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Literature review

Incidence and pathophysiology of heart failure in patients with poorly controlled diabetes mellitus: a narrative review

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ABSTRACT

Introduction: Type 2 diabetes mellitus constitutes a growing public health problem and is closely associated with heart failure, even in the absence of coronary artery disease or hypertension.

Objective:to describe the international evidence on the incidence, pathophysiology, predictors, diagnosis, and treatment of heart failure in patients with poorly controlled type 2 diabetes mellitus.

Methods:a narrative review of the literature published between 2020 and 2025 in PubMed, Scopus, and SciELO was conducted using MeSH terms related to “diabetes mellitus type 2”, “heart failure”, and “diabetic cardiomyopathy”. Original studies, reviews, and international clinical guidelines were included.

Results: The prevalence of heart failure in patients with type 2 diabetes mellitus reaches up to 22% in the outpatient population and 50% in hospitalized patients. Pathophysiological

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mechanisms include insulin resistance, glucotoxicity, lipotoxicity, chronic inflammation, and interstitial fibrosis, which favor both heart failure with reduced ejection fraction and heart failure with preserved ejection fraction. Relevant predictive factors are HbA1c > 8 %, diabetes duration > 10 years, and elevated NT-proBNP. Early diagnosis using biomarkers and advanced echocardiography improves risk stratification. SGLT2 inhibitors and GLP-1 agonists have demonstrated benefits in reducing hospitalizations and mortality.

Conclusions: Poorly controlled diabetes mellitus constitutes an independent determinant of heart failure. Early identification and a multidisciplinary approach are essential to improve prognosis and reduce the healthcare burden.

Keywords: Type 2 diabetes mellitus; Heart failure; Diabetic cardiomyopathy; Pathophysiology; Treatment.

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Introduction

Diabetes mellitus (DM) has become a global public health problem in recent years.Currently, approximately 463 million adults aged 20–79 years have diabetes, representing 9.3% of the global population in this age group. This number is projected to increase to 578 million (10.2%) by 2030 and 700 million (10.9%) by 2045. (1) Heart failure (HF) has been recognized as a complication of diabetes mellitus, which can occur even in the absence of coronary artery disease, hypertension, or valvular heart disease. The coexistence of both conditions presents a complex clinical challenge due to the interaction of various pathophysiological mechanisms that accelerate the development and progression of heart failure. (2)

Heart failure occurs when the heart muscle does not pump blood as effectively as it should. When this happens, blood often backs up, and fluid can accumulate in the lungs, causing shortness of breath. (3) In 2021, leading international scientific societies for heart failure

developed a new “Universal Definition of Heart Failure” that places great importance on the determination of natriuretic peptides. This definition states that in a patient with typical symptoms and/or signs caused by a structural and/or functional cardiac abnormality, plus elevated natriuretic peptide (NP) levels or objective evidence of cardiogenic or systemic pulmonary congestion, a diagnosis of heart failure can already be suspected, pending the necessary echocardiogram to determine its cause and phenotype. (4) In the specific case of diabetes, heart failure 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 itself, to the point that women with diabetes have a five times greater risk, and twice as much in men with diabetes. Heart failure is also the leading cause of hospitalization in these patients. (4)

The prevalence of heart failure (HF) in patients with type 2 diabetes mellitus is 22% in the United States and 50% in patients hospitalized for HF. Lipotoxicity, insulin resistance, and hyperglycemia are key factors in the pathophysiology of HF in diabetic patients. (2) The prevalence of both conditions is expected to increase over time. Although each conditionEach is individually associated with considerable morbidity and mortality, often occurs together, complicates management, negatively affects patient outcomes, and increases the cost of care. (5)The American Diabetes Association (ADA) estimates that 50% of patients with diabetes mellitus (DM) will develop heart failure (HF) during their lifetime. DM predisposes to HF, and HF predisposes to DM. In elderly diabetic patients, and especially in diabetic women, an indirect sign of acute coronary ischemia is often manifested by the onset of clinical destabilization of HF. (6)

The DIABET-IC study conducted in Spain reported a cumulative incidence of heart failure (HF) of 15% over 5 years in patients with HbA1c > 8%, and that the prevalence and incidence of HF in patients with type 2 diabetes (T2D) are very high. The incidence of HF is around 3% per year, which is almost eight times higher than that found in large studies conducted in the general population. (7) This review aims to describe the international evidence on the incidence, pathophysiology, predictors, diagnosis, and treatment of HF in patients with poorly controlled T2D. It synthesizes the most recent evidence, highlighting the importance

of early identification of heart failure in patients with type 2 diabetes mellitus and a multidisciplinary approach to improve prognosis.

Methods

A narrative review of the scientific literature published between January 2020 and December 2025 was conducted. The PubMed, Scopus, SciELO, and Redalyc databases were searched using the DeCS/MeSH descriptors “Diabetes Mellitus, Type 2,” “Heart Failure,” “Diabetic Cardiomyopathy,” and “Cardiovascular Complications.” Original articles, systematic reviews, clinical guidelines, and international consensus statements in English and Spanish were included. Case reports and publications without full-text access were excluded. Selection was made independently by the authors, prioritizing studies with the highest level of evidence and clinical relevance.

Ethical considerations

This study is a narrative review of the scientific literature based exclusively on information previously published in academic and scientific sources. Therefore, the study did not require informed consent or approval from a research ethics committee. However, the ethical principles of scientific research were respected during the preparation of the manuscript, ensuring proper citation of the sources consulted and respect for the intellectual property of the original authors.

Development

Heart failure is a clinical syndrome characterized by cardinal symptoms such as dyspnea, edema, and fatigue, which may be accompanied by elevated jugular venous pressure, peripheral edema, and pulmonary crackles. It results from a structural and/or functional abnormality of the heart that causes elevated intracardiac pressures and/or inadequate cardiac output, which may occur at rest and/or during exercise. (4)

Heart failure is the common end syndrome of various heart diseases: hypertensive, ischemic, and/or asymptomatic alterations of ventricular function. (6)

Heart failure with preserved ejection fraction (HFpEF) is a heterogeneous syndrome with several underlying etiological and pathophysiological factors. The presence of diabetes could identify an important phenotype, with implications for therapeutic strategies. (8) Type 2 diabetes mellitus (T2DM) and heart failure with reduced ejection fraction (HFrEF) often coexist, and the combination of these two diseases indicates a considerably worse outcome than either one alone.It is more frequent in patients with type 2 diabetes and presents earlier and with a worse prognosis, causing the highest number of hospitalizations in elderly patients with diabetes. Therefore, glycemic control must be carefully managed. (6, 9)

Glycemic control, measured by glycated hemoglobin (HbA1c), is an important biomarker for assessing the severity of diabetes and is believed to be associated with the development of heart failure. (9)

Pathophysiology

For decades, there has been talk of a cardiomyopathy specific and exclusive to diabetes mellitus (DM), with specific alterations and changes at the cardiac level, regardless of the coexistence or absence of other associated cardiovascular risk factors. This is known as diabetic cardiomyopathy. (6) The true underlying mechanism of the feedback loop between type 2 diabetes mellitus (T2DM) and heart failure (HF) is insulin resistance, while hyperglycemia represents a subsequent mechanism that contributes to this feedback interaction.

Both factors produce multiple pathophysiological changes in the cardiovascular system, including endothelial dysfunction, impaired energy efficiency, lipotoxicity, inflammatory activation, accumulation of oxygen derivatives, and hyperglycemia-induced cardiomyopathy. (10)Poorly controlled diabetes mellitus induces diabetic cardiomyopathy through interrelated mechanisms: glucotoxicity and advanced glycation end products (AGEs), insulin resistance and lipotoxicity, endothelial dysfunction, chronic inflammation, alterations in intracellular calcium, and interstitial fibrosis. These processes generate ventricular stiffness,

diastolic dysfunction, cardiomyocyte apoptosis, and adverse remodeling, with progression to heart failure with reduced or preserved ejection fraction. (2, 11)

Predictive factors

These include HbA1c > 8%, DM duration > 10 years, microalbuminuria, visceral obesity, metabolic syndrome, and elevated NT-proBNP and high-sensitivity troponins. (12) The study by Sibille et al. (8) identified diabetes as a significant predictor of mortality and hospitalization for heart failure (HR: 1.72 [1.1–2.6], p = 0.011, adjusted for age, BMI, NYHA functional class, and renal function). In these patients, lower HbA1c levels, < 7%, were associated with a worse prognosis (HR: 2.07 [1.1–4.0], p = 0.028, adjusted for age, BMI, hemoglobin, and NT-proBNP levels). Furthermore, having an HbA1c greater than 7% was associated with a higher likelihood of developing later stages of heart failure. For example, people with very early stages of HF are 1.5 to 1.8 times more likely to develop later stages of HF.

The CHARM study (Candesartan in Heart Failure: Assessment of Reduction in Mortality and Morbidity) showed that cardiovascular risk increased with higher HbA1c levels. However, another cohort study of more than 6,000 patients, by Aguilar et al., showed a U-shaped curve, with better survival in the group of patients with HbA1c between 7.1% and 7.8%. (13) Furthermore, diabetes mellitus (DM) was associated with the development of heart failure more rapidly and at a younger age. This relationship holds true even after accounting for other factors that increase the risk of heart disease. (14)

Diagnosis

When it comes to diagnosis, time is of the essence. The goal is to make an early diagnosis in order to begin applying corrective measures and drugs with proven prognostic benefit, capable of reducing hospitalizations for heart failure. (4) The diagnosis of heart failure is established by the association of typical signs and symptoms and objective evidence of ventricular dysfunction. The medical history and physical examination remain fundamental for diagnosis, although many signs and symptoms of heart failure are nonspecific and do not allow this entity to be distinguished from other clinical problems. (6)

Heart failure symptoms associated with elevated natriuretic peptides should alert clinicians to the likelihood of heart disease in diabetic patients. Echocardiography is the next step to assess structural abnormalities and systolic and diastolic function.

The PONTIAC study evaluated the strategy of routine NT-proBNP measurement in diabetic patients at high cardiovascular risk for the early detection of ventricular dysfunction. Those with values greater than 125 pg/ml received early treatment for heart failure and specialized follow-up, and demonstrated a reduction in death and hospitalizations for cardiovascular causes. (15)

Additional tests and findings of heart failure

For diagnostic confirmation, it is essential to objectively demonstrate ventricular dysfunction using an imaging technique, preferably echocardiography or, failing that, echocardiography. (16)

Clinical findings in IC may include:

- Advanced echocardiography showing: diastolic dysfunction, left ventricular hypertrophy, reduction of global longitudinal strain, and elevation of filling pressures. (17)
- Cardiac magnetic resonance imaging: diffuse interstitial fibrosis, myocardial fatty infiltration, adverse remodeling. Electrocardiogram (ECG): persistent sinus tachycardia, left bundle branch block, left ventricular hypertrophy, supraventricular and ventricular arrhythmias, pathological Q waves or ST-T changes. (17)
- Chest X-ray (X-ray): cardiomegaly, vascular redistribution, Kerley B lines, pleural effusion, alveolar edema in a “butterfly wing” pattern. (18)
- Determination of serum biomarkers: elevated NT-proBNP/BNP, high-sensitivity troponin, galectin-3, soluble ST2, high-sensitivity PCR. (10)
- Stress tests and ambulatory monitoring: exercise intolerance, nocturnal hypertension, “non-dipper” pattern, arrhythmias on Holter. (18)

Treatment

The American Heart Association/American College of Cardiology (AHA/ACC) jointly classified heart failure (HF) into stages to implement therapeutic measures along the cardiovascular continuum of HF. This consensus classification into stages A to D has allowed for the systematic establishment of therapeutic recommendations. (10) International guidelines for the treatment of heart failure are similar for patients with and without diabetes.

However, analyses of the diabetic subgroup of many current therapies suggest that this population may behave differently, as they have a higher risk of events and may also present a greater number of complications. (11)Evidence confirms that poorly controlled diabetes mellitus is a determining factor in the development of heart failure, with its own pathophysiological mechanisms that justify considering diabetic cardiomyopathy as a separate entity. The main objectives in the care of diabetic patients with heart disease are reducing the number of cardiovascular events and short- and long-term mortality, as well as trying to maintain the highest possible level of functionality and quality of life. (6)

Early identification using biomarkers and advanced imaging allows for risk stratification and personalized therapy. SGLT2 inhibitors have demonstrated consistent benefits in reducing hospitalizations and mortality, positioning them as first-line therapy. The 2023 update of the European Society of Cardiology (ESC) Guidelines incorporates evidence from recent studies with SGLT2 inhibitors—dapagliflozin and empagliflozin—which have shown effectiveness in reducing hospitalizations and emergency department visits regardless of the patient's left ventricular ejection fraction (LVEF). (4)

The results of the Cardiovascular Outcome Event Trial in Type 2 Diabetes Mellitus Patients (EMPA-REG OUTCOME) study with empagliflozin have demonstrated a reduction in events, heart failure destabilization, and cardiovascular death in patients with type 2 diabetes and associated cardiovascular disease. Empagliflozin resulted in a 35% reduction in hospitalizations for heart failure. (6) The integration of multidisciplinary protocols is essential to reduce the burden of disease. Therefore, the treatment goals are to improve patients' clinical status, functional capacity, and quality of life, prevent hospitalizations, and reduce mortality.

Preventing or avoiding precipitating factors and ensuring that patients and their families/caregivers can recognize the symptoms and signs of decompensation, along with close follow-up in primary care, is a crucial measure in the treatment and prevention of hospitalizations. Structured educational measures and coordinated follow-up between primary and hospital care can reduce hospitalizations by up to 30%. (4) Treatment with sodium-glucose cotransporter 2 inhibitors significantly reversed cardiac remodeling, improving left ventricular systolic and diastolic function, mass, and end-diastolic volume, especially in patients with HFrEF and among those taking empagliflozin compared to other SGLT2 inhibitors. This reversal of remodeling may be a mechanism responsible for the favorable clinical effects of SGLT2 inhibitors on heart failure. The use of SGLT2i was associated with significant improvements in diastolic cardiac function, plasma NT-proBNP levels, and KCCQ scores in patients with type 2 diabetes with or without chronic heart failure, but did not significantly affect structural cardiac parameters indexed by body surface area. (9, 19)

Glucagon-like peptide-1 receptor agonists (GLP-1 receptor agonists) have demonstrated cardiovascular safety in clinical trials, and two drugs in this group, liraglutide and semaglutide, have even shown a reduction in cardiovascular risk. Furthermore, GLP-1 receptor agonists do not increase the risk of hospitalizations for heart failure. (10) Regarding studies with GLP-1 receptor agonists, the neutrality of the Evaluation of LIXisenatide in Acute Coronary Syndrome (ELIXA) study is noteworthy. The Liraglutide Effect and Action in Diabetes: Evaluation of Cardiovascular Outcome Results (LEADER) study with liraglutide in patients with type 2 diabetes and high cardiovascular risk showed that cardiovascular deaths were lower in the liraglutide group (219 patients, 4.7%) than in the placebo group (278, 6.0%), HR 0.78; Likewise, the rates of acute myocardial infarction (AMI), stroke, and hospitalization for heart failure were lower (without statistical significance) in the liraglutide group than in the control group. (6)

The prevalence of heart failure (HF) and type 2 diabetes (T2D) is increasing worldwide, and recent scientific evidence demonstrates a higher cardiovascular risk in patients with HF and diabetes. These situations necessitate that healthcare professionals initiate preventive

measures early in these patients. However, the pathophysiological changes of type 2 diabetes, alone or in conjunction with other cardiovascular risk factors, can favor the development of heart failure with reduced ejection fraction (HFrEF), heart failure with reduced ejection fraction (HFrEF), or heart failure with reduced ejection fraction (HFpEF). (10) High-risk patients benefit from aggressive management of risk factors, including control of hypertension, cholesterol, low-density lipoproteins, glycemic control, renal protection, and lifestyle interventions. (17)

Proper diabetes control decreases the likelihood of heart failure progression and reduces cardiovascular complications. Heart failure in diabetic patients is associated with a higher risk of hospitalization and mortality, so an individualized and multidisciplinary approach is essential to optimize quality of life and clinical outcomes. (14)

The reviewed evidence confirms that poorly controlled type 2 diabetes mellitus (T2DM) is a determining factor in the development of heart failure. The interaction between insulin resistance, glucotoxicity, lipotoxicity, and chronic inflammation promotes the development of diabetic cardiomyopathy, now considered a distinct entity. This phenomenon explains the high prevalence of heart failure in diabetic patients, even in the absence of coronary artery disease or hypertension.

Recent studies, such as DIABET-IC and EMPA-REG OUTCOME, demonstrate that the cumulative incidence of heart failure in poorly controlled diabetics is significantly higher than in the general population, and that the use of SGLT2 inhibitors reduces hospitalizations and mortality. However, controversy persists regarding the optimal HbA1c range, as some studies suggest a U-shaped relationship between HbA1c levels and cardiovascular prognosis.

Early identification using biomarkers (NT-proBNP, high-sensitivity troponins) and advanced imaging techniques (echocardiography, magnetic resonance imaging) allows for risk stratification and personalized treatment. However, gaps remain in the characterization of heart failure subphenotypes in diabetic patients and in the integration of multidisciplinary strategies involving endocrinologists, cardiologists, and primary care.

In this context, structured education and coordinated follow-up have been shown to reduce hospitalizations by up to 30%, which underlines the importance of complementary non-pharmacological interventions.

Limitations of the study

This is a narrative review, susceptible to selection bias. Heterogeneity exists among the included studies, which limits the robustness of some conclusions, particularly regarding HbA1c. A structured diagnostic-therapeutic algorithm is not proposed, nor is there in-depth analysis of heart failure subphenotypes or the clinical implementation of therapies; furthermore, the discussion of new lines of research is limited.

Conclusions

Poorly controlled type 2 diabetes mellitus significantly increases the risk of heart failure, with its own pathophysiological mechanisms justifying the consideration of diabetic cardiomyopathy as a separate entity. Early detection using biomarkers and advanced imaging is essential to improve prognosis and reduce complications. SGLT2 inhibitors are currently the first-line therapy in diabetic patients with heart failure, while GLP-1 agonists provide additional cardiovascular safety. Future research is needed to define the optimal HbA1c range and personalized treatment strategies in patients with type 2 diabetes and heart failure.

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Conflicts of interest

The authors declare that there are no financial, personal, or professional conflicts of interest.

Authorship contribution

Raúl Leyva Castro:conceptualization, research, methodology, project management, writing, editing, validation.

Yenisleidy Rivero Ferrer:data curation, resources, monitoring, formal analysis, visualization.

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