Università *Magna Græcia* di Catanzaro

Dipartimento di Medicina Sperimentale e Clinica

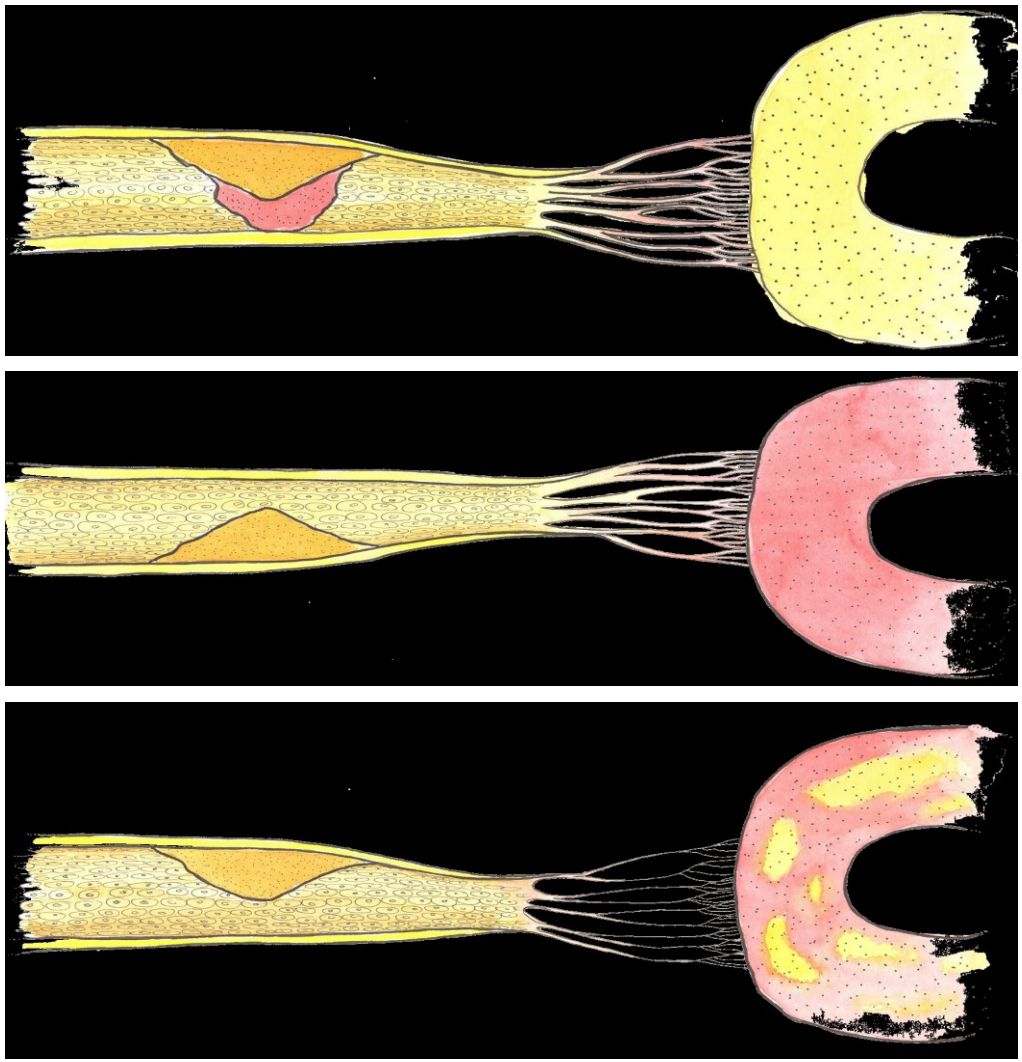
Cattedra di Medicina Interna ed U.O. Malattie Cardiovascolari

Prof. Francesco Perticone

Update Scompenso Cardiaco:

Trattamento Chirurgico o Farmacologico?

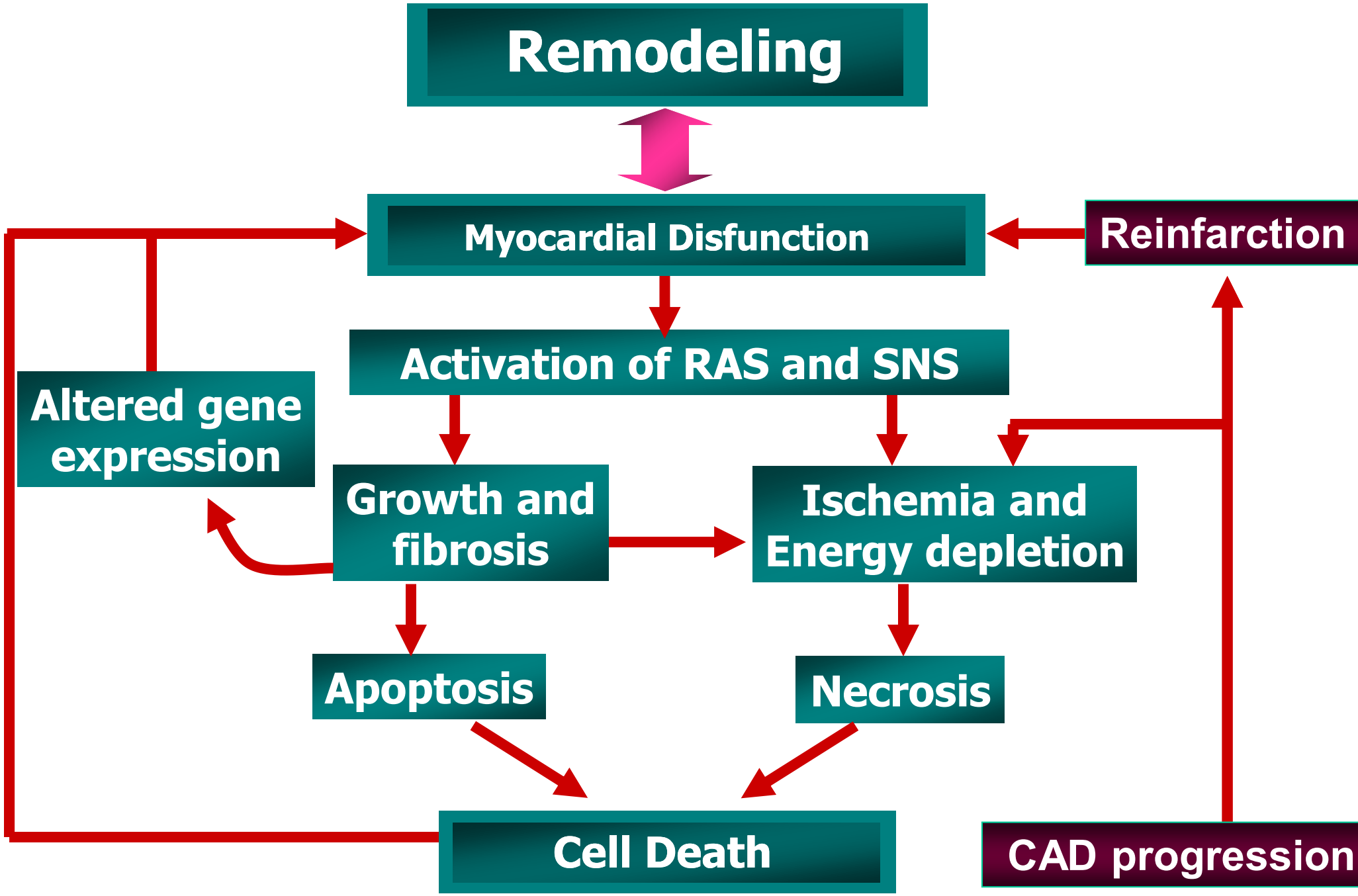
“R E A L T Á”

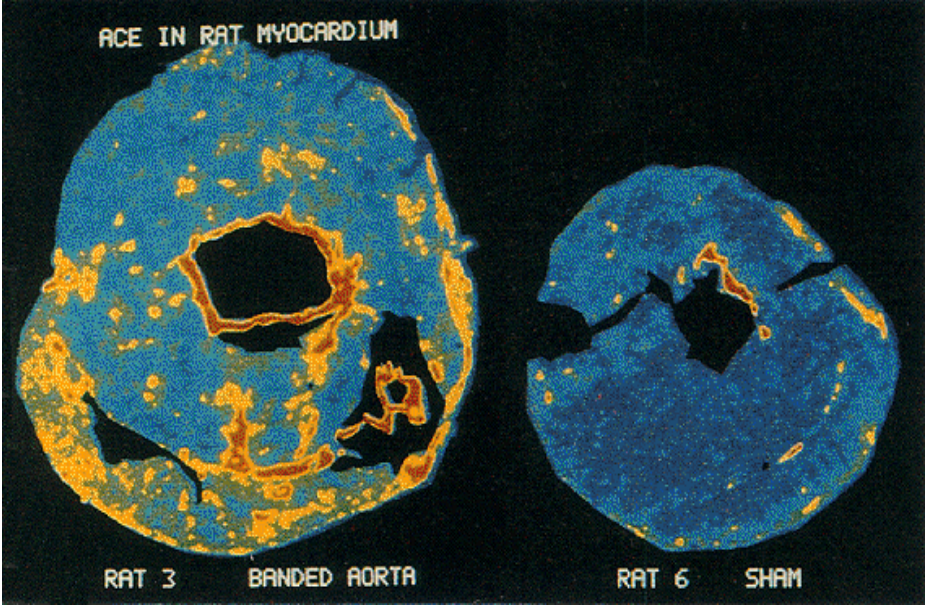


Ischemia

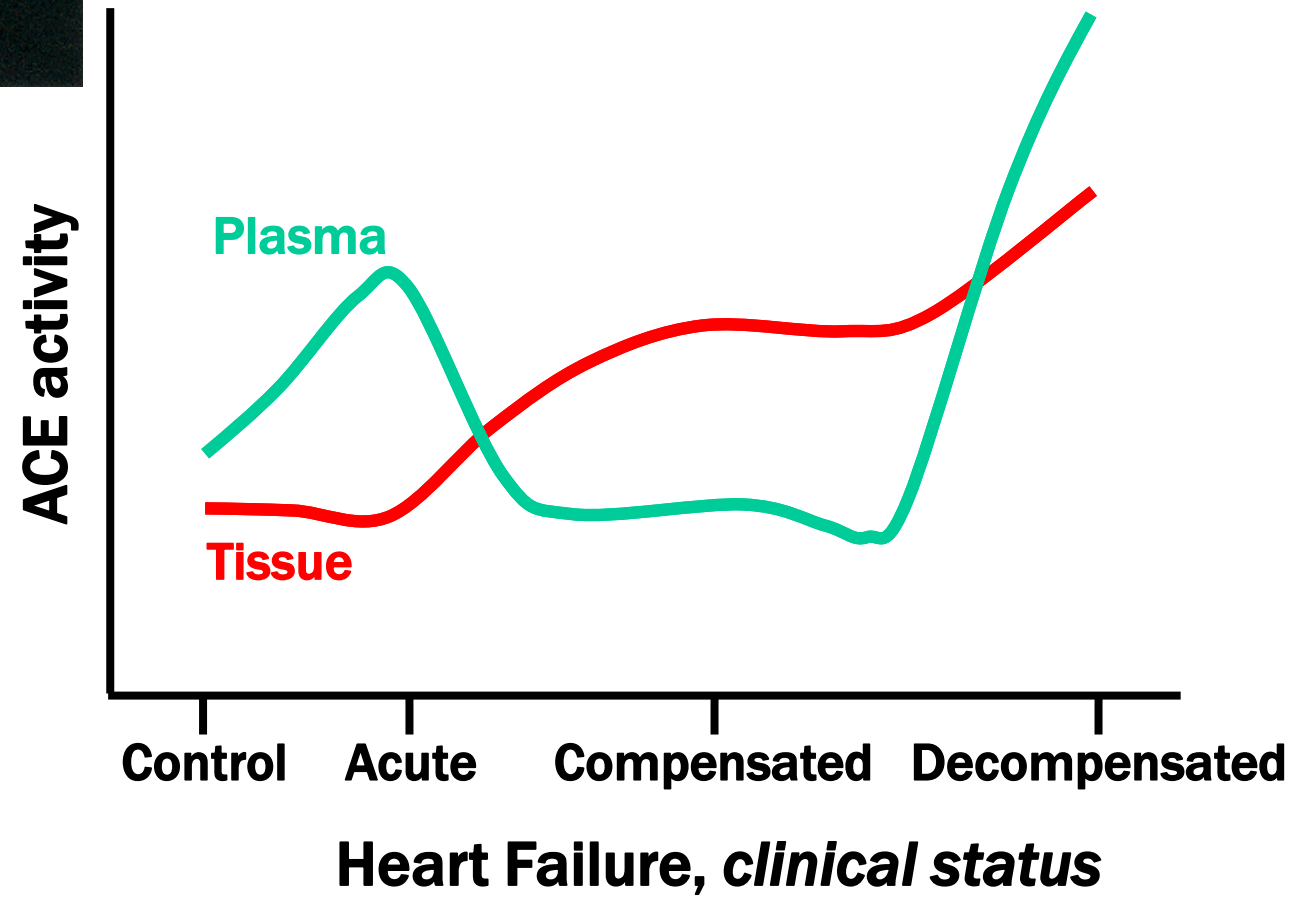
Ricanalizzazione & riperfusione

“ No reflow “


Remodeling
Myocardial Disfunction
Reinfarction
Activation of RAS and SNS
Altered gene expression
Growth and fibrosis
Ischemia and Energy depletion
Apoptosis
Necrosis
Cell Death
CAD progression

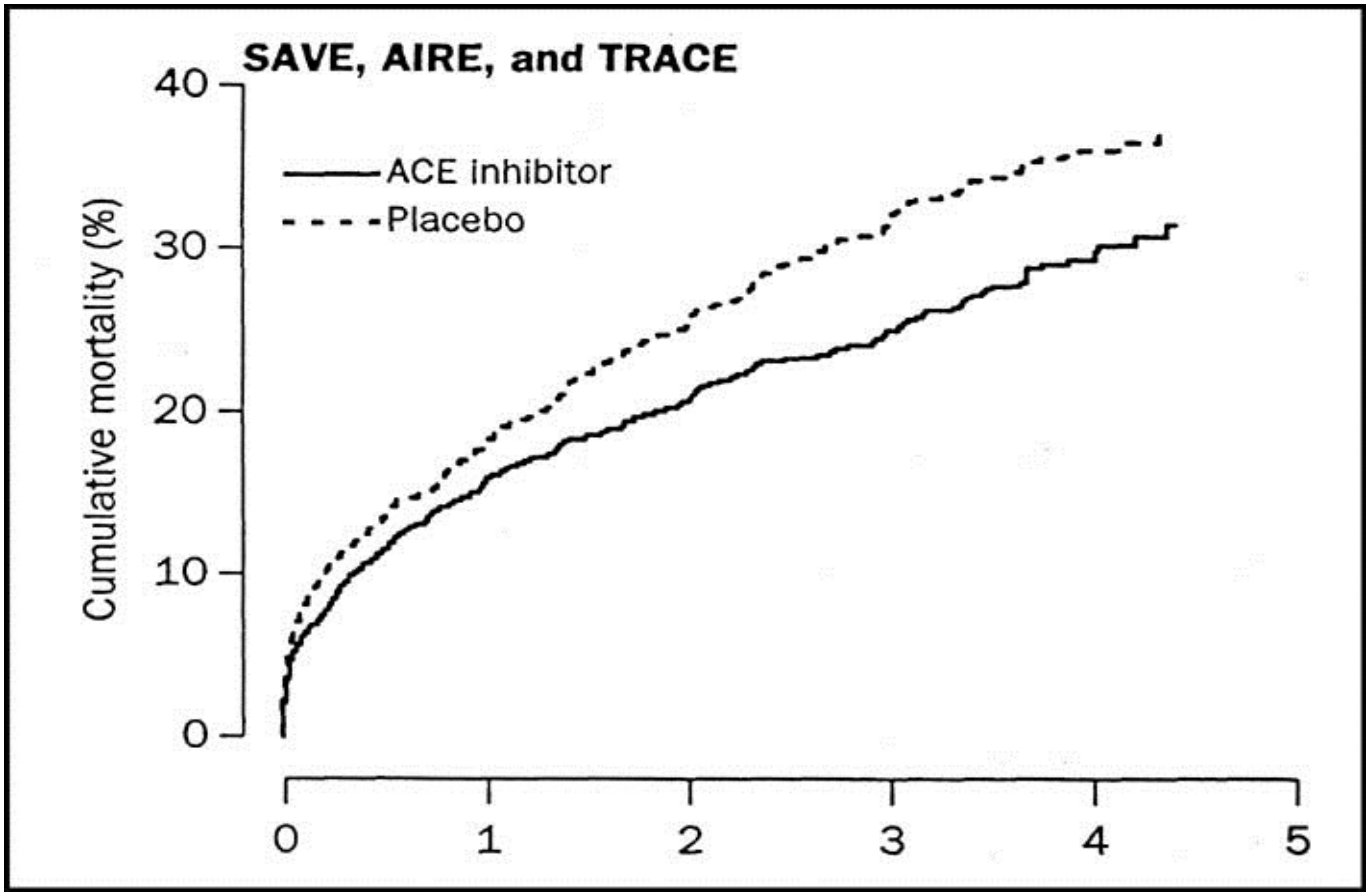


ACE Activity in Heart Failure



ACE inibitori nel post-infarto

Metanalisi degli studi SAVE, AIRE e TRACE del trattamento con ACE-inibitori in pazienti con scompenso cardiaco o disfunzione ventricolare sinistra nel corso di infarto miocardico



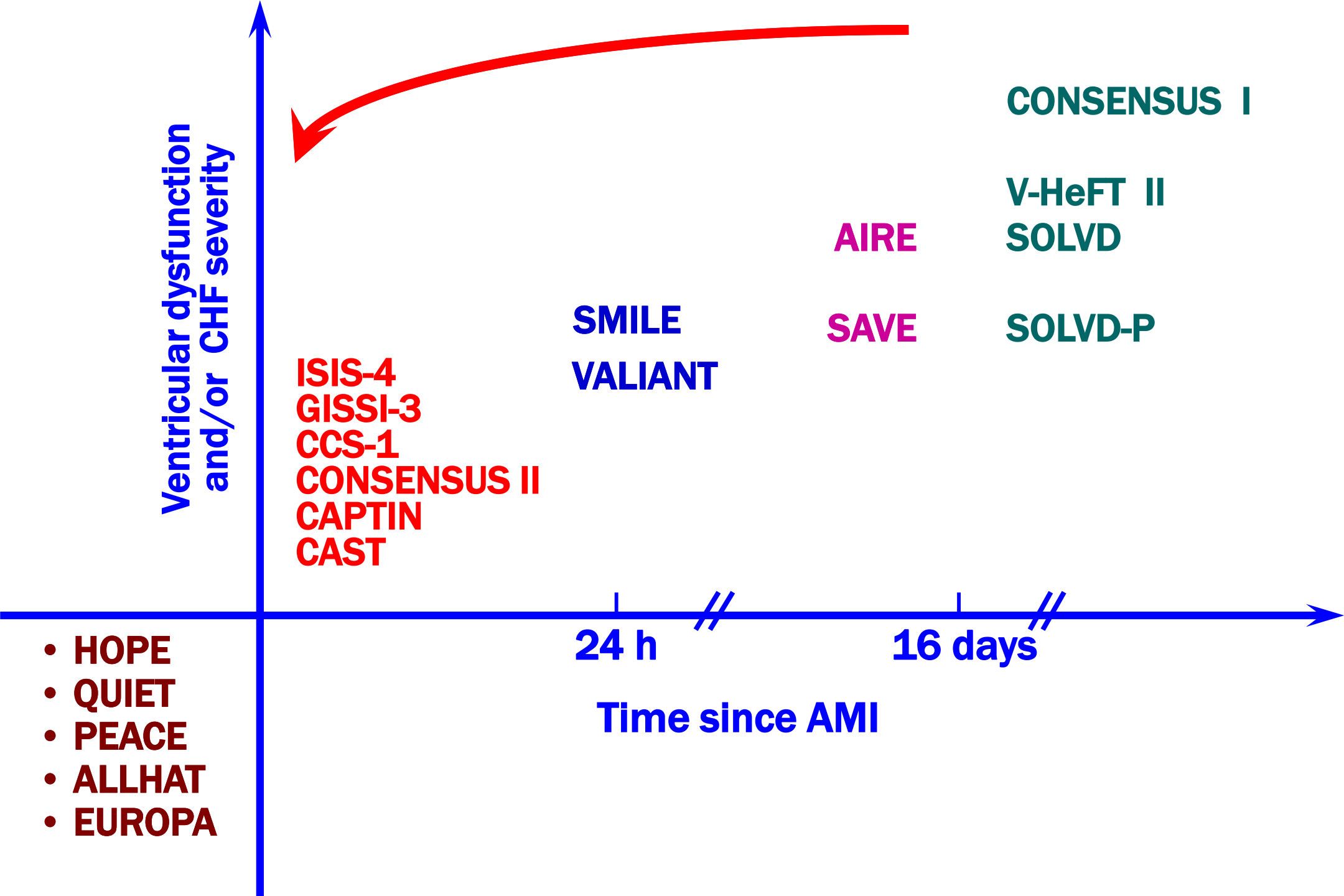
mortalità

controlli	23.4%
trattati	29.1%

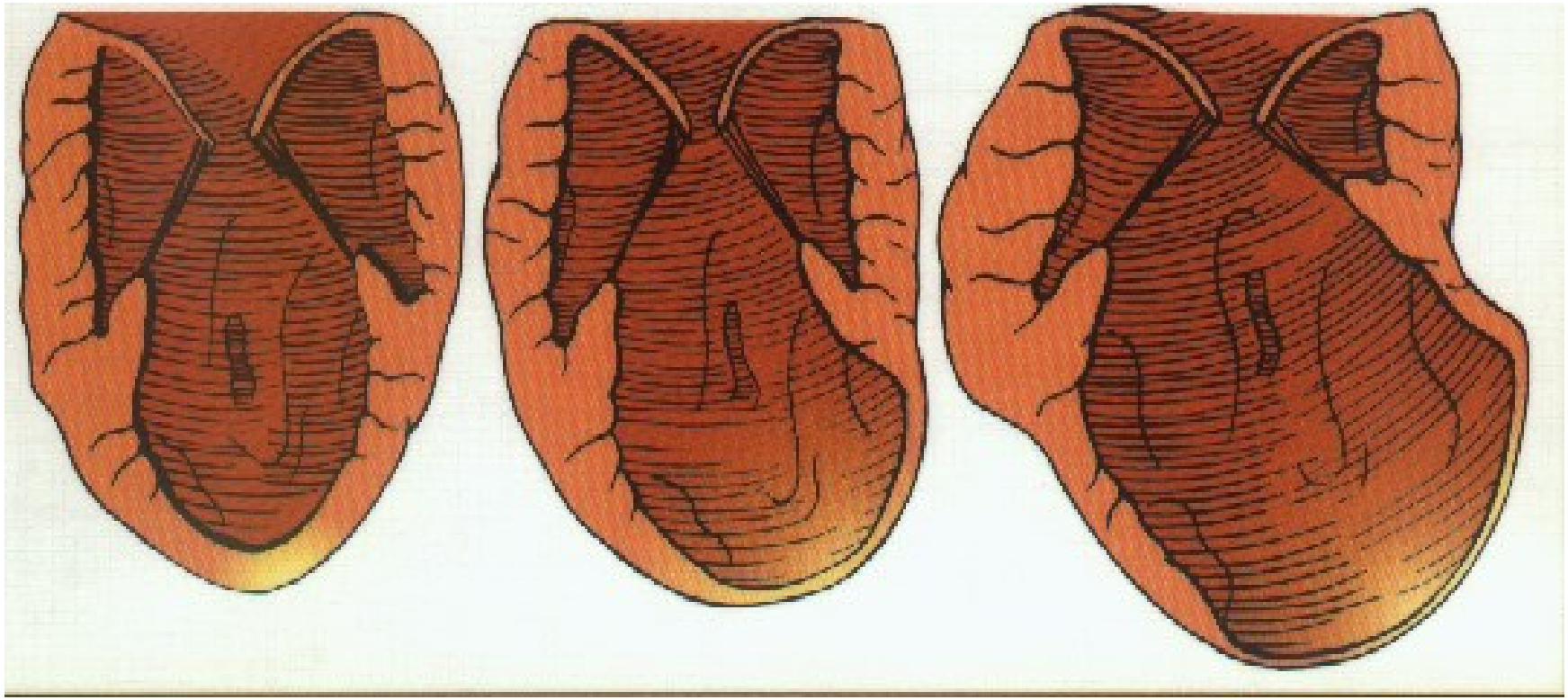
OR (95% IC)

0.74 (0.66-0.83)

(ACE Inhibitor Myocardial Infarction Collaborative Group, Lancet, 2000)


Ventricular dysfunction and/or CHF severity
CONSENSUS I
V-HeFT II
AIRE
SOLVD
SMILE
SAVE
SOLVD-P
VALIANT
ISIS-4
GISSI-3
CCS-1
CONSENSUS II
CAPTIN
CAST
24 h
16 days
Time since AMI
• HOPE
• QUIET
• PEACE
• ALLHAT
• EUROPA

Rimodellamento Ventricolare dopo IMA



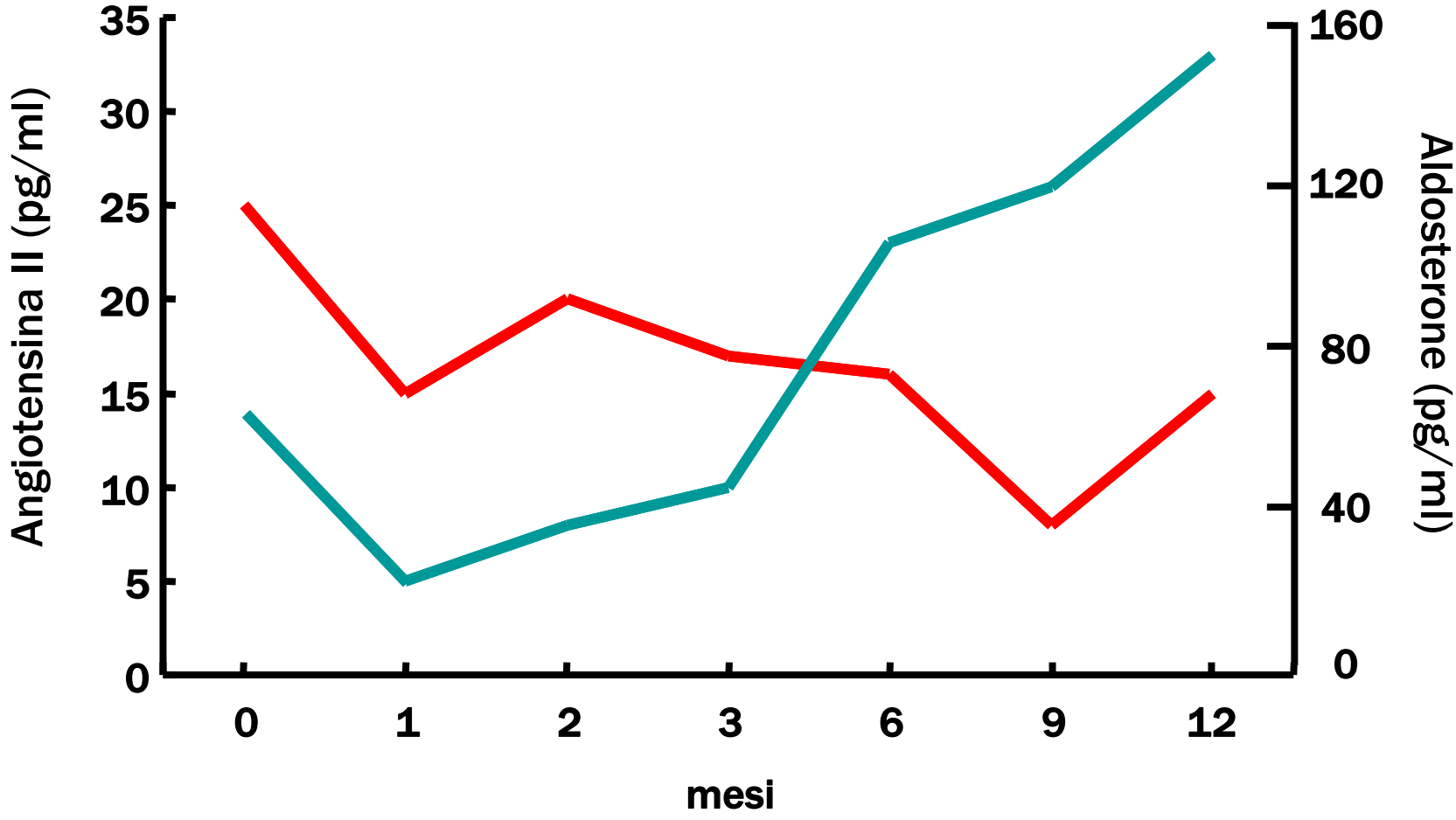
Fase acuta

Rimodellamento

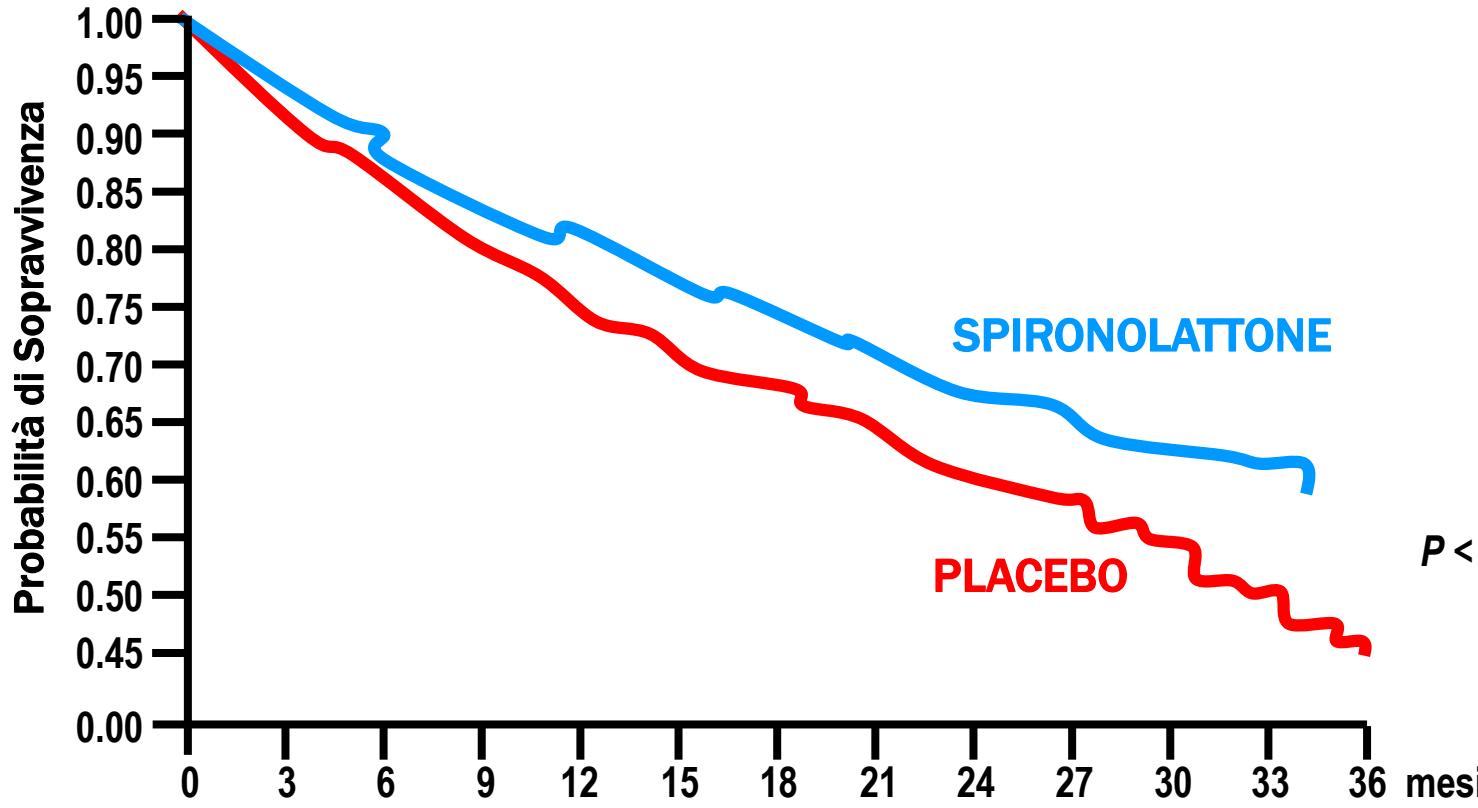
precoce

tardivo

Il Fenomeno dell'Escape del Sistema RAA in Corso di ACE-inibizione



RALES



N° a rischio													
Placebo	841	775	723	678	628	592	565	483	379	280	179	92	36
Spironolattone	822	766	739	698	669	639	608	526	419	316	193	122	43

B Pitt et al. *N Engl J Med* 1999;709-717

Pharmacologic Effects

vs

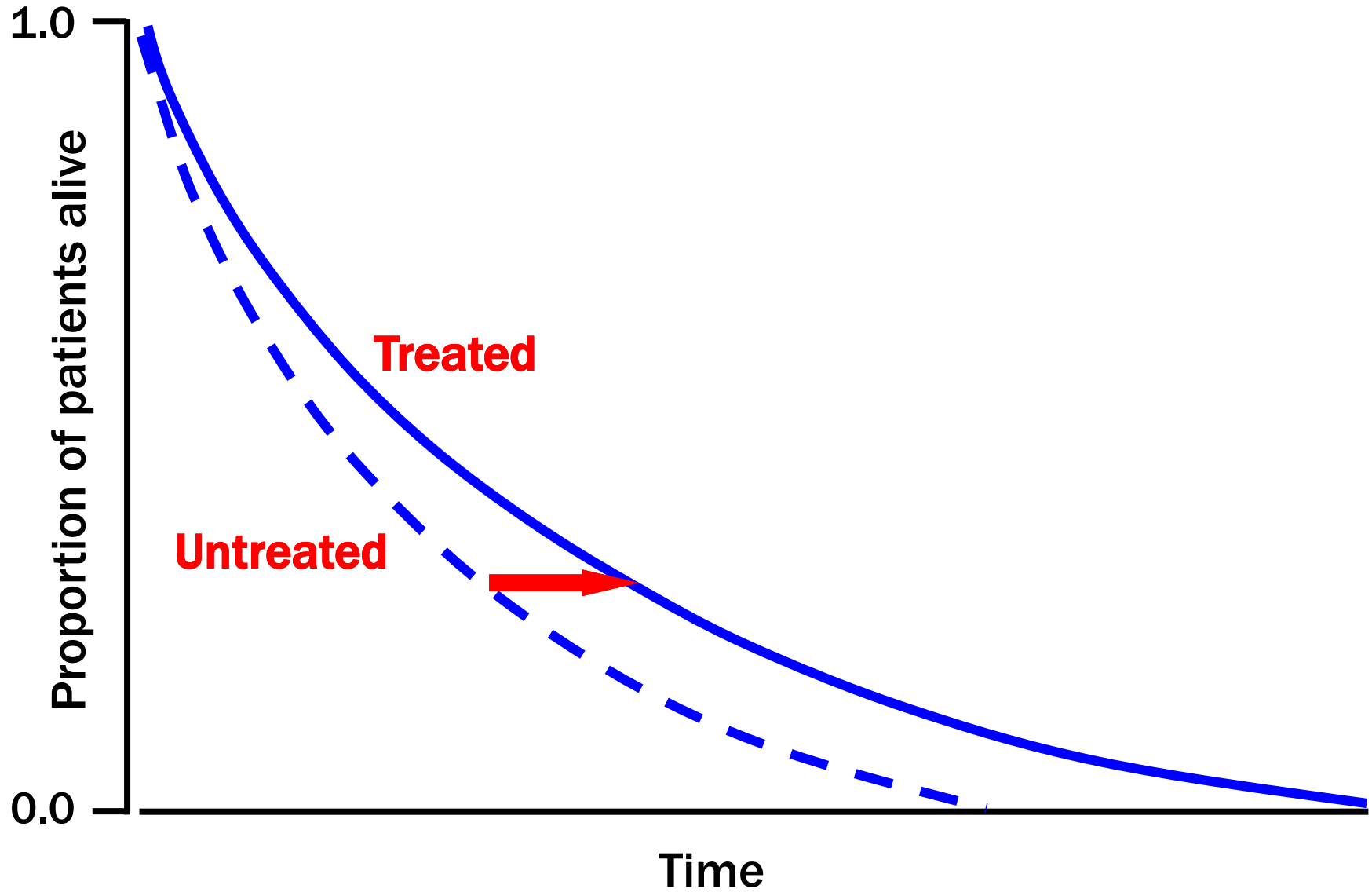
Biologic Effects

Le “sorprese” dei grandi trial

Ace-inibitori, sartani e ....

- prevenzione primaria della disfunzione ventricolare e dello scompenso
- prevenzione degli eventi coronarici
- prevenzione degli eventi cerebrovascolari
- prevenzione della fibrillazione atriale
- prevenzione del diabete mellito

The Concept of ADLG (Average Duration of Life Gained)



Qual' è la reale capacità degli ACE-I di prolungare la sopravvivenza ?

Modello clinico	↓ rischio relativo	ADLG
CONSENSUS I	27 %	9 mesi
SOLVD	16 %	3 mesi
GISSI / ISIS / CCS	7 %	1 mese
TRACE	18 %	15 mesi

Randomised Clinical Trials in CHF

Trial	Annualized placebo mortality rate
CONSENSUS	58.0 %
RALES	24.0 %
COPERNICUS	18.5 %
BEST	16.6 %
CIBIS II	13.2 %
V-HeFT II	12.5 %
SOLVD-T	11.8 %
US CARVEDILOL	11.1 %
MERIT-HF	11.0 %
SAVE	10.5 %
ELITE II	10.4 %
Val-HeFT	10.0 %
ELITE I	8.7 %

Heart Failure

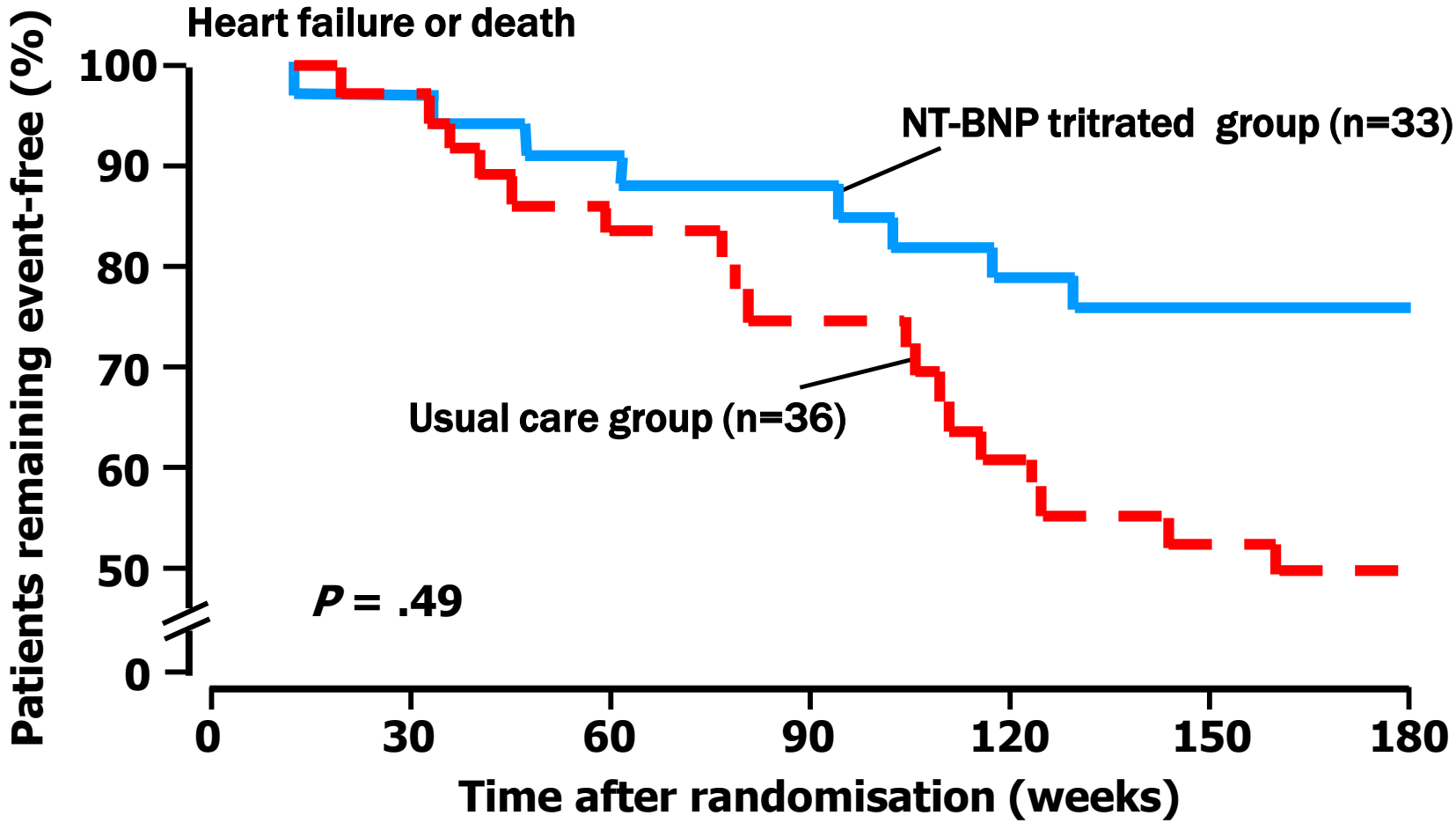
Pathophysiological Abnormalities

- structural remodeling and dilation of LV
- reduced myocytes shortening and wall motion
- Na retention and circulatory congestion
- vasoconstriction and vascular remodeling
- neurohormonal activation

ATTIVAZIONE SIMPATICA
CONSEGUENZE SFAVOREVOLI

- **Aumento del lavoro cardiaco**
- **Riduzione della perfusione coronarica**
- **Aumento del pre e post-carico**
- **Ritenzione idrica e congestione del circolo**
- **Ischemia e necrosi miocardica**
- **Ipokaliemia e aritmie**

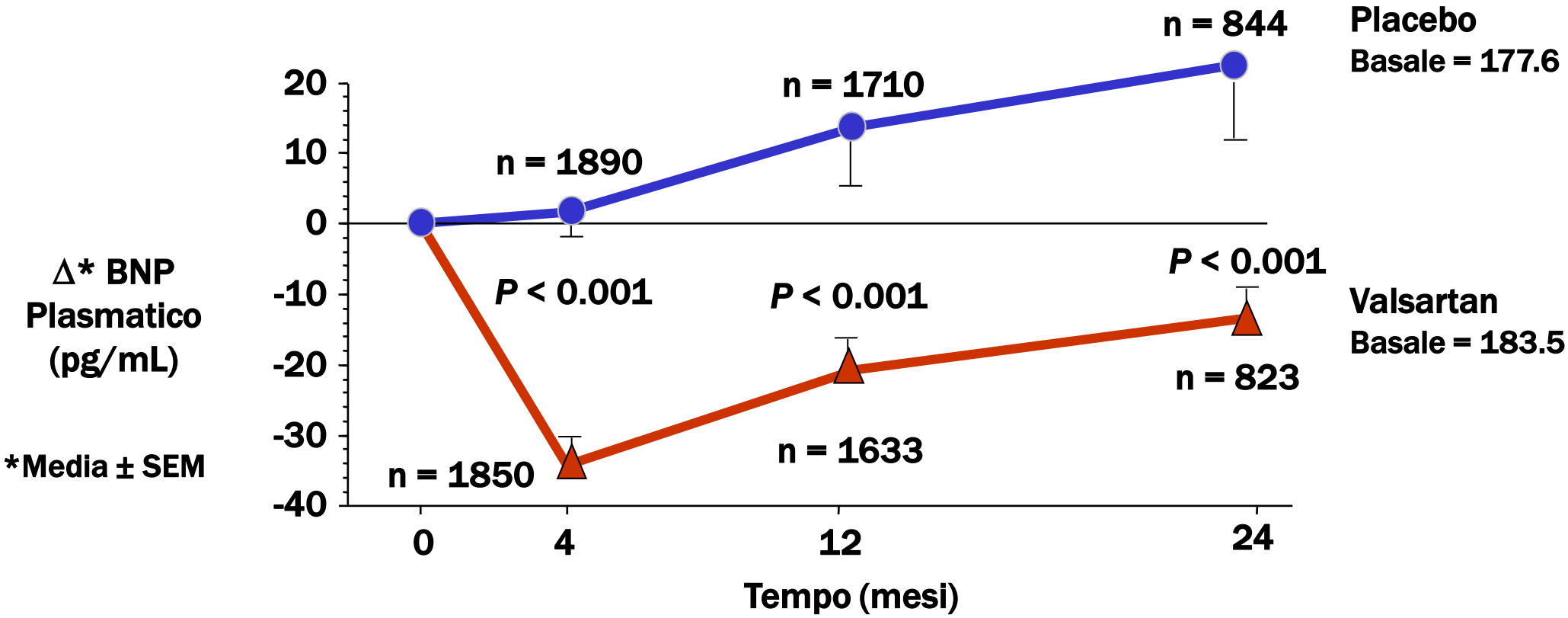
Terapia Ottimizzata per lo Scompenso: Importanza della Normalizzazione del BNP



Troughton et al. *Lancet.* 2000;355:1125-30.

Val-HeFT

Variazione dei Livelli Plasmatici di BNP



Latini R et al. *J Card Fail*. 2001;7(Suppl 2):Abstract 198.

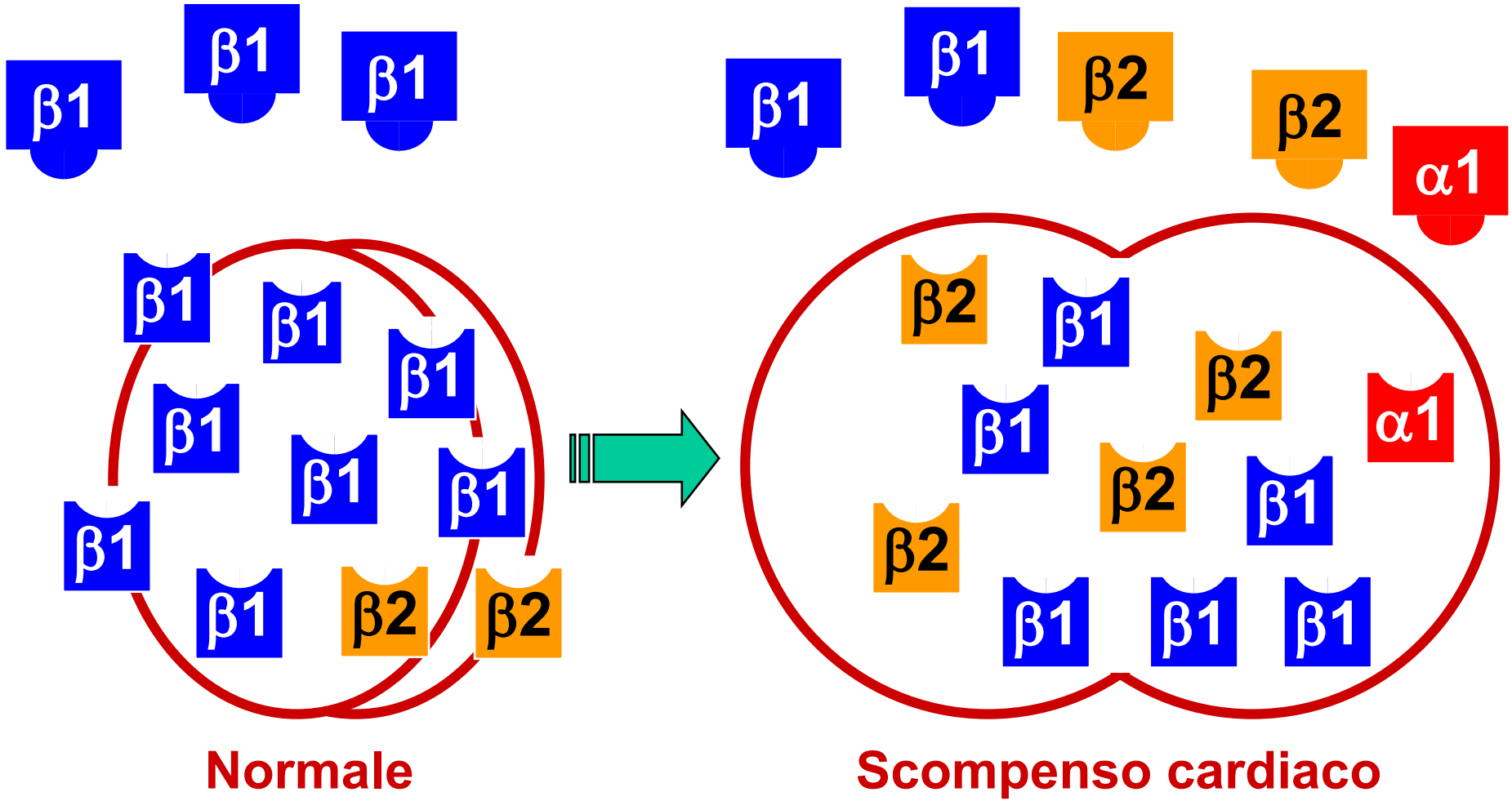
β-Blockade in Mild-to-Moderate Heart Failure

Mortality Reduction

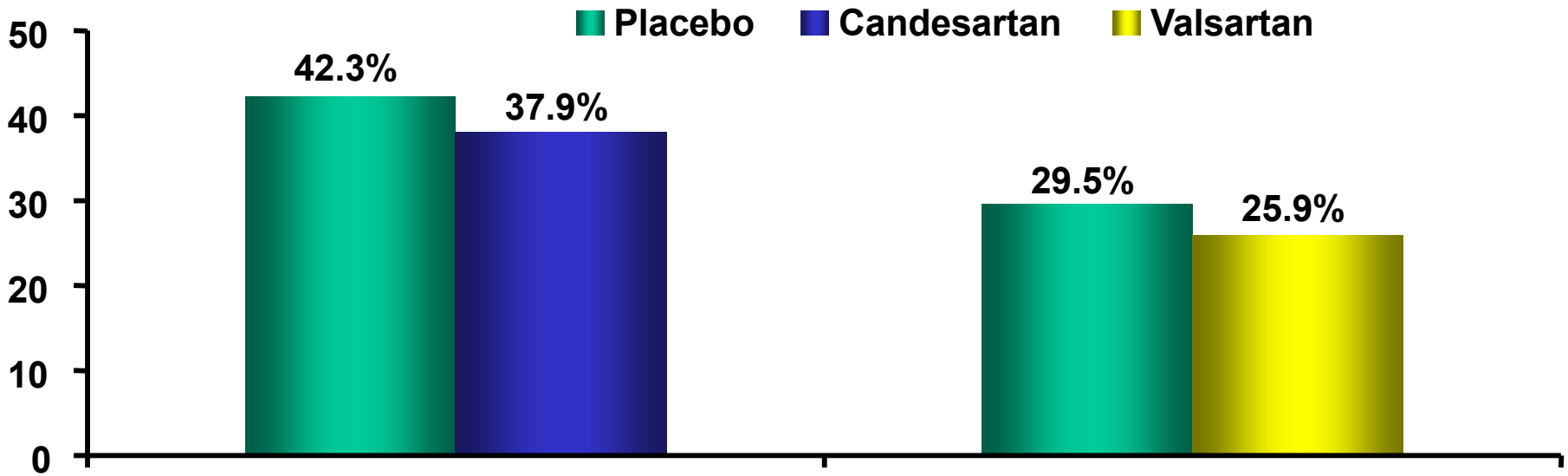
Trial	*n*	*Reduction in relative risk*	*p value*
CIBIS-I	*641*	*-20%*	*ns*
CIBIS-II	*2647*	*-34%*	*p<0.0001*
ANZ	*415*	*-23%*	*ns*
US Carvedilol	*1094*	*-65%*	*p<0.001*
MERIT-HF	*3991*	*-34%*	*p=0.0062**

*Adjusted for two interim analyses

Lo Scompenso Cardiaco Modifica la Densità dei Recettori Adrenergici nel Miocardio



CHARM-Added and Val-HeFT (CV death or hospitalization for HF)

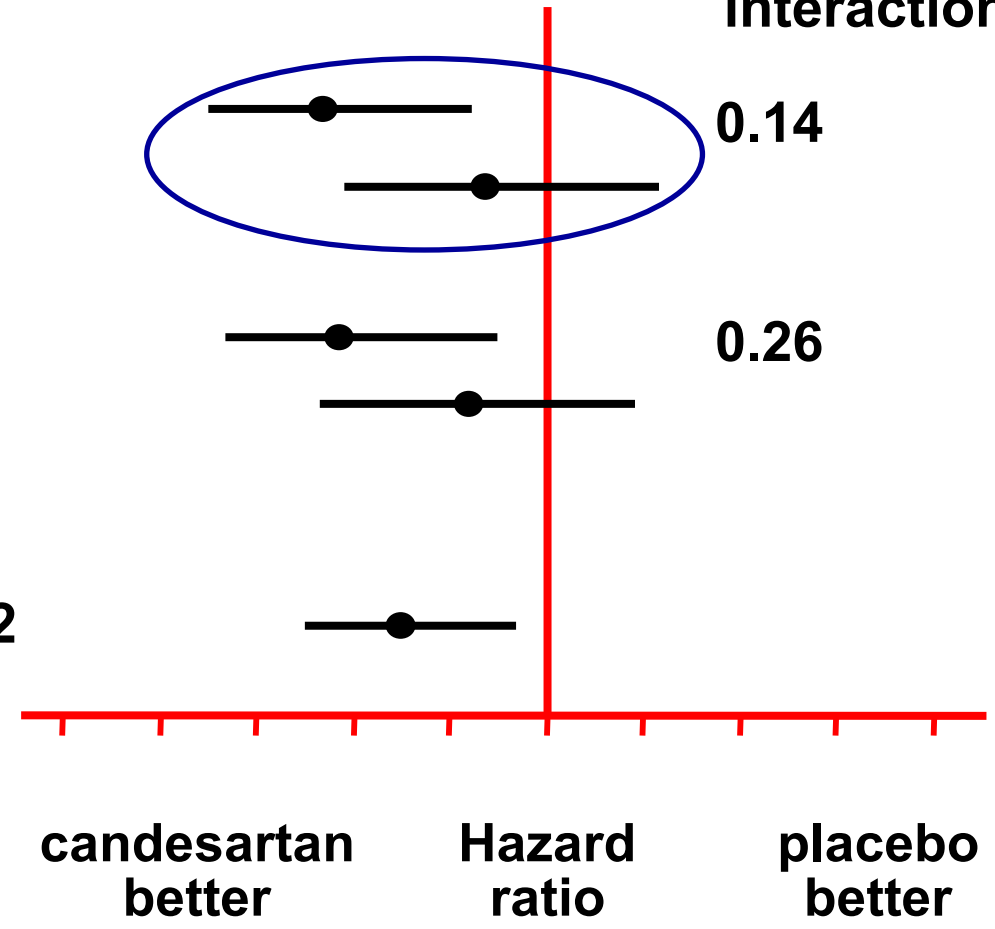


	Placebo	Candesartan	Placebo	Valsartan
Events/treated	538/1272	483/1276	737/2499	650/2511
%	42.3	37.9	29.5	25.9
HR		0.85		0.86
95% CI		0.75-0.96		0.77-0.95
P value		0.011		0.004

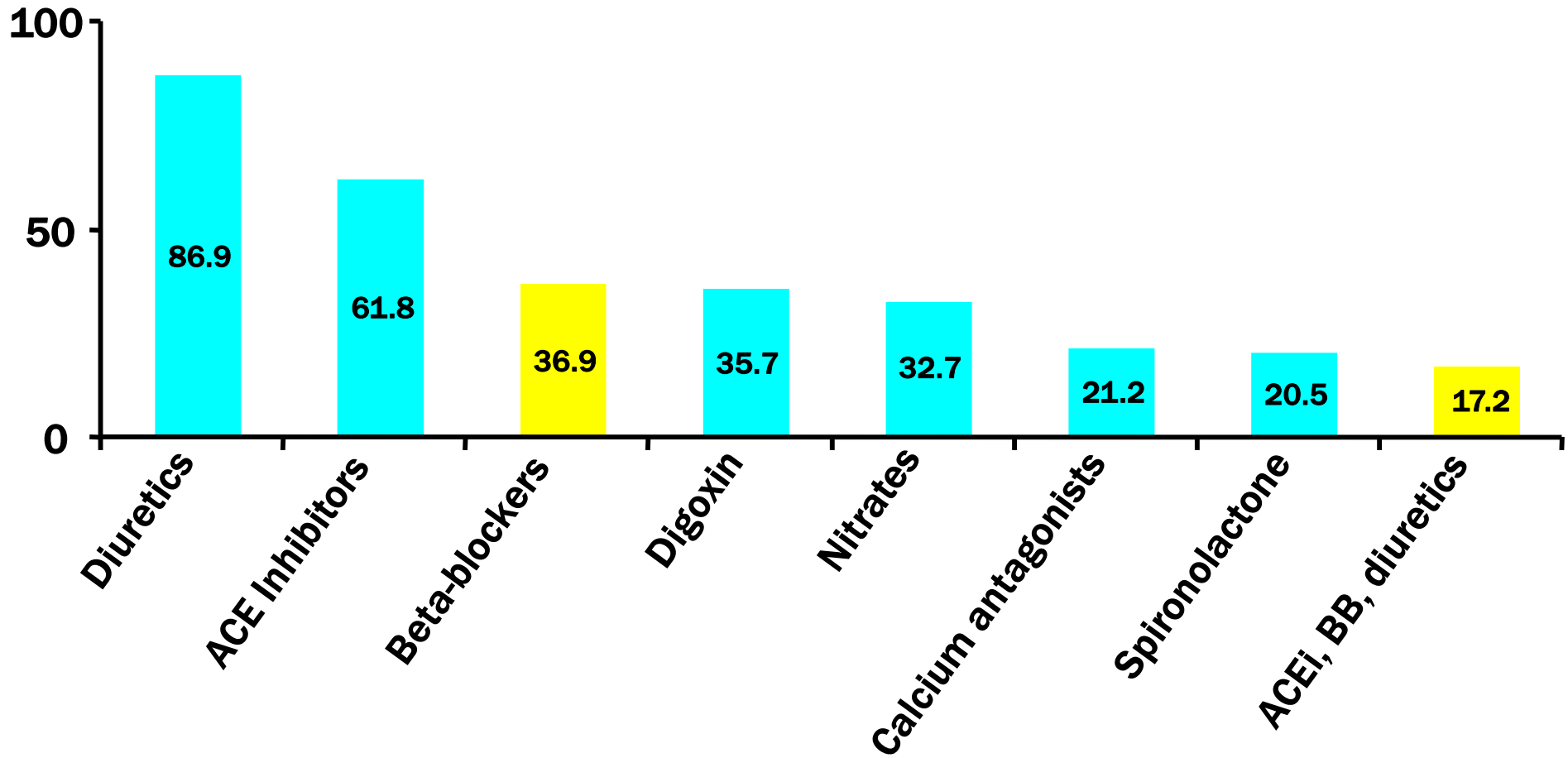
Granger CB et al. *Lancet*. 2003;362:772-776.
Cohn JN et al. *N Engl J Med.* 2001;345:1667-1675.

CHARM-Added: Prespecified subgroups, CV death or CHF hosp.

		Candesartan	Placebo	p-value for treatment interaction
Beta-blocker	Yes	223/702	274/711	0.14
	No	260/574	264/561	
Recom. dose of ACE inhib.	Yes	232/643	275/648	0.26
	No	251/633	263/624	
All patients		483/1276	538/1272	



Utilisation of β Blockade for CHF in Clinical Practice



Komajda M et al. Eur Heart J 2003

Perceptions

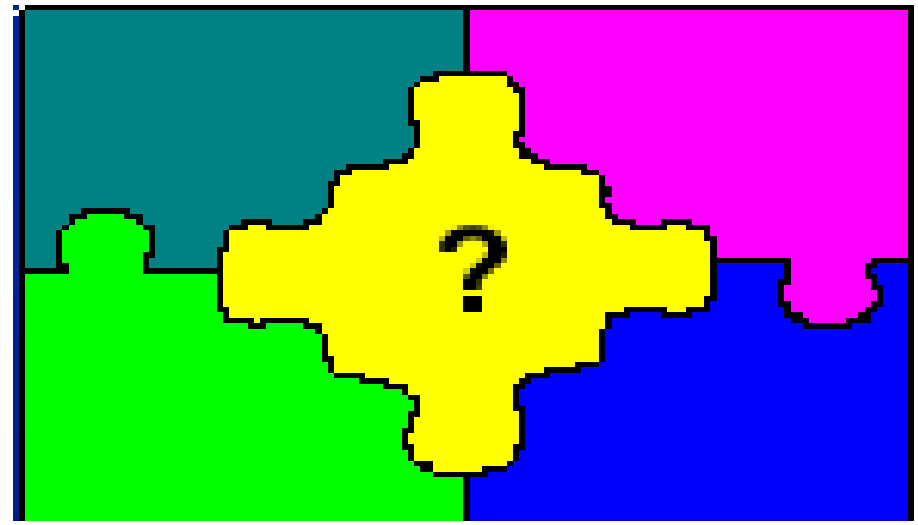
Regarding Tolerability of β Blockade in CHF

- Complexity in initiation and up-titration
- Risk of intolerance and / or worsening of CHF symptom status esp. with initiation
- Delay in beneficial effects on outcomes
- All of the above esp. true in patients with advanced disease

Esistono differenze di trattamento a seconda dei medici?

Cardiologo

Internista



Geriatra

Medico di MG

CHF Hospitalization: Specialty Related Disparities in Practice Patterns and Outcome

	Cardiologi	Internisti	P
NYHA I-II	<15%	50%	0.01
Età media	68±19	72±6	0.01
Ecocardiogramma	49%	34%	0.01
Uso diuretici	87%	76%	0.02
Inotropi ev	9%	1,3%	0.02
Reospedalizzazione	30%	44%	0.04

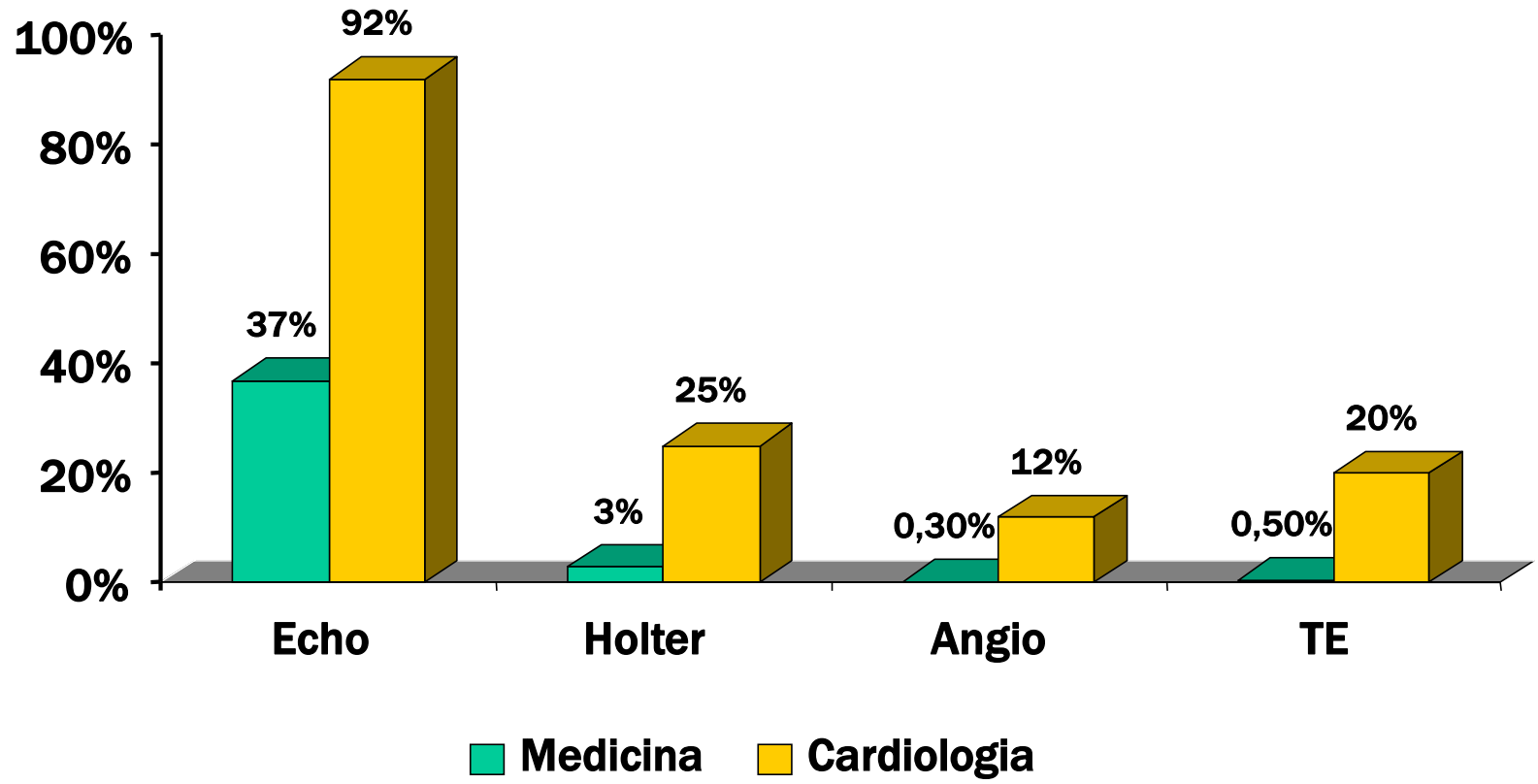
Reis SE et al. J Am Coll Cardiol 1997;30:733-8

Differences Between Practioners and Cardiologists in Diagnosis and Management of Heart Failure: A Survey in Every-day Practice

	Cardiologi	GP	P
Maschi	78%	42%	<0.001
Età Media	64,2	78,2	<0.001
Eco	97%	12%	<0.001
Rx Torace	84%	51%	<0.001
Coronarografia	26%	3%	<0.001
C. Ischemica	56%	31%	<0.001
ACE-I	76%	40%	<0.001
Betabloccanti	30%	8,7%	<0.001
Spironolattone	32%	11%	<0.001
Dicumarolici	29%	6,8%	<0.001

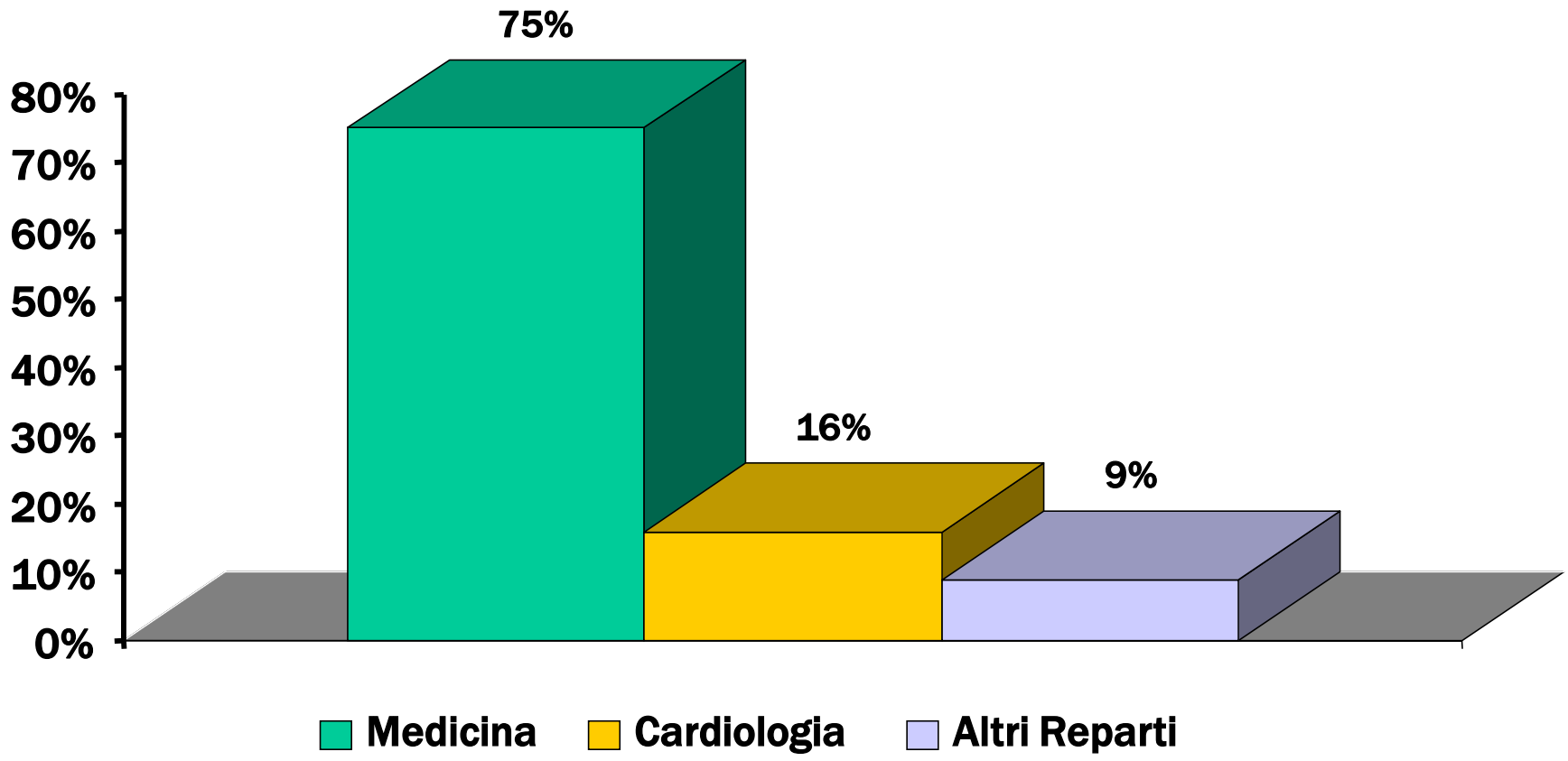
Rutten FH et al. Eur J Heart Failure 2003;5:337-44

Procedure eseguite durante il ricovero



Eur Heart J 2001;22:506

DRG 127 in Lombardia, Liguria e Toscana
1997



TEMISTOCLE

(hearT failurE epideMIological STudy FADOI-ANMCO in itaLian pEople)

TERAPIA FARMACOLOGICA DURANTE LA DEGENZA

	Medicine (n. 1338)	Cardiologie (n. 789)	p
Inotropi	14.3%	25.6%	<.0001
ACE-inibitori	73.0%	70.5%	NS
Digitale	70.2%	64.4%	0.0056
Furosemide	95.5%	95.7%	NS
Spironolattone	34.4%	52.1%	<.0001
Betabloccanti	7.3%	15.7%	<.0001
ARBs	5.2%	9.2%	0.0003
Amiodarone	10.7%	25.9%	<.0001

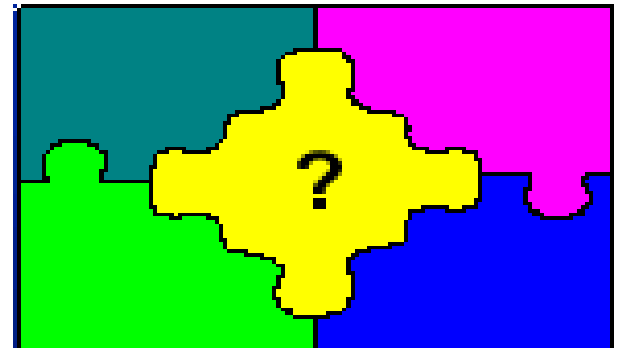
TEMISTOCLE

(hearT failurE epideMIological STudy FADOI-ANMCO in itaLian pEople)

TERAPIA FARMACOLOGICA ALLA DIMISSIONE

	Medicine (n. 1259)	Cardiologie (n. 748)	p
Inotropi	5.9%	5.2%	NS
ACE-inibitori	75.8%	71.0%	0.02
Digitale	61.5%	59.9%	NS
Furosemide	85.5%	89.6%	0.0082
Spironolattone	31.3%	49.1%	<.0001
Betabloccanti	8.7%	17.8%	<.0001
ARBs	6.2%	9.2%	0.012
Amiodarone	8.1%	22.9%	<.0001

Chi Deve Fare Che Cosa?



The explosion in HF devices, part 1: Culture, economics, and unresolved issues

I think there is an ethical imperative to consider implanting these devices into all these patients

Some cardiologists are leaping onto devices as cure-alls when patients aren't even on maximal medical therapy

This represents a real ethical dilemma that in this country we tend not to be very good at facing directly

The trial experience is in a relatively select group

In Sweden there is not the money for this, so we don't screen

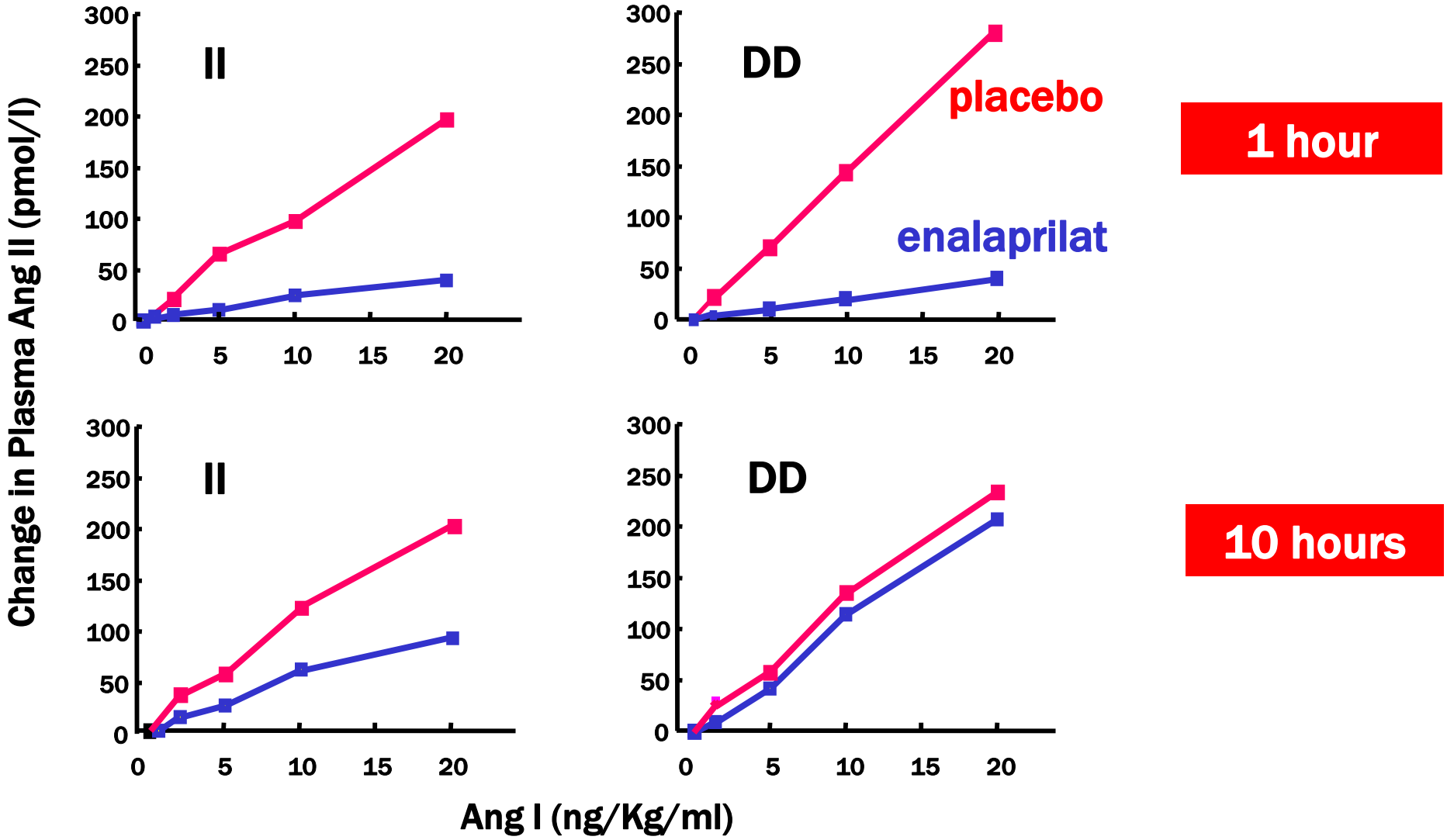
We may be changing their mode of death from a sudden arrhythmic death to drowning by heart failure

Reduction in all-cause and cardiac mortality in the overall study group (n=713)

End point	Relative risk reduction	95% CI	Adjusted p
All-cause mortality	0.36	0.15 to 0.68	0.03
Cardiac mortality	0.39	0.16 to 0.78	0.04

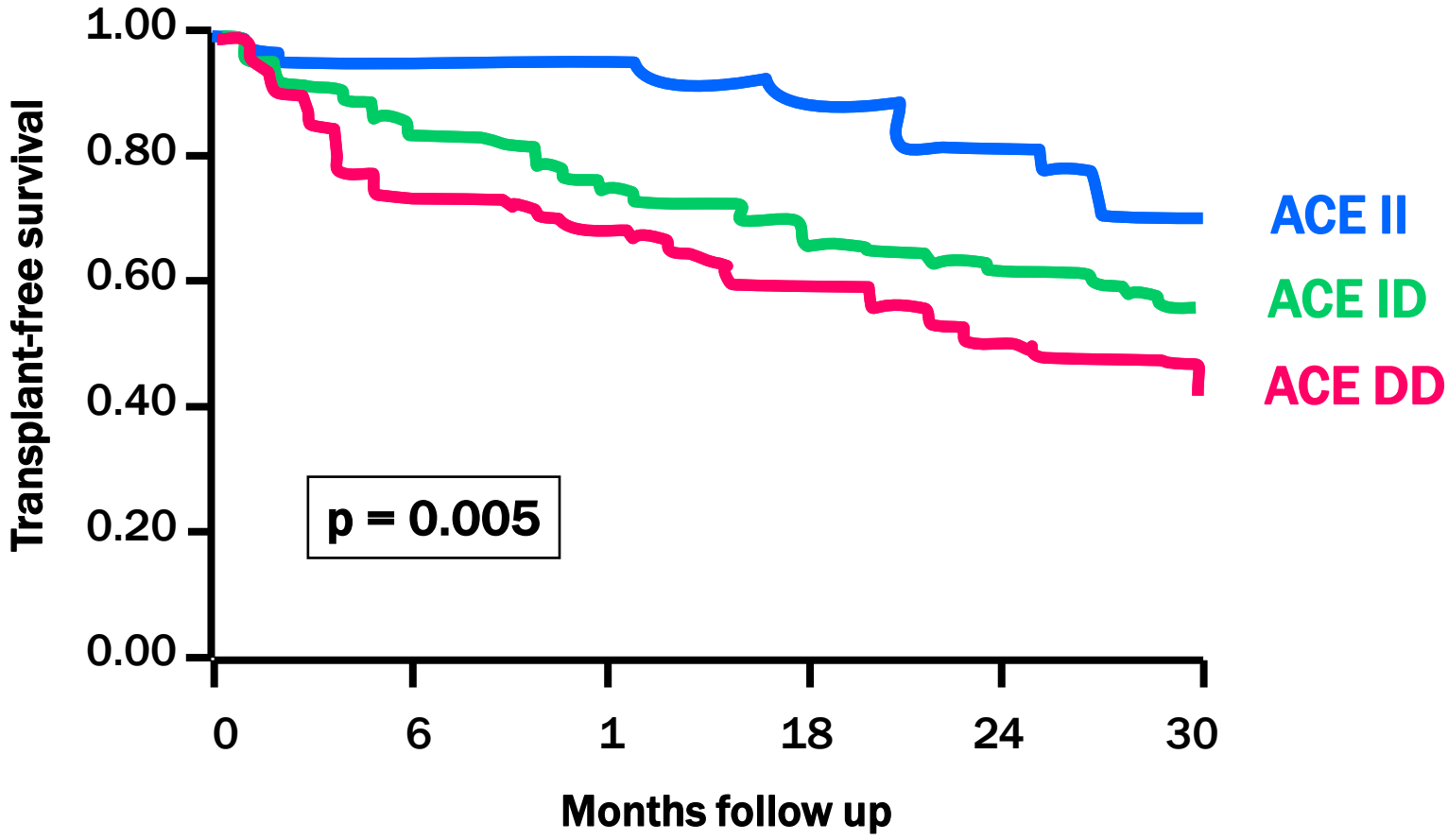
Mitchell LB et al. *J Am Coll Cardiol* 2003; 42:81-87.

Changes in Plasma Ang II Levels During Ang I Infusion



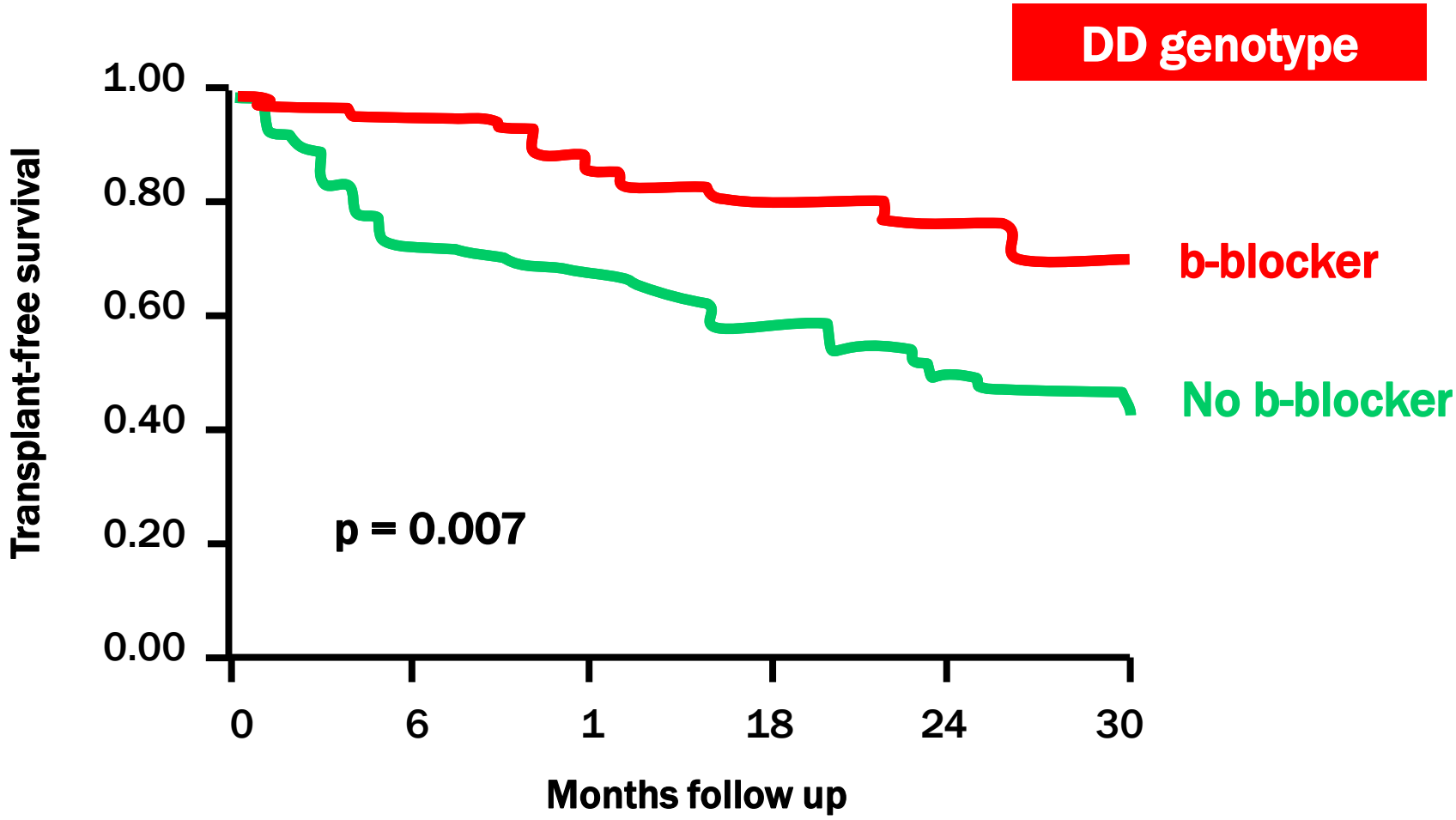
Ueda S et al. Hypertension 1998

ACE Polymorphism and β-Blocker Therapy



McNamara DM et al. Circulation 2001;103:1644

ACE Polymorphism and β-Blocker Therapy



McNamara DM et al. Circulation 2001;103:1644