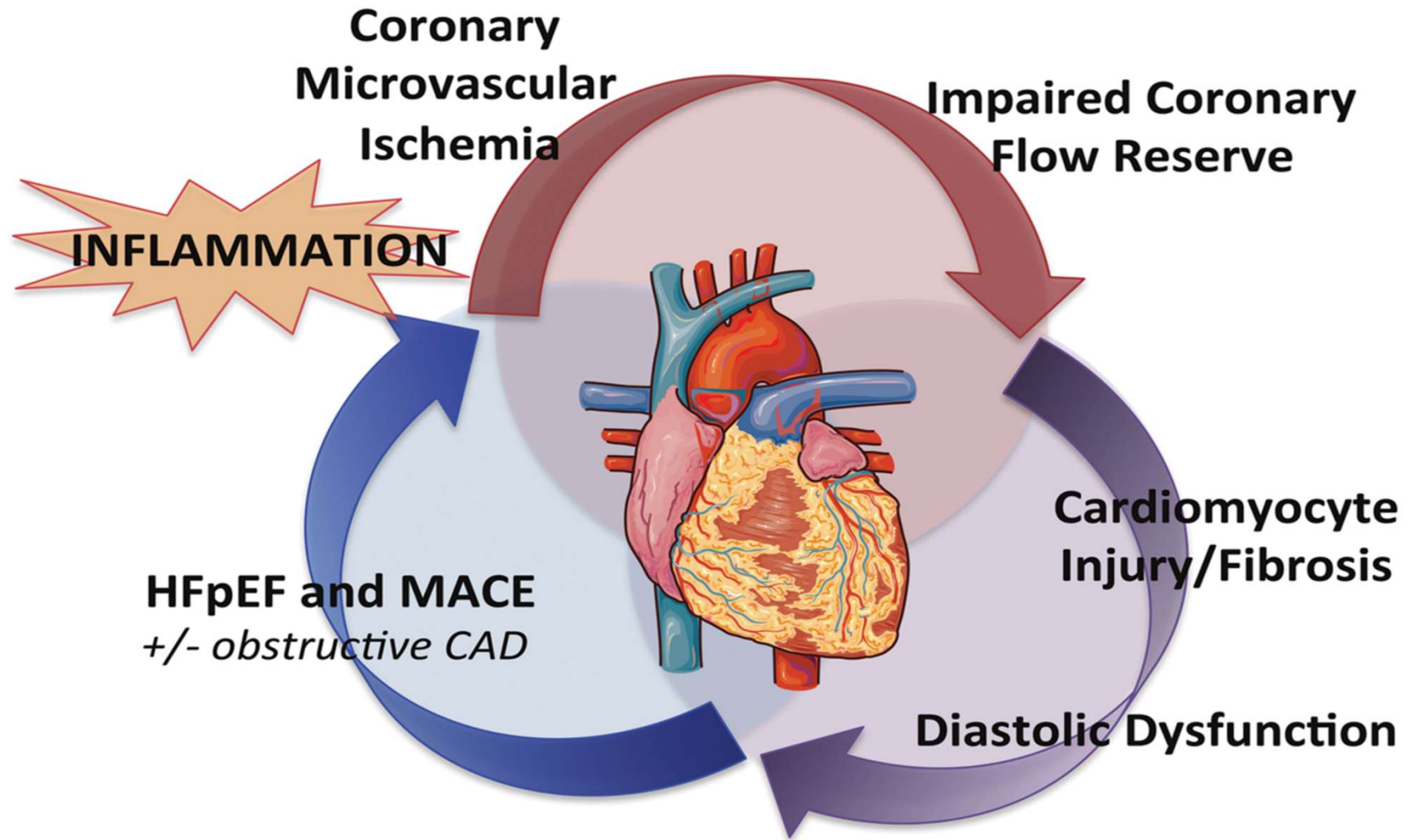


Complexity of HFrEF

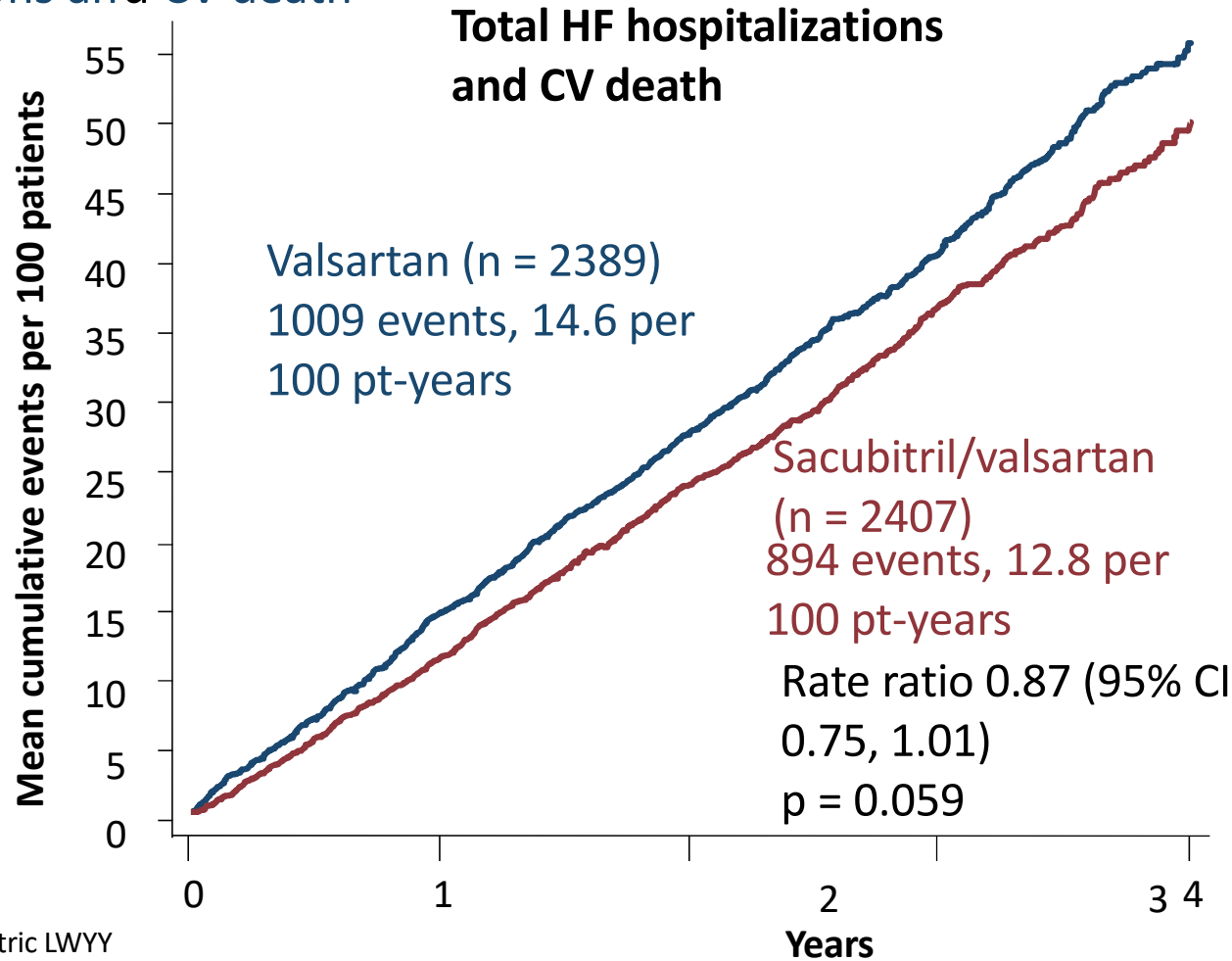


Angiotensin–Neprilysin Inhibition in Heart Failure with Preserved Ejection Fraction

S.D. Solomon, J.J.V. McMurray, I.S. Anand, J. Ge, C.S.P. Lam, A.P. Maggioni, F. Martinez, M. Packer, M.A. Pfeffer, B. Pieske, M.M. Redfield, J.L. Rouleau, D.J. van Veldhuisen, F. Zannad, M.R. Zile, A.S. Desai, B. Claggett, P.S. Jhund, S.A. Boytsov, J. Comin-Colet, J. Cleland, H.-D. Düngen, E. Goncalvesova, T. Katova, J.F. Kerr Saraiva, M. Lelonek, B. Merkely, M. Senni, S.J. Shah, J. Zhou, A.R. Rizkala, J. Gong, V.C. Shi, and M.P. Lefkowitz, for the PARAGON-HF Investigators and Committees

PARAGON-HF primary results

Recurrent event analysis of total HF hospitalizations and CV death*

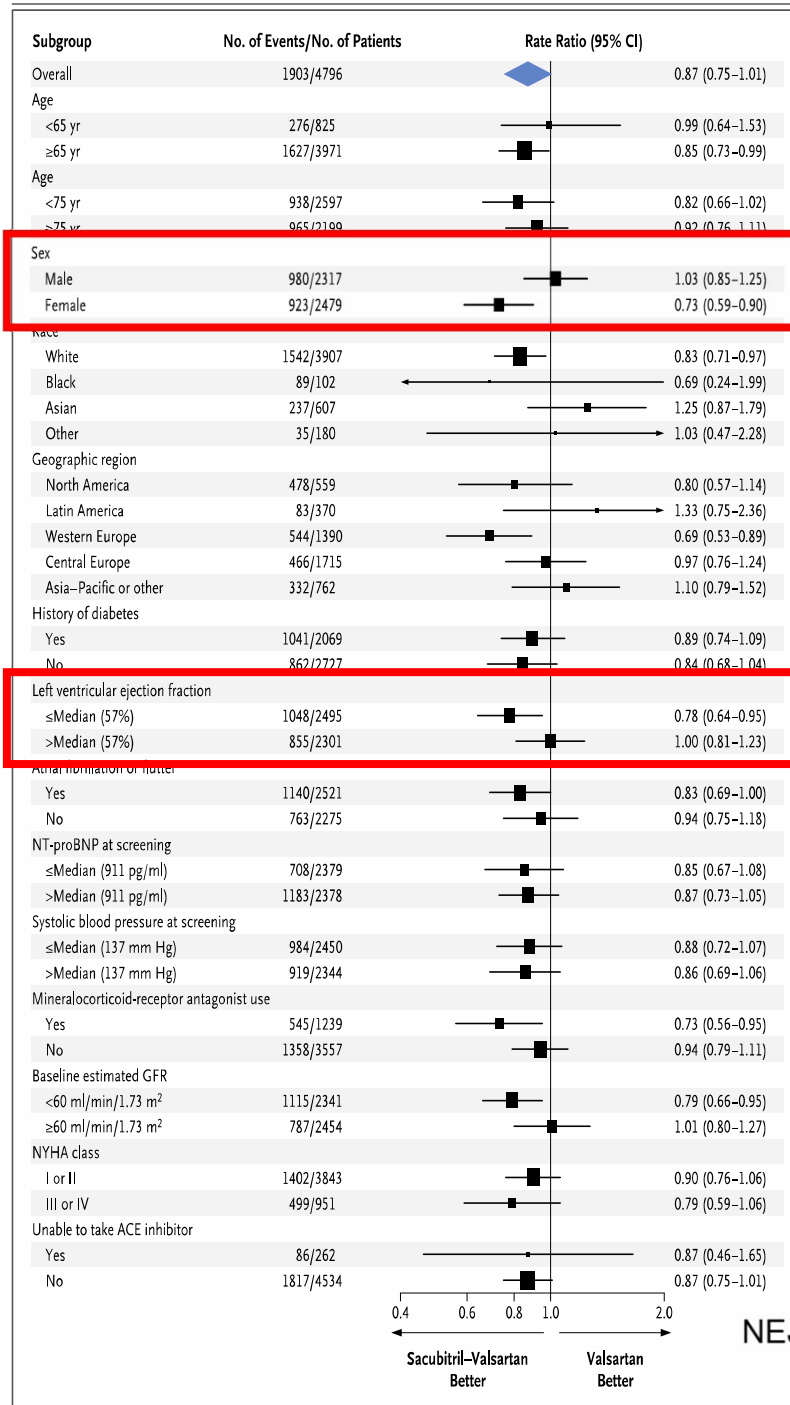


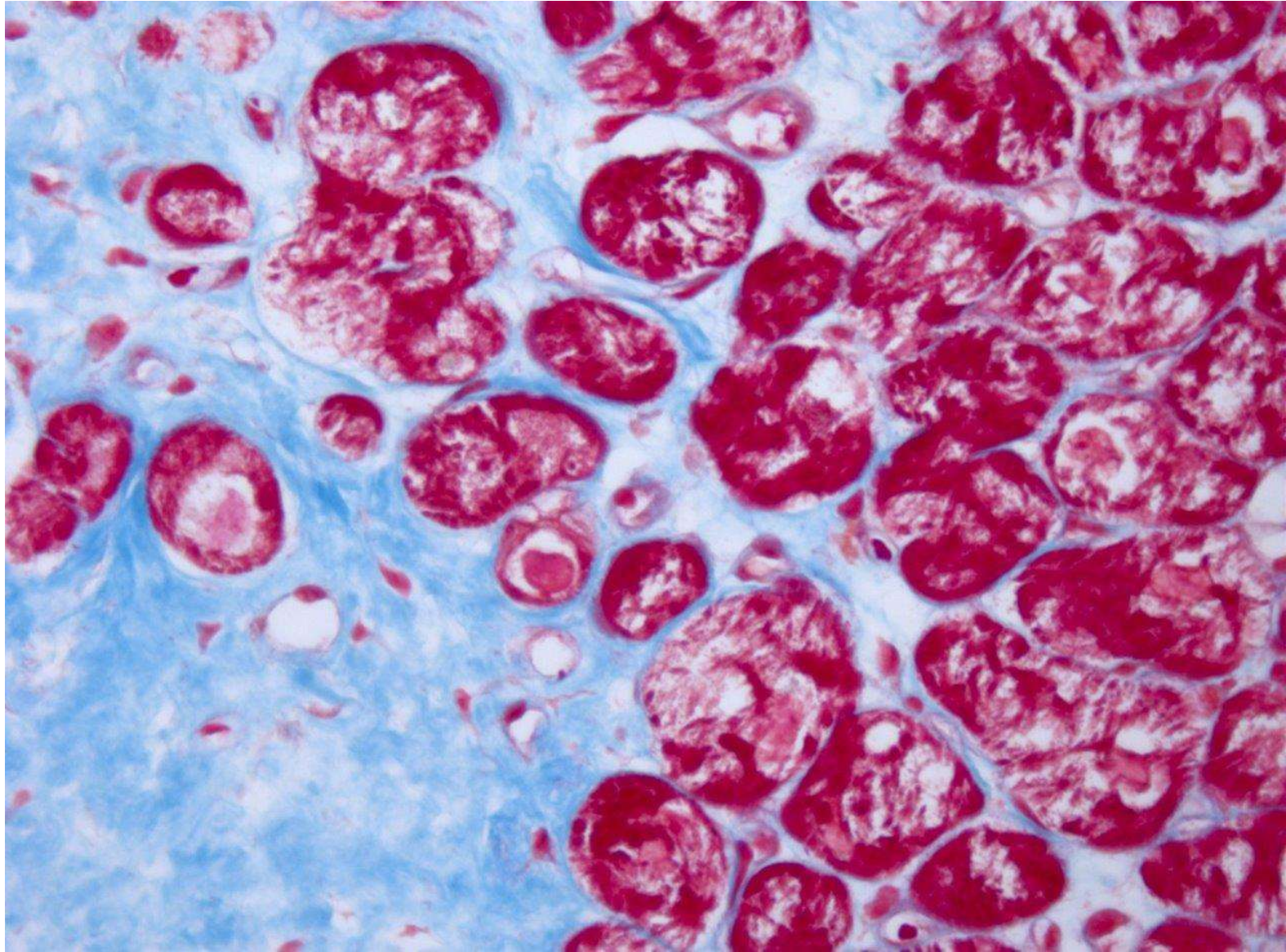
*Semiparametric LWYY method.

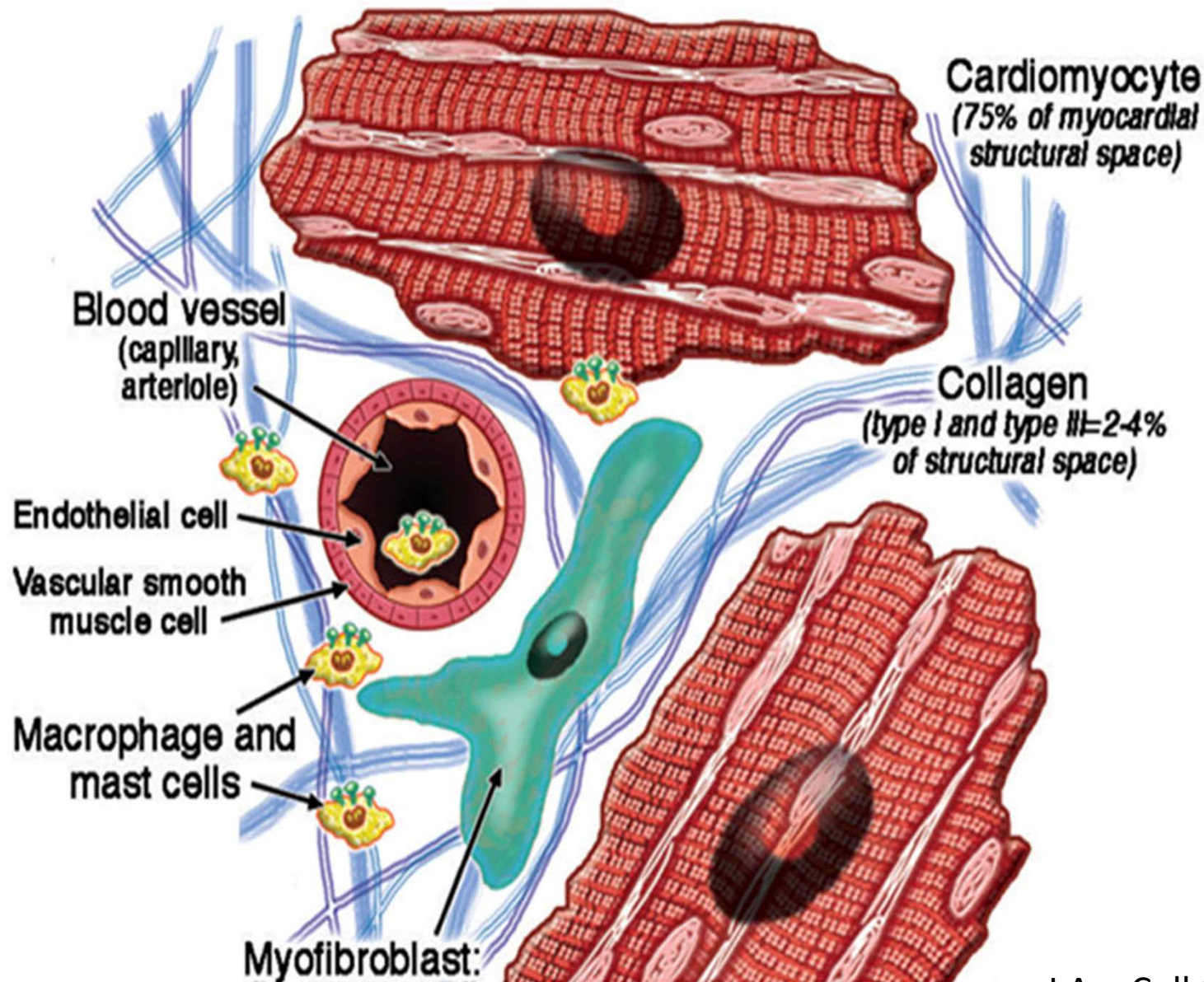
ORIGINAL ARTICLE

Angiotensin–Neprilysin Inhibition in Heart Failure with Preserved Ejection Fraction

S.D. Solomon, J.J.V. McMurray, I.S. Anand, J. Ge, C.S.P. Lam, A.P. Maggioni, F. Martinez, M. Packer, M.A. Pfeffer, B. Pieske, M.M. Redfield, J.L. Rouleau, D.J. van Veldhuisen, F. Zannad, M.R. Zile, A.S. Desai, B. Claggett, P.S. Jhund, S.A. Boytsov, J. Comin-Colet, J. Cleland, H.-D. Düngen, E. Goncalvesova, T. Katova, J.F. Kerr Saraiva, M. Lelonek, B. Merkely, M. Senni, S.J. Shah, J. Zhou, A.R. Rizkala, J. Gong, V.C. Shi, and M.P. Lefkowitz, for the PARAGON-HF Investigators and Committees

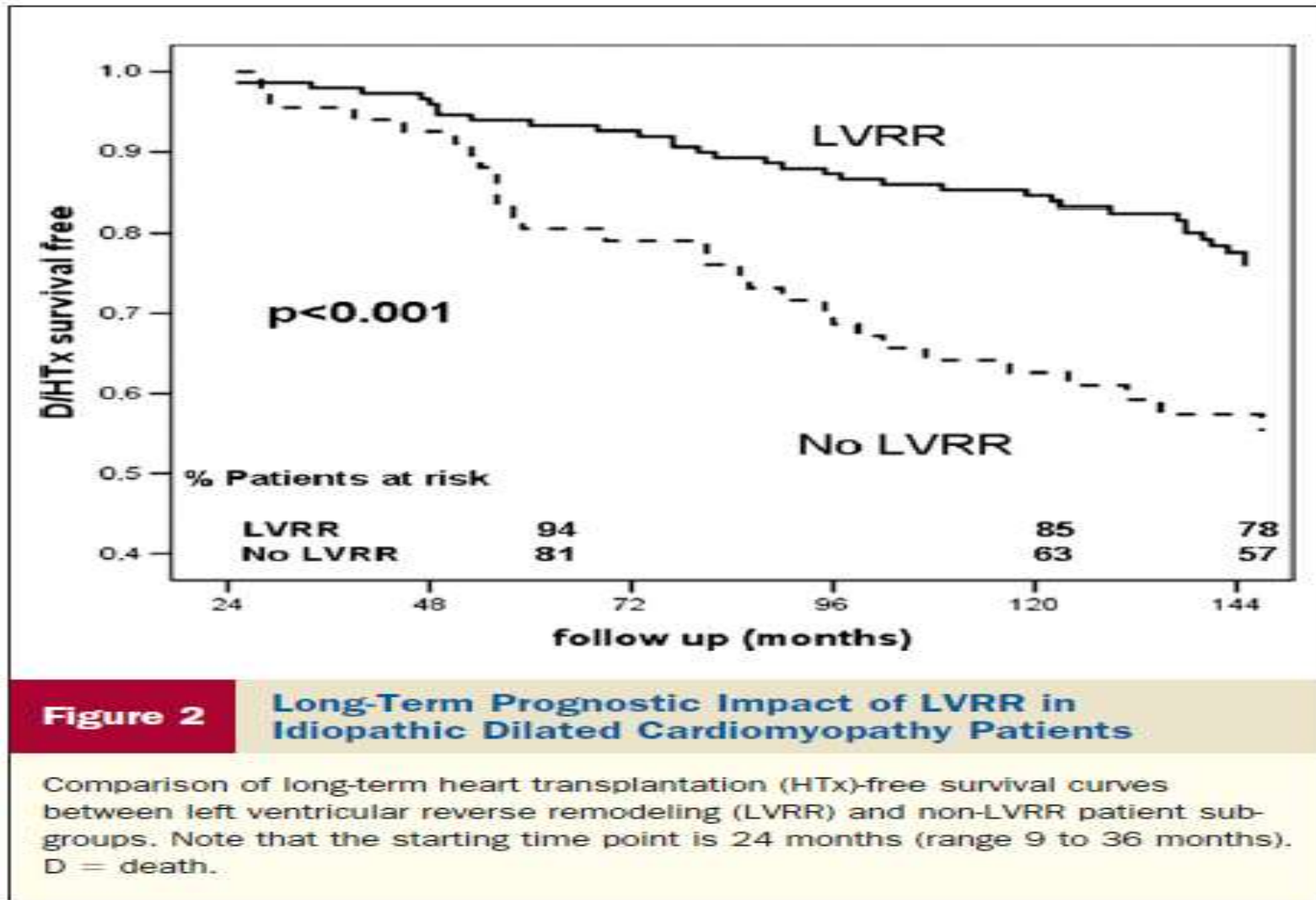






Normal Heart is composed not only by Cardiomyocytes but by a complex interaction of different cell types.

LVRR in DCM – PROGNOSTIC ROLE

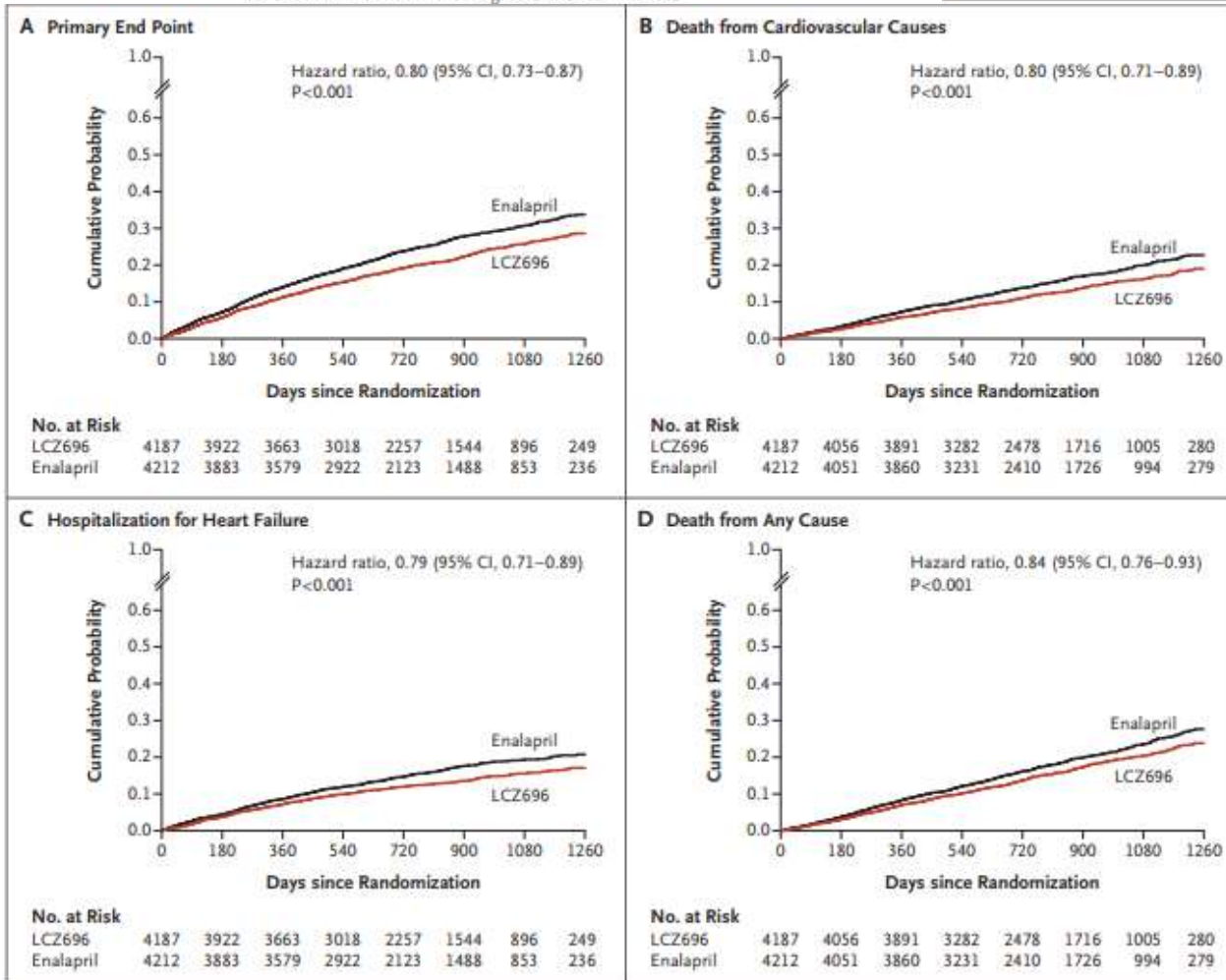


Angiotensin–Neprilysin Inhibition versus Enalapril in Heart Failure

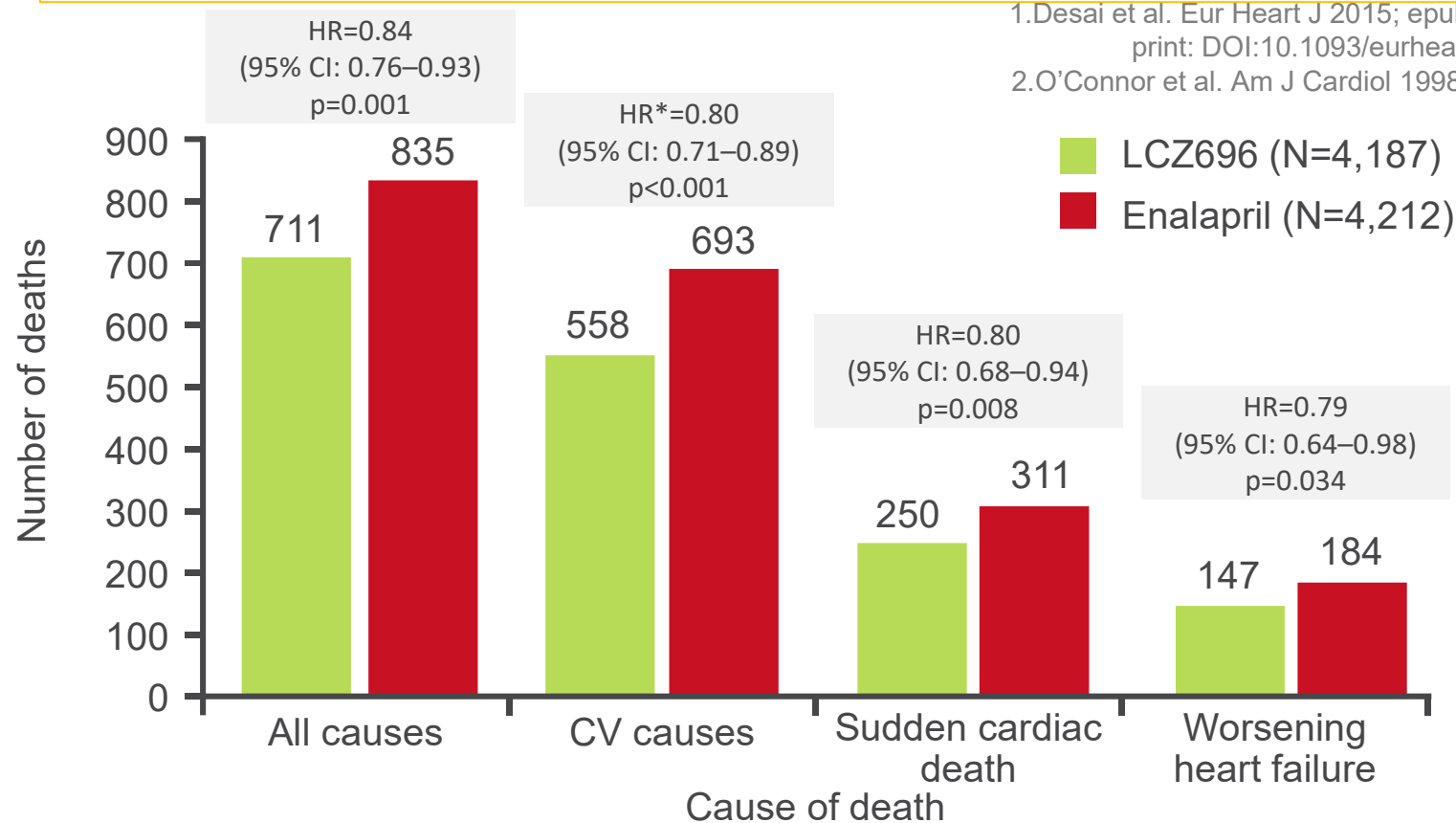
John J.V. McMurray, M.D., Milton Packer, M.D., Akshay S. Desai, M.D., M.P.H., Jianjian Gong, Ph.D., Martin P. Lefkowitz, M.D., Adel R. Rizkala, Pharm.D., Jean L. Rouleau, M.D., Victor C. Shi, M.D., Scott D. Solomon, M.D., Karl Swedberg, M.D., Ph.D., and Michael R. Zile, M.D., for the PARADIGM-HF Investigators and Committees*

Table 2. Primary and Secondary Outcomes.*

Outcome	LCZ696 (N=4187)	Enalapril (N=4212)	Hazard Ratio or Difference (95% CI)	P Value
Primary composite outcome — no. (%)				
Death from cardiovascular causes or first hospitalization for worsening heart failure	914 (21.8)	1117 (26.5)	0.80 (0.73–0.87)	<0.001
Death from cardiovascular causes	558 (13.3)	693 (16.5)	0.80 (0.71–0.89)	<0.001
First hospitalization for worsening heart failure	537 (12.8)	658 (15.6)	0.79 (0.71–0.89)	<0.001
Secondary outcomes — no. (%)				
Death from any cause	711 (17.0)	835 (19.8)	0.84 (0.76–0.93)	<0.001
Change in KCCQ clinical summary score at 8 mo†	-2.99±0.36	-4.63±0.36	1.64 (0.63–2.65)	0.001
New-onset atrial fibrillation‡	84 (3.1)	83 (3.1)	0.97 (0.72–1.31)	0.83
Decline in renal function§	94 (2.2)	108 (2.6)	0.86 (0.65–1.13)	0.28

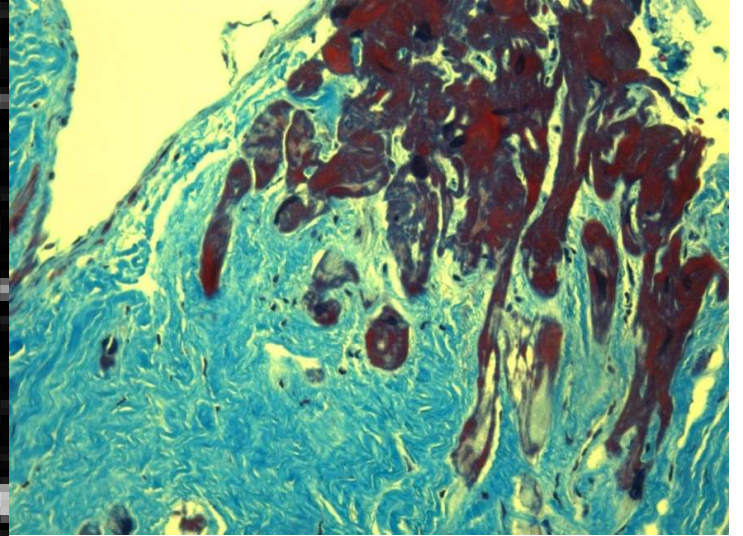


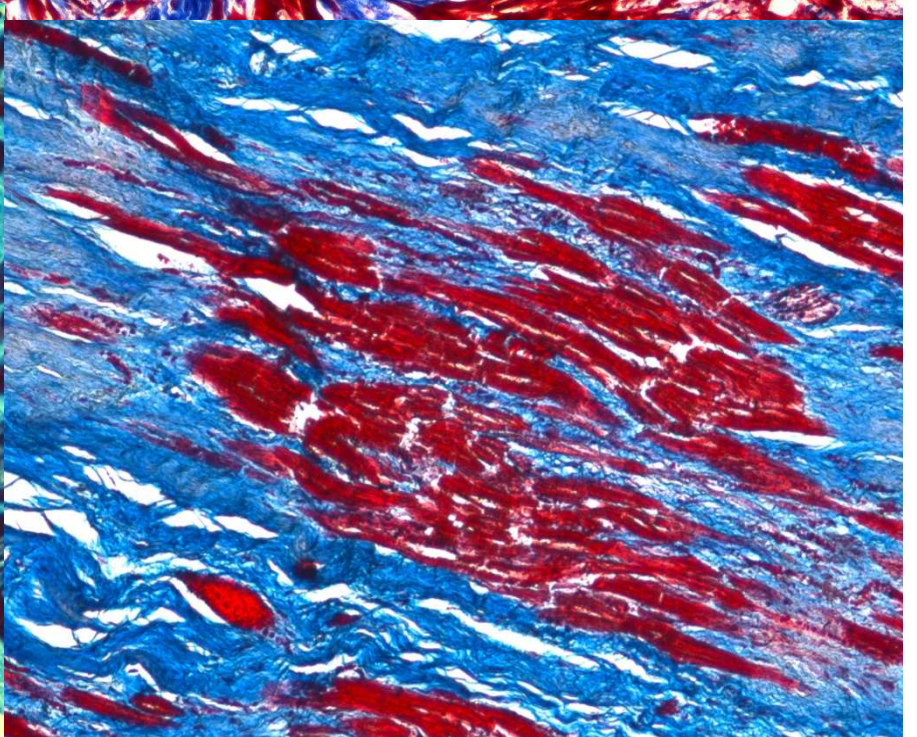
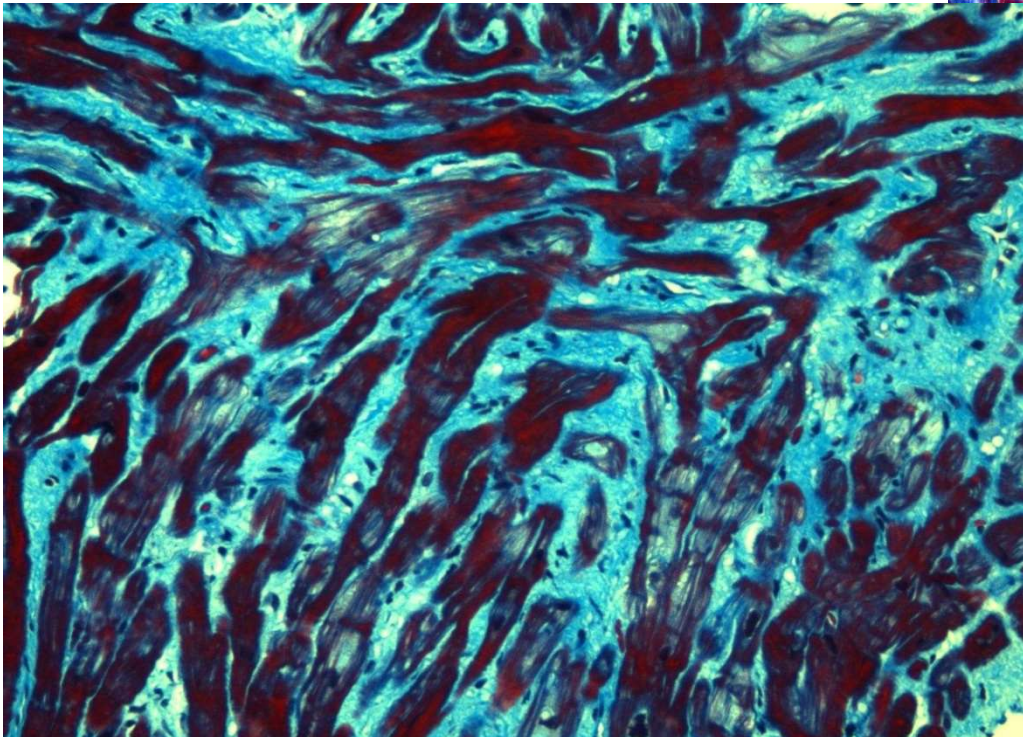
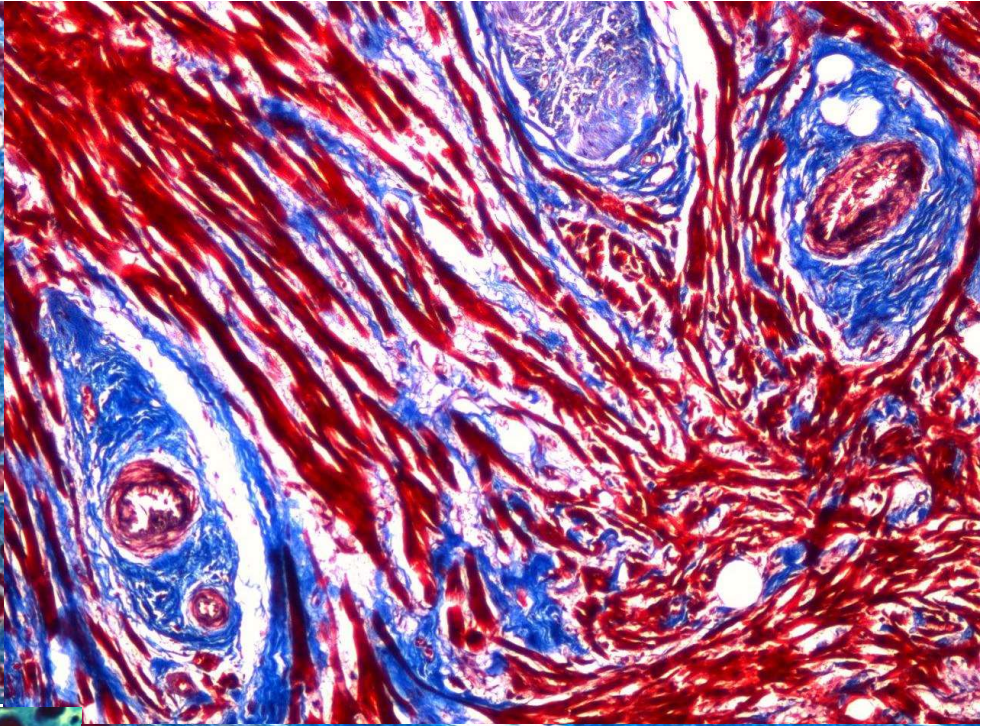
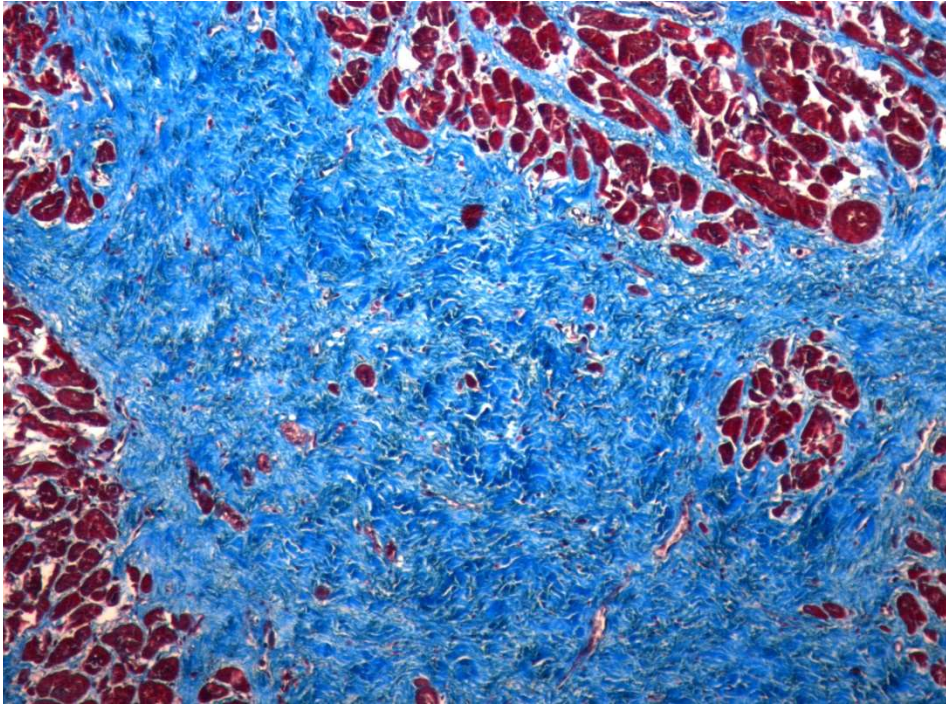
Effect of the angiotensin-receptor-neprilysin inhibitor LCZ696 compared with enalapril on mode of death in heart failure patients



1.Desai et al. Eur Heart J 2015; epub ahead of print: DOI:10.1093/eurheartj/ehv186;

2.O'Connor et al. Am J Cardiol 1998;82:881–7



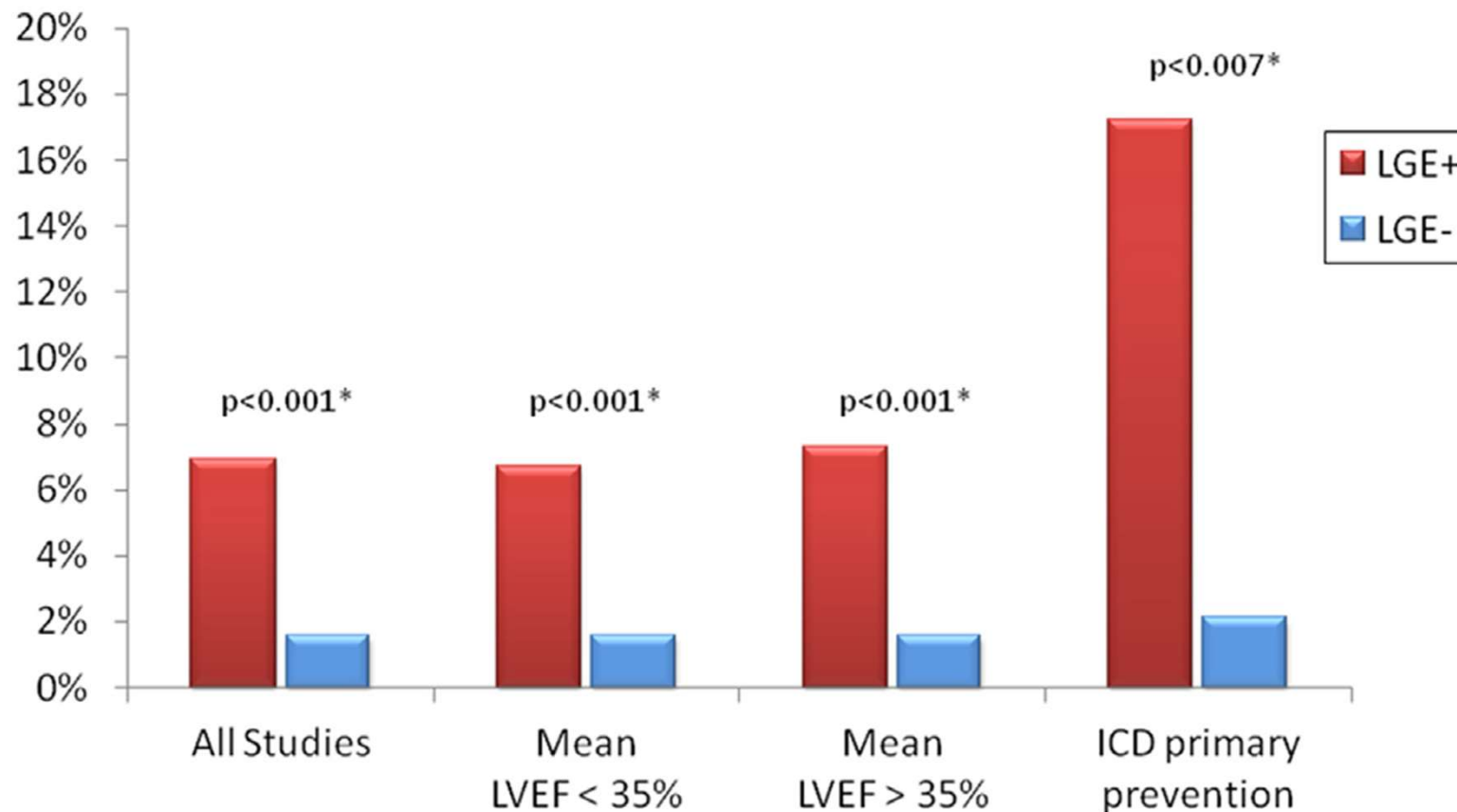


Late Gadolinium Enhancement and the Risk for Ventricular Arrhythmias or Sudden Death in Dilated Cardiomyopathy

Systematic Review and Meta-Analysis

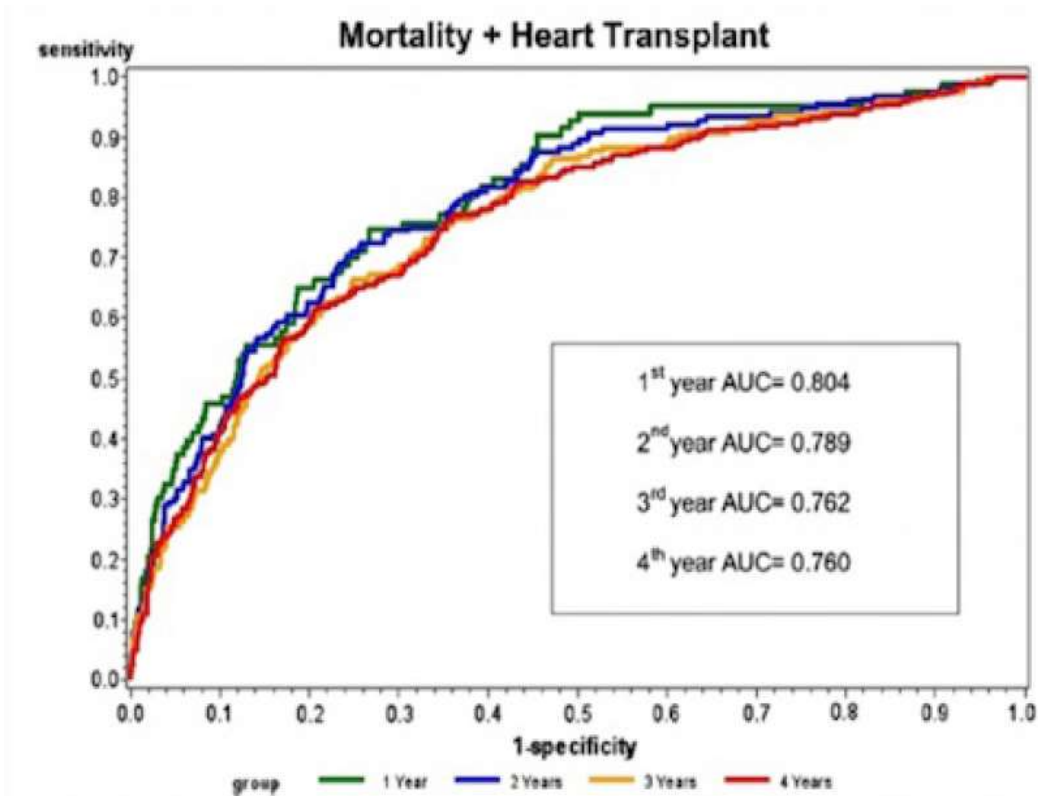


Annual Rate of the Arrhythmic Endpoint According to Late Gadolinium Enhancement Status



Metabolic exercise test data combined with cardiac and kidney indexes, the MECKI score: A multiparametric approach to heart failure prognosis

MECKI score (Metabolic Exercise and Cardiac and Kidney Indexes)



2716 HF patients

1. VO2 di picco %
2. VE/VCO2 slope
3. HGB
4. Sodiemia
5. FE
6. GFR (MDRD)

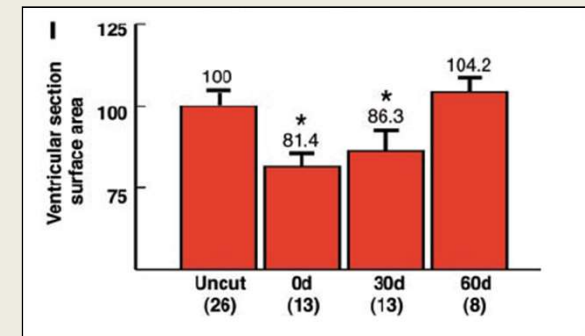
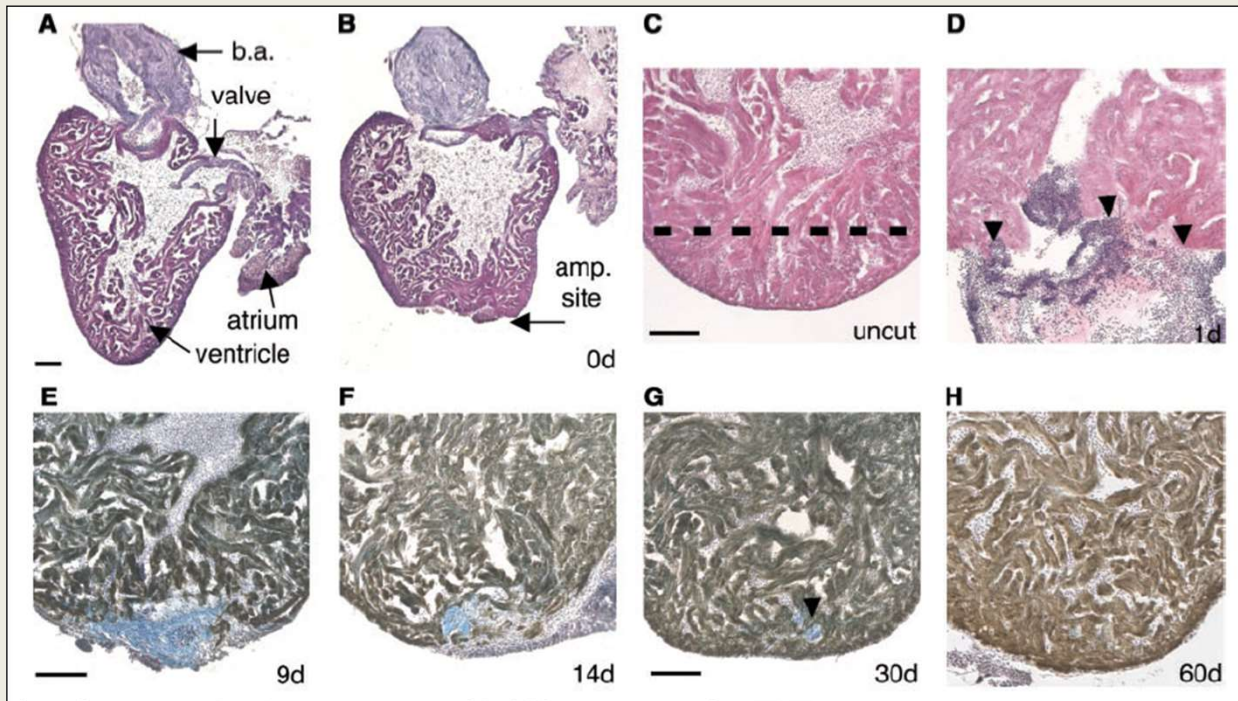
www.cardiologicomonzino.it/Clinica/Cardiologia/Pages/MeckiScore.aspx



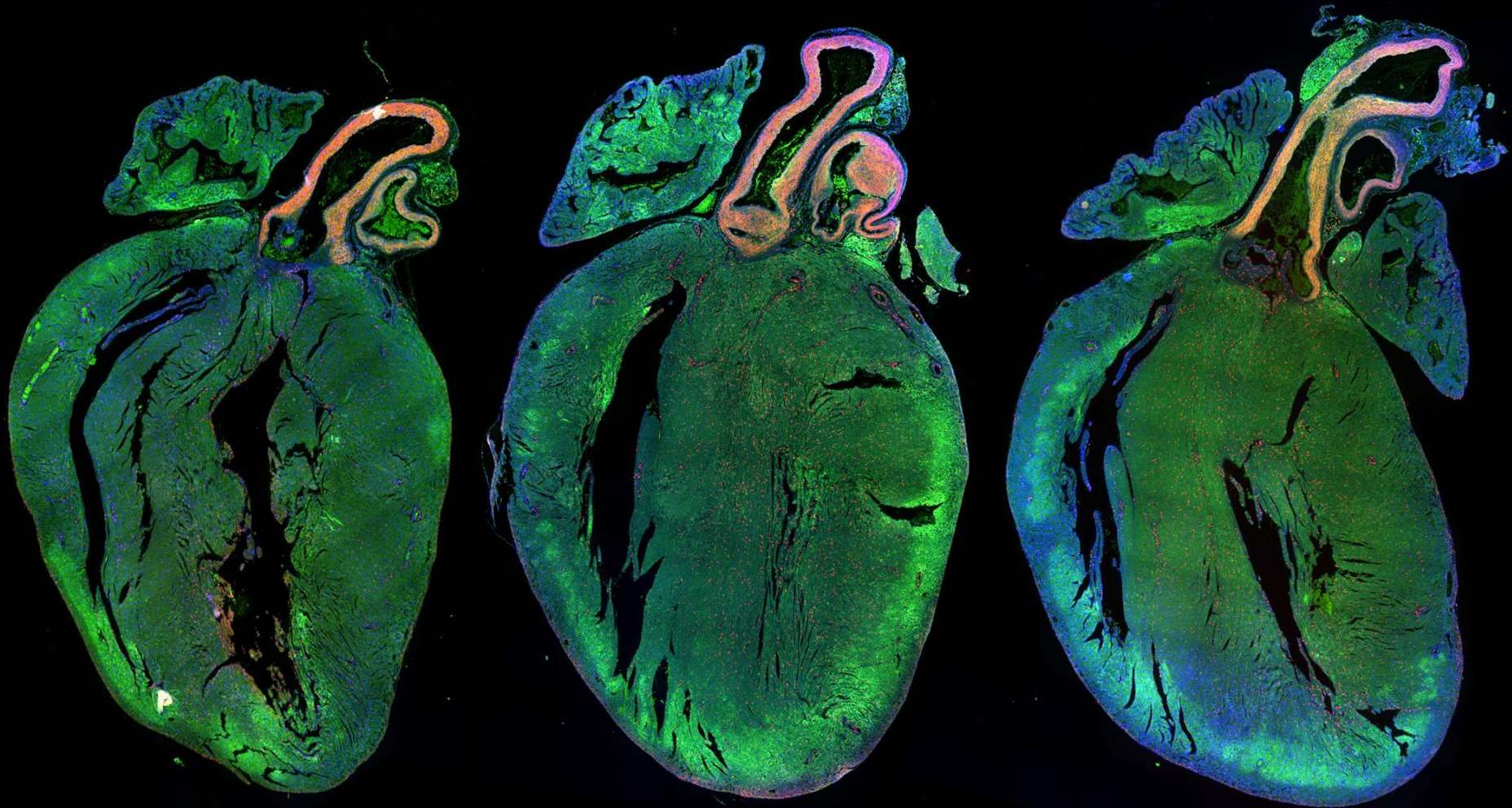
Heart Regeneration in Zebrafish
Kenneth D. Poss, *et al.*
Science **298**, 2188 (2002);
DOI: 10.1126/science.1077857



Why do newt and zebrafish hearts regenerate and mammalian hearts do not?

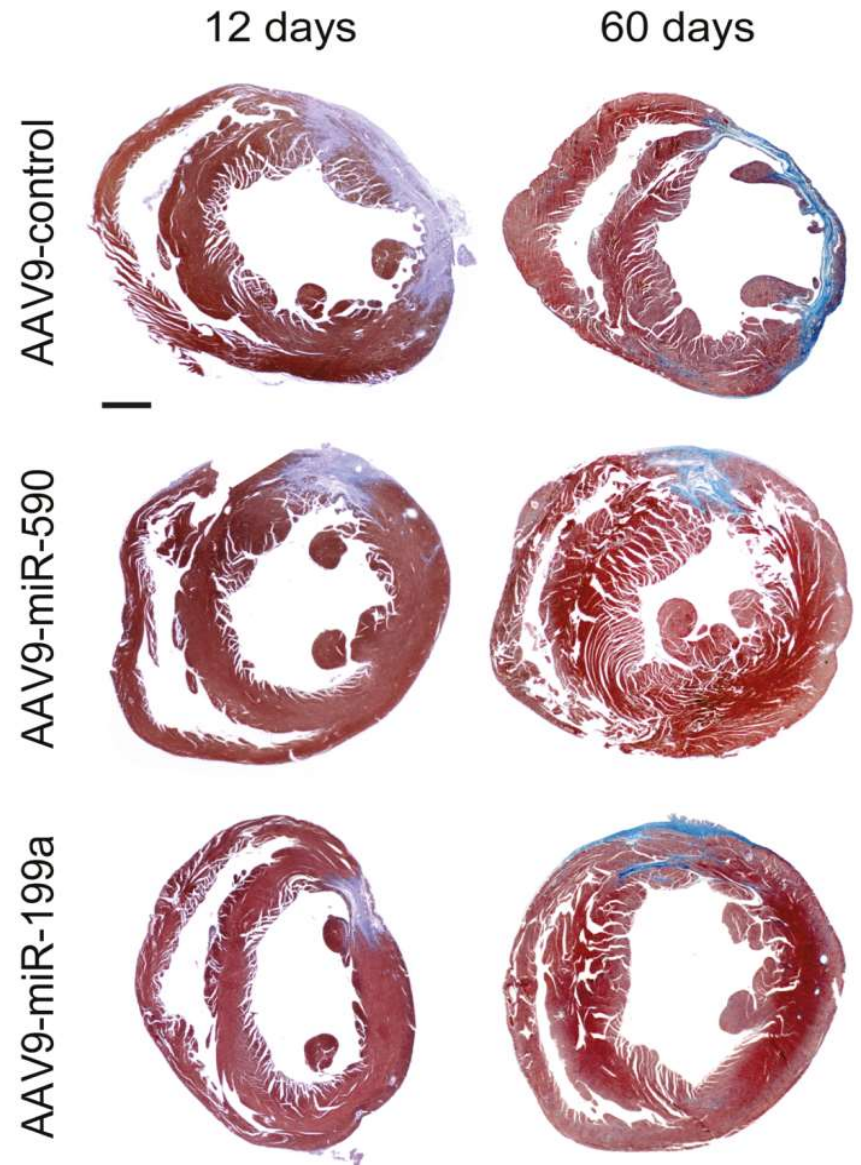
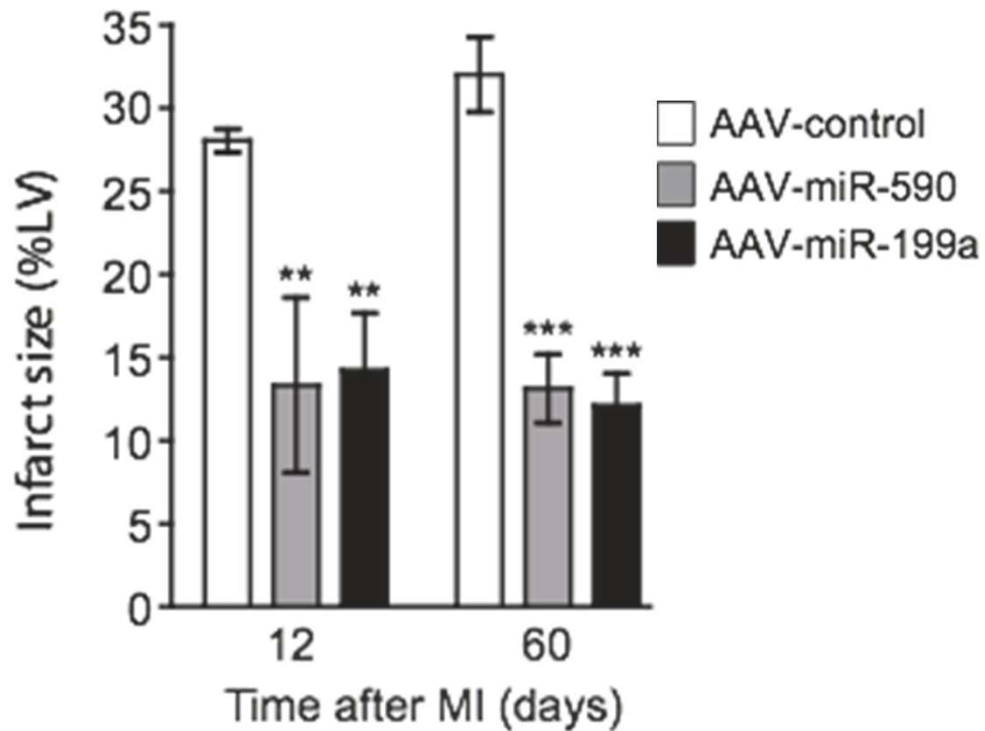
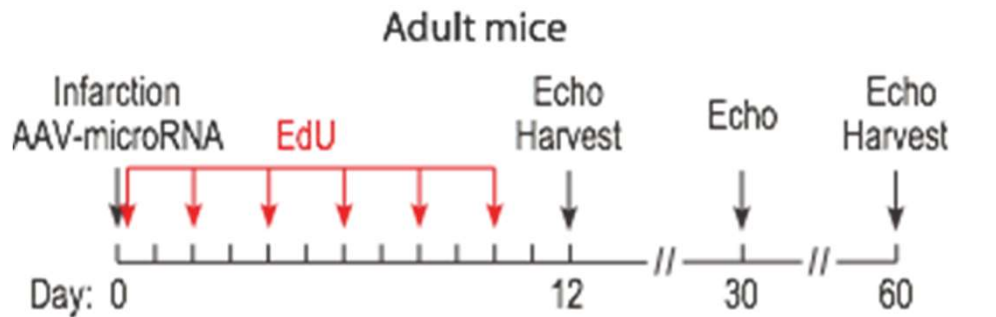


miRNAs increasing myocardial proliferation *in vivo* – newborn rat heart



α -actinin Hoechst EdU

miR-590 and miR-199a markedly reduce infarct size



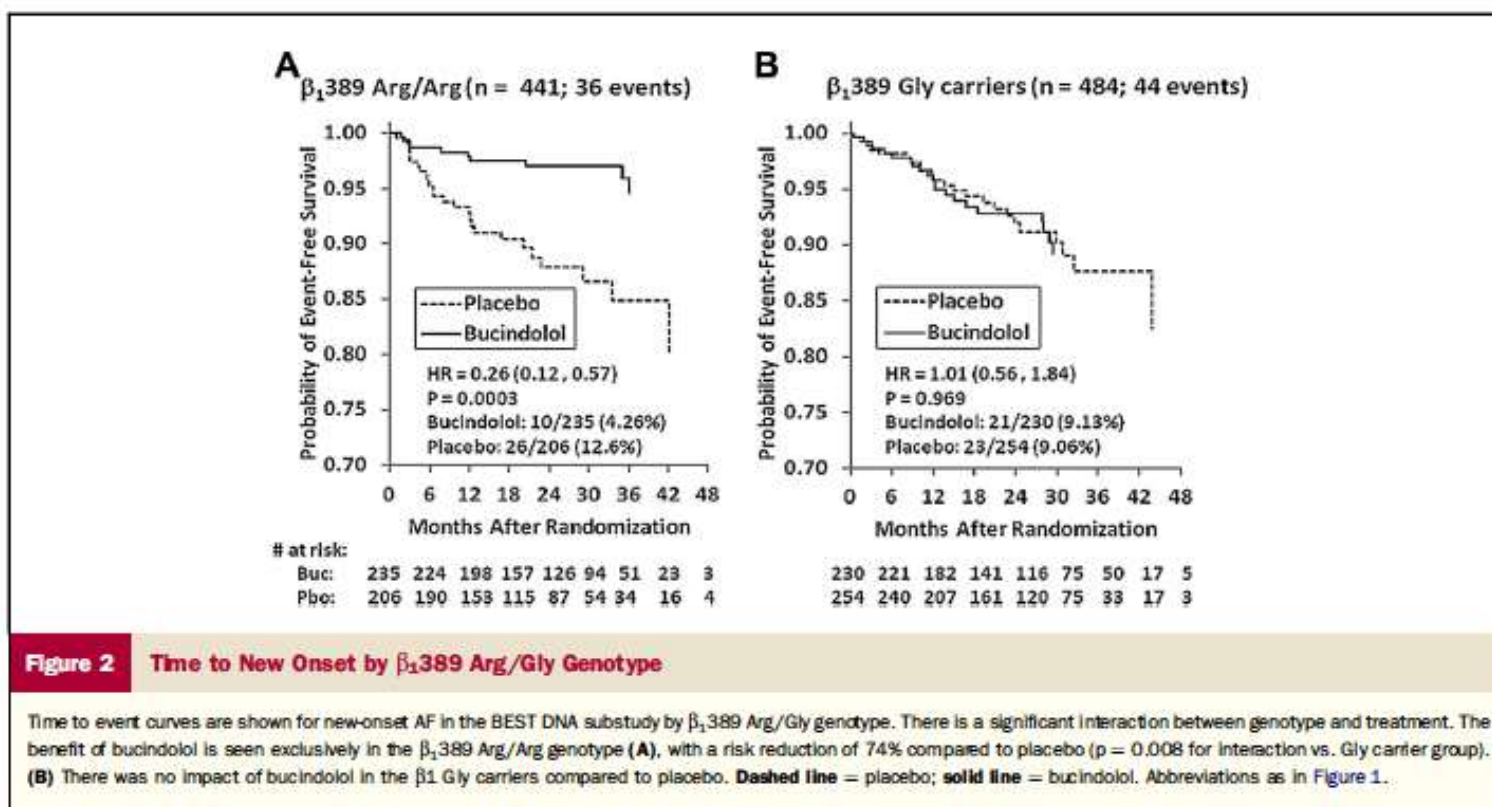
Masson Trichrome staining

Prevention of Atrial Fibrillation by Bucindolol Is Dependent on the β_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 Fiazat, PHARM.D,|| 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

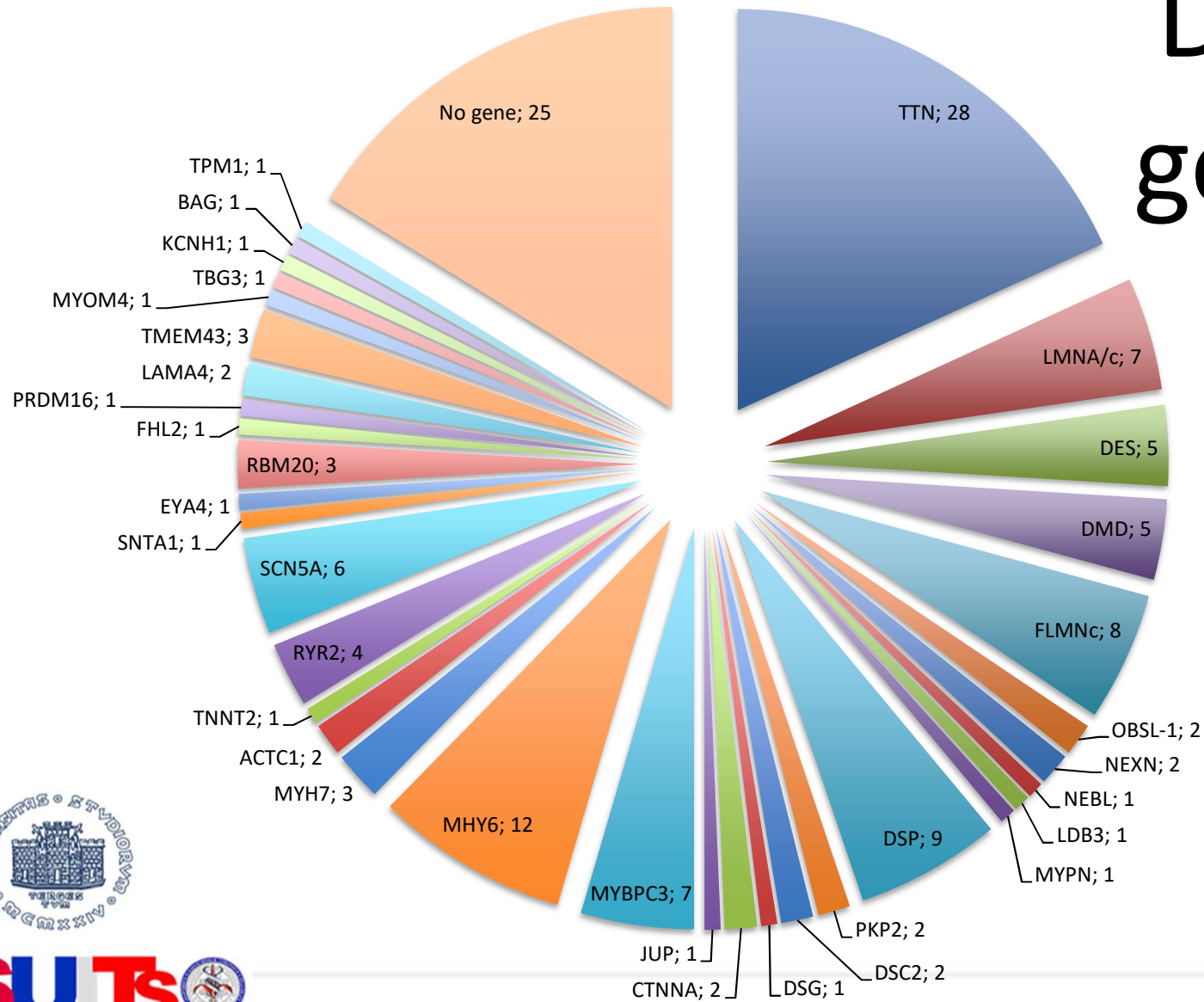
Conclusions

Bucindolol was associated with a significant, quantitatively large decrease in new-onset AF in the entire BEST cohort that was observed exclusively in the β_1 389 Arg/Arg genotype.



Heart Muscle Disease Registry of Trieste

DCM genes

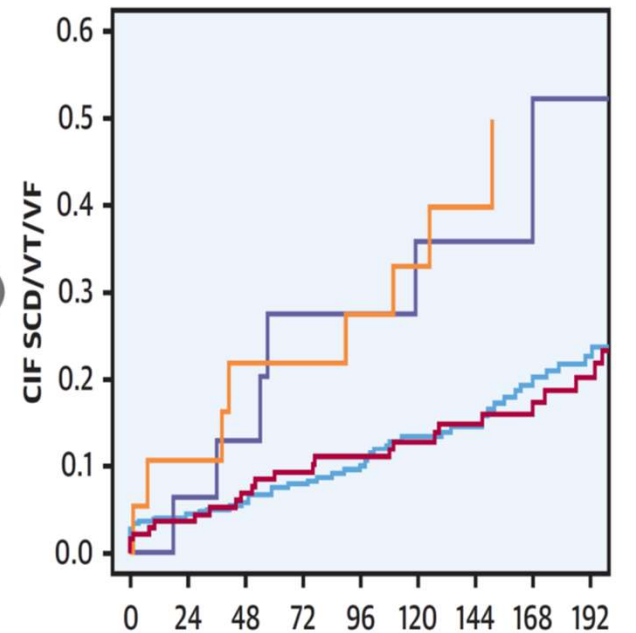
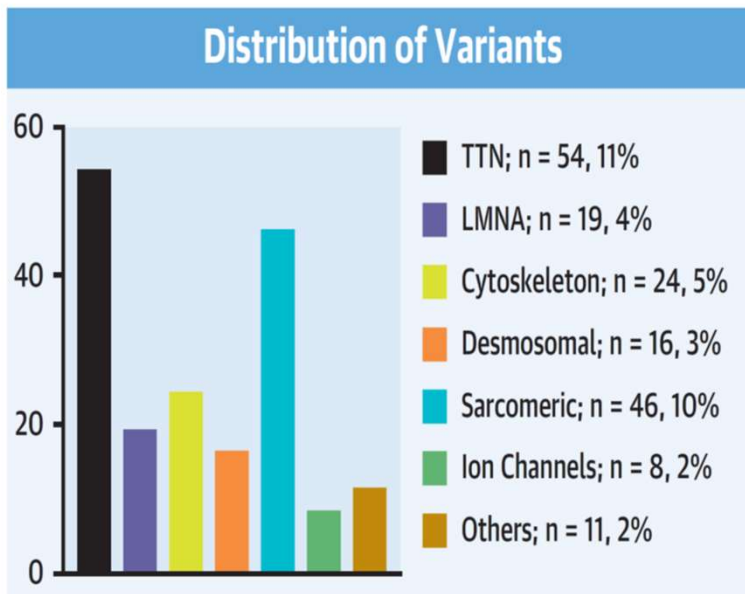




Genetic Risk of Arrhythmic Phenotypes in Patients With Dilated Cardiomyopathy



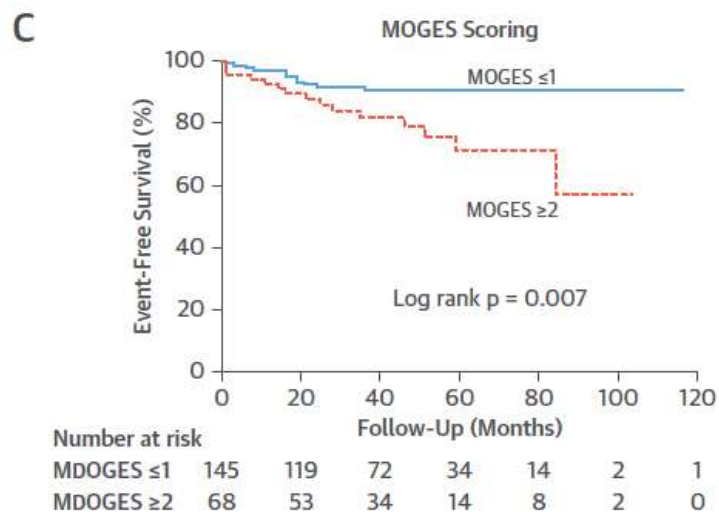
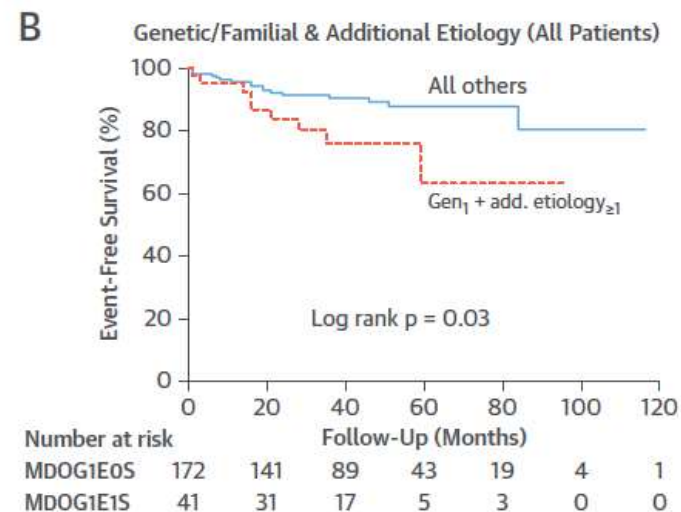
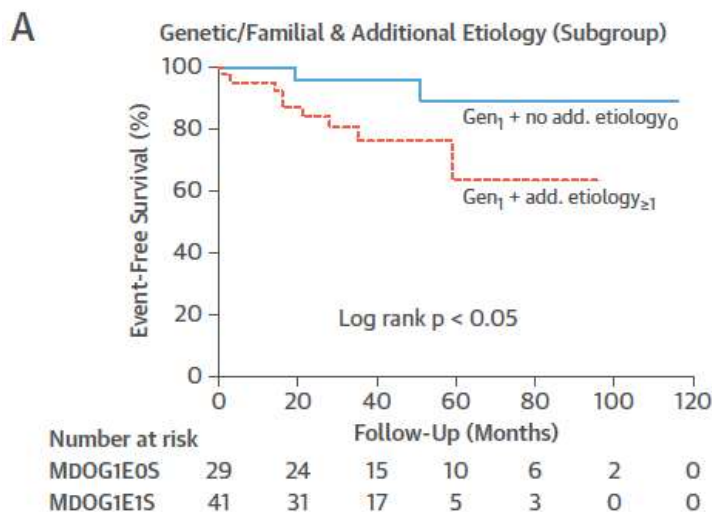
Marta Gigli, MD,^{a,b,*} Marco Merlo, MD,^{a,*} Sharon L. Graw, PhD,^b Giulia Barbati, PhD,^c Teisha J. Rowland, PhD,^b Dobromir B. Slavov, PhD,^b Davide Stolfo, MD,^a Mary E. Haywood, PhD,^b Matteo Dal Ferro, MD,^a Alessandro Altinier, MD,^a Federica Ramani, PhD,^a Francesca Brun, MD,^a Andrea Cocciolo, MD,^{a,b} Ilaria Puggia, MD,^{a,b} Gaetano Morea, MD,^{a,b} William J. McKenna, MD, DSc,^{d,e} Francisco G. La Rosa, MD,^f Matthew R.G. Taylor, MD, PhD,^b Gianfranco Sinagra, MD,^a Luisa Mestroni, MD^b



— Variant Negative — LMNA**
— Desmosomal Genes** — Remaining Carriers

Prognostic Relevance of Gene-Environment Interactions in Patients With Dilated Cardiomyopathy

Applying the MOGE(S) Classification



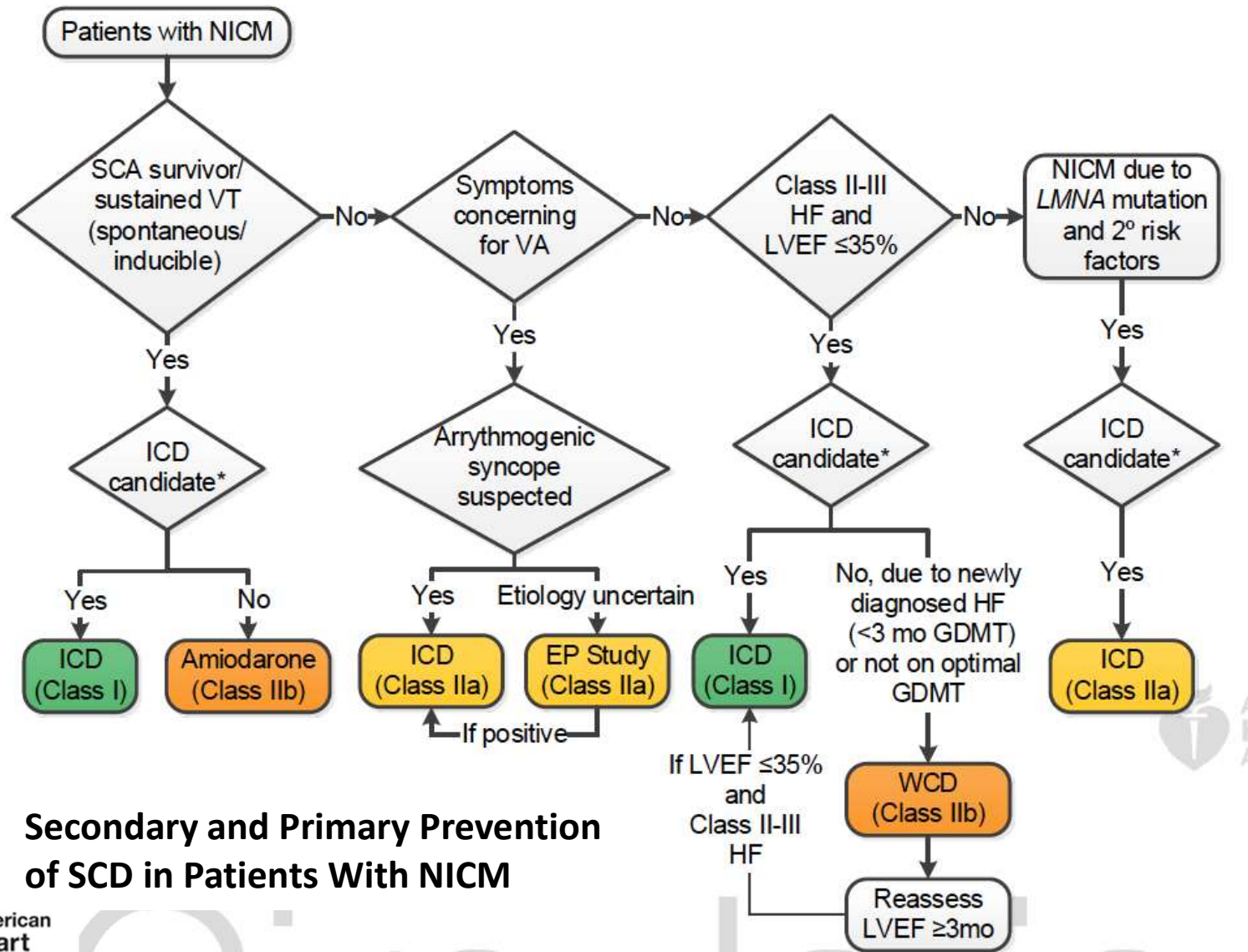
Editorial

Lamin A/C Cardiomyopathy Cutting Edge to Personalized Medicine

Gianfranco Sinagra, MD; Matteo Dal Ferro, MD; Marco Merlo, MD

the correct way to follow in personalizing risk stratification in DCM: the independent variable should be the specific mutation, rather than any clustering attempt (ie, mutation type, mutation position, gene or gene clusters). These clusters, in fact, may help the clinician get a rough orientation but do not allow a truly personalized medicine. Multicenter studies are needed to fill the gap in knowledge of the multiple and heterogeneous genotype–phenotype correlations promoting the onset of DCM in mutation carriers, and Lamin A/C might represent, once again, the starting point.

2017 AHA/ACC/HRS Guideline for Management of Patients With Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death



Secondary and Primary Prevention of SCD in Patients With NICM

2019 HRS Expert Consensus Statement on Evaluation, Risk Stratification, and Management of Arrhythmogenic Cardiomyopathy

Jeffrey A. Towbin, MS, MD (Chair),^{1,2} William J. McKenna, MD, DSc (Vice-Chair),³ Dominic J. Abrams, MD, MRCP, MBA,⁴ Michael J. Ackerman, MD, PhD,^{5,*} Hugh Calkins, MD, FHRS, CCDS,⁶ Francisco C.C. Darrieux, MD, PhD,^{7,†} James P. Daubert, MD, FHRS,⁸ Christian de Chillou, MD, PhD,^{9,‡} Eugene C. DePasquale, MD,^{10,§} Milind Y. Desai, MD,^{11,¶} N.A. Mark Estes, III, MD, FHRS, CCDS,¹² Wei Hua, MD, FHRS,^{13,¶} Julia H. Indik, MD, PhD, FHRS,¹⁴ Jodie Ingles, MPH, PhD, FHRS,^{15,**} Cynthia A. James, ScM, PhD, CGC,⁶ Roy M. John, MBBS, PhD, CCDS, FHRS,¹⁶ Daniel P. Judge, MD,^{17,††} Roberto Keegan, MD,^{18,19,‡‡} Andrew D. Krahn, MD, FHRS,²⁰ Mark S. Link, MD, FHRS,^{21,§§} Frank I. Marcus, MD,¹⁴ Christopher J. McLeod, MBChB, PhD, FHRS,⁵ Luisa Mestroni, MD,²² Silvia G. Priori, MD, PhD,^{23,24,25} Jeffrey E. Saffitz, MD, PhD,²⁶ Shubhayan Sanatani, MD, FHRS, CCDS,^{27,¶¶} Wataru Shimizu, MD, PhD, FHRS,^{28,##} J. Peter van Tintelen, MD, PhD,^{29,30} Arthur A.M. Wilde, MD, PhD,^{24,29,31} Wojciech Zareba, MD, PhD³²

COR	LOE	Recommendations	References
IIa	C-LD	In individuals with FLNC ACM and an LVEF <45%, an ICD is reasonable.	34

Variants in FLNC are associated with several skeletal and cardiac myopathies. Recognition of FLNC has recently been recognized as an ACM, resulting, in part, from the identification of truncation variants in 28 unrelated cardiomyopathy patients referred to a gene testing laboratory in Spain.³⁴ Familial evaluation led to the identification of 54 individuals with a FLNC variant. SCD and arrhythmias treated by an ICD were frequent. In the 12 patients with SCD, the mean LVEF was 39.6% ± 12%.

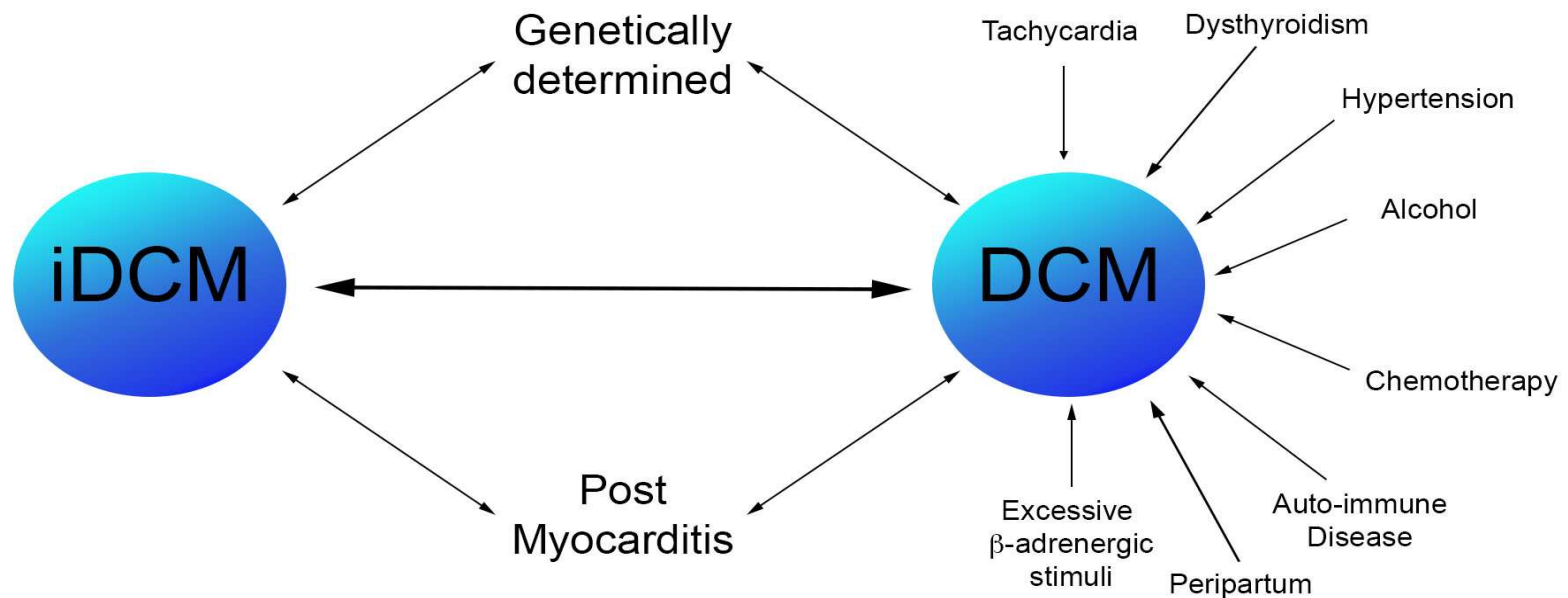


Evolving concepts in dilated cardiomyopathy

Marco Merlo¹, Antonio Cannatà¹, Marco Gobbo¹, Davide Stolfo¹, Perry M. Elliott²,
and Gianfranco Sinagra^{1*}

¹Cardiovascular Department 'Ospedali Riuniti' and University of Trieste, Trieste, Italy; and ²Centre for Heart Muscle Disease, Institute of Cardiological Sciences, University College London and St. Bartholomew's Hospital, London, UK

Received 10 September 2017; revised 30 October 2017; accepted 12 November 2017



Trajectories of Cardiovascular Risk Factors and Incidence of Atrial Fibrillation Over a 25-Year Follow-Up

The ARIC Study (Atherosclerosis Risk in Communities)

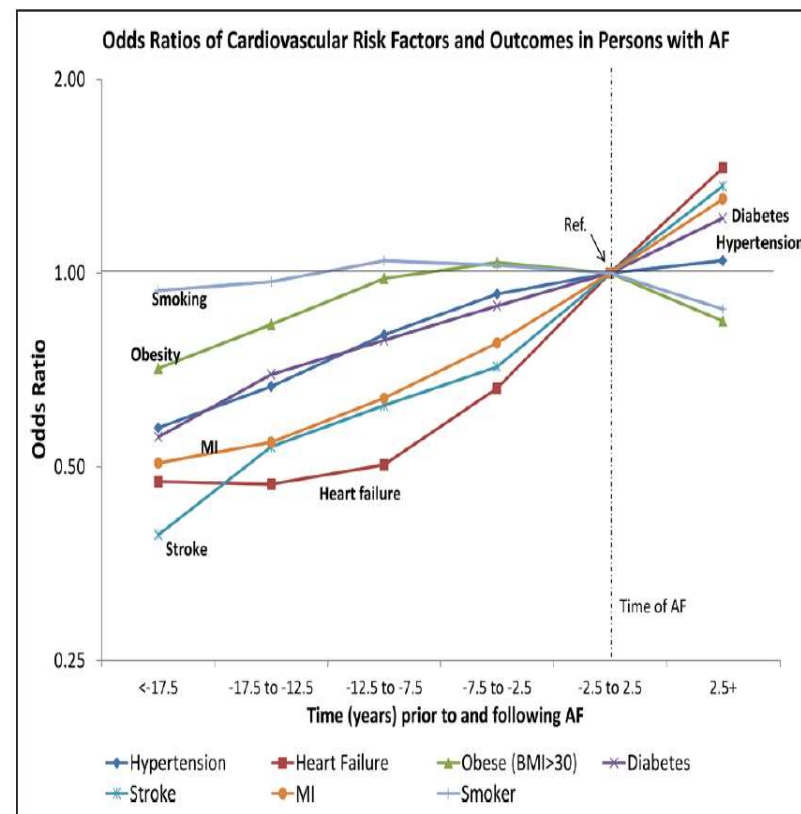


Figure 2. Odds ratios (ORs) of cardiovascular risk factors and outcomes over time based on atrial fibrillation (AF) status and adjusted for age, race, and sex.

An OR <1 or >1 can be interpreted as a lower or higher odds, respectively, of the risk factor or cardiovascular outcome at a particular time period compared with the odds at the time of AF diagnosis date. MI indicates myocardial infarction.

Temporal trends and patterns in heart failure incidence: a population-based study of 4 million individuals

Nathalie Conrad, Andrew Judge, Jenny Tran, Hamid Mohseni, Deborah Hedgecott, Abel Perez Crespillo, Moira Allison, Harry Hemingway, John G Cleland, John J V McMurray, Kazem Rahimi

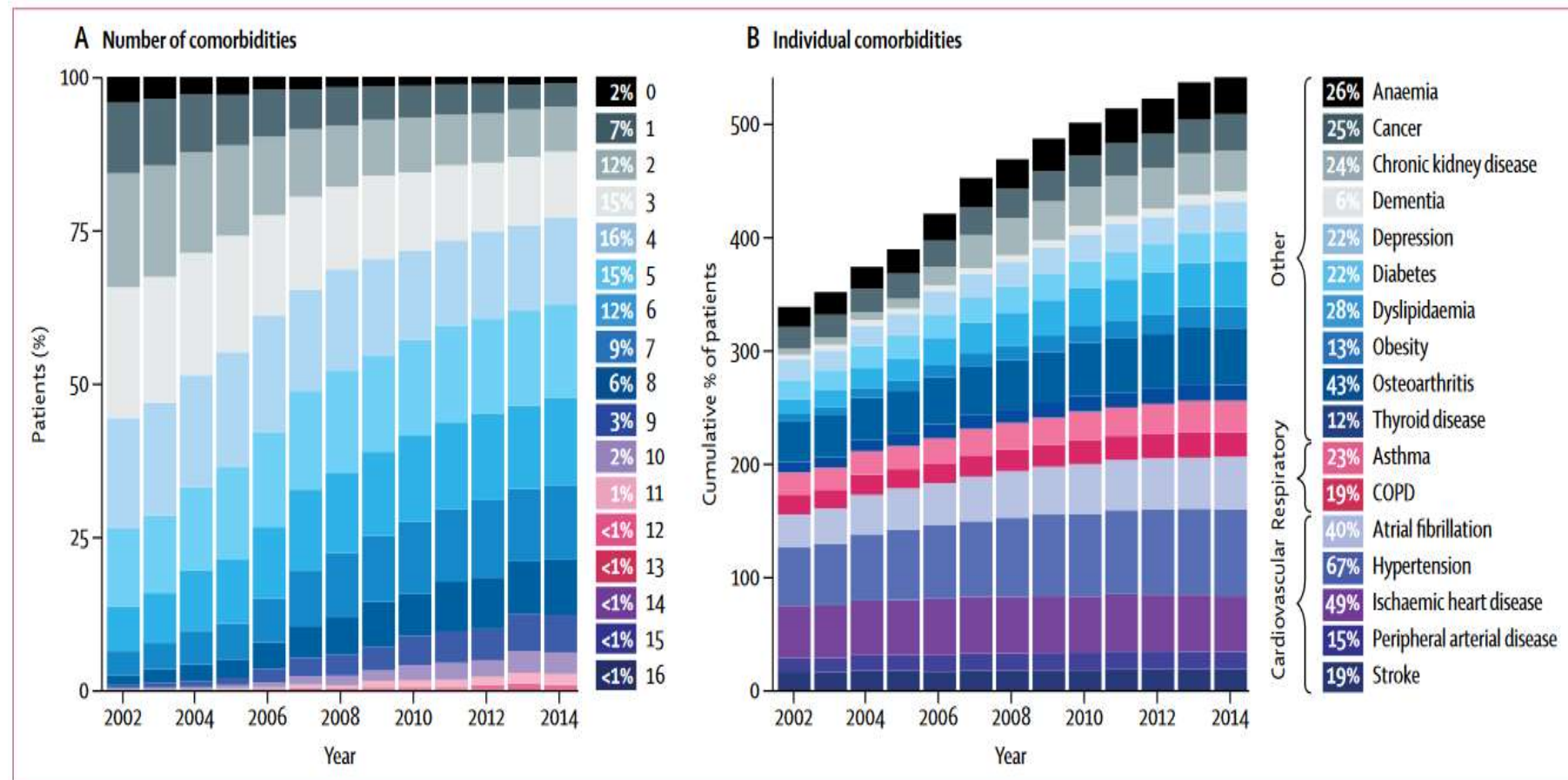
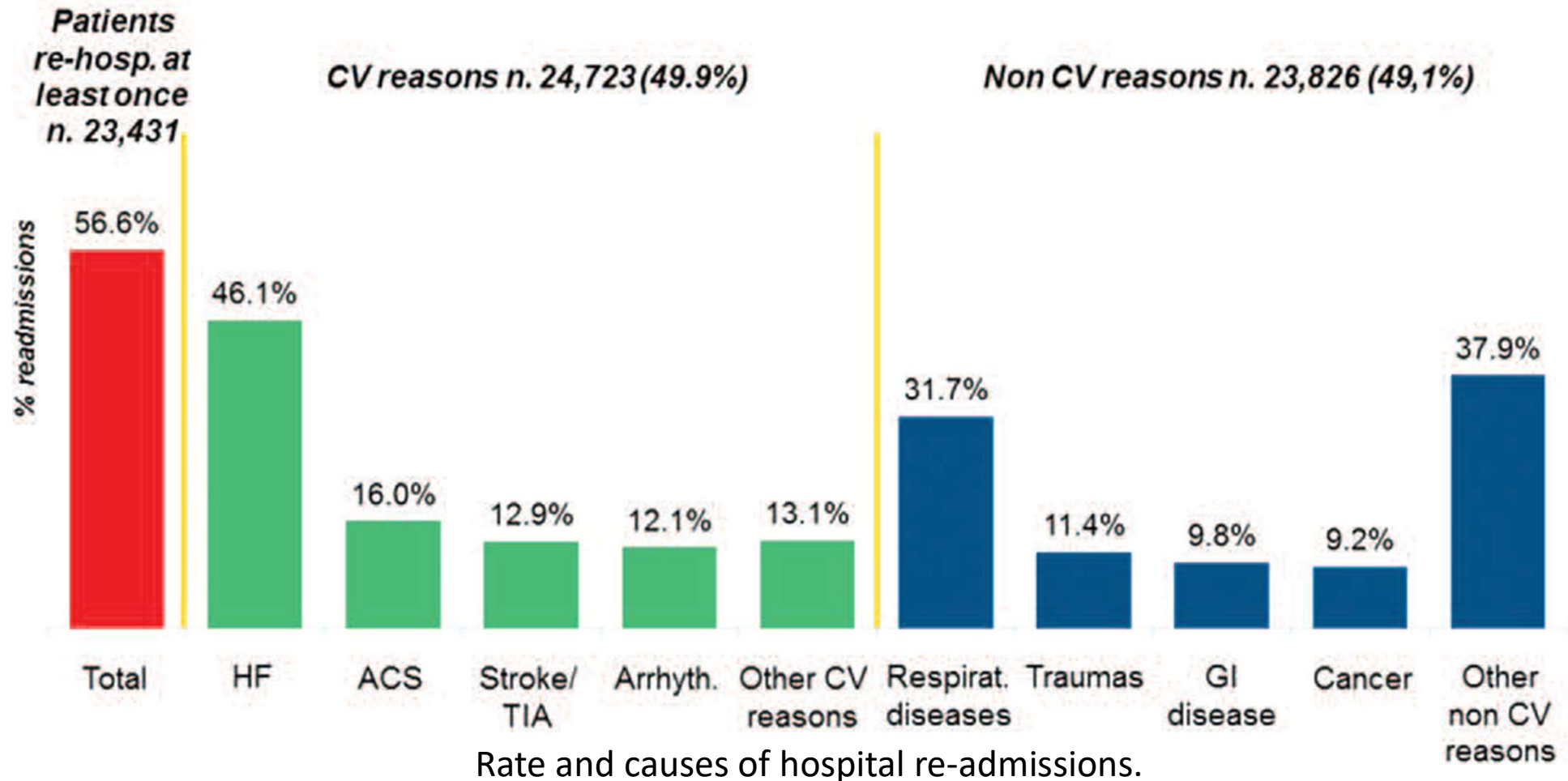


Figure 2: Temporal trends in comorbidities among patients diagnosed with incident heart failure, from 2002 to 2014

The real-world evidence of heart failure: findings from 41 413 patients of the ARNO database



Total number of readmissions = 48,548
(2.1 per patient)



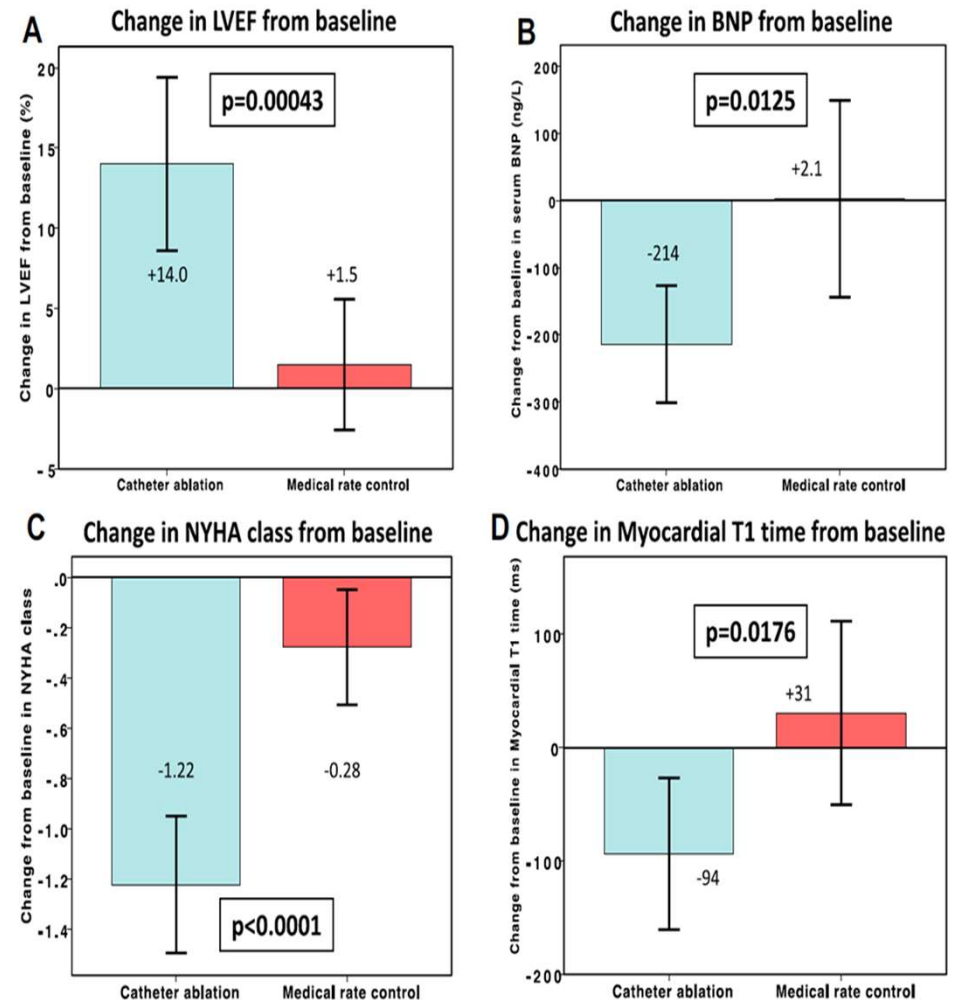
Regression of Diffuse Ventricular Fibrosis Following Restoration of Sinus Rhythm With Catheter Ablation in Patients With Atrial Fibrillation and Systolic Dysfunction

A Substudy of the CAMERA MRI Trial

Sandeep Prabhu, MBBS,^{a,b,c,d,*} Ben T. Costello, MBBS,^{a,b,*} Andrew J. Taylor, MBBS, PhD,^{a,b,e} Sarah J. Gutman, MBBS,^{a,b} Aleksandr Voskoboinik, MBBS,^{a,b,c,d} Alex J.A. McLellan, MBBS, PhD,^{a,b,c,d} Kah Y. Peck, MBBS,^a Hariharan Sugumar, MBBS,^{a,b,c,d} Leah Iles, MBBS, PhD,^{a,b,e} Bhupesh Pathik, MBBS,^{c,d} Chrishan J. Nalliah, MBBS,^{c,d} Geoff R. Wong, MBBS,^{c,d} Sonia M. Azzopardi, CC Bc RN,^{a,b} Geoffrey Lee, MChB, PhD,^c Justin Mariani, MBBS, PhD,^{a,b,e} David M. Kaye, MBBS, PhD,^{a,b,e} Liang-Han Ling, MBBS, PhD,^{a,b,d} Jonathan M. Kalman, MBBS, PhD,^{c,d} Peter M. Kistler, MBBS, PhD,^{a,b,d}

FIGURE 1 Comparison of 6-Month Outcomes by Treatment Arm

Ventricular remodeling and diffuse fibrosis – Comparison between treatment arms



Catheter ablation was associated with (A) a significant improvement in LVEF, (B) a reduction in serum BNP, and (C) a reduction in NYHA functional class. (D) This was accompanied by a reduction in myocardial T1 times consistent with a regression of diffuse fibrosis. Bars represent 95% confidence intervals. BNP = brain natriuretic peptide; LVEF = left ventricular ejection fraction; NYHA = New York Heart Association.

Prabhu *et al.*

Regression of Fibrosis in AF and Systolic Dysfunction

JACC: CLINICAL ELECTROPHYSIOLOGY VOL. 4, NO. 8, 2018

AUGUST 2018:999-1007

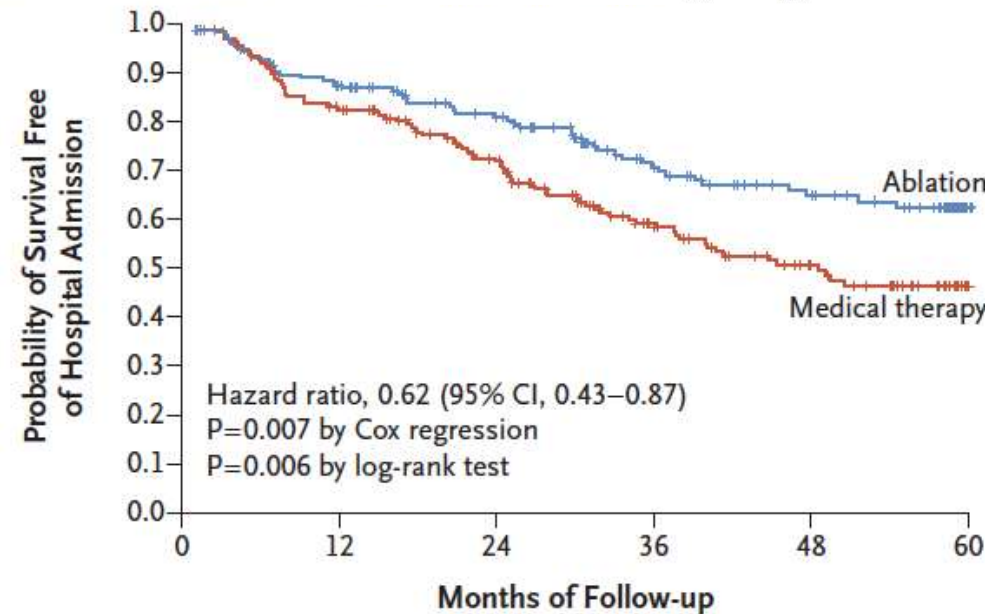
Catheter Ablation for Atrial Fibrillation with Heart Failure

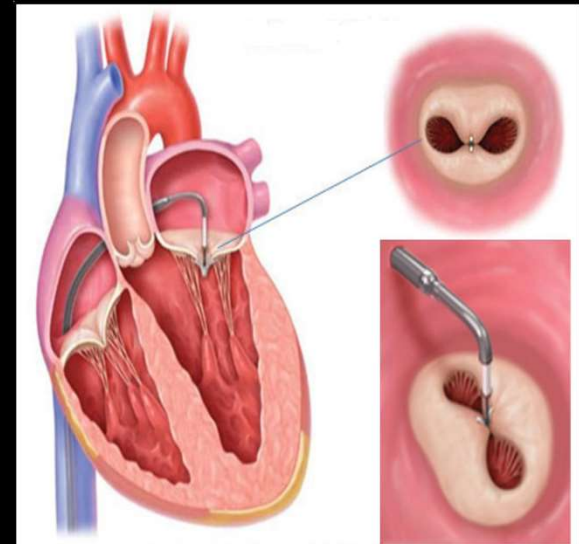
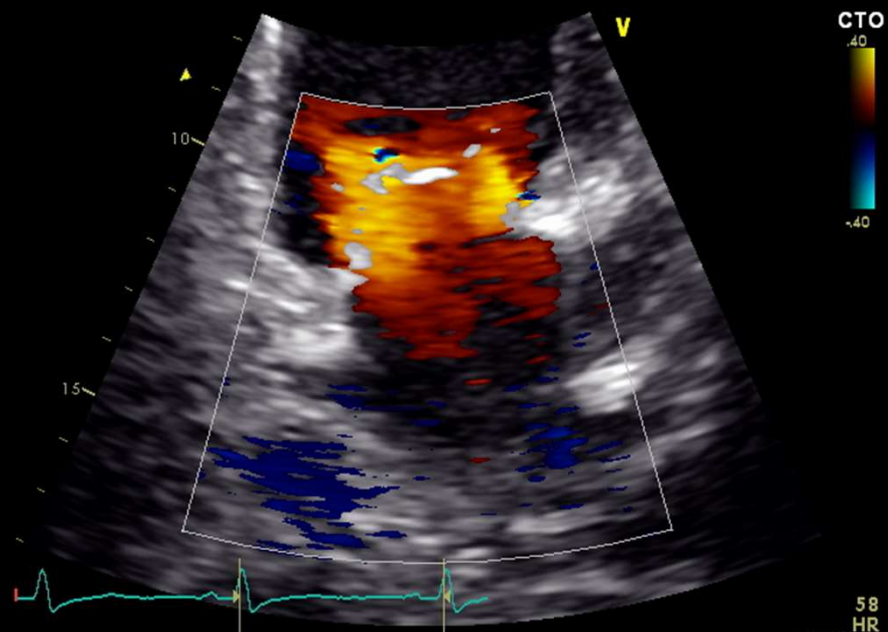
Nassir F. Marrouche, M.D., Johannes Brachmann, M.D., Dietrich Andresen, M.D., Jürgen Siebels, M.D., Lucas Boersma, M.D., Luc Jordaens, M.D., Béla Merkely, M.D., Evgeny Pokushalov, M.D., Prashanthan Sanders, M.D., Jochen Proff, B.S., Heribert Schunkert, M.D., Hildegard Christ, M.D., Jürgen Vogt, M.D., and Dietmar Bänsch, M.D., for the CASTLE-AF Investigators*

Subgroup	Ablation no. of events/no. of patients	Medical Therapy no. of events/no. of patients	Hazard Ratio (95% CI)	P Value Interact
Type of atrial fibrillation				0.90
Paroxysmal	17/54	34/64	0.60 (0.34–1.08)	
Persistent	34/125	48/120	0.64 (0.41–0.99)	
CRT-D implanted				0.60
No	37/131	57/132	0.65 (0.43–0.98)	
Yes	14/48	25/52	0.54 (0.28–1.04)	
ICD indication				0.20
Primary	43/160	72/163	0.57 (0.39–0.83)	
Secondary	8/19	10/21	1.03 (0.41–2.62)	
Sex				0.36
Female	9/23	12/29	0.93 (0.39–2.21)	
Male	42/156	70/155	0.58 (0.39–0.84)	
Age				0.17
<65 yr	18/96	34/99	0.48 (0.27–0.85)	
≥65 yr	33/83	48/85	0.79 (0.50–1.23)	
NYHA functional class				0.06
II	20/101	46/109	0.42 (0.25–0.72)	
III	22/50	26/49	0.89 (0.51–1.58)	
LVEF				0.01
<25%	20/34	15/27	1.36 (0.69–2.65)	
≥25%	29/130	61/145	0.48 (0.31–0.74)	
Cause of heart failure				0.56
Nonischemic	26/107	29/88	0.74 (0.43–1.25)	
Ischemic	25/72	53/96	0.60 (0.37–0.97)	
Diabetes				0.06
No	32/136	48/117	0.52 (0.33–0.81)	
Yes	19/43	34/67	1.01 (0.58–1.78)	
Hypertension				0.88
No	12/50	19/48	0.59 (0.28–1.21)	
Yes	39/129	63/136	0.63 (0.42–0.93)	
Amiodarone use				0.66
No	37/122	61/133	0.65 (0.43–0.97)	
Yes	13/55	18/46	0.55 (0.27–1.13)	
Digitalis use				0.68
No	41/146	52/124	0.65 (0.43–0.98)	
Yes	9/31	27/56	0.56 (0.26–1.19)	
Beta-blocker use				0.47
No	4/12	4/9	1.01 (0.25–4.05)	
Yes	46/165	75/171	0.60 (0.42–0.87)	

Characteristic	Treatment Type	
	Ablation (N=179)	Medical Therapy (N=184)
Age — yr		
Median	64	64
Range	56–71	56–73.5
Male sex — no. (%)	156 (87)	155 (84)
Body-mass index†		
Median	29.0	29.1
Range	25.9–32.2	25.9–32.3
New York Heart Association class — no./total no. (%)		
I	20/174 (11)	19/179 (11)
II	101/174 (58)	109/179 (61)
III	50/174 (29)	49/179 (27)
IV	3/174 (2)	2/179 (1)
Cause of heart failure — no. (%)‡		
Ischemic	72 (40)	96 (52)
Nonischemic	107 (60)	88 (48)
Type of atrial fibrillation — no. (%)		
Paroxysmal	54 (30)	64 (35)
Persistent	125 (70)	120 (65)
Long-standing persistent (duration >1 year)	51 (28)	55 (30)
Left atrial diameter		
Total no. of patients evaluated	162	172
Median — mm	48.0	49.5
Interquartile range — mm	45.0–54.0	5.0–55.0
Left ventricular ejection fraction		
Total no. of patients evaluated	164	172
Median — %	32.5	31.5
Interquartile range — %	25.0–38.0	27.0–37.0
CRT-D implanted — no. (%)§	48 (27)	52 (28)
ICD implanted — no. (%)§	131 (73)	132 (72)
Dual-chamber	128 (72)	123 (67)
Single-lead device with “floating” atrial sensing dipole	3 (2)	9 (5)
Indication for ICD implantation — no. (%)		
Primary prevention	160 (89)	163 (89)
Secondary prevention	19 (11)	21 (11)
History of amiodarone use — no./total no. (%)¶		
Failure	78/175 (45)	82/176 (47)
Unacceptable side effects	21/175 (12)	24/176 (14)
Nonuse	76/175 (43)	70/176 (40)

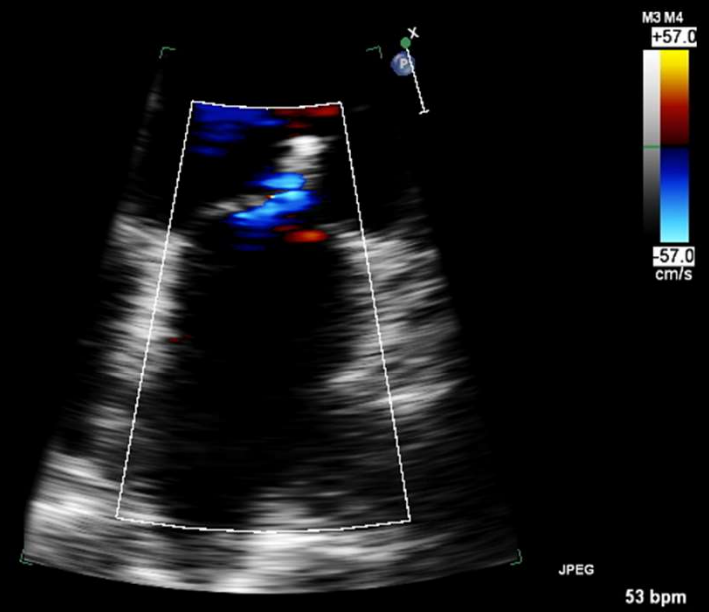
Death or Hospitalization





2D
67%
C 52
P Bassa
APen

CF
70%
2.5MHz
WF Alto



Key Inclusion Criteria

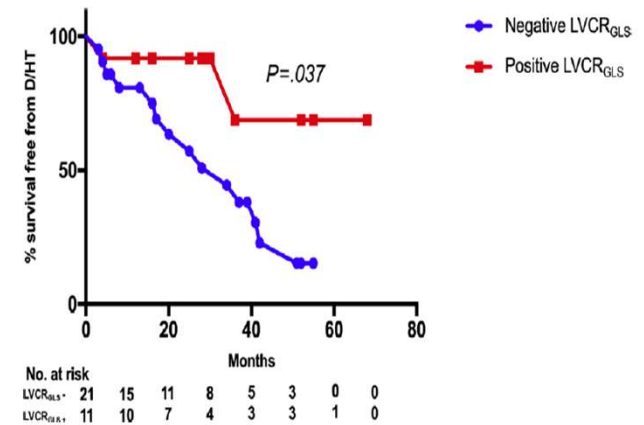
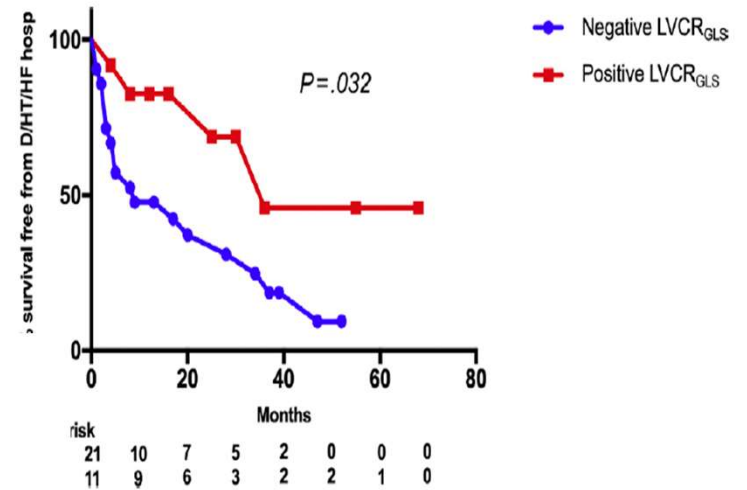
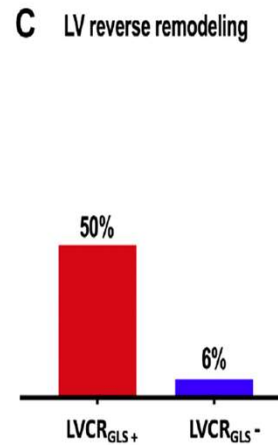
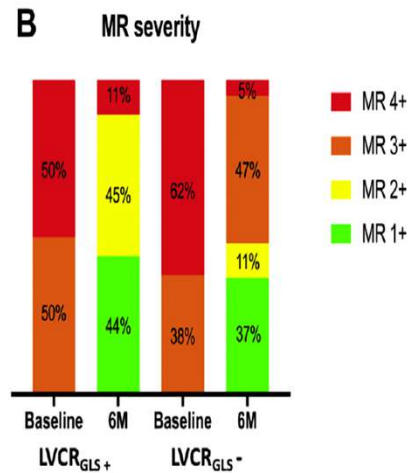
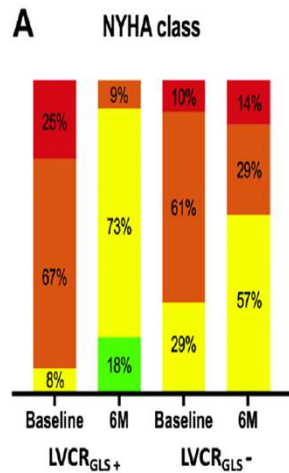
1. Ischemic or non-ischemic cardiomyopathy with LVEF 20%-50% and LVESD \leq 70 mm
2. Moderate-to-severe (3+) or severe (4+) secondary MR confirmed by an independent echo core laboratory prior to enrollment (US ASE criteria)
3. NYHA functional class II-IVa (ambulatory) despite a stable maximally-tolerated GDMT regimen and CRT (if appropriate) per societal guidelines
4. Pt has had at least one HF hospitalization within 12 months and/or a BNP \geq 300 pg/ml* or a NT-proBNP \geq 1500 pg/ml*
5. Not appropriate for mitral valve surgery by local heart team assessment
6. IC believes secondary MR can be successfully treated by the MitraClip

Key Exclusion Criteria

1. ACC/AHA stage D HF, hemodynamic instability or cardiogenic shock
2. Untreated clinically significant CAD requiring revascularization
3. COPD requiring continuous home oxygen or chronic oral steroid use
4. Severe pulmonary hypertension or moderate or severe right ventricular dysfunction
5. Aortic or tricuspid valve disease requiring surgery or transcatheter intervention
6. Mitral valve orifice area $<4.0 \text{ cm}^2$ by site-assessed TTE
7. Life expectancy <12 months due to non-cardiac conditions

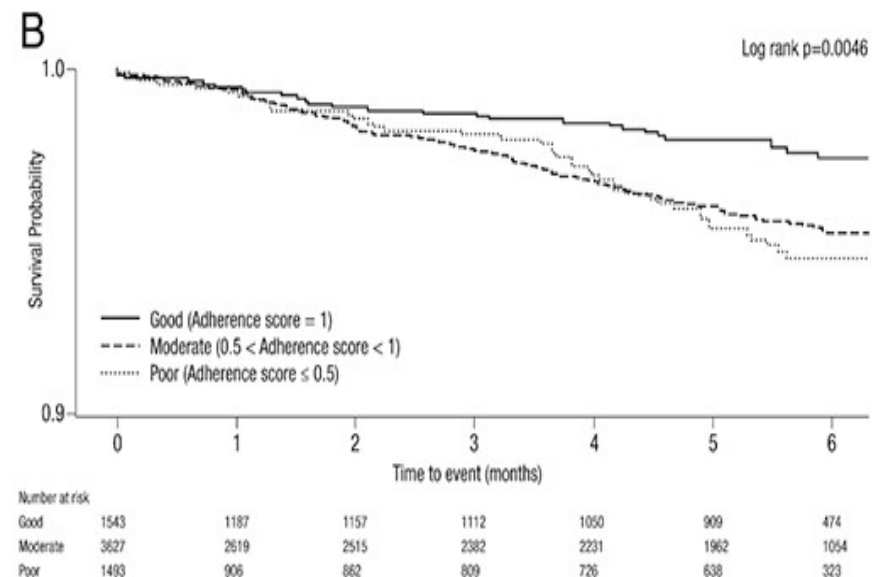
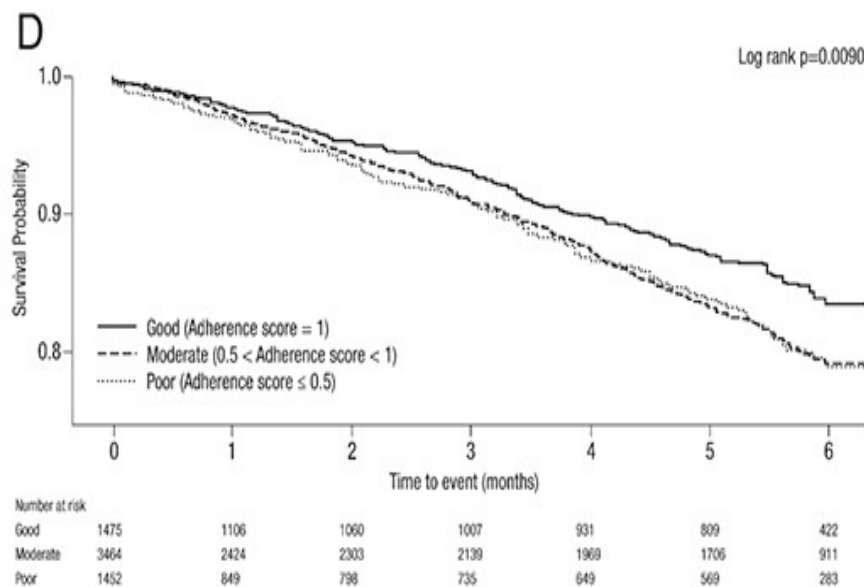
Prognostic Value of Global Longitudinal Strain-Based Left Ventricular Contractile Reserve in Candidates for Percutaneous Correction of Functional Mitral Regurgitation: Implications for Patient Selection

Antonio De Luca, MD, Davide Stolfo, MD, Thomas Caiffa, MD, Renata Korcova, MD, PhD, Giulia Barbati, PhD, Giancarlo Vitrella, MD, Serena Rakar, MD, Andrea Perkan, MD, Gabriele Secoli, MD, Bruno Pinamonti, MD, Marco Merlo, MD, and Gianfranco Sinagra, MD, FESC, Trieste, Italy



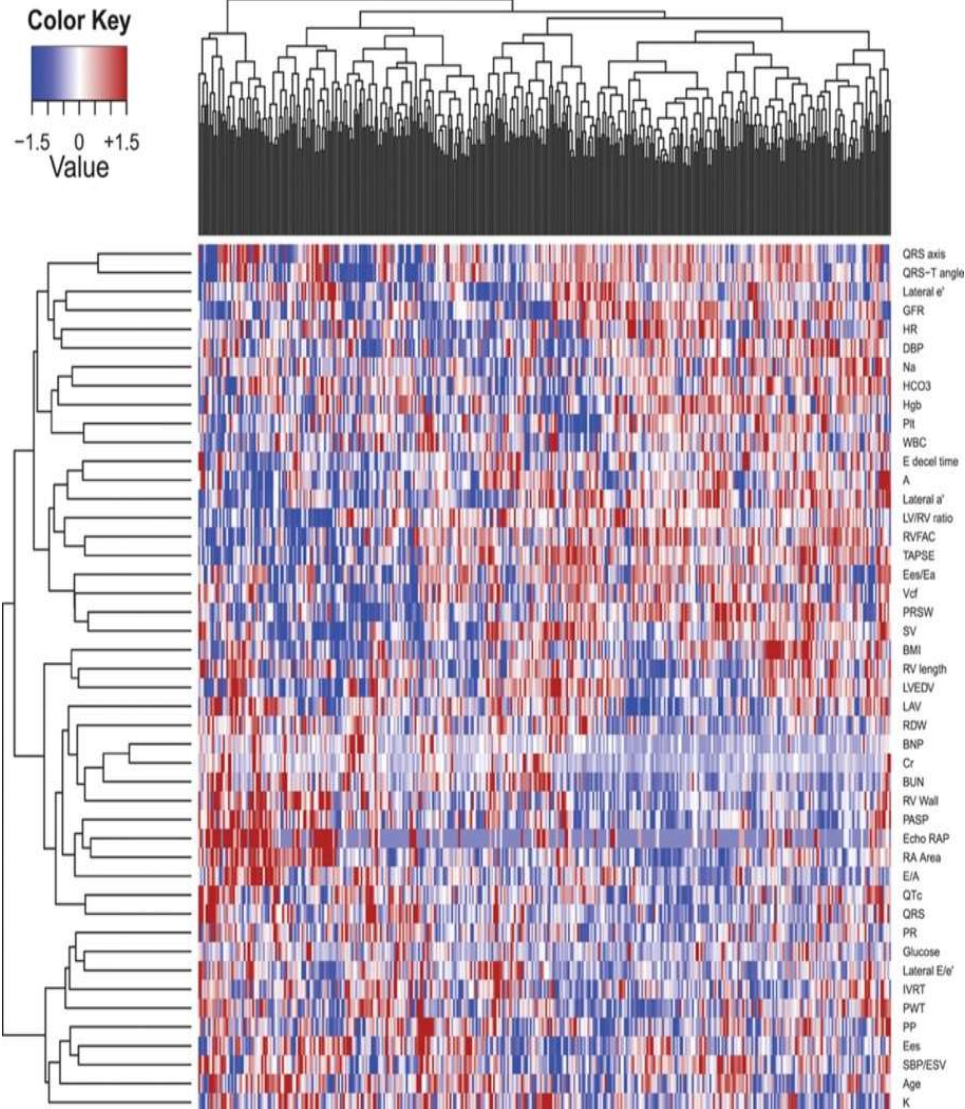
Physicians' guideline adherence is associated with better prognosis in outpatients with HFrEF: the QUALIFY international registry

Cardiovascular (CV) mortality CV hospitalization or CV death



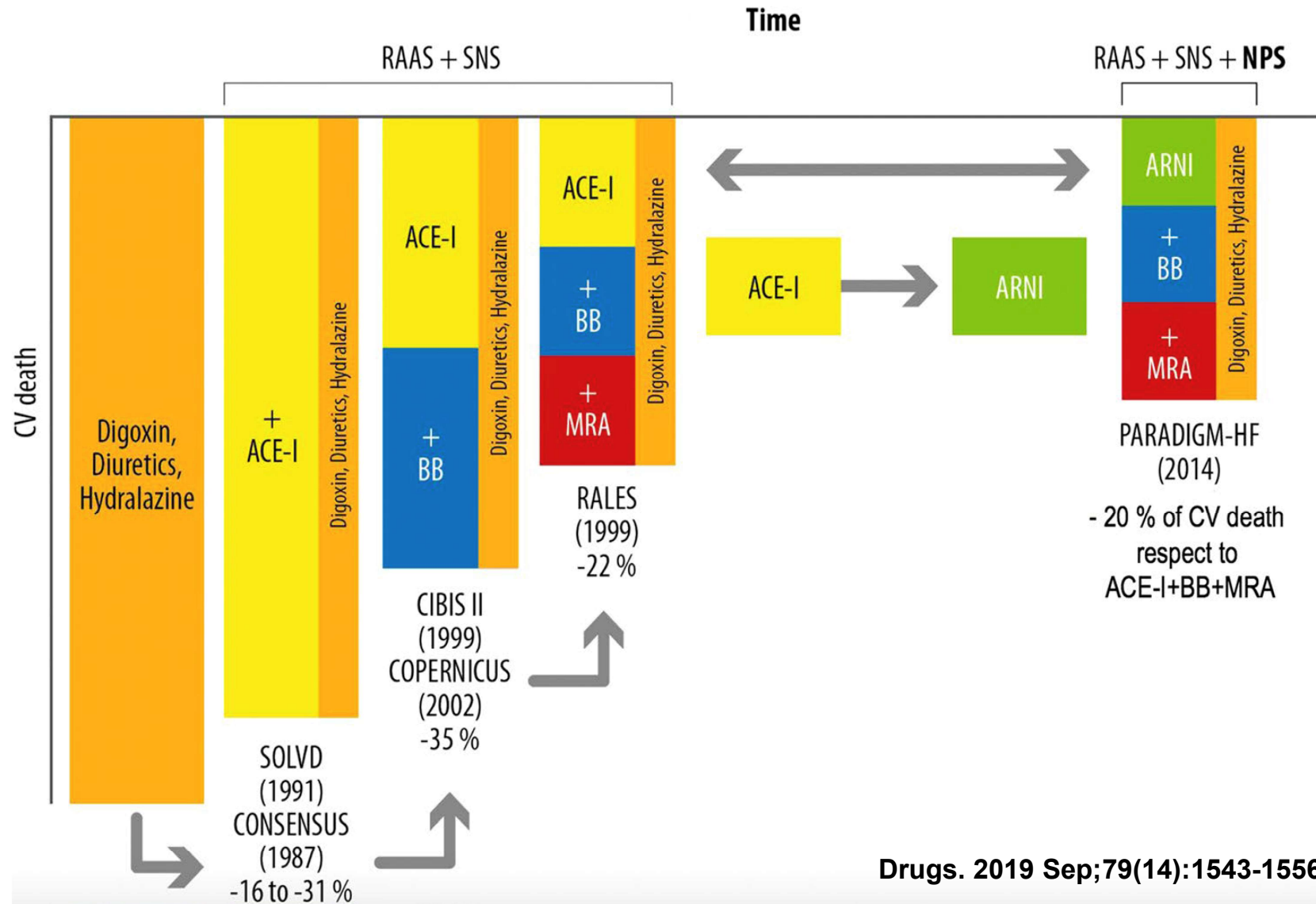
Phenomapping for Novel Classification of Heart Failure With Preserved Ejection Fraction

Sanjiv J. Shah, Daniel H. Katz, Senthil Selvaraj, Michael A. Burke, Clyde W. Yancy, Mihai Gheorghiu, Robert O. Bonow, Chiang-Ching Huang, Rahul C. Deo



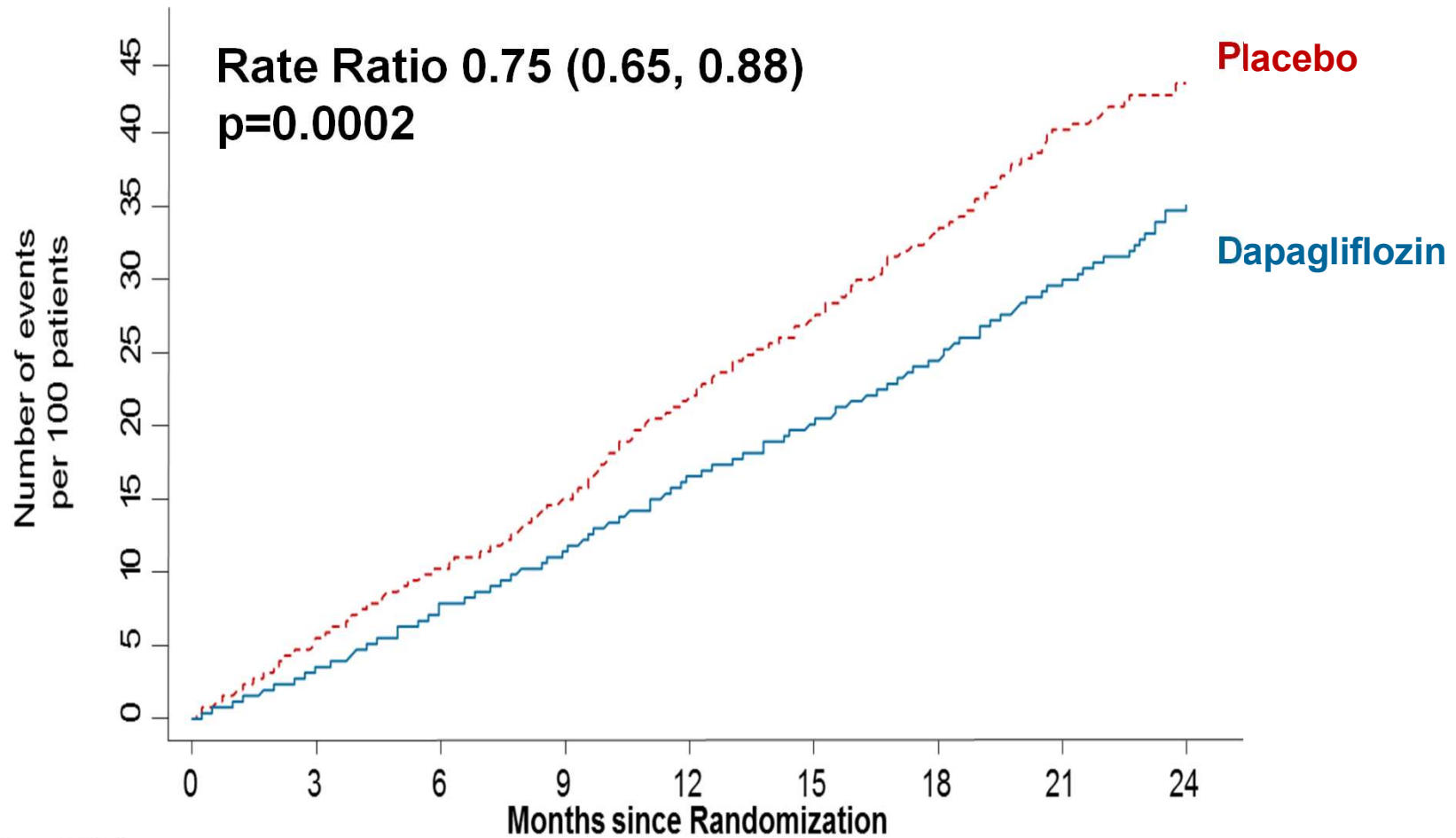
Sacubitril/Valsartan: Updates and Clinical Evidence for a Disease-Modifying Approach

Enrico Fabris¹  · Marco Merlo¹ · Claudio Rapezzi² · Roberto Ferrari^{3,4} · Marco Metra⁵ · Maria Frigerio⁶ · Gianfranco Sinagra¹



Total HF hospitalizations and CV death

Including first and repeat hospitalizations

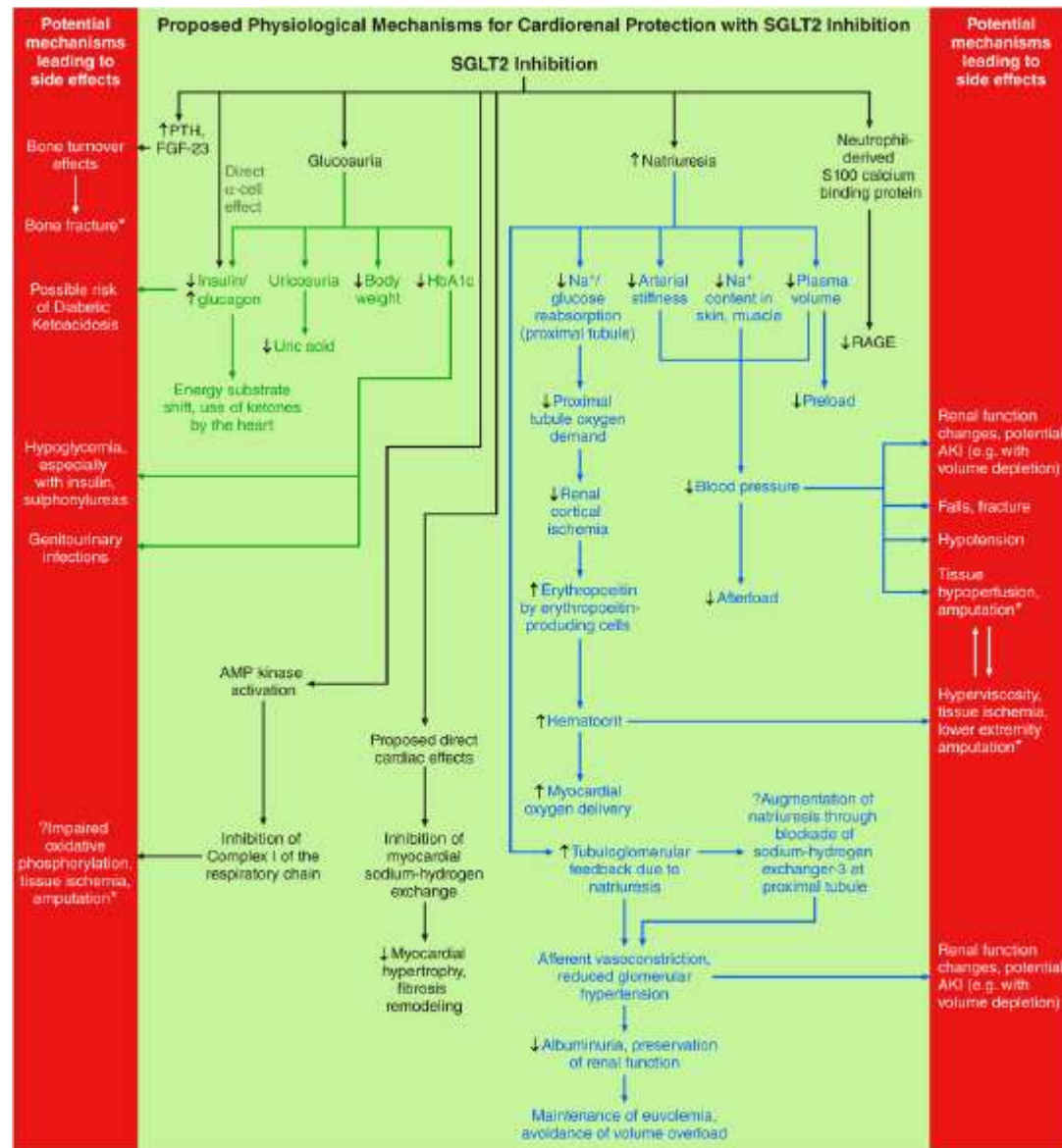


Number at Risk	0	3	6	9	12	15	18	21	24
Dapagliflozin	2373	2339	2293	2248	2127	1664	1242	671	232
Placebo	2371	2330	2279	2230	2091	1636	1219	664	234

Sodium Glucose Cotransporter-2 Inhibition in Heart Failure

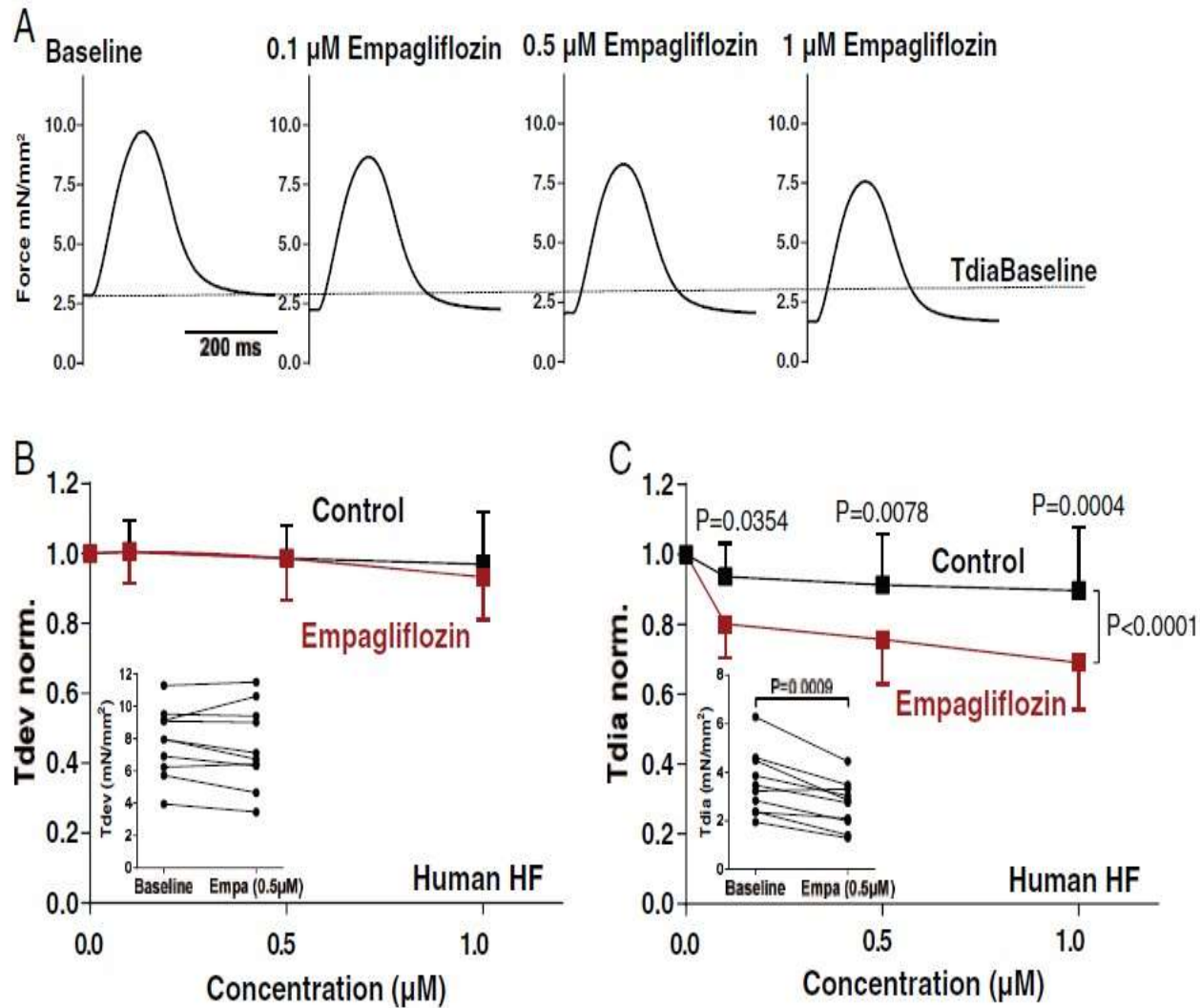
Potential Mechanisms, Clinical Applications, and Summary of Clinical Trials

Yuliya Lytvyn, PhD*
 Petter Bjornstad, MD*
 Jacob A. Udell, MD, MPH
 Julie A. Lovshin, MD, PhD
 David Z.I. Cherney, MD, PhD



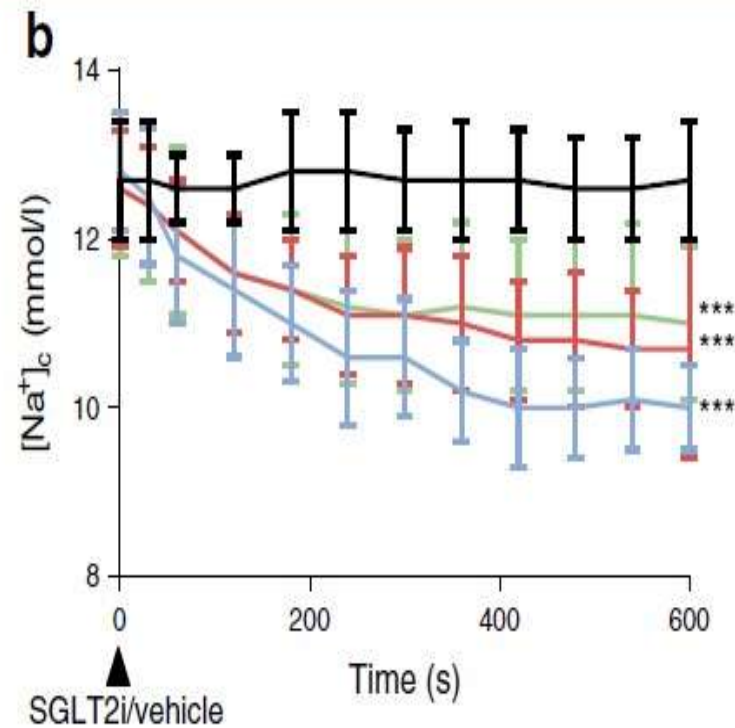
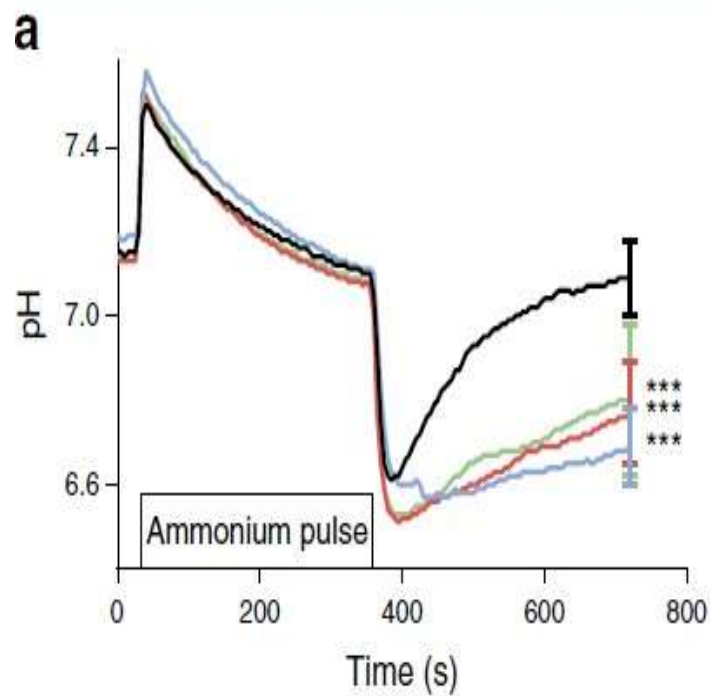
Cardiovascular, heart failure and renal benefits

Empagliflozin reduces diastolic tension in human HF



SGLT2-I Class effect:

EMPA, CANA and DAPA inhibit NHE activity and reduce $[Na^+]_c$



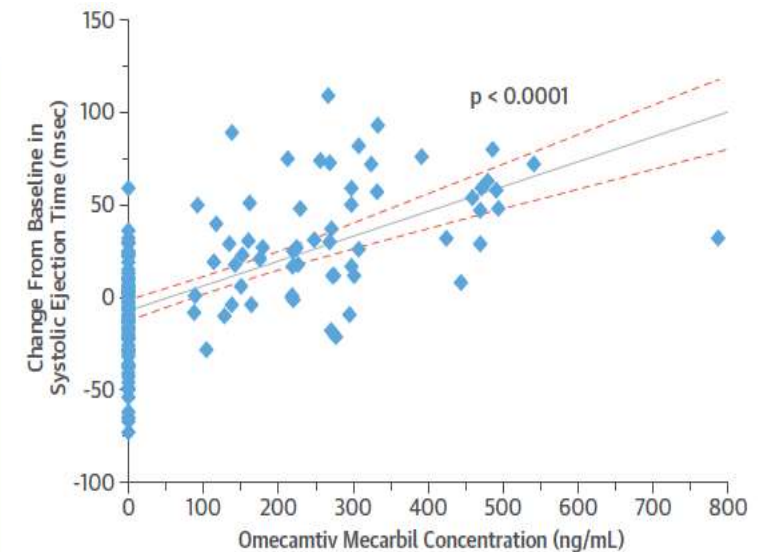
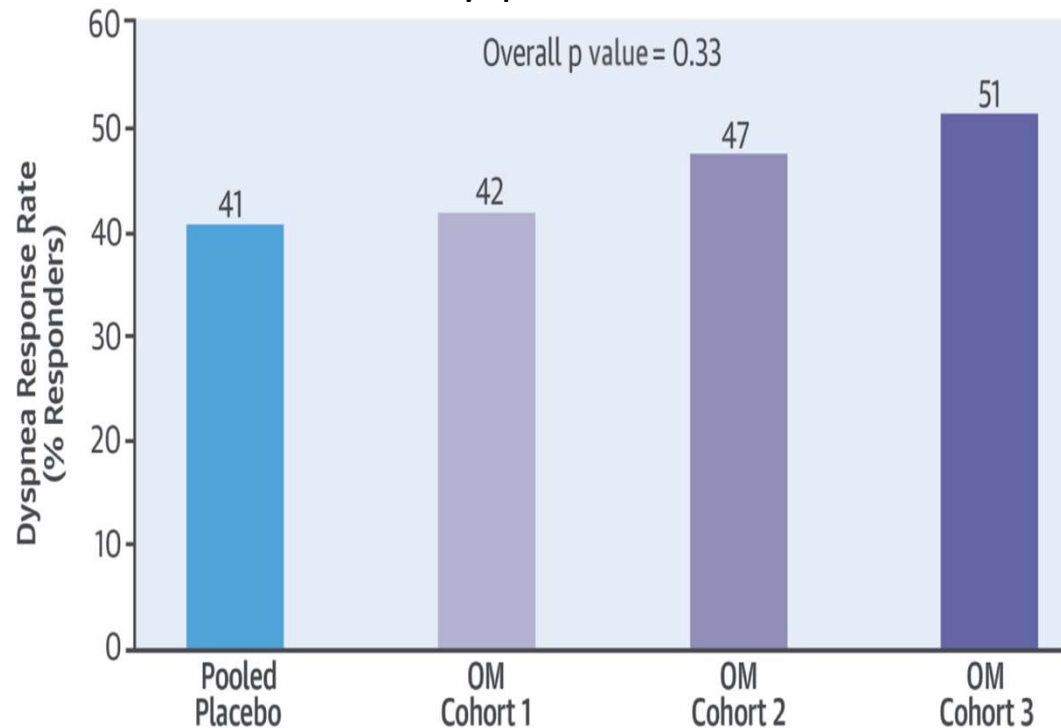
*Uthman et al., Diabetologia
2018; 61:722–726*

Acute Treatment With Omecamtiv Mecarbil to Increase Contractility in Acute Heart Failure



Prospective, phase II, randomized, double-blind, placebo-controlled, dose-escalation, sequential-cohort trial comparing OM (n=303) with placebo (n=303) in patients with AHF

Effect of OM on Dyspnea in Acute Heart Failure

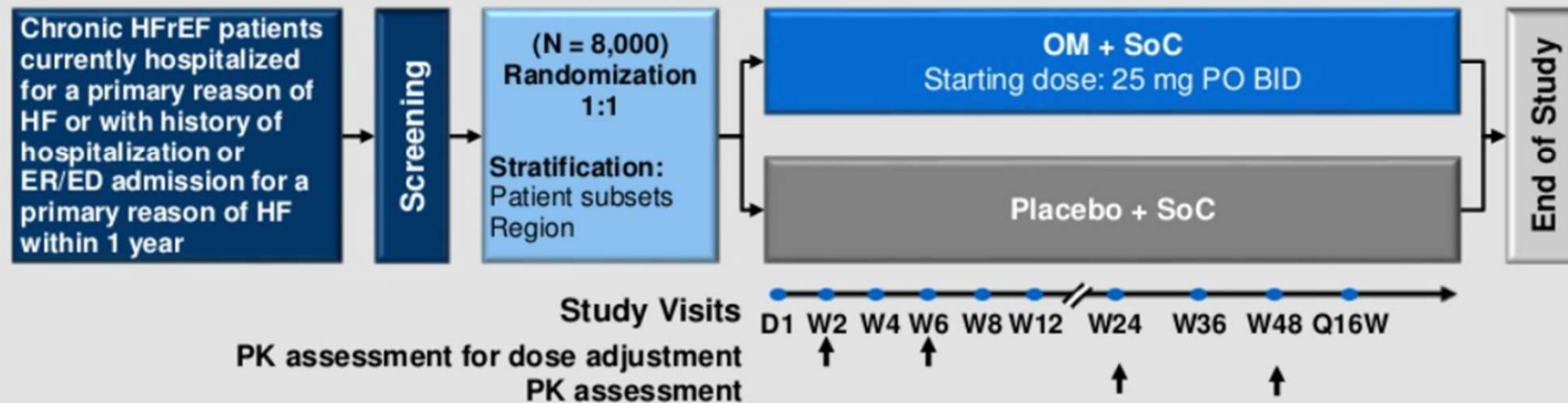


Systolic ejection time increased as corresponding plasma omecamtiv level rose in 89 pts from the echocardiographic study.

In patients with AHF, IV OM did not meet the primary endpoint of dyspnea improvement, but it was generally well tolerated, it increased Systolic Ejection Time, and it may have improved dyspnea in the high-dose group



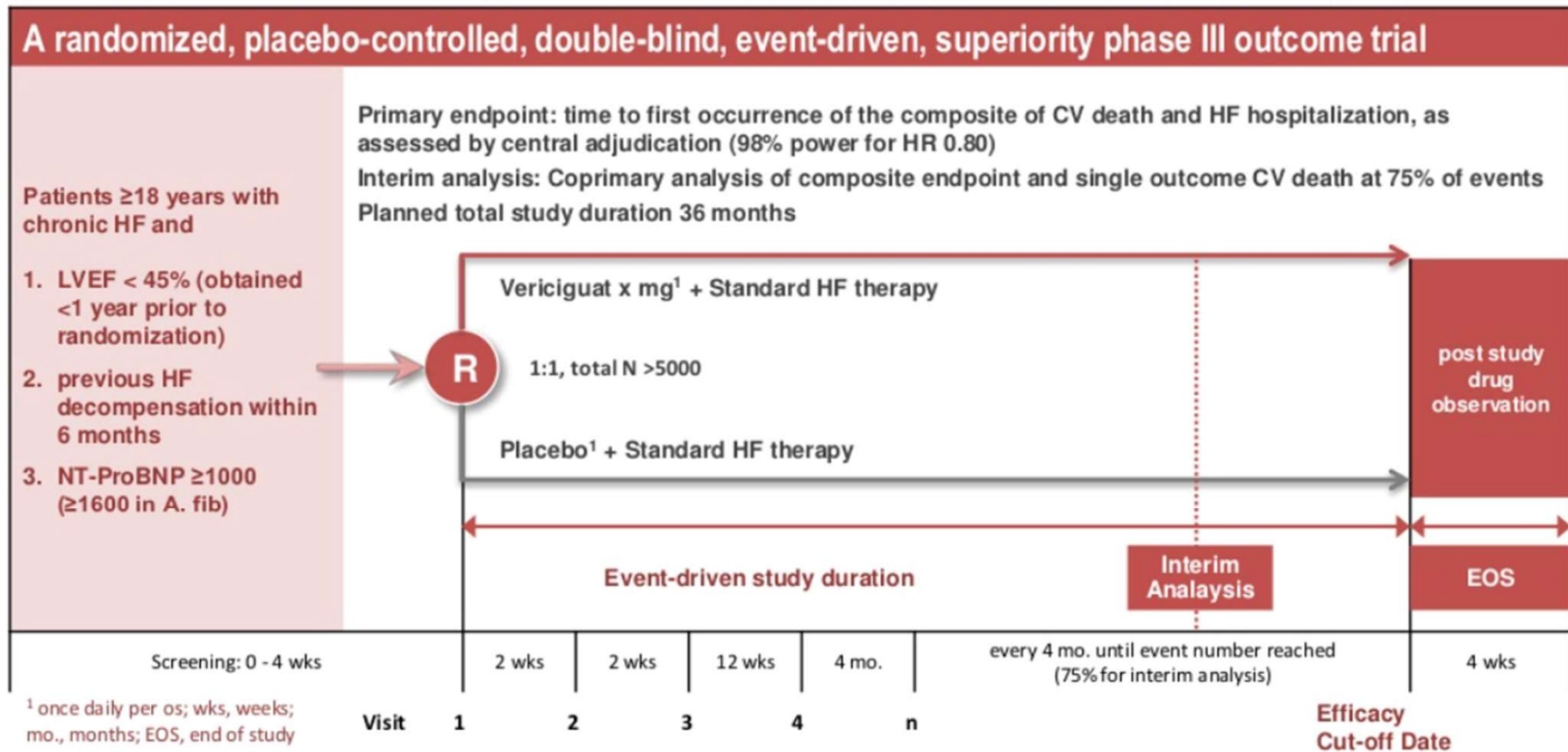
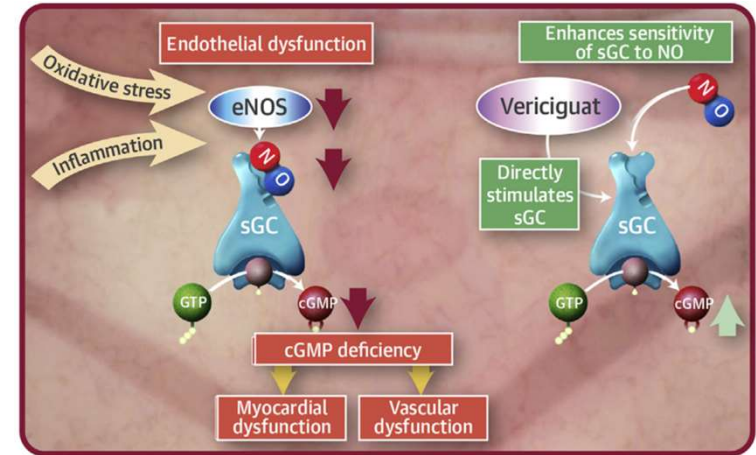
STUDY DESIGN AND TREATMENT SCHEMA



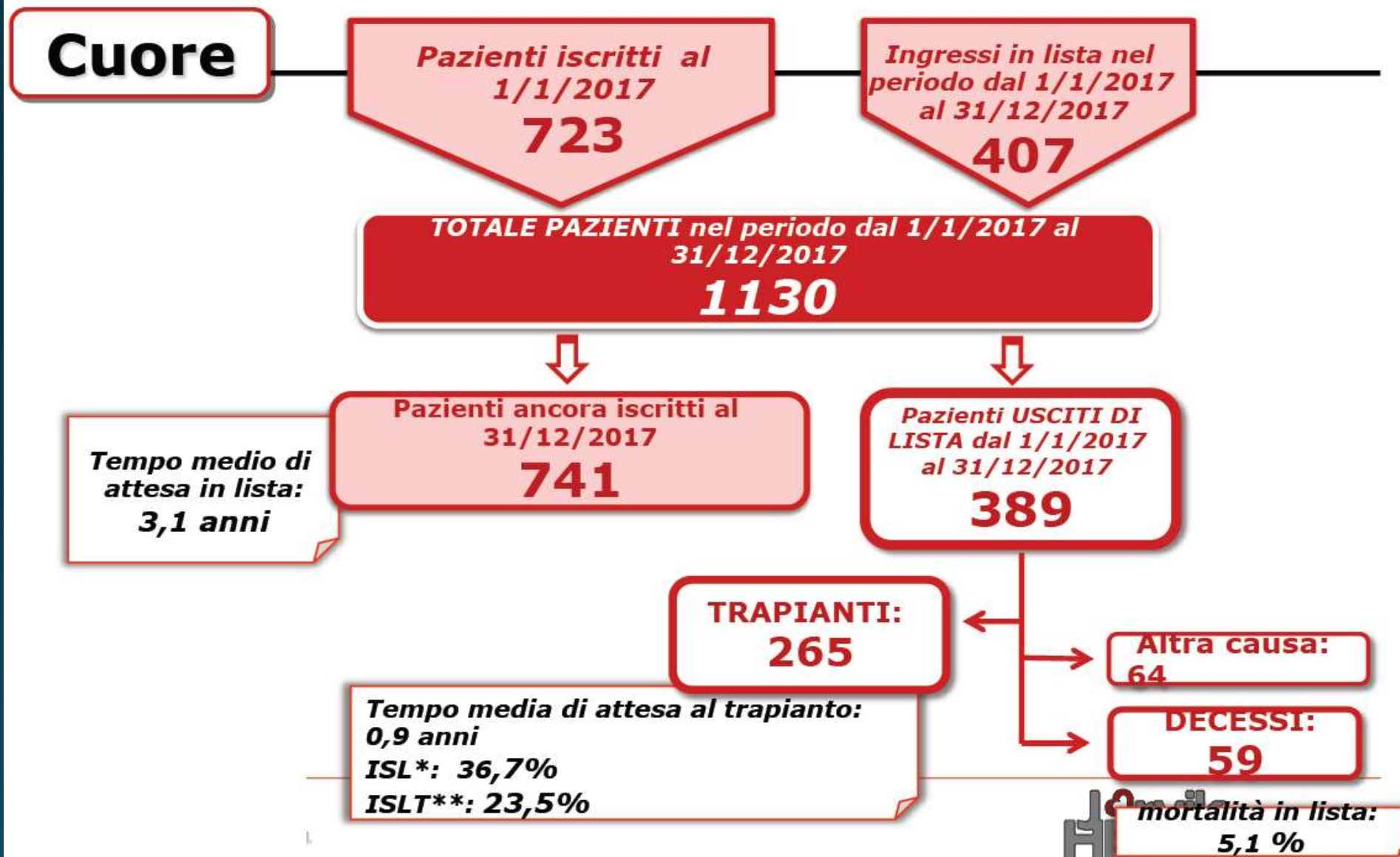
- Randomized, double-blind, placebo-controlled, parallel-group, multicenter, CV outcomes study for oral OM in subjects with HFrEF
 - Approximately 25% or more of the total planned enrollment will include subjects who are hospitalized at randomization
 - Enrollment of subjects with atrial fibrillation will be limited to 20% of each enrollment setting

A Multicenter, Randomized, Double-Blind, Placebo-Controlled Trial of the Efficacy and Safety of the Oral Soluble Guanylate Cyclase Stimulator

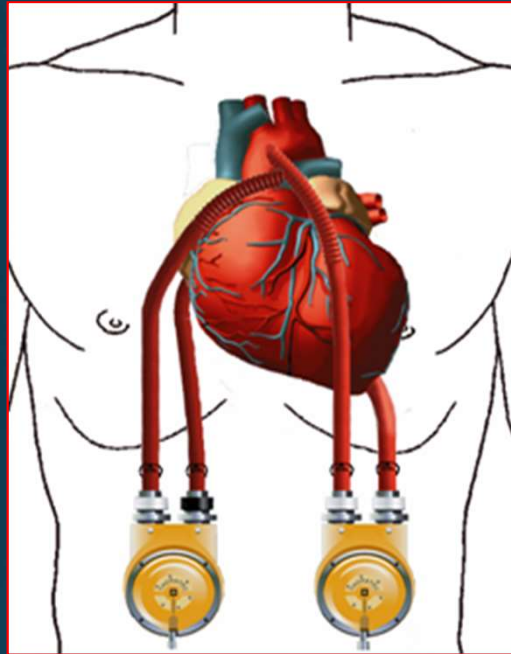
The VICTORIA Trial



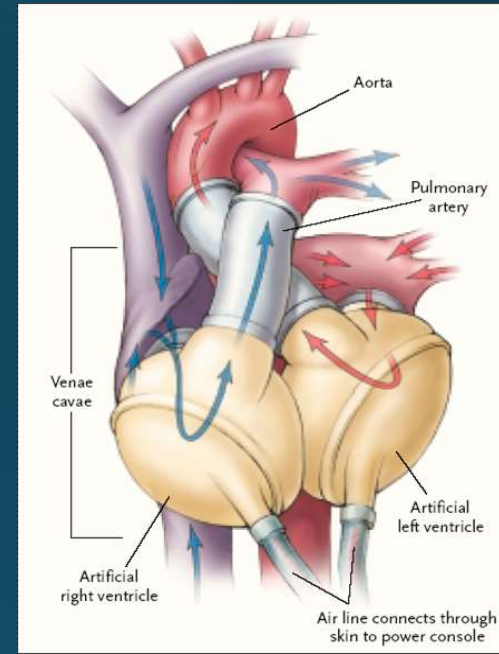
Flussi Lista di attesa 1/1/2017 - 31/12/2017



Overview of Long-term MCS

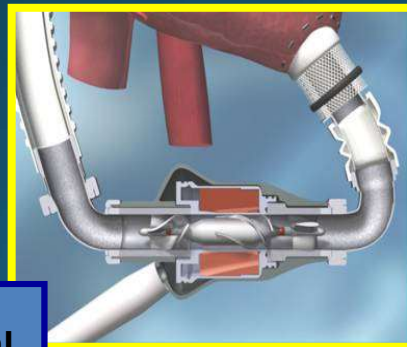


Pulsatile



Axial

Jarvic 2000

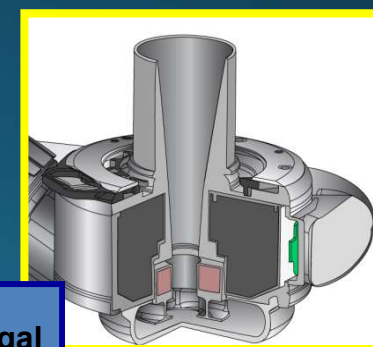


HeartMate II



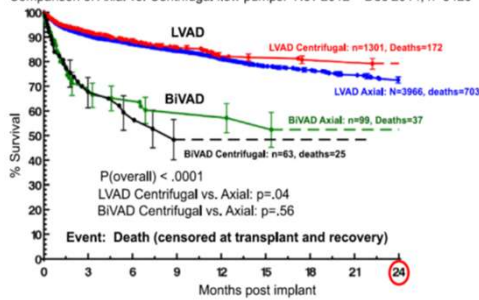
Centrifugal

HeartWare



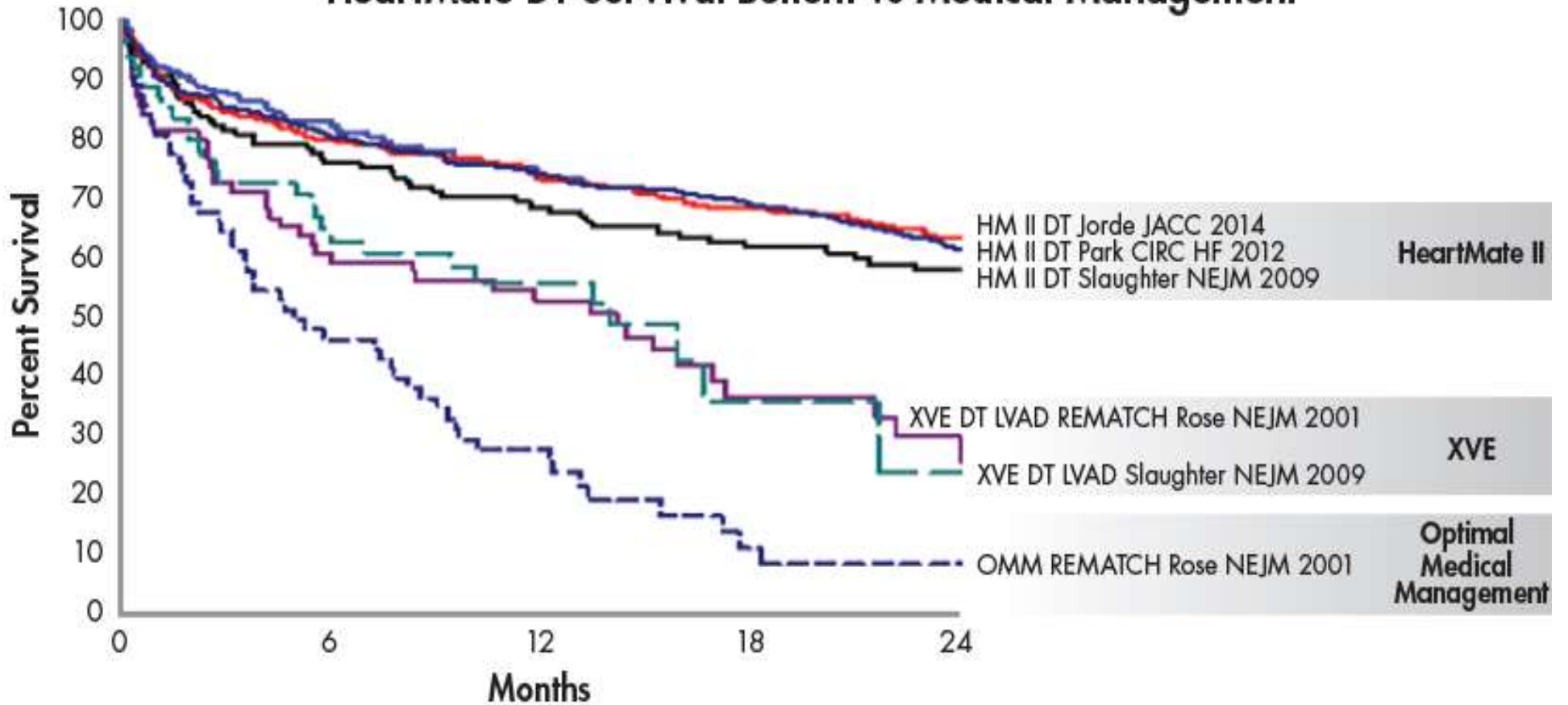
HeartMate III

Comparison of Axial vs. Centrifugal flow pumps: Nov 2012 – Dec 2014, n=5429



1

HeartMate DT Survival Benefit vs Medical Management



1. Jorde UP, Khushwaha SS, Tatoes AJ, et al. Two-Year Outcomes in the Destination Therapy Post-FDA-Approval Study with a Continuous Flow Left Ventricular Assist Device: A Prospective Study Using the INTERMACS Registry. Presented at the ISHLT annual meeting, April 25, 2013.

Proprietary and confidential — do not distribute

2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure

ESC GUIDELINES



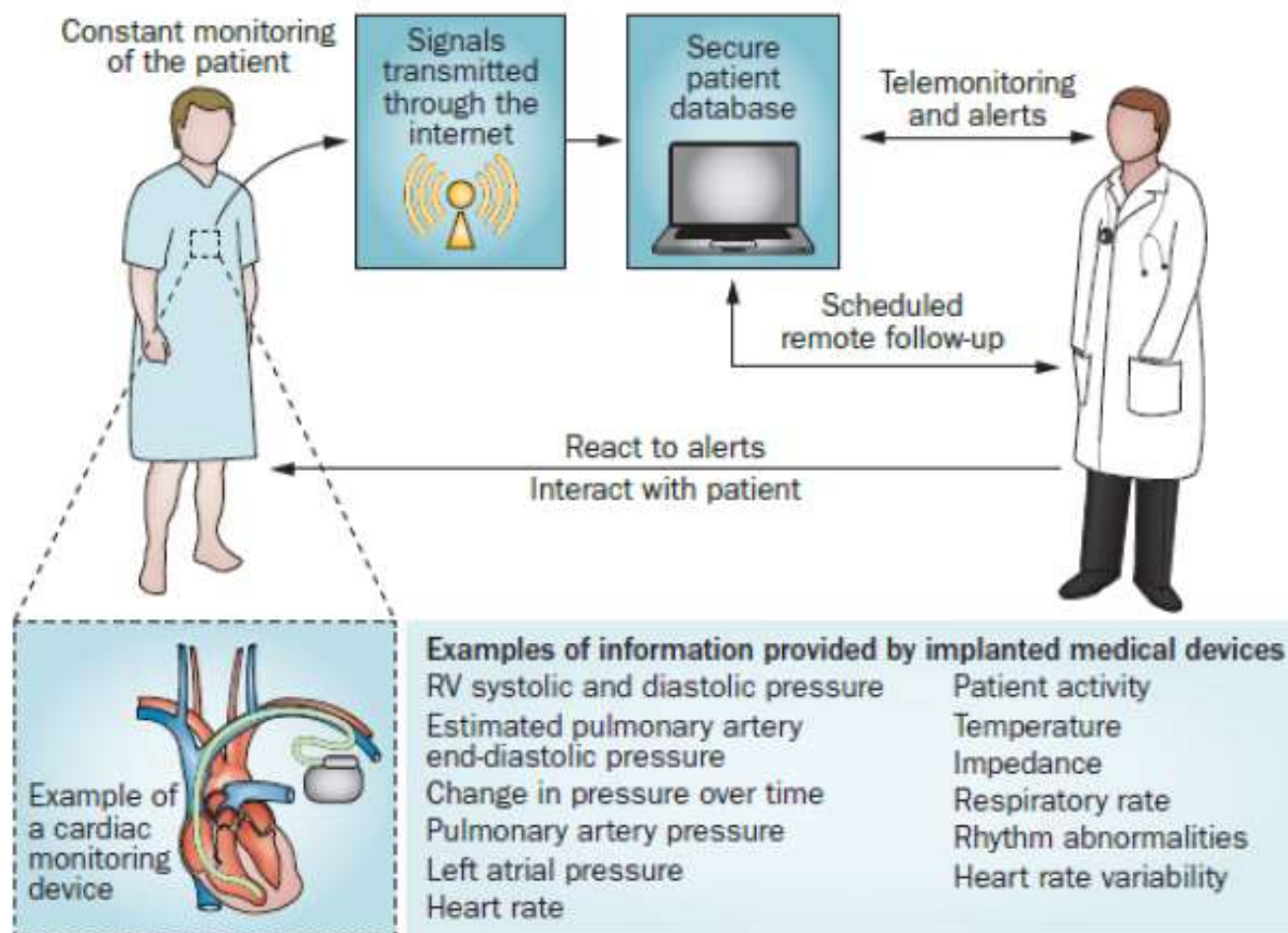
Candidates to LVAD

Patients with >2 months of severe symptoms despite optimal medical and device therapy and more than one of the following:
LVEF <25% and, if measured, peak VO ₂ <12 mL/kg/min.
≥3 HF hospitalizations in previous 12 months without an obvious precipitating cause.
Dependence on i.v. inotropic therapy.
Progressive end-organ dysfunction (worsening renal and/or hepatic function) due to reduced perfusion and not to inadequate ventricular filling pressure (PCWP ≥20 mmHg and SBP ≤80–90 mmHg or CI ≤2 L/min/m ²).
Absence of severe right ventricular dysfunction together with severe tricuspid regurgitation.

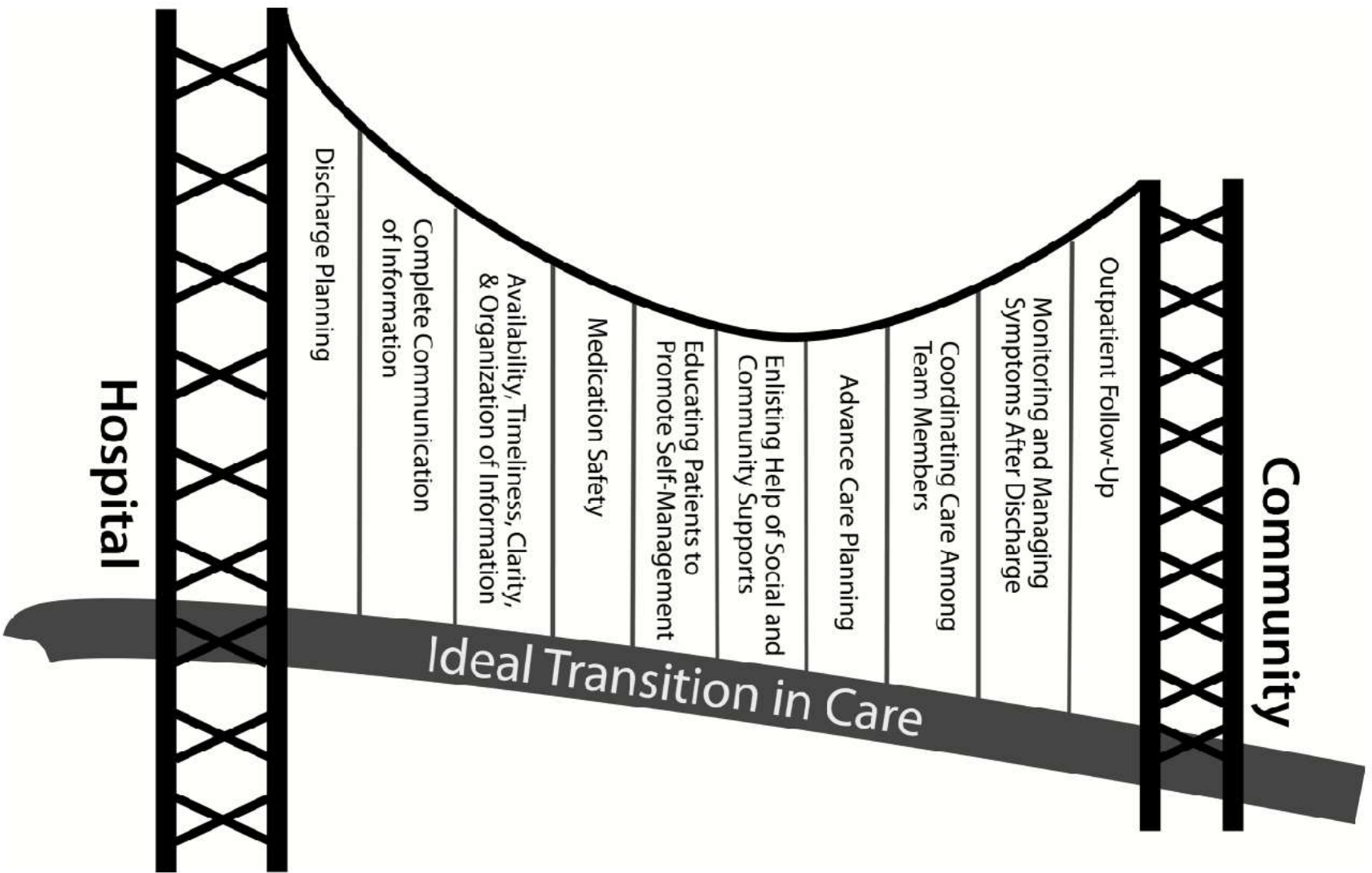
Recommendations	Class ^a	Level ^b
An LVAD should be considered in patients who have end-stage HFrEF despite optimal medical and device therapy and who are eligible for heart transplantation in order to improve symptoms, reduce the risk of HF hospitalization and the risk of premature death (Bridge to transplant indication).	IIa	C
An LVAD should be considered in patients who have end-stage HFrEF despite optimal medical and device therapy and who are not eligible for heart transplantation to, reduce the risk of premature death.	IIa	B

Trials of implantable monitoring devices in heart failure: which design is optimal?

William T. Abraham, Wendy G. Stough, Ileana L. Piña, Cecilia Linde, Jeffrey S. Borer, Gaetano M. De Ferrari, Roxana Mehran, Kenneth M. Stein, Alphons Vincent, Jay S. Yadav, Stefan D. Anker and Faiez Zannad



What are the Ideal Components in the Transition in Care?



Burke RE, et al. *J Hosp Med* 2013;8:102-9.

JCM 200182

Editorial



The evolving care of the elderly with heart failure: from the “high-tech” to the “high-touch” approach

Giovanni Pulignano^a, Donatella Del Sindaco^b, Andrea Di Lenarda^c and Gianfranco Sinagra^c





Il Cardiologo fra superspecializzazione e necessità di un percorso unitario per i pazienti

".... specializzazione che spesso frammenta i contesti, la globalità, la complessità. La specializzazione "as-trae" ossia estrae un oggetto dal suo insieme, ne rifiuta i legami e le interconnessioni con l'ambiente, lo inserisce in un settore concettuale astratto che è quello della disciplina compartimentata, in cui le frontiere spezzano arbitrariamente la sistemicità e la multidimensionalità dei fenomeni..."
(Edgar Morin 2003)

