
Concomitant Diabetes Mellitus and Heart Failure

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Abstract: The prevalence of patients with concomitant diabetes mellitus (DM) and heart failure (HF) is growing exponentially. Patients with HF and DM show specific metabolic, neurohormonal, and structural heart abnormalities, which potentially contribute to worse HF outcomes than seen in patients without comorbid DM. Subgroup analysis of recent trials suggest that patients with HF and DM may respond differently to standard therapy, and data are emerging on the possible increase in the risk of hospitalizations for HF in patients with DM treated with specific class of antidiabetic agents, pointing to the need of developing specific medications to be tested in dedicated future studies to address the unique metabolic and hemodynamic alterations seen in these patients. (Curr Probl Cardiol 2015;40:7–43.)

Introduction

The prevalence of patients with concomitant heart failure (HF) and diabetes mellitus (DM) is growing exponentially with the aging of the general population. Approximately 40% of patients hospitalized with HF and reduced ejection fraction (EF) have DM¹ with an important epidemiologic, clinical, and economic influence. Patients with

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HF and DM show specific metabolic, neurohormonal, and structural heart abnormalities, which potentially contribute to worse outcomes than seen in patients without comorbid DM.^{2,3}

Notably, subgroup analyses of recent trials conducted in hospitalized patients with HF who had DM showed a different response to standard medication, with these patients being more prone to develop side effects than patients with the same degree of HF but without DM,⁴ and a bidirectional effect of therapy in patients with or without DM.⁵ Conversely, data are emerging on the possible increase in the risk of hospitalizations for HF in patients with DM treated with specific class of antidiabetic agents.^{6,7} These data, although should be cautiously interpreted in the context of post hoc analyses, suggest the need to identify or develop a targeted therapy to be tested in dedicated future studies, particularly in patients hospitalized for acute HF with concomitant DM.

Epidemiology

The prevalence of patients with both HF and DM in the general population is estimated at 0.5% in men and 0.4% in women.⁸ The public health burden of HF and DM is substantial: HF afflicts 1%-2% of the general population, increasing to >5%-10% in subjects aged >65 years,⁹ whereas the prevalence of DM worldwide is estimated at 5%-6%,¹⁰ and it is predicted to increase to >8% of the adult population by 2030.¹¹ The prevalence of both diseases is increasing worldwide with the aging of the general population: 1.5%-2% of individuals older than 65 have both HF and DM and the prevalence is expected to grow exponentially in the next decades.¹² In addition, these prevalence figures tend to underestimate the true effect as they do not adequately account for undiagnosed HF in patients with preserved EF or impaired fasting glucose.^{8,13}

Gary S. Francis: There are now emerging data that HF with preserved EF (HFpEF) also presents with multiple phenotypes, including metabolic abnormalities and coronary microvascular inflammation (Paulus WJ, Tschöpe C. *JACC* 2013; 62:263-271). Likewise, HFpEF, similarly to HF with reduced EF, is strongly associated with DM. Compared to nondiabetic HFpEF patients, diabetic HFpEF patients tend to be younger, more obese, more likely hypertensive, have more renal function impairment, and more vascular disease. HFpEF patients with diabetes have more left ventricular (LV) hypertrophy, a trend toward higher LV filling pressures, less exercise tolerance, and more need for hospitalization (Lindman BR, Dávila-Román VG, Mann DL, et al. *Cardiovascular Phenotypes in HFpEF Patients with and without Diabetes. JACC* 2014; 64:541-549). About 30%-40% of patients with HFpEF have DM,

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