Endocrinol Nutr. 2015;62(7):350–355

ENDOCRINOLOGÍA Y NUTRICIÓN

www.elsevier.es/endo

REVIEW ARTICLE

What's new in heart failure in the patient with type 2 diabetes?☆

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Received 16 February 2015; accepted 3 June 2015
Available online 26 September 2015

KEYWORDS
Type 2 diabetes mellitus;
Heart failure

Abstract Type 2 diabetes mellitus (T2DM) is considered an independent risk factor of heart failure (HF). It has been observed that diabetics have a higher risk of heart failure than non-diabetics. However, many aspects are still unknown; for example, the existence of a particular myocardiopathy common to T2DM, the pathogenesis of the HF associated with T2DM that is still not sufficiently clear, its role in the prognosis of HF, or the influence of anti-diabetic treatments on the outcome of the HF. An attempt is made in this review to summarize all those findings that have been published in the past 5 years as regards this interesting question, placing special emphasis on those questions still unresolved.

PALABRAS CLAVE
Diabetes mellitus tipo 2;
Insuficiencia cardiaca

¿Qué hay de nuevo en insuficiencia cardiaca en el paciente con diabetes tipo 2?

Resumen La diabetes mellitus tipo 2 (DMT2) es considerada un factor de riesgo independiente para insuficiencia cardiaca (IC). Se ha visto que los diabéticos tienen un riesgo mayor de IC que los no diabéticos. Sin embargo, muchos aspectos son aún desconocidos, por ejemplo la propia existencia de una miocardiopatía propia de la DMT2, la patogénesis de la IC relacionada con la DMT2 que tampoco está suficientemente aclarada, su papel en el pronóstico de la IC, o la influencia de los tratamiento antidiabéticos en la evolución de la IC. En esta revisión intentaremos resumir todos aquellos hallazgos que han sido publicados en los últimos 5 años en relación con esta interesante cuestión, haciendo especial hincapié en aquellas cuestiones no resueltas.

☆ Please cite this article as: Camafort M. ¿Qué hay de nuevo en insuficiencia cardiaca en el paciente con diabetes tipo 2? Endocrinol Nutr. 2015;62:350–355.
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Introduction

Type 2 diabetes mellitus (T2DM) is one of the non-communicable diseases representing the greatest threat to public health, both because of its prevalence and increasing incidence and because most diabetic patients are at risk of suffering and dying from cardiovascular disease (CVD). Thus, T2DM is considered to be an independent risk factor for atherosclerotic cardiovascular disease and, of course, also for heart failure (HF). Diabetic women have been found to have a five times greater risk of HF than non-diabetic women, and this risk is 2.4 times greater in males.[1–3] Different factors may explain this, such as the fact that T2DM is often associated with high blood pressure (HBP) and, thus, to increased cardiovascular complications such as CVD or the subsequent development of HF.[4] In Spain, a recent study conducted in the Basque Country showed a 73.7% prevalence of HBP in T2DM. On the other hand, the prevalence of chronic diseases related to diabetes such as ischemic heart disease was 11.5%, while the prevalence rate of heart failure was 4.3%.[5] There are however many unknown aspects, such as the possible existence of a T2DM-induced cardiomyopathy, a proposal based on post-mortem findings, or the demonstration of the presence of systolic and diastolic dysfunction in patients with T2DM. The pathogenesis of this disease has also not been fully elucidated, and its role in HF prognosis and the potential impact of antidiabetic treatment on the course of HF are also far from clear.[1]

This review will try to summarize all the findings reported over the past five years related to this interesting question, with special attention being paid to pending issues.

Methods

A literature search was conducted of relevant computer databases in the field of health, the most important being MEDLINE (through PubMed). All studies published from January 1, 2010 to February 1, 2015 were examined as the basis for this review. Search criteria included the terms *heart failure*, restricted to *MESH major topic* or *title and abstract*, and *type 2 diabetes mellitus*, also restricted to *MESH major topic* or *title and abstract* combined with the *AND* operator.

The search encompassed clinical trials, meta-analyses, and reviews, as well as clinical practice guidelines; studies not written in English, German, French, or Spanish were excluded. Of the 83 studies selected, articles that did not provide new responses were finally excluded at the author's discretion, in an attempt to select those studies which were considered to be the most relevant or to have the greatest practical implications.

Once the studies had been reviewed, this review was divided into sections devoted to HF prevention in T2DM, the pathophysiology of HF in T2DM, the prognostic role of T2DM in HF, and the impact of T2DM therapy on HF (Tables 1 and 2).

Table 1 Key new findings in the prevention of HF associated with T2DM.

The risk of HF in T2DM is associated with U-shaped HbA1c levels (higher and lower HbA1c levels are related to a greater risk of HF)[6]
The risk of HF is not significantly different in diabetics on intensive blood glucose control and those on standard treatment[7]
Intensive treatment of CVRFs associated with T2DM significantly increases exercise capacity in patients with HF, while standard treatment decreases exercise capacity[8]

Table 2 Recent key findings in the pathophysiology of HF associated with T2DM.

Autonomic neuropathy may play a role as a link between T2DM and the occurrence of HF[9]
Diastolic dysfunction occurs in more than 50% of patients with T2DM and mainly correlates with diabetes duration, HbA1c levels, and the presence of obesity and diabetic microangiopathy[10]
Independent predictors of asymptomatic LV dysfunction in T2DM include advanced age and the presence of valve calcifications and signs of concentric LV remodeling[4]

Prevention of heart failure

More intensive blood glucose control has been shown to decrease the risk of microvascular disease in patients with T2DM, but it has not been shown to be associated with a reduction in the risk of macrovascular events. It is also known that poor blood glucose control is associated with an increased risk of HF, but it is not known whether improved blood glucose control decreases that risk. Thus, for example, a U-shaped association of the risk of HF with glycosylated hemoglobin (HbA1c) levels has recently been reported, so that the highest and lowest HbA1c levels are related to a greater risk of HF.[6]

This question was analyzed in a recent meta-analysis to find out whether intensive blood glucose control decreased the incidence of fatal or nonfatal HF. For this purpose, the authors analyzed a total of 37,229 patients from eight randomized clinical trials followed up for 2.3–10.1 years. A total of 1469 events were found (55% in the group on intensive T2DM treatment). No significant difference was found between the risk of HF for patients with intensive blood glucose control and those on standard treatment (OR: 1.20; 95% CI: 0.96–1.48). The only finding was that intensive blood glucose control with thiazolidinediones increased the risk of heart failure.[7]

An additional pending issue is whether intensive and global control of cardiovascular risk factors (CVRFs), as compared to standard control, may contribute to the prevention of HF in patients with T2DM. This issue was analyzed in a recent study by Ofstad et al. This study enrolled 100 patients with ≥ 1 CVRF who were randomized to two arms (intensive vs standard management of overall CVR). The ability to prevent HF was assessed through improvement in left ventricular function, as measured by echocardiography and the results of a stress test. Stress capacity, as measured by ergometry, significantly increased in patients on intensive treatment and decreased in those on standard treatment ($p = 0.014$). There were no significant changes between the groups in the echocardiographic parameters tested.[8]