Hospital Universitario Clínico San Carlos
SaludMadrid
Comunidad de Madrid

Madrid, 16 de Noviembre de 2017

SÉPTIMAS JORNADAS CIENTÍFICAS DEL

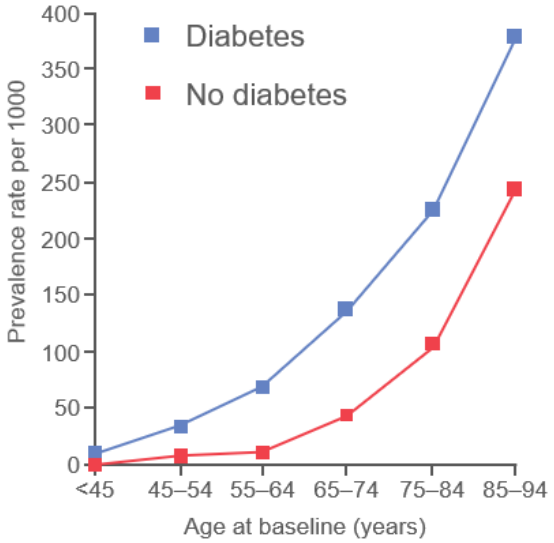
CEIPC

Comité Español Interdisciplinario para la Prevención Cardiovascular

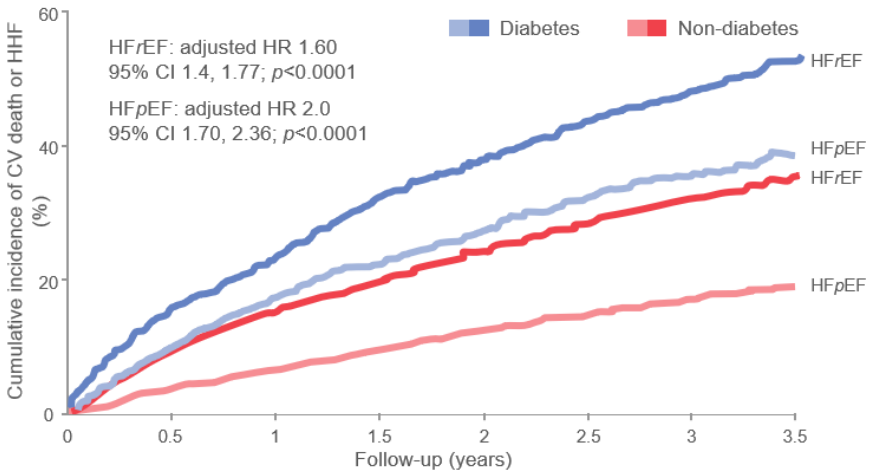
Diabetes e Insuficiencia Cardiaca

Dr. Ramón Bover Freire
Unidad de Insuficiencia Cardiaca
Servicio de Cardiología

Introducción



Los pacientes con DM tienen un riesgo 2-3 veces mayor de desarrollar IC[1]



En los pacientes con IC, la presencia de DM incrementa en un 60-80% la probabilidad de hospitalización o mortalidad CV[2-4]*

*Synthesised based on data from two clinical studies – see Notes for details

1. Gilbert RE *et al*. *Lancet* 2015;385:2107; 2. Amaral N *et al*. *Diab Vasc Dis Res* 2015;12:239; 3. Cubbon RM *et al*. *Diab Vasc Dis Res* 2013;10:330. MacDonald MR et al. Eur Heart J 2008;29:1377.

Introducción

- 1,5-2% de los mayores de 65 años tienen IC y DM.
- 40-50% de los pacientes ingresados con IC presentan DM.
- ¿Mayor probabilidad de efectos secundarios?
- ¿Diferente respuesta a los tratamientos?

El diagnóstico y el tratamiento de la IC en pacientes con/sin DM es esencialmente el mismo

11.6 Diabetes

Dysglycaemia and diabetes are very common in HF, and diabetes is associated with poorer functional status and worse prognosis. In patients with HFrEF, interventions that reduce morbidity and mortality confer similar benefit in the presence or absence of diabetes.[320] For

Concomitant Diabetes Mellitus and Heart Failure

Alessandra Dei Cas, MD, PhD, Gregg C. Fonar
Mihai Gheorghiade, MD, and Javed Butler, M

EDITORIAL COMMENT

Diabetes Mellitus in Patients With Heart Failure

Bad for All, Worse for Some*

Neda Dianati-Maleki, MD, MSc, Javed Butler, MD, MPH, MBA

Clinical diabetic cardiomyopathy: a two-faced disease with restrictive and dilated phenotypes

Petar M. Seferović[1] and Walter J. Paulus[2]*

STATE-OF-THE-ART PAPER

Impact of Diabetes on Epidemiology, Treatment, and Outcomes of Patients With Heart Failure

Alessandra Dei Cas, MD, PhD,* Sadiya S. Khan, MD,† Javed Butler, MD, MPH,‡ Robert J. Mentz, MD,§ Robert O. Bonow, MD, MS,‖ Angelo Avogaro, MD, PhD,¶ Diethelm Tschoepe, MD,# Wolfram Doehner, MD, PhD,** Stephen J. Greene, MD,‖ Michele Senni, MD,†† Mihai Gheorghiade, MD,‖ Gregg C. Fonarow, MD‡‡

REVIEW Open Access

Diagnostic approaches for diabetic cardiomyopathy

A. Lorenzo-Almorós[1], J. Tuñón[2], M. Orejas[2], M. Cortés[2], J. Egido[1,3] and Ó. Lorenzo[1,3*]

Diagnóstico IC



Definición

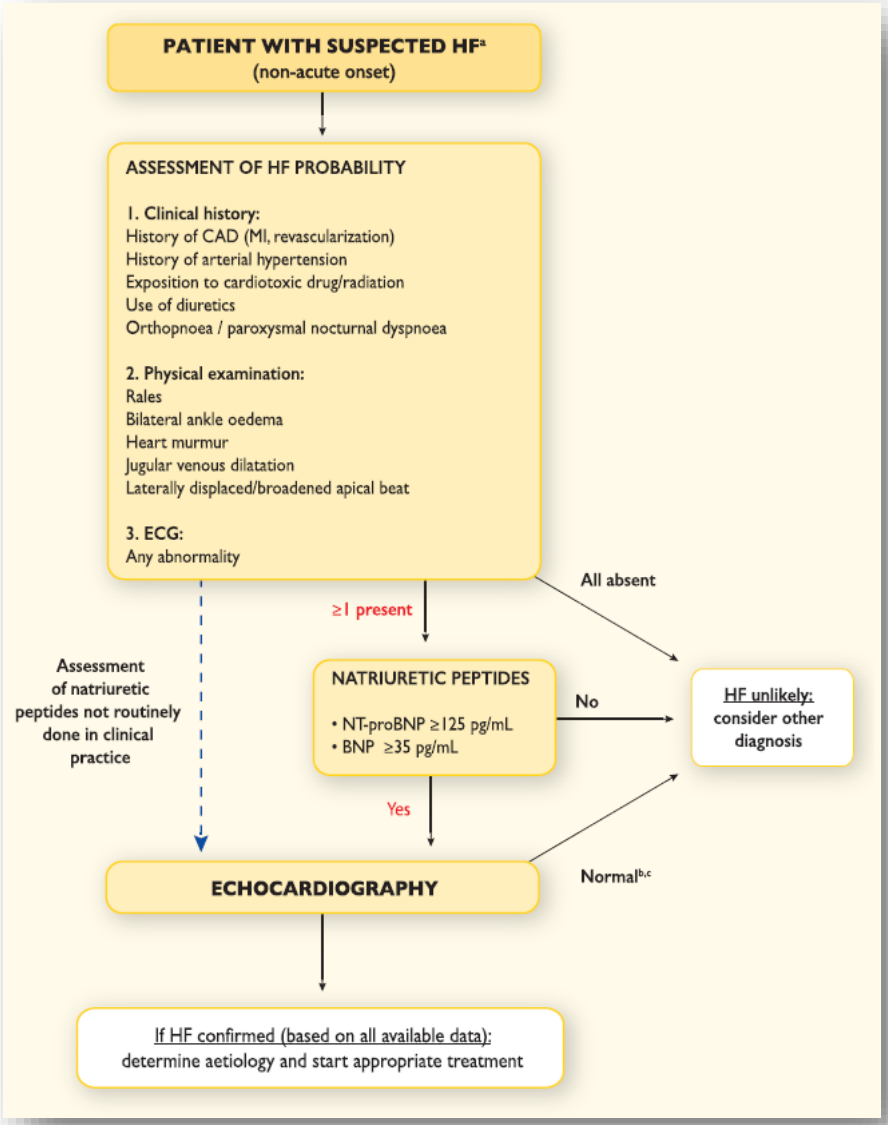
" Heart Failure is a clinical syndrome characterized by typical symptoms (e.g. breathlessness, ankle swelling and fatigue) that may be accompanied by signs (e.g. elevated jugular venous pressure, pulmonary crackles and peripheral oedema) caused by a structural and/or functional cardiac abnormality, resulting in a reduced cardiac output and/ or elevated intracardiac pressures at rest or during stress "

Prevención

Recommendations to prevent or delay the development of overt heart failure or prevent death before the onset of symptoms

Recommendations	Class [a]	Level [b]	Ref [c]
Treatment of hypertension is recommended to prevent or delay the onset of HF and prolong life.	I	A	126, 129, 150, 151
Treatment with statins is recommended in patients with or at high-risk of CAD whether or not they have LV systolic dysfunction, in order to prevent or delay the onset of HF and prolong life.	I	A	137–140, 152
Counselling and treatment for smoking cessation and alcohol intake reduction is recommended for people who smoke or who consume excess alcohol in order to prevent or delay the onset of HF.	I	C	131–134
Treating other risk factors of HF (e.g. obesity, dysglycaemia) should be considered in order to prevent or delay the onset of HF.	IIa	C	130, 141, 153–155
Empagliflozin should be considered in patients with type 2 diabetes in order to prevent or delay the onset of HF and prolong life.	IIa	B	130
ACE-I is recommended in patients with asymptomatic LV systolic dysfunction and a history of myocardial infarction in order to prevent or delay the onset of HF and prolong life.	I	A	5, 144, 145
ACE-I is recommended in patients with asymptomatic LV systolic dysfunction without a history of myocardial infarction, in order to prevent or delay the onset of HF.	I	B	5
ACE-I should be considered in patients with stable CAD even if they do not have LV systolic dysfunction, in order to prevent or delay the onset of HF.	IIa	A	142
Beta-blocker is recommended in patients with asymptomatic LV systolic dysfunction and a history of myocardial infarction, in order to prevent or delay the onset of HF or prolong life.	I	B	146
ICD is recommended in patients: a) with asymptomatic LV systolic dysfunction (LVEF ≤30%) of ischaemic origin, who are at least 40 days after acute myocardial infarction, b) with asymptomatic non-ischaemic dilated cardiomyopathy (LVEF ≤30%), who receive OMT therapy, in order to prevent sudden death and prolong life.	I	B	149, 156–158

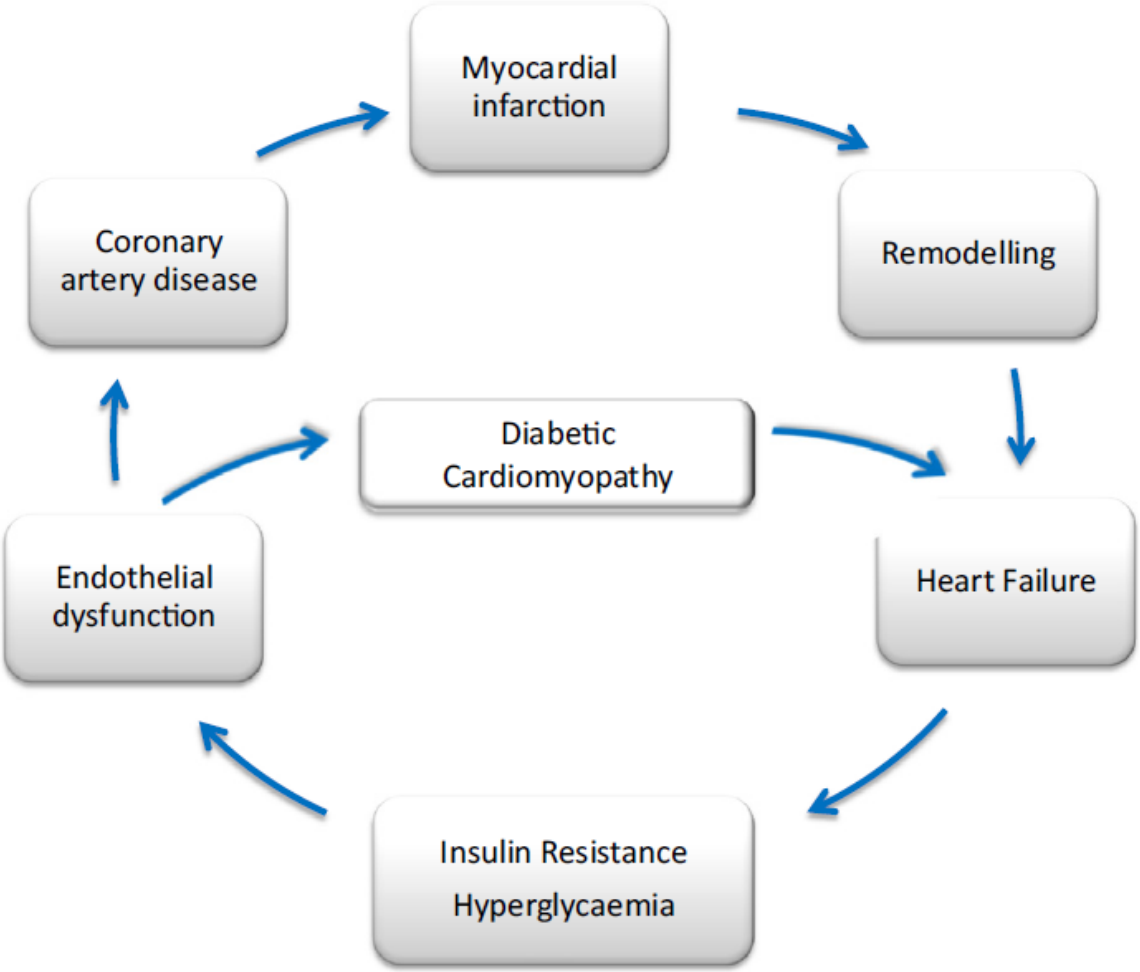
Nuevo Algoritmo Diagnóstico
Contexto clínico NO agudo



Pruebas Diagnósticas
Otras recomendaciones

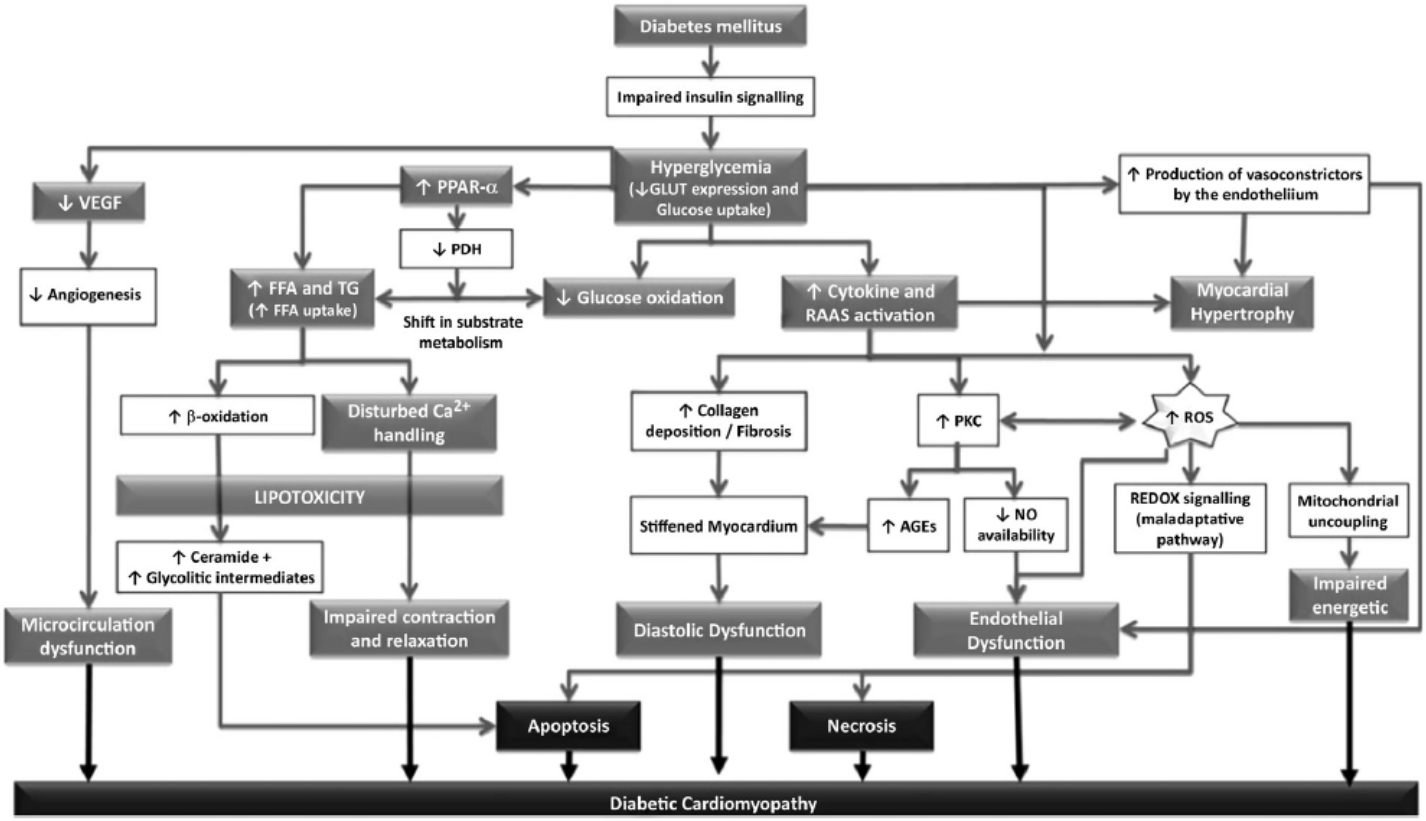
Recommendations for diagnostic tests in patients with heart failure

Recommendations	Class [a]	Level [b]	Ref [c]
The following diagnostic tests are recommended/should be considered for initial assessment of a patient with newly diagnosed HF in order to evaluate the patient's suitability for particular therapies, to detect reversible/treatable causes of HF and co-morbidities interfering with HF:			
- haemoglobin and WBC - sodium, potassium, urea, creatinine (with estimated GFR) - liver function tests (bilirubin, AST, ALT, GGTP) - glucose, HbA1c - lipid profile - TSH - ferritin, TSAT = TIBC	I	C	
- natriuretic peptides	IIa	C	
Additional diagnostic tests aiming to identify other HF aetiologies and comorbidities should be considered in individual patients with HF when there is a clinical suspicion of a particular pathology (see Table 3.4 on HF aetiologies).	IIa	C	
A 12-lead ECG is recommended in all patients with HF in order to determine heart rhythm, heart rate, QRS morphology, and QRS duration, and to detect other relevant abnormalities. This information is needed to plan and monitor treatment.	I	C	
Exercise testing in patients with HF:			
- is recommended as a part of the evaluation for heart transplantation and/or mechanical circulatory support (cardiopulmonary exercise testing);	I	C	119, 120
- should be considered to optimize prescription of exercise training (preferably cardiopulmonary exercise testing);	IIa	C	
- should be considered to identify the cause of unexplained dyspnoea (cardiopulmonary exercise testing).	IIa	C	
- may be considered to detect reversible myocardial ischaemia.	IIb	C	
Chest radiography (X-ray) is recommended in patients with HF to detect/exclude alternative pulmonary or other diseases, which may contribute to dyspnoea. It may also identify pulmonary congestion/oedema and is more useful in patients with suspected HF in the acute setting.	I	C	
Right heart catheterization with a pulmonary artery catheter:			
- is recommended in patients with severe HF being evaluated for heart transplantation or mechanical circulatory support;	I	C	
- should be considered in patients with probable pulmonary hypertension assessed by echocardiography in order to confirm pulmonary hypertension and its reversibility before the correction of valve/structural heart disease;	IIa	C	
- may be considered in order to adjust therapy in patients with HF who remain severely symptomatic despite initial standard therapies and whose haemodynamic status is unclear.	IIb	C	
EMB should be considered in patients with rapidly progressive HF despite standard therapy when there is a probability of a specific diagnosis which can be confirmed only in myocardial samples and specific therapy is available and effective.	IIa	C	93
Thoracic ultrasound may be considered for the confirmation of pulmonary congestion and pleural effusion in patients with AHF.	IIb	C	121
Ultrasound measurement of inferior vena cava diameter may be considered for the assessment of volaemia status in patients with HF.	IIb	C	



CurrProblCardiol,January2015

FIGURE 1 Pathophysiologic Abnormalities in Diabetes and Heart Failure



Multiple pathophysiologic mechanisms are activated and modulated by the presence of diabetes mellitus, resulting in abnormalities in the myocardial substrate unique to patients with diabetes mellitus and heart failure. Adapted with permission from Falcao-Pires I, Leite-Moreira AF. Heart Fail Rev 2012;17:325-44. AGE = advanced glycation end product; FFA = free fatty acid; GLUT = glucose transporter facilitators; PDH = pyruvate dehydrogenase; PKC = protein kinase C; PPAR = peroxisome proliferator-activated receptor; RAAS = renin-angiotensin-aldosterone system; REDOX = oxidation and reduction; ROS = reactive oxygen species; TG = triglyceride; VGEF = vascular endothelial growth factor.

Hospital Universitario Clínico San Carlos
SaludMadrid
Comunidad de Madrid
Instituto CardioVascular

Miocardiopatía diabética - Fenotipos

- Diagnóstico: exclusión de todas las demás etiologías posibles.
- Fenotipo dilatado (DM1):
  - Remodelado excéntrico y disfunción ventricular.
  - Favorecido por fenómenos de autoinmunidad.
  - Muerte de cardiomiocitos.
  - Desarrolla IC-FEr.
- Fenotipo restrictivo (DM2):
  - Remodelado concéntrico, HVI, dilatación de AI, disfunción diastólica.
  - Favorecido por hiperglucemia, lipotoxicidad, hiperinsulinemia.
  - Disfunción endotelial microvascular coronaria.
  - Desarrolla IC-FEp.
- ¿Fenotipos evolutivos? Parece que no.
- Tratamiento de ambos según Guías.

	DMCMP with restrictive/HFPEF phenotype	DMCMP with dilated/HFREF phenotype
Hyperglycaemia	+++	+
Lipotoxicity	+++	+
AGEs deposition	+++	+++
Microvascular rarefaction	+++	+++
Autoimmunity	–	+++
Insulin resistance/ Hyperinsulinaemia	+++	–

European Heart Journal (2015) 36, 1718-1727

Miocardiopatía diabética - Fenotipos

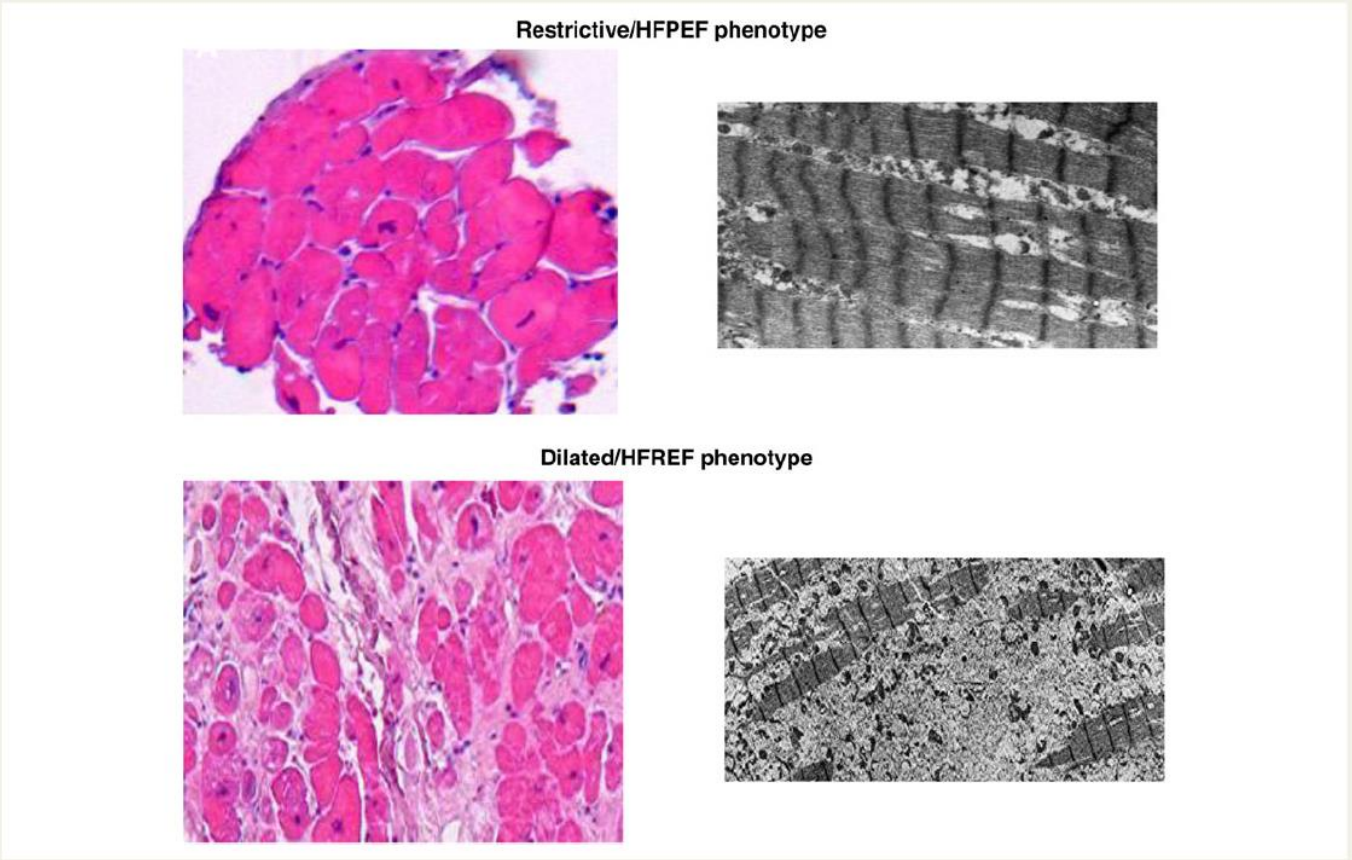


Figure 1 Myocardial structure in restrictive/ heart failure with preserved ejection fraction (HFPEF) and dilated/ heart failure with reduced ejection fraction (HFREF) phenotypes. In the restrictive/ heart failure with preserved ejection fraction phenotype cardiomyocytes are hypertrophied, collagen is laid down in-between cardiomyocytes (reactive fibrosis) (left-hand panel) and sarcomeric structure is preserved (right hand panel). In the dilated/ heart failure with reduced ejection fraction phenotype, cardiomyocytes are small and damaged, collagen is laid down over larger areas (replacement fibrosis) (left-hand panel) and sarcomeres have disappeared (right hand panel). Reproduced with permission from Van Heerebeek *et al.*[19,30]

European Heart Journal (2015) 36, 1718-1727

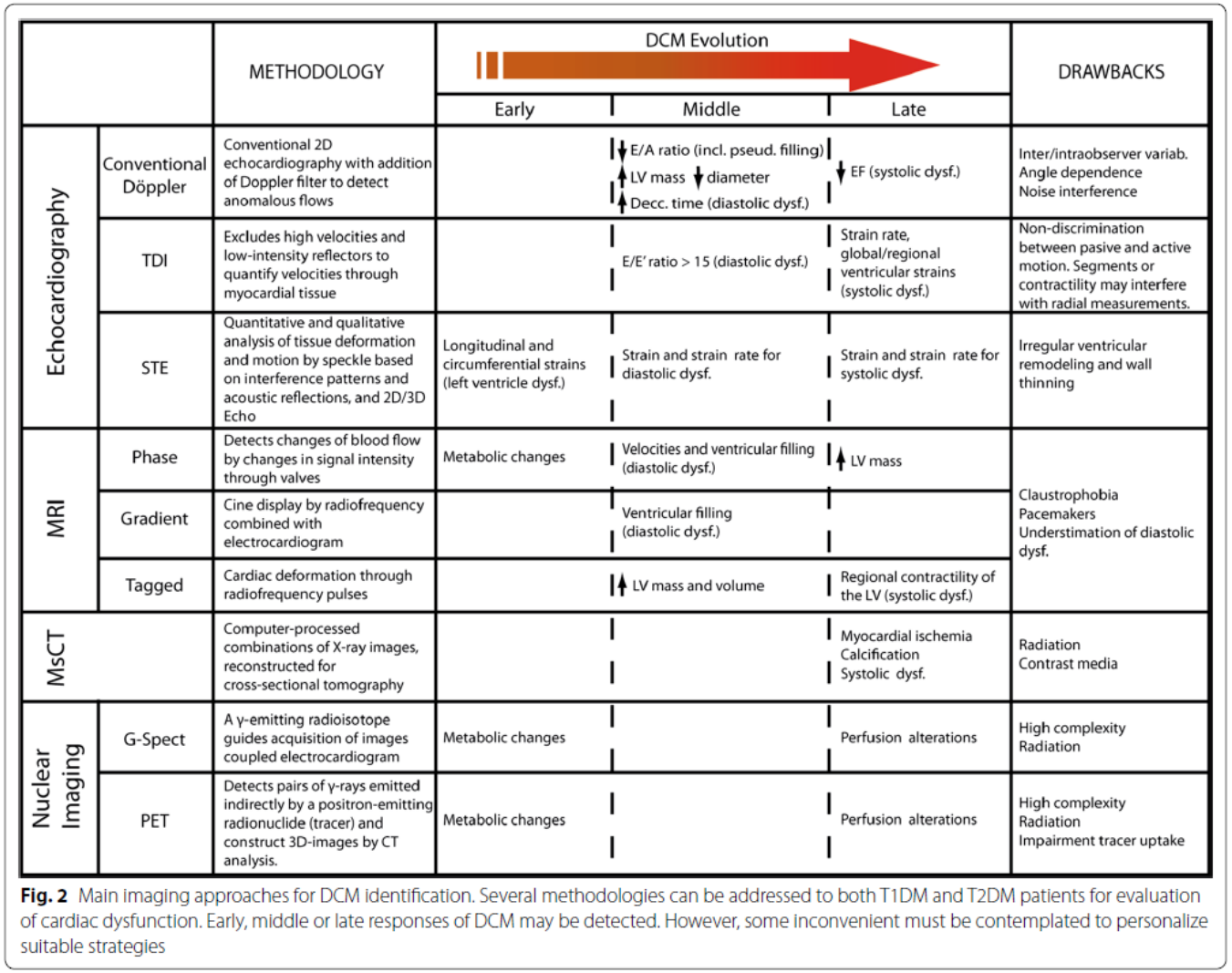
Miocardiopatía diabética - Fenotipos

- Fenotipo dilatado: La DM incrementa la probabilidad de MCD (1.75; 95% CI: 1.71–1.79).
  - Con peores características hemodinámicas: peor FEVI.
- Fenotipo restrictivo:
  - Peor presentación clínica, más hospitalizaciones, menos capacidad de esfuerzo, más HVI, más rigidez ventricular.
- Peor pronóstico en ambos: más hospitalizaciones por IC, mayor mortalidad.
  - ¿Por mayor isquemia miocárdica o directamente por la DM?

	DMCMP with restrictive/HFPEF phenotype	**DMCMP with dilated/HFREF phenotype**
Diagnosis		
	DM (mainly T2DM, obese)	DM (mainly longstanding T1DM)
	Dyspnoea and signs of congestion, S4 Gallop	Dyspnoea and signs of congestion, S3 Gallop
	No coronary, valvular, or congenital cardiac disease	No coronary, valvular, or congenital cardiac disease
	No arterial hypertension	No arterial hypertension
	No infiltrative heart disease in endomyocardial biopsy	No inflammation or virus in endomyocardial biopsy
	LVEF $\geq$50%	LVEF $<$50%
	LVEDVI $\leq$97 mL/m^2	LVEDVI $>$97 mL/m^2
	Diastolic LV dysfunction	
Treatment		
	Diuretics	ACEIs, ARBs, β-blockers, mineralocorticoid-receptor antagonists, ivabradine
		Resynchronization

European Heart Journal (2015) 36, 1718-1727

Diagnóstico por imagen



		METHODOLOGY	DCM Evolution: Early	DCM Evolution: Middle	DCM Evolution: Late	DRAWBACKS
Echocardiography	Conventional Döppler	Conventional 2D echocardiography with addition of Doppler filter to detect anomalous flows		↓E/A ratio (incl. pseud. filling) ↑LV mass ↓diameter ↑Decc. time (diastolic dysf.)	↓EF (systolic dysf.)	Inter/intraobserver variab. Angle dependence Noise interference
	TDI	Excludes high velocities and low-intensity reflectors to quantify velocities through myocardial tissue		E/E' ratio > 15 (diastolic dysf.)	Strain rate, global/regional ventricular strains (systolic dysf.)	Non-discrimination between pasive and active motion. Segments or contractility may interfere with radial measurements.
	STE	Quantitative and qualitative analysis of tissue deformation and motion by speckle based on interference patterns and acoustic reflections, and 2D/3D Echo	Longitudinal and circumferential strains (left ventricle dysf.)	Strain and strain rate for diastolic dysf.	Strain and strain rate for systolic dysf.	Irregular ventricular remodeling and wall thinning
MRI	Phase	Detects changes of blood flow by changes in signal intensity through valves	Metabolic changes	Velocities and ventricular filling (diastolic dysf.)	↑LV mass	Claustrophobia Pacemakers Understimation of diastolic dysf.
	Gradient	Cine display by radiofrequency combined with electrocardiogram		Ventricular filling (diastolic dysf.)		
	Tagged	Cardiac deformation through radiofrequency pulses		↑LV mass and volume	Regional contractility of the LV (systolic dysf.)	
MsCT		Computer-processed combinations of X-ray images, reconstructed for cross-sectional tomography			Myocardial ischemia Calcification Systolic dysf.	Radiation Contrast media
Nuclear Imaging	G-Spect	A γ-emitting radioisotope guides acquisition of images coupled electrocardiogram	Metabolic changes		Perfusion alterations	High complexity Radiation
	PET	Detects pairs of γ-rays emitted indirectly by a positron-emitting radionuclide (tracer) and construct 3D-images by CT analysis.	Metabolic changes		Perfusion alterations	High complexity Radiation Impairment tracer uptake

Fig. 2 Main imaging approaches for DCM identification. Several methodologies can be addressed to both T1DM and T2DM patients for evaluation of cardiac dysfunction. Early, middle or late responses of DCM may be detected. However, some inconvenient must be contemplated to personalize suitable strategies

Lorenzo-Almorós et al. Cardiovasc Diabetol (2017) 16:28

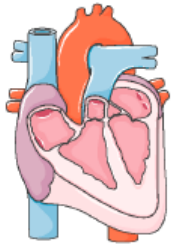
¿Mito o realidad?

Arguments for and against the existence of diabetic cardiomyopathy in ...

Type 1 diabetes

For:
- Increased risk of heart failure despite insulin treatment in most studies
- Diastolic dysfunction
- Systolic and diastolic dysfunction in preclinical models of diabetes
- Many molecular mechanisms overlap with mechanisms in DC of type 2 diabetes

Against:
- Low risk for HF and absence of systolic dysfunction in few long-term studies
- Adjustment for confounders may blunt impairment in diastolic function
- Diastolic dysfunction not specific to diabetes ?
- Insulin treatment normalizes metabolic and molecular abnormalities in preclinical studies and thus maybe also in humans
- Inconsistent evidence of cardiac dysfunction across animal models of type 1 diabetes
- Partially distinct molecular mechanisms compared to DC in type 2 diabetes



Type 2 diabetes

For:
- Increased risk of heart failure
- Diastolic dysfunction
- Left ventricular hypertrophy
- Increased LV mass in type 2 diabetic rodents
- Evidence of mild systolic dysfunction
- Common molecular mechanisms in DC and failing heart
- Confirmation of preclinical data in human DC

Against:
- No convincing evidence for meaningful systolic dysfunction in human DC
- Lack of long-term prospective studies investigating systolic dysfunction/heart failure in diabetic humans in the absence of confounders
- Subclinical systolic and diastolic dysfunction not specific to diabetes?

Int. J. Mol. Sci. 2016, 17, 2136

Pacientes IC-FEp y DM

Comparados con no DM (p <0,01)...

- Signos de congestión más marcados.
- Antecedentes de IAM (28% vs. 22%).
- Mayor IMC (31 vs. 29 kg/m2).
- Peor calidad de vida (MLWHF 48 vs. 40).
- NTproBNP algo más elevado (403 vs. 320 pg/mL).
- Mayores alteraciones estructurales y funcionales cardiacas en Eco (FEVI semejante, mayor masa del VI, mayor dilatación de la AI, signos más marcados de disfunción diastólica).
- Peor pronóstico (hospitalización por IC, muerte CV).

Circulation. 2017;135:724-735.

Tratamiento de la IC



Tratamiento de la IC-FEP

Recommendations for treatment of patients with heart failure with preserved ejection fraction and heart failure with mid-range ejection fraction

Recommendations	Class [a]	Level [b]	Ref [c]
it is recommended to screen patients with HFpEF or HFmrEF for both cardiovascular and non-cardiovascular comorbidities, which, if present, should be treated provided safe and effective interventions exist to improve symptoms, well-being and/or prognosis.	I	C	
Diuretics are recommended in congested patients with HFpEF or HFmrEF in order to alleviate symptoms and signs.	I	B	178, 179

9.1 Effect of treatment on symptoms in heart failure with preserved ejection fraction

Diuretics will usually improve congestion, if present, thereby improving symptoms and signs of HF. The evidence that diuretics improve symptoms is similar across the spectrum of LVEF.[178,179]

Evidence that beta-blockers and MRAs improve symptoms in these patients is lacking. There is inconsistent evidence for an improvement in symptoms in those treated with ARBs (only for candesartan was there an improvement in NYHA class)[309,310] and ACEIs.[311]

9.2 Effect of treatment on hospitalization for heart failure in heart failure with preserved ejection fraction

For patients in sinus rhythm, there is some evidence that nebivolol,[173,312,313] digoxin,[314] spironolactone[301] and candesartan[310] might reduce HF hospitalizations. For patients in AF, beta-blockers do not appear to be effective and digoxin has not been studied. The evidence in support of either ARBs[315] or ACEIs[311] is inconclusive.

9.3 Effect of treatment on mortality in heart failure with preserved ejection fraction

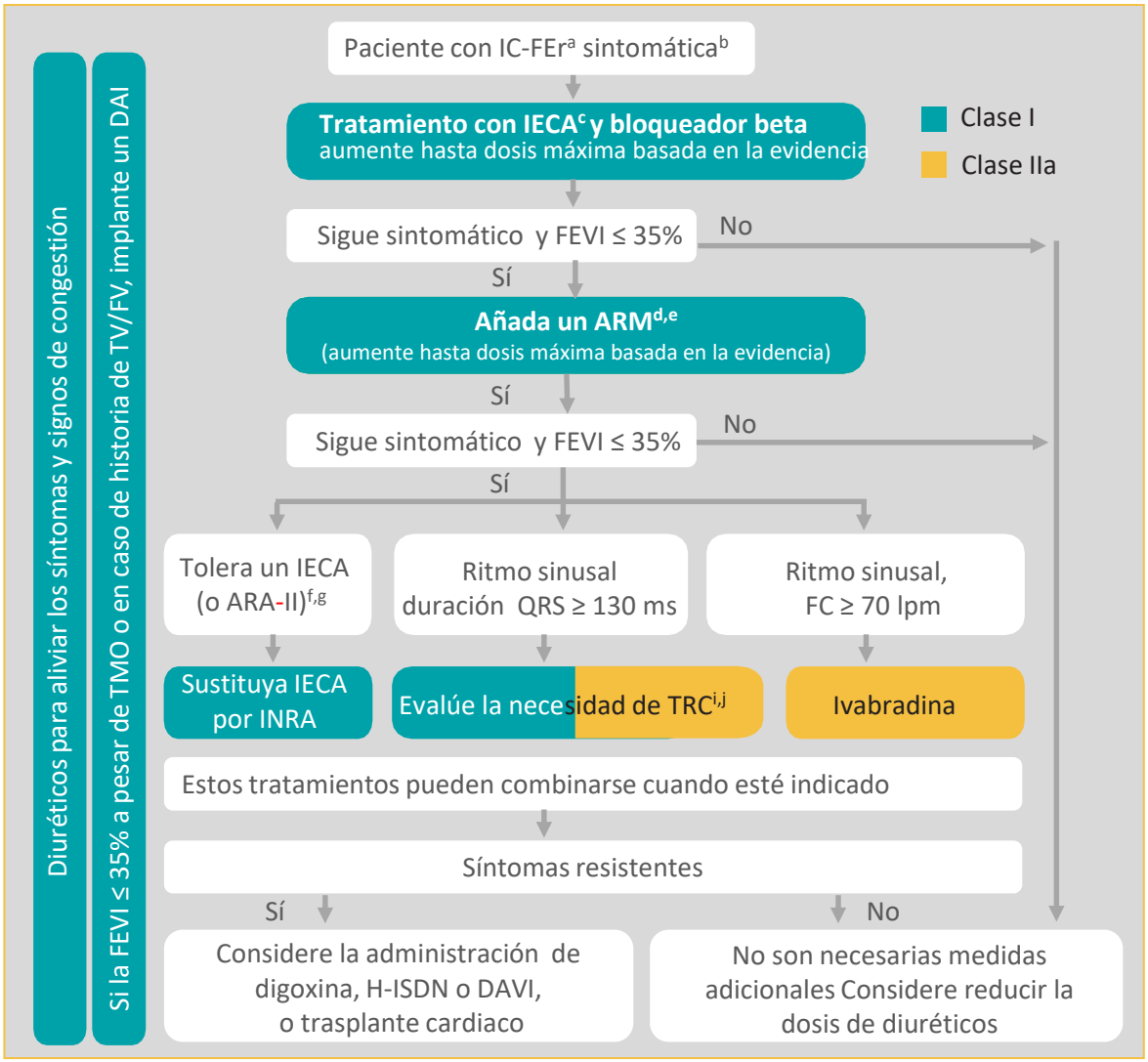
Trials of ACEIs, ARBs, beta-blockers and MRAs have all failed to reduce mortality in patients with HFpEF or HFmrEF. However, in older patients with HFrEF, HFpEF or HFmrEF, nebivolol reduced the combined endpoint of death or cardiovascular hospitalization,[173,312] with no significant interaction between treatment effect and baseline LVEF.[313]

Tratamiento en IC-FER
En todos los pacientes (IA)

Pharmacological treatments indicated in patients with symptomatic (NYHA Class II-IV) heart failure with reduced ejection fraction

Recommendations	Class [a]	Level [b]	Ref [c]
An ACE-I[d] is recommended, in addition to a beta-blocker, for symptomatic patients with HFrEF to reduce the risk of HF hospitalization and death.	I	A	2, 163 –165
A beta-blocker is recommended, in addition an ACE-I[d], for patients with stable, symptomatic HFrEF to reduce the risk of HF hospitalization and death.	I	A	167– 173
An MRA is recommended for patients with HFrEF, who remain symptomatic despite treatment with an ACE-I[d] and a beta-blocker, to reduce the risk of HF hospitalization and death.	I	A	174, 175

Introducción



Rev Esp Cardiol. 2016;69(12):1167.e1-e85

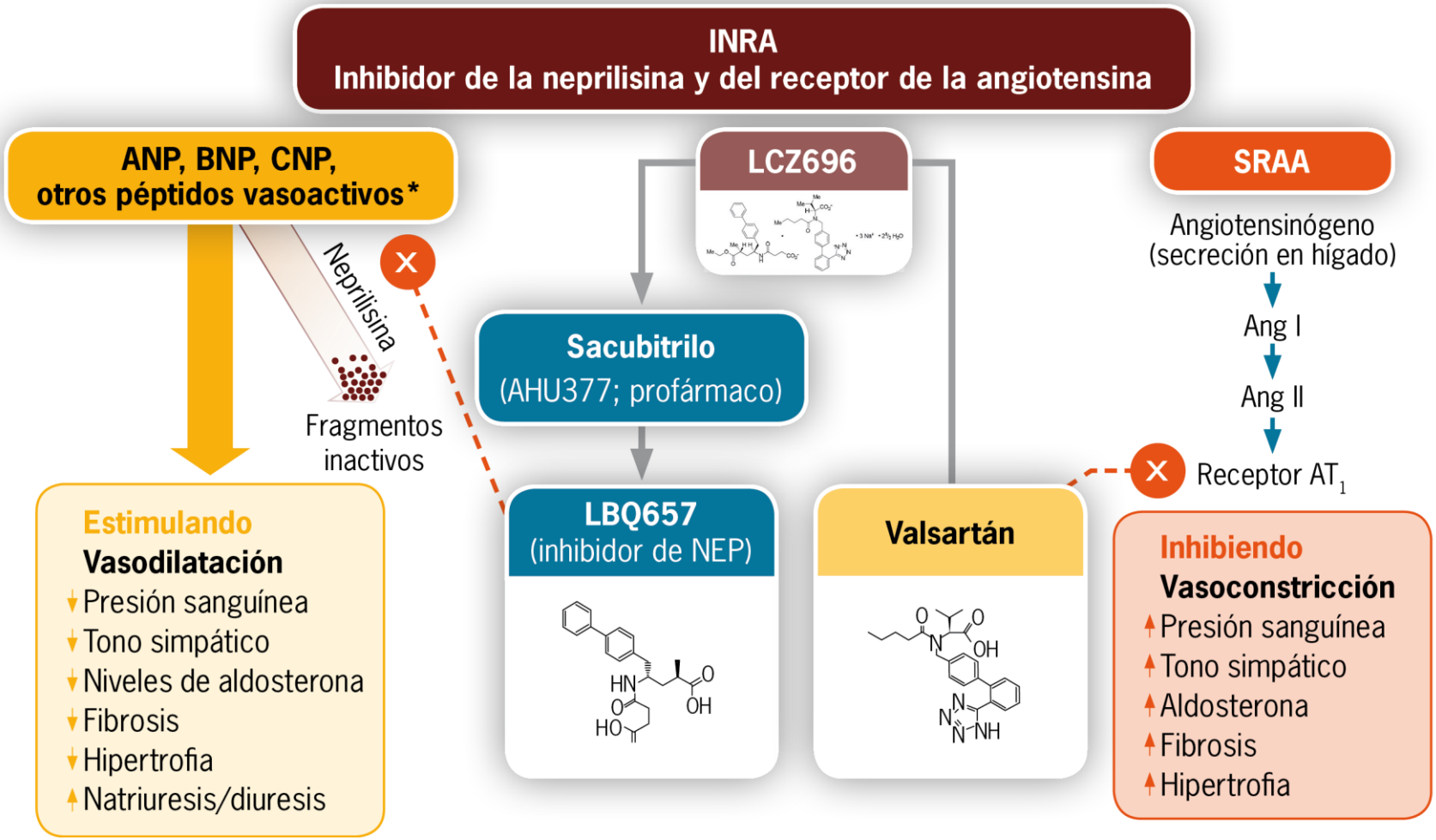
TABLE 1 Major Clinical Trials in Patients With Heart Failure and Subgroup Analyses With Concomitant Diabetes Mellitus

Trial	Primary Outcome	Subgroup of Patients With or Without DM	Average Follow-Up (Months)	Treatment	Results RR or HR (95% CI)	(Ref. #)
SOLVD	Mortality and hospitalization for worsening HF	HF patients with EF <35%	41.4	Enalapril vs. placebo	RR of 0.84 (0.74–0.95) in no DM vs. 1.01 (0.85–1.21) in DM	(35)
SAVE	CV mortality	Recent survivors of MI with EF ≤40%	42	Captopril vs. placebo	RR of 0.82 (0.68–0.99) in no DM vs. 0.89 (0.68–1.16) in DM	(36)
TRACE	All-cause mortality	Patients with LVEF <35% after acute MI	26	Trandalapril vs. placebo	RR of 0.82 (0.69–0.97) in no DM vs. 0.64 (0.45–0.91) in DM (interaction analysis p = 0.3)	(37)
SMILE	Progression to HF	Patients with anterior acute MI not eligible for thrombolytic treatment	12	Zofenopril vs. placebo	RR of 0.79 (0.54–1.15) in no DM vs. 0.44 (0.22–0.87) in DM	(38)
ATLAS	All-cause mortality	High-risk HF patients	46	Lisinopril high dose (32.5–35 mg day^{-1}) vs. low-dose (2.5–5 mg day^{-1})	↓6% RR in no DM patients vs. ↓14% RR in DM high-dose vs. low dose (interaction analysis p = 0.3)	(39)
CHARM	CV death or hospitalization for HF	NYHA functional class II–IV patients (LVEF <40%)	40	Candesartan vs. placebo	RR not significant in no DM vs. that in DM (interaction analysis p = 0.12)	(41)
Val-HeFT	Combined endpoint of CV mortality and morbidity	NYHA functional class II–IV patients	23	Valsartan vs. placebo	↓RR in no DM vs. that in DM (although not significant)	(42)
EPHESUS	Mortality and CV morbidity	Postacute MI patients with LVEF ≤40% and clinical HF	16	Eplerenone vs. placebo	↓RR in no DM vs. that in DM (although not significant; p = 0.59)	(43)
Subgroup analysis	All-cause mortality	NYHA functional class III–IV patients with LVEF <35%	24	Spironolactone vs. placebo	RR of 0.70 (0.60–0.82) in non-DM vs. HR of 0.70 (0.52–0.94) in DM	(44)
BEST	All-cause mortality	NYHA functional class III–IV patients with EF ≤35%	24	Bucindolol vs. placebo	RR of 0.91 (0.74–1.13) in no DM vs. HR of 0.87 (0.73–1.03) in DM	(29)
MERIT-HF	Risk of hospitalization for HF	NYHA functional class III–IV patients with EF <40%	12	Metoprolol vs. placebo	↓37% RR in DM vs. ↓35% in no DM; test of diabetes by treatment interaction was nonsignificant	(30)
CIBIS II	All-cause mortality	NYHA functional class III–IV patients with EF ≤35%	16	Bisoprolol vs. placebo	RR 0.66 (95% CI 0.54–0.81) in no DM vs. RR 0.81 (95% CI 0.51–1.28) in DM (heterogeneity test for interaction p = 0.48)	(32)
COPERNICUS	Combined endpoint All-cause mortality or hospitalization for HF	NYHA functional class IV patients with EF <25%	10.4	Carvedilol vs. placebo	RR of 0.67 (0.52–0.85) in no DM vs. 0.68 (0.47–1.00) in DM	(31)
ASTRONAUT	CV death or HF rehospitalization	Hemodynamically stable patients hospitalized for HF	11.3	Aliskiren vs. placebo	HR of 0.80 (0.64–0.99) in no DM vs. 1.16 (0.91–1.47) in DM; test for interaction p = 0.03	(2)

Hospital Universitario Clínico San Carlos
SaludMadrid
Comunidad de Madrid
INSTITUTO CARDIOVASCULAR

Repasando Sacubitrilo/valsartán

Complejo supramolecular



clinICa
SEGUNDA EDICIÓN

* Sustratos de neprilisina listados en orden de relativa afinidad por NEP: ANP, CNP, Ang II, Ang I, adrenomedulina, sustancia P, bradicinina, endotelina 1, BNP, INRA.

1. Levin et al. N Engl J Med. 1998; 339: 321-328. **2.** Nathisuwan & Talbert. Pharmacotherapy. 2002; 22: 27-42. **3.** Schrier & Abraham. N Engl J Med. 1999; 341: 577-585. **4.** Langenickel & Dole. Drug Discov Today: Ther Strateg. 2012; 9: e131-e139. **5.** Feng et al. Tetrahedron Letters. 2012; 53: 275-276.

1610044238

Subestudios PARADIGM-HF

Sacubitrilo/valsartán en diabéticos…

- S/V reduce los niveles de HbA1c en un 0,26% frente a un 0,16% (95% CI 0.05-0.22 , p=0.0023) comparado con enalapril en pacientes con IC-FEr que también presentan diabetes.
- La introducción del tratamiento con insulina también se redujo en un 29% en los pacientes tratados con S/V (HR 0.71, 95% CI 0.56-0.90, p=0.0052) , en comparación con enalapril a lo largo de los 3 años de seguimiento del estudio PARADIGM-HF.
- No hubo diferencias significativas en los episodios hipoglucémicos entre ambos grupos de tratamiento.

The Lancet Diabetes & Endocrinology March 18, 2017

Tratamiento de la DM, ¿influye en la IC?



Posicionamiento ESC 2017

Non-insulin antidiabetic pharmacotherapy in patients with established cardiovascular disease: a position paper of the European Society of Cardiology Working Group on Cardiovascular Pharmacotherapy

Alexander Niessner[1]*, Juan Tamargo[2], Lorenz Koller[1], Christoph H. Saely[3,4,5], Thomas Andersen Schmidt[6,7], Gianluigi Savarese[8], Sven Wassmann[9], Giuseppe Rosano[10,11], Claudio Ceconi[12], Christian Torp-Pedersen[13,14], Juan Carlos Kaski[15], Keld Per Kjeldsen[16,17,18], Stefan Agewall[19,20], Thomas Walther[21,22], Heinz Drexel[3,4,5,23], and Basil S. Lewis[24,25]

Niessner A, Tamargo J. Eur Heart J. 2017 Nov 8.

Posicionamiento ESC 2017

Patients at risk for heart failure

The EMPA-REG OUTCOME, CANVAS Program, LEADER, SUSTAIN-6, EXSCEL, ELIXA, SAVOR-TIMI 53, EXAMINE, and TECOS study report on the proportion of patients with a diagnosis of HF at randomization which ranges from 10% in the EMPA-REG OUTCOME trial to 28% in the EXAMINE study (Supplementary material online, *Table S4*). Specific data regarding HF are limited to NYHA functional class in two studies.[6,24]

The CANVAS Program, LEADER, SUSTAIN-6, EXSCEL, ELIXA, SAVOR-TIMI 53, EXAMINE, and TECOS trial analysed whether the presence of HF affected the primary outcome but did not find any significant interaction. Heart failure hospitalization was significantly increased in the SAVOR-TIMI 53 study with saxagliptin and in the PROACTIVE study with pioglitazone. Thus, they should not be used in patients at risk for HF or with established HF. According to an analysis of the SAVOR-TIMI 53 study patients with elevated Nt-proBNP or chronic kidney disease (GFR < 60 mL/min) may be at risk for HF.[23] On the contrary, this endpoint was significantly reduced in the EMPA-REG OUTCOME study with empagliflozin and in an exploratory analysis of the CANVAS Program trial.

Niessner A, Tamargo J. Eur Heart J. 2017 Nov 8.

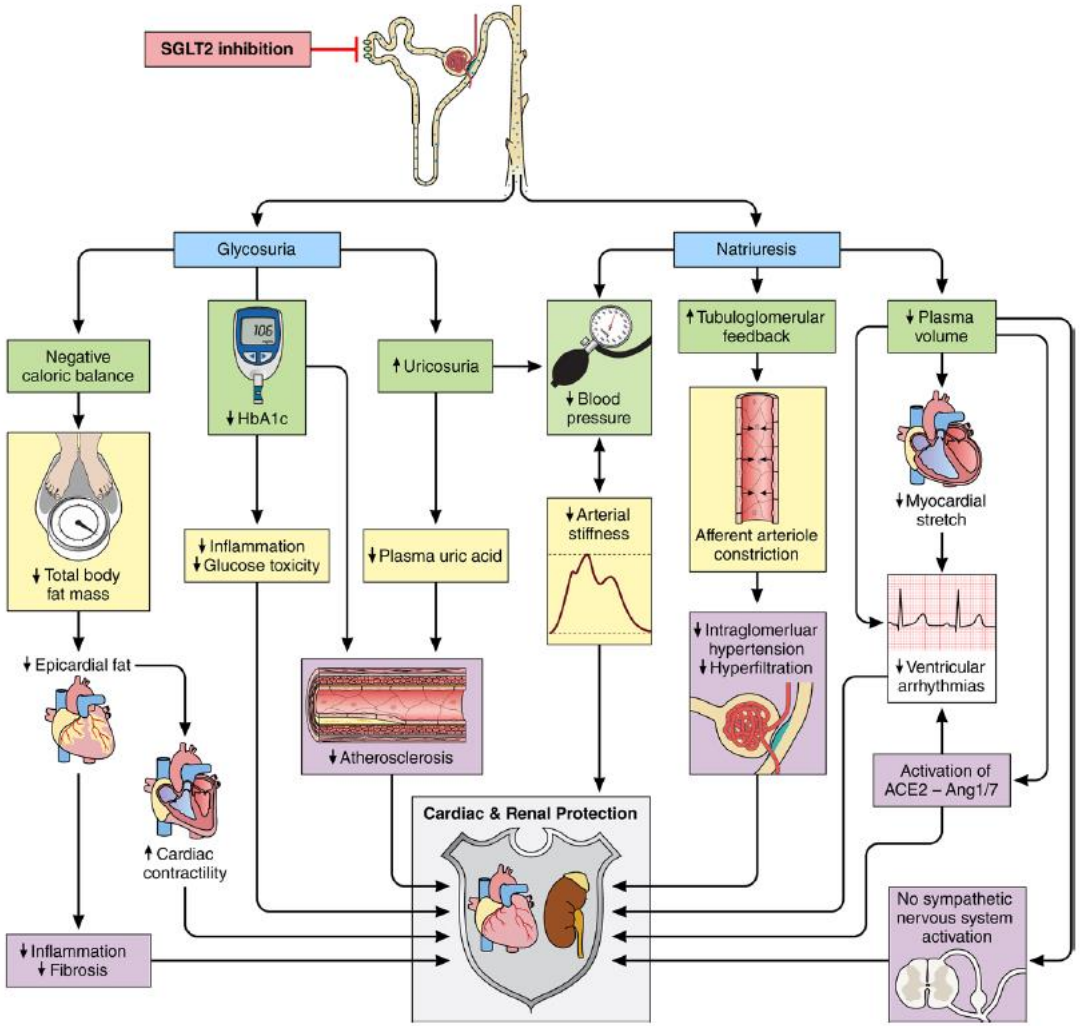
STATE OF THE ART

Sodium Glucose Cotransporter 2 Inhibitors in the Treatment of Diabetes Mellitus

Circulation

Cardiovascular and Kidney Effects, Potential Mechanisms, and Clinical Applications

Hiddo J.L. Heerspink, Bruce A. Perkins, David H. Fitchett, Mansoor Husain and David Z. I. Cherney



Papel de la Cardiología ante las nuevas evidencias



Cardiología y DM2

DM2

Dx - Tratamiento - Gestión Crónica

- Endocrinología
- Atención Primaria
- Cardiología?

- Escaso impacto de la formación
- Dx en eventos (SCA)
- Limitada participación en el tratto.
- No participación en la gestión crónica - HbA1c

FRCV

- Cardiología
- Atención Primaria
- Endocrinología

- Amplio estudio del impacto de la DM2 en la patología CV
- Papel modificador del riesgo y tratto.: DM2 sí/no
- Ausencia de tratto. eficaz de la DM2 para reducir riesgo CV

DM2 como FRCV

Otros factores de riesgo, daño orgánico asintomático o enfermedad	Presión arterial (mmHg)			
	Normal alta PAS 130-139 o PAD 85-89	HTA de grado 1 PAS 140-159 o PAD 90-99	HTA de grado 2 PAS 160-179 o PAD 100-109	HTA de grado 3 PAS ≥ 180 o PAD ≥ 110
Sin otros FR		Riesgo bajo	Riesgo moderado	Riesgo alto
1-2 FR	Riesgo bajo	Riesgo moderado	Riesgo moderado a alto	Riesgo alto
≥ 3 FR	Riesgo bajo a moderado	Riesgo moderado a alto	Riesgo alto	Riesgo alto
Daño orgánico, ERC de grado 3 o diabetes mellitus	Riesgo moderado a alto	Riesgo alto	Riesgo alto	Riesgo alto a muy alto
ECV sintomática, ERC de grado ≥ 4 o diabetes con daño orgánico/FR	Riesgo muy alto	Riesgo muy alto	Riesgo muy alto	Riesgo muy alto

Figura 1. Estratificación del riesgo CV total en categorías de riesgo bajo, moderado, alto y muy alto según los valores de PAS y PAD y la prevalencia de factores de riesgo, daño orgánico asintomático, diabetes mellitus, grado de ERC y ECV sintomática. Los sujetos con PA normal alta en consulta y normal fuera de consulta (hipertensión enmascarada) tienen un riesgo CV en rango de hipertensión. Los sujetos con PA alta en consulta y normal fuera de consulta (hipertensión de bata blanca), especialmente si no tienen diabetes mellitus, daño orgánico, ECV o ERC, tienen un riesgo más bajo que el de la hipertensión persistente con los mismos valores de PA en consulta. CV: cardiovascular; ECV: enfermedad cardiovascular; ERC: enfermedad renal crónica; FR: factor de riesgo; HTA: hipertensión arterial; PA: presión arterial; PAD: presión arterial diastólica; PAS: presión arterial sistólica.

Menos del 20% de la HTA se produce en ausencia de uno o más factores de riesgo

Estratificación del Riesgo CV Global

1. Riesgo muy alto

Sujetos con cualquiera de los siguientes factores:

- ECV documentada en pruebas invasivas o no invasivas (como angiografía coronaria, imagen nuclear, ecocardiografía de estrés, placa carotídea por ultrasonidos), infarto de miocardio, SCA, revascularización coronaria (ICP, CABG) y otros procedimientos de revascularización arterial, ictus isquémico, enfermedad arterial periférica (EAP).
- DM1 o DM2 con uno o más factores de riesgo CV o lesión de órgano diana (como microalbuminuria 30-300 mg/24 h).
- ERC grave (TFG < 30 ml/min/1,73 m²).
- Una estimación SCORE ≥ 10%.

2. Alto riesgo

Sujetos con cualquiera de los siguientes factores:

- Factores de riesgo específicos marcadamente elevados, como dislipemia familiar e hipertensión grave.
- DM1 o DM2, pero sin factores de riesgo CV ni lesión de órgano diana.
- ERC moderada (TFG 30-59 ml/min/1,73 m²).
- Una estimación SCORE ≥ 5% y < 10% para el riesgo a 10 años de ECV mortal.

3. Riesgo moderado

Se considera que un individuo tiene un riesgo moderado cuando su estimación SCORE de riesgo a 10 años es ≥ 1% y < 5%. Numerosas personas de mediana edad entran en esta categoría. Este nivel de riesgo debe modularse con los factores mencionados antes.

4. Bajo riesgo

La categoría de bajo riesgo se aplica a individuos con una estimación SCORE < 1% y en ausencia de otros cualificadores que indicarían un riesgo moderado.

Estas categorías de riesgo son compatibles con las guías sobre el manejo de lípidos de la Sociedad Europea de Aterosclerosis/ESC[70]. La guía conjunta ofrece consejos adicionales sobre la intervención sobre los lípidos basada en estas categorías.

Conclusiones

La estimación del riesgo total sigue siendo una parte fundamental de esta guía. El sistema SCORE se ha actualizado para incluir la estimación del riesgo CV total además del riesgo de muerte CV. Se incluye nueva información sobre la DM y sobre el riesgo relativo, además del riesgo absoluto, para aconsejar a personas jóvenes cuyo riesgo absoluto bajo (por su edad) puede encubrir un riesgo alto y modificable.

Cardiología y DM2

DM2

Dx - Tratamiento - Gestión Crónica

- Endocrinología
- Atención Primaria
- Cardiología?

- Escaso impacto de la formación
- Dx en eventos (SCA)
- Limitada participación en el tratto.
- No participación en la gestión crónica - HbA1c

FRCV

- Cardiología
- Atención Primaria
- Endocrinología

- Amplio estudio del impacto de la DM2 en la patología CV
- Papel modificador del riesgo y tratto : DM2 sí/no
- Ausencia de tratto. eficaz de la DM2 para reducir riesgo CV

Papel del cardiólogo: ¿puede el cardiólogo NO prescribir Empagliflozina?

Check List para el tratamiento con Empaglifozina en Cardiología:

- ☑ DM2 de cualquier tiempo de evolución, adultos.
- ☑ Enfermedad CV establecida (cardiopatía isquémica, ictus, enfermedad vascular periférica; con o sin insuficiencia cardiaca).
- ☑ IMC ≤45, MDRD ≥60 ml/min/1,73 m2.
- ☑ HbA1c ≥7,0% y ≤9,0% SIN tratamiento hipoglucemiante 12 semanas previas ó

  HbA1c ≥7,0% y ≤10,0% CON cualquier tratamiento hipoglucemiante 12 semanas previas.
- ☑ Sin ajuste de dosis por función renal o hepática.
- ☑ Sin interacción con otros fármacos cardiovasculares ni necesidad de ajuste de dosis.
- ☑ Excluidos: SCA, ictus/AIT en los dos meses previos.
- ☑ Precaución: diuréticos de asa (hipovolemia), hipotensión arterial, hipoglucemias si toma insulina o sulfonilureas, infecciones urinarias/genitales previas.

Preservando la continuidad asistencial y el manejo clínico habitual del paciente

Conclusiones

El diagnóstico y el tratamiento de la IC en pacientes con/sin DM es esencialmente el mismo

Lo importante es diagnosticar y tratar adecuadamente la IC y sus frecuentes comorbilidades

¿Tiene el Cardiólogo un nuevo rol en la DM?