SEMI
SOCIEDAD ESPAÑOLA DE MEDICINA INTERNA
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VIII

Grupo de Diabetes y Obesidad

Reunión de Diabetes y Obesidad

31 de Enero y 1 de Febrero de 2014 | Hotel Meliá Castilla. Madrid

VIII
Reunión de Diabetes y Obesidad
31 de Enero y 1 de Febrero de 2014 | Hotel Meliá Castilla. Madrid

Nuevas Terapias en Insuficiencia Cardíaca

Eduardo de Teresa

Málaga

Diabetes e Insuficiencia Cardiaca

- ¿Existe la miocardiopatia diabética?
- Valor pronóstico de la diabetes en la IC
- Tratamiento de la diabetes e IC
- Nuevas terapias en la Insuficiencia Cardiaca

Diabetes e Insuficiencia Cardiaca

- Riesgo IC x2,4 (hombres) o x5 (mujeres) Framingham (1974)

Disfunción diastólica (30-60%)

Afectación vascular
- **Grandes arterias coronarias**
- **Microangiopatía**

Hipertensión arterial

Afectación miocárdica independiente

Diabetes e Insuficiencia Cardiaca

- Afectación vascular
  - Grandes arterias coronarias
  - Microangiopatía
- Hipertensión arterial
- Disfunción diastólica (30-60%)
- Afectación miocárdica independiente

Basic Science for Clinicians

Diabetic Cardiomyopathy Revisited

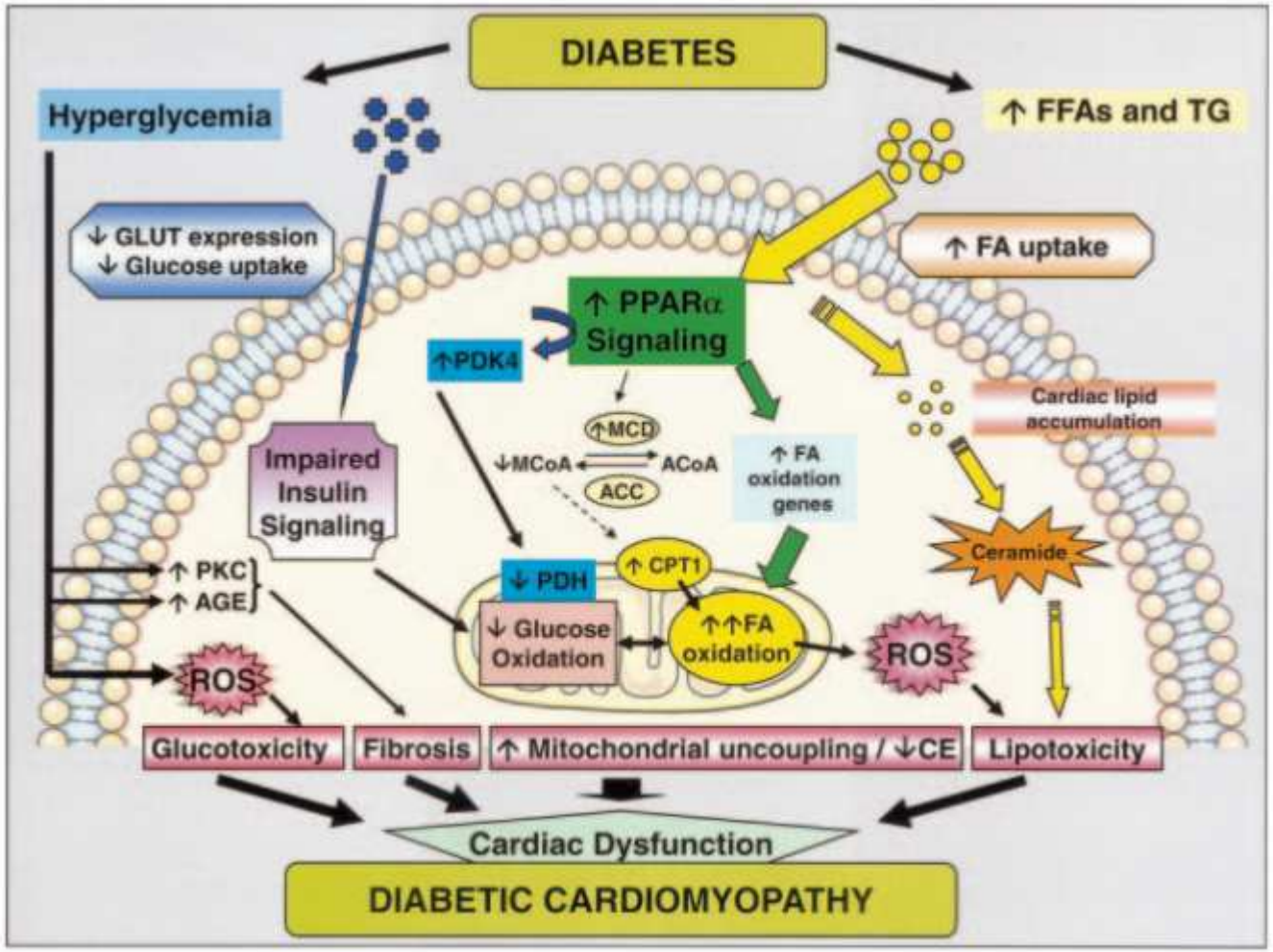
Sihem Boudina, PhD; E. Dale Abel, MBBS, DPhil

Abstract—Diabetes mellitus increases the risk of heart failure independently of underlying coronary artery disease, and many believe that diabetes leads to cardiomyopathy. The underlying pathogenesis is partially understood. Several factors may contribute to the development of cardiac dysfunction in the absence of coronary artery disease in diabetes mellitus. This review discusses the latest findings in diabetic humans and in animal models and reviews emerging new mechanisms that may be involved in the development and progression of cardiac dysfunction in diabetes. **(*Circulation*. 2007;115:3213-3223.)**

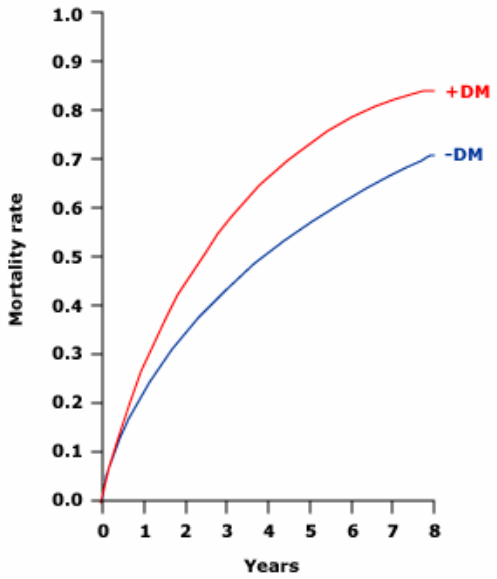
In Vivo and Ex Vivo Data for Cardiac Dysfunction in Animal Models of Type 1 and Type 2 Diabetes Mellitus

	Type 1 Diabetes Mellitus					Type 2 Diabetes Mellitus			
	OVE 26	NOD	BB rats	STZ	Alloxan	ob/ob	db/db	ZF/ZDF	GK
Heart rate			↓ [34,52,58]						
Systolic function	↓ [46]	↓ [50]		↓ [43,45,49,55]	↓ [39]		↓ [30,46,53,59]	↓ [51,61]	
Diastolic function	↓ [46]	↓ [50]	↓ [34,52,58]	↓ [43,45,49]	↓ [39]	↓ [36]	↓ [30,35,46,53,59]	↓ [51,61]	
LV hypertrophy						↑ [33,48]		↑ [37]	↑ [38]
±dP/dt		↓ [50]	↓ [34,52,58]	↓ [45,55]		↑ [32,35]	↑ [35]		
Inotropic response					↓ [39,57]	↓ [33]			
Tolerance to ischemia			↓ [34]	↓ [54,60]	↑ [41]		↓ [31,40,44]	↑ [47,56] ↓ [42]	↑ [47]

Up and down arrows indicate increase and decrease, respectively. Numbers are references. OVE 26 indicates beta cell overexpression of calmodulin; NOD, nonobese diabetic; STZ, streptozocin; ZF/ZDF, Zucker fatty/Zucker diabetic fatty rats; and GK, Goto-Kakizaki rats.

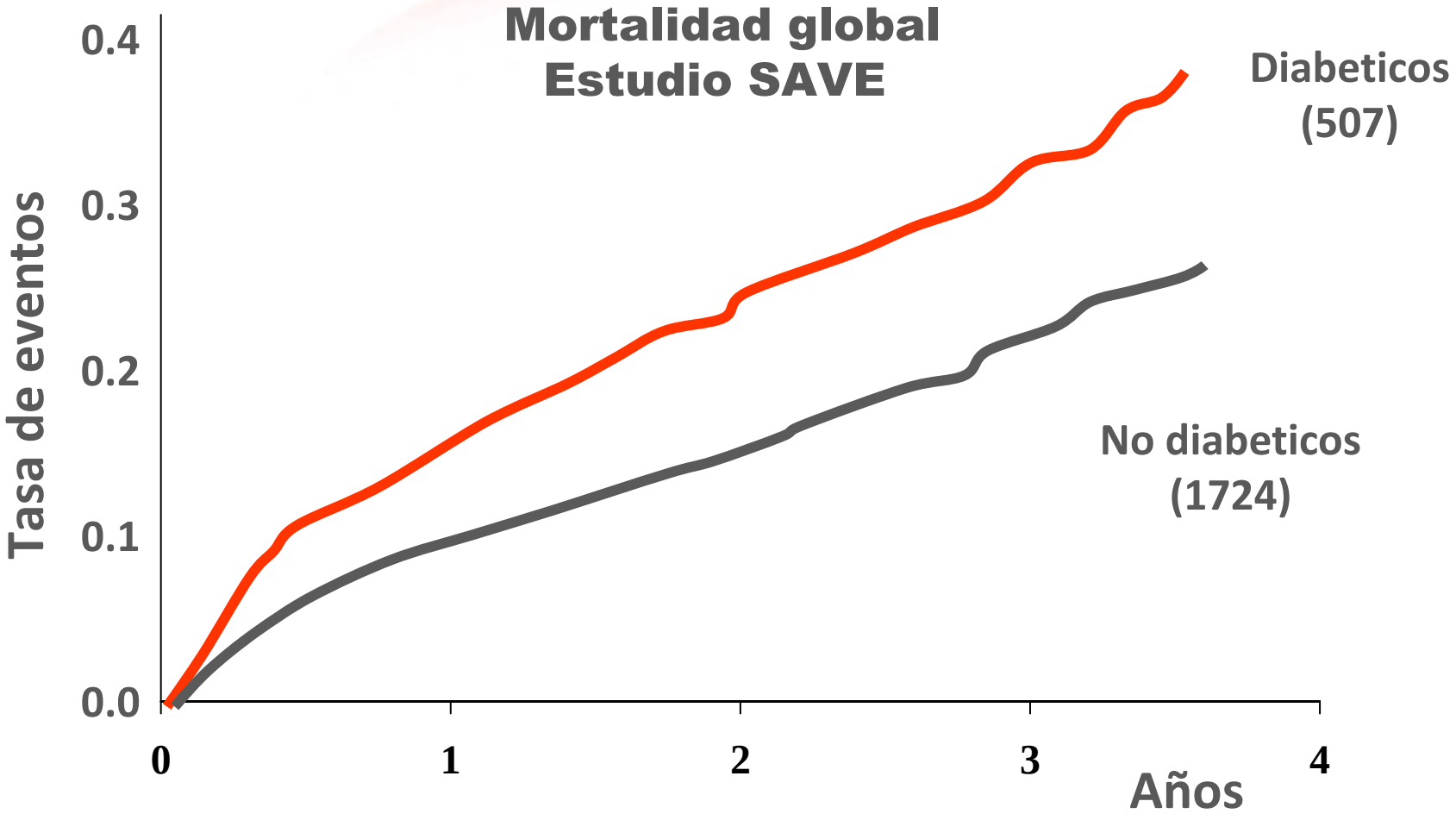

DIABETES
Hyperglycemia
↑ FFAs and TG
↓ GLUT expression
↓ Glucose uptake
↑ FA uptake
↑ PPARα Signaling
↑PDK4
Cardiac lipid accumulation
↑MCD
↓MCoA
ACoA
ACC
↑ FA oxidation genes
Impaired Insulin Signaling
Ceramide
↑ PKC
↑ AGE
↓ PDH
↑ CPT1
↓ Glucose Oxidation
↑↑FA oxidation
ROS
ROS
Glucotoxicity
Fibrosis
↑ Mitochondrial uncoupling / ↓CE
Lipotoxicity
Cardiac Dysfunction
DIABETIC CARDIOMYOPATHY

Cumulative mortality from all causes in patients with heart failure with and without diabetes

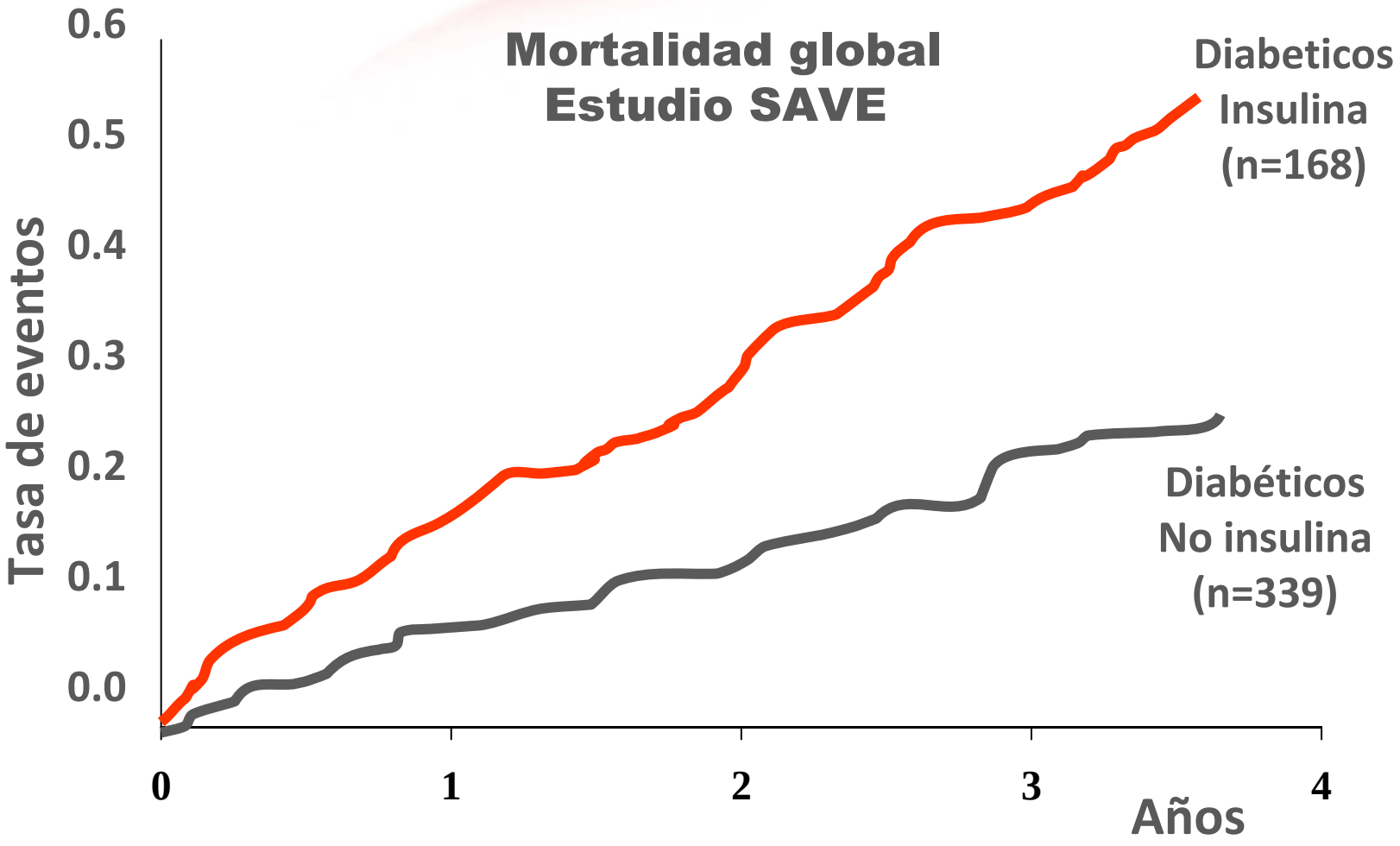


Effect of diabetes on HF mortality. In the DIAMOND-CHF trial of 5491 patients with heart failure (HF), 900 (16 percent) had diabetes mellitus. Mortality for patients with diabetes was significantly higher than for those without diabetes (31 versus 23 percent at one year, adjusted risk ratio 1.5, 95% CI 1.3 to 1.6).

+DM: diabetic patients; -DM: non-diabetic patients.



Jiménez Navarro, JACC 1999



Jiménez Navarro, JACC 1999

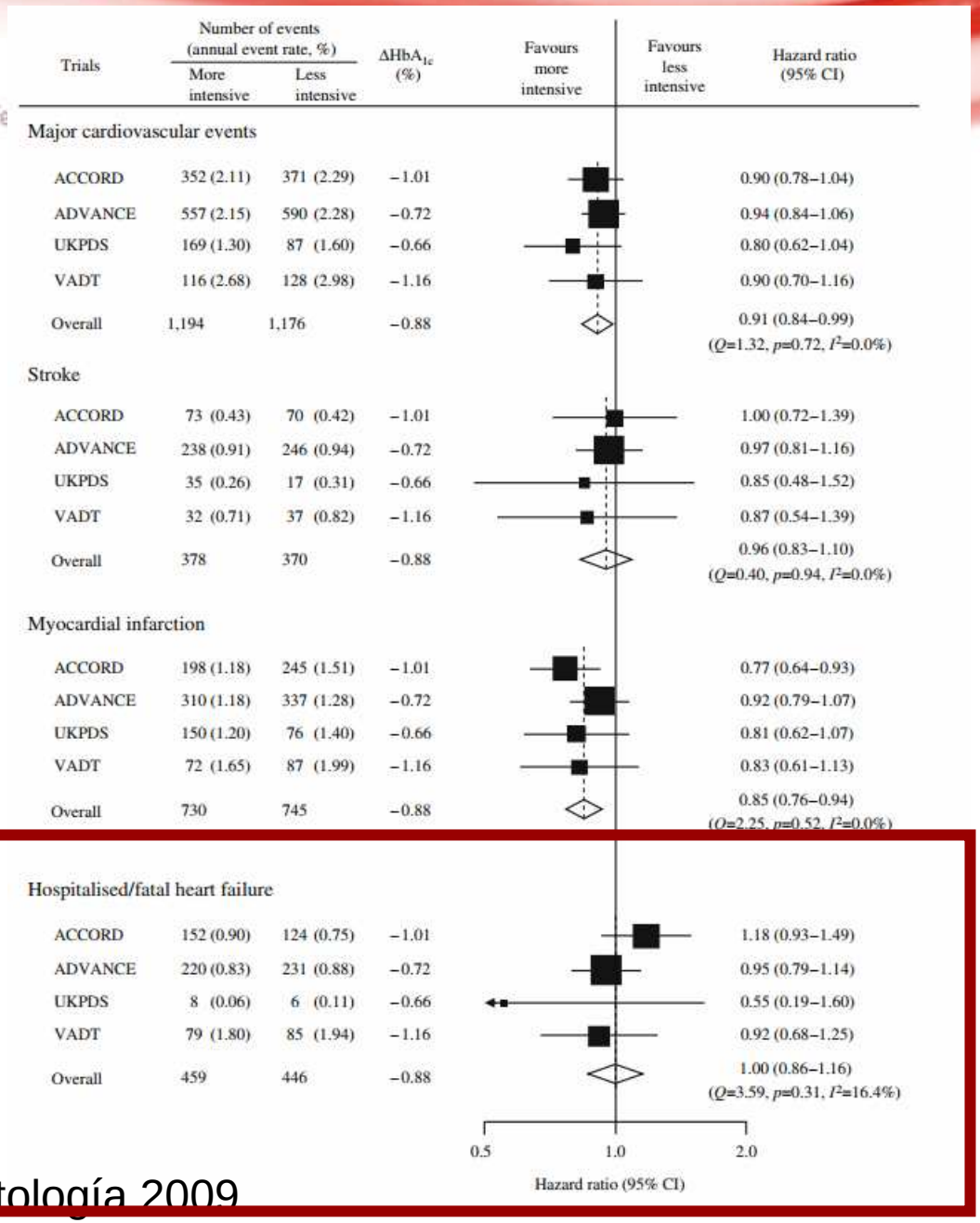
TABLE 2. Number of Events, Persons, Person-Years, and Age-Adjusted Rates per 1000 Person-Years of Heart Failure Hospitalization and/or Death by Hemoglobin A_{1c} Concentration

	All (n=48 858)			Men (n=25 958)			Women (n=22 900)		
Hemoglobin A_{1c}, %	n/N	P-Y	Rate per 10^3 P-Y (95% CI)	n/N	P-Y	Rate per 10^3 P-Y (95% CI)	n/N	P-Y	Rate per 10^3 P-Y (95% CI)
<7	145/10 631	21 963	4.5 (2.9–7.0)	81/5969	12 329	4.5 (2.5–8.2)	64/4662	9634	4.5 (2.4–8.6)
7 to <8	197/10 692	23 417	5.8 (3.8–8.9)	107/5653	12 379	5.9 (3.2–10.6)	90/5039	11 038	5.6 (3.0–10.5)
8 to <9	181/9238	20 808	6.3 (4.1–9.7)	93/4847	10 926	6.0 (3.3–10.9)	88/4391	9882	6.6 (3.5–12.2)
9 to <10	172/7354	16 576	8.3 (5.5–12.6)	100/3817	8528	9.2 (5.2–16.4)	72/3537	8048	7.2 (3.9–13.4)
≥10	240/10 943	23 594	9.2 (6.2–13.8)	135/5672	12 059	10.3 (5.9–17.8)	105/5271	11 536	8.0 (4.4–14.5)
P for linear trend			0.0001			0.0001			0.009

n/N indicates events/persons; P-Y, person-years.

48742 pacientes con DM

Iribarren, Circulation 2001



Turnbull FM, Diabetología 2009

Journal of the American College of Cardiology

Published by Elsevier Inc.

Vol. 49, No. 16, 2007
ISSN 0735-1097/07/$32.00
doi:10.1016/j.jacc.2006.10.077

A Randomized, Placebo-Controlled Trial Assessing the Effects of Rosiglitazone on Echocardiographic Function and Cardiac Status in Type 2 Diabetic Patients With New York Heart Association Functional Class I or II Heart Failure

Henry J. Dargie, MBChB,* Per R. Hildebrandt, MD,† Günter A. J. Riegger, MD,‡ John J. V. McMurray, MD,* Stephen O. McMorn, PhD,§ Jeremy N. Roberts, MSc,‖ Andrew Zambanini, MRCP,§ John P. H. Wilding, DM¶

Glasgow, Scotland; Fredriksberg, Denmark; Regensberg, Germany; Harlow and Liverpool, England; and Oakville, Canada

Table 2 Proportion of Patients With Other Adjudicated Clinical End Points

Adjudicated End Point	PLB, n = 114 n (%)	RSG, n = 110 n (%)	p Value
Cardiovascular hospitalization	15 (13.2)	21 (19.1)	0.465
Definite worsening CHF	4 (3.5)	5 (4.5)	0.858
Possible worsening CHF	0	2 (1.8)	–*
New or worsening edema	10 (8.8)	28 (25.5)	0.005
New or worsening dyspnea	19 (16.7)	29 (26.4)	0.197
Increase in CHF medication	20 (17.5)	36 (32.7)	0.037

*No events occurred in 1 treatment group, preventing analysis using this model.
Abbreviations as in Table 1.

EUROPEAN SOCIETY OF CARDIOLOGY®
European Heart Journal (2012) **33**, 1787–1847
doi:10.1093/eurheartj/ehs104

ESC GUIDELINES

CME

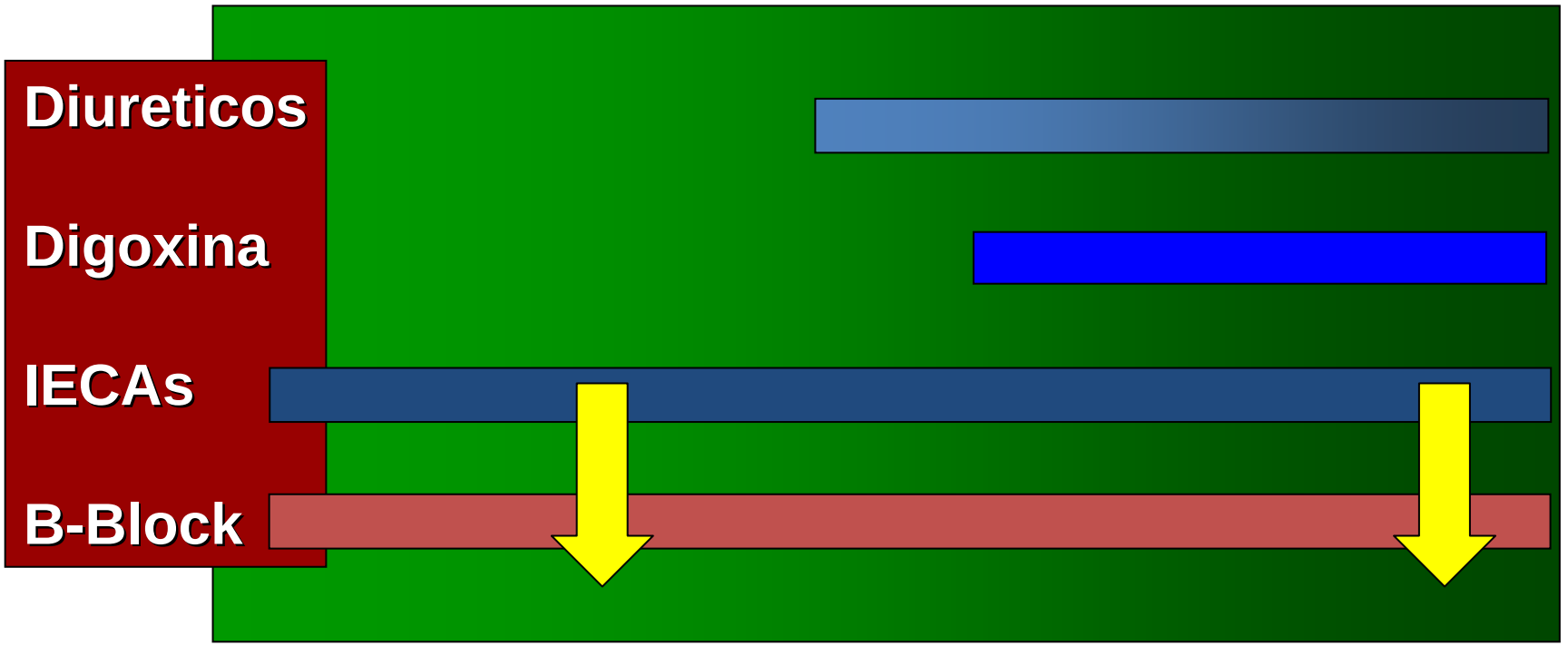
ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2012

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

2. Introduction

The aim of this document is to provide practical, evidence-based guidelines for the diagnosis and treatment of heart failure (HF). The principal changes from the 2008 guidelines[1] relate to:

(i) an expansion of the indication for mineralocorticoid (aldosterone) receptor antagonists (MRAs);
(ii) a new indication for the sinus node inhibitor ivabradine;
(iii) an expanded indication for cardiac resynchronization therapy (CRT);
(iv) new information on the role of coronary revascularization in HF;
(v) recognition of the growing use of ventricular assist devices; and
(vi) the emergence of transcatheter valve interventions.


Diureticos
Digoxina
IECAs
B-Block
Disfunción VI
grado I
grado II
grado III
grado IV

The NEW ENGLAND JOURNAL of MEDICINE

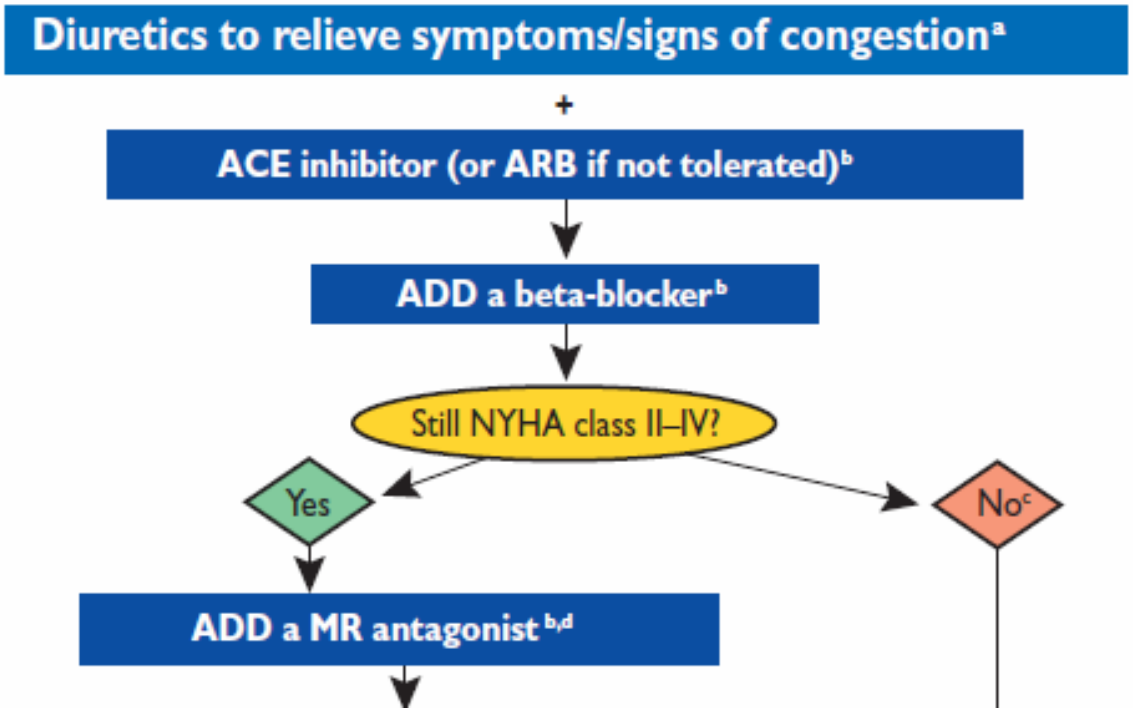
ORIGINAL ARTICLE

Eplerenone in Patients with Systolic Heart Failure and Mild Symptoms

Faiez Zannad, M.D., Ph.D., John J.V. McMurray, M.D., Henry Krum, M.B., Ph.D., Dirk J. van Veldhuisen, M.D., Ph.D., Karl Swedberg, M.D., Ph.D, Harry Shi, M.S., John Vincent, M.B., Ph.D., Stuart J. Pocock, Ph.D., and Bertram Pitt, M.D., for the EMPHASIS-HF Study Group*

ABSTRACT

Ambrovicova, L. Gaspar, E. Goncalvesova, P. Kycina, J. L itvinova, Z. Mikes, J. Murin (LI), P. Poliacik, R. Uhliar; South Africa – E. A. Lloyd, D. Marx, D. P. Naidoo, H. W. Prozesky, K. Sliwa-Hahnle H. Theron; Spain – M. Anguita, E. De Teresa, E. Galve, J. R. G. Juanatey (LI), P. M. M. Orbe, M. Vida; Sweden - U. Ahrem ark, B. Andersson (LI),


Diuretics to relieve symptoms/signs of congestion[a]
+
ACE inhibitor (or ARB if not tolerated)[b]
ADD a beta-blocker[b]
Still NYHA class II–IV?
Yes
No[c]
ADD a MR antagonist[b,d]

TOPCAT: Key outcomes

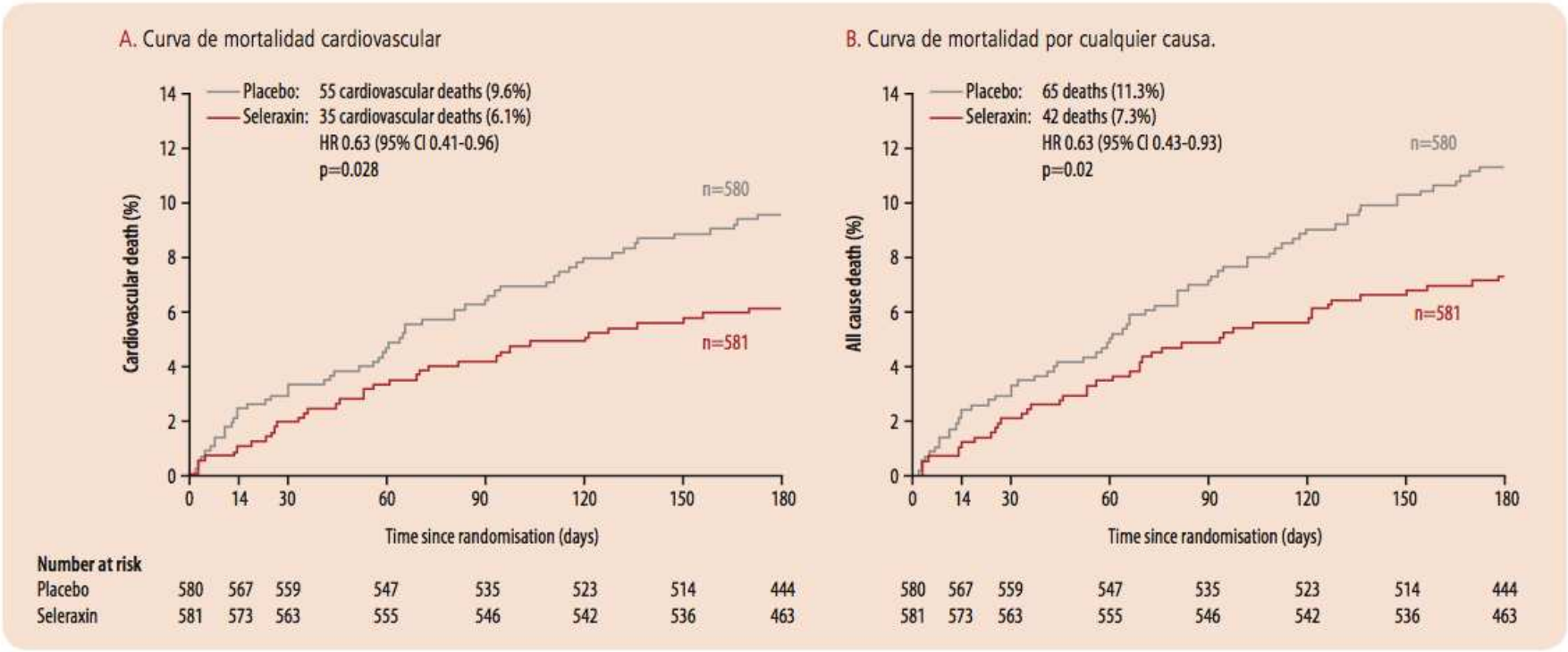
	Spironolactone (n = 1,722)	Placebo (n = 1,723)
Primary composite endpoint of cardiovascular death, heart failure hospitalization, or aborted cardiac arrest	18.6% 5.9 per 100 person-years	20.4% 6.6 per 100 person-years
Components		
Hospitalization for heart failure	12.0% 3.8 per 100 person-years	14.2% 4.6 per 100 person-years
Cardiovascular mortality	9.3% 2.8 per 100 person-years	10.2% 3.1 per 100 person-years
Aborted cardiac arrest	<1%	<1%

Note: The study involved 3,445 participants with heart failure with preserved ejection fraction.

Source: Dr. Pfeffer

IMNG Medical Media

RELAX AHF



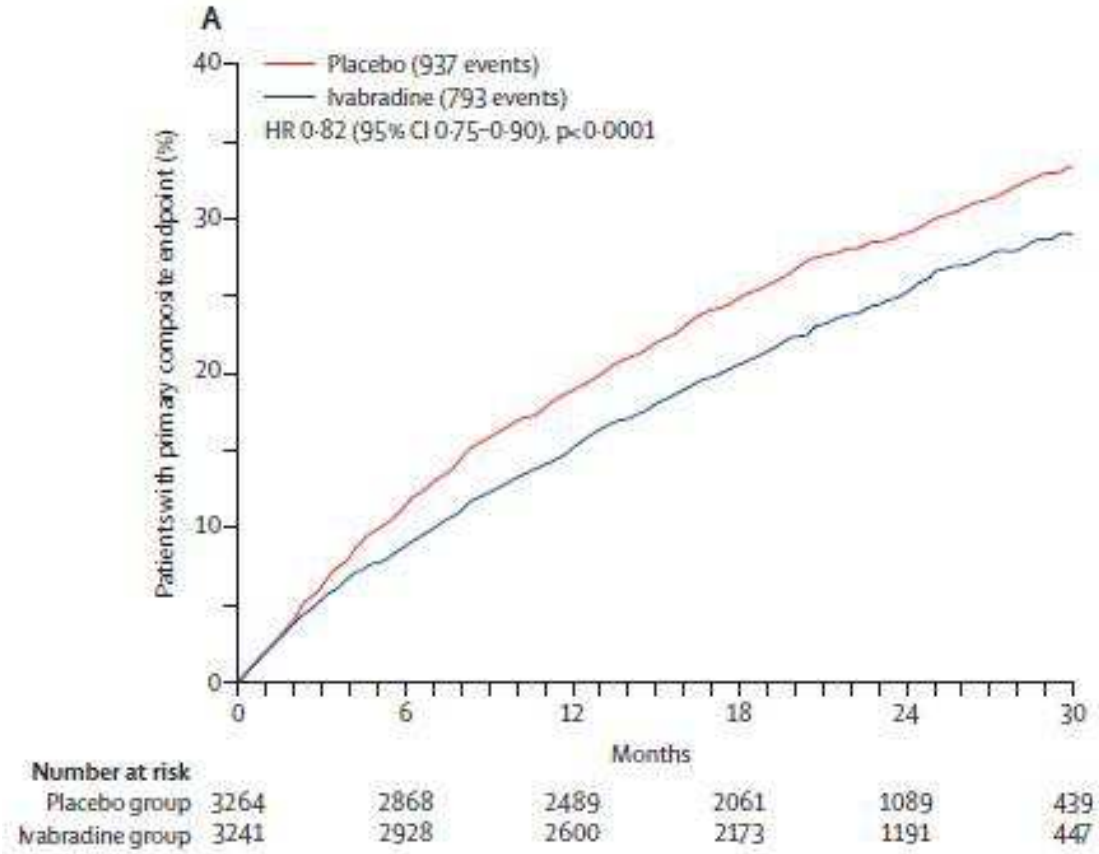
Metra F, Eur Heart J 2013

SHIFT Ivabradina en IC

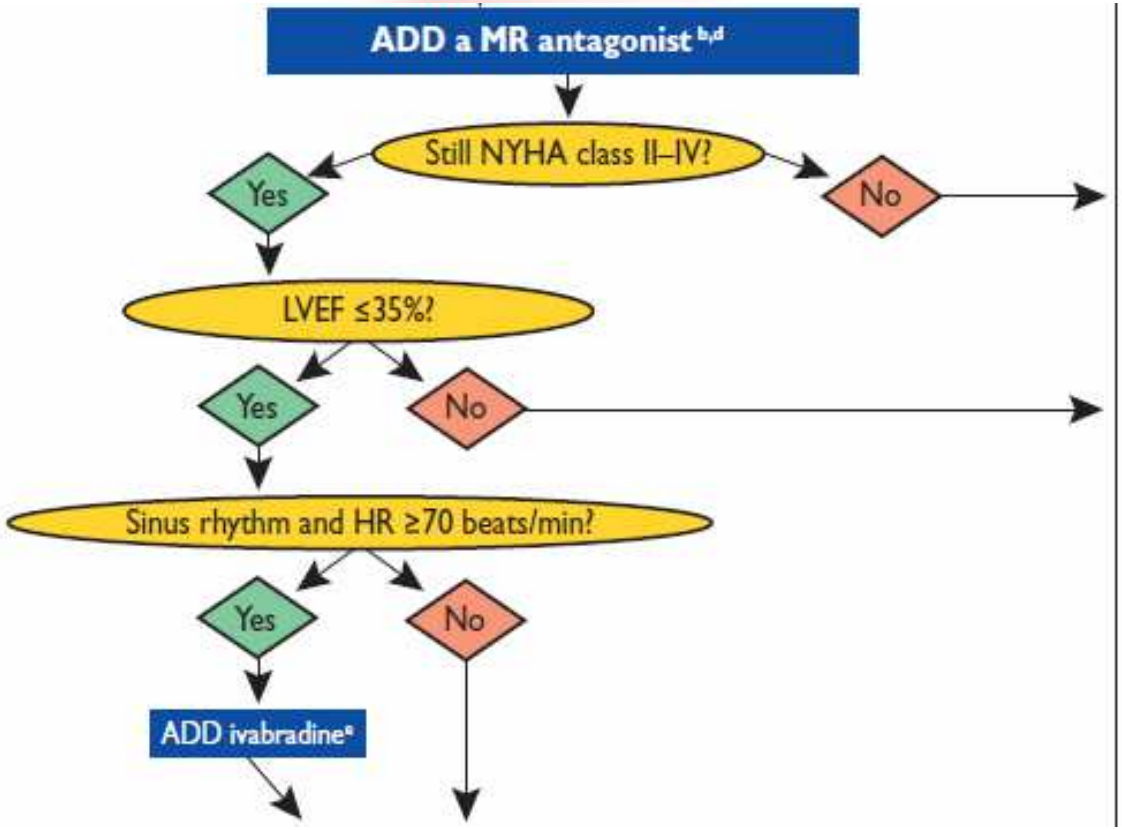
Ivabradine and outcomes in chronic heart failure (SHIFT): a randomised placebo-controlled study

*Karl Swedberg, Michel Komajda, Michael Böhm, Jeffrey S Borer, Ian Ford, Ariane Dubost-Brama, Guy Lerebours, Luigi Tavazzi, on behalf of the SHIFT Investigators**

Swedberg K, Lancet 2010



Swedberg K, Lancet 2010


ADD a MR antagonist [b,d]
Still NYHA class II–IV?
Yes
No
LVEF ≤35%?
Yes
No
Sinus rhythm and HR ≥70 beats/min?
Yes
No
ADD ivabradine[e]

Single Site Left Ventricular Pacing for Cardiac Resynchronization

William G. Stevenson, MD; Michael O. Sweeney, MD

In 1984, de Teresa et al[7] demonstrated that changing the sequence of ventricular activation by pacing could improve cardiac function. Pacing from epicardial leads placed on the right atrium and lateral left ventricular (LV) free wall in patients with LBBB after aortic valve replacement, they noted that left ventricular ejection fraction was maximal when septal and free wall contraction were simultaneous and diminished when septal and free wall motion were dyssyn-

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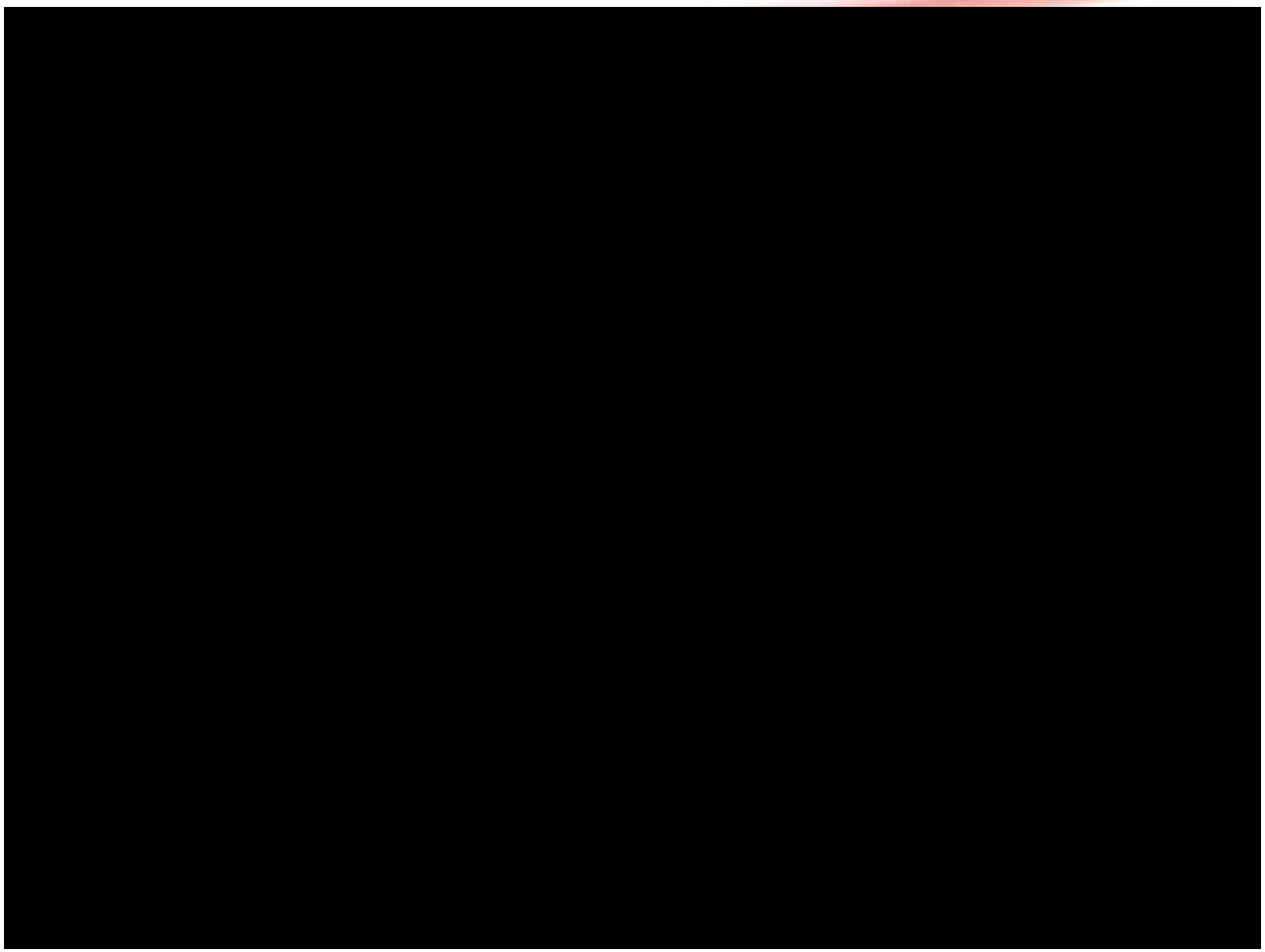
The opinions expressed in this article are not necessarily those of the editors or of the American Heart Association.

From the Cardiovascular Division, Department of Internal Medicine, Brigham and Women's Hospital, Boston, Mass.

Correspondence to William G. Stevenson, MD, Cardiovascular Division, Brigham and Women's Hospital, 75 Francis St, Boston, MA 02115. E-mail wstevenson@partners.org

(*Circulation* 2004;109:1694-1696.)

Circulation is available at http://www.circulationaha.org
DOI: 10.1161/01.CIR.0000126182.49118.52



The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 OCTOBER 1, 2009 VOL. 361 NO. 14

Cardiac-Resynchronization Therapy for the Prevention of Heart-Failure Events

Arthur J. Moss, M.D., W. Jackson Hall, Ph.D., David S. Cannom, M.D., Helmut Klein, M.D., Mary W. Brown, M.S., James P. Daubert, M.D., N.A. Mark Estes III, M.D., Elyse Foster, M.D., Henry Greenberg, M.D., Steven L. Higgins, M.D., Marc A. Pfeffer, M.D., Ph.D., Scott D. Solomon, M.D., David Wilber, M.D., and Wojciech Zareba, M.D., Ph.D., for the MADIT-CRT Trial Investigators*

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 DECEMBER 16, 2010 VOL. 363 NO. 25

Cardiac-Resynchronization Therapy for Mild-to-Moderate Heart Failure

Anthony S.L. Tang, M.D., George A. Wells, Ph.D., Mario Talajic, M.D., Malcolm O. Arnold, M.D., Robert Sheldon, M.D., Stuart Connolly, M.D., Stefan H. Hohnloser, M.D., Graham Nichol, M.D., David H. Birnie, M.D., John L. Sapp, M.D., Raymond Yee, M.D., Jeffrey S. Healey, M.D., and Jean L. Rouleau, M.D., for the Resynchronization–Defibrillation for Ambulatory Heart Failure Trial (RAFT) Investigators

The NEW ENGLAND JOURNAL of MEDICINE

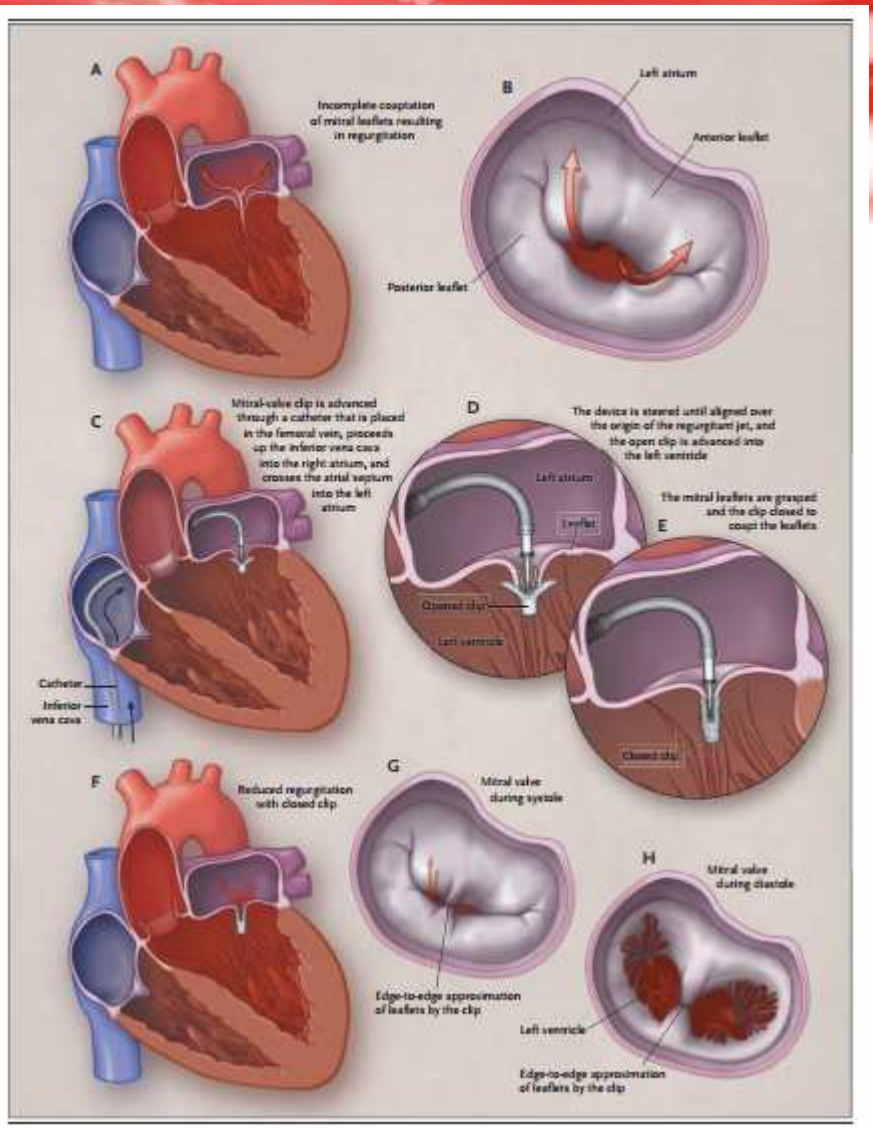
ESTABLISHED IN 1812 DECEMBER 20, 2012 VOL. 367 NO. 25

Strategies for Multivessel Revascularization in Patients with Diabetes

Michael E. Farkouh, M.D., Michael Domanski, M.D., Lynn A. Sleeper, Sc.D., Flora S. Siami, M.P.H., George Dangas, M.D., Ph.D., Michael Mack, M.D., May Yang, M.P.H., David J. Cohen, M.D., Yves Rosenberg, M.D., M.P.H., Scott D. Solomon, M.D., Akshay S. Desai, M.D., M.P.H., Bernard J. Gersh, M.B., Ch.B., D.Phil., Elizabeth A. Magnuson, Sc.D., Alexandra Lansky, M.D., Robin Boineau, M.D., Jesse Weinberger, M.D., Krishnan Ramanathan, M.B., Ch.B., J. Eduardo Sousa, M.D., Ph.D., Jamie Rankin, M.D., Balram Bhargava, M.D., John Buse, M.D., Whady Hueb, M.D., Ph.D., Craig R. Smith, M.D., Victoria Muratov, M.D., M.P.H., Sameer Bansilal, M.D., Spencer King III, M.D., Michel Bertrand, M.D., and Valentin Fuster, M.D., Ph.D., for the FREEDOM Trial Investigators*

Table 3. Kaplan–Meier Estimates of Major Adverse Cardiovascular and Cerebrovascular Events at 30 Days and 12 Months after the Procedure.

Event	30 Days after Procedure			12 Months after Procedure		
	PCI	CABG	P Value	PCI	CABG	P Value
	number (percent)			*number (percent)*		
Major adverse cardiovascular and cerebrovascular events	45 (4.8)	47 (5.2)	0.68	157 (16.8)	106 (11.8)	0.004
Death	8 (0.8)	15 (1.7)	0.12	32 (3.4)	38 (4.2)	0.35
Myocardial infarction	17 (1.8)	15 (1.7)	0.82	54 (5.8)	30 (3.4)	0.02
Stroke	3 (0.3)	16 (1.8)	0.002	8 (0.9)	17 (1.9)	0.06
Repeat revascularization	31 (3.3)	10 (1.1)	0.002	117 (12.6)	42 (4.8)	<0.001



In patients with an indication for valve repair but judged inoperable or at unacceptably high surgical risk, percutaneous edge-to-edge repair may be considered in order to improve symptoms.[250]

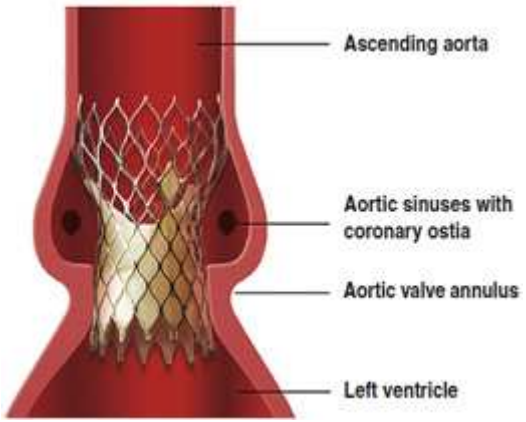
JACC: CARDIOVASCULAR INTERVENTIONS
VOL. 5, NO. 5, 2012

ISSN 1936-8798/$36.00
PUBLISHED BY ELSEVIER INC.
DOI: 10.1016/j.jcin.2012.03.011

Factors Predicting and Having an Impact on the Need for a Permanent Pacemaker After CoreValve Prosthesis Implantation Using the New Accutrak Delivery Catheter System

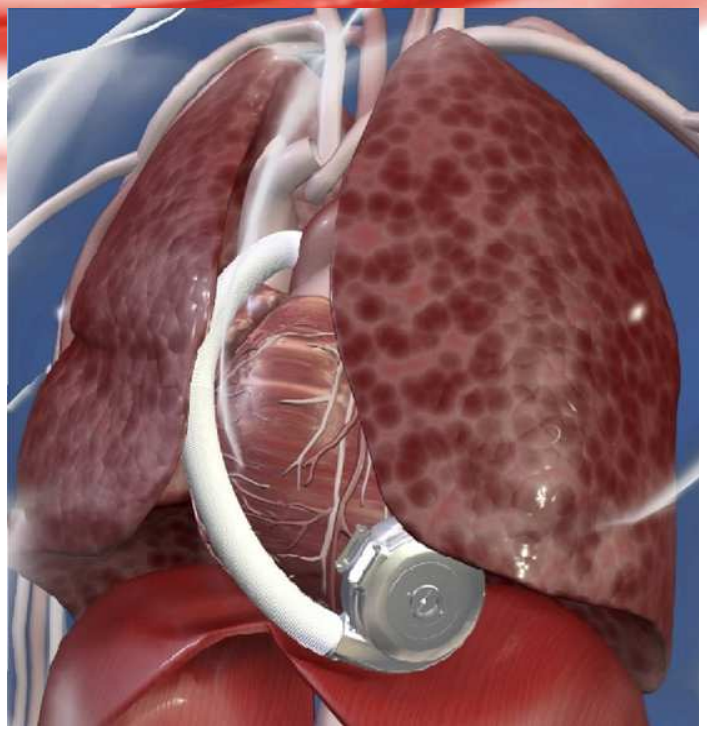
Antonio J. Muñoz-García, MD, PHD, José M. Hernández-García, MD, PHD, Manuel F. Jiménez-Navarro, MD, PHD, Juan H. Alonso-Briales, MD, Antonio J. Domínguez-Franco, MD, Julia Fernández-Pastor, MD, Jose Peña Hernández, MD, Alberto Barrera Cordero, MD, Javier Alzueta Rodríguez, MD, PHD, Eduardo de Teresa-Galván, MD, PHD

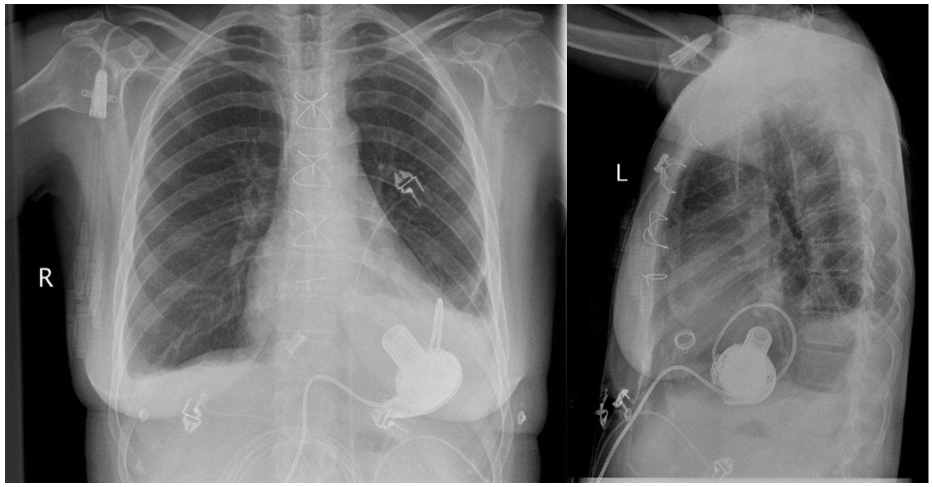
Malaga, Spain

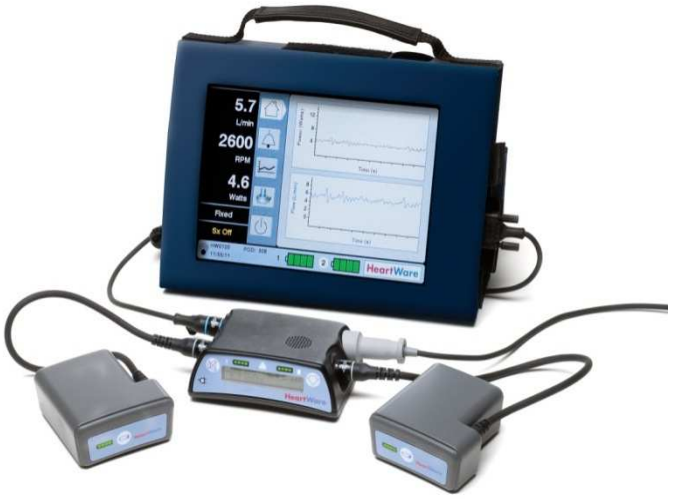


decision-making. In patients not medically fit for surgery (e.g. because of severe pulmonary disease), transcatheter aortic valve replacement should be considered.[248,249]

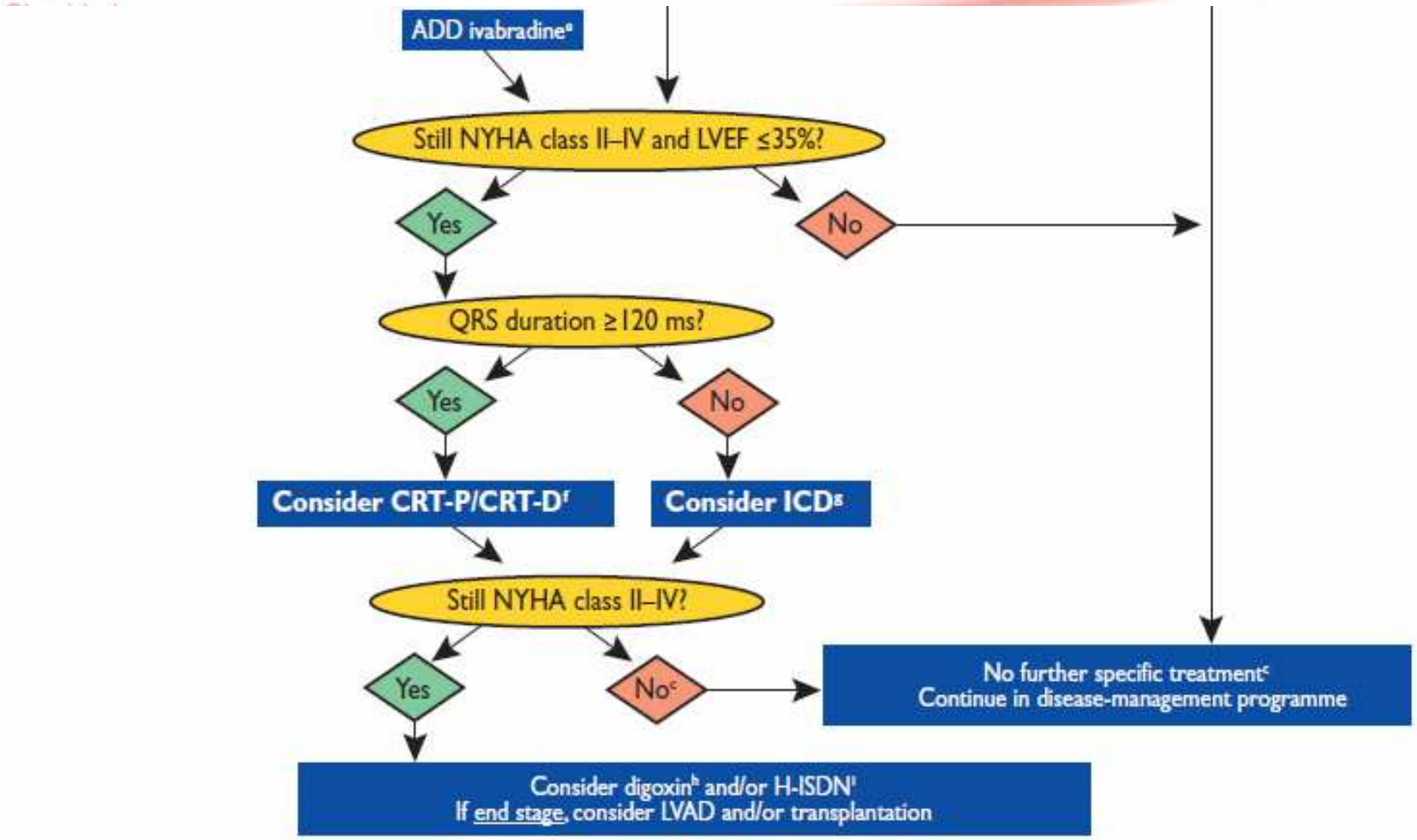
HeartWare Ventricular Assist System







ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2012. Eur Heart J .2012


ADD ivabradine[a]
Still NYHA class II–IV and LVEF ≤35%?
Yes
No
QRS duration ≥120 ms?
Yes
No
Consider CRT-P/CRT-D[f]
Consider ICD[g]
Still NYHA class II–IV?
Yes
No[c]
No further specific treatment[c]
Continue in disease-management programme
Consider digoxin[h] and/or H-ISDN[i]
If end stage, consider LVAD and/or transplantation