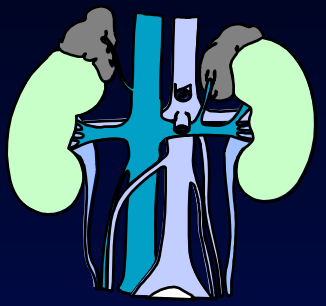
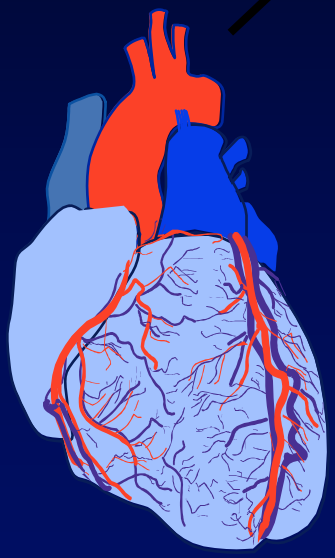
HF treatment: perspectives

- Better ethiological definition and evaluation of precipitating factors and comorbidities
- Better use of drugs and their association/dosages
- Better selection of patients for devices
- Structured long term follow up program with help of telemonitoring
- LVAD as DT
- …Personalized medicine, gene therapy and regenerative medicine

CHF - A complex clinical syndrome





Forward failure

Renal perfusion ↓

Neurohumoral activation

Renin, Angiotensin II ↑

Adrenergic activation

Aldosterone

Apoptosis
Inflammation
Tachycardia

Vasoconstriction

Na^+ and H_2O retention

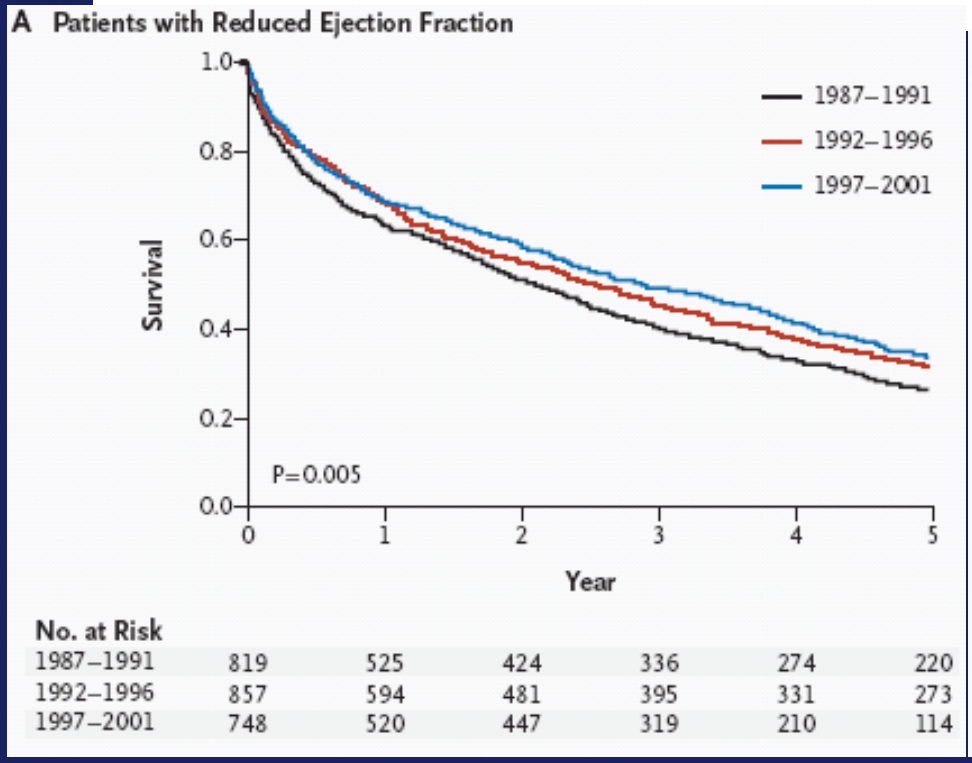
LV function ↓

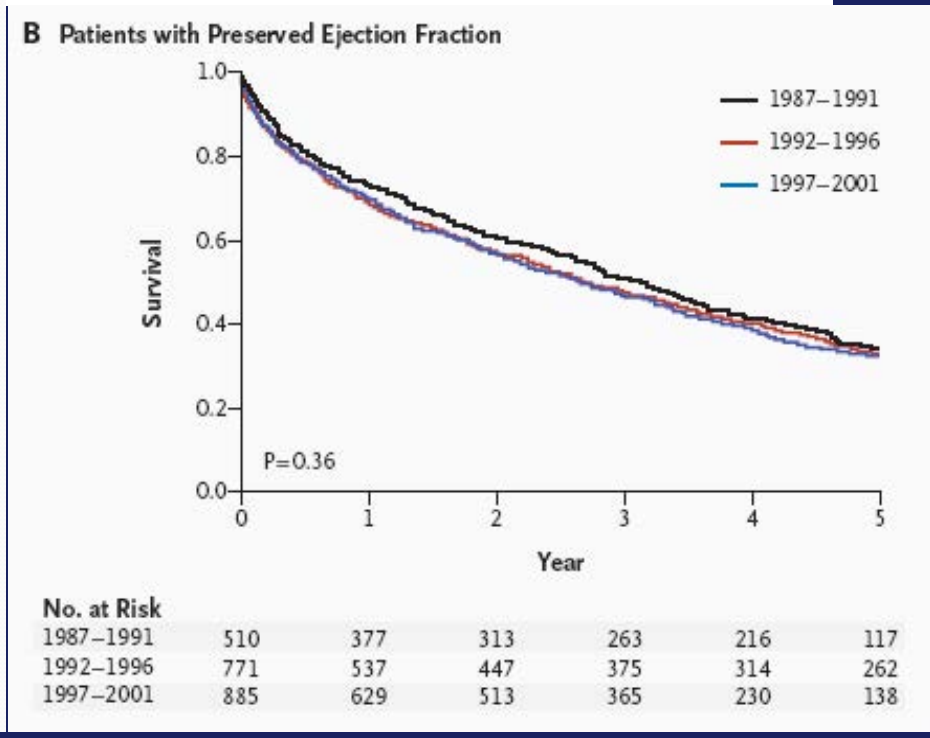
Increased LV afterload, increased O2 demand

Trends in Prevalence and Outcome of Heart Failure with Preserved Ejection Fraction

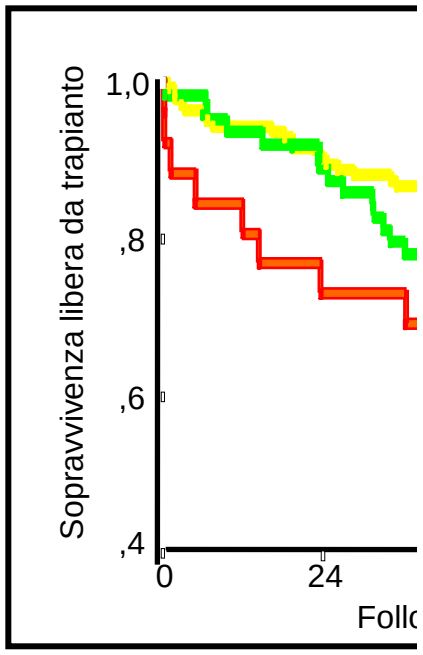
Theophilus E. Owan, M.D., David O. Hodge, M.S., Regina M. Herges, B.S., Steven J. Jacobsen, M.D., Ph.D., Veronique L. Roger, M.D., M.P.H., and Margaret M. Redfield, M.D.

N Engl J Med 2006;355:251-9.





TS DCM Registry - CHANGING MORTALITY in DCM



Di L
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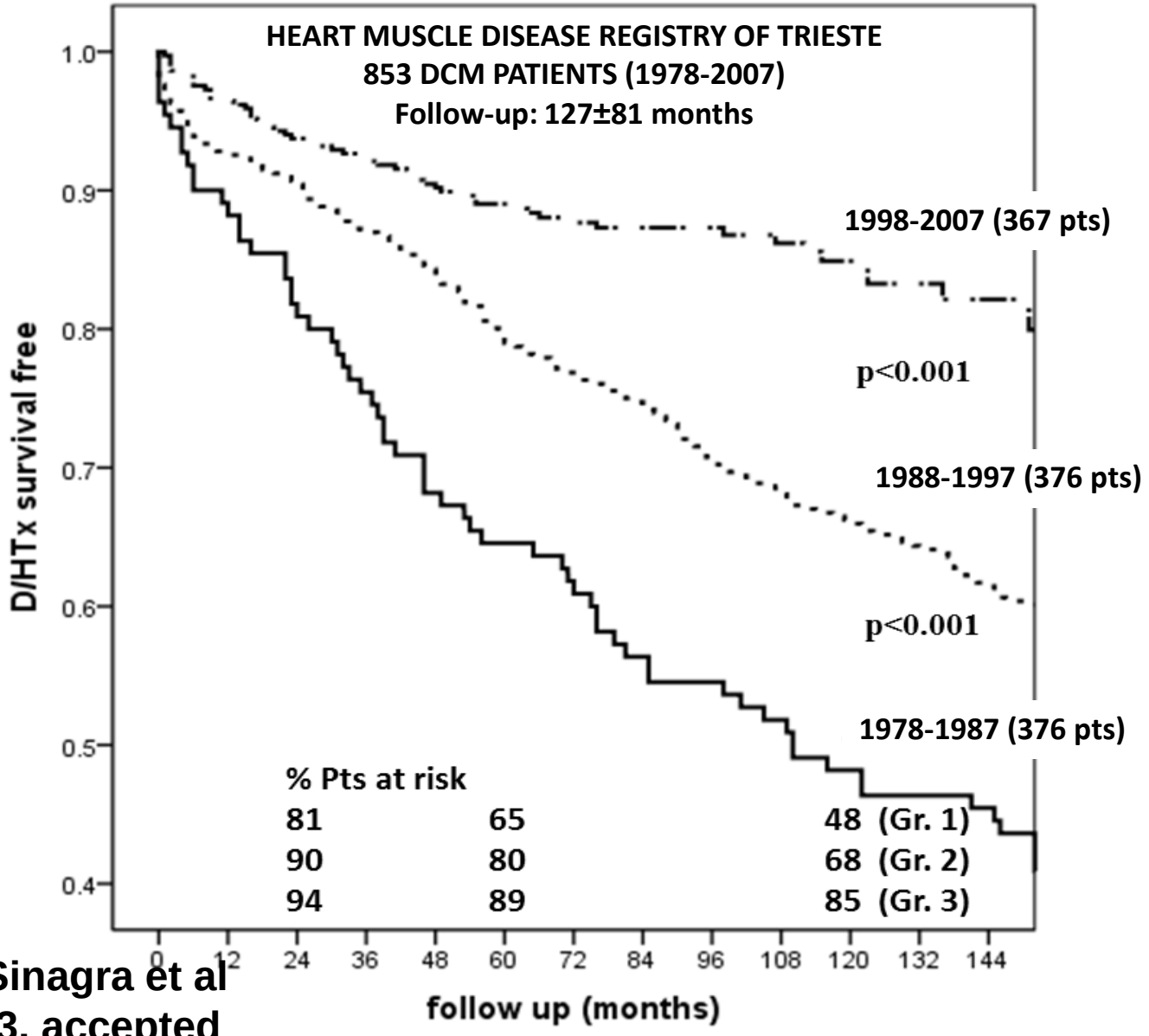


Merlo, Di Lenarda, Sinagra et al
Eur J Heart Fail 2013, accepted

Pharmacological Treatment of Heart Failure

- Simplistic Assumptions:
  - All HF is the same
  - HF remains the same for each patient throughout natural history
  - Drugs metabolised on a similar fashion by all
  - Clinical Trial Dose is appropriate for each patient

Baseline characteristics

	Acute HF (n. 1892)	Chronic HF (n. 3226)	P value
Age (years), mean±SD median [IQR]	69±13 71 [61-79]	66±13 68 [58-76]	<.0001
Age ≥70 years, %	54.2	46.5	<.0001
Females, %	37.4	29.7	<.0001
Ischemic etiology, % *documented by coronary angiography, %*	50.7 *64.3*	40.5 *84.9*	<.0001
BMI (kg/m^2), mean±SD	28.2±5.6	27.7±5.0	0.005
SBP (mmHg), mean±SD	133±29	125±20	<.0001
HR (bpm), mean±SD	88±24	72±14	<.0001
EF (%), mean±SD	38±14	38±13	0.86

Clinical history

	Acute HF (n. 1892)	Chronic HF (n. 3226)	P value
Treated hypertension, %	61.8	58.3	0.015
Diabetes mellitus, %	35.1	29.0	<.0001
History of Atrial Fibrillation, %	43.7	38.6	0.0003
Previous stroke/TIA, %	9.8	10.5	0.42
PAD, %	9.9	11.2	0.16
Renal dysfunction, %	26.0	18.5	<.0001
COPD, %	15.2	15.1	0.96
PM, %	8.3	7.6	0.38
ICD, %	6.0	13.3	<.0001
CRT, %	0.4	1.0	0.02
CRT-D, %	2.9	8.8	<.0001
Previous HF hospitalization, %	56.7	58.6	0.19

Laboratory examinations (at entry/visit)

	Acute HF (n. 1892)	Chronic HF (n. 3226)	P value
Hemoglobin <12g/dL, %	31.6	18.9	<.0001
Creatinine >1.5mg/dL, %	23.0	18.3	0.0001
eGFR <60 ml/min/1.73m^2, %	49.3	40.6	<.0001
eGFR <30 ml/min/1.73m^2, %	9.9	5.1	<.0001
Glycemia >126mg/dL, %	34.7	24.2	<.0001
Sodium <136mEq/L, %	21.9	12.4	<.0001

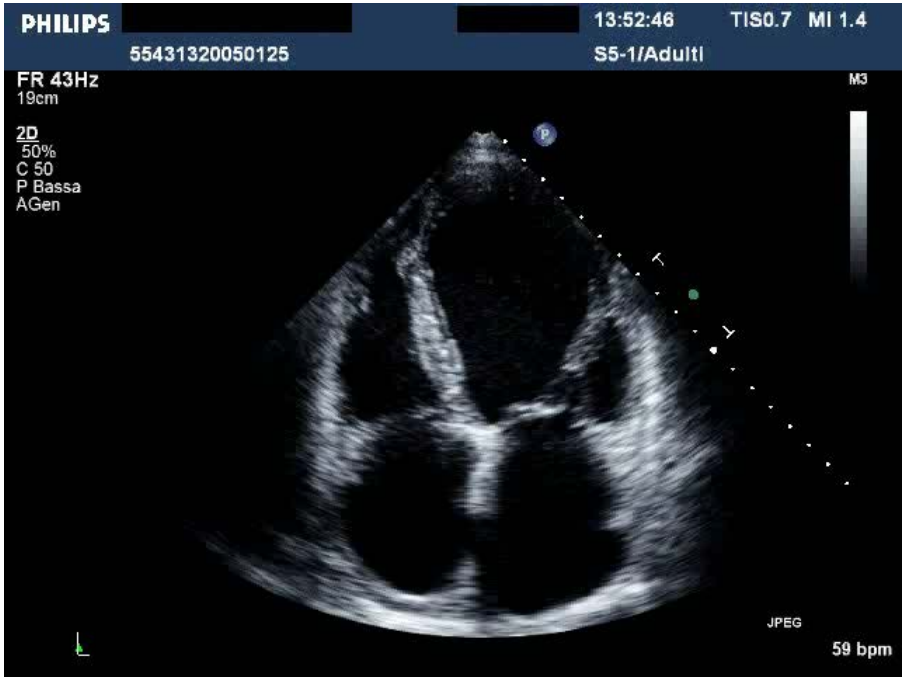
SCC: l'importanza della personalizzazione della terapia

- 35 aa, maschio, NYHA II-III , CMPD, BBsin; FEVsin 30 %

- 77 aa, maschio, NYHA II-III, post-IMA, BBsin; FEVsin 30%

SCC: l'importanza della personalizzazione della terapia

- 35 aa, maschio, NYHA II-III , CMPD, BBsin (QRS 160 msec), RS; BMI 23; FEVsin 30 %; Hb 13.5 g/dl; GFR 87 ml/min
- 77 aa, maschio, NYHA II-III, post-IMA, BBsin (QRS 120 msec); FA; FEVsin 30%; Hb 10 g/dl; DM; GFR 45 ml/min; estesa cicatrice posteriore; ospedalizzazioni recidivanti per SCC e necessità supporto inotropo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13:52:46 TIS0.7 MI 1.4
55431320050125
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19cm
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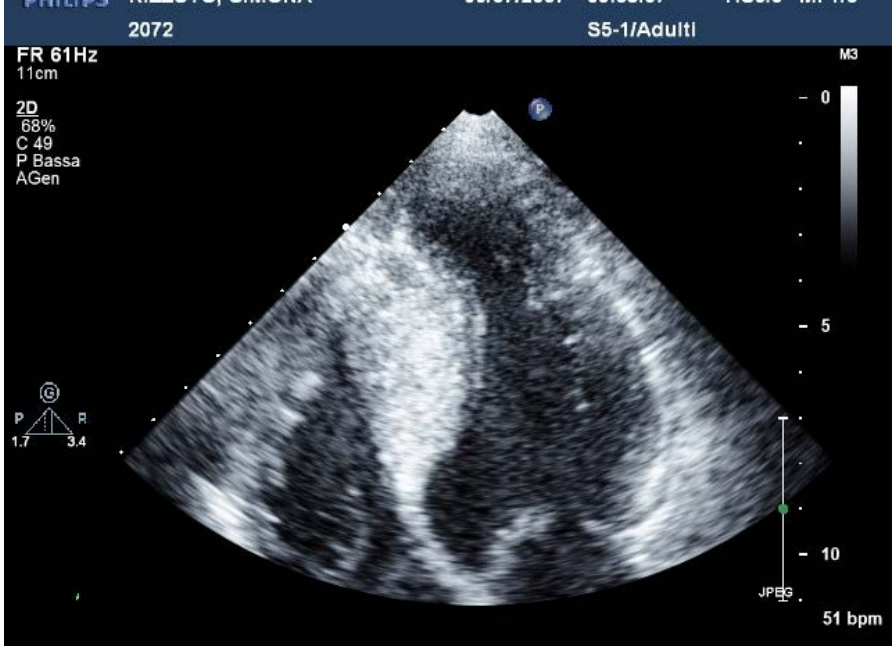
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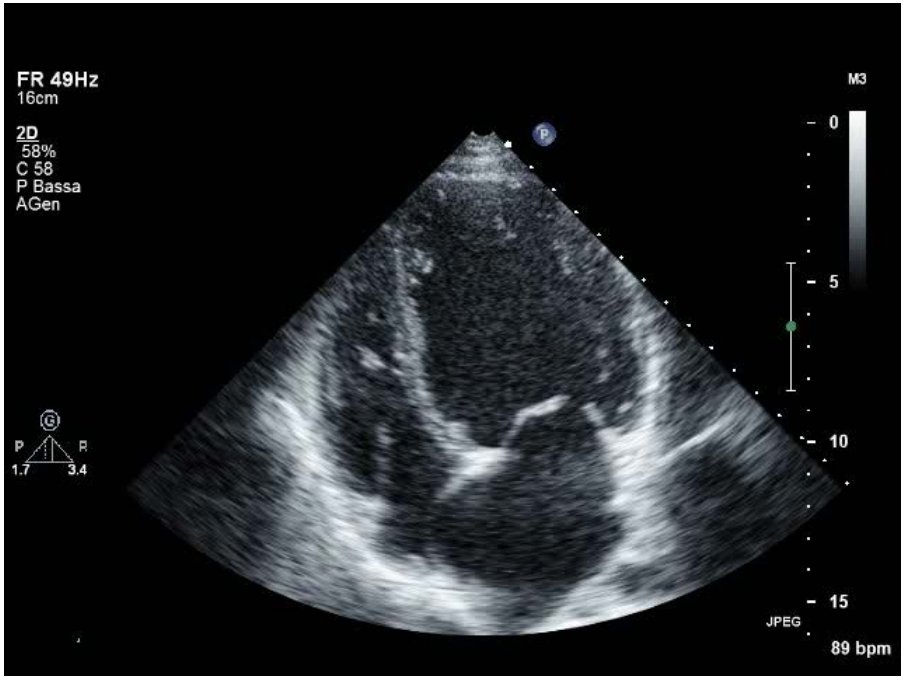
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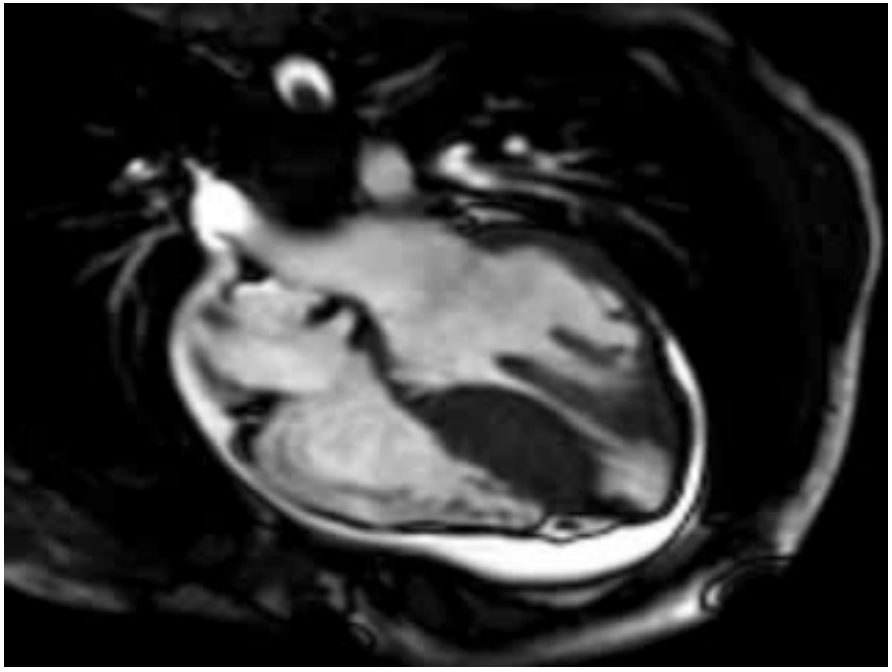
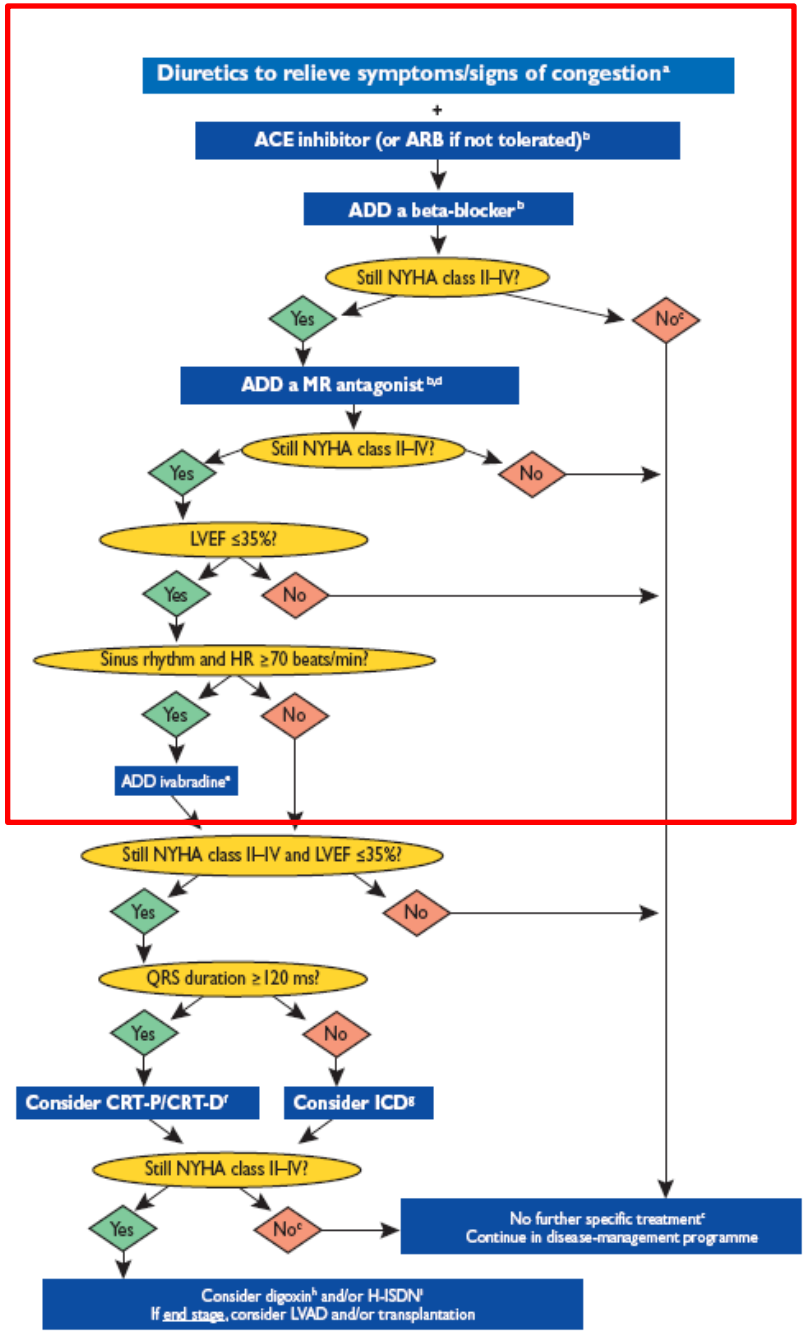
C 58
P Bassa
AGen
M3
0
5
10
15
JPEG
89 bpm





European Heart Journal (2012) **33**, 1787–1847
doi:10.1093/eurheartj/ehs104

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

Authors/Task Force Members: John J.V. McMurray (Chairperson) (UK)*, Stamatis Adamopoulos (Greece), Stefan D. Anker (Germany), Angelo Auricchio (Switzerland), Michael Böhm (Germany), Kenneth Dickstein (Norway), Volkmar Falk (Switzerland), Gerasimos Filippatos (Greece), Cândida Fonseca (Portugal), Miguel Angel Gomez-Sanchez (Spain), Tiny Jaarsma (Sweden), Lars Køber (Denmark), Gregory Y.H. Lip (UK), Aldo Pietro Maggioni (Italy), Alexander Parkhomenko (Ukraine), Burkert M. Pieske (Austria), Bogdan A. Popescu (Romania), Per K. Rønnevik (Norway), Frans H. Rutten (The Netherlands), Juerg Schwitter (Switzerland), Petar Seferovic (Serbia), Janina Stepinska (Poland), Pedro T. Trindade (Switzerland), Adriaan A. Voors (The Netherlands), Faiez Zannad (France), Andreas Zeiher (Germany).

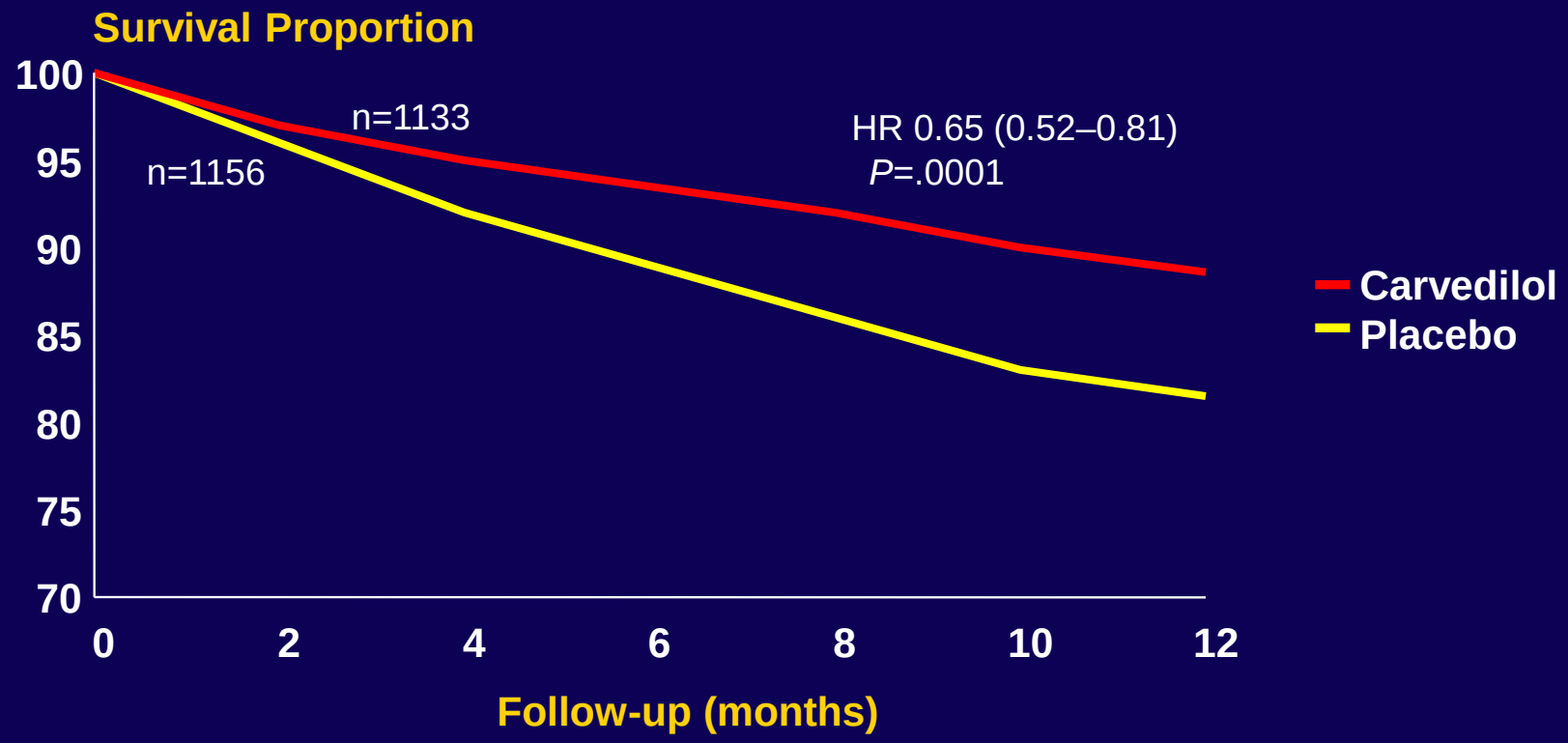
Endpoint PRIMARIO:
Mortalità totale ed Ospedalizzazioni cause Cardiovascolari

SENIORS

Numero di eventi: Nebivololo 332 (31.1%) Placebo 375 (35.3%)

Flather MD. EHJ 2005;26:215-25

Effect of Carvedilol in Severe Heart Failure COPERNICUS



2289 Class IV CHF pts, LVEF <0.25 (not on inotropes × 4 days), ave age 63, LVEF 0.20
Carvedilol 3.125 bid, q 2 wks titration, 75% to target, withdrawal 16% placebo, 13% carvedilol

Packer M et al. *NEJM*. 2001;334:1651–1658.

CLINICAL RESEARCH **Clinical Trials**

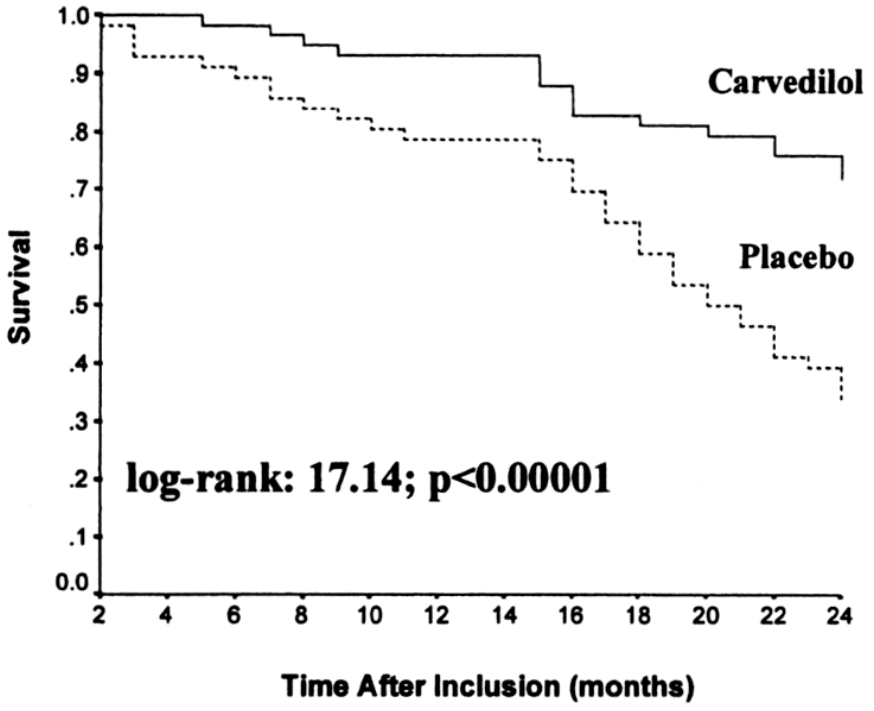
Carvedilol Increases Two-Year Survival in Dialysis Patients With Dilated Cardiomyopathy

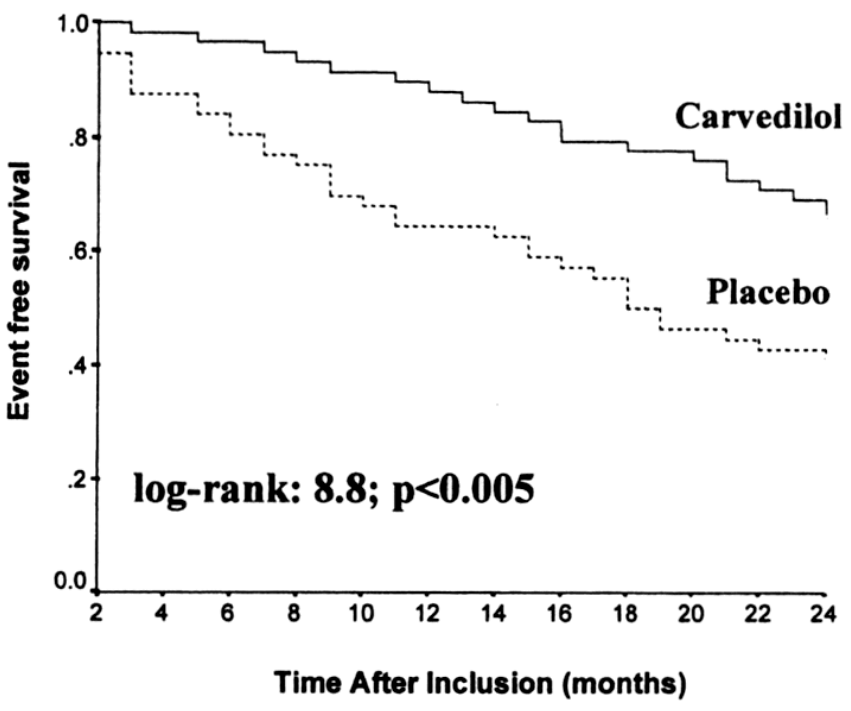
A Prospective, Placebo-Controlled Trial

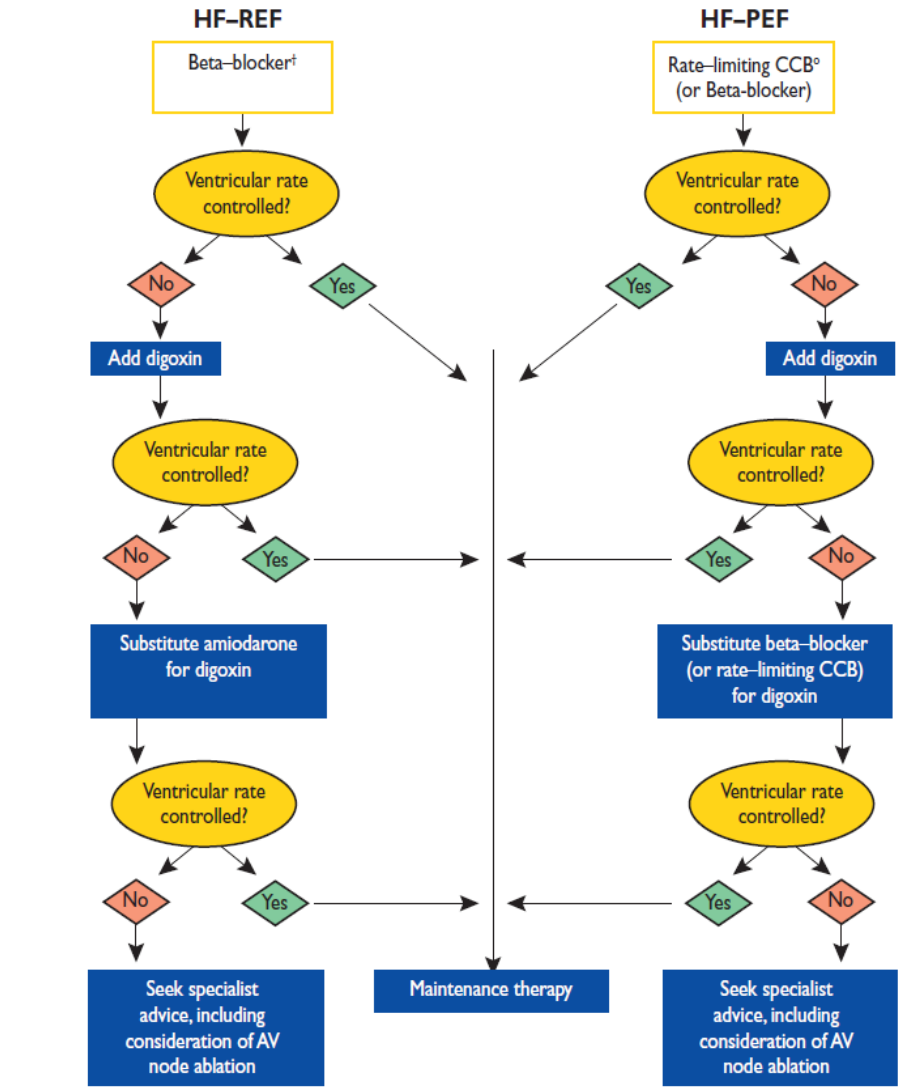
Gennaro Cice, MD,* Luigi Ferrara, MD,* Antonello D'Andrea, MD,* Salvatore D'Isa, MD,* Attilio Di Benedetto, MD,† Antonio Cittadini, MD,‡ Pina Elvira Russo, MD,* Paolo Golino, MD, PHD,* Raffaele Calabrò, MD*

Naples, Italy

J Am Coll Cardiol 2003; 41: 1438-44







*Thrombo-embolism prophylaxis should also be considered in parallel.
†Beta-blocker treatment can cause worsening in acutely decompensated patients with HF-REF (see section on acute heart failure).
°Rate-limiting CCBs should be avoided in HF-REF.
AV = atrioventricular; CCB = calcium-channel blocker; HF-PEF = heart failure with preserved ejection fraction; HF-REF = heart failure with reduced ejection fraction.

Figure 3 Recommendations for controlling the ventricular rate in patients with heart failure and persistent/permanent atrial fibrillation and no evidence of acute decompensation*.

European Heart Journal (2012) **33**, 1787–1847
doi:10.1093/eurheartj/ehs104

European Journal of Heart Failure (2013) **15**, 5–8
doi:10.1093/eurjhf/hfs194

EDITORIAL

Pharmacological treatment of heart failure with preserved ejection fraction: a glimpse of light at the end of the tunnel?

Dirk J. van Veldhuisen[1]* and John J.V. McMurray[2]

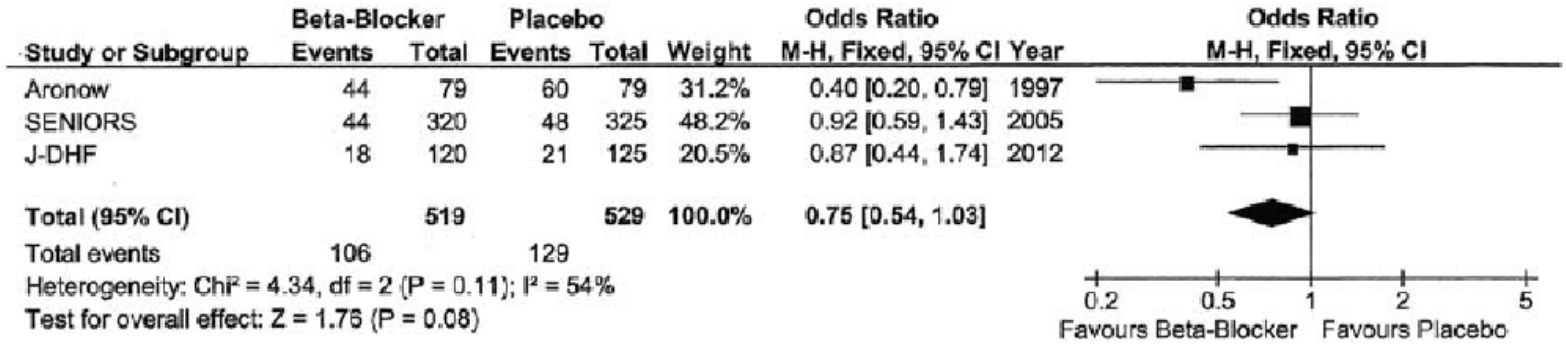
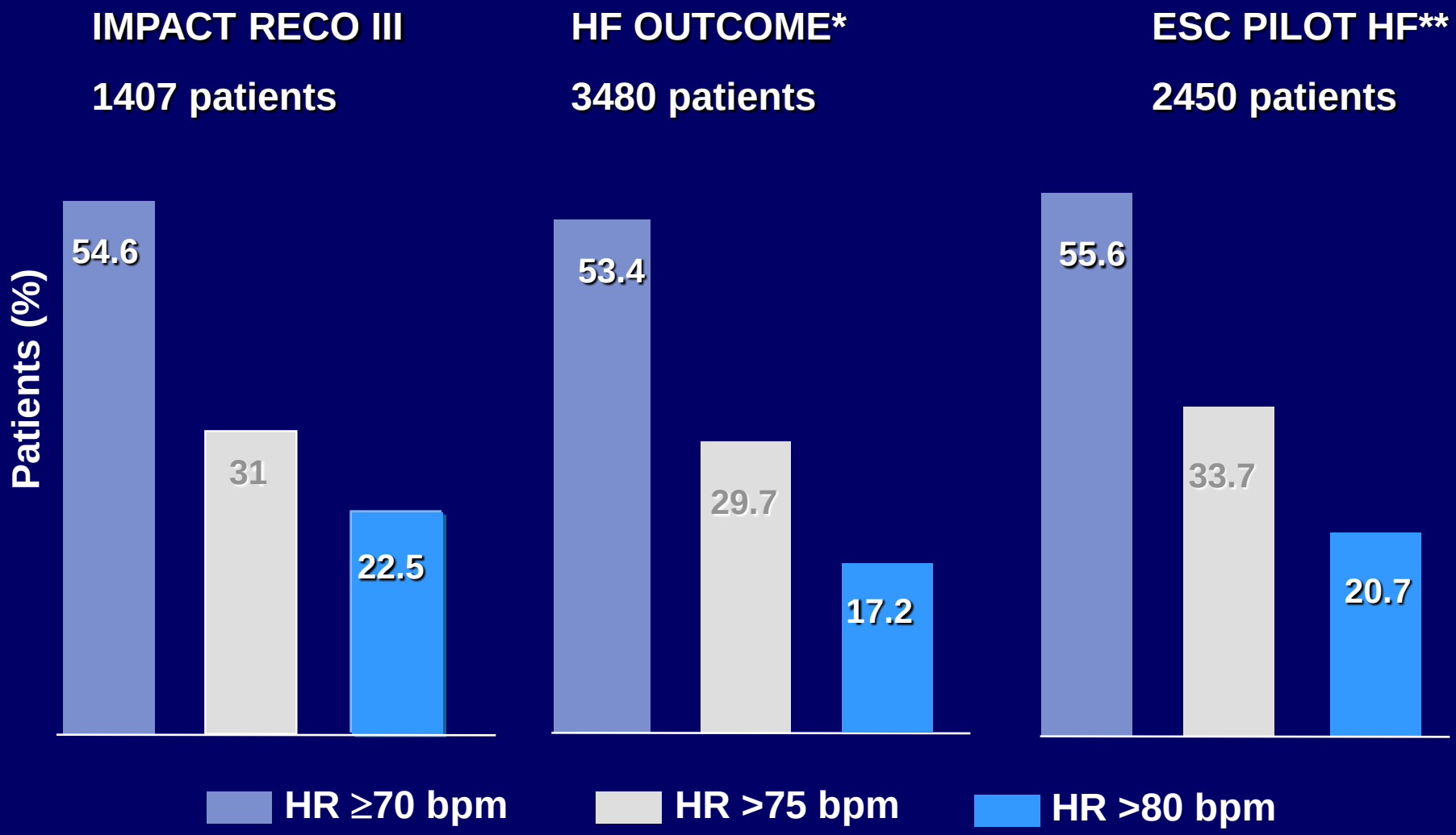


Figure 1 Effect of beta-blockers on all-cause mortality in randomized trials of patients with heart failure with preserved ejection fraction (HFPEF).

HF registries: more than 50% of patients have HR ≥70 bpm

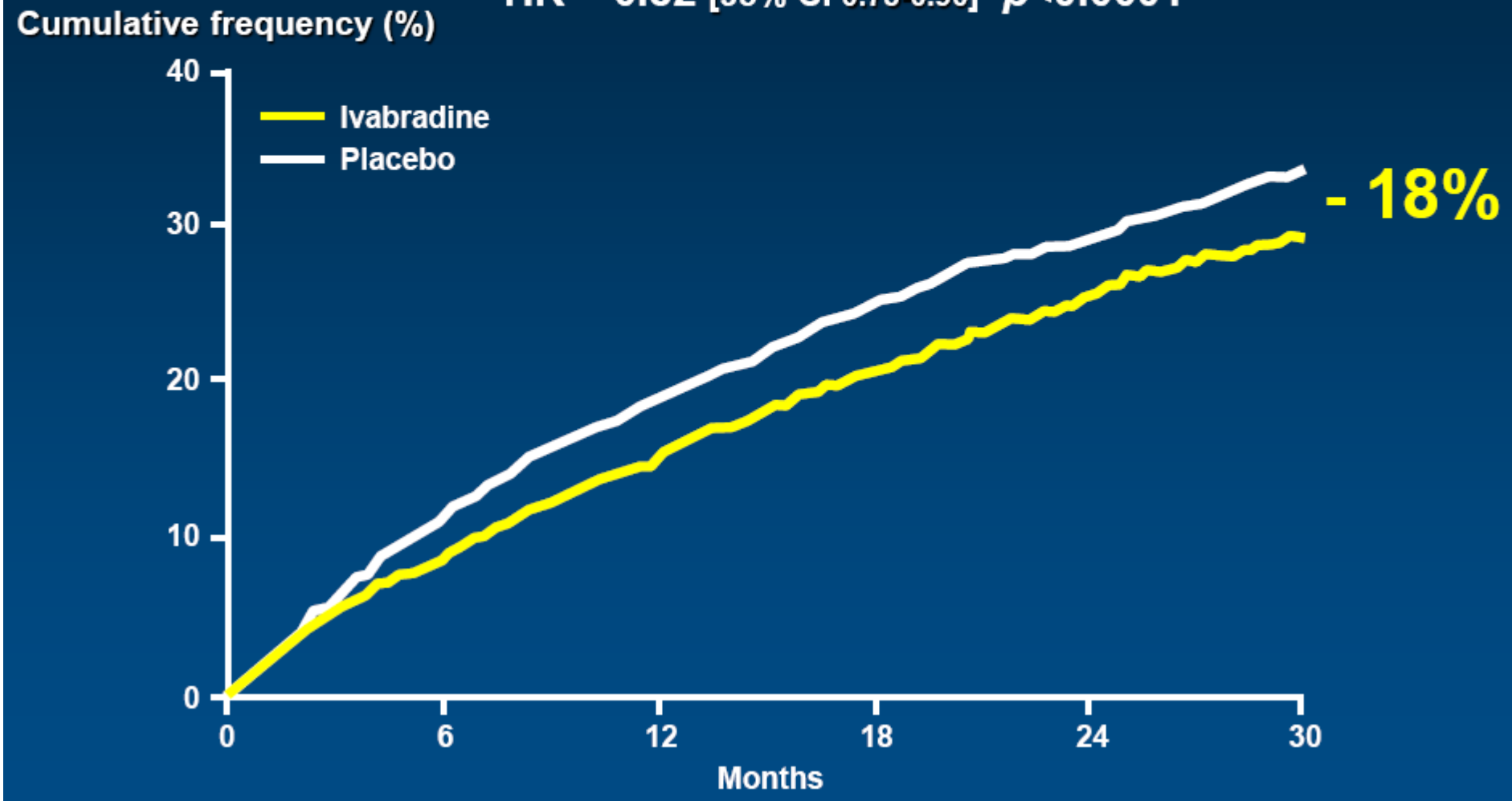


*Courtesy of Prof Tavazzi
**Courtesy of Prof Maggioni

Primary composite endpoint

Ivabradine n=793 (14.5%PY) Placebo n=937 (17.7%PY)

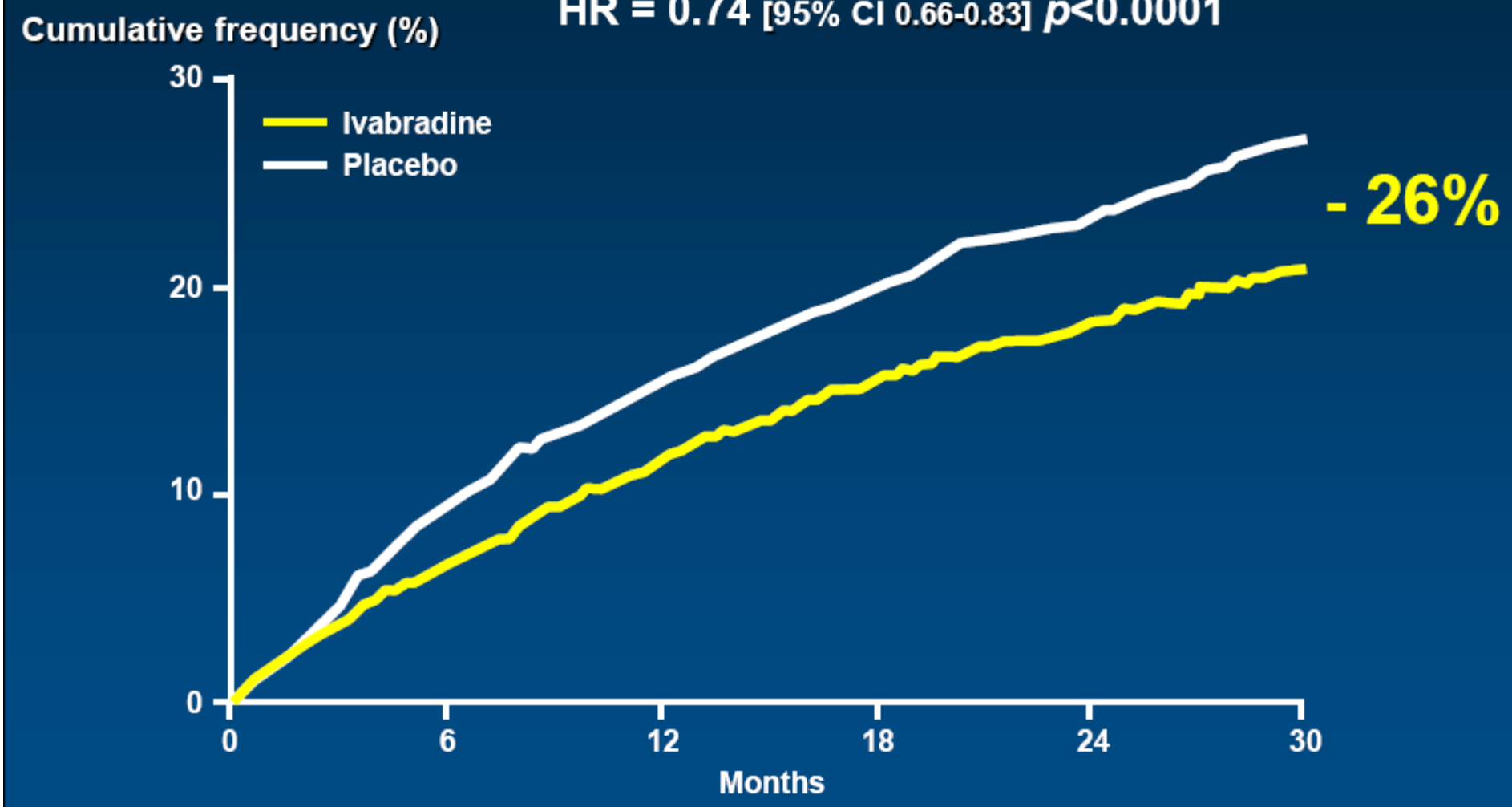
HR = 0.82 [95% CI 0.75-0.90] $p<0.0001$



Hospitalisation for heart failure

Ivabradine n=514 (9.4%PY) Placebo n=672 (12.7%PY)

HR = 0.74 [95% CI 0.66-0.83] $p<0.0001$



European Heart Journal (2012) 33, 1787–1847
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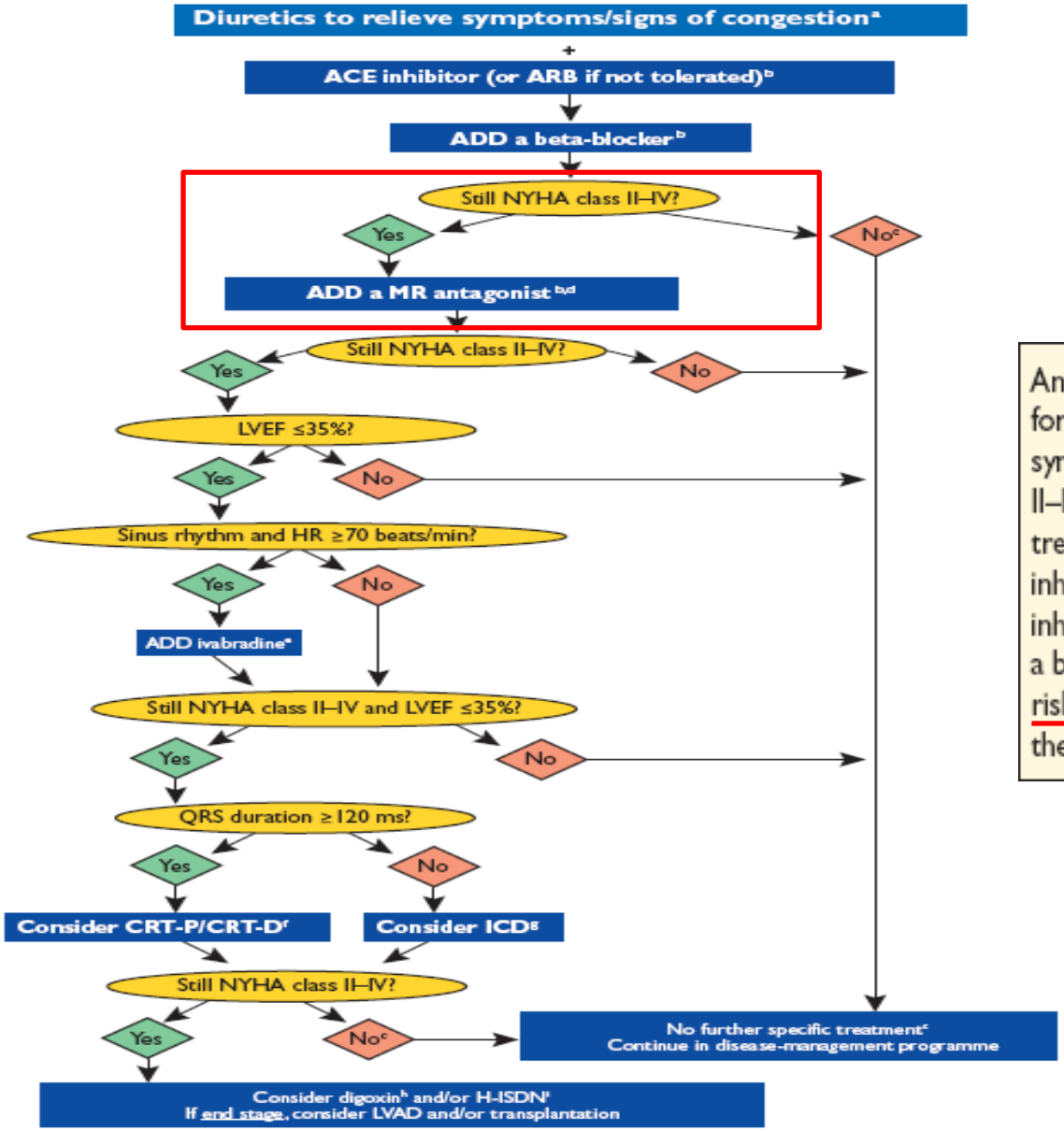
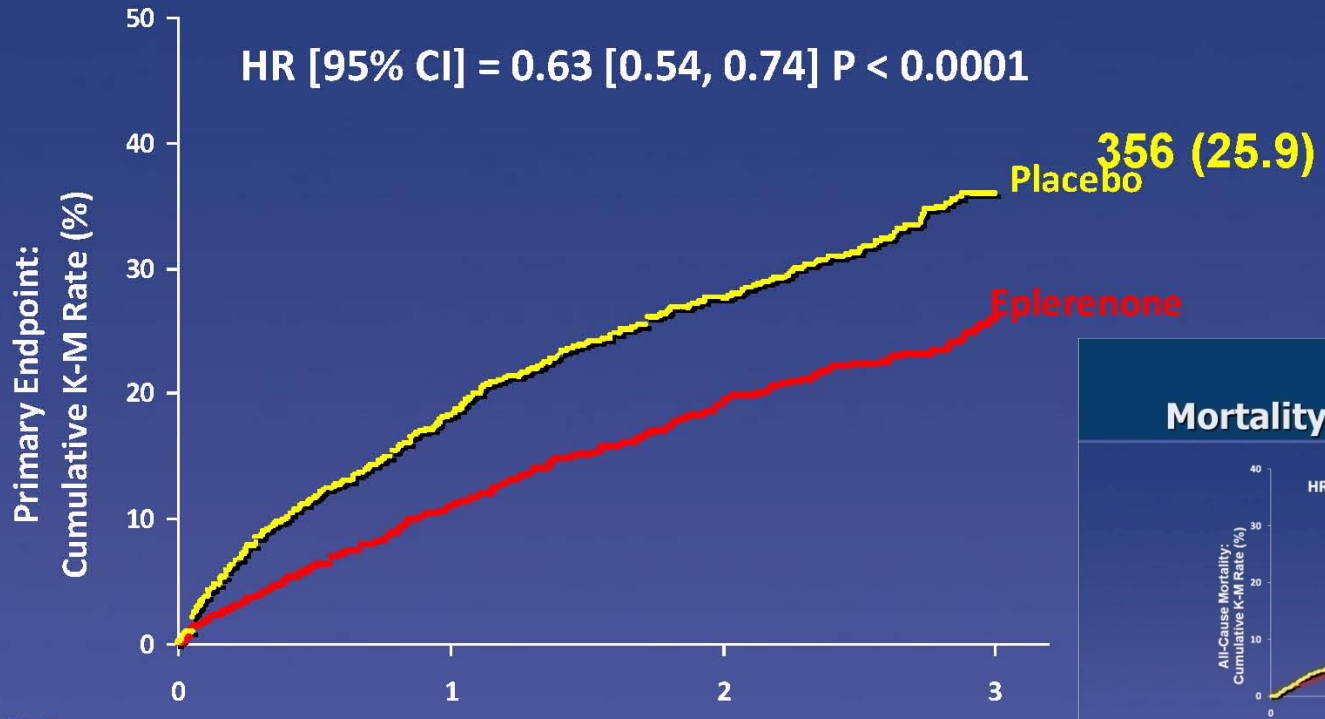


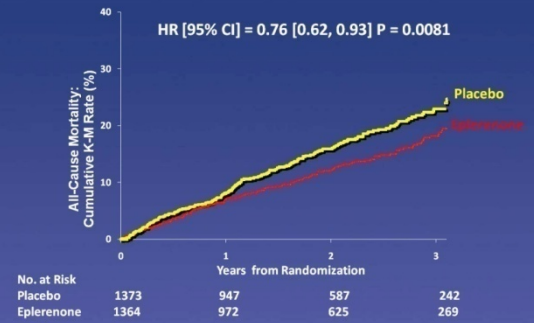
An MRA is recommended for all patients with persisting symptoms (NYHA class II–IV) and an EF ≤35%, despite treatment with an ACE inhibitor (or an ARB if an ACE inhibitor is not tolerated) and a beta-blocker, to reduce the risk of HF hospitalization and the risk of premature death.	I	A

Primary Endpoint Cardiovascular Death or Hospitalization for HF



No. at Risk				
Placebo	1373	848	312	199
Eplerenone	1364	925	562	232

Mortality From Any Cause



*Unadjusted HR, 0.78; 0.64, 0.95; p=0.01

EMPHASIS HF

*Unadjusted HR 0.66; 0.56, 0.78; p<0.0001

Safety - Potassium related issues
(Investigator reported events)

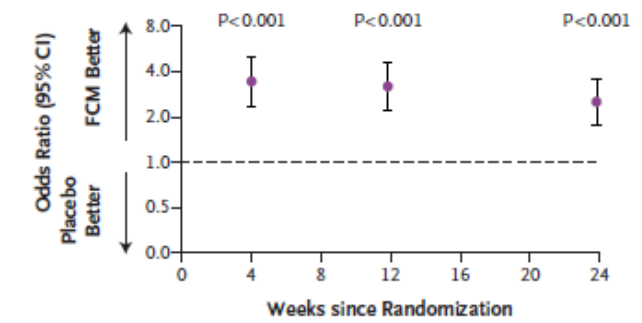
Outcome	Patients with an adverse event leading to drug withdrawal — no. (%) Eplerenone (N=1360)	Placebo (N=1373)	P Value
Hyperkalemia (investigator reported AE)	109 (8)	50 (3.7)	<0.001
Hyperkalemia leading to drug discontinuation	15 (1.1)	12 (0.9)	0.57
Serum K+ > 5.5 mmol/L	158 (11.8)	96 (7.2)	<0.001
Serum K+ > 6.0 mmol/L	33 (2.5)	25 (1.9)	0.29
Hospitalization for hyperkalemia (adjudicated)	4 (0.3)	3 (0.2)	0.85

EMPHASIS HF

ORIGINAL ARTICLE

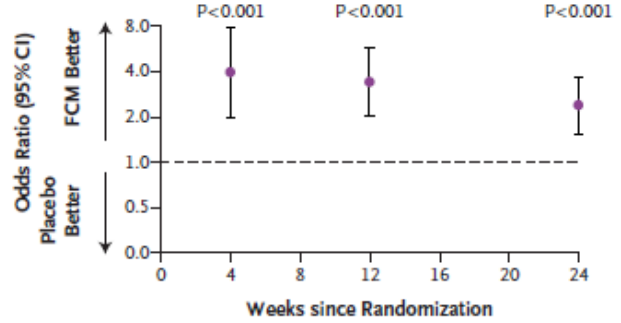
Ferric Carboxymaltose in Patients with Heart Failure and Iron Deficiency

A Self-Reported Patient Global Assessment



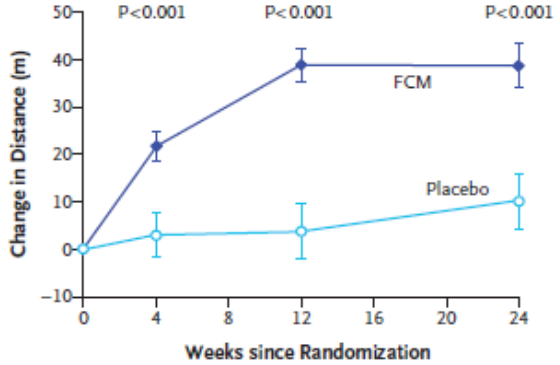
No. of Patients				
FCM	282	291		292
Placebo	146	149		149

B NYHA Functional Class



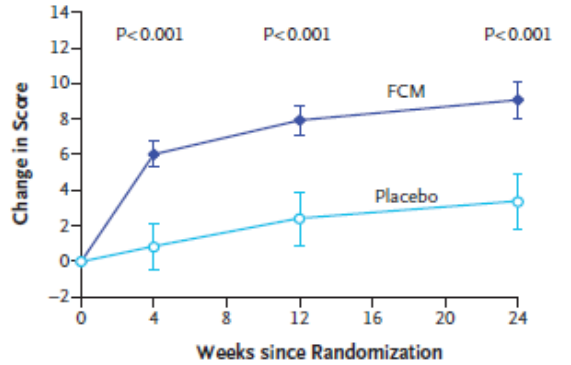
No. of Patients				
FCM	304	287	294	294
Placebo	155	147	150	150

C 6-Minute-Walk Test



FCM				
No. of patients	303	284	280	268
Mean distance (m)	274±6	294±7	312±6	313±7
Placebo				
No. of patients	155	144	141	134
Mean distance (m)	269±9	269±10	272±10	277±10
Mean Study-Treatment Effect	21±6	37±7		35±8

D EQ-5D Visual Analog Scale



FCM				
No. of patients	295	274	283	285
Mean score	54±1	60±1	62±1	63±1
Placebo				
No. of patients	152	140	145	146
Mean score	54±1	54±2	56±2	57±2
Mean Study-Treatment Effect	6±1	6±2		7±2

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MAY 17, 2012 VOL. 366 NO. 20

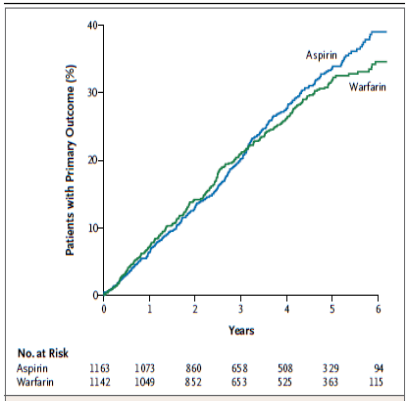


Figure 1. **Cumulative Incidence of the Primary Outcome.**
The primary outcome was the time to the first event in the composite end point of ischemic stroke, intracerebral hemorrhage, or death from any cause.

Warfarin and Aspirin in Patients with Heart Failure and Sinus Rhythm

	Warfarin (N=1142)		Aspirin (N=1163)		Hazard Ratio (95% CI)†	P Value
	no. of patients (%)	*unadjusted rate of events/100 patient-yr*	*no. of patients (%)*	*unadjusted rate of events/100 patient-yr*		
Primary outcome: death, ischemic stroke, or intracerebral hemorrhage						
Composite	302 (26.4)	7.47	320 (27.5)	7.93	0.93 (0.79–1.10)	0.40
Components						
Death	268 (23.5)	6.63	263 (22.6)	6.52	1.01 (0.85–1.20)	0.91
Ischemic stroke	29 (2.5)	0.72	55 (4.7)	1.36	0.52 (0.33–0.82)	0.005
Intracerebral hemorrhage	5 (0.4)	0.12	2 (0.2)	0.05	2.22 (0.43–11.66)	0.35

Aliskiren Trial to Minimize OutcomeS in Patients with HEart failuRE

Predictors for Restoration of Normal Left Ventricular Function in Response to Cardiac Resynchronization Therapy Measured at Time of Implantation

Laura Vitali Serdoz, MD[a], Elisabetta Daleffe, MD[b], Marco Merlo, MD[a], Massimo Zecchin, MD[a], Giulia Barbati, PhD[c], Domenico Pecora, MD[d], Bruno Pinamonti, MD[a], Cecilia Fantoni, MD, PhD[b], Pierpaolo Lupo, MD[b], Andrea Di Lenarda, MD[a], Gianfranco Sinagra, MD, FESC[a], and Riccardo Cappato, MD[b,*]

There are no parameters predicting the individual probability of "full response" to cardiac resynchronization therapy (CRT). The aim of this work was to find prognostic factors of full clinical and echocardiographic responses (i.e., ≥50% left ventricular ejection fraction [LVEF] and New York Heart Association class I) after 1 year of CRT. This was a prospective follow-up study that involved 2 hospitals. Patients (n = 75) with advanced heart failure (64 ± 9 years of age, 87% men, LVEF 24 ± 7%) who received CRT were followed for 17 ± 9 months. Univariate and multivariate regression analyses were used to identify predictors of full CRT response. A nomogram predicting the individual probability of full CRT response during follow-up was calculated. There were 13 patients with restoration of normal LVEF versus 62 without (mean LVEF 56% ± 5% vs 31% ± 8%, respectively, p <0.001). Predictors of full response included cause of heart disease, baseline QRS width, and degree of QRS shortening in response to CRT. Patients with nonischemic heart disease, baseline QRS width ≤150 ms, and QRS shortening ≥40 ms in response to CRT had a >75% probability of restoration of normal LVEF. In conclusion, our nomogram using a combination of cause, baseline QRS width, and degree of QRS shortening in response to CRT allows assessment of individual probability of full response. This observation awaits further confirmation from larger series. (Am J Cardiol 2011;108:75–80)

Vitali-Serdoz L et al. Am J Cardiol 2011;108:75-80.

Ospedali Riuniti di Trieste

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QUARTERLY FOCUS ISSUE: HEART RHYTHM DISORDERS

Viewpoint and Commentary

Critical Appraisal of the Use of Cardiac Resynchronization Therapy Beyond Current Guidelines

Rutger J. Van Bommel, MD, Victoria Delgado, MD, Martin J. Schalij, MD, PhD, Jeroen J. Bax, MD, PhD

Leiden, the Netherlands

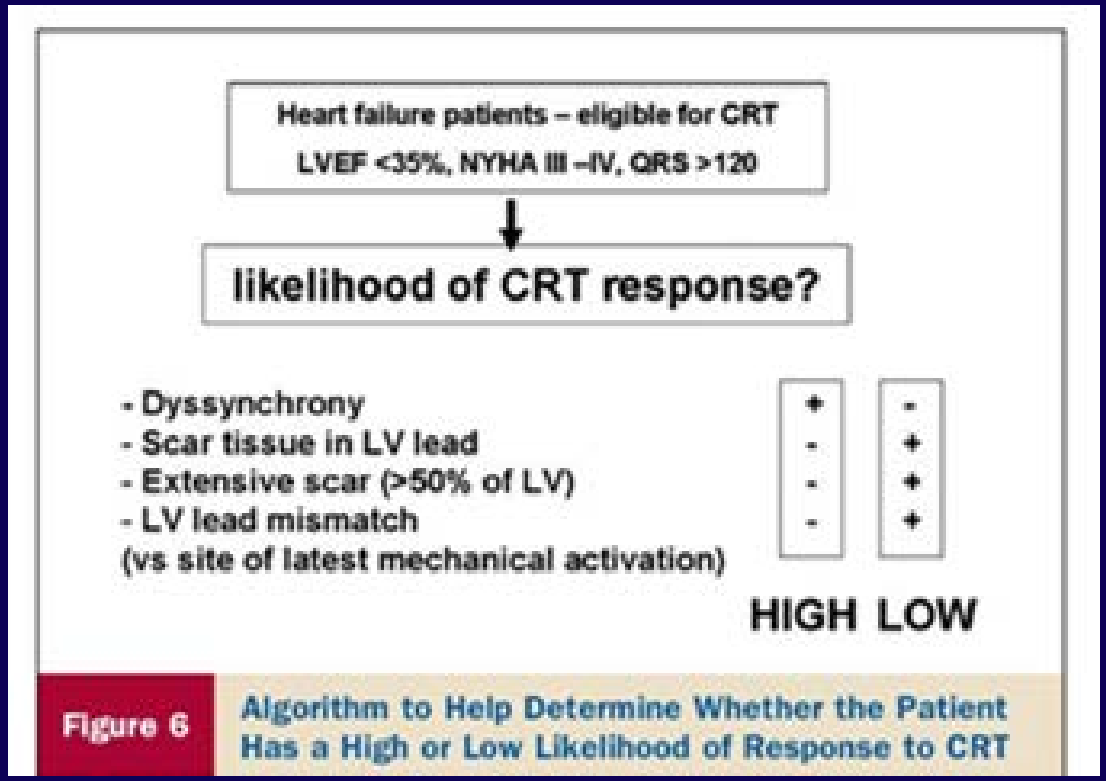
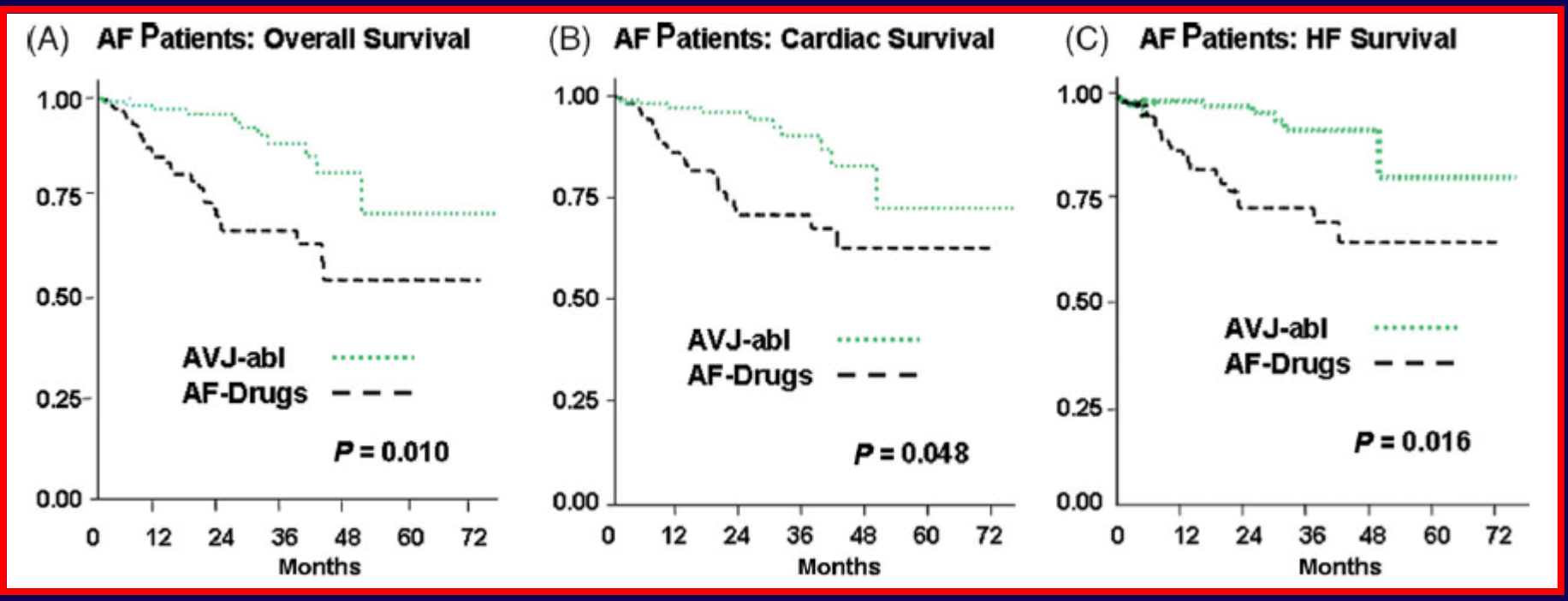


Figure 6 Algorithm to Help Determine Whether the Patient Has a High or Low Likelihood of Response to CRT

J Am Coll Cardiol 2010;56; 754-62

Long-term survival in patients undergoing cardiac resynchronization therapy: the importance of performing atrio-ventricular junction ablation in patients with permanent atrial fibrillation

Maurizio Gasparini[1]*, Angelo Auricchio[2,3], Marco Metra[4], François Regoli[1], Cecilia Fantoni[2,3], Barbara Lamp[5], Antonio Curnis[4], Juergen Vogt[5], and Catherine Klersy[6] for the Multicentre Longitudinal Observational Study (MILOS) Group

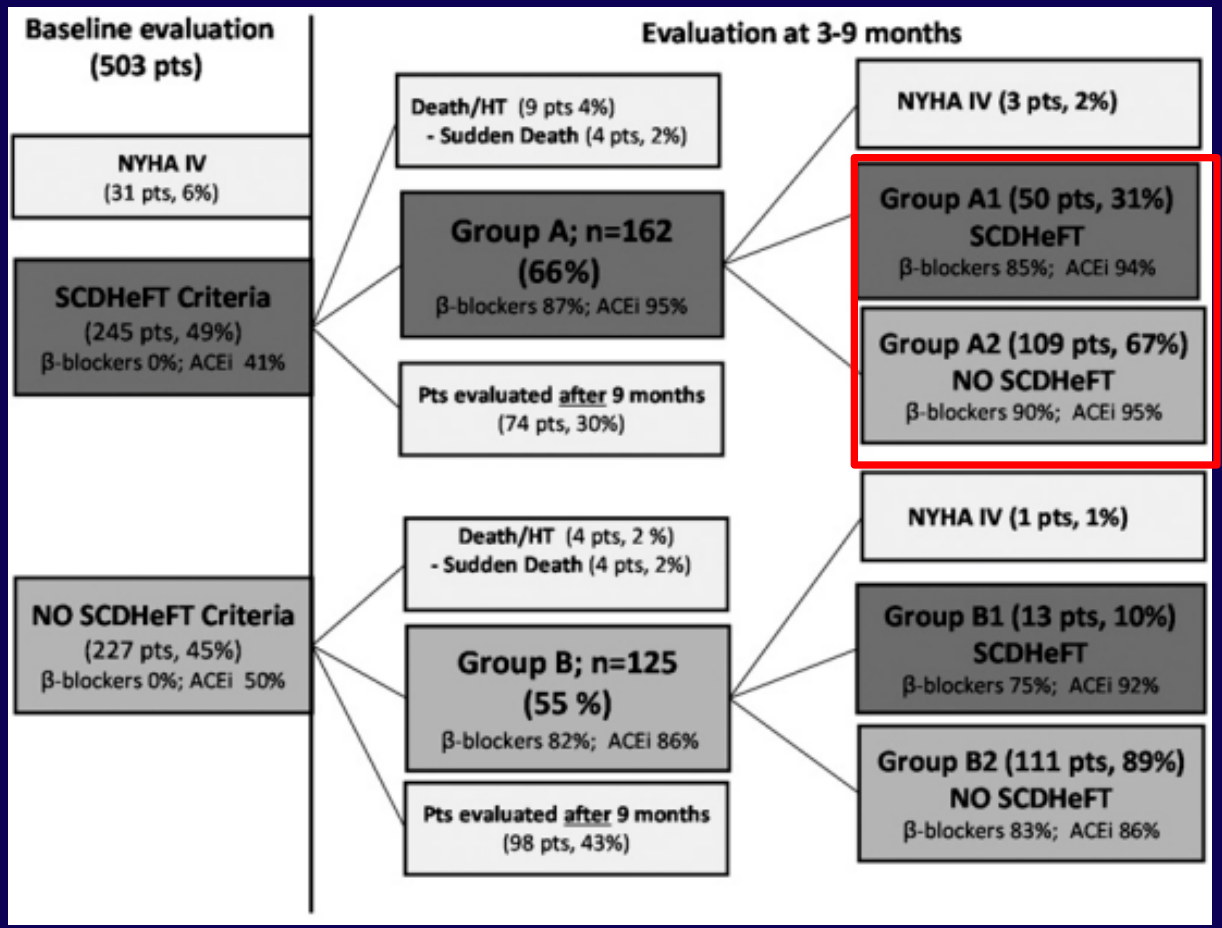


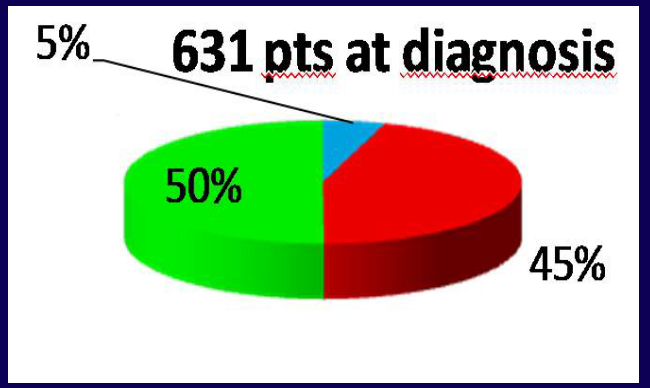
Eur Heart J 2008; 29: 1644–1652.

How Can Optimization of Medical Treatment Avoid Unnecessary Implantable Cardioverter-Defibrillator Implantations in Patients With Idiopathic Dilated Cardiomyopathy Presenting With "SCD-HeFT Criteria?"

Massimo Zecchin, MD[a,*], Marco Merlo, MD[a], Alberto Pivetta, MD[a], Giulia Barbati, PhD[b], Cristina Lutman, MD[a], Dario Gregori, PhD[b], Laura Vitali Serdoz, MD[a], Stefano Bardari, MD[a], Silvia Magnani, MD[a], Andrea Di Lenarda, MD[c], Alessandro Proclemer, MD[d], and Gianfranco Sinagra, MD[a]

Study population and effect of medical treatment optimization on "SCD-HeFT criteria"



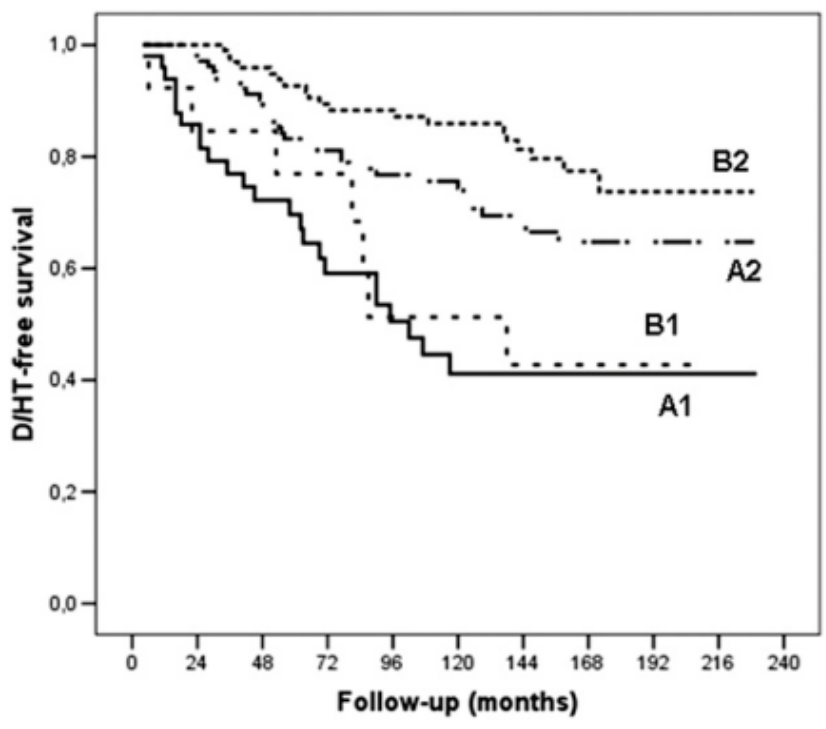


Zecchin et al Am J Cardiol 2012;109:729

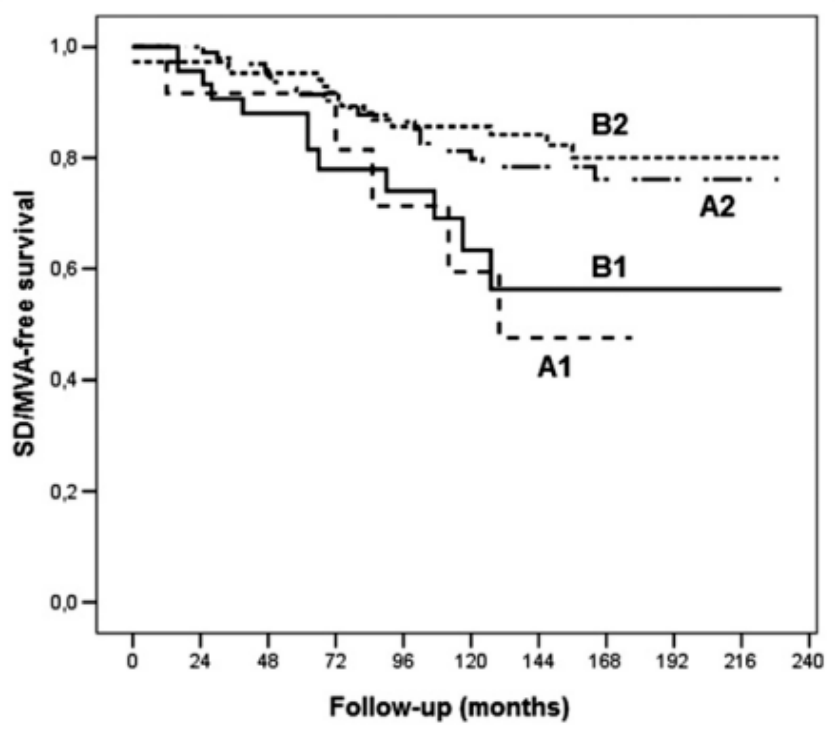
How Can Optimization of Medical Treatment Avoid Unnecessary Implantable Cardioverter-Defibrillator Implantations in Patients With Idiopathic Dilated Cardiomyopathy Presenting With "SCD-HeFT Criteria?"

Massimo Zecchin, MD[a,*], Marco Merlo, MD[a], Alberto Pivetta, MD[a], Giulia Barbati, PhD[b], Cristina Lutman, MD[a], Dario Gregori, PhD[b], Laura Vitali Serdoz, MD[a], Stefano Bardari, MD[a], Silvia Magnani, MD[a], Andrea Di Lenarda, MD[c], Alessandro Proclemer, MD[d], and Gianfranco Sinagra, MD[a]

Long-term survival



Long-term survival free from SD/MVA



A1: baseline "SCD-HeFT criteria" both at first and second evaluation
A2: baseline "SCD-HeFT criteria" at first but not at second evaluation
B1: patients developing "SCD-HeFT criteria" only at second evaluation
B2: patients without "SCD-HeFT criteria" at first or second evaluation

Zecchin et al Am J Cardiol 2012;109:729

European Heart Journal (2012) **33**, 1564–1570
doi:10.1093/eurheartj/ehs112

REVIEW

Frontiers in cardiovascular medicine

Personalized medicine: hope or hype?

Keyan Salari[1], Hugh Watkins[2], and Euan A. Ashley[3]*

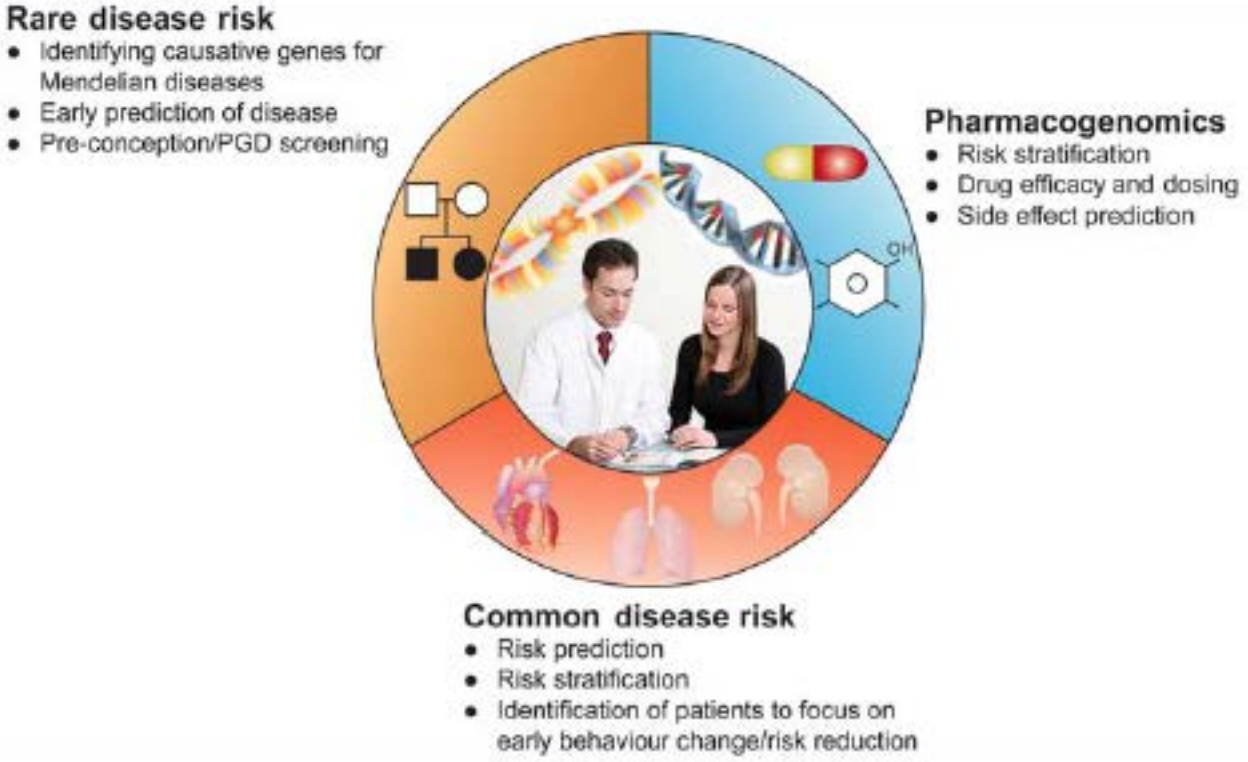
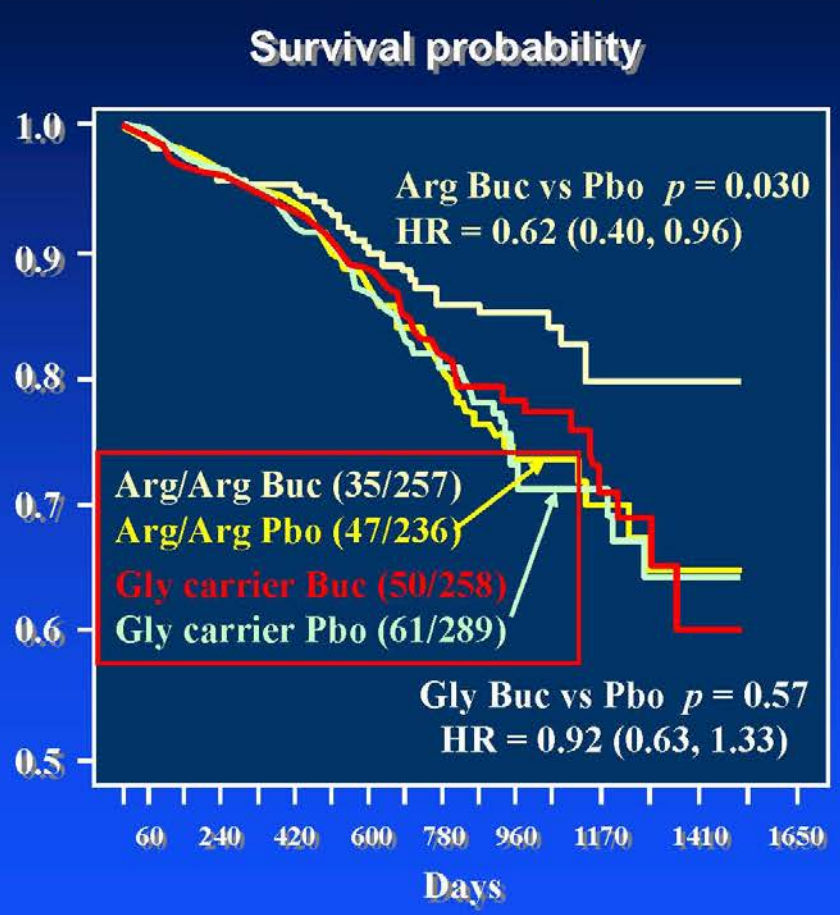
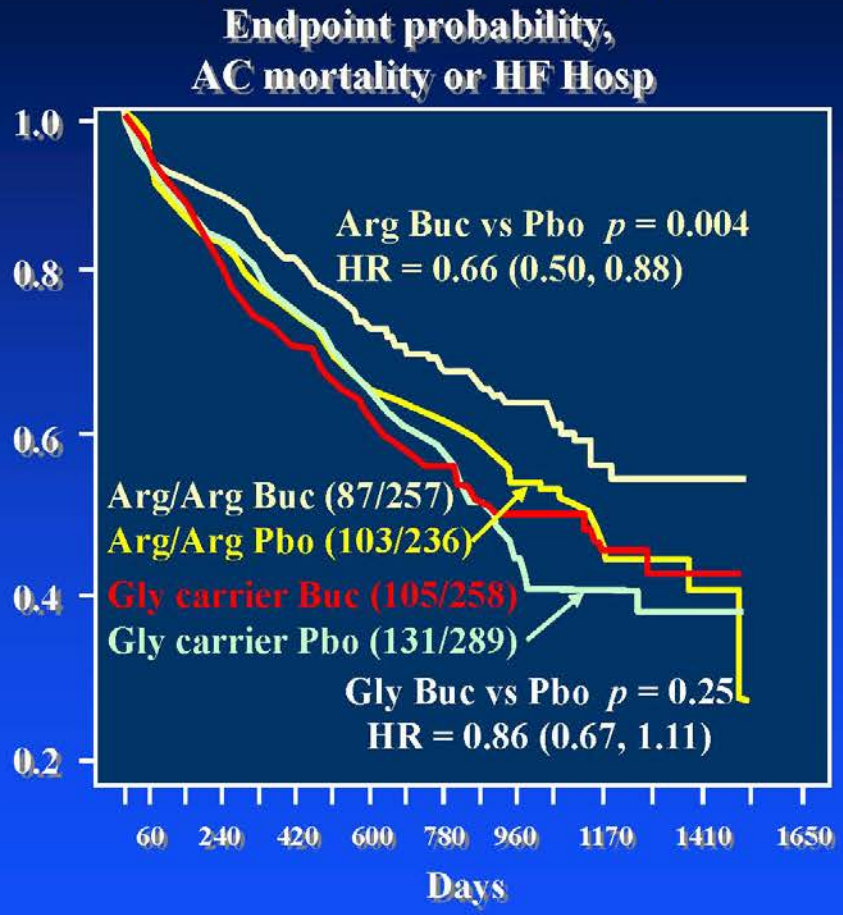


Figure 1 Domains of personalized medicine.

Kaplan-Meier analysis of endpoints in the BEST trial stratified by treatment and β_1–389 genotype





Liggett et al. PNAS 103:11288-11293, 2006

JACC: Heart Failure
Vol. ■, No. ■, 2013

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Prevention of Atrial Fibrillation by Bucindolol Is Dependent on the Beta$_1$389 Arg/Gly Adrenergic Receptor Polymorphism

Ryan G. Aleong, MD,* William H. Sauer, MD,* Gordon Davis, MS,† Guinevere A. Murphy, PHD,† J. David Port, PHD,†‡ Inder S. Anand, MD,§ Mona Fiuzat, PHARMD,|| Christopher M. O'Connor, MD,|| William T. Abraham, MD,¶ Stephen B. Liggett, MD,# Michael R. Bristow, MD, PHD†‡||
Denver and Broomfield, Colorado; Durham, North Carolina; Columbus, Ohio; and Tampa, Florida

Conclusions

Bucindolol was associated with a significant, quantitatively large decrease in new-onset AF in the entire BEST cohort that was observed exclusively in the $\beta_1$389 Arg/Arg genotype.

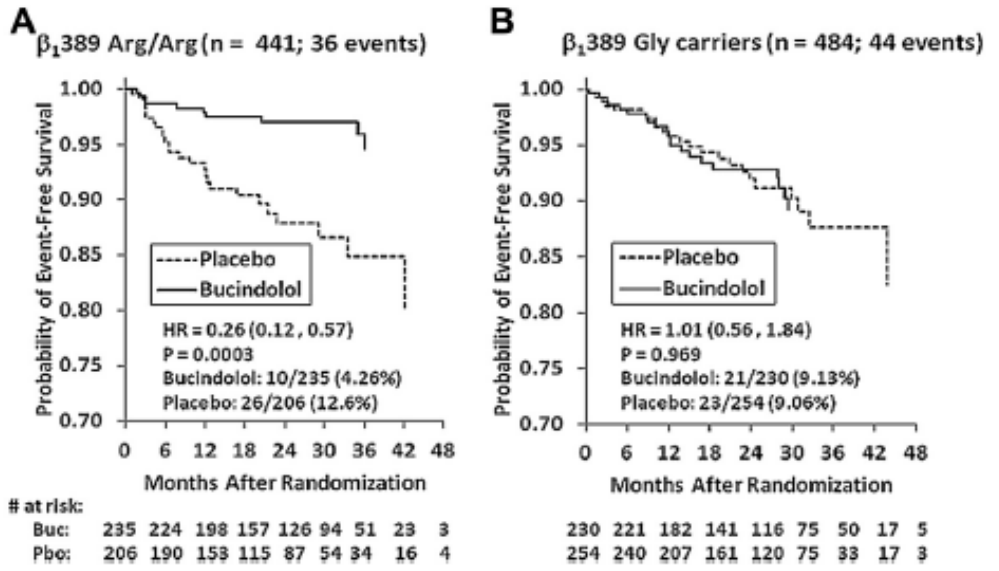


Figure 2 Time to New Onset by $\beta_1$389 Arg/Gly Genotype

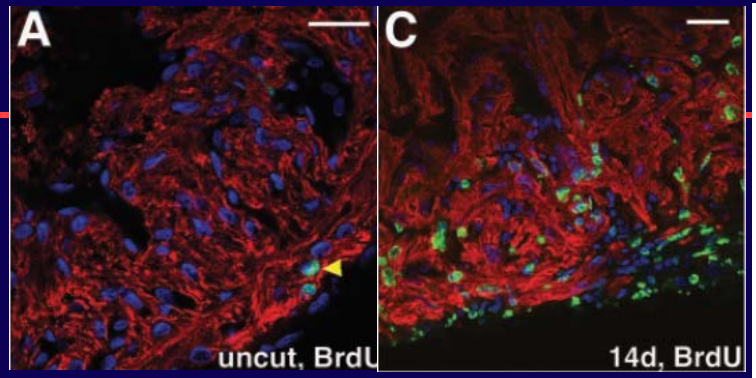
Time to event curves are shown for new-onset AF in the BEST DNA substudy by $\beta_1$389 Arg/Gly genotype. There is a significant interaction between genotype and treatment. The benefit of bucindolol is seen exclusively in the $\beta_1$389 Arg/Arg genotype **(A)**, with a risk reduction of 74% compared to placebo ($p = 0.008$ for interaction vs. Gly carrier group). **(B)** There was no impact of bucindolol in the β1 Gly carriers compared to placebo. **Dashed line** = placebo; **solid line** = bucindolol. Abbreviations as in Figure 1.

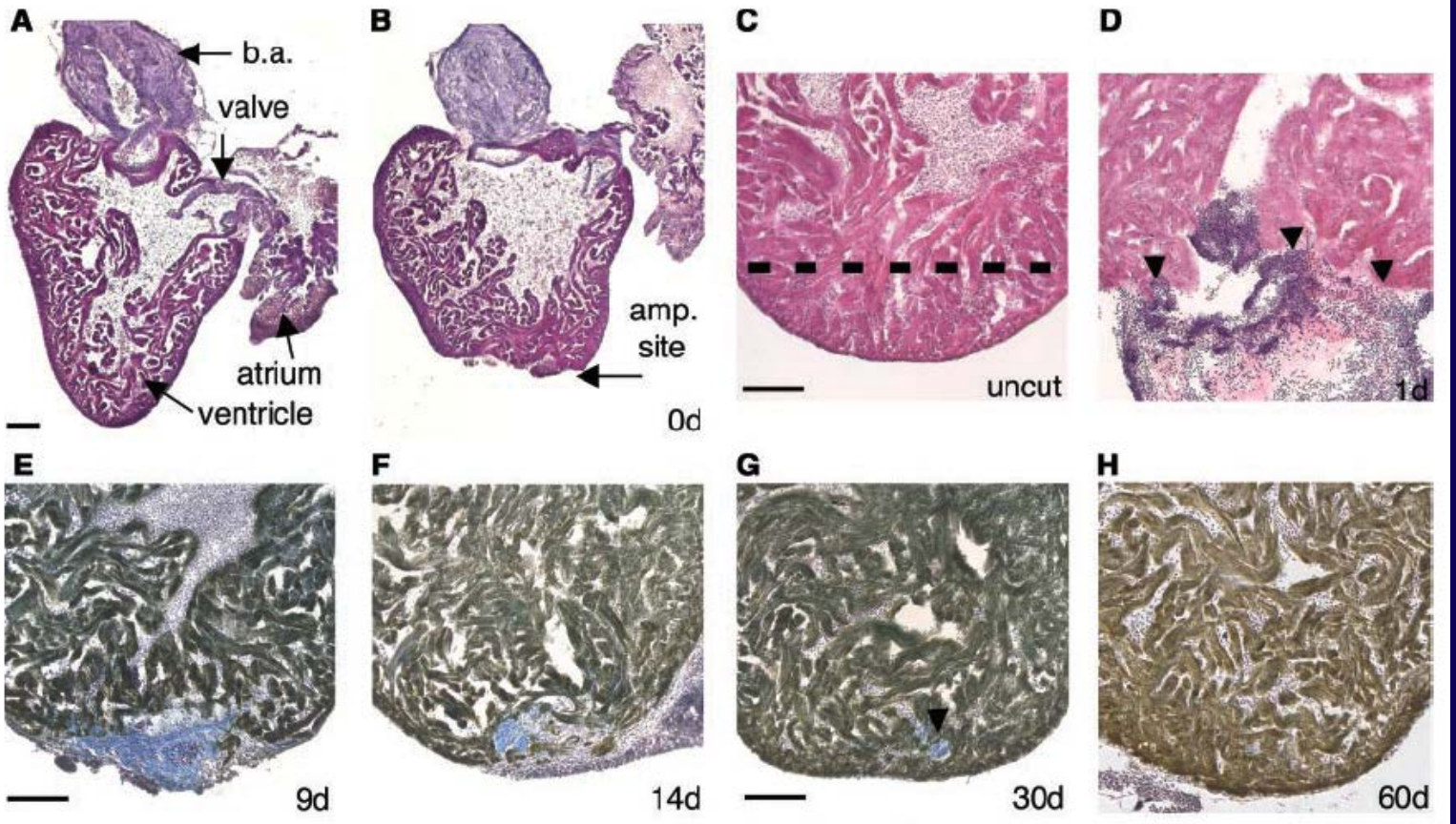
Heart Regeneration in Zebrafish

Kenneth D. Poss,* Lindsay G. Wilson, Mark T. Keating*

Cardiac injury in mammals and amphibians typically leads to scarring, with minimal regeneration of heart muscle. Here, we demonstrate histologically that zebrafish fully regenerate hearts within 2 months of 20% ventricular resection. Regeneration occurs through robust proliferation of cardiomyocytes localized at the leading epicardial edge of the new myocardium. The hearts of zebrafish with mutations in the Mps1 mitotic checkpoint kinase, a critical cell cycle regulator, failed to regenerate and formed scars. Thus, injury-induced cardiomyocyte proliferation in zebrafish can overcome scar formation, allowing cardiac muscle regeneration. These findings indicate that zebrafish will be useful for genetically dissecting the molecular mechanisms of cardiac regeneration.

SCIENCE VOL 298 13 DECEMBER 2002





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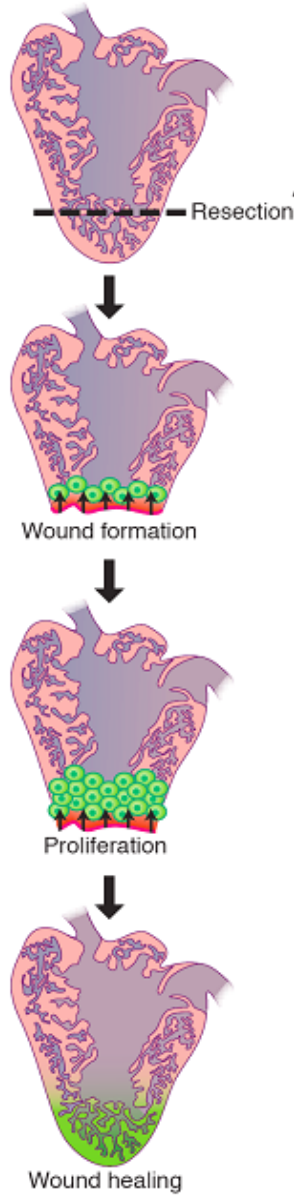
Zebrafish heart



Cardiac Cell Therapy — Mixed Results from Mixed Cells

Anthony Rosenzweig, M.D.

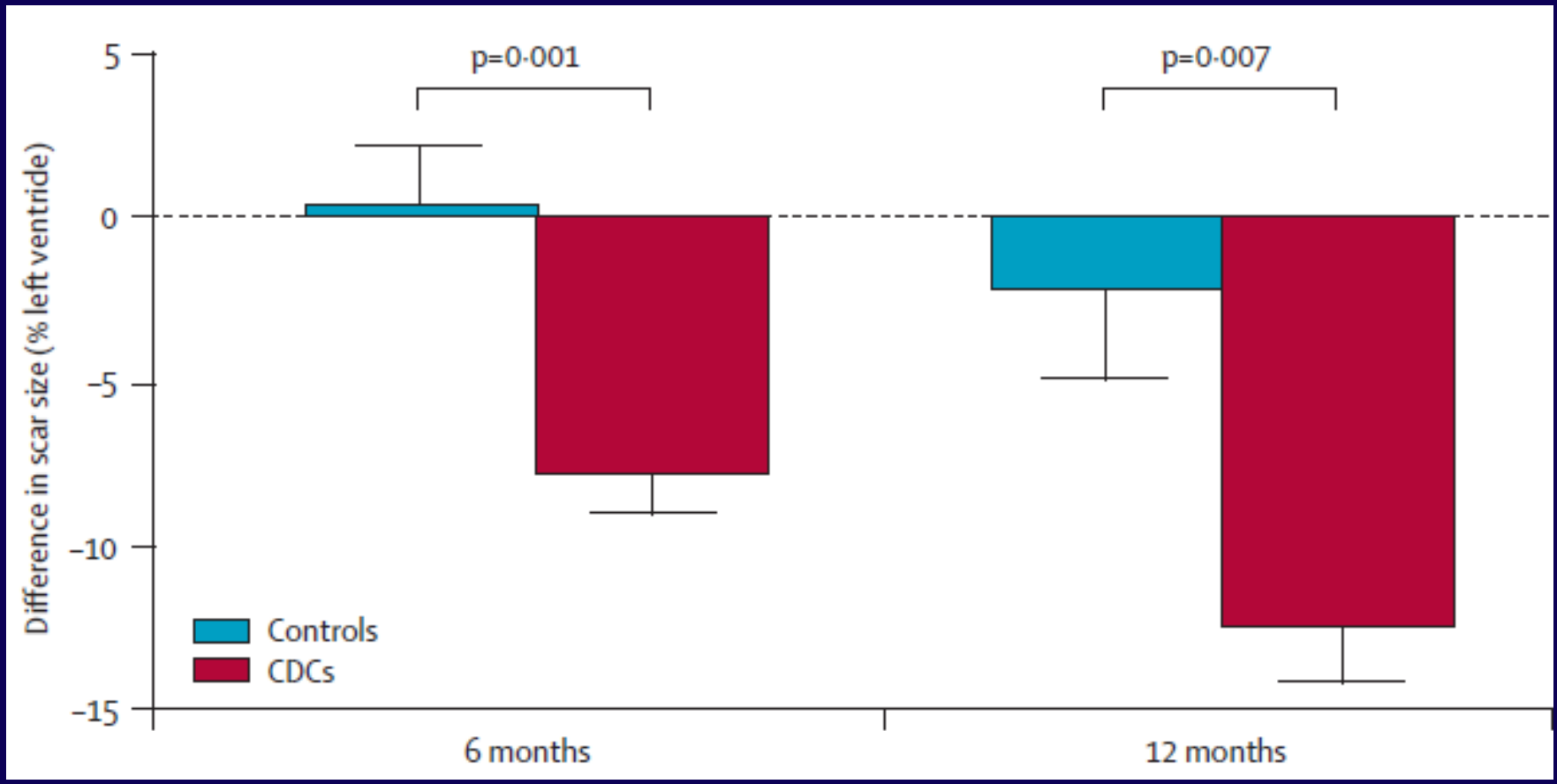
Trial or Investigator Group	Setting	Design	No. of Cells Administered in Treatment Group	Results
BOOST[4,9]	PCI after acute myocardial infarction	Randomized trial 30 patients received BMC; 30 received no infusion LVEF assessed by MRI	Approximately 2.5×10^9 unfractionated BMC	At 6 mo: LVEF 6% greater in BMC group than in control group At 18 mo: no significant difference in LVEF between the 2 groups
Janssens et al.[8]	PCI after acute myocardial infarction	Randomized, double-blind trial 33 patients received BMC; 34 received placebo infusion LVEF was assessed by MRI	Approximately 3×10^8 Ficoll-separated BMC	At 4 mo: no significant difference in overall LVEF; decreased infarct size and better regional function in BMC group
TOPCARE-CHD[6]	Chronic left ventricular dysfunction	Randomized, crossover trial In the second phase, 24 patients received CPC, 28 received BMC, 23 received no infusion LVEF assessed by left ventricular angiography	Approximately 2×10^8 Ficoll-separated BMC or approximately 2×10^7 Ficoll-separated, cultured CPC	At 3 mo: greater increase in LVEF (2.9 percentage points) in BMC group than in CPC group or control group
ASTAMI[7]	PCI after acute myocardial infarction	Randomized trial 47 patients received BMC; 50 received no infusion LVEF assessed by SPECT, echocardiography, and MRI	Approximately 7×10^7 Ficoll-separated BMC	At 6 mo: no significant difference in LVEF between the 2 groups
REPAIR-AMI[5]	PCI after acute myocardial infarction	Randomized, double-blind trial 101 patients received BMC; 98 received placebo infusion LVEF assessed by left ventricular angiography	Approximately 2.4×10^8 Ficoll-separated BMC	At 4 mo: greater absolute increase in LVEF in BMC group than in placebo group (5.5% vs. 3.0%) At 1 yr: reduction in combined adverse clinical events in BMC group as compared with placebo group

NEJM 355;12 2006

Intracoronary cardiosphere-derived cells for heart regeneration after myocardial infarction (CADUCEUS): a prospective, randomised phase 1 trial

Raj R Makkar, Rachel R Smith, Ke Cheng, Konstantinos Malliaras, Louise E J Thomson, Daniel Berman, Lawrence S C Czer, Linda Marbán, Adam Mendizabal, Peter V Johnston, Stuart D Russell, Karl H Schuleri, Albert C Lardo, Gary Gerstenblith, Eduardo Marbán

cMRI



Scar size was unchanged in controls at 6 months (difference of 0.3% [SD 5,4]; p= 0,894 within group)

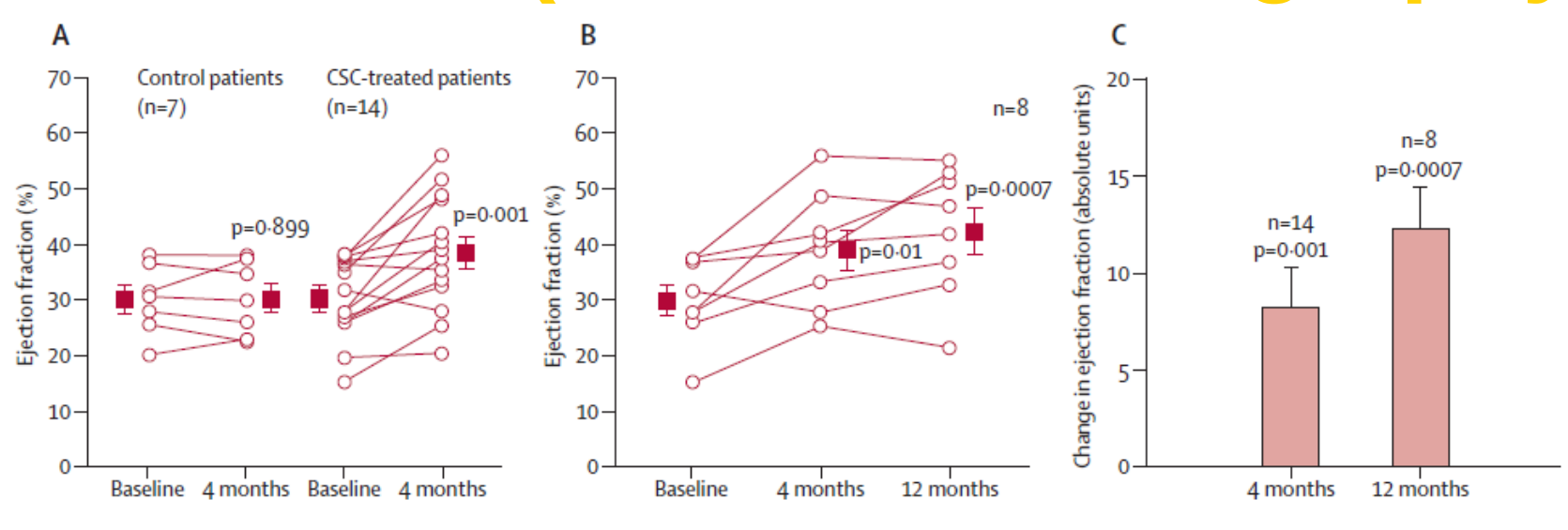
Scar size decreased in patients treated with CDCs (absolute difference –7,7% [4,8]; p<0,0001 within group, p=0,001 between groups)

***Lancet* 2012; 379: 895–904**

Cardiac stem cells in patients with ischaemic cardiomyopathy (SCIPIO): initial results of a randomised phase 1 trial

Roberto Bolli, Atul R Chugh, Domenico D'Amario, John H Loughran, Marcus F Stoddard, Sohail Ikram, Garth M Beache, Stephen G Wagner, Annarosa Leri, Toru Hosoda, Fumihiro Sanada, Julius B Elmore, Polina Goichberg, Donato Cappetta, Naresh K Solankhi, Ibrahim Fahsah, D Gregg Rokosh, Mark S Slaughter, Jan Kajstura, Piero Anversa

LVEF (3D echocardiography)



- 1 month after infusion: mean of 30,3% (SE 1.9) → 35.9% (2,7) (p=0,014)
- 4 months after infusion: 30.3%→ 38,5% (2,8) (p=0,001).
- 1 year of follow up (8 patients): from 39,2% (3,6) at 4 months to 42,5% (4,1) at 1 year (p=0,159)
- The absolute increase in LVEF from baseline was 8,2 EF units (2,0) at 4 months in 14 patients and 12,3 EF units (2,1) at 12 months in eight patients
- No change in 7 control patients (4 months of follow-up)

Cardiac stem cells in patients with ischaemic cardiomyopathy (SCIPIO): initial results of a randomised phase 1 trial

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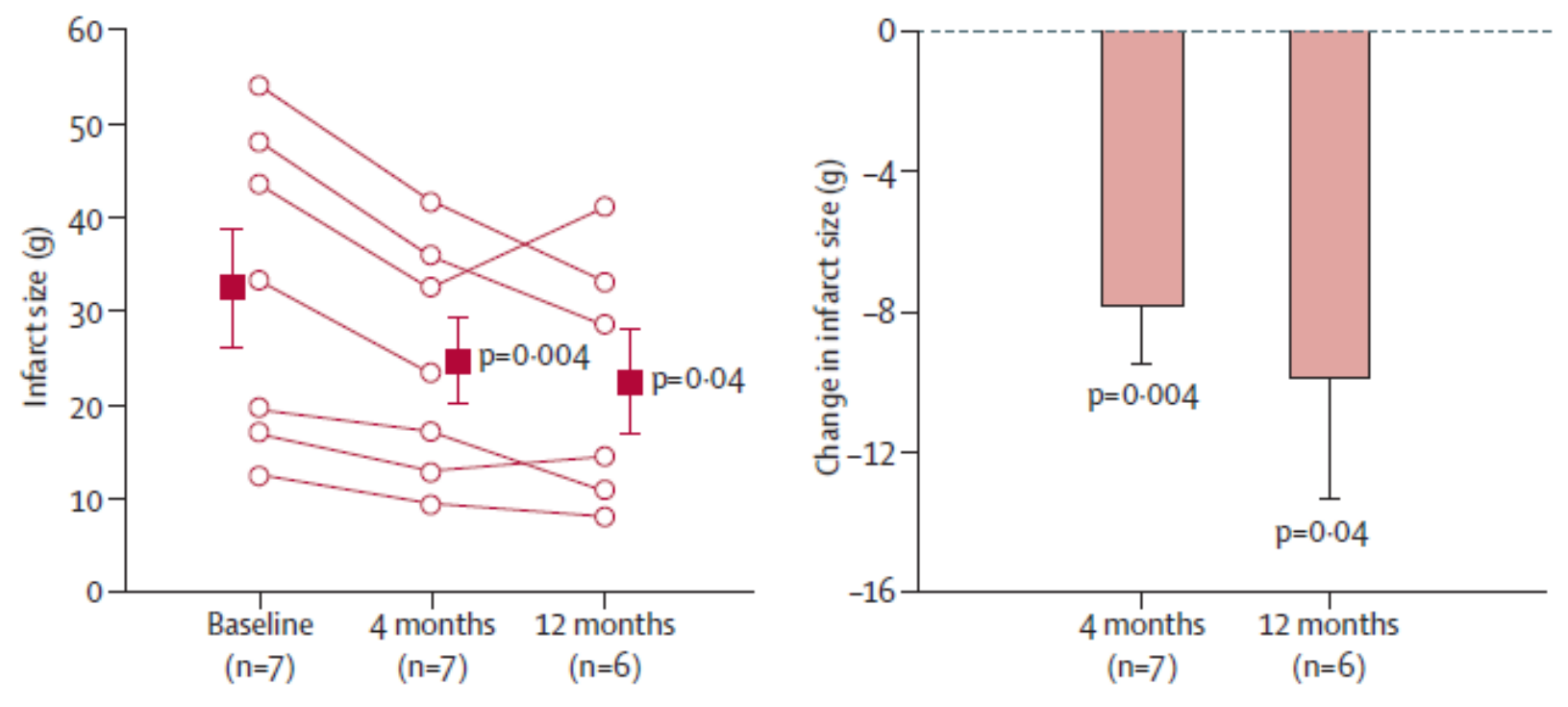
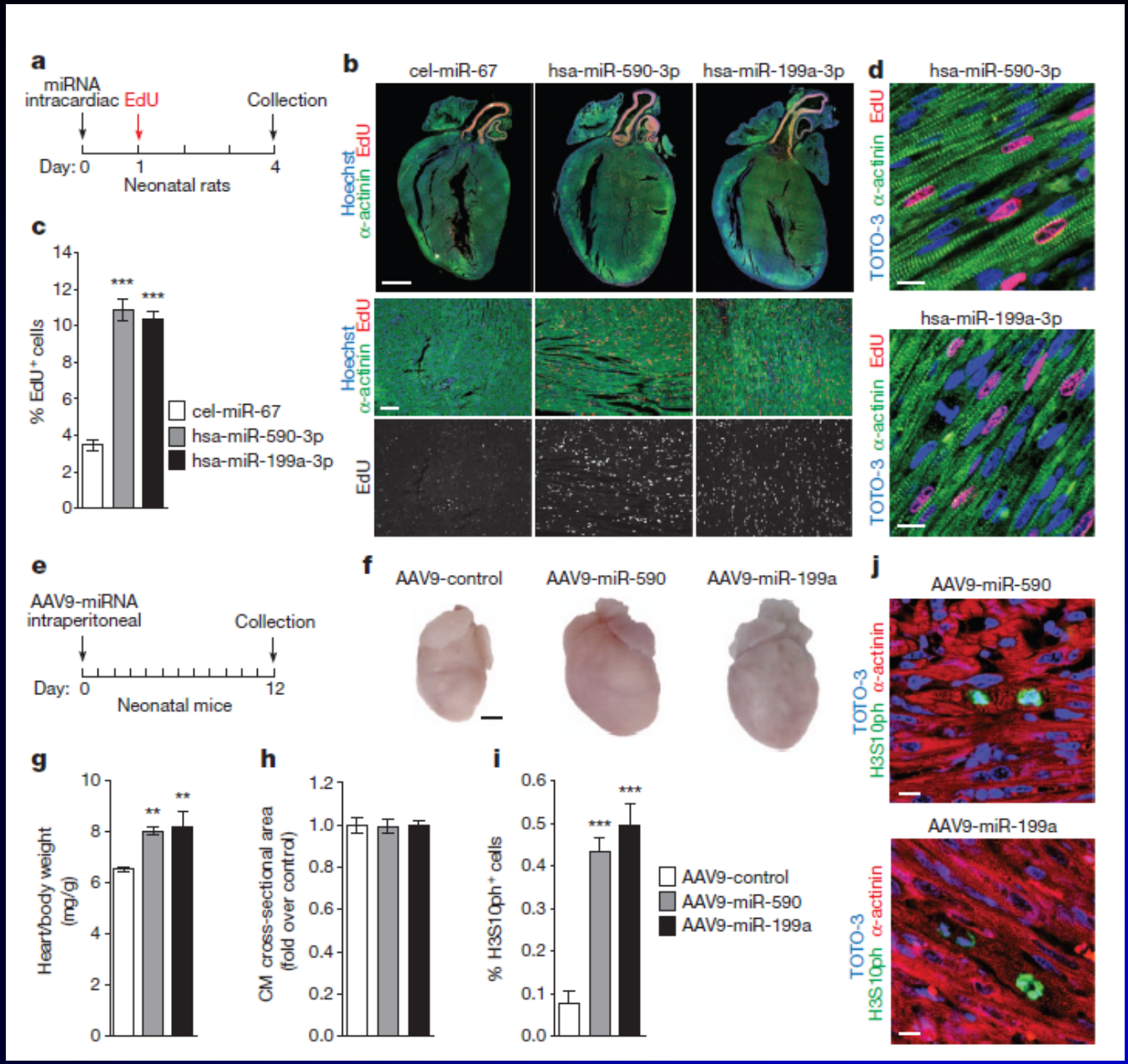


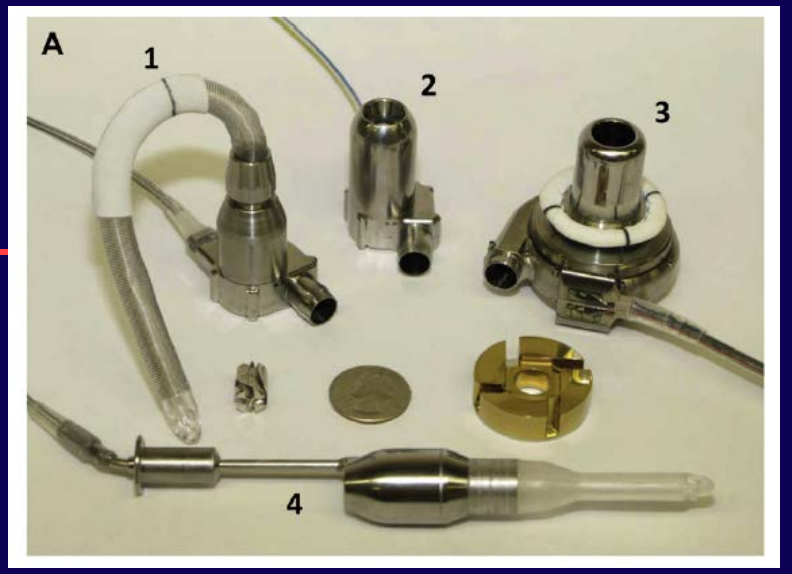
The mean infarct weight: 32,6 g [SE 6,3] before infusion of CSCs, and decreased by 7,8 g (1,7; 24%) at 4 months after treatment and 9,8 g (3,5; 30%)

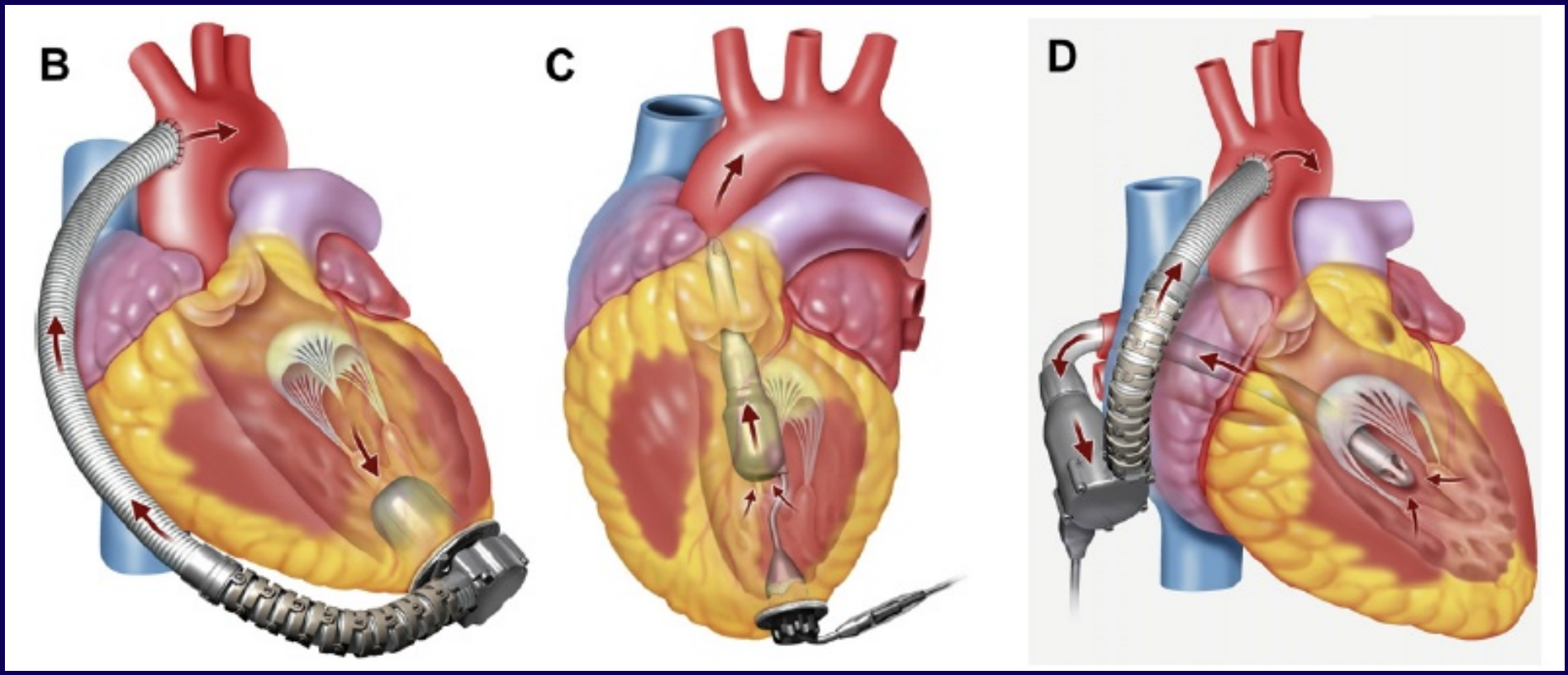


Eulalio, Zacchigna, Dal Ferro….Sinagra and Giacca; NATURE 2012, 492; 377

The Future of Adult Cardiac Assist Devices: Novel Systems and Mechanical Circulatory Support Strategies

Carlo R. Bartoli, PhD[a], Robert D. Dowling, MD[b,*]





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

European Heart Journal (2012) **33**, 1787–1847
doi:10.1093/eurheartj/ehs104

HF treatment: perspectives

- Better ethiological definition and evaluation of precipitating factors and comorbidities
- Better use of drugs and their association/dosages
- Better selection of patients for devices
- Structured long term follow up program with help of telemonitoring
- LVAD as DT
- …Personalized medicine, gene therapy and regenerative medicine