Sex hormone-binding globulin and heart failure hospitalizations in patients with dysglycemia - Experiences from the Outcome Reduction with an Initial Glargine Intervention (ORIGIN) trial

A. Wang Gottlieb1, H. Gerstein2, S. Hess3, S. Lee4, L. Mellbin1, L. Ryden1

1Karolinska Institute, Stockholm, Sweden
2McMaster University, Department of Medicine, Hamilton, Canada
3Global Medical Diabetes, Sanofi, Frankfurt, Germany
4Population Health Research Institute, Hamilton, Canada

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Background: Sex hormone-binding globulin (SHBG), which binds most of the circulating testosterone in blood, is linked to both dysglycemia and a variety of cardiovascular (CV) events. However, few studies have investigated the link between SHBG and heart failure.

Purpose: To investigate the relationship between SHBG levels and heart failure hospitalizations in men and women with dysglycemia.

Methods: The Outcome Reduction with an Initial Glargine Intervention (ORIGIN) trial followed individuals with dysglycemia (impaired fasting glucose, impaired glucose tolerance or diabetes) and high cardiovascular risk for a median of 6.2 years. Incident CV events, including heart failure hospitalizations (defined as heart failure requiring overnight stay at hospital or attendance in an acute care setting) were collected and adjudicated. A subset of patients (n = 8,494) in whom blood samples were stored had SHBG levels analysed. Cox regression was used to estimate hazard ratios (HRs) of heart failure hospitalizations per standard deviation increase of SHBG. Adjustments were made for age, comorbidities, biochemical data (including testosterone) and pharmacological treatment. Analyses were performed separately in men and women.

Results: A total of 5,553 men and 2,848 women were included in whom heart failure hospitalizations were reported in 349 men and 123 women. Median SHBG levels were 35 nmol/L (25-47) in men and 39 nmol/L (27-55) in women. The primary outcome was more frequent in men with SHBG levels above median (n = 208/349 [59.6 %]; p<0.01) whilst no difference was seen for women (n = 69/123 [56.1%]; p = 0.24). A higher SHBG was associated with increased risk of heart failure hospitalizations in men (adjusted HR 1.15, 95% CI 1.03-1.28; p = 0.011) but not in women (adjusted HR 1.13; 95% CI 0.96-1.39; p = 0.14).

Conclusions: In this biomarker substudy within the ORIGIN trial comprising patients with dysglycemia and at high CV risk, increasing levels of SHBG were associated with heart failure hospitalizations independent of testosterone levels in men but not in women.