

The Relationship between Inflammation and Serum Estrogen, Testosterone, and DHEA-S Levels in Obstructive Coronary Artery Disease

Obstrüktif Koroner Arter Hastalığında Enflamasyon ve Serum Östrojen, Testosteron ve DHEA-S Düzeyleri Arasındaki İlişki

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ABSTRACT

Objectives: The relationship between sex hormones such as estrogen, testosterone and coronary artery disease (CAD) has been found to be controversial in various studies. Moreover, recent studies revealed an association between CAD and dehydroepiandrosterone sulphate (DHEA-S) which is an endogenous steroid hormone and the precursor of sex hormones. We aimed to investigate the relationship between serum testosterone, estrogen, DHEA levels and CAD.

Method: A hundred patients enrolled in the study. Patients were divided two groups based on the presence of lesions that causes luminal narrowing more than % 50 in at least one epicardial coronary artery.

Results: Obstructive CAD (O-CAD) was detected in 75 (60 m, 15 f) patients. The mean age was 60.1 ± 14.2 in the O-CAD group and 59.2 ± 11.2 in the Non-O-CAD group. Serum/plasma HbA1c levels and having male gender were significantly higher in the O-CAD group. (p = .002, p = .008). Serum sex hormones were shown to have no significant differences between groups.

Conclusion: Our data showed that there is no significant relationship between serum sex hormone levels and O-CAD.

Key Words: Coronary artery disease, inflammation, sex hormones

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ÖZET

Amaç: Östrojen, testosteron gibi cinsiyet hormonları ve koroner arter hastalığı (KAH) arasındaki ilişki çeşitli çalışmalarda farklı sonuçlar nedeniyle tartışmalıdır. İlaveeten, KAH ile endojen steroid hormonu ve seks hormonlarının öncüsü olan dehidroepiandrosteron sülfat (DHEA-S) arasında ilişki olduğunu bilinmektedir. Bu çalışmada; serum testosteron, östrojen, DHEA-S düzeyleri ve KAH arasındaki ilişkiyi araştırmayı amaçladık.

Yöntem: Çalışmaya göğüs ağrısı şikayeti ile kardiyoloji polikliniğine başvuran ve koroner anjiyografi planlanan yüz hasta kaydedildi. Hastalar en az bir epikardiyal koroner arterde % 50'den fazla lümen daralmasına neden olan lezyonların varlığına göre iki gruba ayrıldı.

Bulgular: Obstrüktif KAH (O-KAH) 75 hastada tespit edildi. Ortalama yaş O-KAH grubunda 60.1 ± 14.2 ve Obstrüktif olmayan KAH grubunda 59.2 ± 11.2 idi. Serum cinsiyet hormonlarının gruplar arasında önemli bir farklılık göstermediği saptandı.

Sonuç: Verilerimiz, serum seks hormonu seviyeleri ile O-KAH arasında anlamlı bir ilişki olmadığını saptamıştır.

Anahtar Sözcükler: Koroner arter hastalığı, enflamasyon, cinsiyet hormonları

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INTRODUCTION

Cardiovascular diseases are the most important cause of death in the adult population in developed countries. Obstructive coronary artery disease (CAD) is less commonly seen among women compared with men (1). This is especially evident in premenopausal women and is frequently explained by the antiatherogenic effects of estrogen (2). The relationship between testosterone and cardiovascular diseases is, however, more uncertain. While some studies on the subject have shown that higher testosterone levels in men increase the CAD risk (3), in others, lower testosterone levels were found to be more important in terms of cardiovascular risk (4). On the other hand, some studies have found that the testosterone levels are neutral in CAD (5). Dehydroepiandrosterone (DHEA) is an endogenous, steroid prohormone secreted from the adrenal gland in both women and men. There are many studies showing that its decreasing amounts with age increase the risk of CAD (6). The purpose of this study is to investigate whether there is a relationship between the presence of obstructive CAD and serum estrogen, testosterone, and DHEA levels in patients who underwent coronary angiography (CAG) due to stable CAD pre-diagnosis and to investigate the effects of these hormones on lipid and inflammation parameters.

METHODS

A total of 100 consecutive patients, who were evaluated for chest pain at the inpatient or outpatient cardiology clinic and underwent CAG were included in the study. Men and postmenopausal women patients, aged 18-80 years, who were evaluated for chest pain at the inpatient or outpatient cardiology clinic, were planned for and underwent CAG between January 1, 2015 and December 31, 2015 sequentially. The patients were divided into two groups: those who had a lesion with >50% luminal narrowing in at least one coronary artery (O-CAD) and those who had not (Non-O-CAD) in CAG. All of the women included in the study were in the postmenopausal period.

All laboratory parameters measured on admission hospital. Peripheral venous blood samples were obtained from all participants at the emergency department, collected in tubes with EDTA for the hematological test and dry tubes for biochemical tests and analyzed urgently. K3-EDTA (Grainer Bio-One GmbH) and VACUETTER Z Serum Sep Clot Activator venous blood collection tubes were used for laboratory samples. White blood cell count, hemoglobin and hematocrit (HCT) measurements were determined by an automated hematology analyzer XE1200 (Sysmex, Kobe, Japan). The biochemical measurements were performed using a molecular analyzer (Roche Diagnostics, Mannheim, Germany). Left ventricular ejection fraction (LVEF) was evaluated by a modified biplane Simpson method in two-dimensional echocardiography (Vivid 3 system; General Electric Company, Milwaukee, WI) within 24 hours of admission hospital.

Patients with malignancy that secrete sex hormones, intracranial malignancy, women who have had menstruation in the last two years, use sex hormones exogenously for any reason and/or refusing to participate in the study were excluded from this study.

The present study was conducted by the Declaration of Helsinki and was approved by the local ethics. The volunteers were informed about the study and their written consent was obtained.

Coronary angiography

All procedures were performed in our hospital and recorded in digital media for quantitative analysis. All of the patients underwent CAG within 24-36 h of first hospital admission. CAG was performed by the Judkins technique using a femoral artery with a 6- or 7-French guiding catheter.

Statistical analysis

Data were analyzed using the IBM SPSS 22.0 Statistical Package Program for Windows (IBM SPSS, Inc., IL, USA). The Shapiro-Wilk test was used to test the normality of distribution. Continuous variables with normal distribution were expressed as mean \pm standard deviation but continuous variables for all parameters were not distributed normally, so data were presented as median and interquartile range and categorical variables were expressed as the number of patients and percentages. Student t-test was used for comparison of mean values and Chi-square or Fisher's Exact test was used to compare categorical variables as appropriate. The Mann-Whitney U test was used to compare continuous variables that were not distributed normally. The differences between groups were statistically significant with a p value of < 0.05. analysis.

RESULTS

The mean age of the patients was 59.2 ± 11.7 in O-CAD and 60.1 ± 14.2 in Non-O-CAD. The demographic and clinical characteristics of the patient groups are summarized in Table 1. Hypertension, glycated haemoglobin (HbA1C), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), *C-reactive protein* (CRP), and creatinine levels were evaluated as risk factors in both groups. The HbA1C level was significantly higher in O-CAD ($p=0.02$) (Table 1).

Table 1: Baseline Characteristics of the Participants

	O-CAD n=75	Non-O-CAD n=25	p value
Female/Male, n (%)	15/60 (20%/80%)	12/13 (48%/52%)	0.008
Age, years	60.1 ± 14.2	59.2 ± 11.7	0.777
Hypertension, n (%)	44(58%)	10(40%)	0.082
Creatinine, (mg/dl)	1.1 ± 0.8	1.5 ± 2.4	0.334
CRP, (mg/L)	30.1 ± 67.7	18.8 ± 51.8	0.447
HbA1C, (%)	6.4 ± 2.4	5.3 ± 1.0	0.002

The testosterone, estrogen, and DHEA-S levels were 6.7 ± 33.9 nmol/L, 15.2 ± 10.7 nmol/L, and 106.1 ± 70.3 nmol/L in O-CAD, while they were 2.1 ± 1.6 nmol/L, 18.1 ± 17.0 nmol/L, and 118.4 ± 80.1 nmol/L in Non-O-CAD group, respectively. No significant difference was found in terms of serum sex hormone levels between the groups (Table 2).

Table 2: Sex hormone levels

	O-CAD n=75	Non-O-CAD n=25	p value
Estrogen, (nmol/L)	15.2 ± 10.7	18.1 ± 17.0	0.314
Testosterone, (nmol/L)	6.7 ± 33.9	2.1 ± 1.6	0.499
DHEA-S, (nmol/L)	106.1 ± 70.3	118.4 ± 80.1	0.466

DISCUSSION

The theory and published studies concerning the relationship between the serum sex hormones, estrogen and testosterone, and CAD are quite contradictory. It is generally accepted that estrogen, the main sex hormone in women, has a protective role against atherosclerosis. In contrast, the detection of high levels of estradiol and estrone after myocardial infarction in men suggests that exposure to estrogen causes atherosclerosis. There are also studies suggesting that estrogen plays a role in the formation of atherogenic lipid profile in men with obstructive CAD (7, 8). However, the relationship between hyperestrogenemia and CAD in men could not be confirmed in many studies, suggesting that stress induced by ischemia may play a role in the elevation of estradiol (9). In our study, there was no difference between the serum estrogen levels of O-CAD group, consisting of men and postmenopausal women with obstructive CAD, and non-O-CAD group. In a group of patients with similar demographic characteristics but with acute coronary syndrome, serum estrogen levels were negatively correlated with CAD severity but they were positively correlated with matrix metalloproteinase (MMP) and CRP levels (10). In that study, it was suggested that the decrease of serum estrogen levels increased CRP and MMP levels. The fact that our patient group consisted of people with stable CAD may have resulted in different results. In another study on patients with stable CAD, a minor and not statistically significant decrease in estrogen levels was shown in postmenopausal women while estrogen levels in men did not have a significant difference between patients with and without CAD (11). Although the decrease in serum testosterone levels in men is associated with CAD in general, there are also studies suggesting that there is no significant relationship between them (12). In a study, which found that the serum testosterone levels were slightly elevated in the group with obstructive CAD among postmenopausal women, this difference was not significant among men (11).

Serum DHEA-S, an endogenous steroid secreted from the adrenal gland at whose levels decrease by aging, is the precursor of estrogen and testosterone. There are studies showing that there is an association between low DHEA-S levels and CAD and all-cause mortality (6). Similarly, it was reported in many studies that this relationship was more prominent in men and that there was no relationship in women (13). In the Women's Ischemia Syndrome Evaluation (WISE) study, while low DHEA levels in women were associated with higher cardiovascular and total mortality, no association could be found with CAD severity (14). It is argued that DHEA-S deficiency may cause adverse events by increasing inflammation and endothelial dysfunction (15). Although there was no relationship between DHEA-S and obstructive CAD in men and postmenopausal women in our study, a weak correlation between DHEA-S and CRP in the group with obstructive CAD supports this view.

As it is known, cardiovascular mortality is the most important cause of death, especially in older ages, although the prevalence of obstructive CAD is lower among women than men. The investigation of the mechanistic relationship between DHEA-S and atherosclerosis and larger studies on this topic will contribute to the development of new perspectives on this subject.

Conflict of interest

No conflict of interest was declared by the authors.

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