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Fund "Nauka" Project № 19017 Resume – Competition-Based Session 2019: "Dynamics in the serum levels of male sex hormones following an acute coronary syndrome"

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The sexual dysfunction is a common problem following a myocardial infarction (MI) – a fact that is supported by numerous studies. Additional contribution to the development of sexual dysfunction are conditions like hearth insufficiency, hormonal imbalance, atherosclerotic hearth disease and depression – all of them frequent among MI survivors. In different studies, the association between serum testosterone levels, MI survival rates and the long term prognosis are in focus but both the results and the populations included vary greatly. Another aspect of the hormonal changes occurring in the context of acute physiological stress is the alteration in the functional state of the adrenal cortex, associated with immunomodulation and the adaptation to MI.

In the present study, the goal is to clarify the short-term (6th month) dynamics in the pituitary-adrenal and the pituitary-gonadal axis determined by the ration cortisol/DHEA-S in men following an acute coronary syndrome (ACS) and their prognostic value to the development of hypogonadism and sexual dysfunction.

In order for this to be achieved, the following parameters will be studied: 1) the testosterone level and its fractions, LH, FSH 48 h after the event and then again after 6 months; 2) the ejection fraction at the time of the event and again on the 6^{th} month; 3) the ration DHEA-S/cortisol at the time of the event and again on the 6^{th} month; 4) to determine the likelihood of sexual dysfunction prior to the event and again in the recovery period.

Accomplishing the goal of the research would give opportunity to asses simultaneously, for the first time, the pituitary-adrenal and the pituitary-gonadal axis after ACS. This would lead to expanding the knowledge of the pathophysiological mechanisms that play a role in the adaptation to acute events. The analysis of the data will allow the research team to determine the importance behind the changes concerning the incidence of hypogonadism and quality of life. That would possibly lead to the development of screening tools.

Having in mind the stated problems and the growing population of MI survivors, the question about the decrease in testosterone and sexual dysfunction becomes especially relevant.

Achieved results:

In the period 2020-2023, the results of the study were published and a dissertation was defended. This led to the PhD of the PhD student Savi Shishkov. 4 full-text articles were published, participation in a national congress was achieved.

As a consequence of the scientific research the following results were obtained:

The expected T dynamics was observed in the acute period after the onset of myocardial ischemia. Additionally, lower T levels were found in the subgroup of patients with ST-elevation. The observed dynamics violated the usual associations with body mass index, in contrast to the group of patients with chronic coronary syndrome. This suggests that in the context of ACS, the usual risk factors for hypothyroidism give way to the stronger influence of myocardial ischemia. Myocardial ischemia affects the gonadal axis by mechanisms other than activation of the CHA axis, which could not be indicated by the present study.

On the other hand, an association of glomerular filtration rate and age with DHEA-S emerged, independent of patients' risk characteristics or severity of ACS. For this reason, in agreement with other investigators, the project team assumed that DHEA-S is an expression of general health status or plays a role in the pathogenesis of ischemic cardiac pathology, but its low levels are not a consequence of the occurrence of ACS.

SHBG, on the other hand, is associated with some established risk characteristics of patients with ACS and CHD. This, in the project team's opinion, makes cardiovascular risk a suitable additional marker and at the same time allows a more detailed hormonal assessment (determination of svT and bioT).

Both absolute hormone values and hormone ratios demonstrated correlations with clinical and biochemical parameters. The oT/LH ratios differed in patients with and without diabetes mellitus, suggesting hypothalamic dysfunction exacerbated in the course of ACS. Aromatization index, expressed by the oT/oE ratio, was better associated with cardiovascular risk factors better than either index alone.

These observations support the original hypothesis that examining the hormonal axes in their direct interaction with each other yields more information relative to each indicator alone.

Based on this, testosterone to LH ratio, testosterone to estradiol ratio as well as the albumin value could be added to the usual risk characteristics, given the associations of these parameters with the lipid profile and the GRACE score. The K/D ratio as an expression of the balance between the functional status of different areas in the adrenal cortex also showed an association with metabolic abnormalities and risk characteristic.