Rafael González-Manzanares, MD, PhD.
Cardiology Unit. Hospital Universitario Reina Sofía, Córdoba.
Instituto Maimónides de Investigación Biomédica (IMIBIC), Córdoba. Spain.

Heart failure and diabetes mellitus:

understanding this close relationship and the new treatment paradigm

Type 2 diabetes mellitus (T2DM) is one of the greatest pandemics of our century. Historically, both healthcare professionals and patients have focused on controlling blood sugar levels to prevent classic complications such as kidney damage, vision loss, or myocardial infarction. However, in recent years, medical science has shed light on an undeniable clinical reality: heart failure (HF) is one of the most common, lethal, and paradoxically underdiagnosed cardiovascular complications in people with diabetes (1).

This article aims to explore the profound relationship between diabetes and HF. We will examine how diabetes affects cardiac structure, the simple tools currently available for early diagnosis, and, most importantly, how new treatments have revolutionized our ability not only to prolong life but also to dramatically improve patients' quality of life.

THE SIZE OF THE PROBLEM

It is estimated that people with diabetes have between two and five times higher risk of developing HF compared to the general population without diabetes. In fact, HF is often the first cardiovascular complication to appear in a patient with type 2 diabetes, surpassing myocardial infarction or stroke in frequency.

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» In recent and highly representative studies, such as the Spanish national registry DIABET-IC, which evaluated patients with type 2 diabetes treated in cardiology and endocrinology clinics, it was found that nearly 40% (39.2%) of these patients already had HF at the time of evaluation. Even more striking, during a three-year follow-up, the incidence of new cases was 7.6%. Globally, it is estimated that up to 22% of all patients with diabetes have some degree of this cardiac condition (2).

Despite these alarming figures, HF remains an underestimated complication. Part of the problem lies in the fact that early symptoms, such as fatigue or shortness of breath, are often mistakenly attributed to age, poor physical condition, or excess weight, delaying a crucial diagnosis (3).

WHAT IS "DIABETIC CARDIOMYOPATHY" AND HOW DOES IT DAMAGE THE HEART?

To understand HF, it is helpful to visualize the heart as a muscular pump responsible for filling with oxygenated blood and ejecting it to the rest of the body. When this pump fails, the body does not receive the oxygen it needs, and fluids accumulate in the lungs and legs (congestion).

In people with diabetes, the heart suffers direct and progressive damage that physicians refer to as **"diabetic cardiomyopathy"**, defined as deterioration of cardiac function occurring even in the absence of obstructive coronary artery disease or severe hypertension (4). This damage manifests mainly through 2 major phenotypes:

1. **Diabetes, obesity, and heart failure with preserved ejection fraction (HFpEF)**

   This is currently the most frequent and fastest-growing phenotype in patients with type 2 diabetes. It is closely associated with obesity, particularly "visceral adiposity" (fat accumulated around abdominal organs and the heart itself). Traditionally, excess glucose was considered the sole culprit. However, we now know that visceral fat is not merely an energy store but an active and toxic organ that releases inflammatory substances (adipokines) into the bloodstream. This chronic inflammation causes fat to accumulate directly within cardiac muscle cells. As a result of this inflammatory and toxic environment, the cardiac muscle becomes thick (hypertrophy) and stiff (fibrosis). In this scenario, the heart preserves its pumping strength (hence "preserved ejection fraction"), but due to its stiffness, it loses its ability to relax[5]. If it cannot relax properly, it cannot fill efficiently, leading to increased intracardiac pressure transmitted to the lungs, causing extreme fatigue and dyspnea.

2. **Diabetes, ischemic disease, and heart failure with reduced ejection fraction (HFrEF)**

   This 2nd profile is the most classic. In this case, chronically elevated blood glucose levels, along with factors such as hypercholesterolemia and smoking, damage blood vessel walls. This accelerates atherosclerosis (formation of fatty plaques that obstruct coronary arteries). When arteries become blocked, the heart suffers from lack of oxygen and myocardial infarctions may occur. The heart tissue that survives an infarction becomes weakened and scarred. As healthy muscle mass is lost, the heart becomes enlarged and weak. Due to its inability to contract effectively, the amount of blood ejected with each beat decreases (hence "reduced ejection fraction").

In people with diabetes, HFpEF is more frequent in women, and HFrEF in men[6]. Regardless of phenotype (stiff or weak heart), the final outcome is similar: a profound decline in physical capacity, recurrent hospitalizations, and reduced life expectancy.

STAGES OF THE DISEASE AND EARLY DIAGNOSIS

One of the most important concepts in modern cardiology is that HF does not begin when the patient experiences dyspnea; it begins much earlier, silently. Clinical practice guidelines classify HF into different stages (A, B, C, and D) (7):

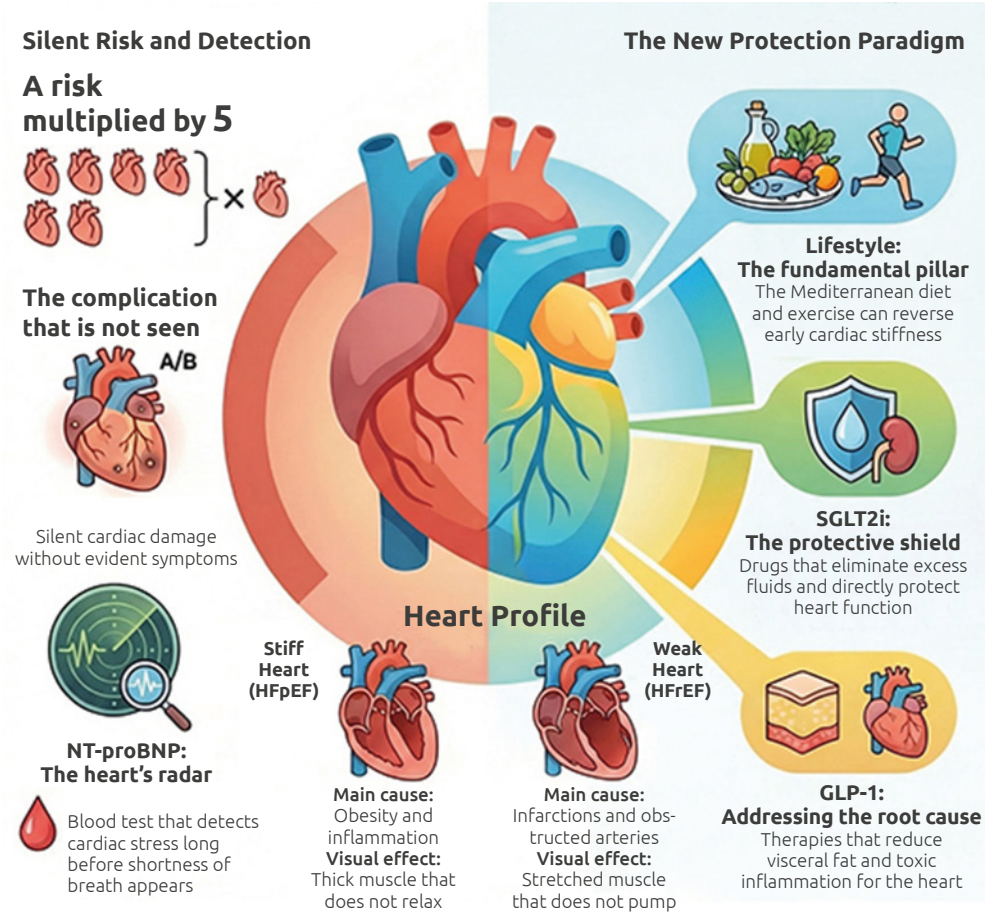
- **Stage A (high risk):** any person with diabetes is already in this stage. Simply having diabetes places the heart at risk, even if the patient feels completely healthy.
- **Stage B (pre-HF):** structural heart damage already exists (e.g., stiffness) or overload detectable by blood tests, but the patient remains asymptomatic.
- **Stages C and D (symptomatic and advanced disease):** evident symptoms appear, such as dyspnea on exertion, orthopnea, or swelling of ankles and legs (edema).

The major current goal is to detect the disease in stages A and B, before irreversible damage occurs. To achieve early and accurate diagnosis, healthcare professionals rely on three fundamental and widely accessible tools:

1. **Blood biomarkers (NT-proBNP).** This is perhaps the most revolutionary early detection tool. NT-proBNP is a protein released by the heart when it is under stress. It can be measured with a simple blood test. If elevated in a person with diabetes, it is a warning sign of silent cardiac suffering. Conversely, normal levels are highly reassuring and practically rule out HF.

2. **Electrocardiogram (ECG).** A rapid, painless test that records the heart's electrical activity. It detects silent myocardial infarctions, cardiac hypertrophy, and importantly, arrhythmias. Patients with diabetes and HF are at high risk of atrial fibrillation, which must be detected to prevent thromboembolism and stroke.

3. **Echocardiogram.** This is a cardiac ultrasound and the gold standard for visualizing the problem. It assesses chamber size, wall thickness, valve function, and calculates ejection frac- »



NT-PROBNP IS A PROTEIN RELEASED BY THE HEART INTO THE BLOODSTREAM WHEN IT IS UNDER STRESS. IT CAN BE MEASURED WITH A SIMPLE BLOOD TEST. IF A PERSON WITH DIABETES UNDERGOES THIS TEST AND LEVELS ARE ELEVATED, IT IS A WARNING SIGN THAT THE HEART IS SUFFERING SILENTLY

» tion, allowing differentiation between HFrEF and HFpEF.

TREATMENT: A HISTORIC PARADIGM SHIFT

A decade ago, diabetes treatment focused almost exclusively on lowering blood glucose. However, major clinical trials demonstrated that glycemic control alone did not always reduce cardiovascular mortality. Today, we are experiencing a complete paradigm shift. The modern approach is holistic and organ-protective. The goal is no longer just a number on the glucometer, but the use of strategies and medications that protect the heart and kidneys while addressing underlying obesity.

1. Lifestyle: the fundamental pillar

Treatment must begin with lifestyle foundations: nutrition and exercise. A Mediterranean diet is recommended, along with prudent salt restriction in patients with fluid retention. Aerobic exercise is essential, improving oxygen utilization and even partially reversing cardiac stiffness in early stages. In patients with severe obesity, significant weight loss reduces visceral fat and HF hospitalization risk.

2. SGLT2 inhibitors: the protective shield

SGLT2 inhibitors were initially developed as oral antidiabetic agents promoting urinary glucose excretion. However, they have proven to be true "cardiovascular heroes." Beyond glucose lowering, they reduce sodium and fluid overload. At the cellular level, they improve cardiac metabolic efficiency. They are now a cornerstone of HF treatment, significantly reducing hospitalizations and mortality in both HFrEF and HFpEF (8). Proper genital hygiene is recommended to reduce urinary infection risk.

3. GLP-1 receptor agonists and dual therapies: addressing the root cause

GLP-1 receptor agonists are medications »

» (generally injectable) that mimic intestinal satiety hormones. They act in the brain by reducing appetite, which leads to clinically significant weight loss. In the context of HFpEF associated with obesity, these drugs are rewriting the story. By promoting weight loss, they drastically reduce the size of visceral adipose tissue and systemic inflammation. Recent and promising clinical trials have demonstrated that diabetic and obese patients with HF treated with GLP-1 have a better prognosis, experience improvement in quality of life, and show a notable increase in their capacity for exercise (9, 10).

4. Classical treatments and drugs to avoid

For patients with weak hearts (HFrEF), classical cardiological treatment remains essential. This includes medications that block stress hormones and fluid retention, such as beta-blockers, mineralocorticoid receptor antagonists, and the revolutionary neprilysin inhibitors and angiotensin receptor blockers, such as sacubitril/valsartan. Finally, it is crucial to recognize that not all oral antidiabetic drugs are beneficial for the heart. Older medications such as thiazolidinediones (glitazones) or certain dipeptidyl peptidase-4 (DPP-4) inhibitors (such as saxagliptin) are contraindicated or discouraged in patients at risk of HF, as they may promote fluid retention and cause swelling, thereby worsening the clinical condition. D

CONCLUSIONS

1. HF is undoubtedly one of the most serious threats facing individuals with diabetes mellitus. The coexistence of both diseases imposes a significant burden on quality and expectancy of life. However, the outlook has never been more promising.

2. Today, we have simple tools such as NT-proBNP that act as early warning systems, detecting cardiac stress long before symptoms appear.

3. The current therapeutic arsenal, led by SGLT2 inhibitors and GLP-1 receptor agonists, allows us to target the metabolic root of the problem.

4. The current challenge for endocrinologists, cardiologists, and primary care physicians is to implement these screening and treatment strategies proactively and in a multidisciplinary manner.

5. For patients, the message is clear: diabetes does not inevitably condemn the heart. With active weight control, proper nutrition, exercise, and appropriate medication, it is possible to protect the heart and ensure an active and healthy future.

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