

### Type 2 Diabetes and Heart Failure: Key Messages to Remember

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#### COLUMN ARTICLE

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#### INTRODUCTION

In the last three decades an increase in the prevalence of both type 2 diabetes (T2DM) and heart failure (HF) occurred in most countries all over the world. The aim of this mini review is to present some key messages about the epidemiology, pathophysiology, prognostic implication and management of this association.

**Message 1:** Patients with HF have a four-fold higher prevalence of T2DM (20%) than patients without HF (4 - 6%) [1,2] and this rises to 40% in T2DM patients hospitalized for HF [3]. Furthermore, the risk to develop HF is 2.5-fold increased for patients with T2DM12 and 1.7-fold for patients with impaired glucose tolerance (IGT) or insulin resistance compared with normal (non-diabetic) individuals, respectively. In patients with HF, data from observational and clinical trials demonstrate an increased risk for new-onset T2DM compared to patients without HF [4].

**Message 2:** T2DM worsens prognosis for patients with HF with reduced ejection fraction (HF<sub>r</sub>EF), but even more with heart failure with preserved ejection fraction (HF<sub>p</sub>EF), by increasing the risk of death and hospitalization. Patients with T2DM have a 75% higher risk of CV death or HF hospitalization compared with those without T2DM. This effect on the HF prognosis occurs in both ischemic and non-ischemic etiology of HF [5].

**Message 3:** The pathophysiology of HF in T2DM include 3 important factors: coronary artery disease (most common), hypertension and diabetic cardiomyopathy related to changes in myocardial cell function, a fibrosis and remodeling. The risk factors for development of HF in T2DM include age, duration of DM, insulin use ischemic HD, peripheral arterial disease, poor glycemic control, serum creatinine and microalbuminuria. Also, the predictors for the development of T2DM in HF patient include; elevated body mass index and waist circumference history of smoking, elevated glucose or HbA1c, higher systolic blood pressure, longer duration of HF, diuretic therapy, higher NYHA functional class [6].

**Message 4:** In the treatment of T2DM in HF patient The association between HbA1c and mortality among patients

with HF is consistently U shaped, with the lowest mortality in patients with HbA1c 7% to 8%. So, it is better to avoid intensive glycemic control or persistent hyperglycemia [7].

**Message 5:** Regarding selection of antidiabetics in HF patient with diabetes the following points are to be considered [6]:

- Metformin is safe and can be used in HF patient except in patient e GFR < 30 ml and those liable to lactic acidosis as cardiogenic shock.
- Sodium glucose co-transporter 2 (SGLT2) inhibitors are recommended as it proved effective in large clinical trials to improve both diabetes and heart failure.
- Glucagon-like peptide-1 (GLP1) agonist like liraglutide, exenatide lixisenatide and semaglutide can be used safely in HF patient.
- Dipeptidyl Peptidase-4 (DDP4) Inhibitors are neutral in patient with HF except saxagliptin which increase HF hospitalization.
- Insulin and insulin analogs can be used if needed for glycemic control in HF patient with some cautions regarding hypoglycemia, weight gain and salt and water retention.
- Sulfonyl urea better avoided in HF patient for fear of hypoglycemia weight gain and possible increase CV outcome. However, glimepiride had proved neutral effect regarding CV outcome in CAROLINA trial.
- Thiazolidinedione (TZD) are contraindicated in patient with heart failure for its effect on salt and water retention and aggravation of HF.

**Message 6:** In management of HF in T2DM the following points to be considered [6,8]:

- All heart failure therapy including devices showed similar benefit in HFrEF patients with diabetes as without diabetes.
- ACE inhibitors, ARBs, and ARNI have favorable effects on the development of DM and glycemic control in patients with HFrEF and should be used according to guideline recommendations.

- Spironolactone may modestly worsen glycemic control in patients with DM and HFrEF and eplerenone may be safer in this situation.
- Carvedilol might have more favorable effects on glycemic control than metoprolol succinate and bisoprolol.
- Ivabradine has beneficial effect in HF patient with and without DM.

**Message 7:** Lifestyle management should be integral to the care of patients with DM and HF. DM is linked to obesity, inactivity, and poor dietary choices, which in turn are linked to cardiovascular diseases, including HF. Exercise can improve functional capacity for patients with DM and HF. Rehabilitation program can improve physical capacity and quality of life in diabetic patient with heart failure.

**Message 8:** Diabetic patient can benefit from advanced HF therapy as cardiac transplantation and left ventricular assist devices (LVAD) as nondiabetic patient though some consideration regarding patient selection and use of immune suppressive therapy and combined heart and kidney transplantation may be needed.

**Message 9:** Management of HF and T2DM association need the collaborative approach with management team including cardiologist, endocrinologist, dietician, physical therapist and nursing staff.

**Message 10:** There are many gaps of knowledge in this association that need future trial including [9]:

- The role of insulin resistance in HF.
- Pleotropic effects of antidiabetics especially metformin.
- New methods for patient monitoring other than patient symptoms and biomarkers.
- The benefit of SGLT2 inhibitors in HF without DM.

## DISCLOSURE

No conflict of interest.

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