XVI Reunión de Insuficiencia Cardíaca Y Fibrilación auricular.
Zaragoza 20 y 21 de marzo de 2014

Grupo de Insuficiencia Cardíaca y Fibrilación Auricular de la Fundación Española de Medicina Interna (FEMI)

NUEVAS EVIDENCIAS EN EL TRATAMIENTO DE LA IC Y SUS COMORBILIDADES

CARDIOPATÍA ISQUÉMICA

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Departament de Salut

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CARDIOPATÍA ISQUÉMICA e IC

Guión

- Prevalencia IC en la Cardiopatía Isquémica (CI)
- Fisiopatología de la IC en la CI
- Tratamiento farmacológico
- Dispositivos en miocardiopatía isquémica
- Revascularización miocárdica e IC
- Tratamiento en la fase aguda de la IC
- Terapia celular e ingeniería tisular miocárdica
- Cirugía de la IC en pacientes con CI
- Perspectivas futuras del tratamiento de la IC y CI

Demographics and Concomitant Diseases of Hospitalized Patients with HF in Registries

	ADHERE (n=107,920)	EURO HF (n=11,327)	OPTIMIZE-HF (n=34,059)
Mean age (y)	75	71	73
Women (%)	52	47	52
Prior HF (%)	75	65	87
LVEF <40%	51	46	52
Coronary artery disease (%)	57	68	50
Hypertension (%)	72	53	71
Diabetes (%)	44	27	42
Atrial fibrillation (%)	31	43	31
Renal insufficiency (%)	30	18	NA

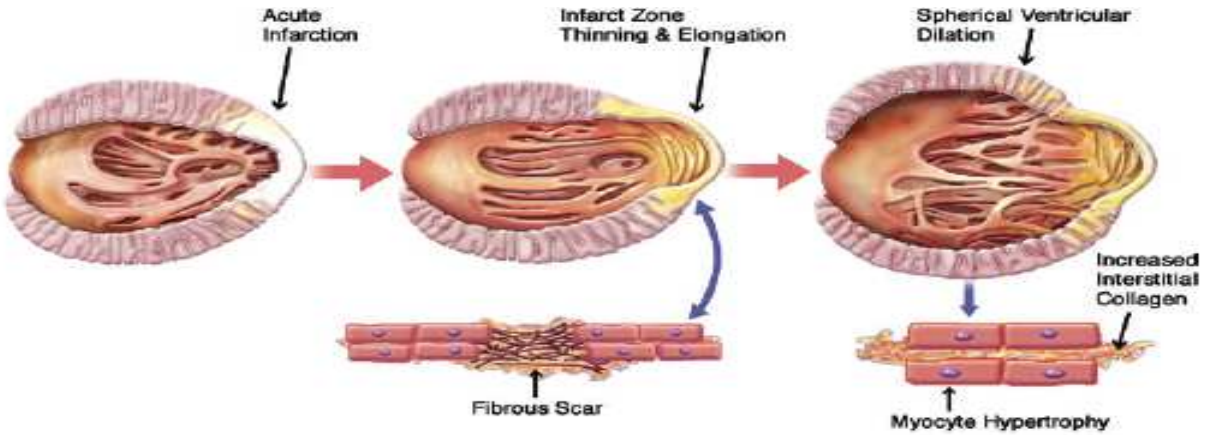
Fonarow GC. *Am Heart J* 2008;155:200–207

PROGRESIÓN DE LA INSUFICIENCIA CARDIACA EN LA CI

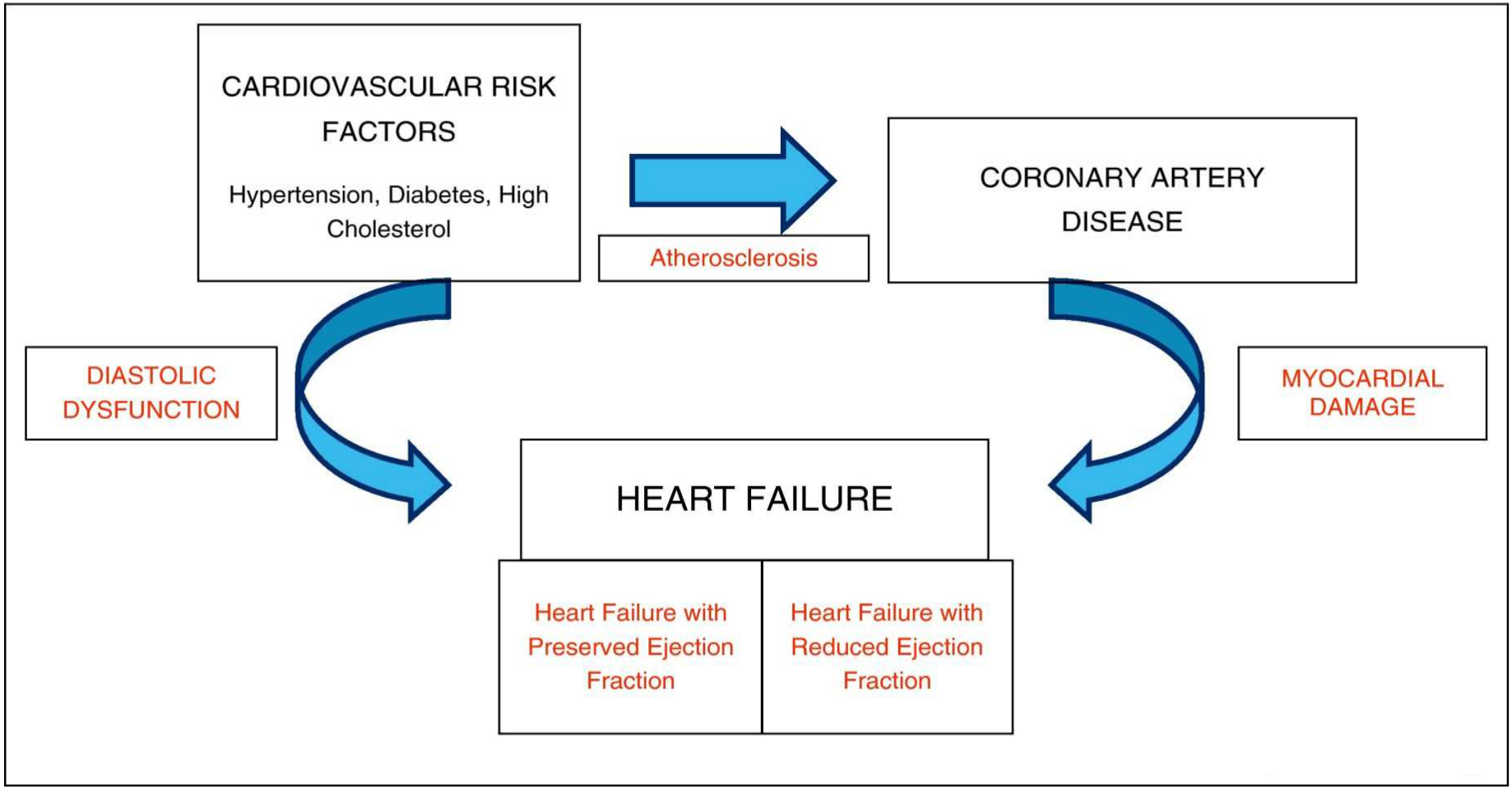
INJURIA / AGRESIÓN MIOCÁRDICA

- **DILATACIÓN VENTRICULAR**
- **ESFERICIDAD VENTRICULAR**
- **REMODELADO VENTRICULAR**
- **DISFUNCIÓN SISTÓLICA Y DIASTÓLICA**
- **SINDROME CLÍNICO DE INSUFICIENCIA CARDIACA**

EMPEORAMIENTO DE LA INSUFICIENCIA CARDÍACA



Relationship between cardiovascular risk factors, coronary artery disease and heart failure.

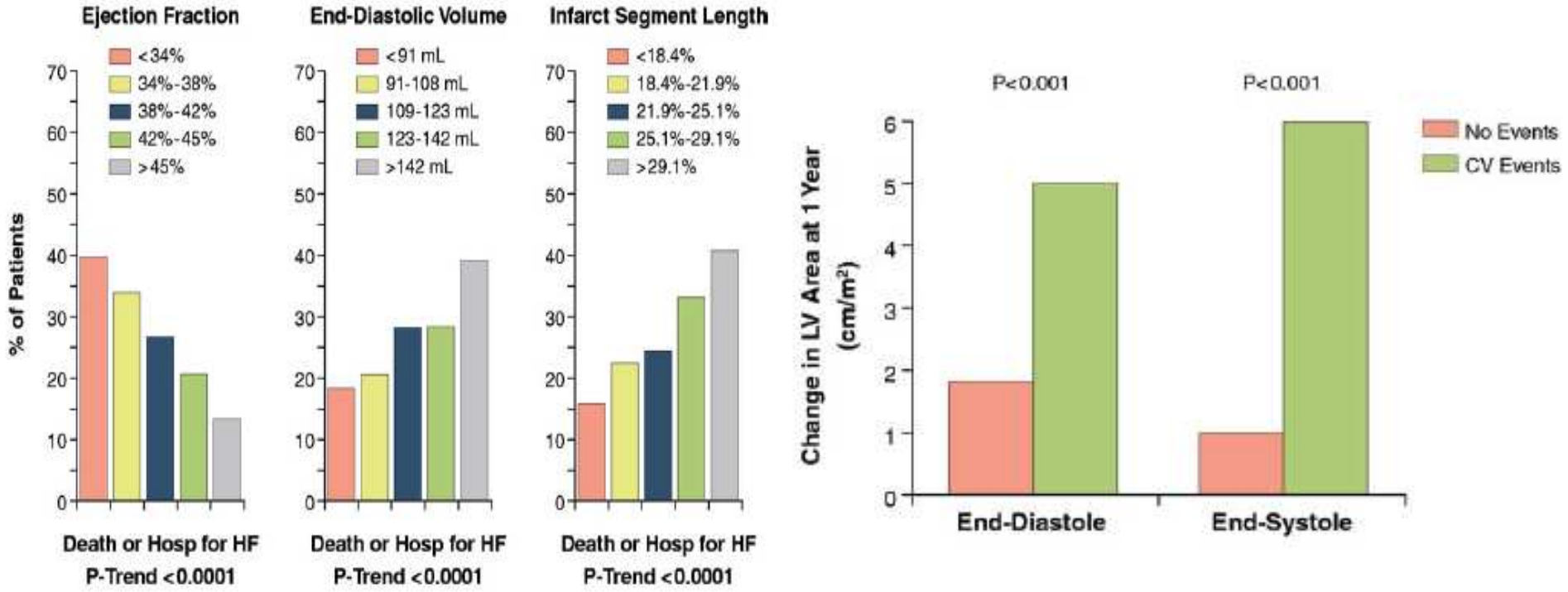


Clare J Taylor , Richard Hobbs. Current Opinion in Pharmacology. 2013;13:205 – 9.

…. el problema es el remodelado del ventrículo izquierdo

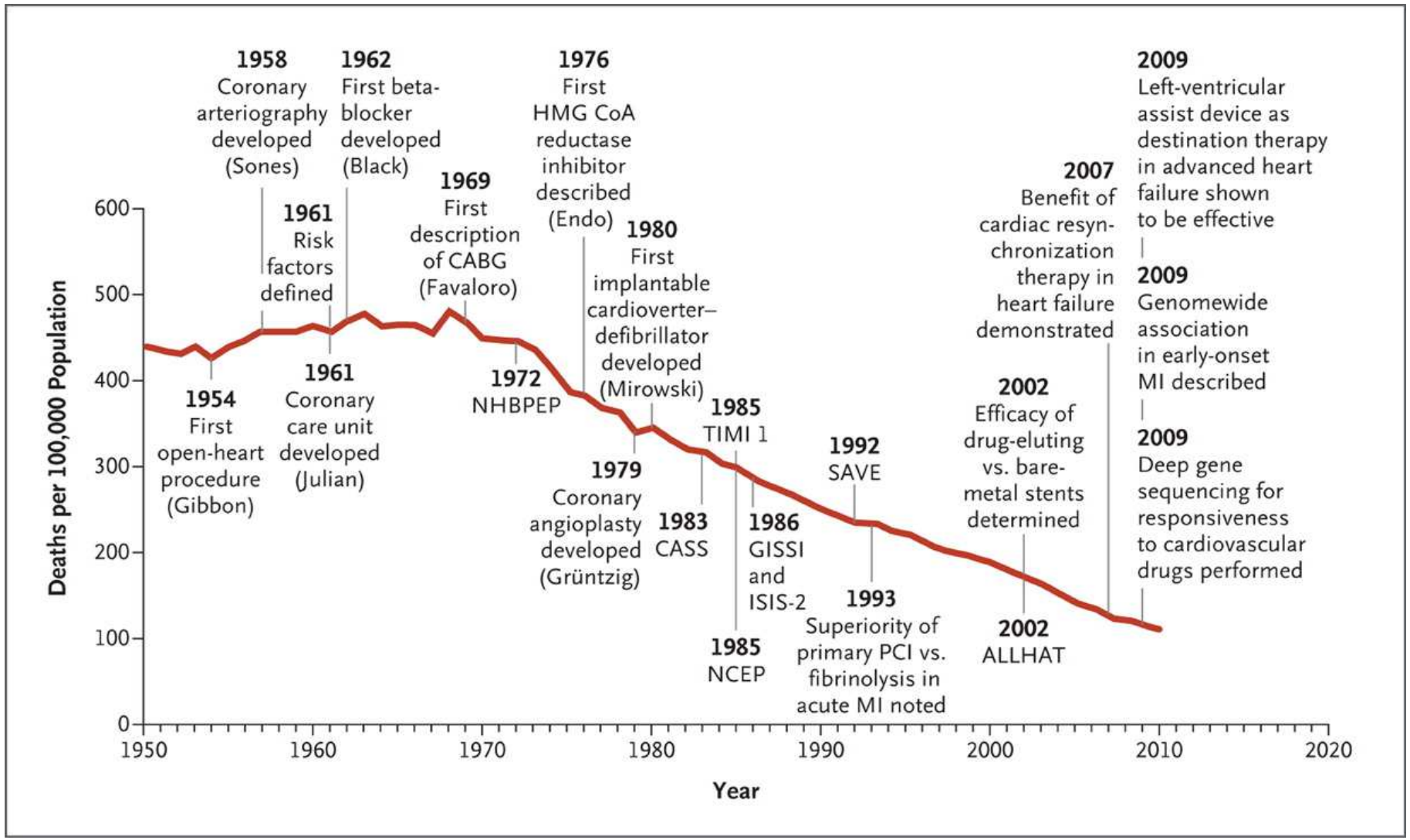
PRONÓSTICO DE LA IC Y REMODELADO VENTRICULAR

Subestudio ecocardiográfico del VALIANT (post-IAM)



Kostam MA et al. J Am Coll Cardiol Img. 2011;4:98 –108.

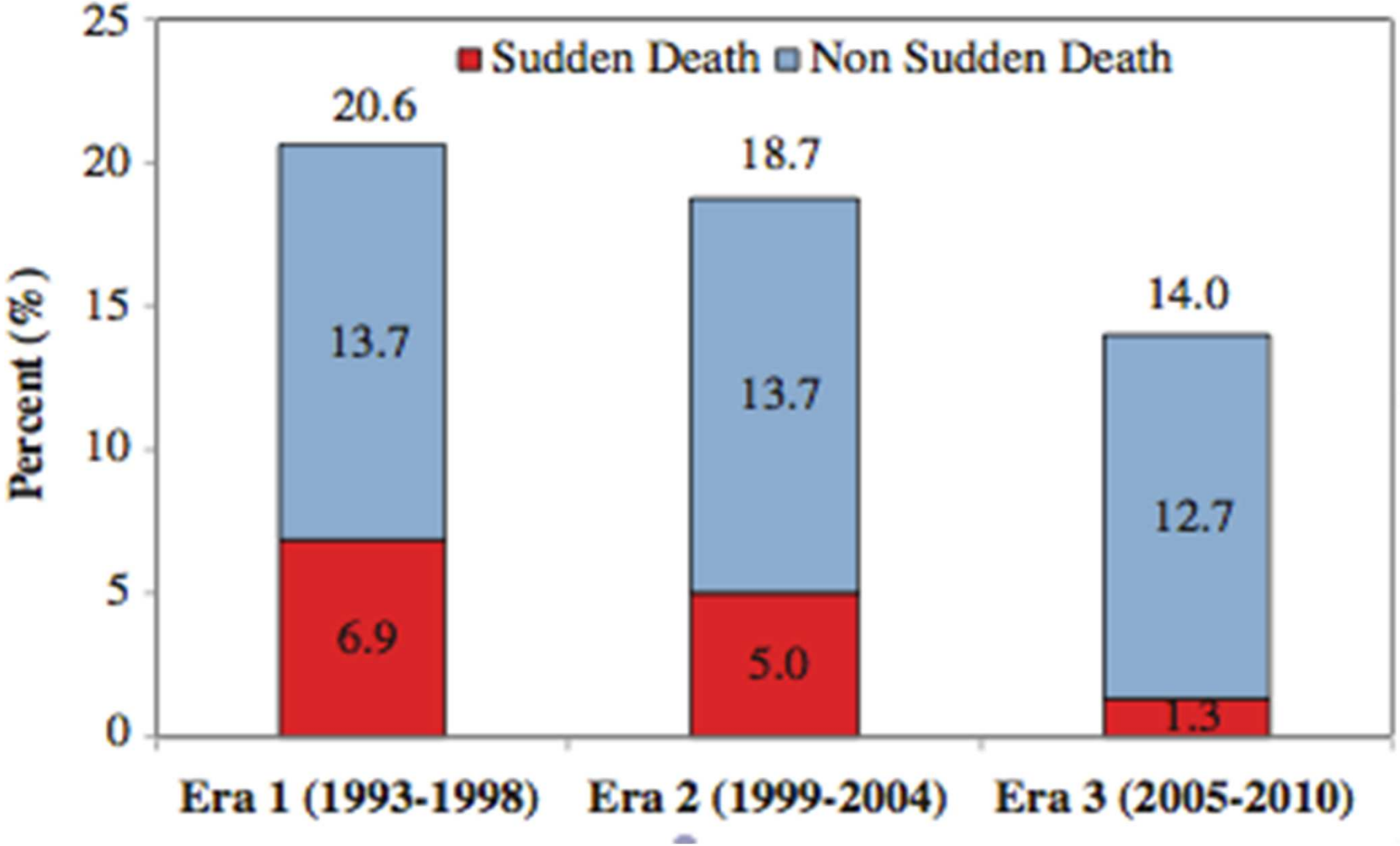
Decline in Deaths from Cardiovascular Disease in Relation to Scientific Advances.



Nabel EG, Braunwald E. N Engl J Med 2012;366:54-63.

Temporal Trends in Treatment and Outcomes for Advanced Heart Failure With Reduced Ejection Fraction From 1993-2010: Findings From a University Referral Center.

n=2507



Loh J et al. Circulation: Heart Failure. 2013;6:411-419.

2013 ESC guidelines on the management of stable coronary artery disease

The Task Force on the management of stable coronary artery disease of the European Society of Cardiology

Task Force Members: Gilles Montalescot* (Chairperson) (France), Udo Sechtem* (Chairperson) (Germany), Stephan Achenbach (Germany), Felicita Andreotti (Italy), Chris Arden (UK), Andrzej Budaj (Poland), Raffaele Bugiardini (Italy), Filippo Crea (Italy), Thomas Cuisset (France), Carlo Di Mario (UK), J. Rafael Ferreira (Portugal), Bernard J. Gersh (USA), Anselm K. Gitt (Germany), Jean-Sebastien Hulot (France), Nikolaus Marx (Germany), Lionel H. Opie (South Africa), Matthias Pfisterer (Switzerland), Eva Prescott (Denmark), Frank Ruschitzka (Switzerland), Manel Sabaté (Spain), Roxy Senior (UK), David Paul Taggart (UK), Ernst E. van der Wall (Netherlands), Christiaan J.M. Vrints (Belgium).

European Heart Journal Advance Access published August 30, 2013

EUROPEAN SOCIETY OF CARDIOLOGY®

European Heart Journal
doi:10.1093/eurheartj/eht296

ESC GUIDELINES

Objetivos del tratamiento farmacológico en la enfermedad arterial coronaria estable (EACE)

1. Alivio de los síntomas
2. Prevención de los eventos CV

↓

Aparición de disfunción ventricular izquierda

7.1.3 Pharmacological management of stable coronary artery disease patients

7.1.3.1 Aims of treatment

The two aims of the pharmacological management of stable CAD patients are to obtain relief of symptoms and to prevent CV events.

Relief of anginal symptoms: rapidly acting formulations of nitroglycerin are able to provide immediate relief of the angina symptoms once the episode has started or when the symptom is likely to occur (immediate treatment or prevention of angina). Anti-ischaemic drugs—but also lifestyle changes, regular exercise training, patient education and revascularization—all have a role to play in minimizing or eradicating symptoms over the long term (long-term prevention).

To prevent the occurrence of CV events: efforts to prevent MI and death in coronary disease focus primarily on reducing the incidence of acute thrombotic events and the development of ventricular dysfunction. These aims are achieved by pharmacological or lifestyle interventions which: (i) reduce plaque progression; (ii) stabilize plaque, by reducing inflammation and (iii) prevent thrombosis, should plaque rupture or erosion occur. In patients with severe lesions in coronary arteries supplying a large area of jeopardized myocardium, a combined pharmacological and revascularization strategy

2013 ESC guidelines on the management of stable coronary artery disease

Angina/ischaemia[d] relief			
Short-acting nitrates are recommended.	I	B	3, 329
First-line treatment is indicated with ß-blockers and/or calcium channel blockers to control heart rate and symptoms.	I	A	3, 331
For second-line treatment it is recommended to add long-acting nitrates or ivabradine or nicorandil or ranolazine, according to heart rate, blood pressure and tolerance.	IIa	B	177, 307, 3, 199, 284, 286, 308, 319-321, 328, 364
For second-line treatment, trimetazidine may be considered.	IIb	B	313, 315
According to comorbidities/tolerance it is indicated to use second-line therapies as first-line treatment in selected patients.	I	C	-
In asymptomatic patients with large areas of ischaemia (>10%) ß-blockers should be considered.	IIa	C	-
In patients with vasospastic angina, calcium channel blockers and nitrates should be considered and beta-blockers avoided.	IIa	B	3, 365

European Heart Journal. 2013

Saxagliptin and Cardiovascular Outcomes in Patients with Type 2 Diabetes Mellitus

SAVOR-TIMI 53 trial

Table 2. Prespecified Clinical End Points.*

End Point	Saxagliptin (N=8280)	Placebo (N=8212)	Hazard Ratio (95% CI)	P Value
	no. (%)			
Cardiovascular death, myocardial infarction, or stroke: primary efficacy end point	613 (7.3)	609 (7.2)	1.00 (0.89–1.12)	0.99
Cardiovascular death, myocardial infarction, stroke, hospitalization for unstable angina, heart failure, or coronary revascularization: secondary efficacy end point	1059 (12.8)	1034 (12.4)	1.02 (0.94–1.11)	0.66
Death from any cause	420 (4.9)	378 (4.2)	1.11 (0.96–1.27)	0.15
Death from cardiovascular causes	269 (3.2)	260 (2.9)	1.03 (0.87–1.22)	0.72
Myocardial infarction	265 (3.2)	278 (3.4)	0.95 (0.80–1.12)	0.52
Ischemic stroke	157 (1.9)	141 (1.7)	1.11 (0.88–1.39)	0.38
Hospitalization for unstable angina	97 (1.2)	81 (1.0)	1.19 (0.89–1.60)	0.24
Hospitalization for heart failure	289 (3.5)	228 (2.8)	1.27 (1.07–1.51)	0.007
Hospitalization for coronary revascularization	423 (5.2)	459 (5.6)	0.91 (0.80–1.04)	0.18
Doubling of creatinine level, initiation of dialysis, renal transplantation, or creatinine >6.0 mg/dl (530 μmol/liter)	194 (2.2)	178 (2.0)	1.08 (0.88–1.32)	0.46
Hospitalization for hypoglycemia	53 (0.6)	43 (0.5)	1.22 (0.82–1.83)	0.33

Prior heart failure — no. (%) 1056 (12.8) Saxag vs 1049 (12.8) vs plac

Scirica BM et al. N Engl J Med 2013; 369:1317-1326

Alogliptin after Acute Coronary Syndrome in Patients with Type 2 Diabetes

EXAMINE trial

Table 3. Major Safety End Points.

End Point	Placebo (N = 2679)	Alogliptin (N = 2701)	Hazard Ratio for Alogliptin Group (95% CI)	P Value*
	no. (%)			
Primary end point†	316 (11.8)	305 (11.3)	0.96 (≤1.16)‡	0.32
Components of primary end point				
Death from cardiovascular causes	111 (4.1)	89 (3.3)	0.79 (0.60–1.04)	0.10
Nonfatal myocardial infarction	173 (6.5)	187 (6.9)	1.08 (0.88–1.33)	0.47
Nonfatal stroke	32 (1.2)	29 (1.1)	0.91 (0.55–1.50)	0.71
Principal secondary end point§	359 (13.4)	344 (12.7)	0.95 (≤1.14)‡	0.26
Other end points				
Death from any cause	173 (6.5)	153 (5.7)	0.88 (0.71–1.09)	0.23
Death from cardiovascular causes¶	130 (4.9)	112 (4.1)	0.85 (0.66–1.10)	0.21

Congestive heart failure 744 (27.8) Plac. vs 757 (28.0) Alogl.

In addition, alogliptin neither induced new-onset heart failure nor worsened heart-failure outcomes in patients with a history of heart failure before randomization.

White WB et al. N Engl J Med 2013;369:1327-35.

Vildagliptin in Ventricular Dysfunction Diabetes (VIVIDD) trial

254 patients with type 2 diabetes mellitus, Glycated haemoglobin (HbA1c) 6.5 to 10%, and NYHA class I to III were randomized to vildagliptin 50mg bid (n=128) or placebo (n=126)

Results:

- The mean increase in the ejection fraction by 52 weeks (primary endpoint) was 4.1 in the vildagliptin group versus 3.5 in the placebo group (P=0.670, confirming non-inferiority) and that the mean glycated haemoglobin (HbA1c) difference between vildagliptin and placebo at 16 weeks (secondary endpoint) was 0.62% (P<0.001).
- Additionally vildagliptin, in comparison to placebo showed unexpected increases in left ventricular end-diastolic volume (LVEDV, p=0.007), end systolic volume (LVESV, p=0.06) and stroke volume (p=0.002). By 52 weeks BNP had fallen by 14%, relative to baseline, in the placebo group versus 28% in the vildagliptin group.
- Worsening of HF occurred in 22 patients in the placebo group versus 23 in the vildagliptin group; and death from any cause occurred in four patients in the placebo group versus 11 in the vildagliptin group

John McMurray, HFA 2013

John McMurray, HFA 2013

“I think that the real take home message from this study is that we know virtually nothing about the effects of treatment for diabetes in patients with heart failure”

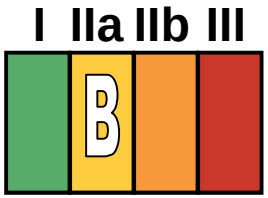
Pharmacological Treatment for Stage C HF*r*EF

No Benefit

Anticoagulation is not recommended in patients with chronic HF*r*EF without AF, a prior thromboembolic event, or a cardioembolic source.

No Benefit

Statins are not beneficial as adjunctive therapy when prescribed solely for the diagnosis of HF in the absence of other indications for their use.



Omega-3 polyunsaturated fatty acid (PUFA) supplementation is reasonable to use as adjunctive therapy in patients with NYHA class II-IV symptoms and HF*r*EF or HF*p*EF, unless contraindicated, to reduce mortality and cardiovascular hospitalizations.

Nuevos anticoagulantes orales en IC y CI: COMMANDER HF

Clinical Protocol

A Randomized, Double-blind, Event-driven, Multicenter Study Comparing the Efficacy and Safety of Oral Rivaroxaban with Placebo for Reducing the Risk of Death, Myocardial Infarction or Stroke in Subjects with Chronic Heart Failure and Significant Coronary Artery Disease Following a Hospitalization for Exacerbation of Heart Failure

COMMANDER HF Study

Protocol RIVAROXHFA3001; Phase 3
BAY 59-7939/16302

- **The trial will assess the safety and efficacy of 2.5 mg twice daily rivaroxaban compared to placebo (on a background of standard treatment) in reducing the risk of death, myocardial infarction (MI) or stroke in 5,000 patients with chronic HF and significant CAD following hospitalization.**

- **The primary efficacy outcome is the composite of all-cause mortality, MI, or stroke.**

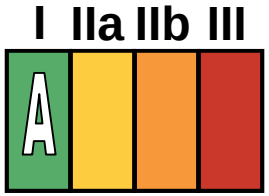
- **The principal safety outcome is the composite of fatal bleeding or bleeding into a critical space with a potential for permanent disability.**

- **Patients on sinus rythm**

Treatment of HFpEF

Recommendations	COR	LOE
Systolic and diastolic blood pressure should be controlled according to published clinical practice guidelines	I	B
Diuretics should be used for relief of symptoms due to volume overload	I	C
Coronary revascularization for patients with CAD in whom angina or demonstrable myocardial ischemia is present despite GDMT	IIa	C
Management of AF according to published clinical practice guidelines for HFpEF to improve symptomatic HF	IIa	C
Use of beta-blocking agents, ACE inhibitors, and ARBs for hypertension in HFpEF	IIa	C
ARBs might be considered to decrease hospitalizations in HFpEF	IIb	B
Nutritional supplementation is not recommended in HFpEF	III: No Benefit	C

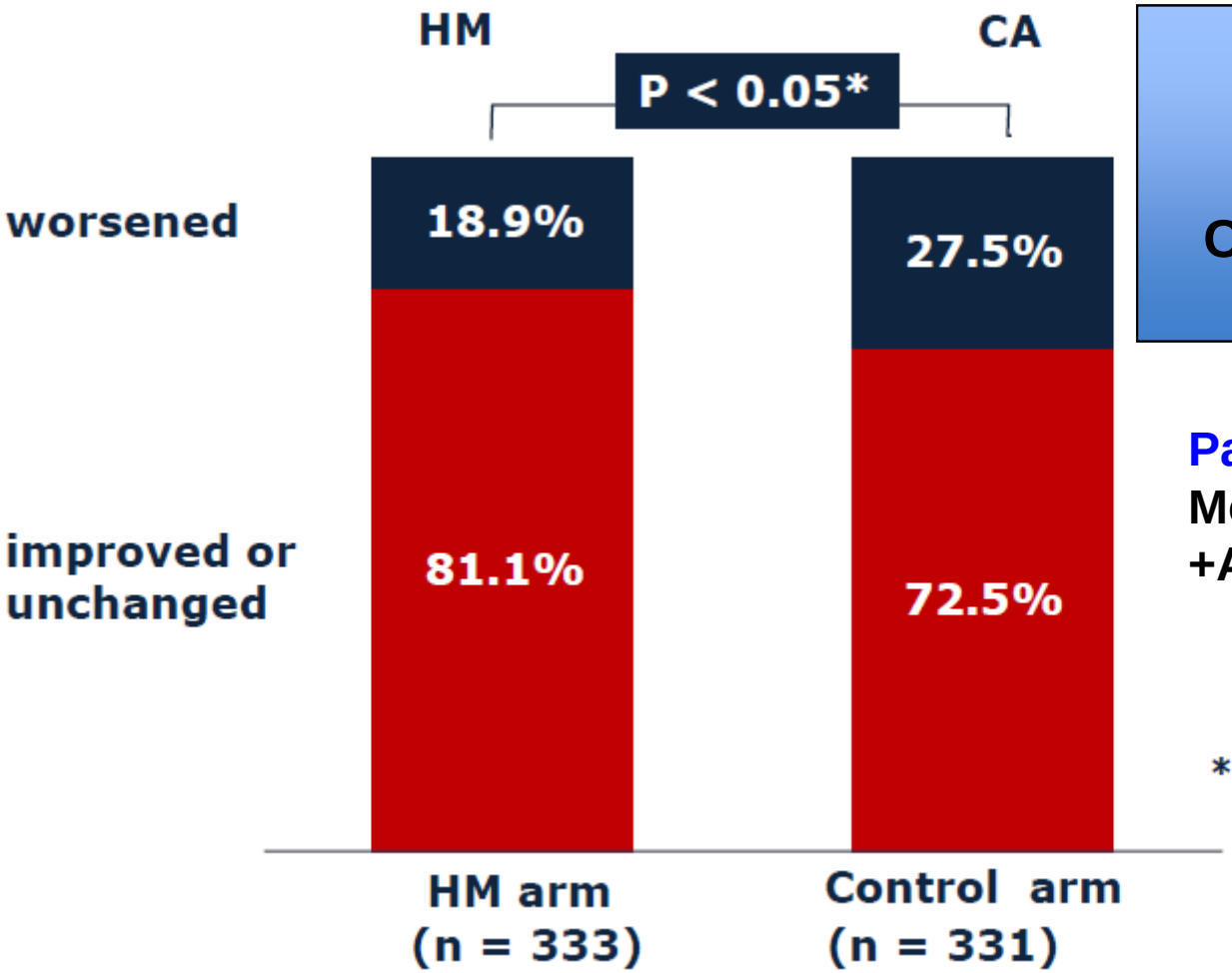
Device Therapy for Stage C HFrEF



ICD therapy is recommended for primary prevention of SCD to reduce total mortality in selected patients with nonischemic DCM or ischemic heart disease at least 40 days post-MI with LVEF of 35% or less, and NYHA class II or III symptoms on chronic GDMT, who have reasonable expectation of meaningful survival for more than 1 year.

CRT is indicated for patients who have LVEF of 35% or less, sinus rhythm, left bundle-branch block (LBBB) with a QRS duration of 150 ms or greater, and NYHA class II, III, or ambulatory IV symptoms on GDMT.

In-Time Study: The Influence of Implant-Based Home Monitoring on the Clinical Status of Heart Failure Patients with Impaired Left Ventricular Function



664 aleatorizados
NYHA :II-IV
FEVI :<0.35
CRT-D 58% Bicameral :42%

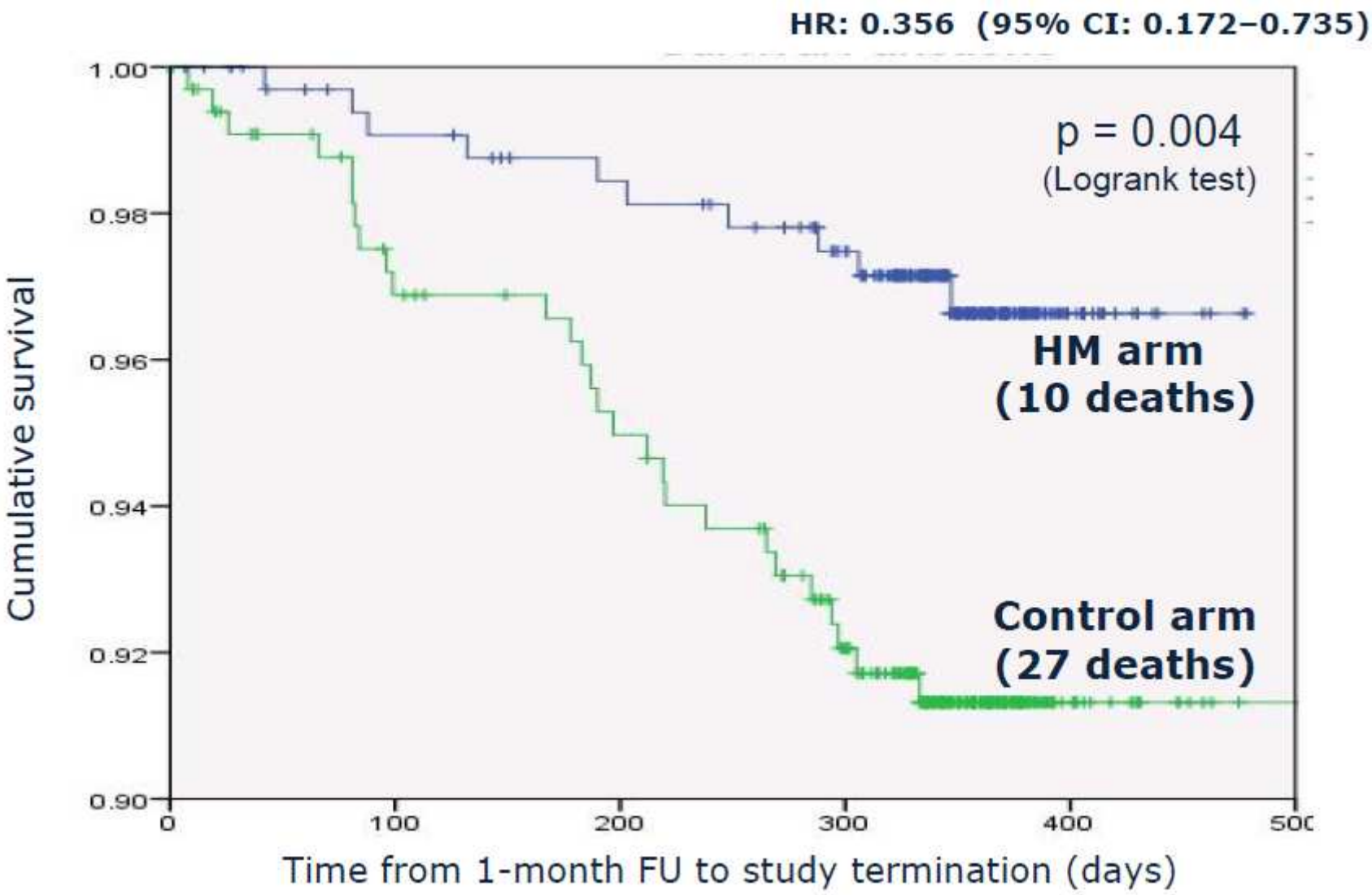
Packer score modificado:
Mortalidad +Rehosp.por IC +Autoevaluacion NYHA

*χ2 test

HINDRICKS G. ESC 2013

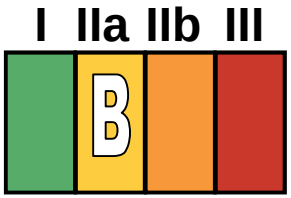
IN-TIME

All-cause mortality



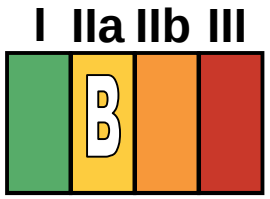
HINDRICKS G. ESC 2013

Surgical Interventional Treatment of HF



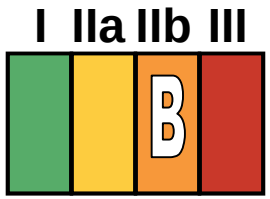
CABG or medical therapy is reasonable to improve morbidity and cardiovascular mortality for patients with severe LV dysfunction (EF <35%), HF, and significant CAD.

Coronary artery revascularization via CABG or percutaneous intervention is indicated for patients (HFpEF and HFrEF) on GDMT with angina and suitable coronary anatomy, especially for a left main stenosis (>50%) or left main equivalent disease.

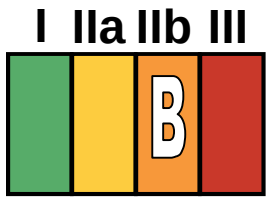


CABG to improve survival is reasonable in patients with mild to moderate LV systolic dysfunction (EF 35% to 50%) and significant (≥70% diameter stenosis) multivessel CAD or proximal LAD coronary artery stenosis when viable myocardium is present in the region of intended revascularization.

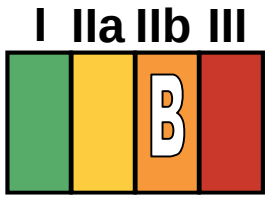
Surgical/Percutaneous/Transcatheter Interventional Treatment of HF



CABG may be considered with the intent of improving survival in patients with ischemic heart disease with severe LV systolic dysfunction (EF <35%), and operable coronary anatomy whether or not viable myocardium is present.



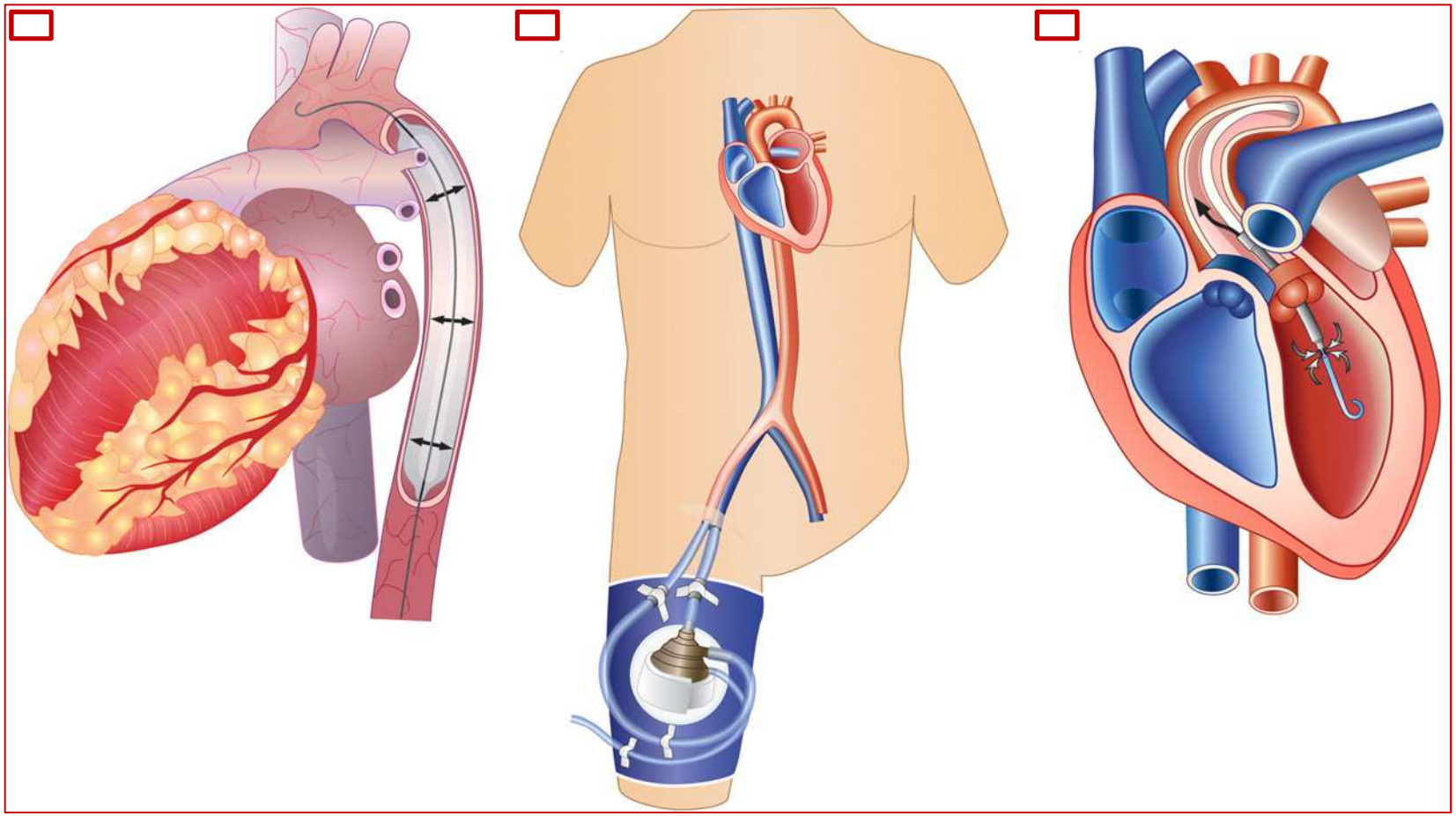
Transcatheter mitral valve repair or mitral valve surgery for functional mitral insufficiency is of uncertain benefit and should only be considered after careful candidate selection and with a background of GDMT.



Surgical reverse remodeling or LV aneurysmectomy may be considered in carefully selected patients with HF*r*EF for specific indications including intractable HF and ventricular arrhythmias.

Esquemas de los dispositivos de AVM percutánea usados en el shock cardiogénico

Aportan GC < 5 l /min



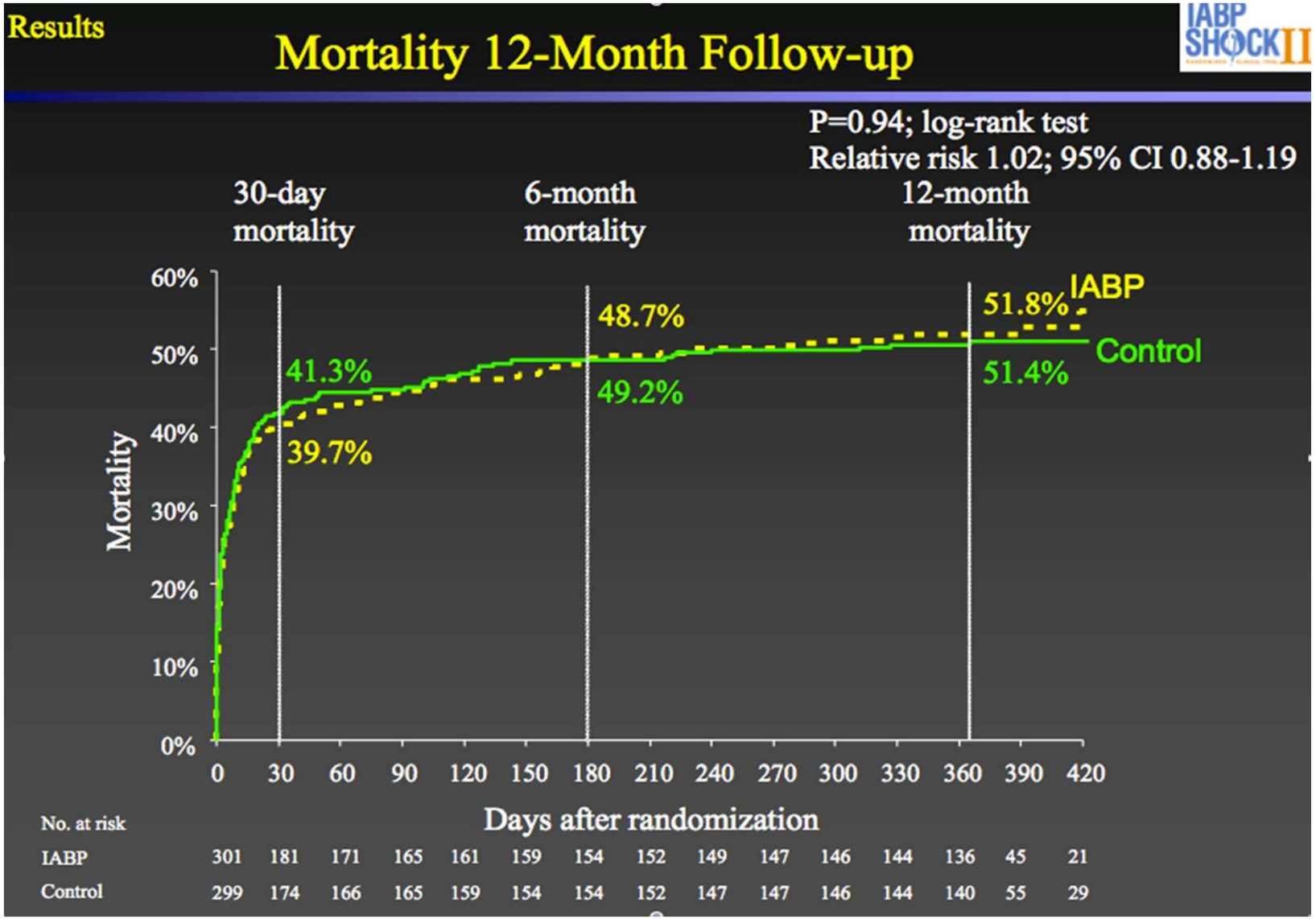
Balón de contrapulsación intraaórtico (BCIA)

Tandem Heart ™

Impella 2.5 ®.

Thiele H et al. Eur Heart J 2010;31:1828-1835

Intraaortic balloon support for myocardial infarction with cardiogenic shock.



THIELE H. ESC 2013

Intraaortic balloon support for myocardial infarction with cardiogenic shock.

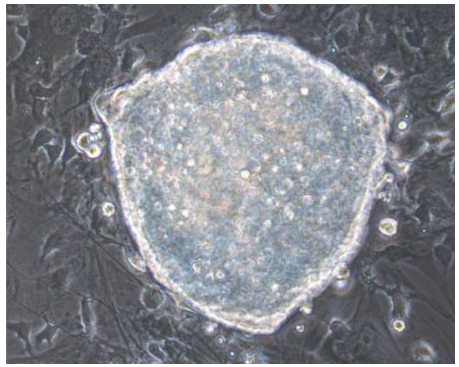
Results

Multivariable Predictors of 12-Month Mortality

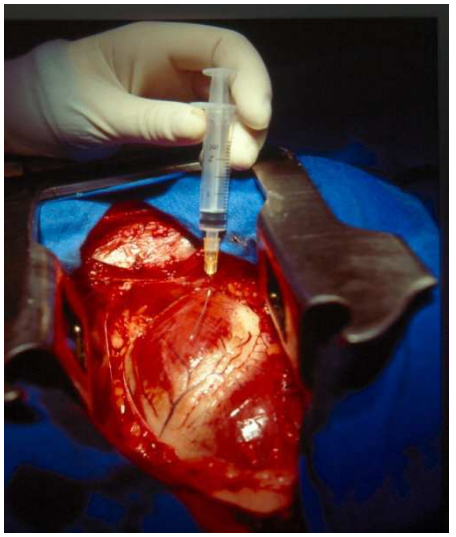
IABP SHOCK II

	Univariable		Stepwise multivariable	
Variable	Hazard Ratio (95% CI)	P-Value	Hazard Ratio (95% CI)	P-Value
Single vessel coronary artery disease	0.68 (0.51-0.92)	0.01	-	-
Mechanical ventilation	1.23 (0.98-1.55)	0.07	-	-
Cold, clammy skin and extremities	1.55 (1.11-2.17)	0.01	-	-
Current smoking	0.63 (0.49-0.81)	<0.001	-	-
History of arterial hypertension	1.33 (1.03-1.72)	0.03	-	-
Hemoglobin, mmol/l	0.87 (0.81-0.94)	<0.001	-	-
Hematocrit, %	0.15 (0.04-0.63)	0.01	-	-
Sinus rhythm	0.78 (0.60-1.01)	0.06	-	-
ST-elevation myocardial infarction	0.76 (0.60-0.95)	0.02	-	-
Age, per 10 years	1.33 (1.20-1.47)	<0.001	1.25 (1.12-1.39)	<0.001
History of stroke	2.18 (1.53-3.11)	<0.001	2.00 (1.37-2.93)	<0.001
Baseline serum lactate, per 10 mmol/l	1.43 (1.29-1.57)	<0.001	1.24 (1.10-1.39)	<0.001
Baseline creatinine, per 100 µmol/l	1.38 (1.24-1.54)	<0.001	1.23 (1.08-1.40)	0.002
Altered mental status	1.73 (1.30-2.30)	<0.001	1.57 (1.15-2.16)	0.005
Oliguria (<30 ml/h)	1.73 (1.38-2.18)	<0.001	1.40 (1.08-1.82)	0.010
pH <7.36 at admission	1.58 (1.24-2.01)	<0.001	1.35 (1.02-1.79)	0.036
Left bundle branch block	1.84 (1.37-2.47)	<0.001	1.41 (1.01-1.98)	0.042

THIELE H. ESC 2013



EMERGENT THERAPIES



CARDIAC CELL THERAPY:
Cardiomyoplasty

CARDIAC TISSUE ENGINEERING:
Bioprotheses for the myocardium

NEO-ORGANOGENESIS:
Bioartificial Heart

Adult Bone Marrow Cell Therapy Improves Survival and Induces Long-Term Improvement in Cardiac Parameters

Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION

American Heart Association

Adult Bone Marrow Cell Therapy Improves Survival and Induces Long-Term Improvement in Cardiac Parameters : A Systematic Review and Meta-Analysis
Vinodh Jeevanantham, Matthew Butler, Andre Saad, Ahmed Abdel-Latif, Ewa K. Zuba-Surma and Buddhadeb Dawn

Metaanálisis de 50 estudios :2650 pacientes

Mejoría FEVI : 3.96% 95 IC (2.90 -5.02 p<0.00001

Reducción Tamaño de Infarto: -4.03 95 IC (-5.47 a-6.25 p<0.00001

Reducción Vol. Telesistólico: -8.91 95% IC (-11.5 a -6.25 p<0.00001

- El trasplante de médula ósea mejora la FEVI, reduce el tamaño de infarto y mejora los parámetros de remodelado en pacientes con cardiopatía isquémica .

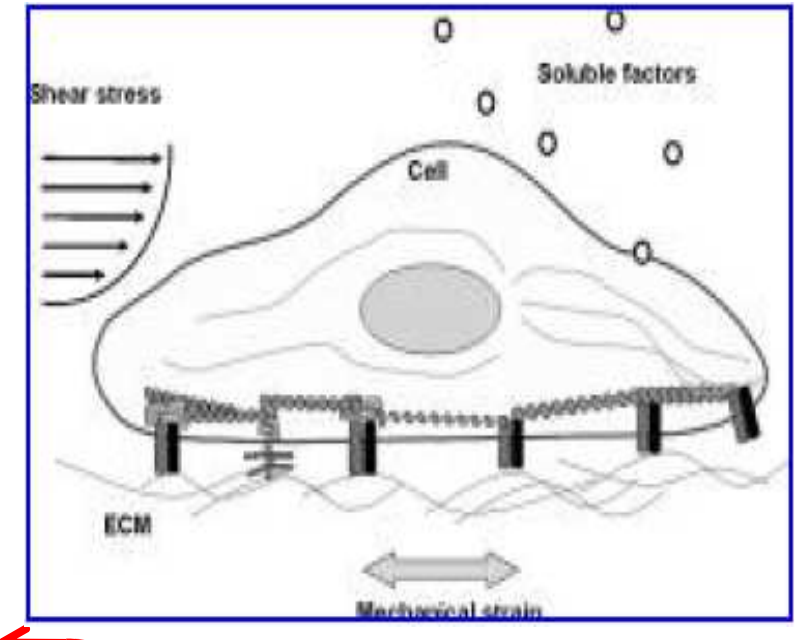
- Los beneficios se mantienen a largo plazo .

- Redujo incidencia de muerte, recurrencia de IAM y trombósis precoz del stent en pacientes con cardiopatia isquémica crónica.

Jeevananthan V et al .Circulation. 2012;126:551-568.

Regenerative Medicine and Tissue Engineering

- Repair/replace damaged tissues
  - Enhance natural regeneration



Cell Source

Embryonic stem cells
Adult stem cells
Progenitor cells

Signals

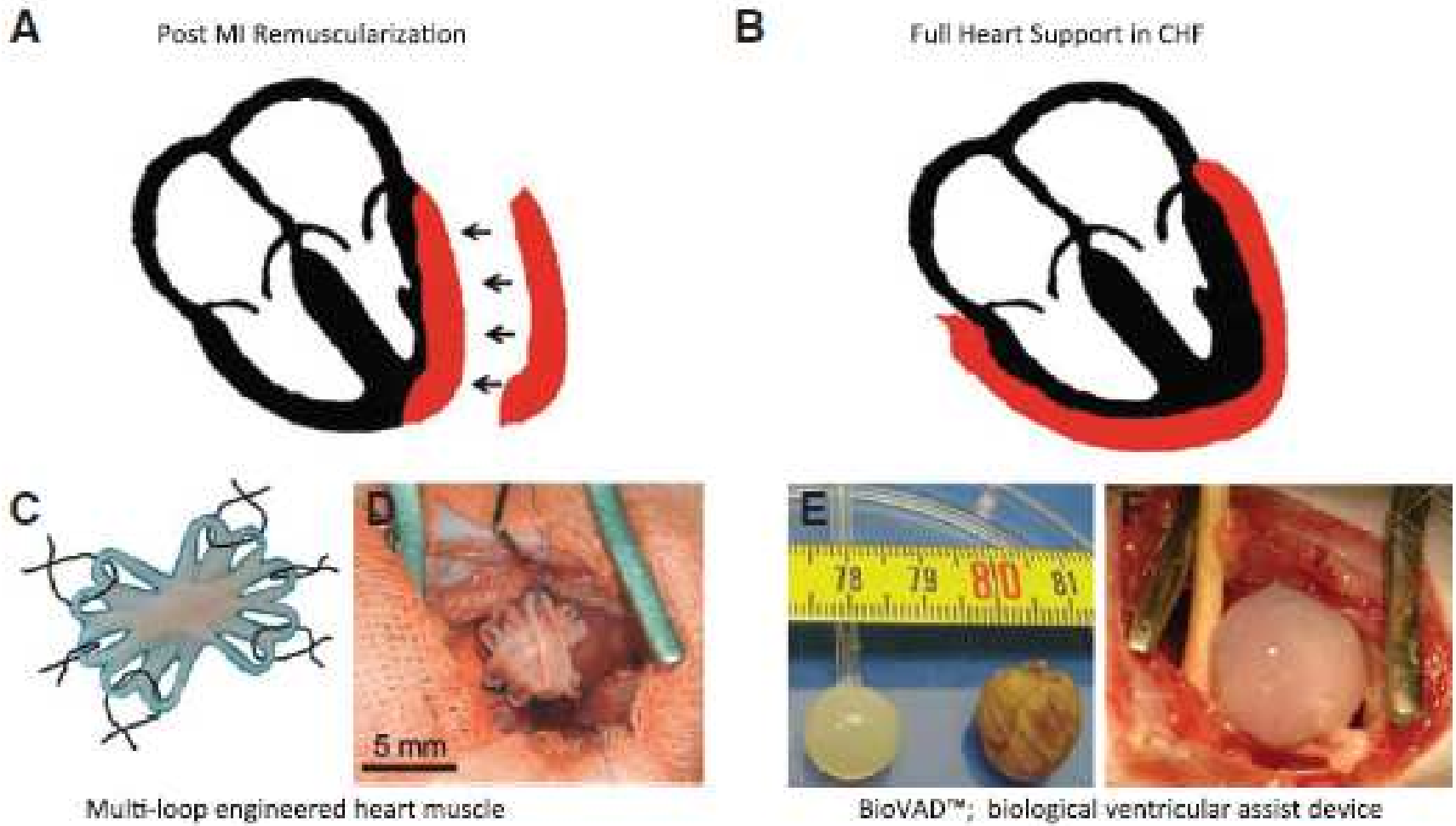
Growth factors
Drugs
Mechanical forces

ECM

Metals
Ceramics
Synthetic polymers
Natural polymers

Regenerative Medicine and Tissue Engineering

“ Patching the Heart ”

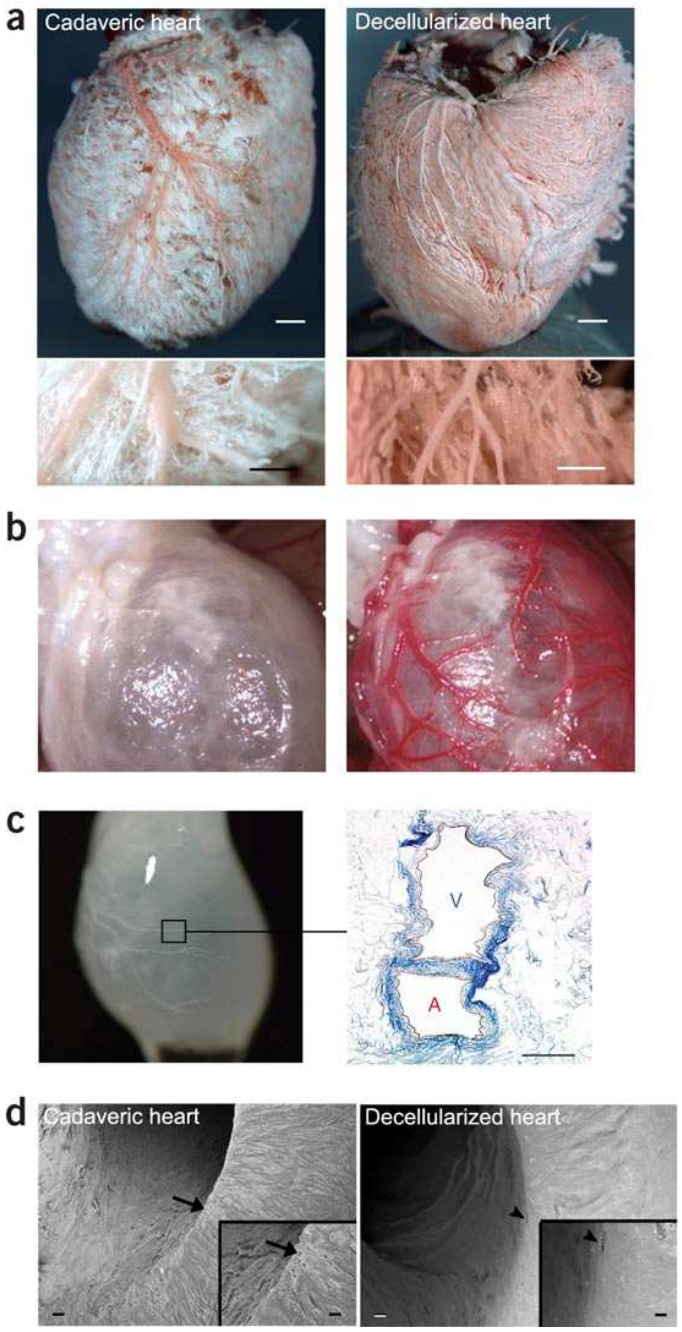


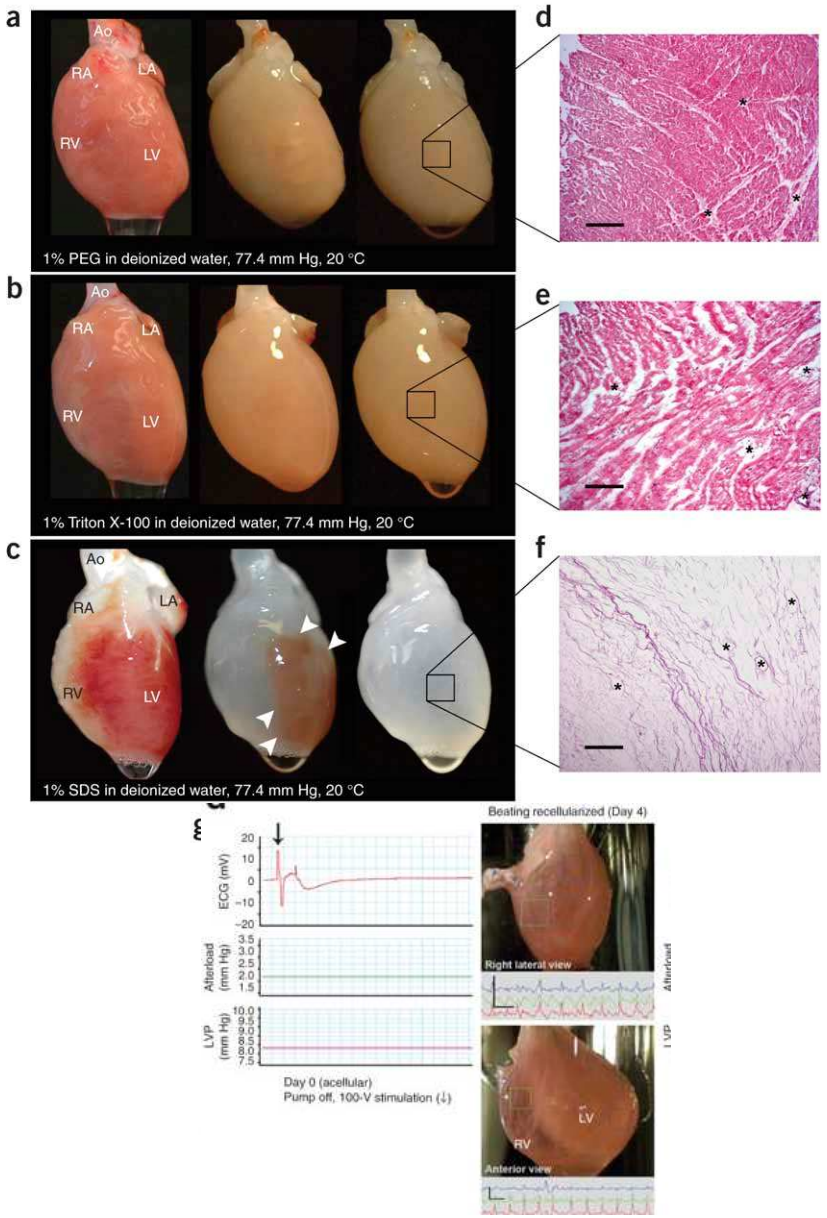
Multi-loop engineered heart muscle

BioVAD™; biological ventricular assist device

Ye L et al. Circ Res. 2013;113:922-32.

NEO-ORGANOGENESIS: Bioartificial Heart

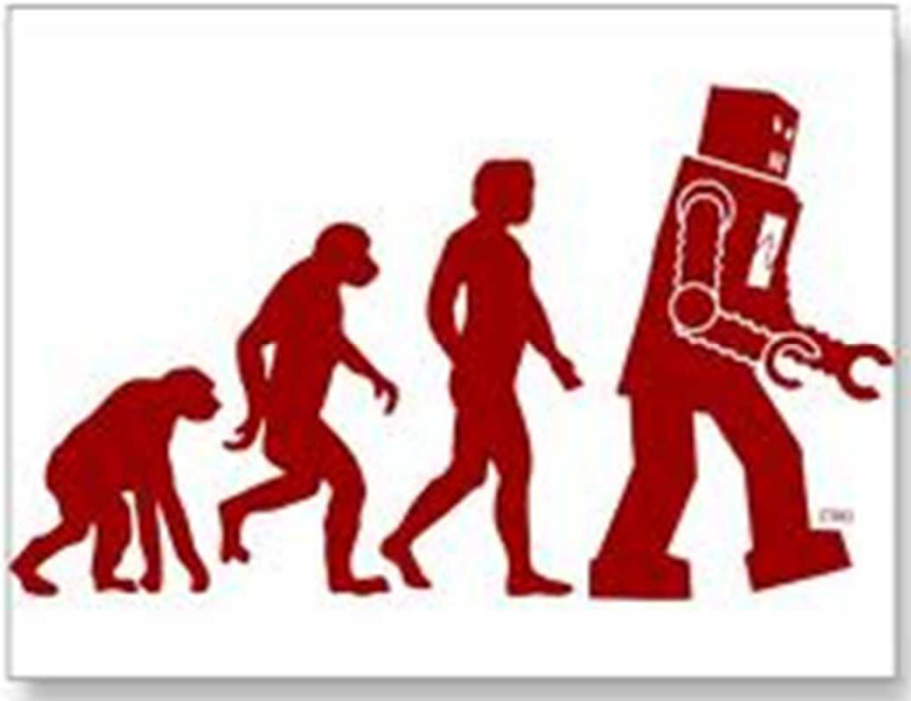


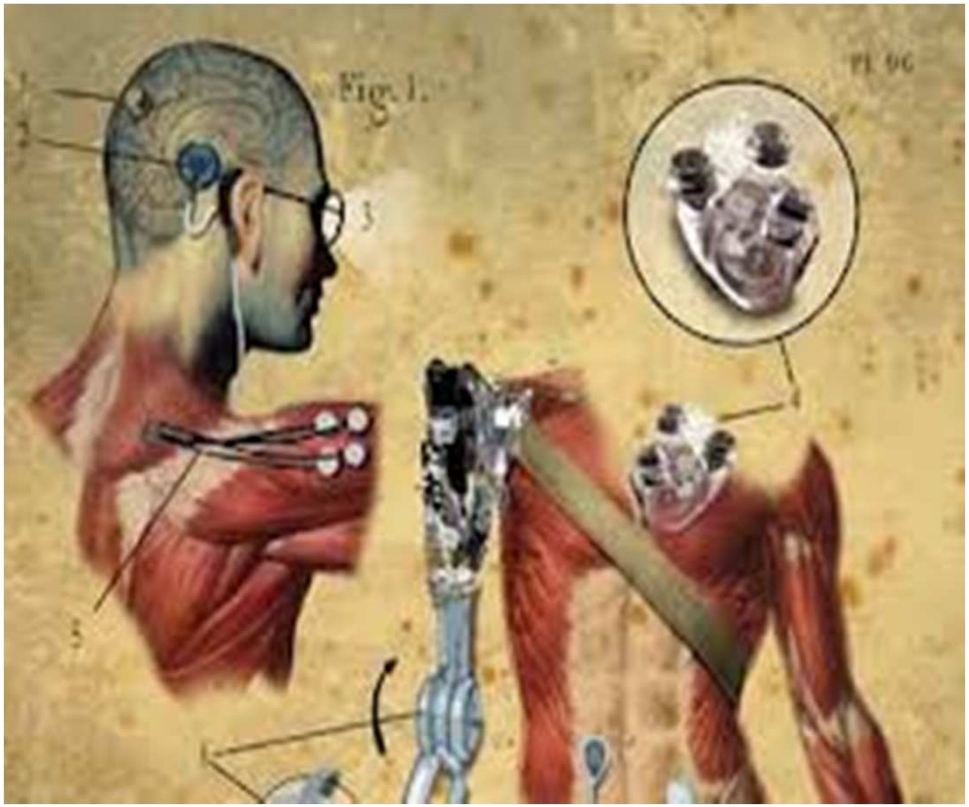


Ott HC et al. Nature Med 2008; 14:213-21

Human evolution

TECHNOLOGICAL PROGRESS

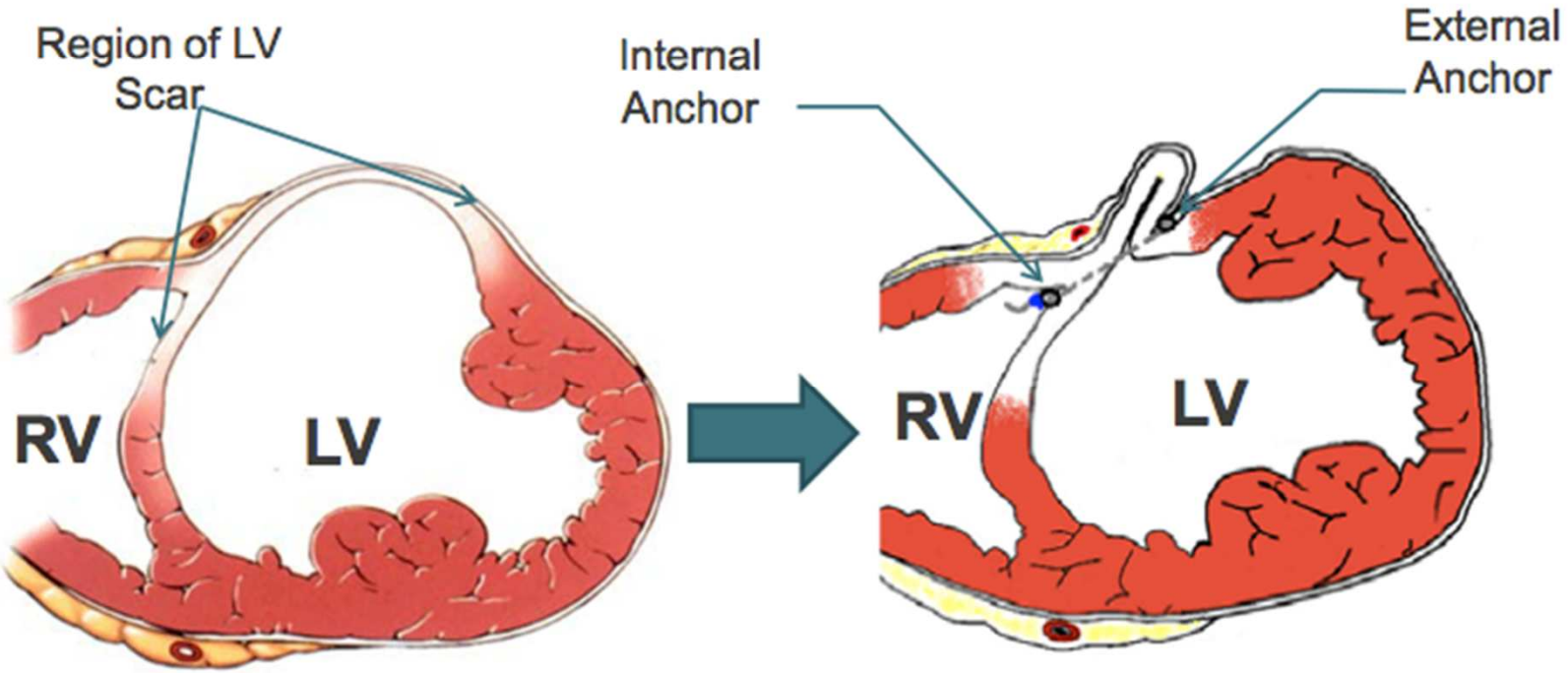




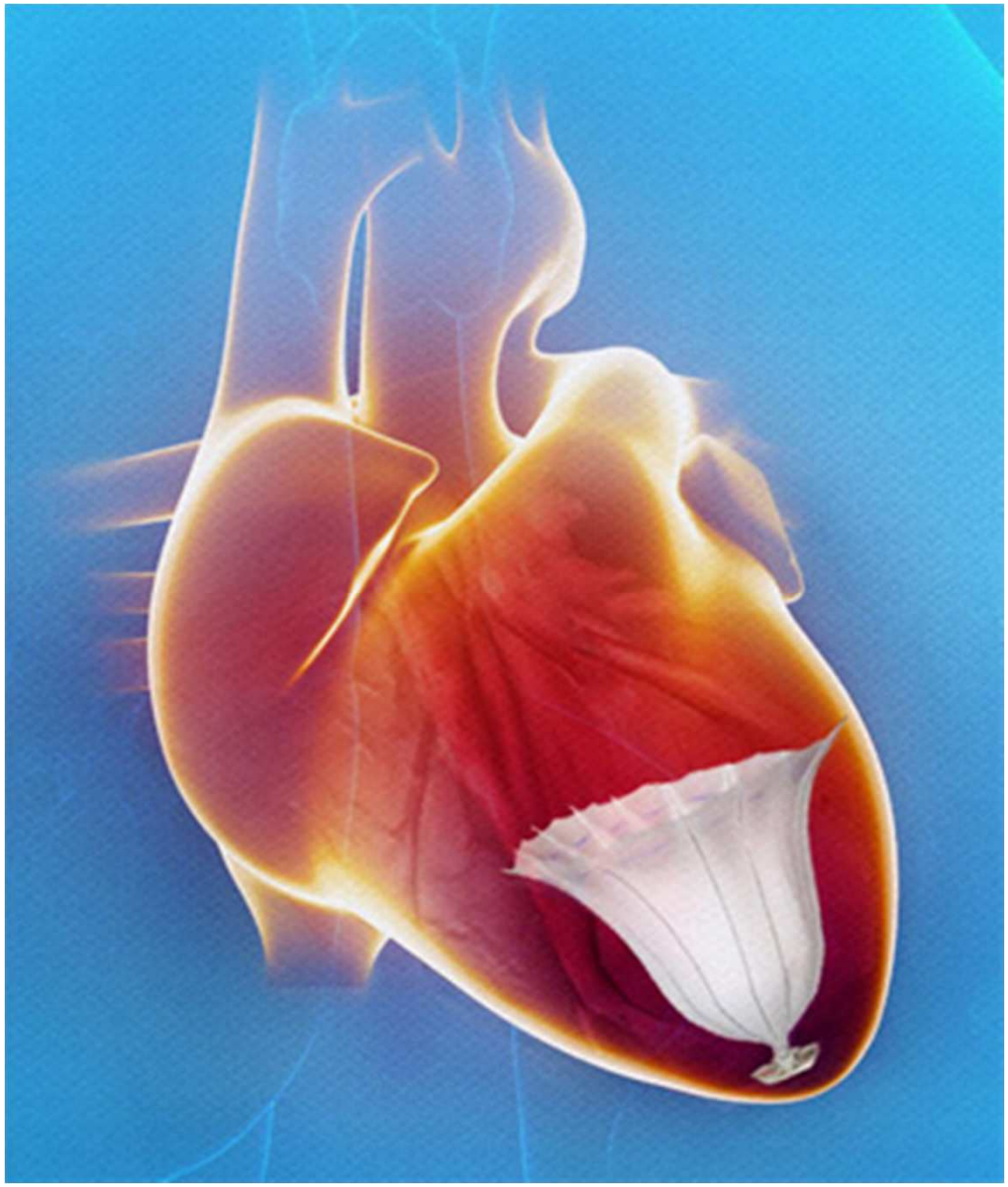
VENTRICULAR RECONSTRUCTION DEVICES

Revivent™

Myocardial Anchoring System



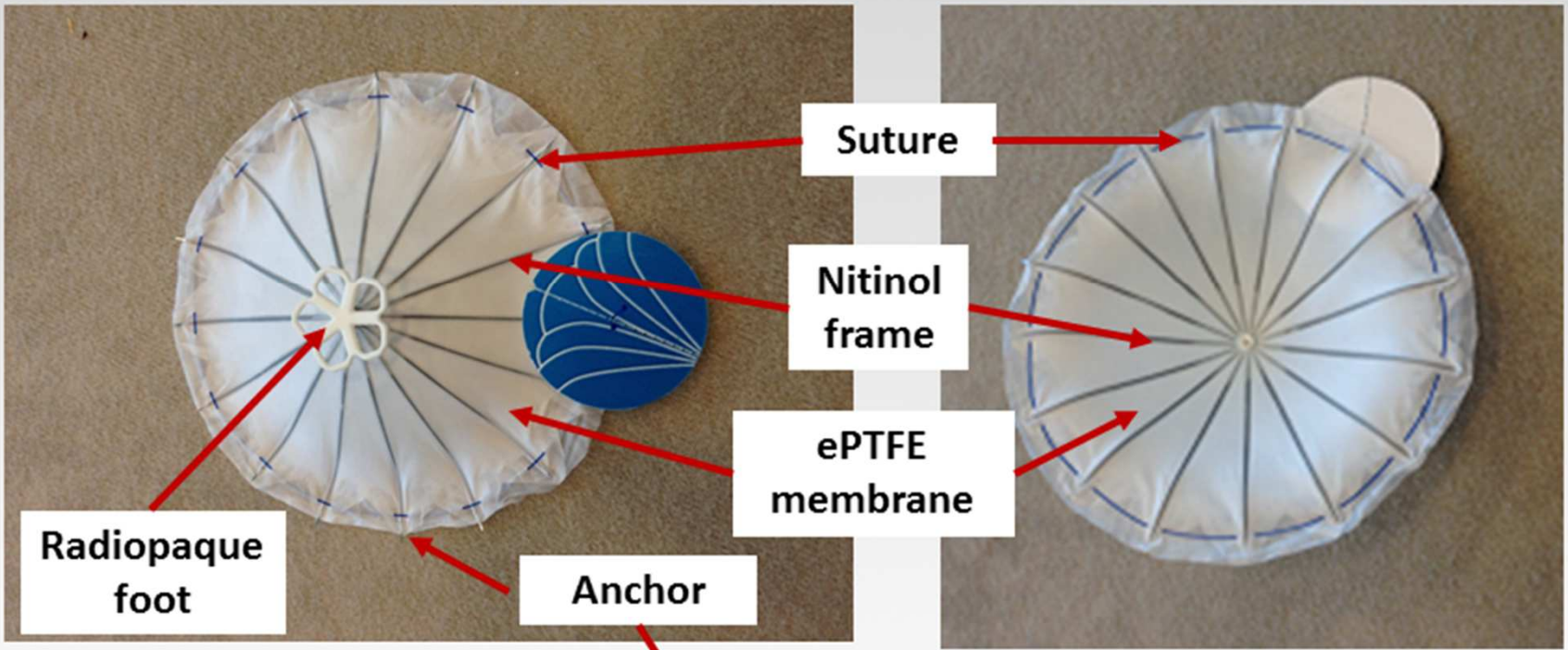
VENTRICULAR RECONSTRUCTION DEVICES



PARACHUTE DEVICE

Parachute™ Device

This is an investigational device, not approved for use in the United States



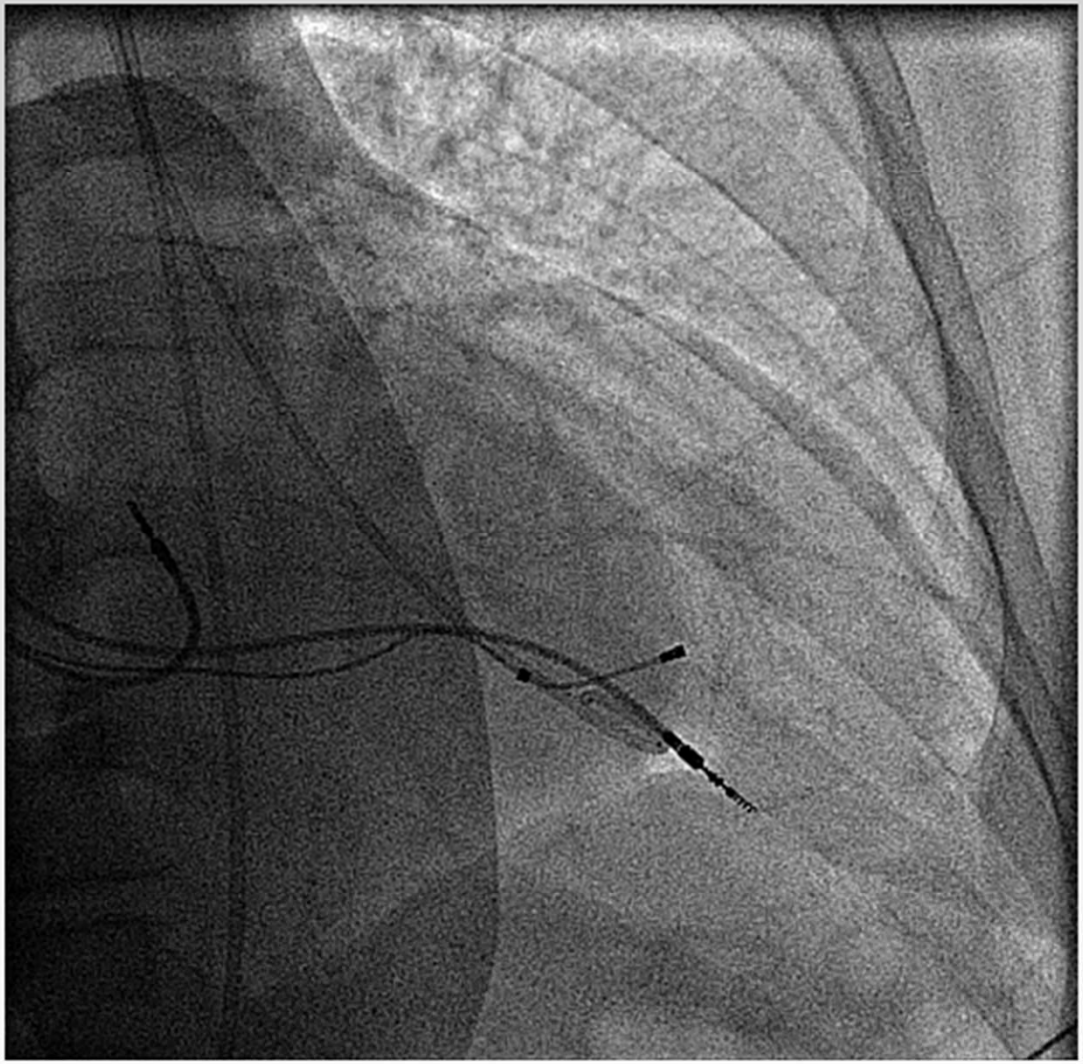
Globally 84 implants to date.
Patients require one year warfarin + aspirin

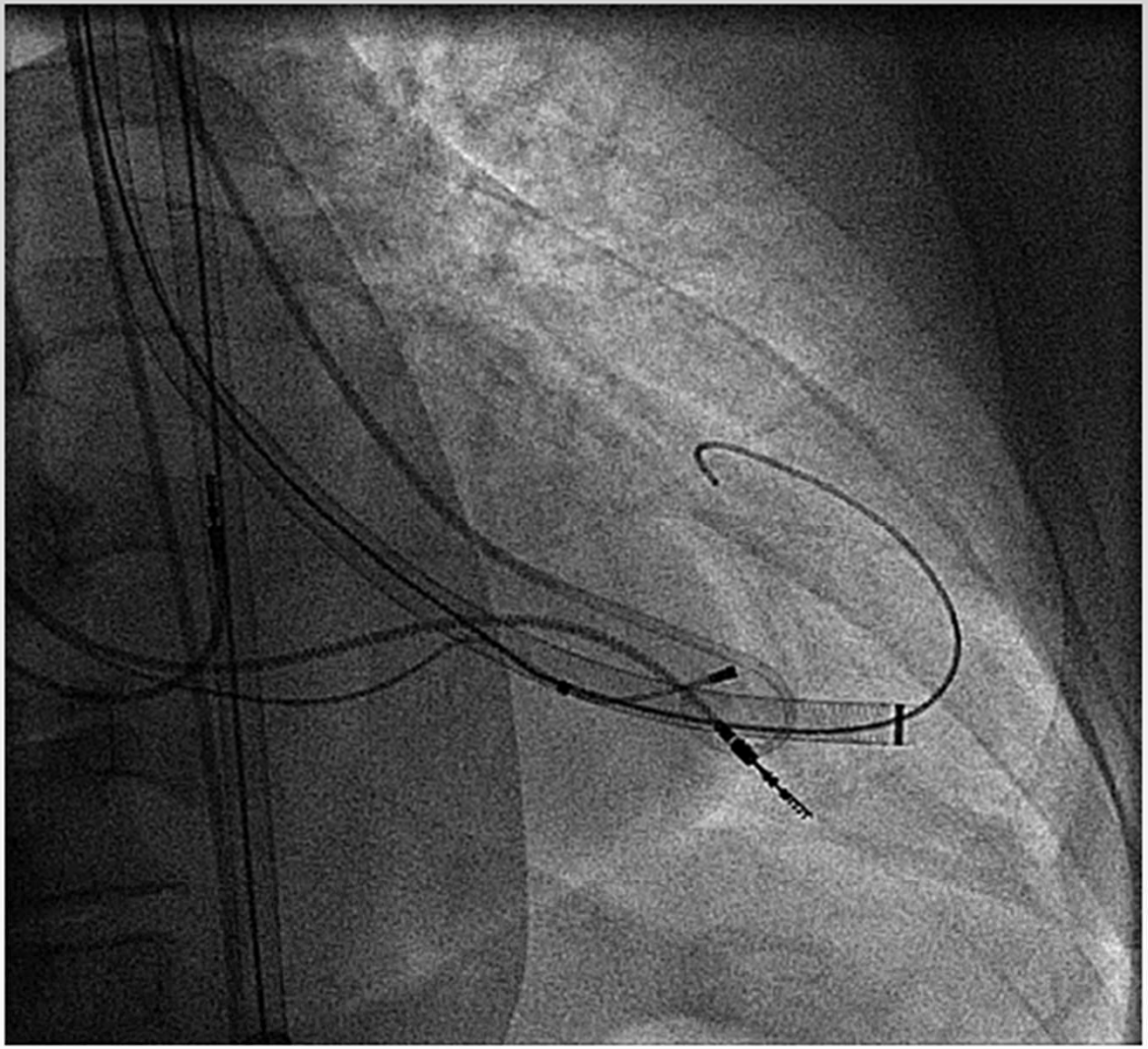
Interventional & Surgery

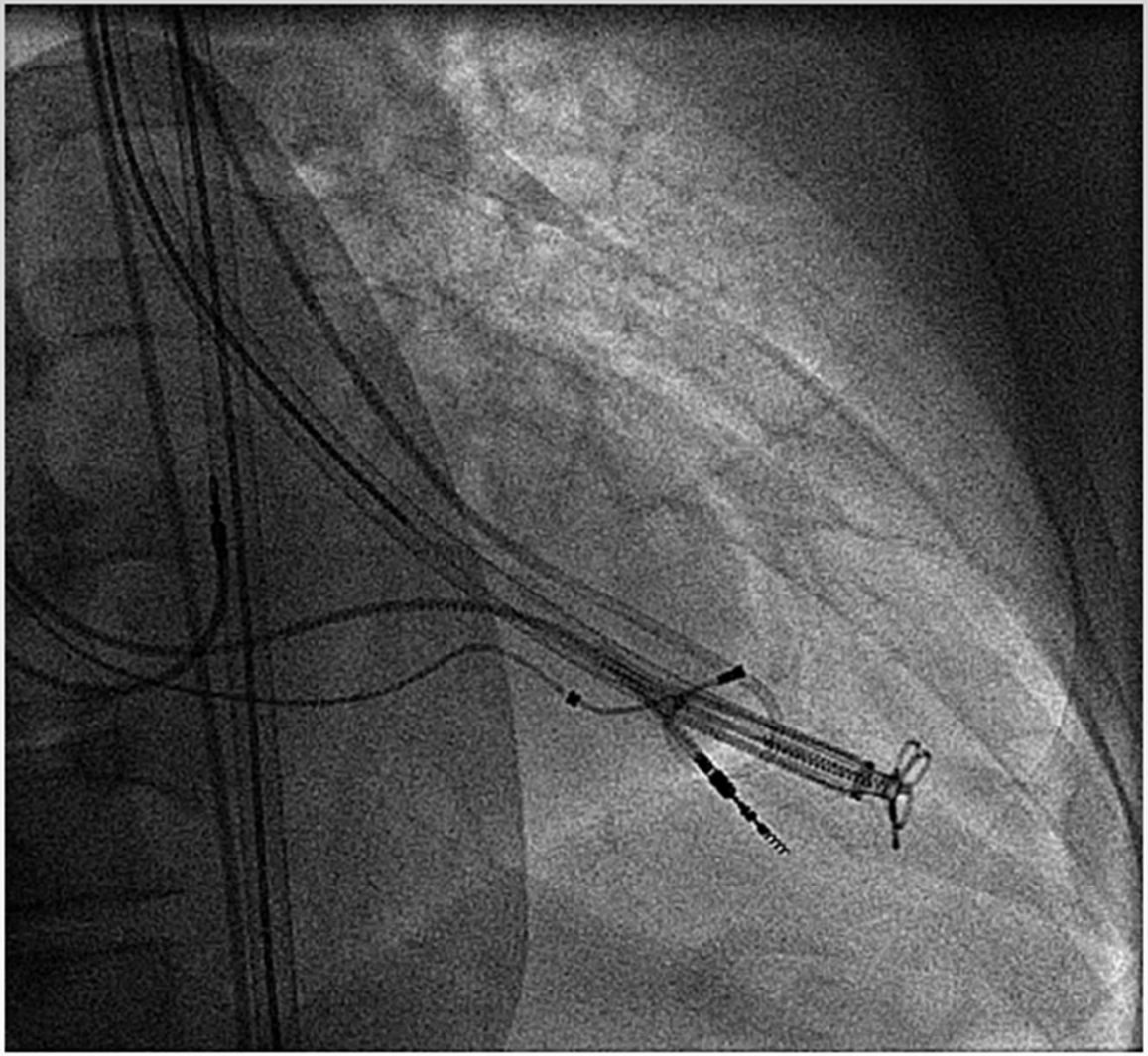
CardioKinetix, Inc., Menlo Park, CA

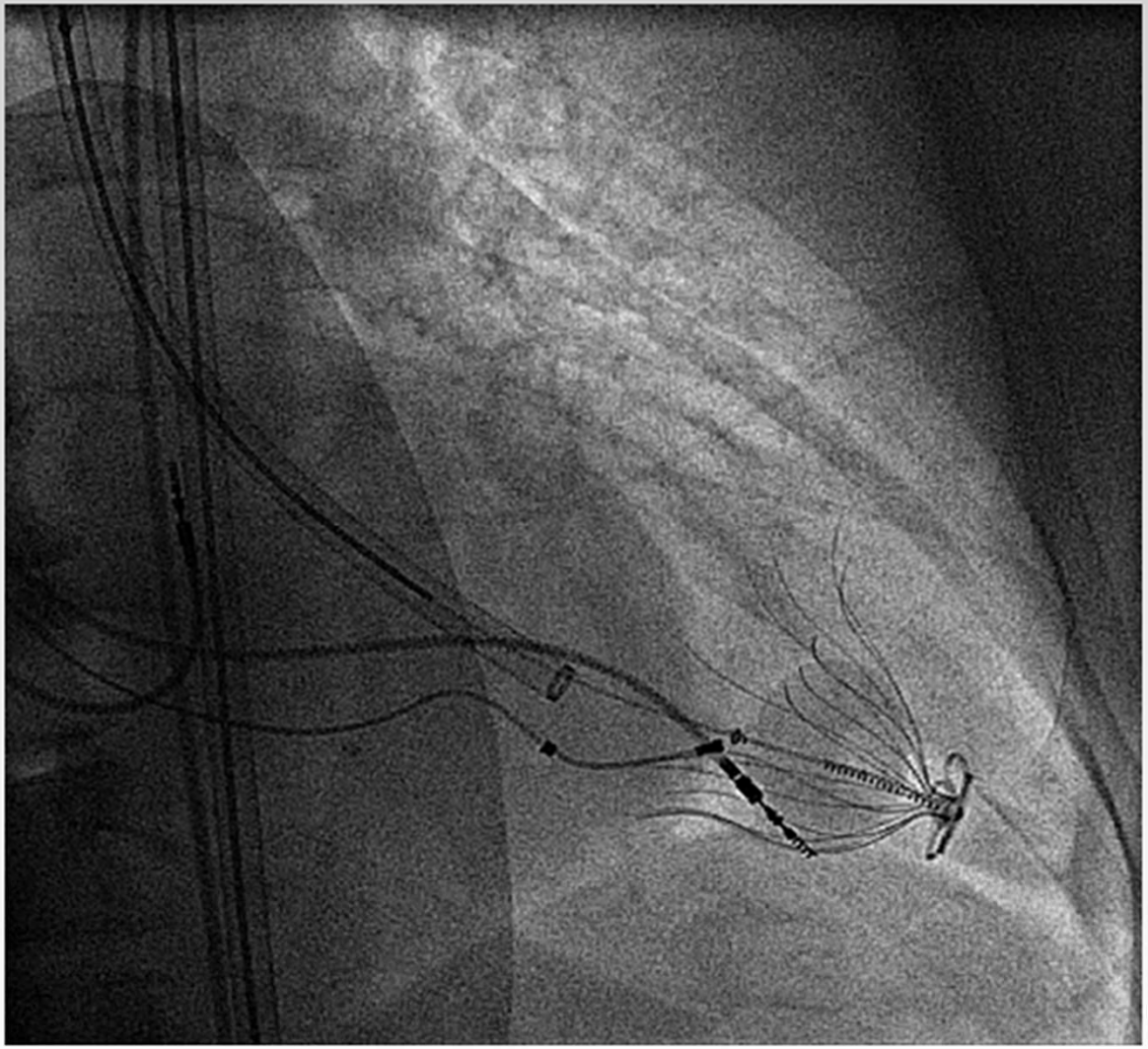
theheart.org from WebMD

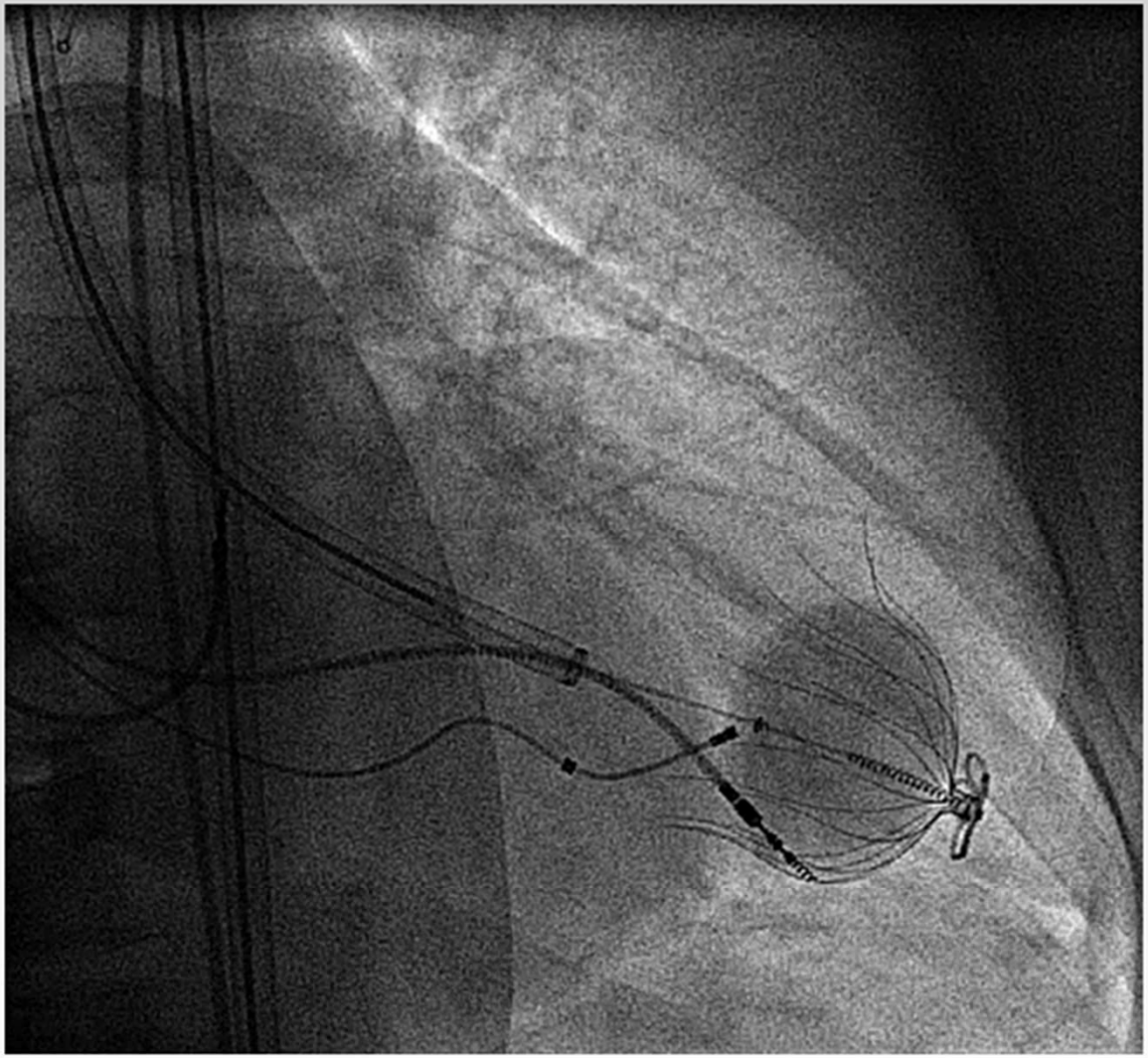
Medscape EDUCATION

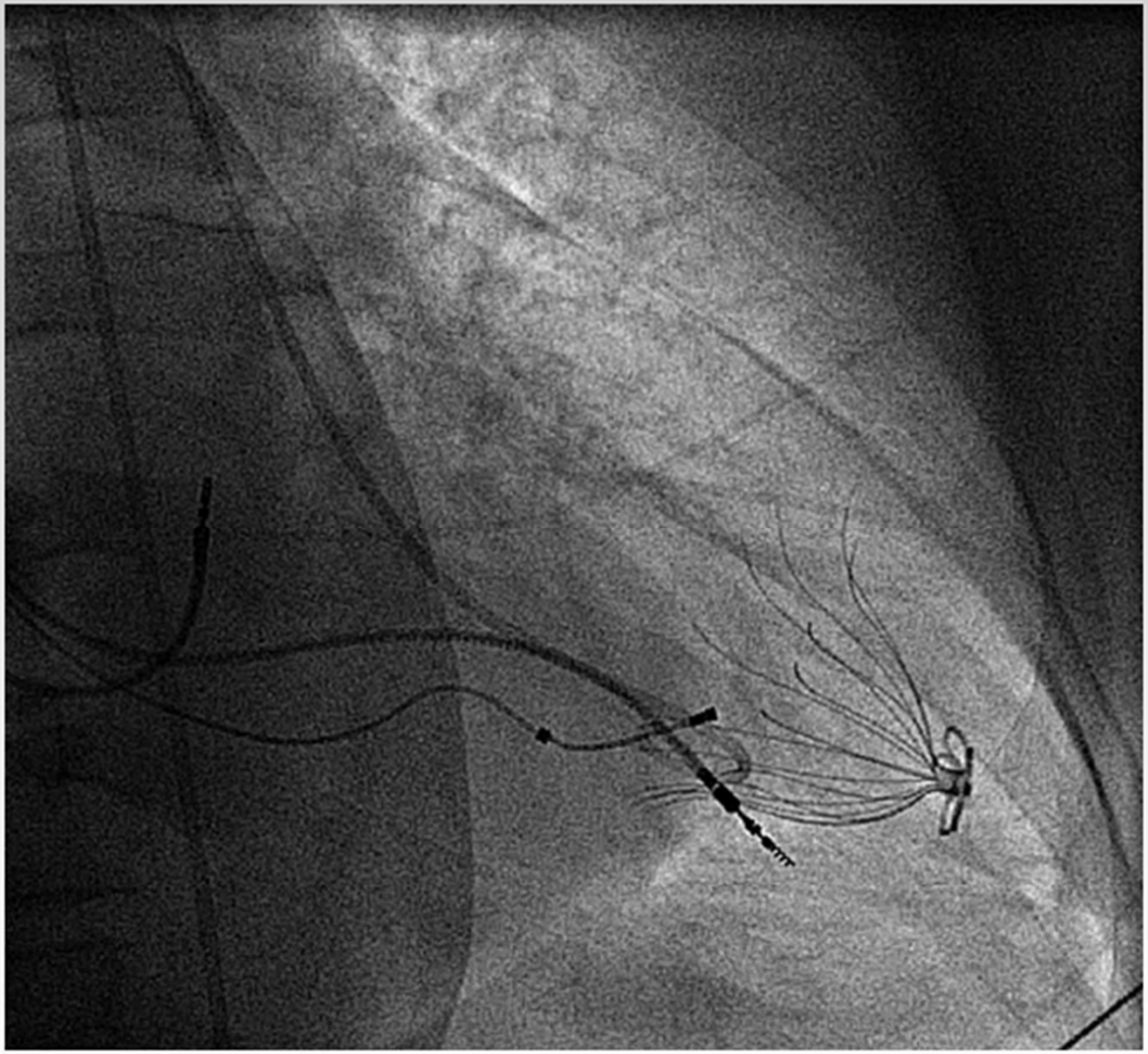


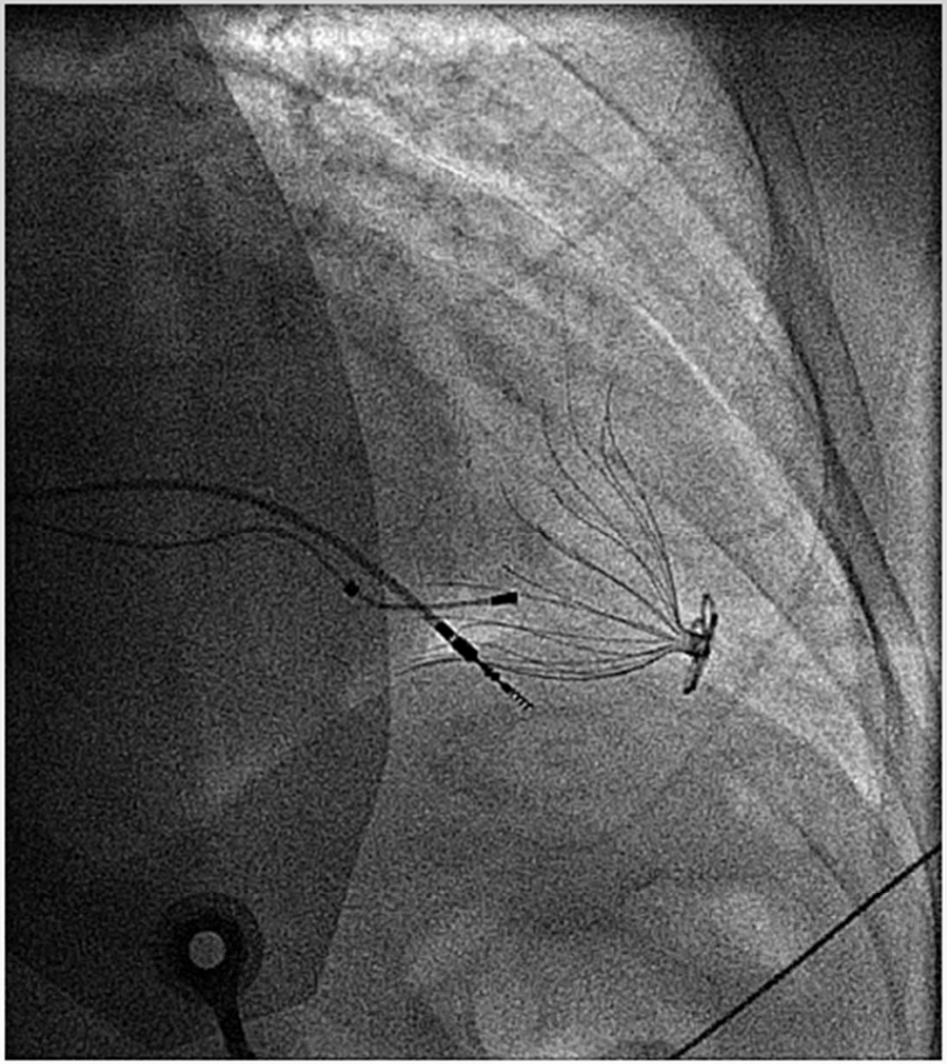


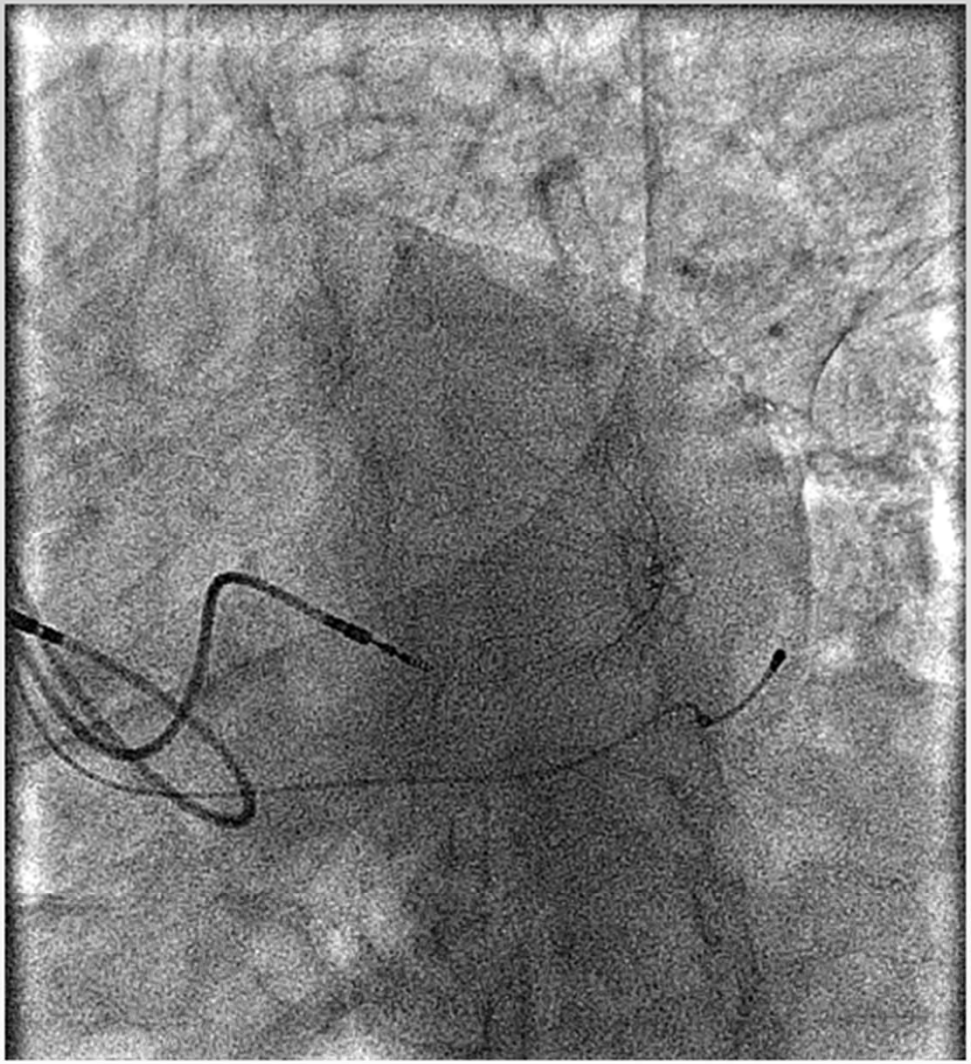






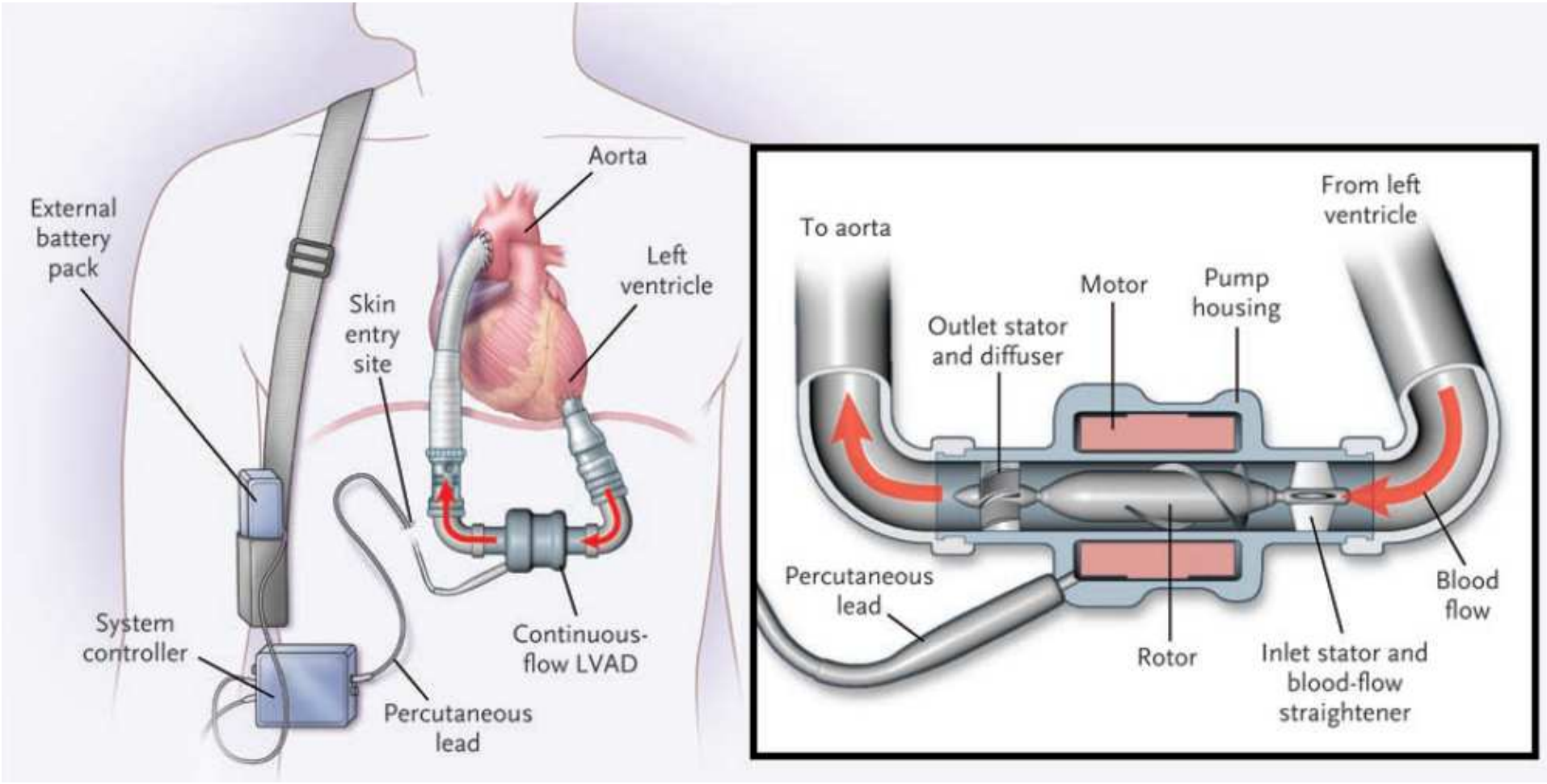






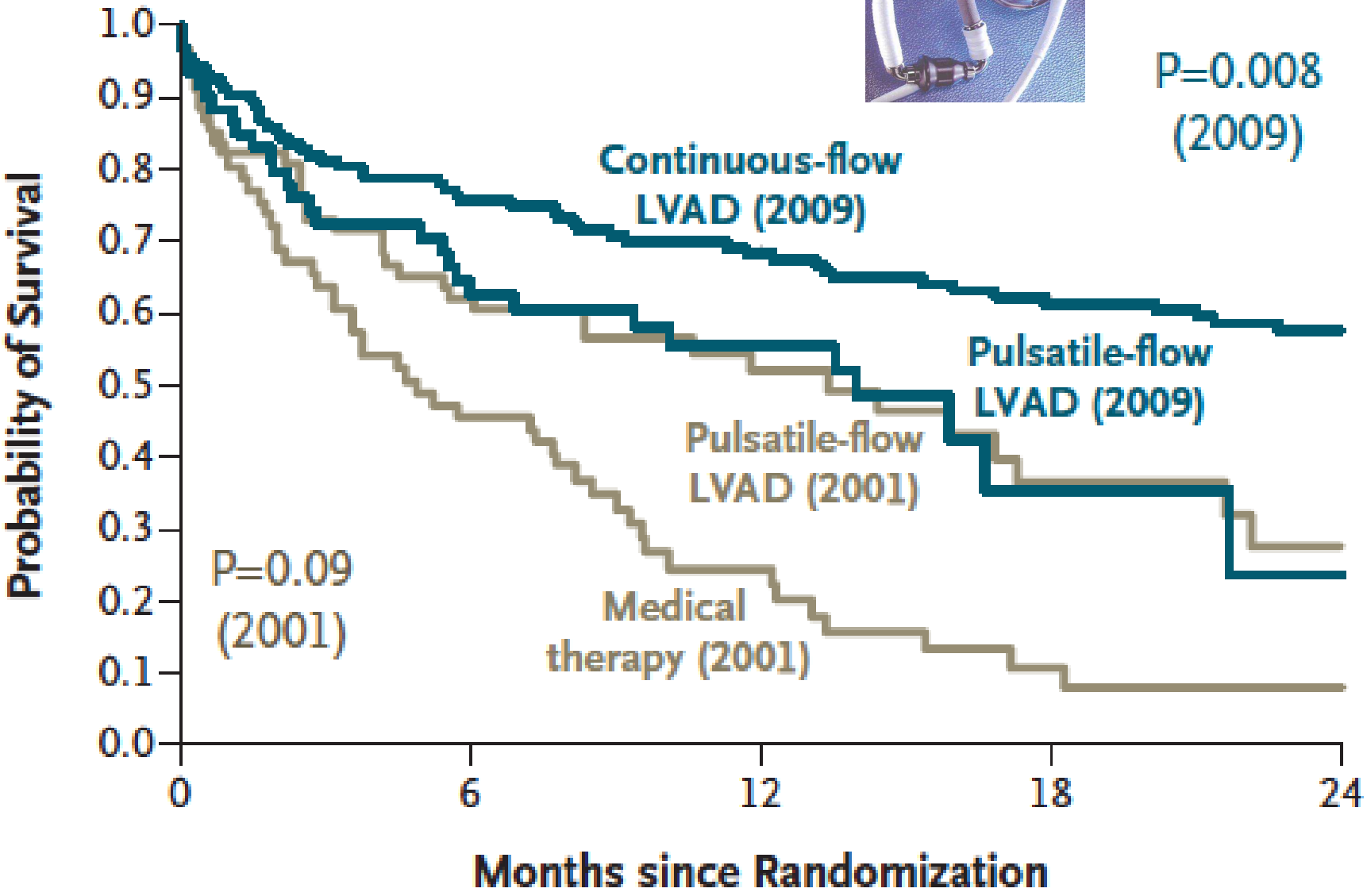
EXCOR Berlin Heart
PUENTE AL TRASPLANTE CARDÍACO

Puente a AV larga duración



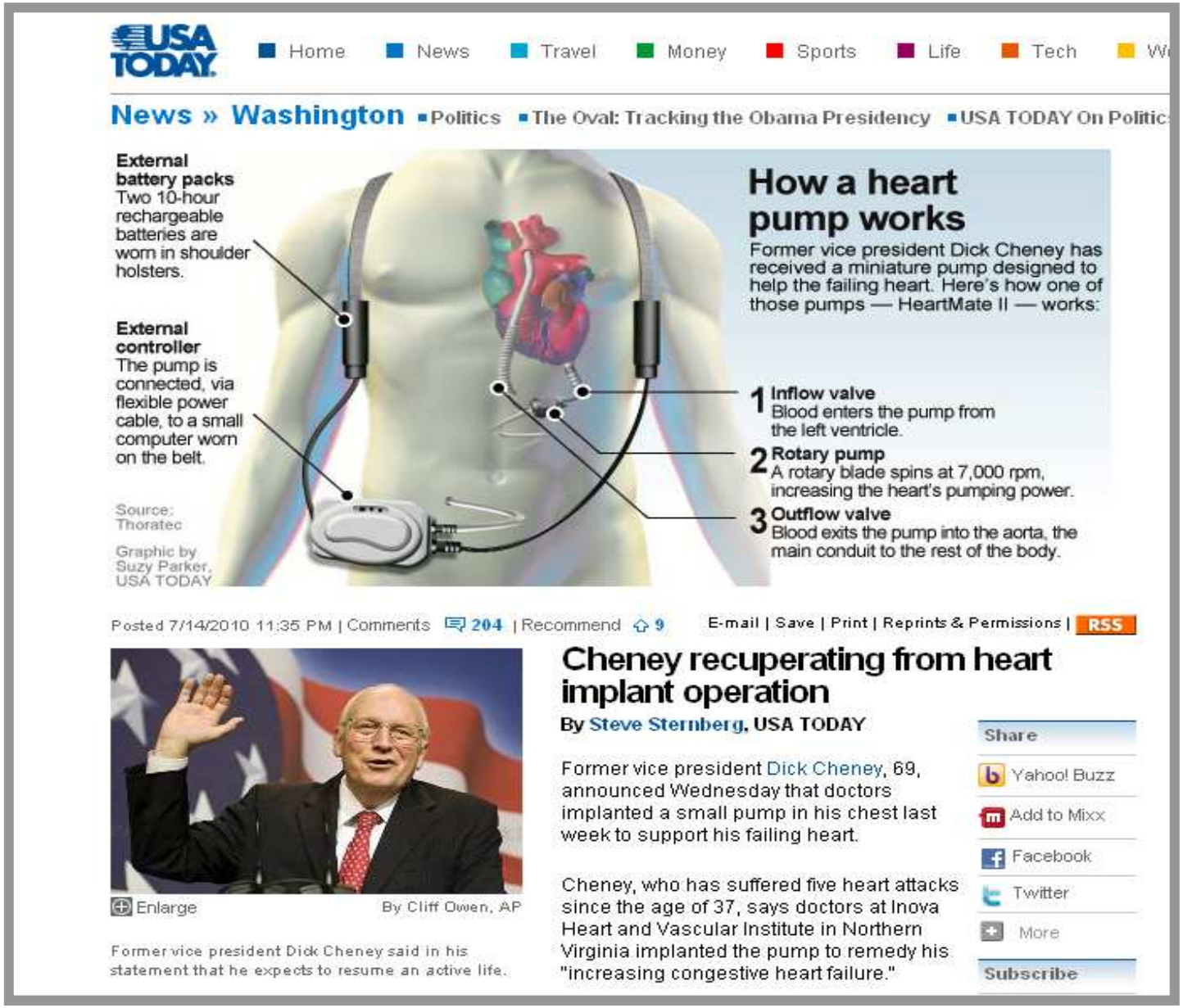
HEART MATE II - INCOR

HEART MATE I VS II



Slaughter et al. NEJM 2009;361:2241

ASISTENCIA VENTRICULAR COMO TERAPIA DEFINITIVA EN CARDIOPATIA AVANZADA



CORAZÓN ARTIFICAL TOTAL: CARMAT

BIOMEDICINE NEWS

6 COMMENT

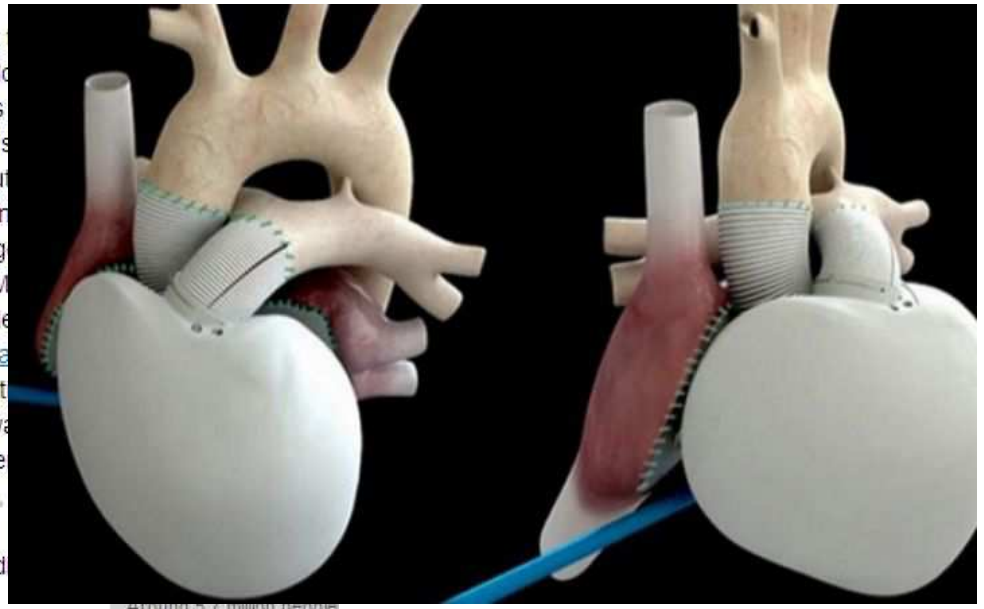
The Latest Artificial Heart: Part Cow, Part Machine

A French company is preparing to test a complex artificial heart that combines biology with machinery.

By Susan Young on May 30, 2013

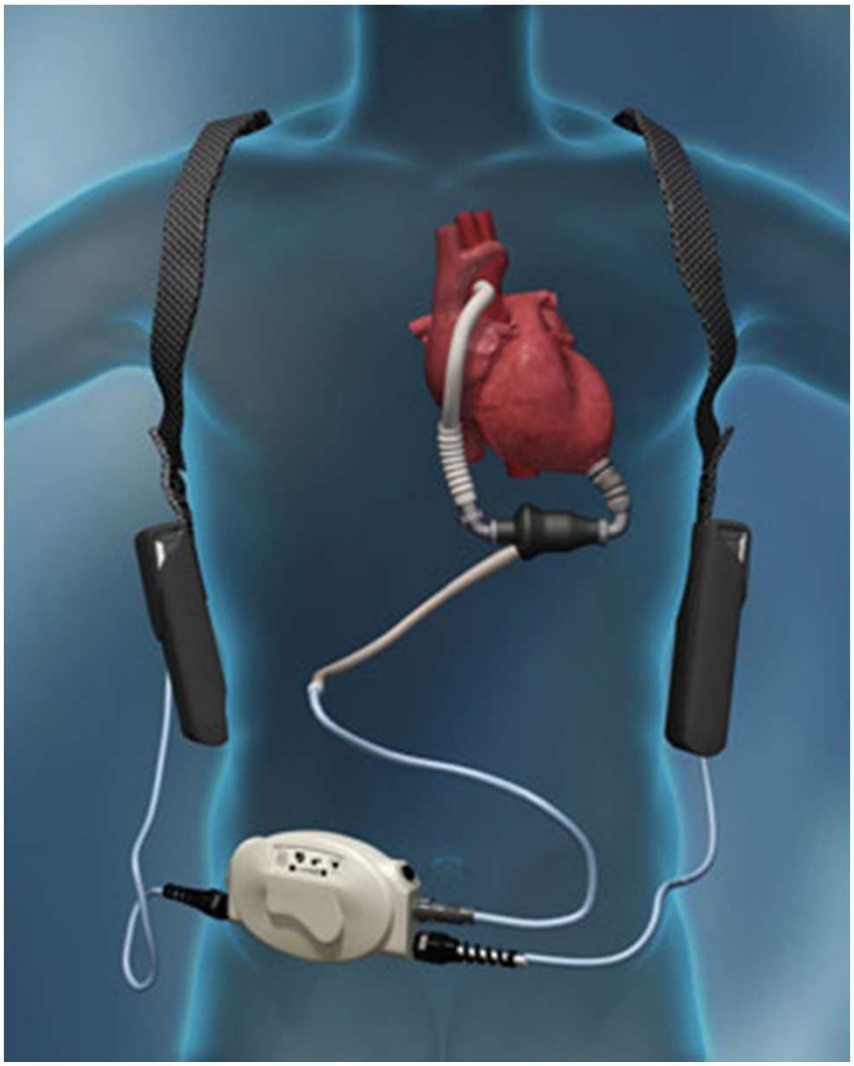
A new kind of artificial heart
combines synthetic and biol
materials as well as sensors
software to detect a patient's
of exertion and adjust output
accordingly is to be tested in
patients at four cardiac surg
centers in Europe and the M
East. If the "bioprosthetic" de
made by the Paris-based Ca
proves to be safe and effect
could be given to patients wa
for a heart transplant. Curre
only one fully artificial heart,
by Tucson, Arizona-based
SynCardia, has U.S., Canad
and European regulatory approval for use in patients.

Cardio cyborg: This rendering shows the biological valves at the top of Carmat's artificial



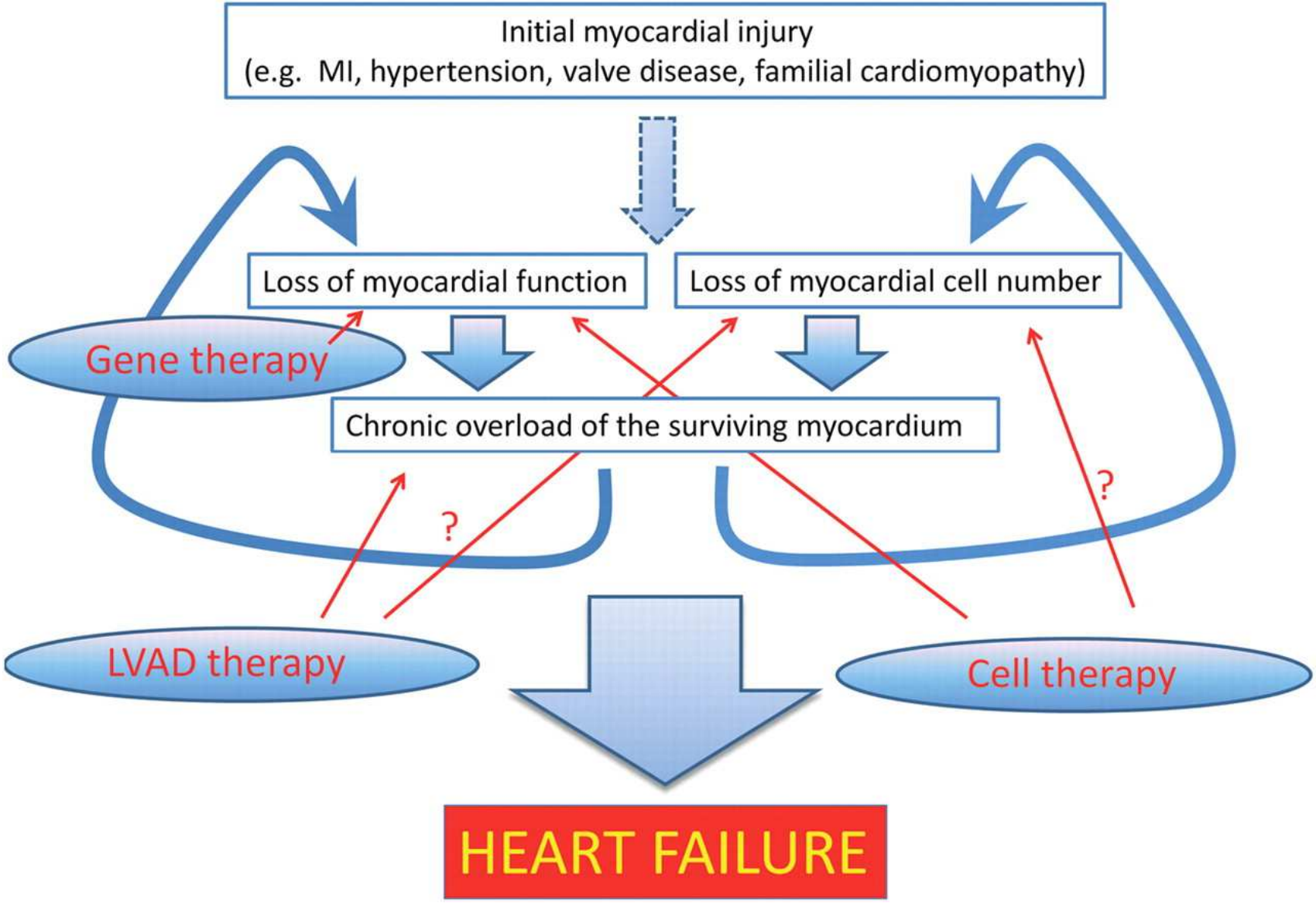
Around 5.7 million people in the U.S. have heart failure, meaning their

VADS: physiological approach to cellular recovery in heart failure.



VADs as a BRIDGE TO REPAIR

Schematic representation of the physiological approach to cellular recovery in heart failure.



Ibrahim M et al. Eur J Cardiothorac Surg 2012;ejcts.ezs067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