

EDITORIAL

Heart failure in people with diabetes and obesity, can it be prevented?



Insuficiencia cardíaca en personas con diabetes y obesidad: ¿se puede prevenir?

Jesús María de la Hera^{a,b,*}, Elías Delgado^{b,c,d,e}^a Servicio de Cardiología, Área del Corazón, Hospital Universitario Central de Asturias, Oviedo, Asturias, Spain^b Instituto de Investigación Sanitaria del Principado de Asturias (ISPA), Oviedo, Asturias, Spain^c Servicio de Endocrinología, Hospital Universitario Central de Asturias, Oviedo, Asturias, Spain^d Facultad de Medicina, Universidad de Oviedo, Oviedo, Asturias, Spain^e Centro de Investigación Biomédica en Red, Enfermedades Raras (CIBERER), Instituto de Salud Carlos III, Madrid, Spain

To the Editor,

Diabetes Mellitus (DM) is closely associated with the future development of heart failure (HF), as it doubles its likelihood.¹ Obesity is also a predisposing factor for HF² and, given the increasing prevalence of both conditions in our environment,^{1,2} it seems appropriate to focus on early diagnosis and prevention of HF in this group of patients. Of note that controlling weight and blood glucose alone is not enough. For example, in the case of type 2 diabetes (T2DM), it is known that despite optimal control of cardiovascular risk factors, the risk of HF persists, unlike in the prevention of ischemic heart disease, where these measures have proven effective.³ Therefore, HF-related strategies in patients with T2DM and obesity should be updated.

Why do patients with obesity and diabetes develop HF?

Both obesity and T2DM are often associated with conditions that increase the risk of HF, such as hypertension (HTN), insulin resistance, and oligoalbuminuria. Additionally, in the case of T2DM, there is a higher prevalence of ischemic heart disease and atrial fibrillation (AF), which also increase the likelihood of HF. Regarding pathophysiology, multiple mechanisms have been involved, such as activation of the renin-angiotensin system, the formation of advanced glycation end-products, dysautonomia, and the activation of sodium-hydrogen exchangers.¹

One aspect that should be highlighted is that HF develops progressively, and in this sense, 4 stages of involvement are proposed (stages A, B, C, and D).¹ Stage A consists of patients who are at risk for the future development of HF, including all patients with DM or obesity. Stage B: structural or functional heart impairment, but without any signs or symptoms of HF; Stage C: patients also exhibit signs or symptoms of HF, and Stage D: patients with advanced HF. Ideally, we should focus on patients at Stage A, identify Stage B (where HF prevention measures would be imple-

* Corresponding author.

E-mail address: jesusdelahera@gmail.com (J.M. de la Hera).

mented), or, failing that, diagnose HF in the early stages of Stage C to avoid hospital admissions. Therefore, prevention and early diagnosis of HF are parallel measures, depending on the stage of our patients.

How is HF diagnosed?

We must understand the current diagnostic process for HF, as it is key to its early detection. Traditionally, the Framingham criteria have been used, which identify patients with overt HF meaning that diagnosis would come late. Currently, the diagnosis of HF is based on clinical suspicion, with suggestive signs and symptoms, mainly in patients at risk of developing HF (T2DM, HTN, obesity, AF, and previous heart disease). Measurement of natriuretic peptides (NT-proBNP) in blood and an electrocardiogram (ECG) should be requested for these patients.⁴ Although the ECG does not diagnose HF, if it is strictly normal, it is very unlikely that the patient has HF. With NT-proBNP levels <125 pg/mL, HF can be ruled out. However, in the presence of higher levels, it is recommended to complete the study with an echocardiogram, as this test allows a definitive diagnosis of HF. This approach would enable earlier diagnosis, reducing the number of admissions. In the UK public health system, experience shows that HF diagnosis is mainly established in the hospital (up to 80% overall), and of those established in the Primary Care setting, very few diagnoses follow the described and recommended protocol based on the clinical practice guidelines.⁵ In our setting, a collaborative project between Primary Care and Cardiology has demonstrated that this model can work in a coordinated way. However, it has also revealed that in most patients from the Primary Care setting, this approach is not followed.⁶

How should we interpret NT-proBNP values?

Although the negative predictive value of this parameter to exclude the presence of HF is well established, we should also be aware of other aspects of interest in its use, such as: 1) obese patients have lower values, so the cut-off points should be reduced; 2) there are cardiac (myocarditis, AF, etc.) and extracardiac (chronic obstructive pulmonary disease, pulmonary embolism, advanced age, renal disease, etc.) causes that can also elevate NT-proBNP levels; and 3) the definitive diagnosis of HF must currently be established via echocardiography.⁴

Are the strategies of several scientific societies the same in the prevention/diagnosis of HF?

Although both the European⁷ and American⁸ guidelines recognize HF as a significant health problem, their strategies are different. The European guidelines promote early diagnosis of HF by selectively using NT-proBNP and always integrating it into the process, with basic cardiovascular examination and ECG. Therefore, proactive identification of HF signs or symptoms, even if subtle, is necessary, and it is at this moment when actions are recommended. The American model recommends systematic annual measurement of

natriuretic peptides in all T2DM patients and referral to cardiology if these are abnormal (>125 pg/mL). Therefore, most patients identified as pathological will be categorized as Stage B (functional impairment due to elevated natriuretic peptides), and only in the presence of signs/symptoms of HF, and with an echocardiogram confirming it, would the patient be categorized as Stage C. In our environment, this might not be sustainable from a health care perspective due to the overload of echocardiographic studies and cardiology consultations that could be generated, especially when it has not been conclusively proven that the American Diabetes Association (ADA) strategy is more effective. In defense of the ADA model, the PONTIAC study (NT-proBNP selected prevention of cardiac events in a population of diabetic patients without a history of cardiac disease)⁹ allowed the identification of higher-risk T2DM patients with elevated NT-proBNP levels, in whom intensive HTN control measures reduced the 2-year incidence rate of the primary composite of death or cardiovascular hospitalization by 65%. The limitation of this study is that it was conducted in a pre-current era with more widespread use of sodium-glucose cotransporter-2 inhibitors (SGLT2i) and would require NT-proBNP measurement in all T2DM patients. This is partially being addressed with the emergence of clinical risk scales that optimize the use of natriuretic peptides and better identify patients at risk of HF.¹⁰

How should HF be prevented in patients with obesity or diabetes?

Initially, we should identify higher-risk patients, who are those with associated HTN, AF, chronic kidney disease with oligoalbuminuria, structural or valvular heart disease, or cancer survivors. Regarding gender, women with diabetes have a higher risk of developing HF (47% higher in type 1 diabetes and 9% in T2DM).¹¹ It is difficult to know whether this is due to an independent gender-related factor or to the greater comorbidities and psychosocial aspects present in women. Another important aspect in diabetic patients is the duration of DM. It has been shown that for every 5 years of DM, the risk of developing HF increases by 17%¹²; this is another reason for early diagnosis of DM and special monitoring in patients with longer DM duration. Similarly, good glycemic control, without hypoglycemia, also decreases the incidence of HF.¹ Continuing with general measures, HTN control is very effective in reducing HF, both in DM and obesity. For every 10 mmHg-reduction in systolic blood pressure, the risk of HF, stroke, and overall mortality drops by 28%, 27%, and 13%,¹ respectively.

In the pharmacological aspect, SGLT2i are the cornerstone for preventing and treating HF in diabetic patients.⁴ Finerenone—a non-steroidal mineralocorticoid receptor antagonist—has shown a 22% reduction in the incidence of HF in T2DM patients with chronic kidney disease,¹³ and its use can effectively complement SGLT2i.

In obese individuals, bariatric surgery reduces the incidence of HF by 50% according to results from a meta-analysis of non-randomized trials,¹⁴ and early data with semaglutide (a GLP-1 receptor agonist, arGLP1) in patients with HF and preserved ejection fraction are promising, with improved quality of life.¹⁵

In the case of type 1 diabetes, HF incidence is also high, and we should also be proactive regarding prevention and early diagnosis. However, evidence on specific outcomes is limited, and the use of SGLT2i, arGLP1, or finerenone is not yet generally recommended for these patients.

In summary, strategies to prevent HF in people with DM and obesity should include lifestyle changes, optimal HTN and glycemia control, identification of higher-risk patients, AF screening, early diagnosis using NT-proBNP, echocardiography, and broader use of SGLT2i, and in specific scenarios, finerenone and arGLP1.

Declaration of Generative AI and AI-assisted technologies in the writing process

The authors declare that no artificial intelligence tools were used in the preparation and writing of this manuscript.

Funding

None declared.

Declaration of competing interest

None declared.

References

- Pandey A, Khan MS, Patel KV, Bhatt DL, Verma S. Predicting and preventing heart failure in type 2 diabetes. *Lancet Diabetes Endocrinol.* 2023;11:607–24.
- Suthahar N, Meems LMG, Withaar C, Gorter TM, Kieneker LM, Gansevoort LT, et al. Relative fat mass, a new index of adiposity, is strongly associated with incident heart failure: data from PREVEND. *Sci Rep.* 2022;12:147.
- Rawshani A, Rawshani A, Franzén S, Sattar N, Eliasson B, Svensson AM, et al. Risk factors, mortality, and cardiovascular outcomes in patients with type 2 diabetes. *N Engl J Med.* 2018;379:633–44.
- McDonagh TA, Metra M, Adamo M, Gardner RS, Baumbach A, Böhm M, et al. 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: Developed by the Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC) With the special contribution of the Heart Failure Association (HFA) of the ESC. *Eur Heart J.* 2021;42:3599–726.
- Roalfe AK, Lay-Flurrie SL, Ordóñez-Mena JM, Goyder CR, Jones NR, Hobbs FDR, et al. Long term trends in natriuretic peptide testing for heart failure in UK primary care: a cohort study. *Eur Heart J.* 2021;43:881–91.
- Cuevas Pérez J, Moro Quesada D, Alonso Fernández V, Prieto-Díaz MÁ, Prieto García B, Herrero Puente P, et al. Atención primaria y péptidos natriuréticos: diseño de un proceso asistencial para la mejora en el diagnóstico de la insuficiencia cardíaca. *Medicina de Familia. SEMERGEN.* 2024;50, <http://dx.doi.org/10.1016/j.semerg.2024.102224>.
- Marx N, Federici M, Schütt K, Müller-Wieland D, Ajjan RA, Antunes MJ, et al. 2023 ESC Guidelines for the management of cardiovascular disease in patients with diabetes: developed by the task force on the management of cardiovascular disease in patients with diabetes of the European Society of Cardiology (ESC). *Eur Heart J.* 2023;44:4043–140.
- American Diabetes Association Professional Practice Committee. 10. Cardiovascular Disease and Risk Management: Standards of Care in Diabetes—2024. *Diabetes Care.* 2024;47 Supplement.1:S179–218.
- Huelsmann M, Neuhold S, Resl M, Strunk G, Brath H, Francesconi C, et al. PONTIAC (NT-proBNP selected prevention of cardiac events in a population of diabetic patients without a history of cardiac disease): a prospective randomized controlled trial. *J Am Coll Cardiol.* 2013;62:1365–72.
- Razaghizad A, Oulousian E, Randhawa VK, Ferreira JP, Brophy JM, Greene SJ, et al. Clinical prediction models for heart failure hospitalization in type 2 diabetes: a systematic review and meta-analysis. *J Am Heart Assoc.* 2022;11:e024833, <http://dx.doi.org/10.1161/JAHA.121.024833>.
- Ohkuma T, Komorita Y, Peters SAE, Woodward M. Diabetes as a risk factor for heart failure in women and men: a systematic review and meta-analysis of 47 cohorts including 12 million individuals. *Diabetologia.* 2019;62:1550–60.
- Echouffo-Tcheugui JB, Zhang S, Florido R, Hamo C, Pankow JS, Michos ED, et al. Duration of diabetes and incident heart failure: the ARIC (Atherosclerosis Risk In Communities) study. *JACC Heart Fail.* 2021;9:594–603.
- Agarwal R, Filippatos G, Pitt B, Anker SD, Rossing P, Joseph A, et al. FIDELIO-DKD and FIGARO-DKD investigators. Cardiovascular and kidney outcomes with finerenone in patients with type 2 diabetes and chronic kidney disease: the FIDELITY pooled analysis. *Eur Heart J.* 2022;43:474–84.
- Van Veldhuisen SL, Gorter TM, van Woerden G, de Boer RA, Rienstra M, Hazebroek EJ, et al. Bariatric surgery and cardiovascular disease: a systematic review and meta-analysis. *Eur Heart J.* 2022;43:1955–69.
- Butler J, Shah SJ, Petrie MC, Borlaug BA, Abildstrøm SZ, Davies MJ, et al., STEP-HFpEF Trial Committees and Investigators. Semaglutide versus placebo in people with obesity-related heart failure with preserved ejection fraction: a pooled analysis of the STEP-HFpEF and STEP-HFpEF DM randomised trials. *Lancet.* 2024, [http://dx.doi.org/10.1016/S0140-6736\(24\)00469-0](http://dx.doi.org/10.1016/S0140-6736(24)00469-0). S0140-6736(24)00469-0. Epub ahead of print.