

XXXVII CONGRESO

ASOCIACIÓN SOCIEDAD EXTREMEÑA DE CARDIOLOGÍA

Novedades terapéuticas en insuficiencia cardíaca

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Novedades



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

The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC)

Developed with the special contribution of the Heart Failure Association (HFA) of the ESC

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2016 ACC/AHA/HFSA Focused Update on New Pharmacological Therapy for Heart Failure: An Update of the 2013 ACCF/AHA Guideline for the Management of Heart Failure

A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Failure Society of America

Developed in Collaboration With the International Society for Heart and Lung Transplantation

Insuficiencia Cardíaca Aguda



Recommendations for the management of patients with acute heart failure: pharmacotherapy

Recommendations	Class ^a	Level ^b	Ref ^c
Diuretics			
Intravenous loop diuretics are recommended for all patients with AHF admitted with signs/symptoms of fluid overload to improve symptoms. It is recommended to regularly monitor symptoms, urine output, renal function and electrolytes during use of i.v. diuretics.	I	C	
In patients with new-onset AHF or those with chronic, decompensated HF not receiving oral diuretics the initial recommended dose should be 20–40 mg i.v. furosemide (or equivalent); for those on chronic diuretic therapy, initial i.v. dose should be at least equivalent to oral dose.	I	B	540, 548
It is recommended to give diuretics either as intermittent boluses or as a continuous infusion, and the dose and duration should be adjusted according to patients' symptoms and clinical status.	I	B	548
Combination of loop diuretic with either thiazide-type diuretic or spironolactone may be considered in patients with resistant oedema or insufficient symptomatic response.	IIb	C	549
Vasodilators			
i.v. vasodilators should be considered for symptomatic relief in AHF with SBP >90 mmHg (and without symptomatic hypotension). Symptoms and blood pressure should be monitored frequently during administration of i.v. vasodilators.	IIa	B	537, 550–555
In patients with hypertensive AHF, i.v. vasodilators should be considered as initial therapy to improve symptoms and reduce congestion.	IIa	B	537, 551–554
Inotropic agents – dobutamine, dopamine, levosimendan, phosphodiesterase III (PDE III) inhibitors			
Short-term, i.v. infusion of inotropic agents may be considered in patients with hypotension (SBP <90 mmHg) and/or signs/symptoms of hypoperfusion despite adequate filling status, to increase cardiac output, increase blood pressure, improve peripheral perfusion and maintain end-organ function.	IIb	C	
An intravenous infusion of levosimendan or a PDE III inhibitor may be considered to reverse the effect of beta-blockade if beta-blockade is thought to be contributing to hypotension with subsequent hypoperfusion.	IIb	C	
Inotropic agents are not recommended unless the patient is symptomatically hypotensive or hypoperfused because of safety concern.	III	A	556, 557
Vasopressors			
A vasopressor (norepinephrine preferably) may be considered in patients who have cardiogenic shock, despite treatment with another inotrope, to increase blood pressure and vital organ perfusion.	IIb	B	558
It is recommended to monitor ECG and blood pressure when using inotropic agents and vasopressors, as they can cause arrhythmia, myocardial ischaemia, and in the case of levosimendan and PDE III inhibitors also hypotension.	I	C	540, 559–563
In such cases intra-arterial blood pressure measurement may be considered.	IIb	C	
Thrombo-embolism prophylaxis			
Thrombo-embolism prophylaxis (e.g. with LMWH) is recommended in patients not already anticoagulated and with no contra-indication to anticoagulation, to reduce the risk of deep venous thrombosis and pulmonary embolism.	I	B	564
Other drugs			
For acute control of the ventricular rate in patients with atrial fibrillation: a. digoxin and/or beta-blockers should be considered as the first-line therapy. ^d b. amiodarone may be considered.	IIa IIb	C B	565–567
Opiates may be considered for cautious use to relieve dyspnoea and anxiety in patients with severe dyspnoea but nausea and hypopnea may occur.	IIb	B	568, 569

Recommendations regarding renal replacement therapy in patients with acute heart failure

Recommendations	Class ^a	Level ^b	Ref ^c
Ultrafiltration may be considered for patients with refractory congestion, who failed to respond to diuretic-based strategies.	IIb	B	578–580
Renal replacement therapy should be considered in patients with refractory volume overload and acute kidney injury.	IIa	C	

Recommendations regarding management of patients with cardiogenic shock

Recommendations	Class ^a	Level ^b	Ref ^c
In all patients with suspected cardiogenic shock, immediate ECG and echocardiography are recommended.	I	C	
All patients with cardiogenic shock should be rapidly transferred to a tertiary care center which has a 24/7 service of cardiac catheterization, and a dedicated ICU/CCU with availability of short-term mechanical circulatory support.	I	C	
In patients with cardiogenic shock complicating ACS an immediate coronary angiography is recommended (within 2 hours from hospital admission) with an intent to perform coronary revascularization.	I	C	
Continuous ECG and blood pressure monitoring are recommended.	I	C	
Invasive monitoring with an arterial line is recommended.	I	C	
Fluid challenge (saline or Ringer's lactate, >200 ml/15–30 min) is recommended as the first-line treatment if there is no sign of overt fluid overload.	I	C	
Intravenous inotropic agents (dobutamine) may be considered to increase cardiac output.	IIb	C	
Vasopressors (norepinephrine preferable over dopamine) may be considered if there is a need to maintain SBP in the presence of persistent hypoperfusion.	IIb	B	558
IABP is not routinely recommended in cardiogenic shock.	III	B	585, 586
Short-term mechanical circulatory support may be considered in refractory cardiogenic shock depending on patient age, comorbidities and neurological function.	IIb	C	

Table 13.3 Patients potentially eligible for implantation of a left ventricular assist device

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 for implantation of mechanical circulatory support in patients with refractory heart failure

Recommendations	Class ^a	Level ^b	Ref ^c
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).	Ila	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.	Ila	B	605, 612, 613

Heart transplantation is an accepted treatment for end-stage HF.^{614,615} Although controlled trials have never been conducted, there is a consensus that transplantation—provided that proper selection criteria are applied—significantly increases survival, exercise capacity, quality of life and return to work compared with conventional treatment.

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Acute and Advanced Heart Failure Knowledge Centre

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News & Perspective

Serelaxin Again Bombs in Acute Heart Failure: RELAX-AHF-2

Patrice Wendling

March 23, 2017

WASHINGTON, DC — Serelaxin (RLX030, Novartis) failed to meet its primary end points in acute heart failure in the [RELAX-AHF-2](#) study, putting its future in jeopardy.

An update of the phase 3 data showed serelaxin did not significantly reduce the rate of cardiovascular death through day 180 or worsening heart failure through day 5 in acute heart-failure patients when added to standard therapy, according to the company^[1].

The first-in-class recombinant form of human hormone relaxin 2 reduced dyspnea in the [RELAX-AHF](#) trial but questions about its mortality benefit remained.

The drug was subsequently shot down for the treatment of acute HF in 2014 by [US Food and Drug Administration](#) reviewers, who cited insufficient

Insuficiencia Cardíaca Crónica



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 spironolactone³⁰¹ and candesartan³¹⁰ 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 ARBs³¹⁵ or ACEIs³¹¹ is inconclusive.

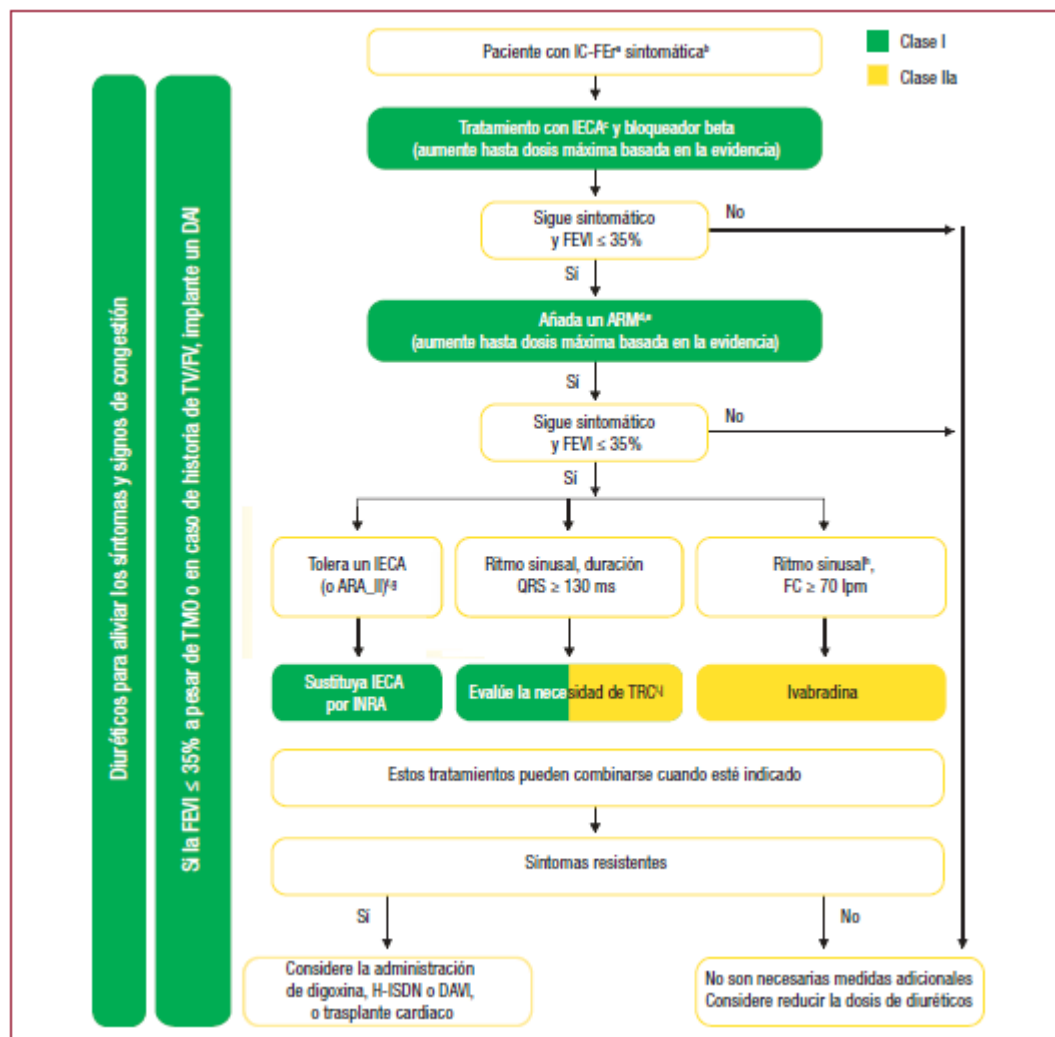
9.3 Effect of treatment on mortality in heart failure with preserved ejection fraction

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

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



Recommendations for the treatment of stable angina pectoris with symptomatic (NYHA Class II-IV) heart failure with reduced ejection fraction^{112,113}

Recommendations	Class ^a	Level ^b	Ref ^c
Step I			
A beta-blocker (in an evidence-based dose or maximum tolerated) is recommended as the preferred first-line treatment to relieve angina because of the associated benefits of this treatment (reducing the risk of HF hospitalization and the risk of premature death).	I	A	167–173
Step 2: on top of beta-blocker or if a beta-blocker is not tolerated			
Ivabradine should be considered as an anti-anginal drug in suitable HFrEF patients (sinus rhythm and HR ≥70 bpm) as per recommended HFrEF management.	IIa	B	180, 410, 411
Step 3: For additional angina symptom relief – except from any combination not recommended			
A short-acting oral or transcutaneous nitrate should be considered (effective anti-anginal treatment, safe in HF).	IIa	A	183, 184, 409
A long acting oral or transcutaneous nitrate should be considered (effective anti-anginal treatment, not extensively studied in HF).	IIa	B	183, 184
Trimetazidine may be considered when angina persists despite treatment with a beta-blocker (or alternative) to relieve angina (effective anti-anginal treatment, safe in HF).	IIb	A	400–403
Amlodipine may be considered in patients unable to tolerate a beta-blocker to relieve angina (effective anti-anginal treatment, safe in HF).	IIb	B	215, 407
Nicorandil may be considered in patients unable to tolerate a beta-blocker to relieve angina (effective anti-anginal treatment, but safety in HF uncertain).	IIb	C	
Ranolazine may be considered in patients unable to tolerate a beta-blocker to relieve angina (effective anti-anginal treatment, but safety in HF uncertain).	IIb	C	

CRT

Recommendations for cardiac resynchronization therapy implantation in patients with heart failure

Recommendations	Class ^a	Level ^b	Ref ^c
CRT is recommended for symptomatic patients with HF in sinus rhythm with a QRS duration ≥ 150 msec and LBBB QRS morphology and with LVEF $\leq 35\%$ despite OMT in order to improve symptoms and reduce morbidity and mortality.	I	A	261–272
CRT should be considered for symptomatic patients with HF in sinus rhythm with a QRS duration ≥ 150 msec and non-LBBB QRS morphology and with LVEF $\leq 35\%$ despite OMT in order to improve symptoms and reduce morbidity and mortality.	IIa	B	261–272
CRT is recommended for symptomatic patients with HF in sinus rhythm with a QRS duration of 130–149 msec and LBBB QRS morphology and with LVEF $\leq 35\%$ despite OMT in order to improve symptoms and reduce morbidity and mortality.	I	B	266, 273
CRT may be considered for symptomatic patients with HF in sinus rhythm with a QRS duration of 130–149 msec and non-LBBB QRS morphology and with LVEF $\leq 35\%$ despite OMT in order to improve symptoms and reduce morbidity and mortality.	IIb	B	266, 273
CRT rather than RV pacing is recommended for patients with HFrEF regardless of NYHA class who have an indication for ventricular pacing and high degree AV block in order to reduce morbidity. This includes patients with AF (see Section 10.1).	I	A	274–277
CRT should be considered for patients with LVEF $\leq 35\%$ in NYHA Class III–IV ^d despite OMT in order to improve symptoms and reduce morbidity and mortality, if they are in AF and have a QRS duration ≥ 130 msec provided a strategy to ensure bi-ventricular capture is in place or the patient is expected to return to sinus rhythm.	IIa	B	275, 278–281
Patients with HFrEF who have received a conventional pacemaker or an ICD and subsequently develop worsening HF despite OMT and who have a high proportion of RV pacing may be considered for upgrade to CRT. This does not apply to patients with stable HF.	IIb	B	282
CRT is contra-indicated in patients with a QRS duration < 130 msec.	III	A	266, 283–285

Otras comorbilidades

Recommendations for the treatment of other co-morbidities in patients with heart failure

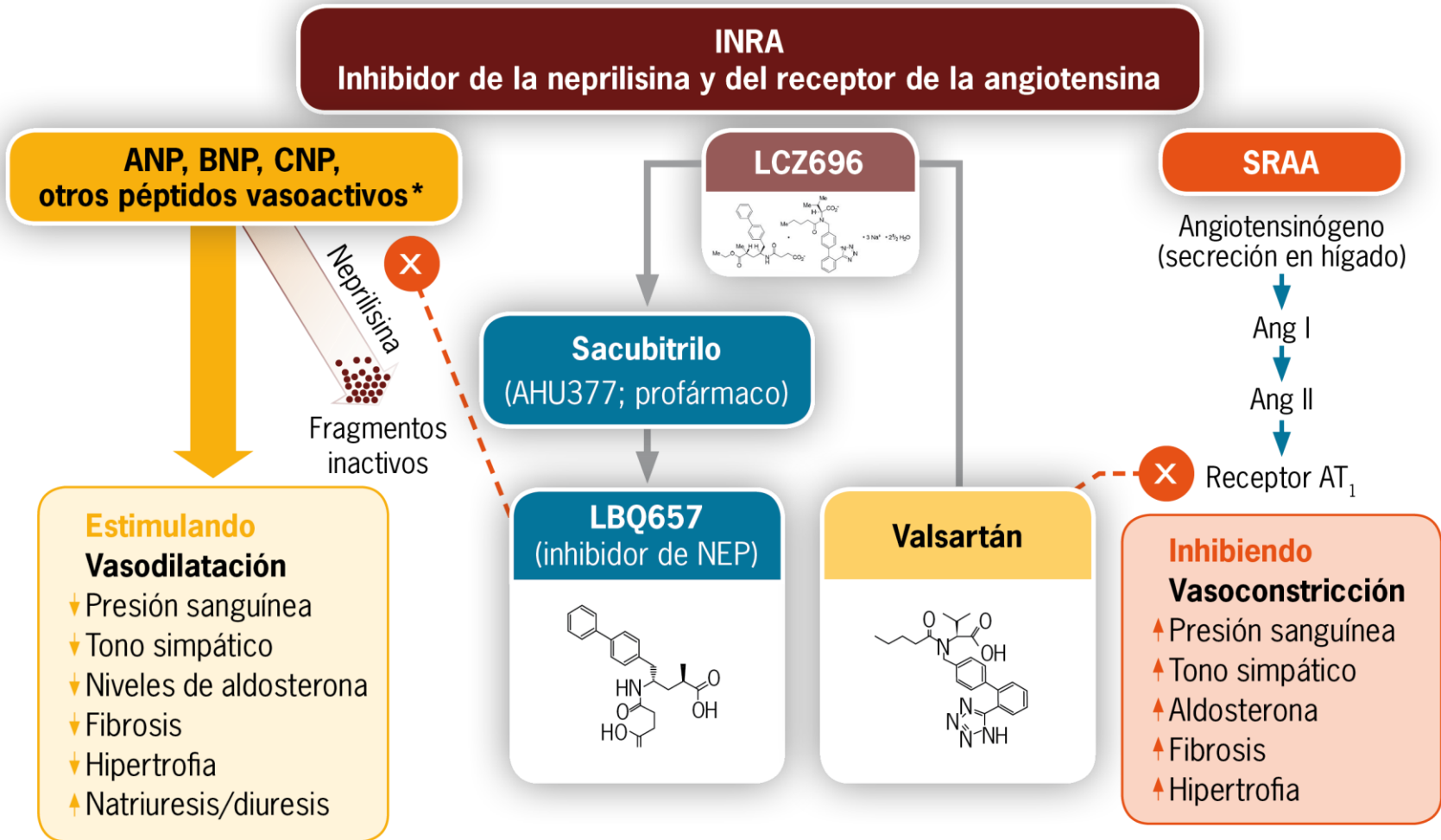
Recommendations	Class ^a	Level ^b	Ref ^c
Iron deficiency			
Intravenous FCM should be considered in symptomatic patients with HFrEF and iron deficiency (serum ferritin <100 µg/L, or ferritin between 100–299 µg/L and transferrin saturation <20%) in order to alleviate HF symptoms, and improve exercise capacity and quality of life.	Ila	A	469, 470
Diabetes			
Metformin should be considered as a first-line treatment of glycaemic control in patients with diabetes and HF, unless contra-indicated.	Ila	C	440, 441

Treatments not recommended of other co-morbidities in patients with heart failure

Recommendations	Class ^a	Level ^b	Ref ^c
Sleep apnoea			
Adaptive servo-ventilation is not recommended in patients with HFrEF and a predominant central sleep apnoea because of an increased all-cause and cardiovascular mortality.	III	B	473
Diabetes			
Thiazolidinediones (glitazones) are not recommended in patients with HF, as they increase the risk of HF worsening and HF hospitalization.	III	A	209, 210
Arthritis			
NSAIDs or COX-2 inhibitors are not recommended in patients with HF, as they increase the risk of HF worsening and HF hospitalization.	III	B	211–213

Sacubitrilo/valsartan

Complejo supramolecular



* 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. 2011; 52: 275-276.

Manejo práctico

- Indicación
- Inicio de la prescripción
- Titulación
- Contraindicaciones / efectos secundarios

Indicación

- S/V 24 mg/26 mg.
- S/V 49 mg/51 mg.
- S/V 97 mg/103 mg.
- 26 mg, 51 mg y 103 mg de valsartán en Entresto son equivalentes a 40 mg, 80 mg y 160 mg de valsartán en otras formulaciones comercializadas.
- Dosis **baja**, **media (de inicio)** y **óptima** semejante a IECAs o BB.

Para aprender las dosis...
-1 +1 mg -3 +3 mg

Indicación

Indicación en Ficha Técnica:

- "S/V está indicado en pacientes adultos para el tratamiento de la insuficiencia cardiaca crónica sintomática con fracción de eyección reducida".

En PARADIGM-HF:

IC crónica

NYHA II-IV

FEVI $\leq 40\%$ (modificado a $\leq 35\%$)

Tratto. óptimo estable en las 4 semanas previas

Subestudios PARADIGM-HF

Beneficios demostrados en...

- pacientes ancianos.
- no diabéticos, diabéticos y prediabéticos.
- en los diferentes grados de severidad de la disfunción ventricular.
- con o sin ingreso previo por IC, e independiente del tiempo desde el mismo.
- con un beneficio equivalente en los pacientes que toleraban previamente sólo dosis bajas de enalapril.
- independientemente del tratamiento concomitante de base del paciente.
-

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

1610044238

¿Cuándo empezar?

En cualquier momento de la historia natural:

- Paciente con reciente diagnóstico y mala respuesta.
- Paciente NYHA II ó III con síntomas estables.
- Paciente NYHA II ó III con síntomas progresivos.
- En primera consulta tras ingreso o Urgencias por descompensación.

Contraindicaciones

- No historia de angioedema.
- No historia de intolerancia a IECA+ARAI.
- No embarazo ni lactancia.
- No toma Aliskireno.
- No insuficiencia hepática grave.
- No diálisis.

PAS < 100 mmHg
K > 5,4 mEq/L

3 Preguntas para saber dosis de inicio

1. Dosis previa de IECA/ARAII	Bajas (Enalapril ≤ 10 mg/d Valsartán ≤ 160 mg/d o equivalentes) o sin tratamiento previo	Medias o Altas (Enalapril > 10 mg/d Valsartán > 160 mg/d o equivalentes)
2. PAS	100 a 110 mmHg	> 110 mmHg
3. FG Insuf. Hepática	≤ 60 ml/min/1,73m ² IH moderada	> 60 ml/min/1,73m ² IH leve
	Cualquiera de las 3 anteriores = DOSIS BAJAS 24/26 mg/ 12 h	Si se cumplen las 3 anteriores = ENTRESTO DOSIS MEDIAS 49/51 mg / 12 h

Titulación a la siguiente dosis cada 2-4 semanas

** Con problemas de tolerabilidad (PAS ≤ 95 mmHg, hipotensión sintomática, hiperpotasemia, disfunción renal) se recomienda un ajuste de los medicamentos concomitantes, reducción temporal de la dosis o interrupción de Entresto*

Efectos secundarios

	Sacubitrilo /valsartán (n= 4.187)	Enalapril (n= 4.212)	p [‡]
Hipotensión			
• Sintomático	588 (14,0)	388 (9,2)	<0,001
• Sintomático con PAS <90 mmHg	112 (2,7)	59 (1,4)	<0,001
Creatinina en sangre elevada			
• ≥2,5 mg/dL	139 (3,3)	188 (4,5)	0,007
• ≥3,0 mg/dL	63 (1,5)	83 (2,0)	0,10
Potasio en sangre elevado			
• >5,5 mmol/L	674 (16,1)	727 (17,3)	0,15
• >6,0 mmol/L	181 (4,3)	236 (5,6)	0,007
Tos	474 (11,3)	601 (14,3)	<0,001
Angioedema (adjudicada por un comité de expertos ciego)			
• Sin tratamiento o solo tratamiento con antihistamínicos	10 (0,2)	5 (0,1)	0,19
• Catecolaminas o glucocorticoides sin hospitalización	6 (0,1)	4 (0,1)	0,52
• Hospitalización sin dispositivo de vía aérea	3 (0,1)	1 (<0,1)	0,31
• Con compromiso de la vía aérea	0	0	---

McMurray et al. N Engl J Med. 2014; 371: 993-1.004.

Interacciones farmacológicas

Fármaco	¿Contraindicado?	Riesgos de la administración concomitante	Observaciones y recomendaciones
IECA	SI	Puede aumentar el riesgo de angioedema.	S/V no se debe iniciar hasta 36 horas después de la última dosis de IECA, o viceversa.
Aliskireno	SI[#]	Está potencialmente asociada con un aumento de la frecuencia de acontecimientos adversos como hipotensión, hiperpotasemia y disminución de la función renal (incluyendo fallo renal agudo) [#] en pacientes con DM o con IR (TFGe <60 ml/min/1,73 m ²)	No se recomienda la combinación de S/V con inhibidores directos de la renina como el aliskireno en pacientes con DM o con IR (TFGe <60 ml/min/1,73 m ²) [#]
ARA-II	NO [±]	±S/V contiene valsartán y por lo tanto no se debe administrar junto con otro medicamento que contenga un ARA-II.	No se recomienda el uso concomitante

Debido al riesgo potencial de angioedema, se recomienda un **LAVADO DE 36h en pacientes que toman IECAs o que los reinician tras Sacubitrilo/valsartán.**

Si toma ARA-II sustituir por Sacubitrilo/valsartán la siguiente toma (no lavado).

Sacubitrilo/valsartán no se debe administrar de forma conjunta con un IECA o un ARA-II.

Experiencia UIC Hospital Clínico San Carlos Primeros 65 pacientes

- 57% varones, edad $64,3 \pm 15,0$ años.
 - NYHA II 74,5%
 - NYHA III 25,5 %
- Etiología: isquémica 57 %, idiopática 40%, resto 3%.
- FEVI media $29,4 \pm 7,9$ %
- Tratamiento previo:
 - 67,4 % IECA; 22,4 % ARAII; 10,3 % ninguno.
 - BB 91%, ARM 83%, Digoxina 14%, diuréticos 86%.
- Dosis de inicio Sacubitrilo/Valsartán: 79 % baja y 21 % media.

Experiencia UIC Hospital Clínico San Carlos

Perfil seguridad:

- Suspensión en 2 pacientes por hipotensión.
- Reducción por hipotensión sintomática en 3 pacientes.
- Suspensión en 1 paciente por ingreso por IC.
- Sin cambios significativos en función renal ni en niveles de potasio.

Pacientes que muestran mejoría sintomática 57%