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The ABC of managing heart failure in patients with type 2 diabetes mellitus

Avoiding complications and improving quality of life from Primary Care

Heart failure (HF) is a complex and prevalent condition in our offices, as well as in the ER and at the hospital setting. People with HF are at high risk for hospitalization, cardiorenal complications, and mortality, which poses a clinical challenge for all health care professionals treating these patients.

In the specific context of diabetes, HF is much more frequent due to the coexistence of common risk factors, such as hypertension or obesity, the presence of ischemic heart disease, extracellular volume expansion, or diabetic cardiomyopathy per se. **Women with diabetes have a 5 times higher risk**, while men with diabetes have a 2 times higher risk. **Heart failure is also the leading cause of hospitalization in these patients**[7, 8].

In recent years, much progress has been made in the treatment of HF, thanks to large cardiovascular safety trials conducted with drugs from the sodium-glucose cotransporter 2 inhibitors (SGLT2i) family, which have demonstrated significant cardiovascular benefits across the entire spectrum of HF in patients with type 2 diabetes mellitus (T2DM). Dapagliflozin and empagliflozin have shown these benefits even in patients without diabetes.

CURRENT DIAGNOSIS OF HEART FAILURE

Heart failure is a clinical syndrome characterized by **cardinal symptoms** (such as dyspnea, ankle swelling, and fatigue) that may be accompanied by **signs** (such as elevated jugular venous pressure, peripheral edema, and pulmonary crepitations).

Heart failure is due to **structural and/or functional cardiac abnormalities** that result in elevated intracardiac pressures and/or inadequate cardiac output, which may present at rest and/or during exercise.

In 2021, major international heart failure societies developed a new **"Universal Definition of Heart Failure".** This definition emphasizes the importance of determining natriuretic peptides (NPs). In a patient with typical clinical symptoms and/or signs caused by a structural and/or functional cardiac abnormality, along with elevated NPs or objective evidence of cardiogenic pulmonary or systemic congestion, a suspected diagnosis of heart failure can already be established. An echocardiogram, when available, will help establish the cause and phenotype of the condition.

This universal classification is particularly important in primary care settings, where access to echocardiography may be delayed. Once the clinical suspicion is established through symptoms, NP levels, and accessible imaging modalities, such as chest X-ray or echocardiography, treatment can be started with drugs that have proven effective across the entire range of left ventricular ejection fraction (LVEF), such as SGLT2 inhibitors - dapagliflozin and empagliflozin - and diuretics, if necessary, to control congestion[2, 4].

Early diagnosis is critical. The goal is to make a timely diagnosis so that corrective measures and prognostically beneficial drugs, capable of reducing heart failure-related hospitalizations, can be initiated as soon as possible.

Natriuretic peptides are essential, not only to rule out heart failure but also to confirm diagnosis ("to rule heart failure in")[5].

In the presence of typical clinical symptoms and/or signs caused by structural and/or functional cardiac abnormalities, elevated NP levels allow for a high-suspicion diagnosis. Easily accessible imaging modalities, such as chest X-rays or echocardiography, can support this diagnosis. NPs improve clinical evaluation by increasing the accuracy of heart failure diagnosis, particularly in cases of uncertainty. Their use reduces costs, improves management and timing, and increases the number of correct diagnoses.

NPs allow us to rule out HF both in the ER and outpatiently, due to their high sensitivity and negative predictive value. They enhance clinical assessment by increasing the ability to distinguish HF, particularly in uncertain situations, regardless of other factors. Their use has a health care impact by reducing costs and improving management and timing, ultimately increasing the number of correct diagnoses.

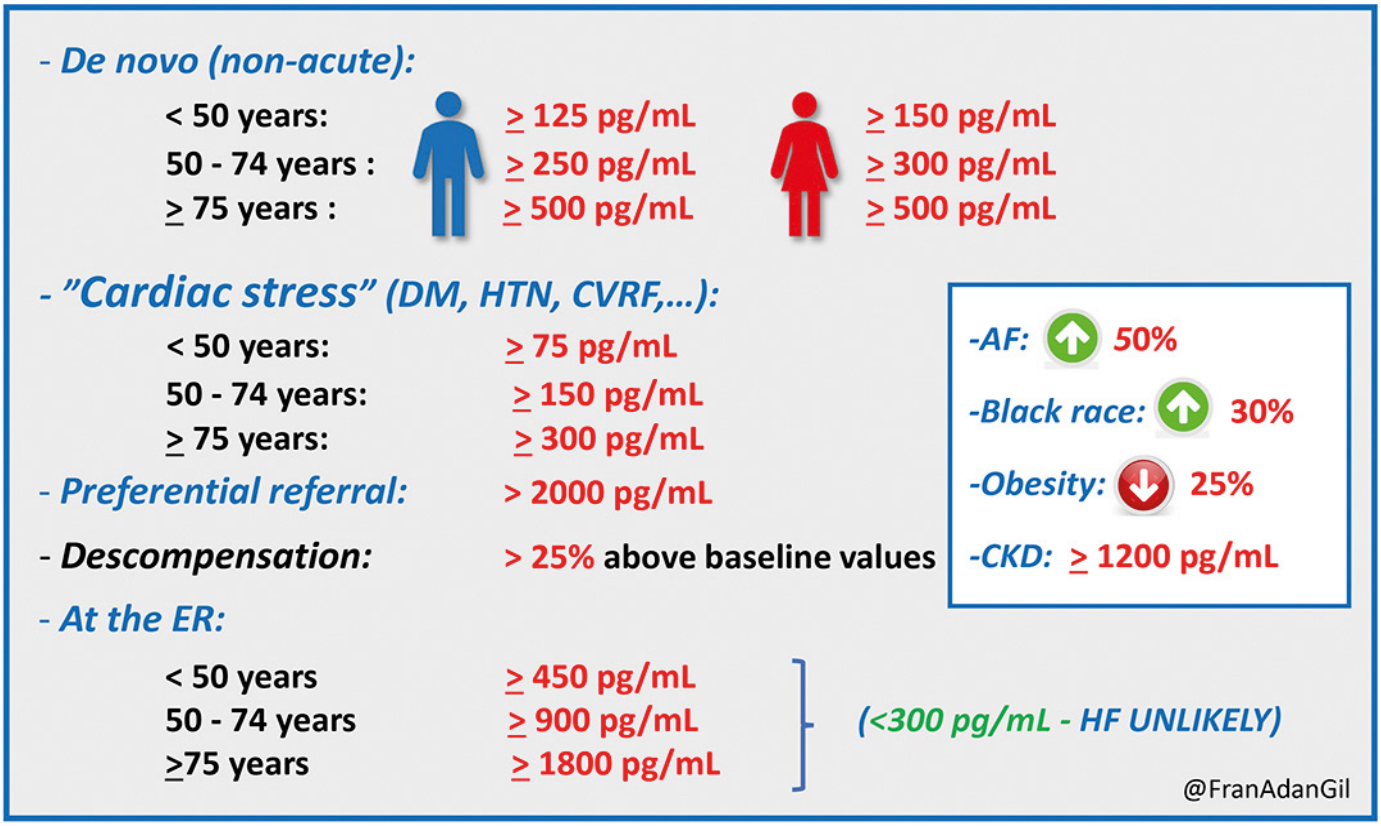
However, NPs are not only useful in the diagnostic process but also throughout the course of the disease, helping monitor clinical progress and detect decompensations early. The following table shows a few reference values *(Table 1)*.

CURRENT MANAGEMENT OF HEART FAILURE

Heart failure with reduced and mildly reduced ejection fraction

Heart failure with reduced and mildly re- »

WOMEN WITH DIABETES HAVE A 5 TIMES GREATER RISK—BEING THIS RISK 2 TIMES HIGHER IN MEN WITH DIABETES. HEART FAILURE IS ALSO THE LEADING CAUSE OF HOSPITAL ADMISSION IN THESE PATIENTS



Bayes-Genis A. et al. (Orcid ID: 0000-0002-3044-197X) Eur J HF 2023 https://doi.org/10.1002/ejhf.2293 ESC HF Guidelines. Eur Heart J 2021;42(36)

TABLE 1. Interpretation of natriuretic peptides (NT pro-BNP)

» **duced ejection fraction** (HFrEF and HFmrEF) is a chronic and progressive disease. These patients have a relatively stable course of the disease until they experience a first hospitalization. From this point, a progressive clinical picture begins, with successive hospitalizations due to acute exacerbations leading to global heart failure.

The targets of treatment are to improve the patient's clinical status, functional capacity, and quality of life, prevent hospitalizations, and reduce mortality. Preventing or avoiding precipitating factors and recognizing signs of decompensation by the patient and their caregivers, along with close follow-up in primary care, is essential for treatment and preventing hospitalizations. Structured educational measures and coordinated follow-up between primary and hospital care can reduce hospitalizations by up to 30%[7].

Nutritionally, the **Mediterranean diet** is recommended, with salt restriction (< 3 grams/day) and maintaining an adequate weight, avoiding very restrictive diets that may not be well tolerated by these patients. Self-monitoring of weight, and even fluid intake and diuresis in NYHA Functional Class III/IV allows for early detection of exacerbations. Routine fluid restriction is not necessary for HF patients, except in cases of decompensated or advanced HF, especially with hyponatremia (< 1.5-2 liters/day).

Regular and moderate physical activity (e.g., walking or cycling for, at least, 30 minutes, 5 times a week) improves exercise tolerance, functional capacity, and quality of life and can reduce hospitalizations.

The treatment of HFrEF is well protocolized, with recommendations to act on all therapeutic targets when possible: sympathetic nervous system, renin-angiotensin-aldosterone system, vasoactive peptide system, and cardiorenal axis, using beta-blockers, ACEIs/ARBs/ARNIs, MRAs, and SGLT2 inhibitors.

In patients in sinus rhythm with a HR > 70 bpm, ivabradine is also an effective alternative for those who remain symptomatic despite optimal therapy. Hydralazine + isosorbide dinitrate or digoxin are se- »

» cond-line drugs that are useful in certain scenarios *(Figure 1)*[7].

New drugs like vericiguat or omecamtiv mecarbil have also shown benefits in reducing hospitalizations or mortality in these patients.

Despite optimal pharmacological treatment, some patients with advanced HFrEF may require other strictly hospital-based therapeutic options, such as mechanical circulatory support, myocardial revascularization, or surgical treatment, among others.

Implantable devices have become effective in both the primary prevention of sudden death with defibrillators and reducing rehospitalizations and overall mortality with cardiac resynchronization therapy.

Regarding HFrEF, currenlt, it tends to be treated similarly to HFrEF, although with a lower level of recommendation, since studies have not been as conclusive.

Heart failure with preserved ejection fraction (HFpEF)

Given the characteristics of these patients—older, highly symptomatic, often with poor quality of life—a key therapy is to alleviate symptoms and improve their quality of life.

In patients with congestion, the first-line therapy includes loop diuretics such as furosemide, torsemide, or bumetanide, which reduce cardiac filling pressures to improve dyspnea symptoms and exercise capacity. These are useful in all types of heart failure (recommendation grade I-B) and may reduce the risk of hospitalization.

In chronic HF, the goal of diuretics is to maintain euvolemia—"dry weight"—with the lowest possible dose. The persistence of congestion should be reevaluated in prolonged treatments, restricting their use in the absence of fluid overload. The need for diuretics is a marker of the degree of disease con- »

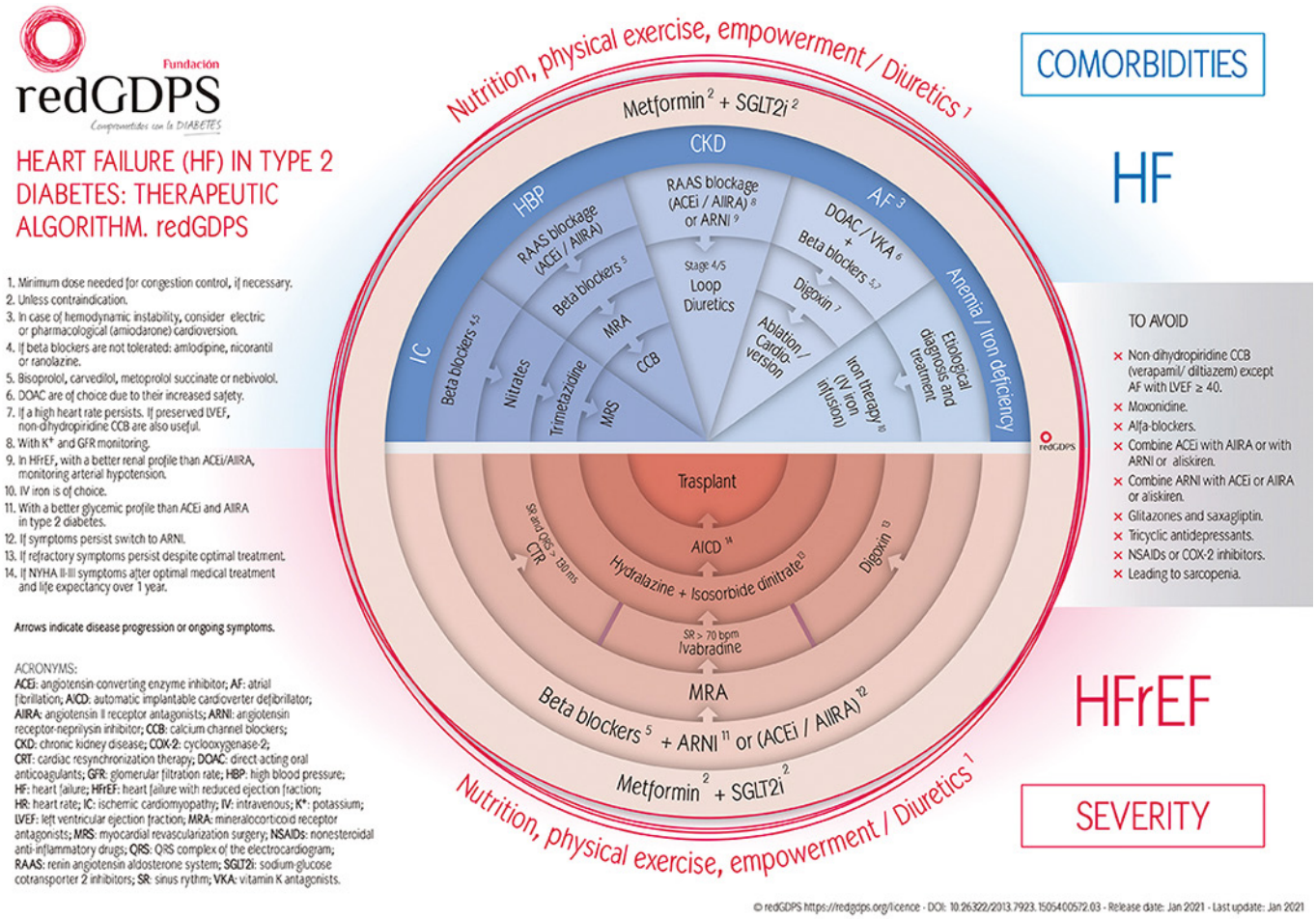


FIGURA 1: Tratamiento de la Insuficiencia Cardiaca con fracción de eyección reducida en DM2

» trol, so any patient who requires 2 or more diuretic tablets per day for control purposes cannot be considered stable, and their baseline therapy should be optimized[8].

The 2023 update of the guidelines published by the European Society of Cardiology (ESC)[4] highlights the evidence from recent studies on SGLT2 inhibitors—dapagliflozin and empagliflozin—that have proven effective in reducing hospitalizations and visits to the ER, regardless of the patient's LVEF.

Therefore, in a patient with a well-founded diagnostic suspicion of HF, while awaiting the ECG to determine their LVEF and possible etiology, treatment with dapagliflozin or empagliflozin should be initiated as soon as possible. This way, the patient can start benefiting from a reduced risk of first or subsequent hospitalizations and an improved quality of life. Since this effect is maintained across the entire spectrum of ejection fraction, these drugs can be continued regardless of the ECG results throughout the course of the disease.

OPTIMIZING THE TREATMENT OF CHRONIC HEART FAILURE

When choosing the appropriate treatment for each clinical situation, key variables such as LVEF, systolic blood pressure, heart rate, glomerular filtration rate, and blood potassium levels should be considered. Various clinical scenarios are defined based on these variables, with the goal of normalizing them as much as possible to optimize treatment (figure 2)[9].

Thus, for example, the use of drugs that cause hypotension, bradycardia, impaired glomerular filtration, or hyperkalemia should be avoided as much as possible or substituted with safer alternatives in these patients, especially if they do not offer a prognostic benefit.

No drug is effective if not taken. These patients are prescribed a large number »

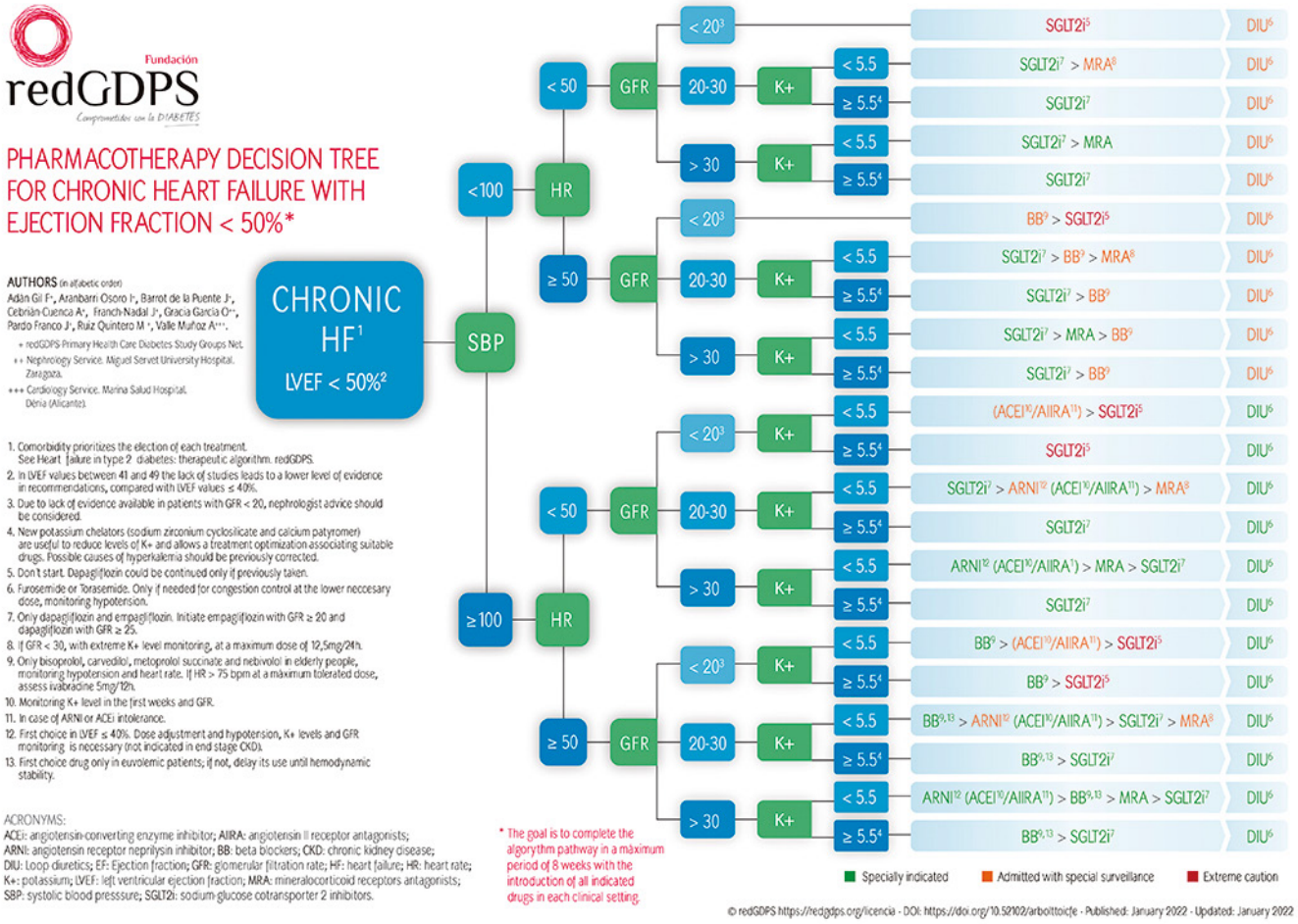


FIGURA 2: Optimización del tratamiento de la Insuficiencia Cardiaca crónica

IN SOME PATIENTS WITH ADVANCED HFREF—WHO MAY REPRESENT UP TO 5% OF THE TOTAL—IT WILL BE NECESSARY TO RESORT TO OTHER STRICTLY HOSPITAL-BASED THERAPEUTIC OPTIONS

» of drugs, which complicates adherence. As a result, they sometimes make decisions to discontinue one or more of their treatments on their own, a factor that is the leading cause of decompensation and hospital admissions in this condition. Therefore, any strategy that helps simplify their treatment (such as fixed-dose combinations or chronotherapy) may improve their adherence.

COMORBIDITY IN CHRONIC HEART FAILURE

The management of comorbidities in HF, particularly HFpEF, is crucial to improving the quality of life and survival of these patients and reducing the significant economic burden of this condition on society. The frequency distribution of patients with comorbidities and HFpEF vs those with HF with reduced ejection fraction (HFrEF), differentiated by men and women, shows that men with HFpEF have a higher number of concurrent diseases—a mean 4—vs patients of both sexes with HFrEF.

In addition to their own comorbidities, there may be other clinical conditions such as anemia, depression, obesity, diabetes, kidney disease, chronic obstructive pulmonary disease (COPD), sarcopenia, or pulmonary hypertension, which are independent risk factors for the development of HF and require specific management.

In conclusion, HF requires a proactive approach from health care professionals to uncover the iceberg of underdiagnosis. Natriuretic peptides are an excellent aid for clinicians during this diagnostic phase. The new evidence in treating this condition has streamlined its management towards therapies that improve prognosis and reduce hospitalizations.

HF is the paradigm of a cross-sectional disease with high associated morbidity, where many professionals are involved, always putting the patient at the center of care. D

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