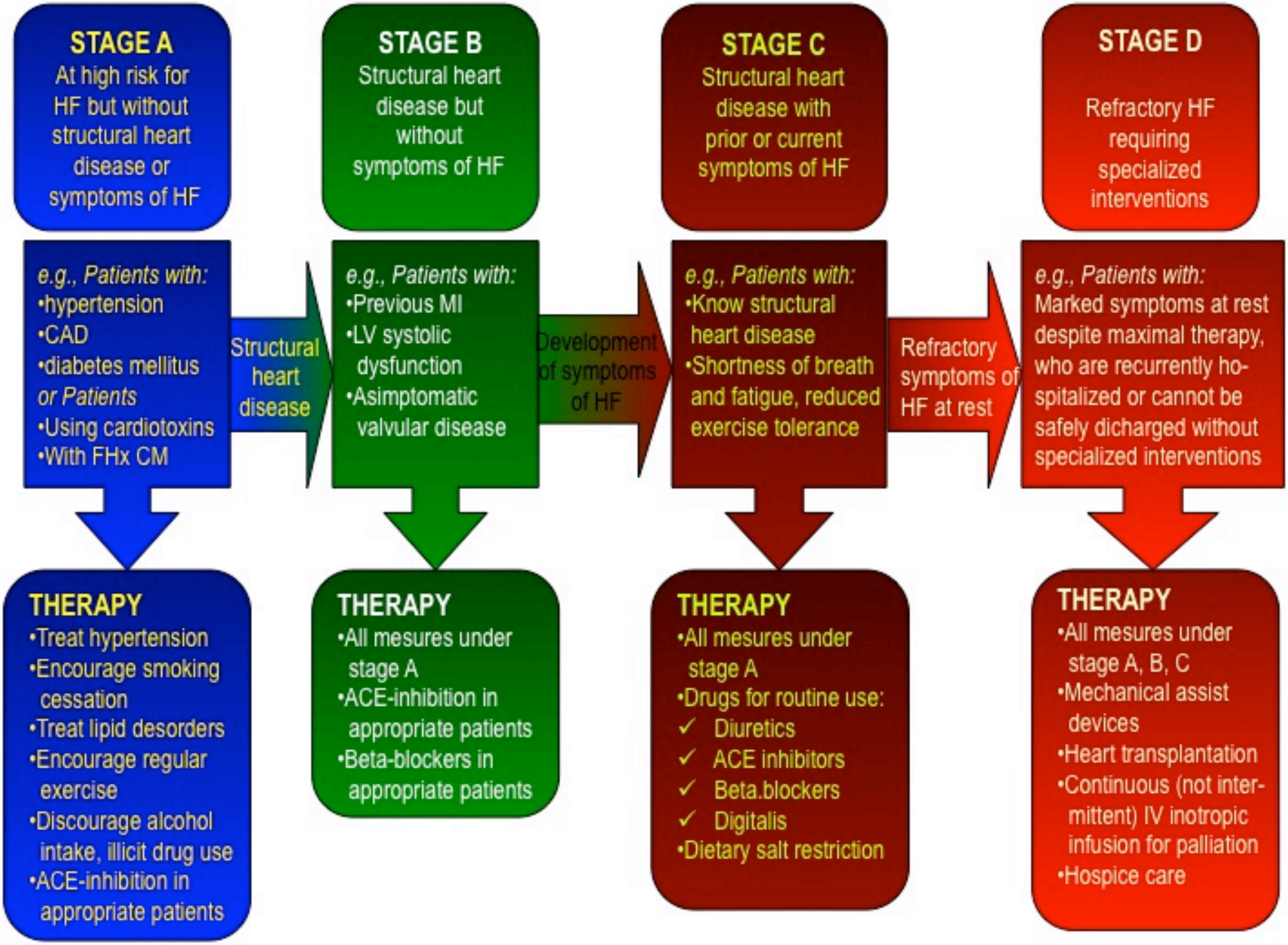
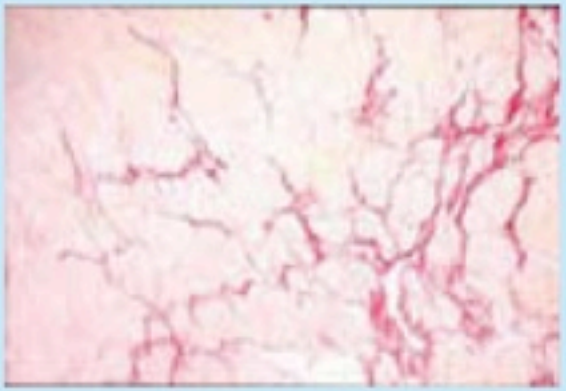
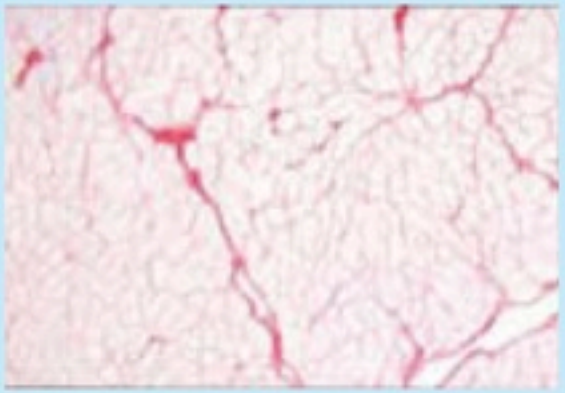

STAGE A
At high risk for HF but without structural heart disease or symptoms of HF
STAGE B
Structural heart disease but without symptoms of HF
STAGE C
Structural heart disease with prior or current symptoms of HF
STAGE D
Refractory HF requiring specialized interventions
e.g., Patients with:
•hypertension
•CAD
•diabetes mellitus
or Patients
•Using cardiotoxins
•With FHx CM
Structural heart disease
e.g., Patients with:
•Previous MI
•LV systolic dysfunction
•Asimptomatic valvular disease
Development of symptoms of HF
e.g., Patients with:
•Know structural heart disease
•Shortness of breath and fatigue, reduced exercise tolerance
Refractory symptoms of HF at rest
e.g., Patients with:
Marked symptoms at rest despite maximal therapy, who are recurrently hospitalized or cannot be safely dicharged without specialized interventions
THERAPY
•Treat hypertension
•Encourage smoking cessation
•Treat lipid desorders
•Encourage regular exercise
•Discourage alcohol intake, illicit drug use
•ACE-inhibition in appropriate patients
THERAPY
•All mesures under stage A
•ACE-inhibition in appropriate patients
•Beta-blockers in appropriate patients
THERAPY
•All mesures under stage A
•Drugs for routine use:
✓ Diuretics
✓ ACE inhibitors
✓ Beta.blockers
✓ Digitalis
•Dietary salt restriction
THERAPY
•All mesures under stage A, B, C
•Mechanical assist devices
•Heart transplantation
•Continuous (not intermittent) IV inotropic infusion for palliation
•Hospice care

(A) - Before



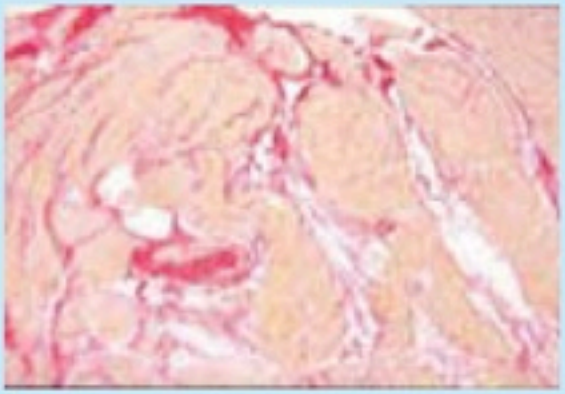
CVF = 5.36%

(A) - After



CVF = 3.26%

(B) - Before



CVF = 9.83%

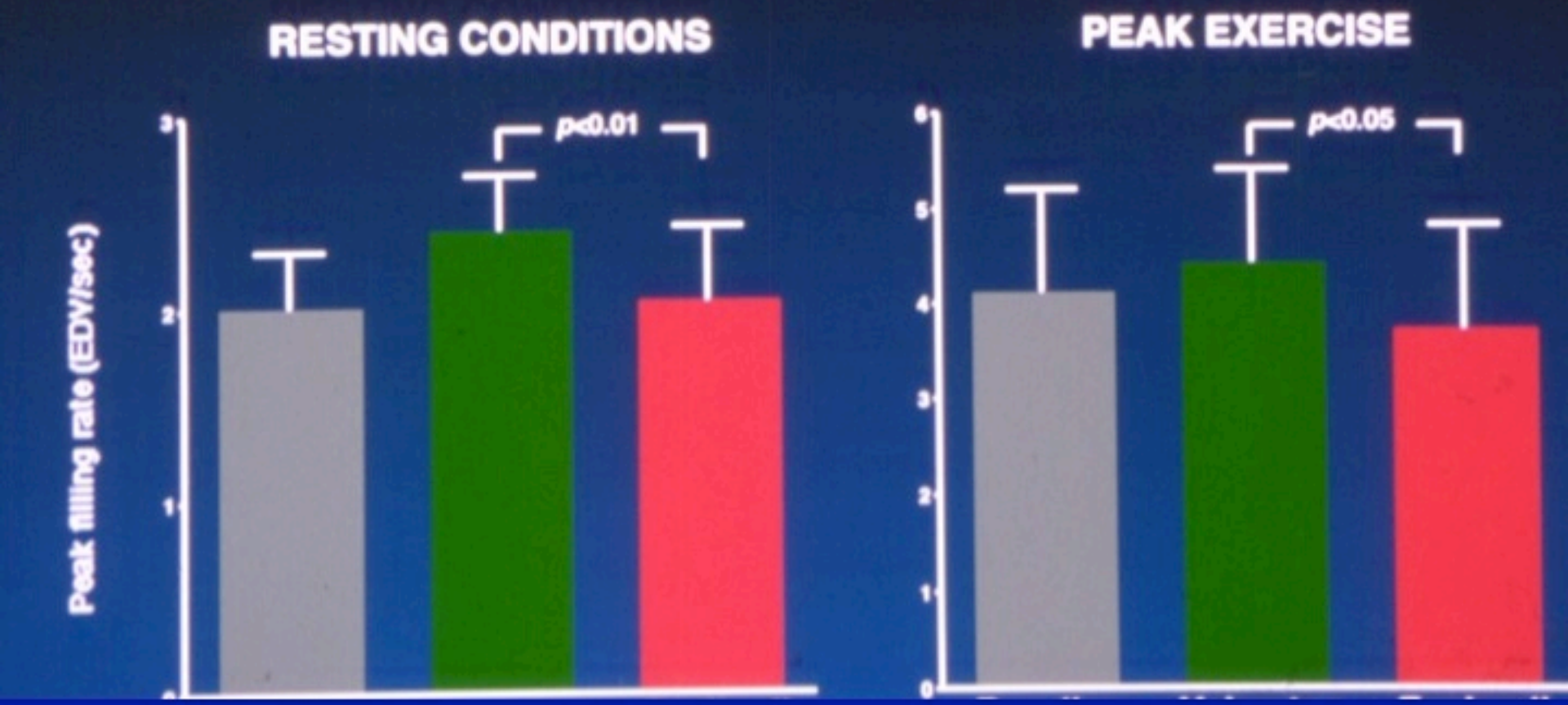
(B) - After

CVF = 2.65%

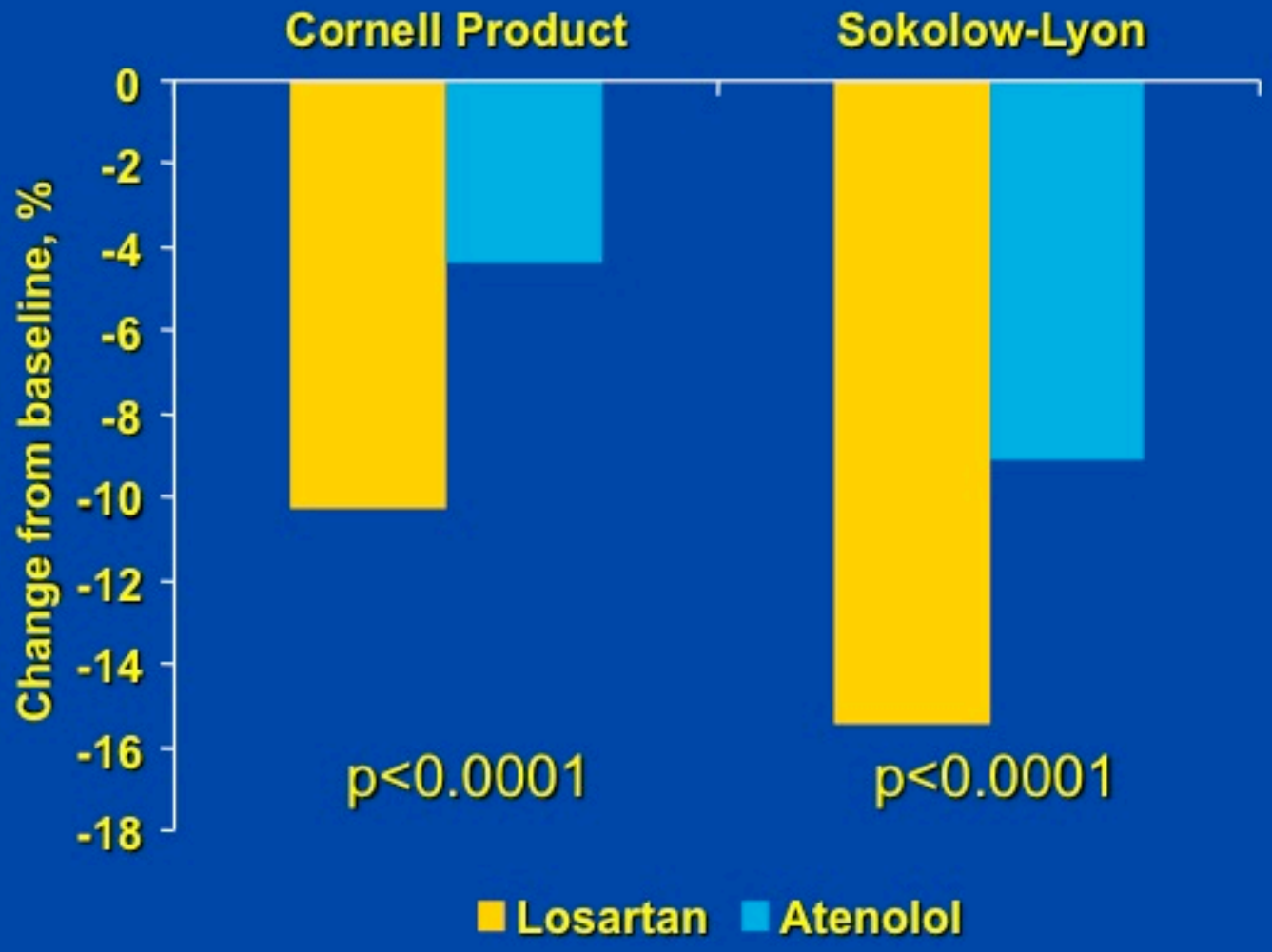
Histological section of myocardial specimen biopsy from a hypertensive patient with nonsevere myocardial fibrosis (A) and a hypertensive patient with severe myocardial fibrosis (B) before and after treatment with losartan. Picrosirius red stain; magnification

Díez J et al. Circulation. 2002;105:2512-2

Left Ventricular Peak Filling Rate in Hypertensive Patients With Impaired Diastolic Function at Randomization

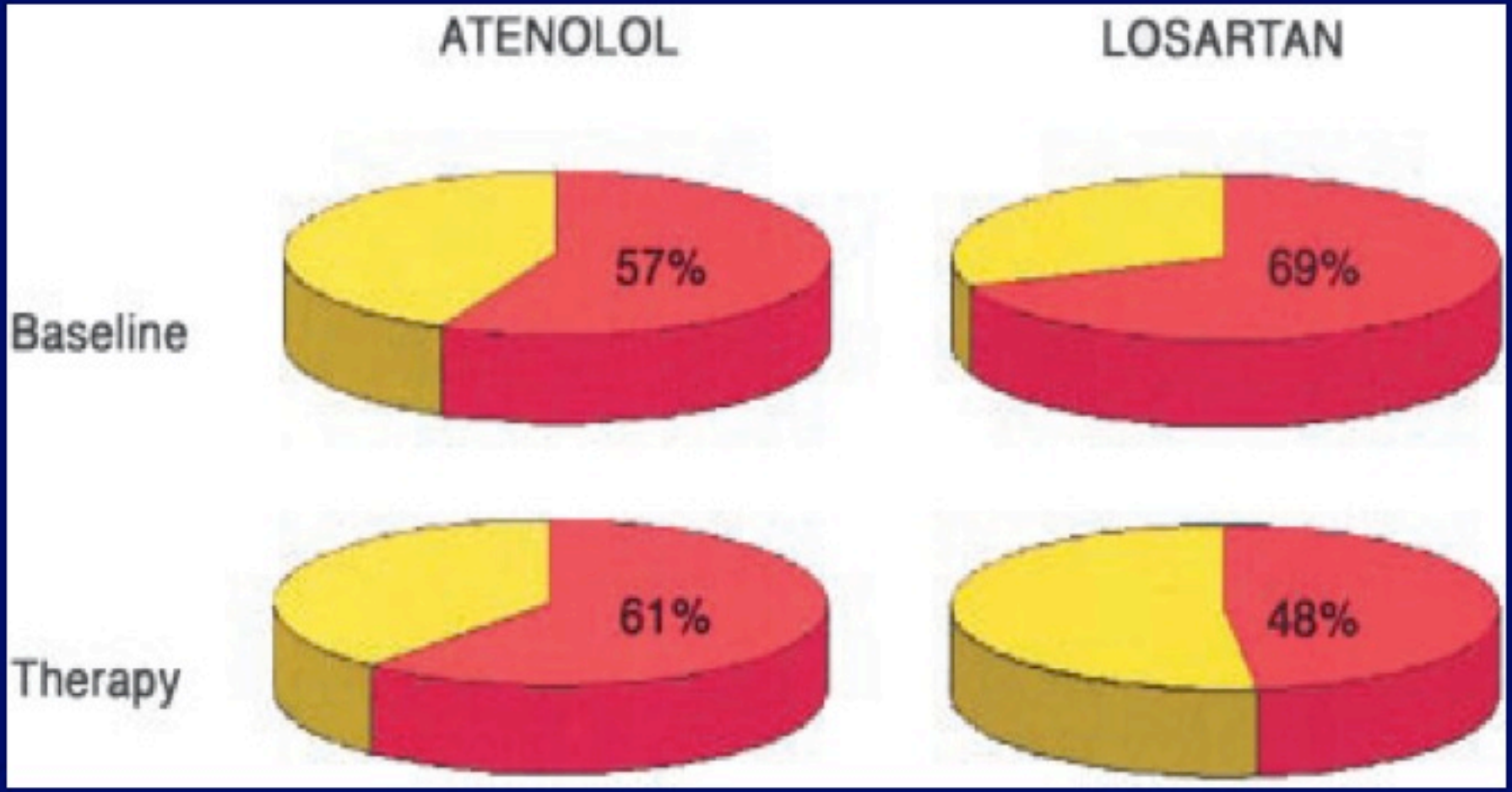


LIFE: ECG-LVH Regression from Baseline

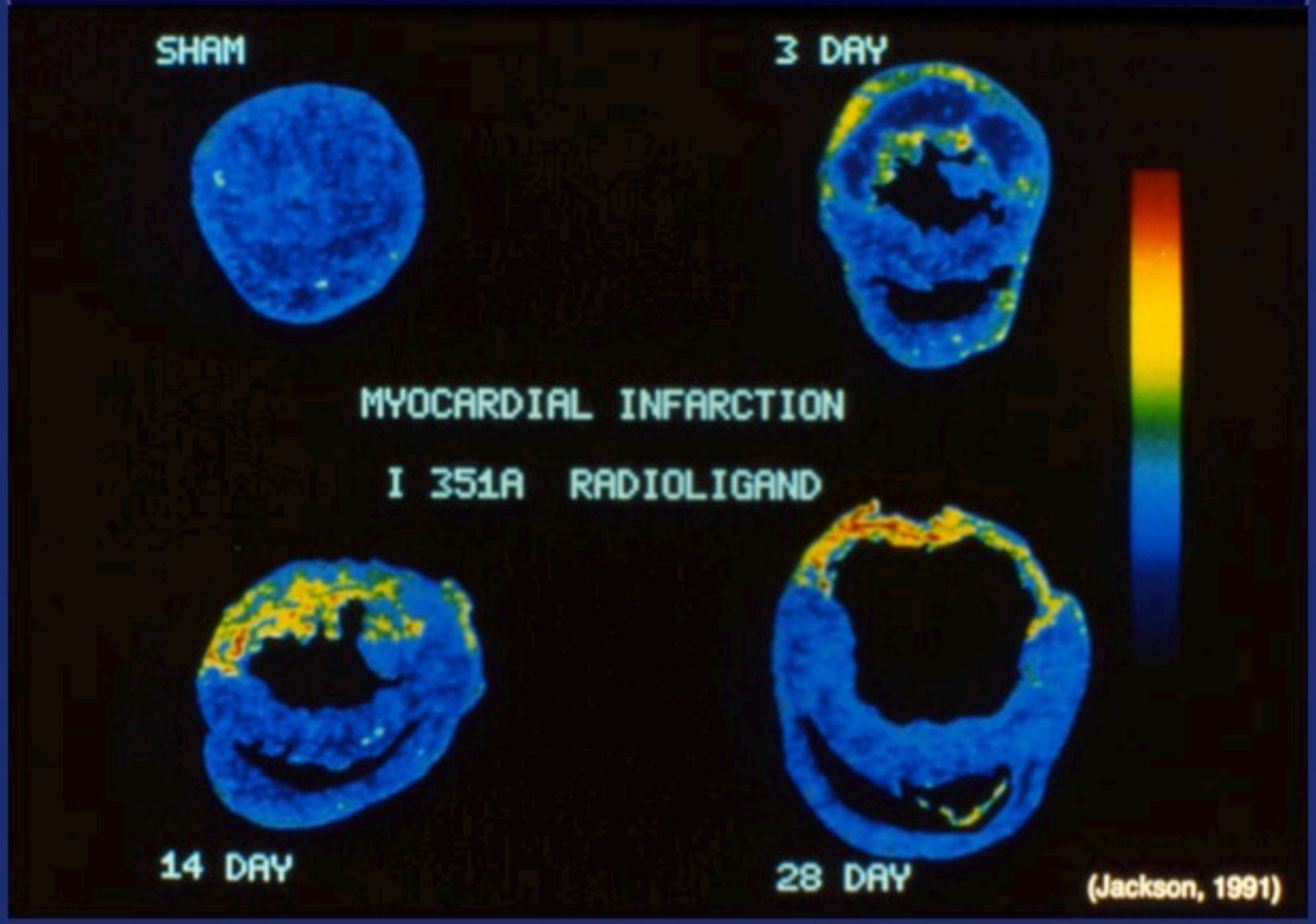


B Dahlof et al. Lancet 2002;359:995-1003

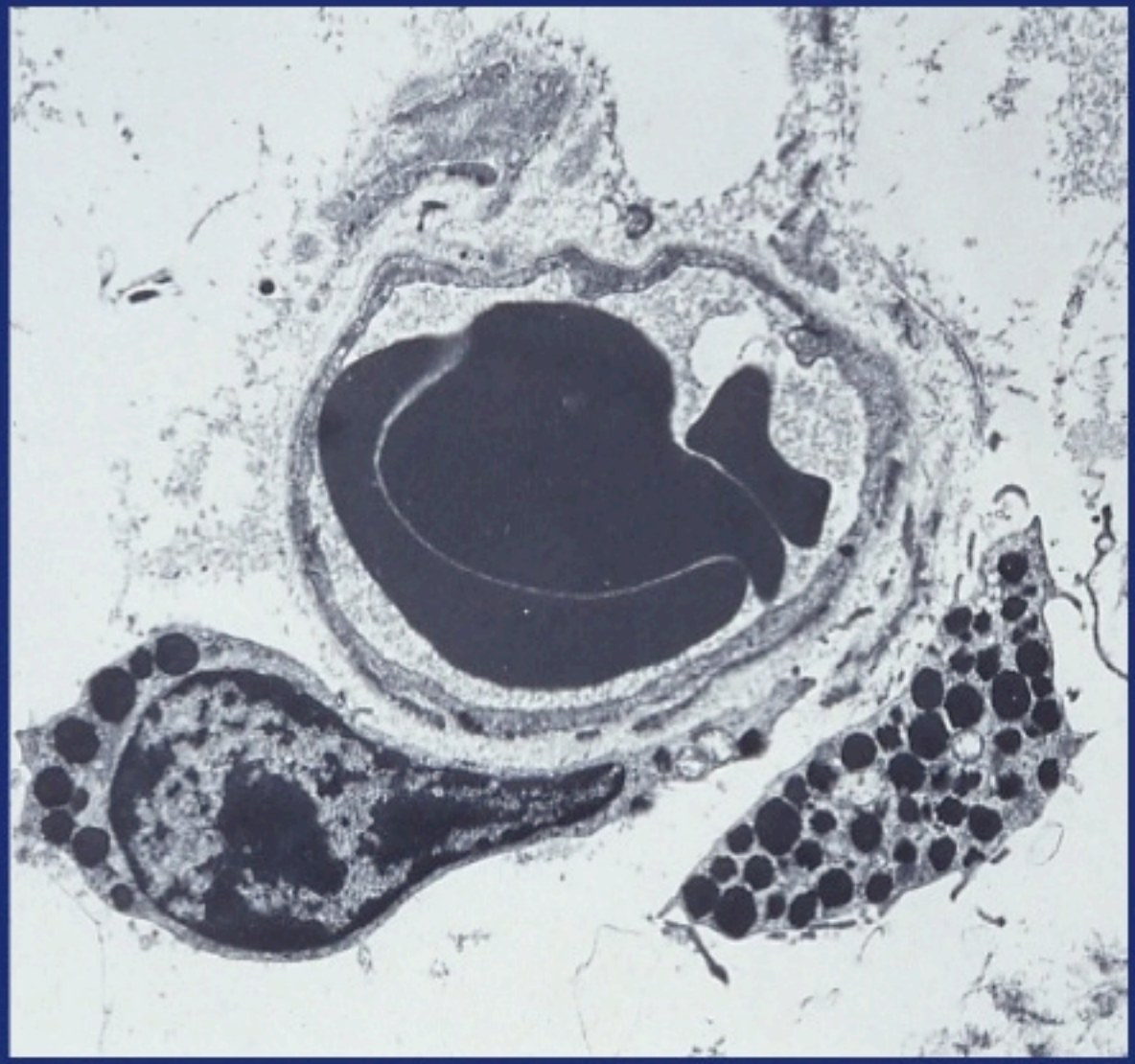
Prevalence of excessive fibrosis in atenolol- and losartan-treated patients at baseline and after 36-week treatment.

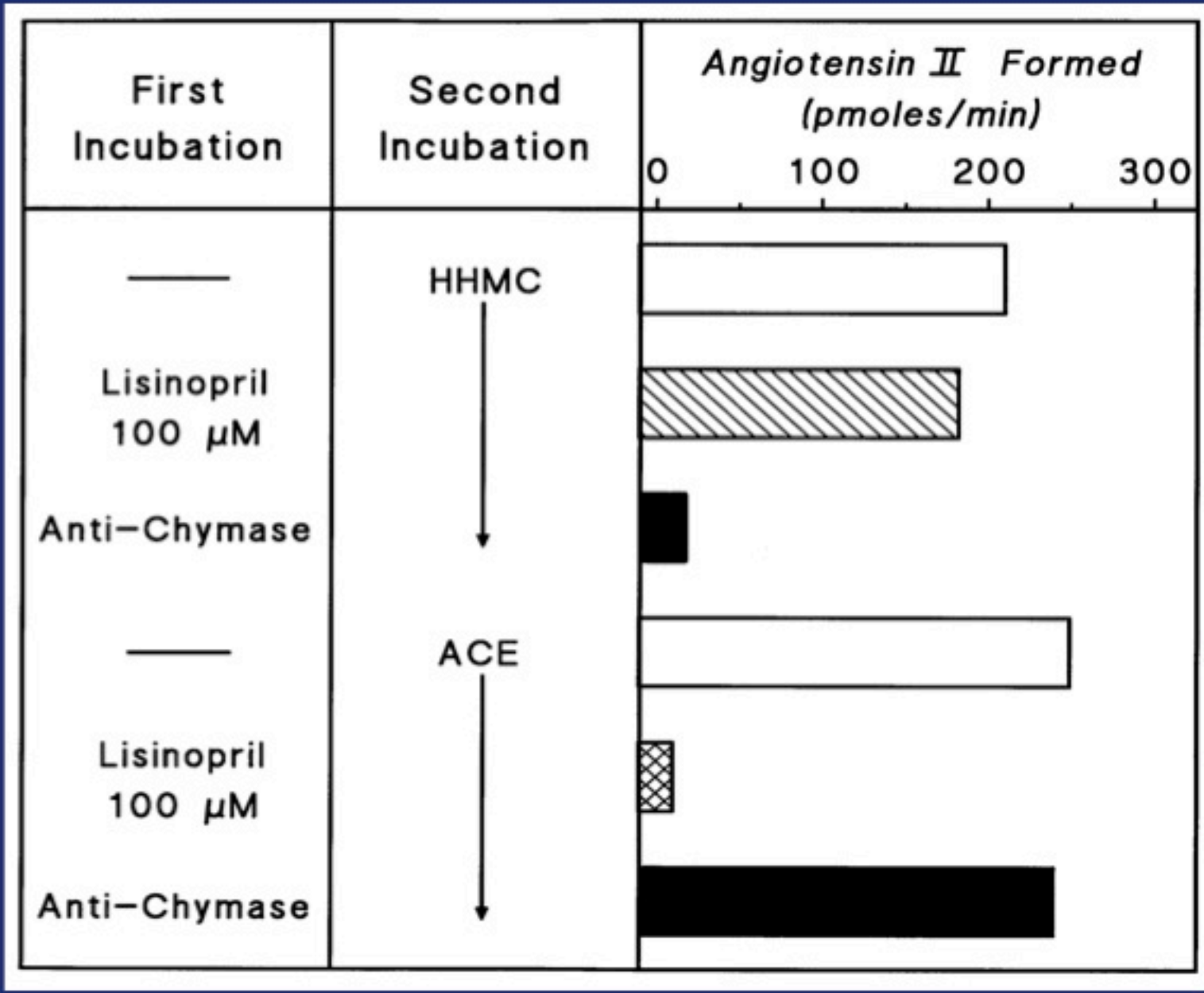


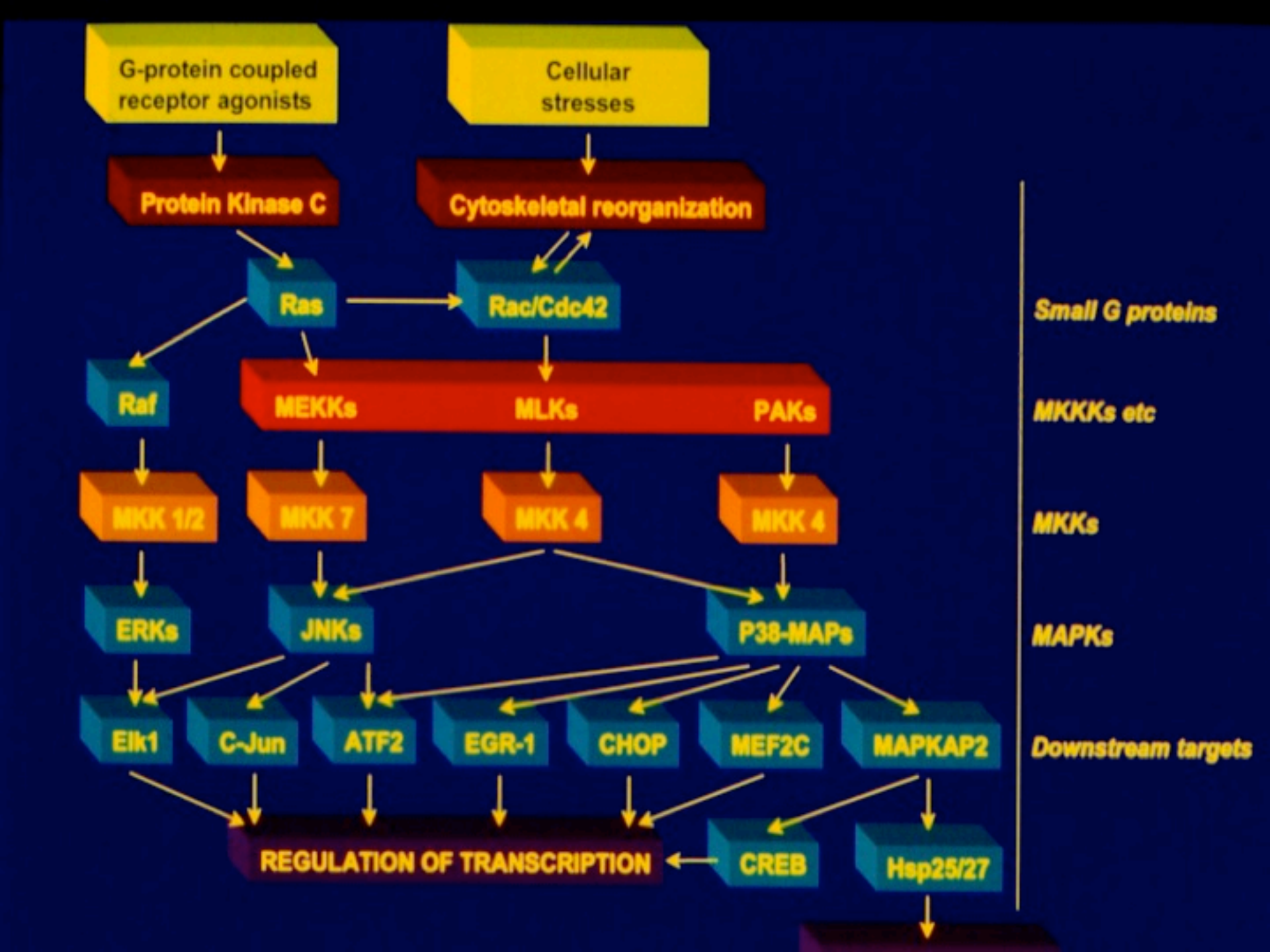
RUOLO DEL SISTEMA RENINA-ANGIOTENSINA NEL POST-INFARTO:CRESCENTE CONCENTRAZIONE DI ACE NEL MIOCARDIO

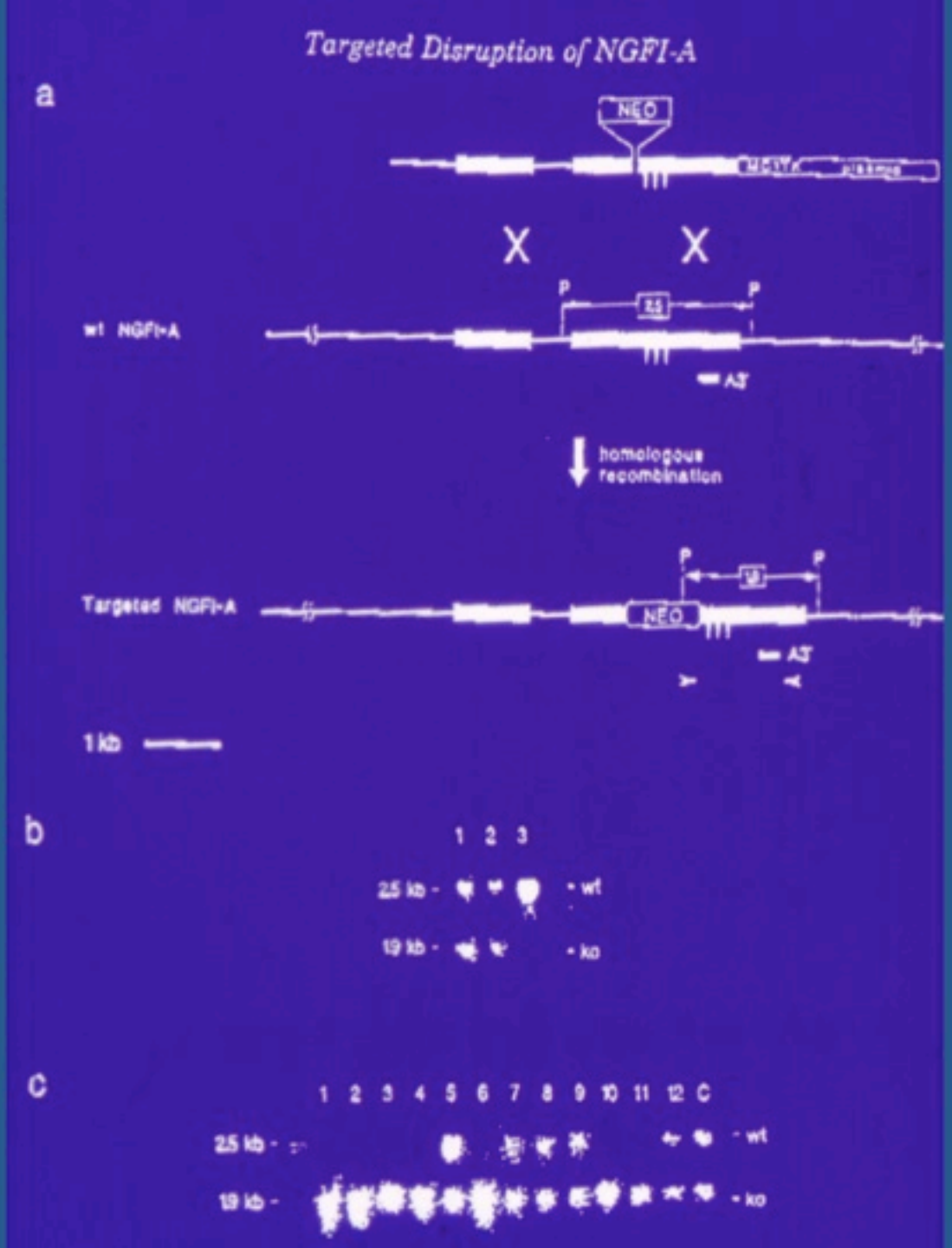


Electron Microscopic Localization of HHMC (III)

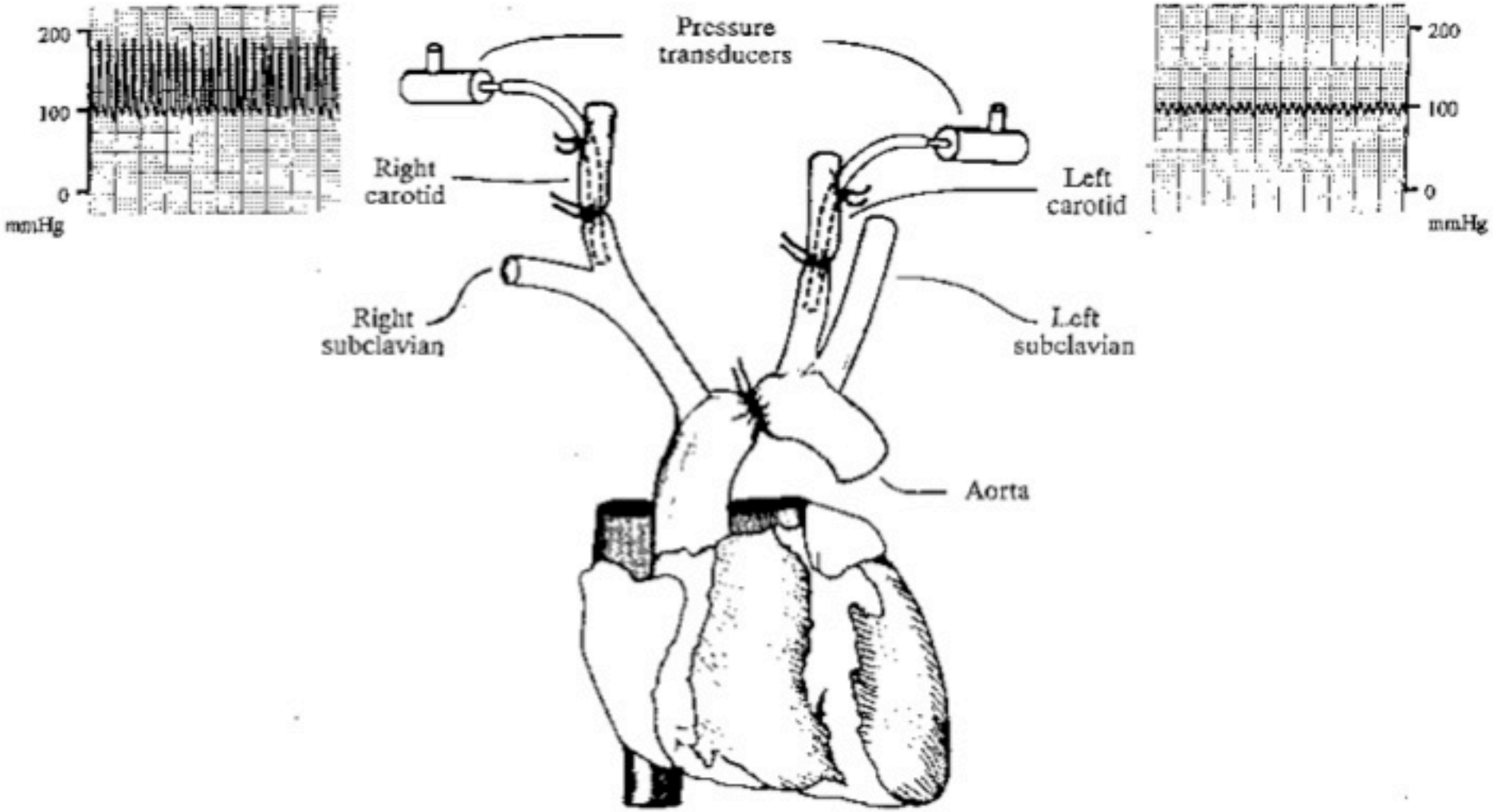



First Incubation
Second Incubation
Angiotensin II Formed (pmoles/min)
0
100
200
300
——
HHMC
Lisinopril 100 μM
Anti–Chymase
——
ACE
Lisinopril 100 μM
Anti–Chymase

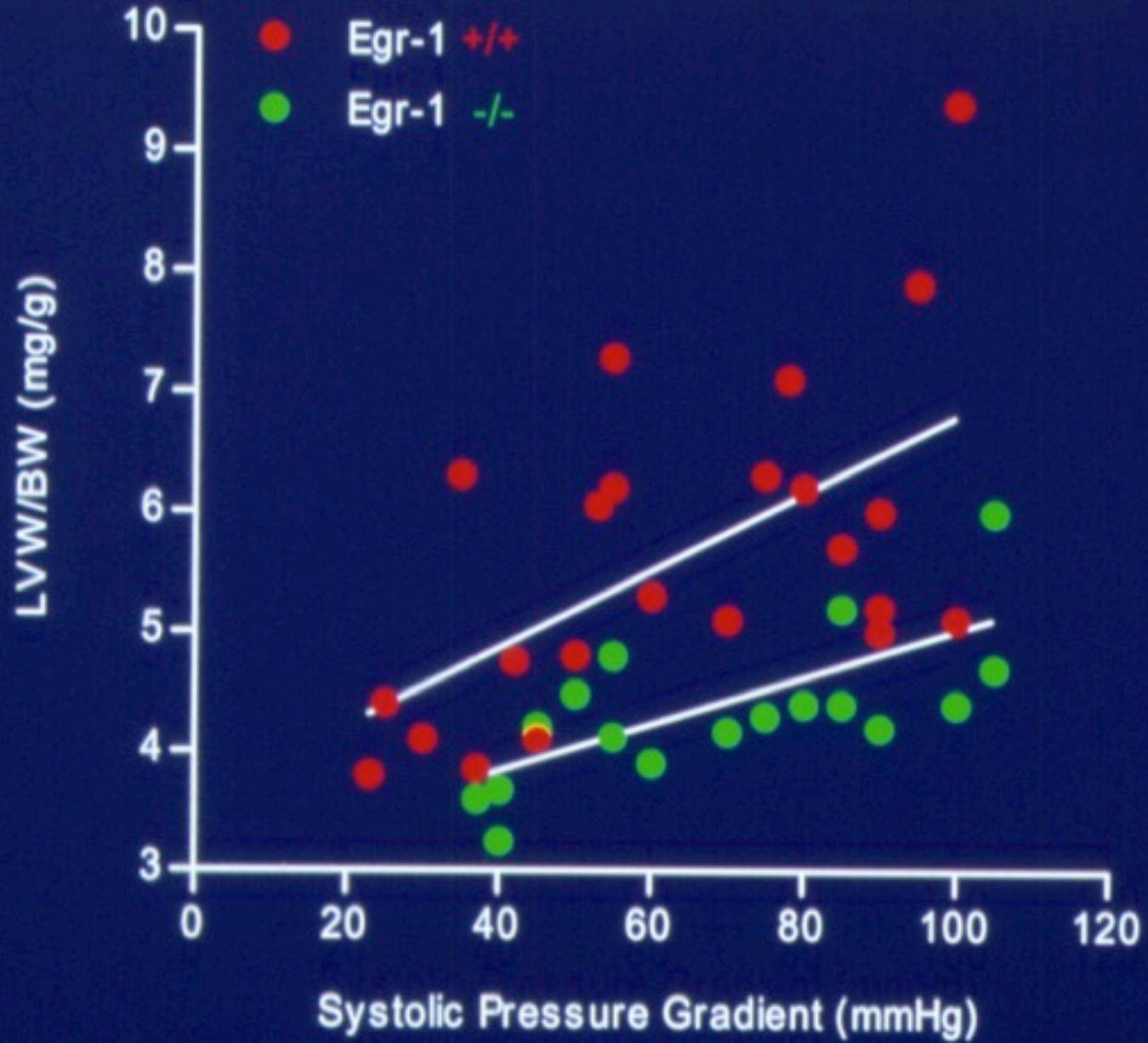

G-protein coupled receptor agonists
Cellular stresses
Protein Kinase C
Cytoskeletal reorganization
Ras
Rac/Cdc42
Raf
MEKKs
MLKs
PAKs
MKK 1/2
MKK 7
MKK 4
MKK 4
ERKs
JNKs
P38-MAPs
Elk1
C-Jun
ATF2
EGR-1
CHOP
MEF2C
MAPKAP2
REGULATION OF TRANSCRIPTION
CREB
Hsp25/27
Small G proteins
MKKKs etc
MKKs
MAPKs
Downstream targets


Targeted Disruption of NGFI-A
a
NEO
X
X
P
2.5
P
wt NGFI-A
AS
homologous
recombination
P
M
P
Targeted NGFI-A
NEO
AS
1 kb
b
1 2 3
2.5 kb -
- wt
19 kb -
- ko
c
1 2 3 4 5 6 7 8 9 10 11 12 C
2.5 kb -
- wt
19 kb -
- ko

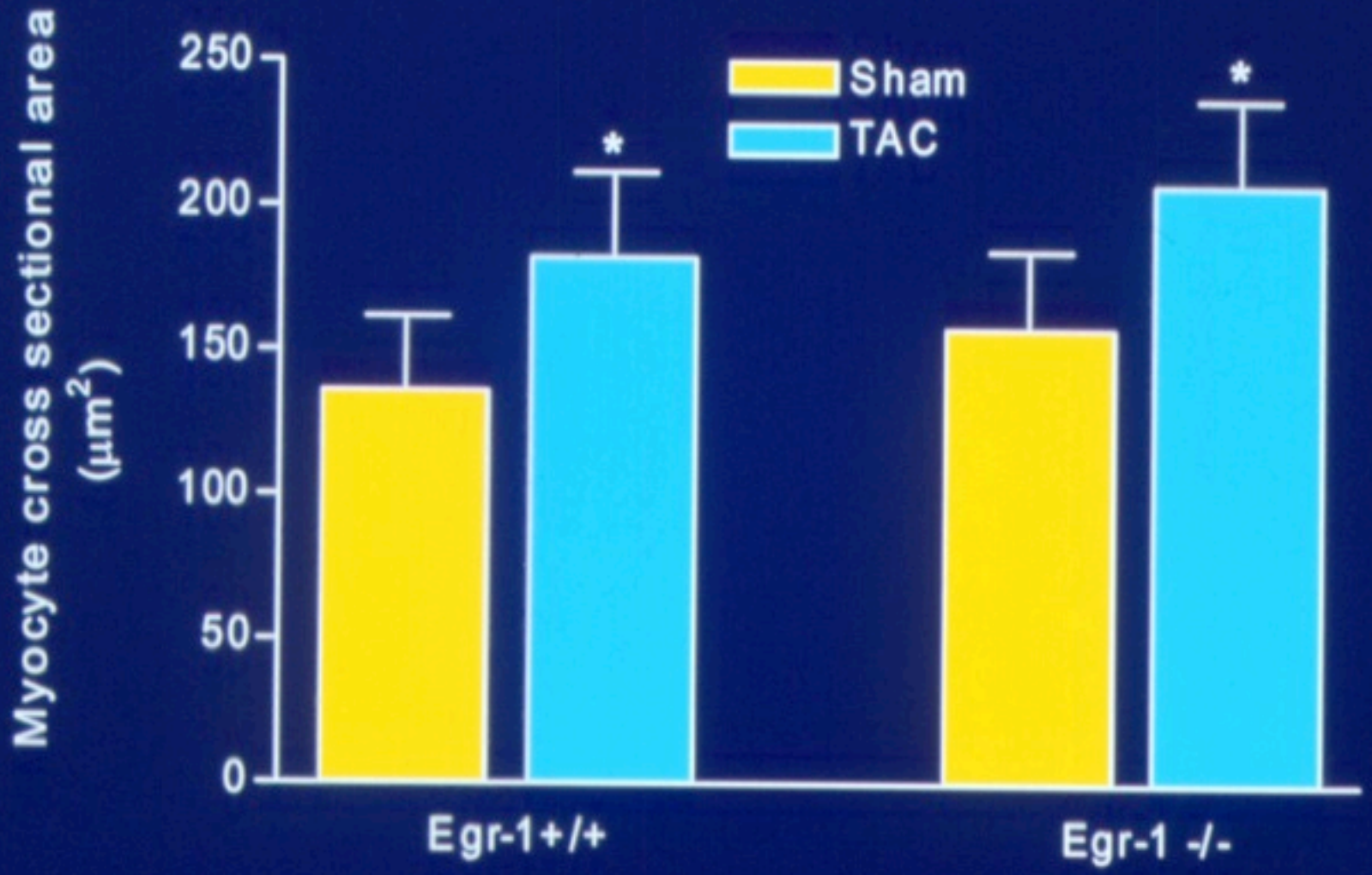
Transverse Aortic Constriction (TAC)



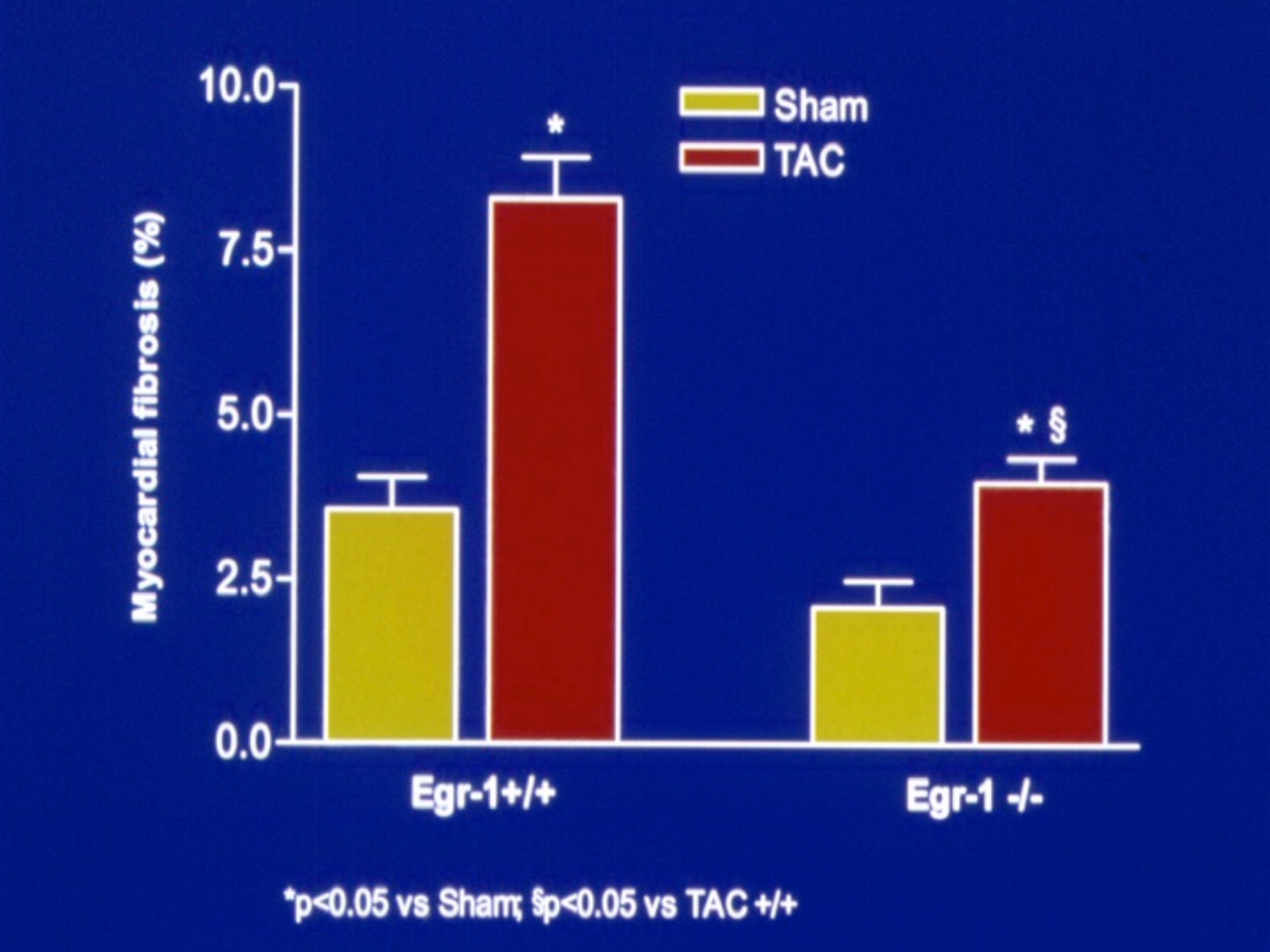
LEFT VENTRICULAR GROWTH DURING CHRONIC PRESSURE OVERLOAD



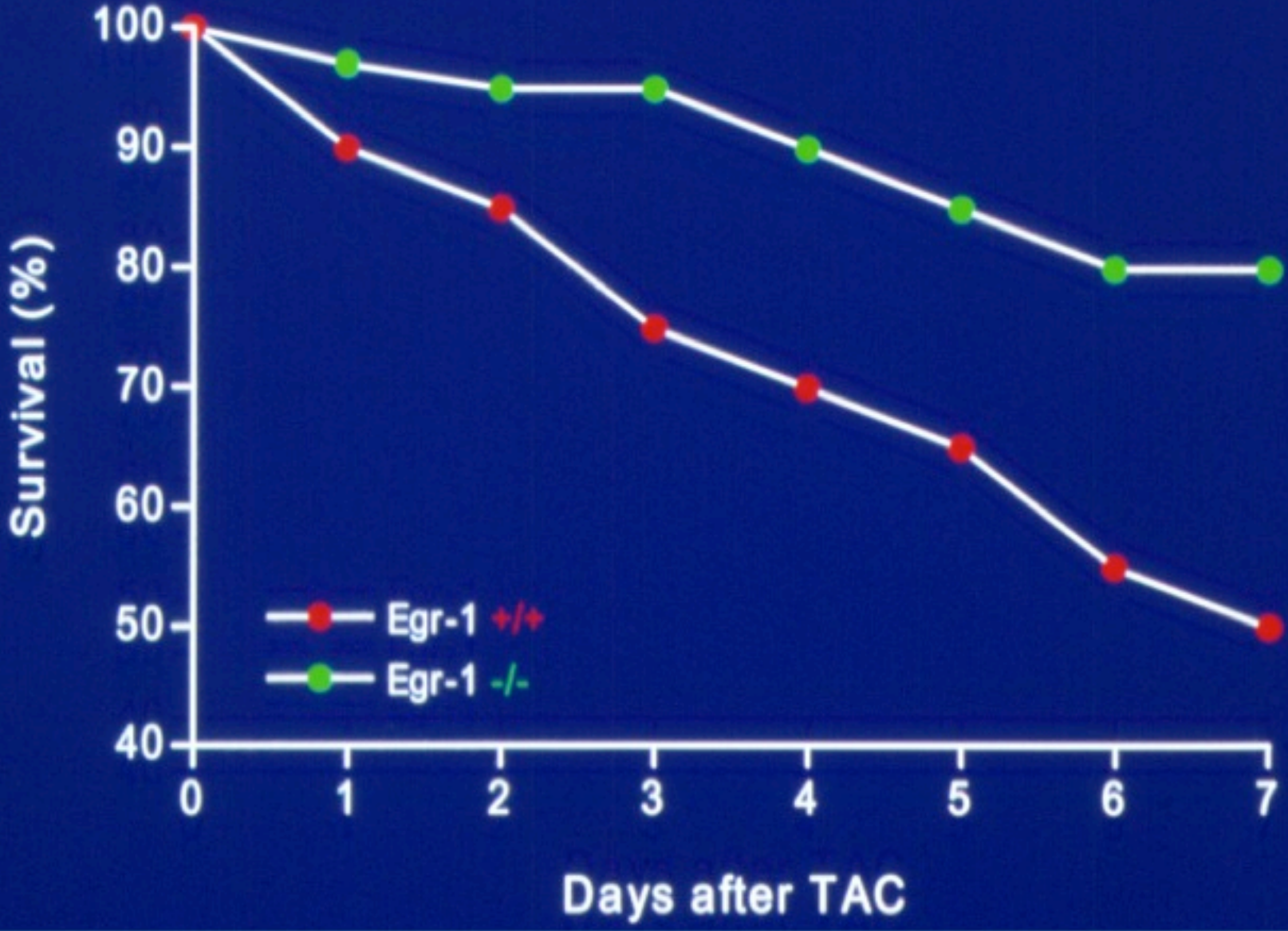
MYOCYTE CROSS SECTIONAL AREA AFTER CHRONIC PRESSURE OVERLOAD



*p<0.05 vs Sham


10.0
7.5
5.0
2.5
0.0
Myocardial fibrosis (%)
Sham
TAC
*
* §
Egr-1+/+
Egr-1 -/-
*p<0.05 vs Sham; §p<0.05 vs TAC +/+

SURVIVAL RATES DURING PRESSURE OVERLOAD

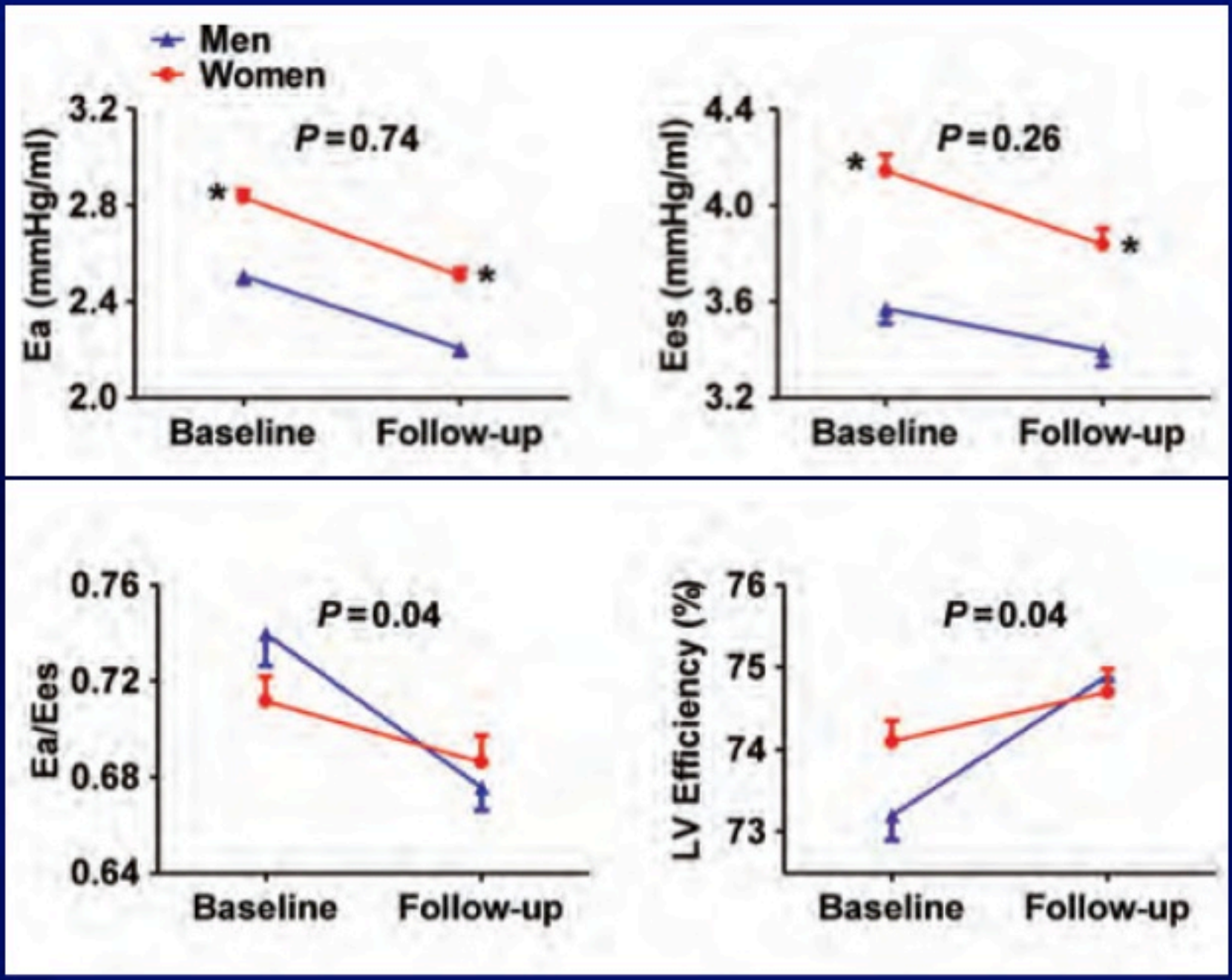


Effect of antihypertensive therapy on ventricular–arterial mechanics, coupling, and efficiency

Carolyn S.P. Lam[1,2*†], Amil M. Shah[3†], Barry A. Borlaug[4], Susan Cheng[3], Anil Verma[5], Joseph Izzo[6], Suzanne Oparil[7], Gerard P. Aurigemma[8], James D. Thomas[9], Bertram Pitt[10], Michael R. Zile[11], and Scott D. Solomon[3]

[1]National University Health System, Tower Block Level 9, 1E Kent Ridge Road, Singapore 119228, Singapore; [2]Boston University School of Medicine, Boston, MA, USA; [3]Brigham and Women's Hospital, Boston, MA, USA; [4]Mayo Clinic, Rochester, MN, USA; [5]Ochsner Heart and Vascular Institute, New Orleans, LA, USA; [6]State University of New York, Buffalo, NY, USA; [7]University of Alabama, Birmingham, AL, USA; [8]University of Massachusetts Medical School, Worcester, MA, USA; [9]Cleveland Clinic Foundation, Cleveland, OH, USA; [10]University of Michigan, Ann Arbor, MI, USA; and [11]RHJ Department of Veterans Affairs Medical Center and the Medical University of South Carolina, Charleston, SC, USA

European Heart Journal (2013) 34, 676–683



European Heart Journal (2013) 34, 676–683

Effect of antihypertensive therapy on ventricular–arterial mechanics, coupling, and efficiency

Carolyn S.P. Lam[1,2*†], Amil M. Shah[3†], Barry A. Borlaug[4], Susan Cheng[3], Anil Verma[5], Joseph Izzo[6], Suzanne Oparil[7], Gerard P. Aurigemma[8], James D. Thomas[9], Bertram Pitt[10], Michael R. Zile[11], and Scott D. Solomon[3]

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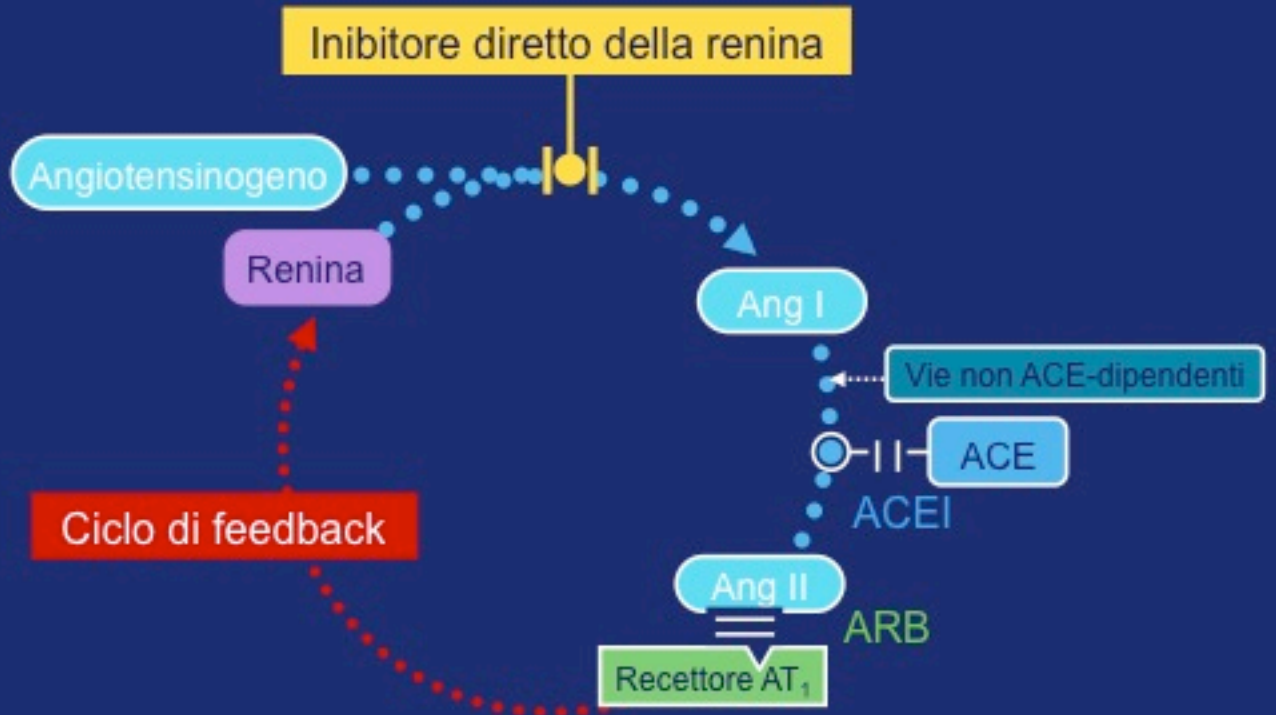
Conclusion

Antihypertensive therapy reduces arterial and ventricular stiffness, enhances ventricular–arterial coupling, reduces cardiac work, and improves LV efficiency, systolic, and diastolic function. Attenuated responses in women and among obese subjects suggest that structure–function changes may be less reversible in these groups, possibly explaining their greater susceptibility to ultimately develop heart failure.

European Heart Journal (2013) 34, 676–683

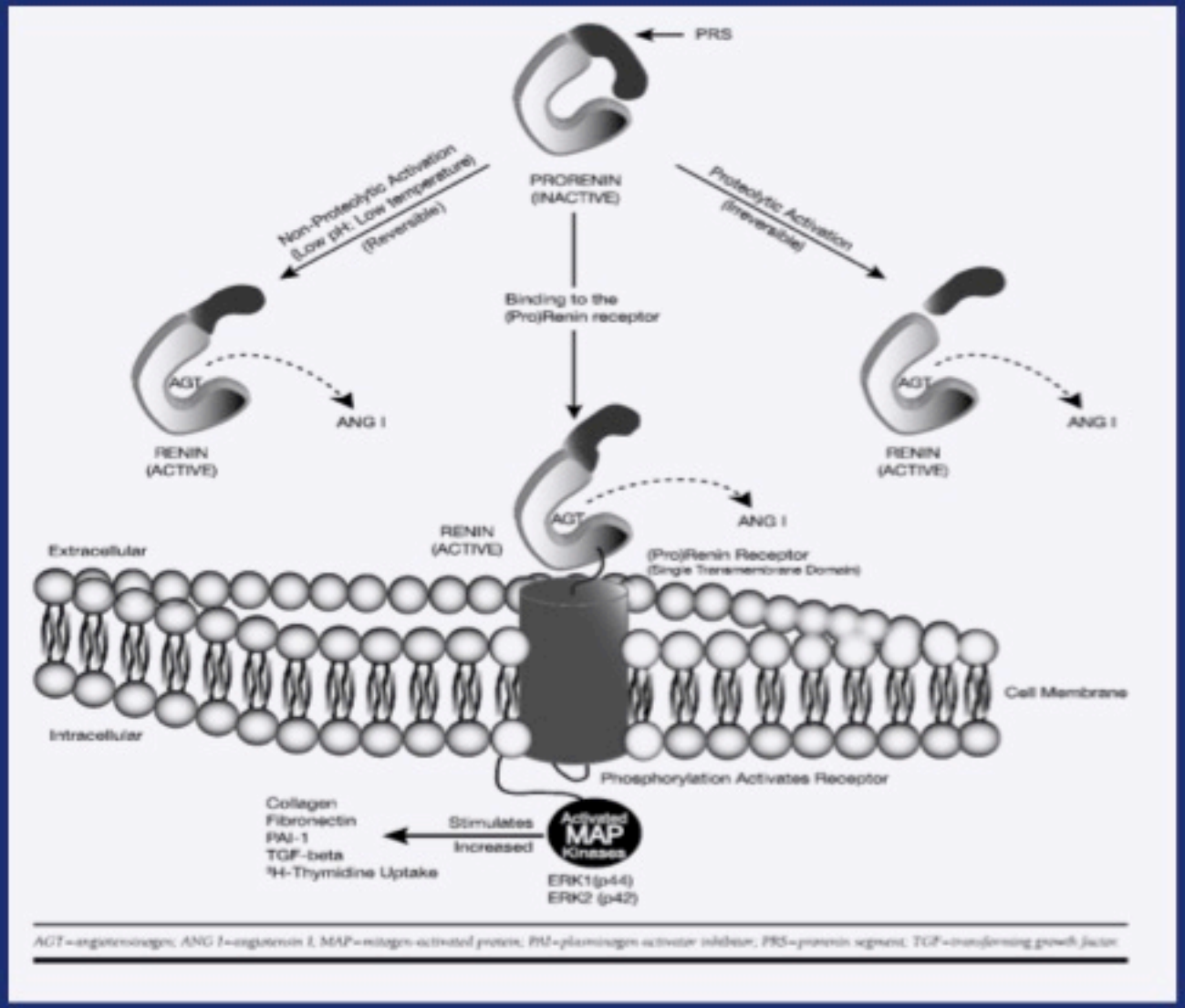
A differenza degli ACE-I e degli ARB, aliskiren riduce l'Ang I, l'Ang II e la PRA



	Ang I	Ang II	Renina	PRA
ACEI	↑	↓	↑	↑
ARB	↑	↑	↑	↑
Aliskiren	↓	↓	↑	↓

Azizi M et al. 2006

Rappresentazione schematica del meccanismo di attivazione del recettore della prorenina



AGT=angiotensinogen; ANG I=angiotensin I; MAP=mitogen-activated protein; PAI=plasminogen activator inhibitor; PRS=prorenin segment; TGF=transforming growth factor

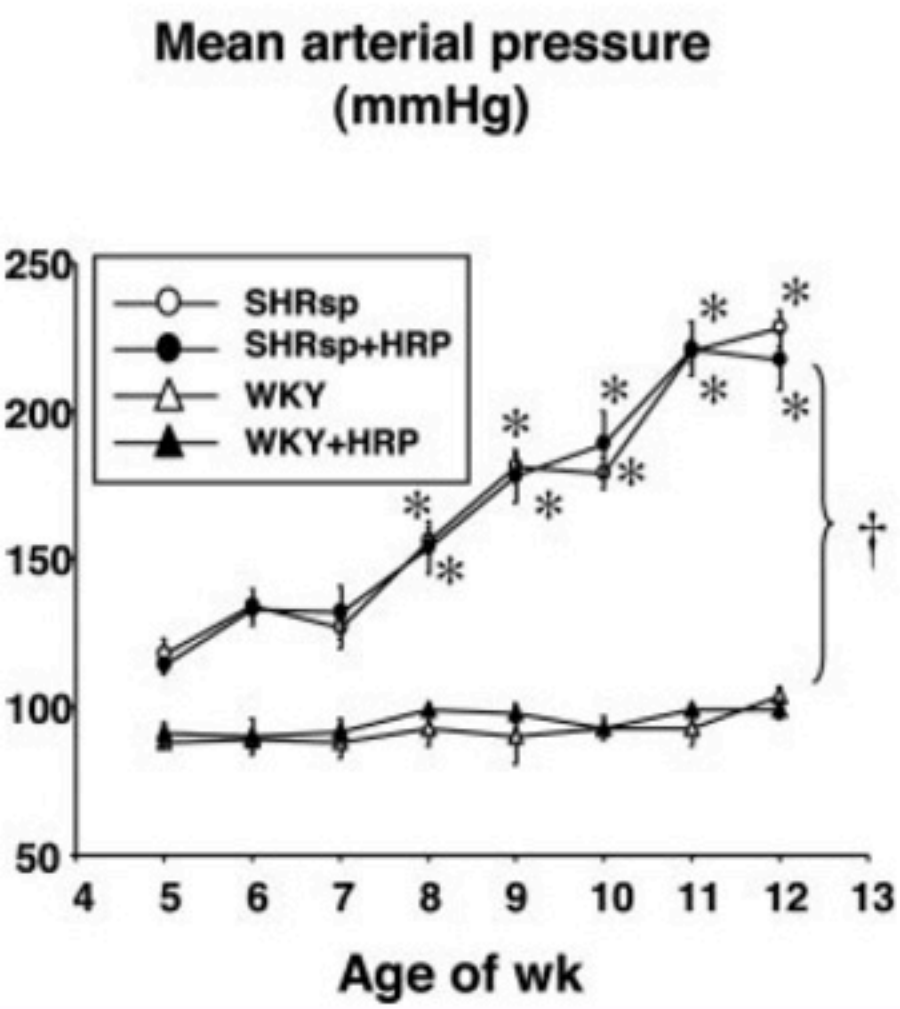
Nguyen G, *et al.* 2007

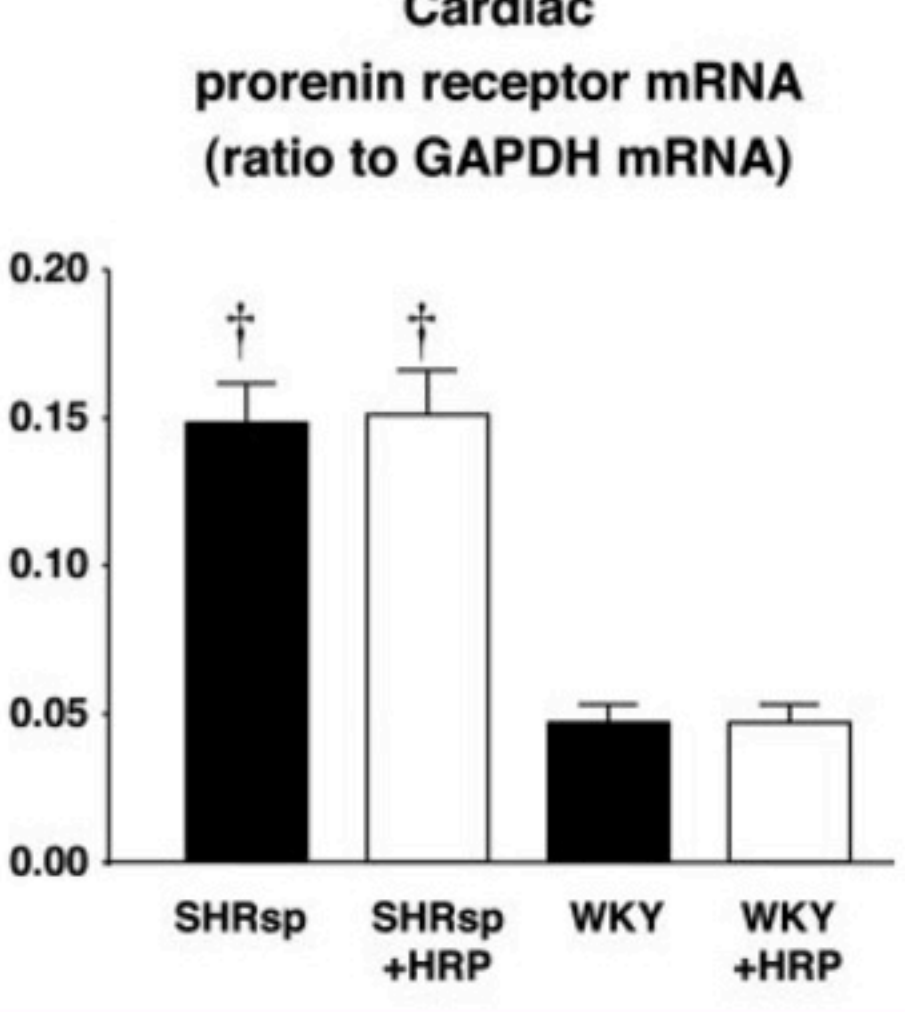
Hypertension
JOURNAL OF THE AMERICAN HEART ASSOCIATION

Nonproteolytic Activation of Prorenin Contributes to Development of Cardiac Fibrosis in Genetic Hypertension

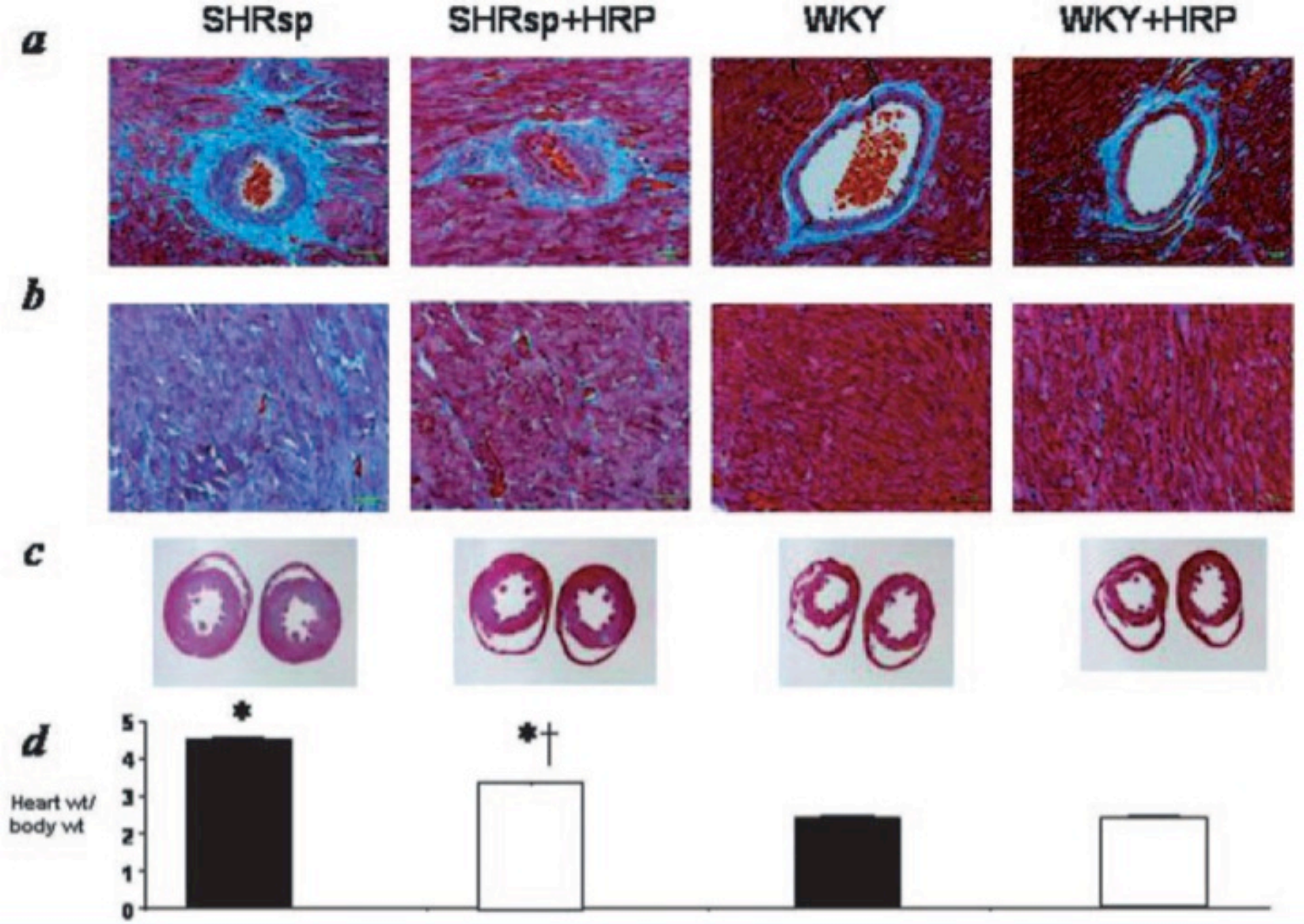
Atsuhiro Ichihara, Yuki Kaneshiro, Tomoko Takemitsu, Mariyo Sakoda, Fumiaki Suzuki, Tsutomu Nakagawa, Akira Nishiyama, Tadashi Inagami and Matsuhiko Hayashi

Hypertension 2006, 47:894-900: originally published online April 3, 2006

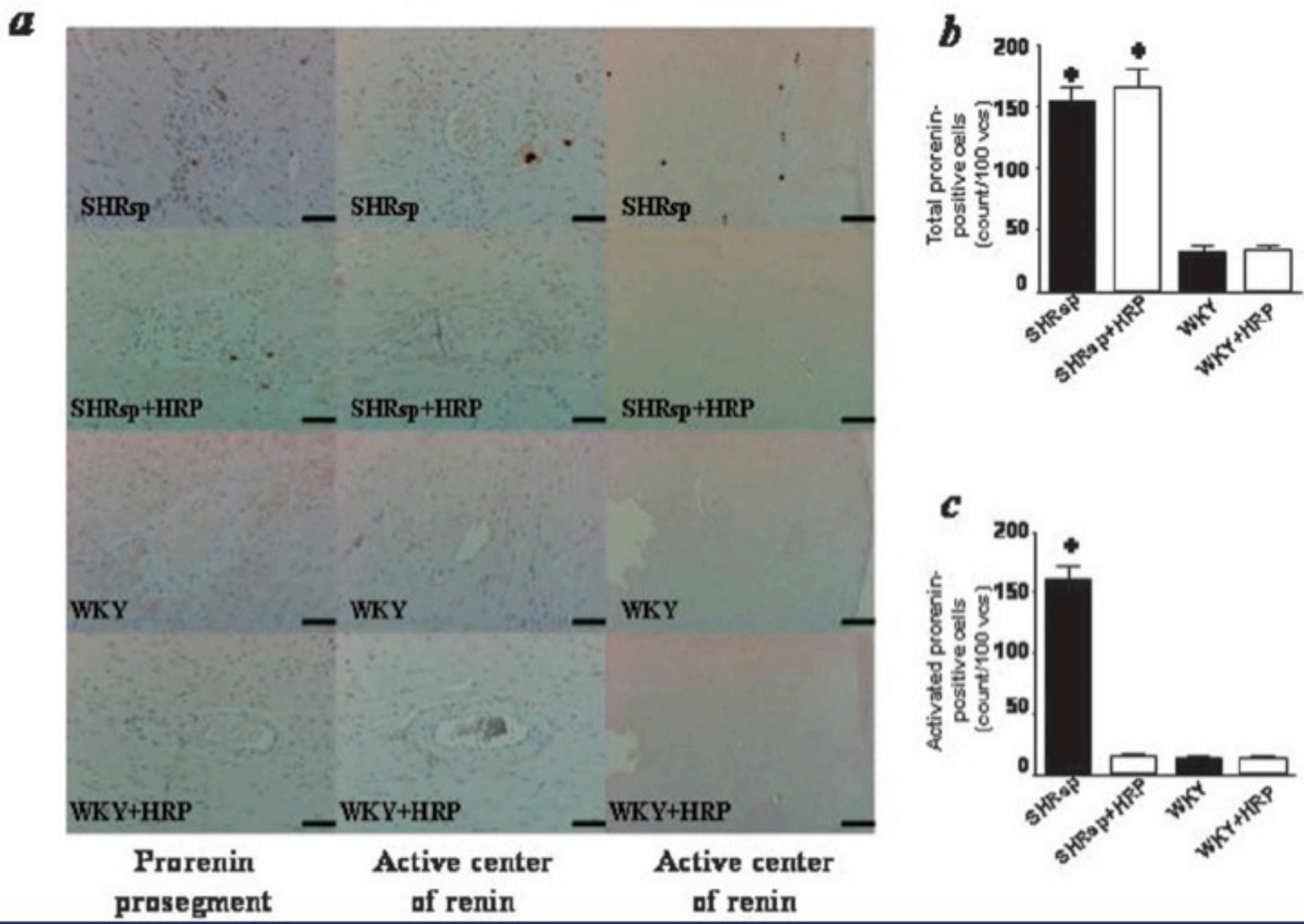




Hypertension. 2006;47:894-90)



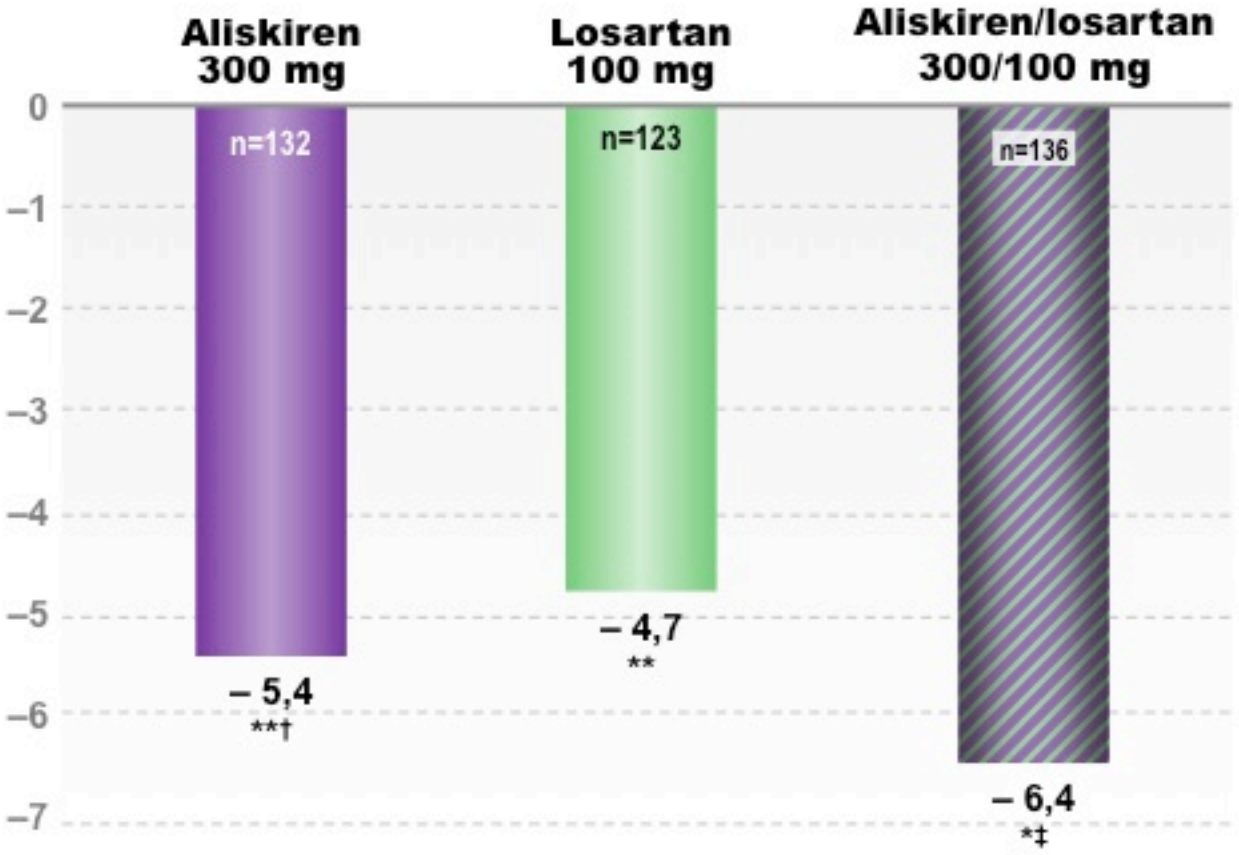
Hypertension. 2006;47:894-90)



Hypertension. 2006;47:894-90)

L'associazione aliskiren/losartan assicura una maggiore riduzione di ~20% dell'IMVS rispetto a losartan in monoterapia

Variazione percentuale media (%) di IMVS dal basale dopo 36 settimane di trattamento



*IMVS: indice di massa ventricolare sinistra

Analisi fra trattamenti basate su dati medi minimi quadrati:

*p<0,0001 vs basale

†p<0,0001 per non inferiorità vs losartan 100 mg; ‡p=0,52 vs losartan 100 mg

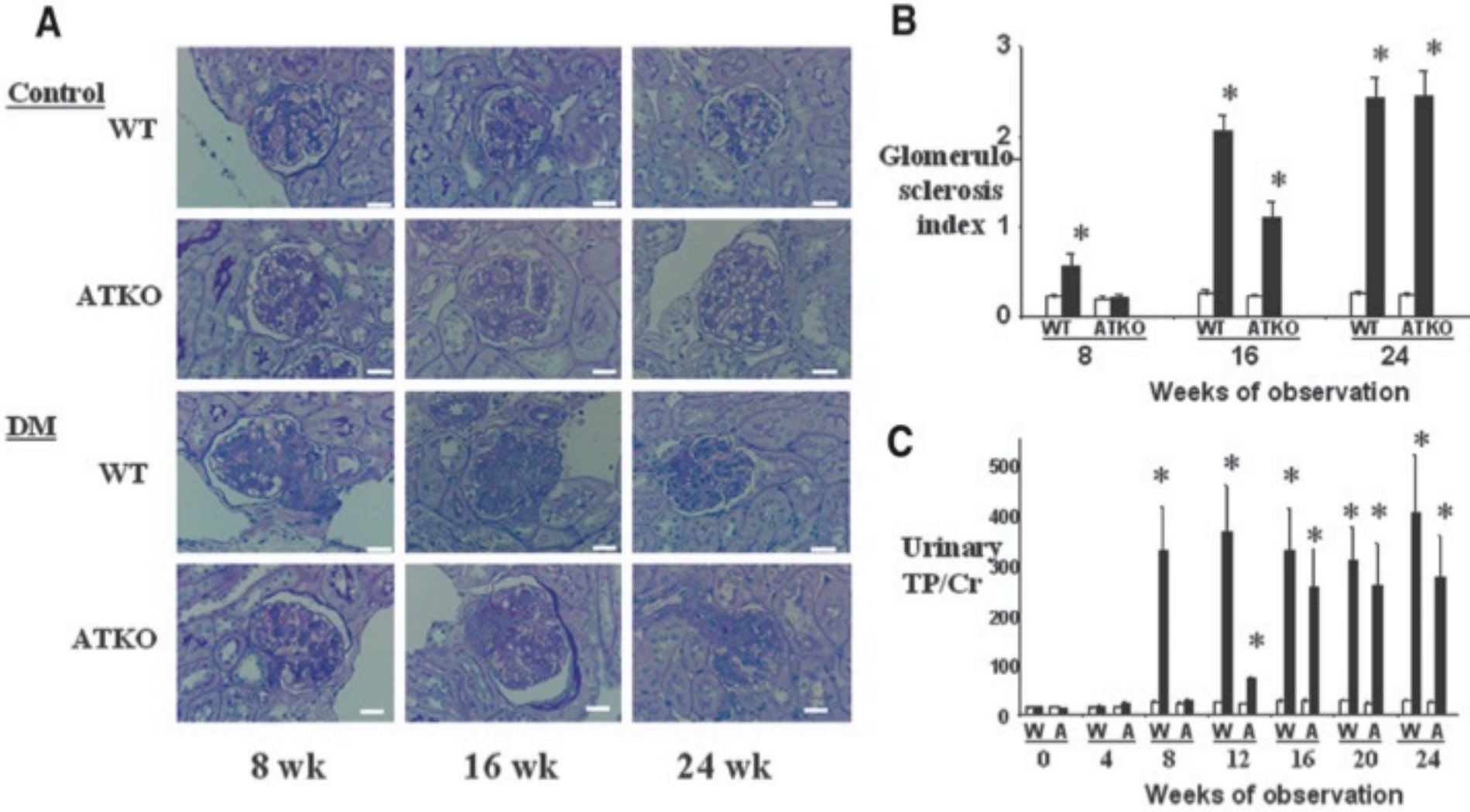
Solomon SD et al, Circulation 2009.

Prorenin Receptor Blockade Inhibits Development of Glomerulosclerosis in Diabetic Angiotensin II Type 1a Receptor–Deficient Mice

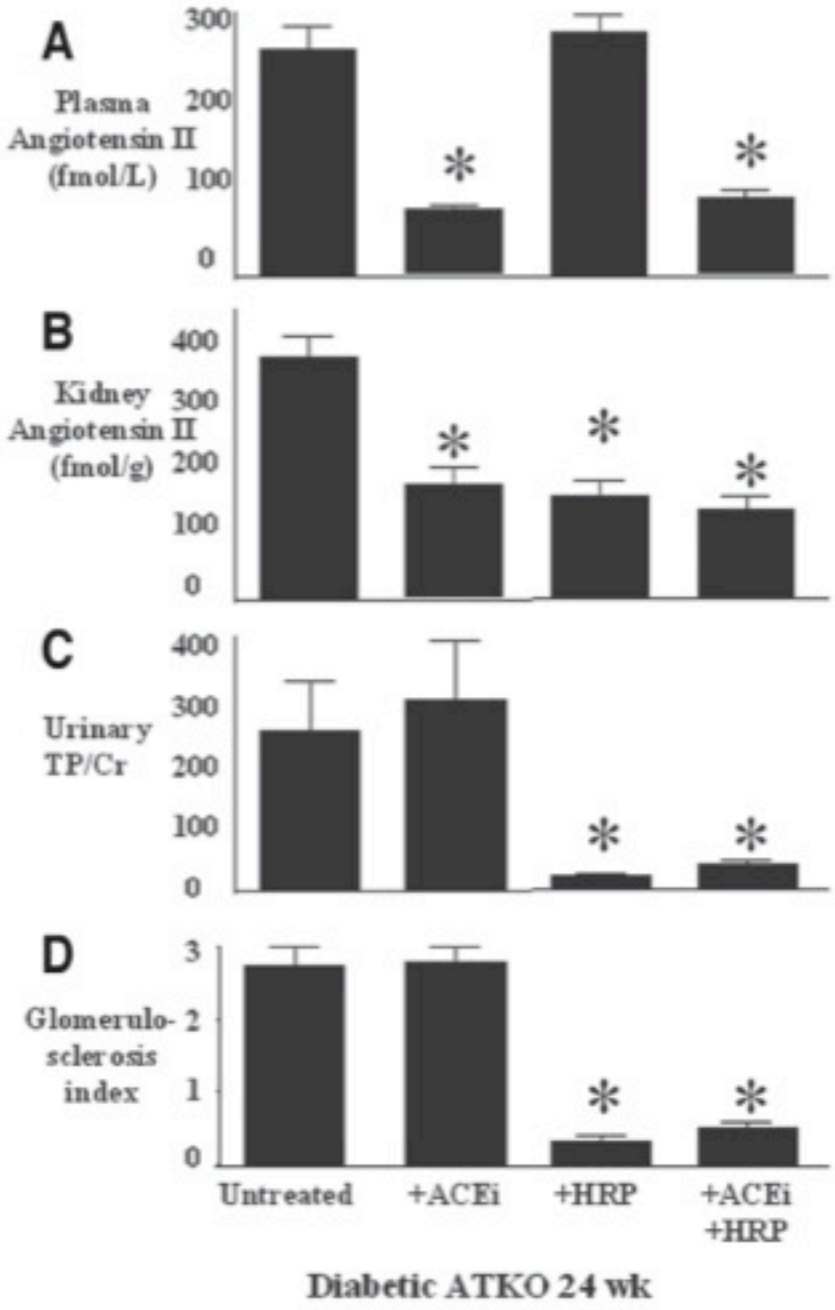
Atsuhiro Ichihara,* Fumiaki Suzuki,†‡ Tsutomu Nakagawa,† Yuki Kaneshiro,* Tomoko Takemitsu,* Mariyo Sakoda,* A.H.M. Nurun Nabi,‡ Akira Nishiyama,§ Takeshi Sugaya,‖ Matsuhiko Hayashi,* and Tadashi Inagami¶

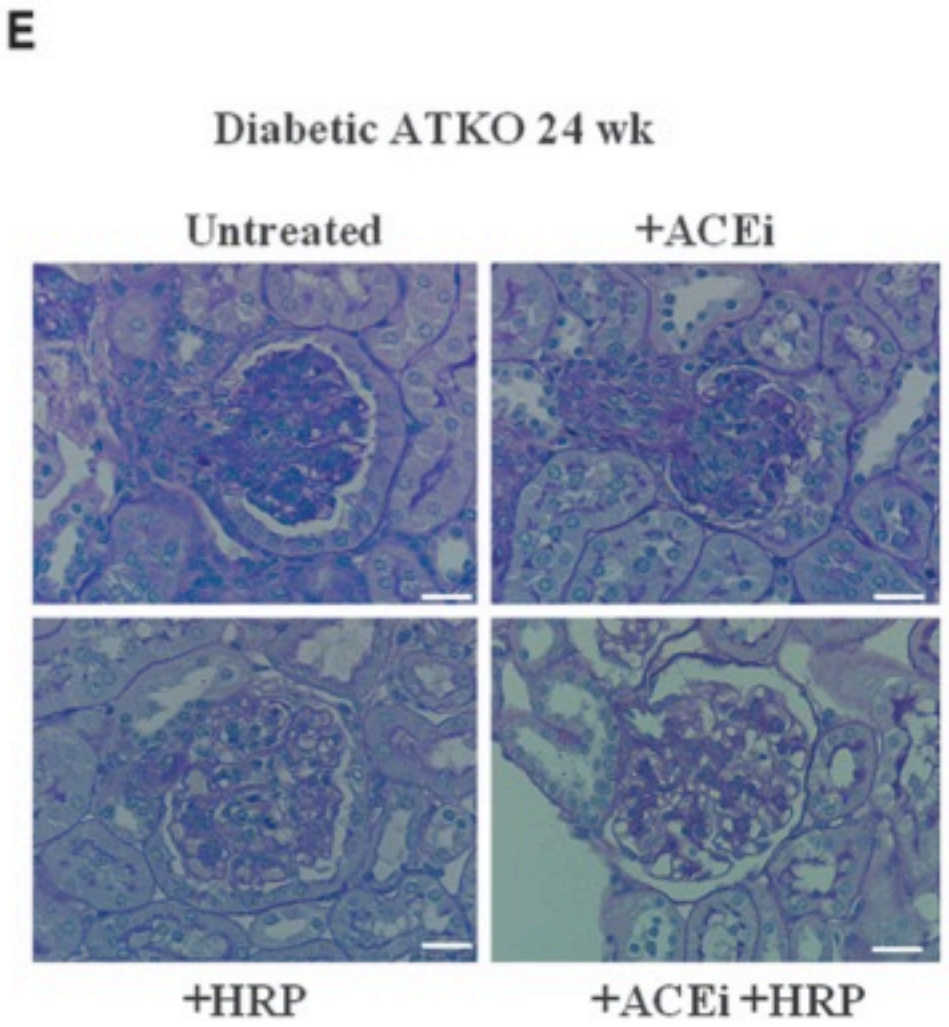
*Department of Internal Medicine, Keio University School of Medicine, Tokyo, †Faculty of Applied Biological Sciences and ‡United Graduate School of Agricultural Science, Gifu University, Gifu, §Department of Pharmacology, Kagawa University School of Medicine, Kagawa, and ‖Nephrology Diseases Research Laboratory, Tanabe Seiyaku, Osaka, Japan; and ¶Department of Biochemistry, Vanderbilt University School of Medicine, Nashville, Tennessee

J Am Soc Nephrol 17: 1950–1961, 2006



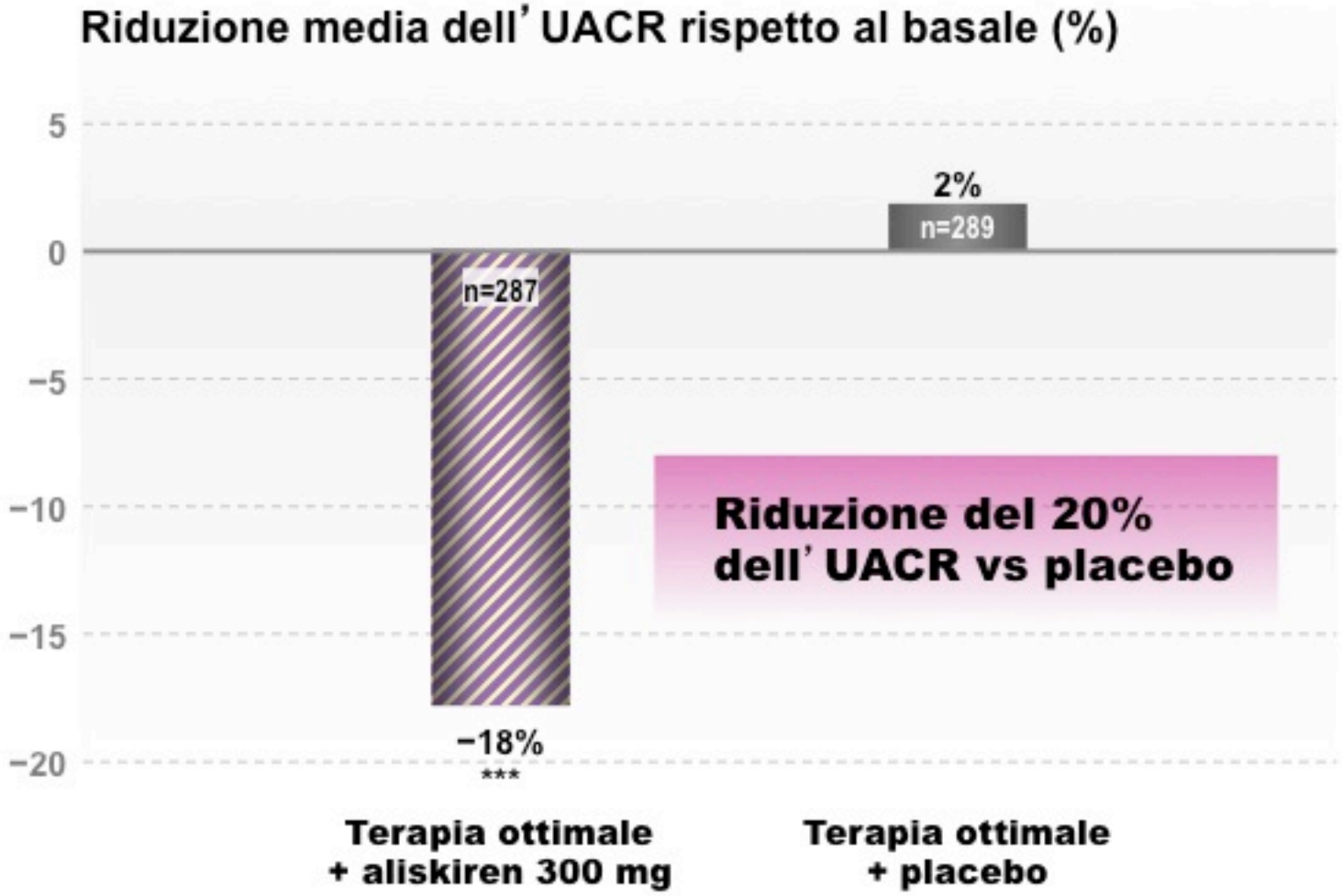
J Am Soc Nephrol 17: 1950–1961, 2006





J Am Soc Nephrol 17: 1950–1961, 2006

Aliskiren riduce significativamente il rapporto urinario albumina/creatinina (UACR) rispetto al placebo



*** p = 0,0009 vs placebo

H-H Parving et al, N Engl J Med 2008.

European Heart Journal Advance Access published March 26, 2012

European Heart Journal
doi:10.1093/eurheartj/ehs057

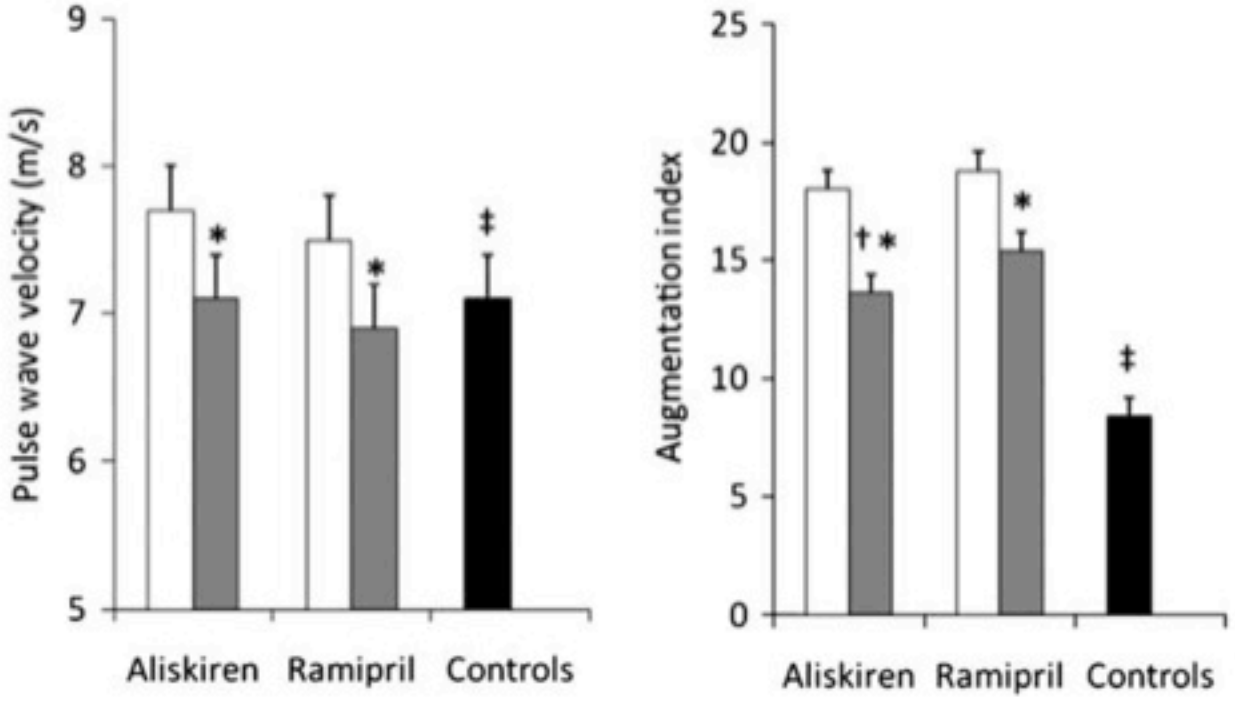
CLINICAL RESEARCH

Effect of aliskiren treatment on endothelium-dependent vasodilation and aortic stiffness in essential hypertensive patients

Agostino Virdis*†, Lorenzo Ghiadoni†, Ahmad Amedeo Qasem, Gianni Lorenzini, Emiliano Duranti, Giulia Cartoni, Rosa Maria Bruno, Giampaolo Bernini, and Stefano Taddei

Department of Internal Medicine, University of Pisa, Pisa, Italy

Received 22 November 2011; revised 1 February 2012; accepted 16 February 2012



Eur Heart J. 2012 Mar 26. [Epub ahead of print]