

To the Editor

In the Scientific statement from the American Heart Association "Drugs that may cause or exacerbate heart failure", insulin is not listed among the drugs that may cause or worsen heart failure (HF) (1). Fluid retention caused by insulin was first reported by Gibson and Larimer in 1925, just a few years after its discovery, and is due to sodium retention at the renal tubular level, as clearly observed by De Fronzo in 1975. The onset or worsening of HF in patients treated with insulin has already been described extensively in the literature and it has been hypothesized that insulin can also cause myocardial steatosis and left ventricular diastolic dysfunction(2). Guidelines for the Treatment of Acute and Chronic Heart Failure of the European Society of Cardiology of 2016 underline how insulin in diabetic patients with HF may cause fluid retention and thus worsening HF (3). In our recent post-hoc analysis of the Valsartan Heart Failure (Val-HeFT) and of the Gruppo Italiano per lo Studio della Sopravvivenza-Heart Failure (GISSI-HF) trials, we found that insulin was associated with increased mortality (HR 1.35 [1.12-1.62] p=0.0015) and more frequent hospital admission for HF (HR 1.37 [1.15-1.65], p=0.01) compared to other anti-diabetic therapies, after adjustment for HF and diabetes severity and other co-morbidities with propensity score (4). A very recent cohort study in 469688 UK people with type 2 diabetes showed that insulin was independently associated with a 47% higher risk of all-cause mortality and a 32% higher risk of incident HF while significant better outcomes were associated to metformin, gliptins and glitazones (5)

Our recent data, associated with the analysis of the literature, show how is compelling to include insulin in the list of drugs that may exacerbate HF, also considering that about one third of patients with HF also has type 2 diabetes mellitus and that 27% of these patients are treated with insulin (GISSI-HF data).

If there are no alternatives to insulin therapy, the administration should be individualized, carefully avoiding hypoglycemia and increase in body weight.

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