

Sex hormone-binding globulin and left ventricular ejection fraction in men with heart failure

 Viktor Čulić^{1,2*},
 Željko Bušić¹,
 Ivan Velat¹

¹University Hospital Centre Split, Split, Croatia

²University of Split School of Medicine, Split, Croatia

KEYWORDS: heart failure, left ventricular ejection fraction, men, sex hormone-binding globulin, testosterone.

CITATION: *Cardiol Croat.* 2024;19(11-12):417. | <https://doi.org/10.15836/ccar2024.417>

***ADDRESS FOR CORRESPONDENCE:** Viktor Čulić, Klinički bolnički centar Split, Šoltanska 1, HR-21000 Split, Croatia. / Phone: +385-21-557-289 / E-mail: viktor.culic@st.t-com.hr

ORCID: Viktor Čulić, <https://orcid.org/0000-0002-4026-0195> • Željko Bušić, <https://orcid.org/0000-0001-5877-3602>
Ivan Velat, <https://orcid.org/0000-0002-5757-3016>

Introduction: The association of circulating testosterone levels with various parameters of cardiac function and wider pathophysiological framework of processes involved in the development and progression of heart failure (HF) syndrome have been well-described¹. However, the links between circulating sex hormone-binding globulin (SHBG) and HF have been less extensively investigated; previous studies have suggested no association² or a low risk of HF with low circulation SHBG levels³.

Patients and Methods: Data on baseline characteristics, cardiovascular risk factors and medications were collected for 196 male patients who were consecutively hospitalized for an acute episode of HF. In addition to baseline laboratory findings, serum concentrations of both SHBG and total testosterone were prospectively recorded. The left ventricular ejection fraction (LVEF) was assessed by the biplane Simpson's method and in accordance with the current guidelines.

Results: The study population consists of 12.8% smokers, 57.1% those with hypertension, 40.3% with diabetes mellitus, 26.5% with hypercholesterolemia and 20.4% of those with previous myocardial infarction. The mean age was 74.2±7.9 years, body mass index 27.5±5.1 kg/m², creatinine clearance 53.5±18.8 mL/min/1.73 m², LVEF 46.4±13.7%, whereas median SHBG was 46.8 nmol/L (interquartile range 32.3 – 62.7) and total testosterone was 10.2 nmol/L (interquartile range 6 – 14.1). In the univariate analysis, plotting the LVEF according to SHBG suggested a non-linear association well described by a cubic polynomial function (Figure 1). In the multivariate analysis, the association of LVEF with testosterone and SHBG was adjusted for all of the above clinical variables. In addition to younger age (p=0.004) and high creatinine clearance (p=0.02), both high circulating serum levels of total testosterone (p<0.0001) and low levels of SHBG (p=0.005) were identified as the independent predictors of LVEF.

Conclusions: The present study concurred evidence suggesting that SHBG is not just a glycoprotein that binds and carries the circulating testosterone, but that it may also be independently involved in biological processes affecting cardiac function in HF. Possible mechanisms Possible pathophysiological and sub-cellular mechanisms of SHBG in HF should be further explored.

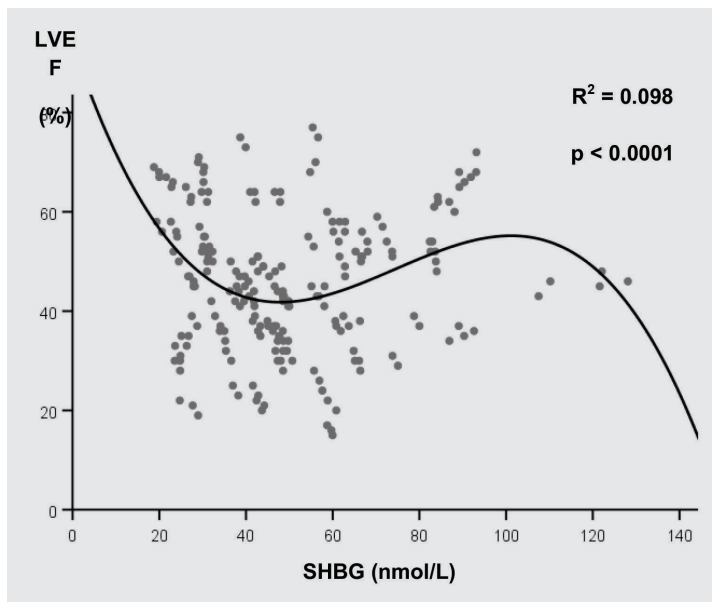


FIGURE 1. Scatterplots depicting the association between sex hormone-binding globulin (SHBG) and left ventricular ejection fraction (LVEF) in male patients with heart failure. A significant association (cubic regression equation: $Y = 93.683 - 2.573x + 0.04x^2 - 0.0002x^3$) was observed in the study population. (Regression equation, R² and p values were obtained from the cubic regression analysis.)

RECEIVED:
September 29, 2024

ACCEPTED:
October 31, 2024



LITERATURE 

1. Bušić Ž, Čulić V. Central and peripheral testosterone effects in men with heart failure: An approach for cardiovascular research. *World J Cardiol.* 2015 Sep 26;7(9):504-10. <https://doi.org/10.4330/wjc.v7.i9.504>
2. Zhao D, Guallar E, Ballantyne CM, Post WS, Ouyang P, Vaidya D, et al. Sex Hormones and Incident Heart Failure in Men and Postmenopausal Women: The Atherosclerosis Risk in Communities Study. *J Clin Endocrinol Metab.* 2020 Oct 1;105(10):e3798-807. <https://doi.org/10.1210/clinem/dgaa500>
3. Yeap BB, Marriott RJ, Antonio L, Raj S, Dwivedi G, Reid CM, et al. Associations of Serum Testosterone and Sex Hormone-Binding Globulin With Incident Cardiovascular Events in Middle-Aged to Older Men. *Ann Intern Med.* 2022 Feb;175(2):159-170. <https://doi.org/10.7326/M21-0551>