Short term effect of sodium glucose cotransporter 2 inhibitors and sacubitril/valsartan on comprehensive geriatric assessment and oxidative stress in elderly with chronic heart failure (from MAGIC-HF)

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Background: Sodium Glucose Cotransporter 2 inhibitors (SGLT2i) and Sacubitril/Valsartan (Sac/Val) have improved clinical prognosis in patients affected by heart failure (HF) with reduced ejection fraction (HFrEF). Cognitive impairment, depression, and poor physical functional performance are a very common comorbidity in patients with HF and result in a worse prognosis.

Purpose: The aim of this study was to evaluate the potential effects of SGLT2i on functional, humoral, and cognitive aspects, assessed by performing a comprehensive geriatric assessment (CGA), and on oxidative stress and platelets activation biomarkers, in a cohort of HFrEF elderly, and any differences between men and women.

Methods: We enrolled 91 HFrEF patients (63 men and 28 women, mean age 73.7±4.7 years) in the "MAgna GraecIa evaluation of Comorbidities in patients with Heart Failure STUDY (MAGIC-HF STUDY). Men and women differed for use of glucagon-like-peptide 1 receptor agonists, antiplatelet drugs, and circulating levels of NADPH Oxidase 2 (Nox-2). SGLT2i therapy was introduced in patients already treated with Sac/Val for at least 12 months who were taking an average dose of 273.6±102.0 mg/die.

Results: After 3 months follow-up, we observed a significant improvement in cognitive, humoral and functional parameters of CGA, NTpro-BNP levels and echocardiographic parameters. Changes (Δ) in Montreal Cognitive Assessment (MoCA) (p=0.015) and Cardiac Index (CI) which were greater in men (p<0.0001) and Geriatric Depression Scale (GDS) which were greater in women (p=0.029). In the whole population, multivariate analysis shows that Δ of CI, Homeostatic model assessment (HOMA), Sp-Selectina, Nox-2 and 8-Isoprostane contributed for 19.7% (p<0.0001), 9.4% (p=0.001), 6.4% (p=0.002), 3.8% (p=0.013) and 2.9% (p=0.004) to Mini mental state examination (MMSE) variability, respectively, and the whole model accounted for a 42.2% of MMSE variation; moreover Δ of HOMA, Sp-Selectina and highly sensitive c-reactive protein (hs-CRP) contributed for 21.6% (p<0.0001), 5.7% (p=0.002) and 4.0% (p=0.014) to MoCA variability, respectively, and the whole model accounted for a 33.3% of MoCA variation. In addition, Δ of Sp-Selectina, Nox-2, CI and HOMA globally contributed for 37.5% of GDS variation (p<0.05); and Δ of HOMA and Sp-Selectina contributed for 30.9% of Short performance physical battery variation (p<0.0001).

Conclusions: This represents the first real-world study carried out in an elderly population suffering from chronic HFrEF with several comorbidities, in which the addition of SGLT2i, in patients already treated with the best medical therapy including Sac/Val, after three months induced important improvements in clinical, humoral, hemodynamic, functional outcomes and cognitive performance. This study shows that echocardiographic and cognitive improvements are greater in men than in women, instead metabolic and humoral improvements are greater in women.