

Research Article

Association between Serum Cortisol Level and Erectile Function in Healthy Men from the General Population

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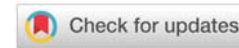
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Abstract

Purpose: The aim of the study is to investigate the association between serum levels of cortisol and erectile function in healthy men aged 45-60 years.

Material and methods: The serum level of cortisol was measured. The international index of erectile function-5 items (IIEF-5) was used to assess the erectile function. Data were gathered on the age of participants, Body Mass Index (BMI), waist circumference, family history of cardiovascular disease, and their habits including alcohol consumption and smoking. Two subgroups were defined, based on the IIEF-5 total score: the normal erectile function group with an IIEF-5 total score ≥ 22 points, and the erectile dysfunction group with an IIEF-5 total score < 22 points.

Results: A positive significant correlation was found between cortisol levels and IIEF-5 total score ($r = 0.299, p = 0.003$). Cortisol level and IIEF-5 total score showed negative significant correlations with BMI ($r = -0.276, p = 0.004$), ($r = -0.193, p = 0.041$), respectively; and waist circumference ($r = -0.319, p = 0.001$), ($r = -0.283, p = 0.003$), respectively. Men with normal erectile function had significantly higher cortisol levels (377 nmol/L vs. 308 nmol/L, $p = < 0.001$); significantly lower BMI (25 kg/m² vs. 27 kg/m², $p = 0.005$), and waist circumference (97 cm vs. 104 cm, $p = < 0.001$) compared to men with erectile dysfunction. In multivariate regression analysis adjusted for the age of participants, alcohol consumption, smoking, and family history of cardiovascular disease, IIEF-5 total score showed a significant negative association only with waist circumference ($\beta = -0.194, p = 0.031, 95\% \text{ CI} = -0.370, -0.018$).

Conclusions: To our knowledge, this is the first study to demonstrate a significant positive association between serum levels of cortisol and erectile function in healthy men. This association seems, however, to be affected by variations in body parameters, mainly waist circumference in such men.

Introduction

The inability to obtain/or sustain an erection efficient enough to undergo sexual activity or insufficient erectile rigidity on three of four sexual occasions, that persists for a minimum of 6 months, is referred to as erectile dysfunction (ED) [1]. ED represents a major health problem worldwide with a significant and steady increase in the number of men looking for medical assistance due to ED over time [2].

Cortisol is essential in stress-respond mechanisms, however, the role of cortisol in the process of erectile function

is still uncertain and results from previous studies were found inconsistent. In line with this, glucocorticoid replacement therapy in men with primary adrenocortical insufficiency was associated with improvement of their sexual function [3], and a similar result was found in men with psychogenic erectile dysfunction [4,5]. On the other hand, other scholars suggested an inhibitory role of cortisol in the process of erectile function in healthy men [6,7].

Worldwide, obesity is getting more attention, particularly considering its association with many health problems. In accordance, a large number of studies indicate obesity as a



contributing factor for common problems such as hypertension, diabetes, vascular disease, and endothelial dysfunction, all of which are also known to contribute to the etiology of ED. In line with this, waist circumference was shown to predict obesity-related health problems [8] and is suggested as the best predictor of erectile dysfunction [9]. Also, obesity is associated with the activation of the hypothalamic-pituitary-adrenal system with overproduction of serum cortisol [10,11].

The present study aimed to investigate the connection between serum level of cortisol and the international index of erectile function-5 items (IIEF-5) total score in 119 community-dwelling healthy men, aged from 45 to 60 years.

Material and methods

The present study is part of a larger study on the association between male sexual function and risk of early cardiovascular disease, conducted on 119 men aged from 45 to 60 years, representing the general population during the period between January 2006 and January 2011. Detailed information about the recruiting process is described elsewhere [12].

In brief, community-dwelling healthy men were randomly invited to participate in the study. Exclusion criteria were history of chronic inflammatory diseases, infection diseases, Cardiovascular Disease (CVD), diabetes, hypertension, psychological disease, as well as use of prescribed medications during the last 6 months prior to inclusion in the study. Men outside the range of 45 to 60 years were also excluded from the study.

Sexual function was estimated with the IIEF-5 questionnaire, based on 5 domains evaluating sexual desire, erectile function, intercourse satisfaction, orgasmic function, and overall satisfaction. Each domain is scored on a 5-point scale with a total score ranging from 5 points to 25 points. Men with a total score ranging from 22-25 points were considered to have normal erectile function, while those with an IIEF-5 total score of less than 22 points were considered to have ED.

Demographic data was also collected regarding age (years), body configuration including Body Mass Index (BMI) (kg/cm²) and waist circumference (cm), lifestyle factors including smoking status (yes, no) and alcohol consumption (yes, no), and presence of family history of CVD (yes, no). The participants who were found eligible had a blood sample taken between 07:00 and 10:00 am for analysis of serum cortisol level (nmol/L).

Hormonal analysis

Plasma samples were stored in the biological bank at -80 °C. Serum cortisol concentration was measured using a Two-step competitive method with ElectroChemiLuminiscenceImmunoassay (ECLIA) detection method based on Ruthenium (Ru) derivatives, which has an intra- and interassay coefficient of variation (CV) of 5%. With a measuring range of 1.5 – 1750 nmol/L and a reference range of 133 – 537 nmol/L. Missing data was found in 13 men.

The main outcome measure was the association between serum cortisol level and the IIEF-5 score representing the erectile function of the men. The present study protocol was reviewed and approved by the institutional review board of Lund University Hospital (Reg. No. 400/2005). Informed consent was submitted by all subjects when they were collected.

Statistical analyses

SPSS software, version 16 (SPSS, Inc; Chicago, IL) was used to run out all the statistical analyses. The correlations between serum level of cortisol (nmol/L), IIEF-5 scores and age (years), BMI (kg/cm²), and waist circumference (cm) were investigated using Spearman's rank test.

The study subjects were then classified into two groups based on the IIEF-5 total score: men with normal erectile function (IIEF-5 total score \geq 22 points), and men with erectile dysfunction (IIEF-5 total score $<$ 22 points). Non-parametric Mann-Whitney U test was used to compare serum levels of cortisol (nmol/L), age (years), BMI (kg/cm²), and waist circumference (cm) means between groups.

Finally, the association between variables that showed significant differences between groups (serum levels of cortisol, BMI, and waist circumference), and IIEF-5 total score (continuous parameter) was investigated in a multivariate regression analysis test balanced for age (continuous years), smoking status (yes, no), alcohol consumption (yes, no), and family history of CVD (yes, no).

Results

The demographic data of the participants is summarized in Table 1. A positive significant correlation between serum level of cortisol and IIEF-5 total score ($r = 0.299$, $p = 0.003$) was found. Negative significant correlations between serum level of cortisol and BMI ($r = -0.276$, $p = 0.004$), and waist circumference ($r = -0.319$, $p = 0.001$) were found. On the

Table 1: Descriptive statistics of the study population.

Variables	n	Mean (±SD) or %	Range
Age (years)	119	55 (±4.0)	46 - 60
BMI (kg/cm ²)	117	27 (±3.0)	20 - 38
Waist circumference (cm)	118	100 (±10)	79 - 132
Smoking:	118		
Never	61	52%	-
Past/current	57	48%	-
Alcohol consumption	116		
Yes	99	85%	-
no	18	15%	-
Family history of CVD	117		
Yes	30	26%	-
No	87	74%	-
Cortisol (nmol/L)	106	339 (±92)	132 - 662

Data are mean (±SD) or (%), range. BMI: Body Mass Index.



contrary, no significant correlation between serum cortisol level and age was found ($p > 0.05$). IIEF-5 total score showed a negative significant correlation with BMI ($r = -0.193$, $p = 0.041$), and with waist circumference ($r = -0.283$, $p = 0.003$). In contrast, the correlation between IIEF-5 total score and age was not significant ($p > 0.05$) (Table 2).

Men showing normal erectile function with IIEF-5 total score ≥ 22 points were associated with a significantly higher serum cortisol level as compared to men showing signs of erectile dysfunction with IIEF-5 total score < 22 points (377 nmol/L vs. 308 nmol/L, $p < 0.001$). The opposite trend was found regarding BMI (25 kg/cm² vs. 27 kg/cm², $p = 0.005$), and waist circumference (97 cm vs. 104 cm, $p < 0.001$). In contrast, age was not significantly different between groups ($p > 0.05$) (Table 3).

In a multivariate regression analysis test adjusted for age (continuous years), smoking status (yes, no), alcohol consumption (yes, no), and given a family history of CVD (yes, no), a negative significant association only between IIEF-5 total score and waist circumference ($\beta = -0.194$, $p = 0.031$, 95% CI = -0.370, -0.018) was found (Table 4).

Discussion

A higher serum level of cortisol was associated with a higher IIEF-5 score. Both cortisol level and IIEF-5 score showed significant negative correlations with BMI and waist circumference. Men with normal erectile function had significantly higher cortisol levels compared to men with

Table 4: Association between erectile function according to IIEF-5 score and serum cortisol levels, BMI, and waist circumference from 119 men from the general population.

Variables	Erectile function (IIEF-5)			
	β	p	95% CI	
			Lower	Higher
Cortisol (nmol/L)	0.007	0.168	-0.003	0.018
BMI (kg/m ²)	0.152	0.546	-0.348	0.652
Waist circumference (cm)	-0.194	0.031	-0.37	-0.018

Statistical analysis was done using multivariate regression analysis tests adjusted for the age of subjects (continuous), smoking (yes, no), alcohol consumption (yes, no), and family history of CVD. A p - value less than 0.05 is considered statistically significant.

erectile dysfunction. The opposite trend was found regarding BMI and waist circumference. In the adjusted multivariate analysis test, the IIEF-5 score showed a significant negative association only with waist circumference. The results indicate an association between erectile function and serum cortisol level, which seems to be affected by changes in body parameters.

It has been reported that gluco- and mineralocorticoid replacement therapy in men with autoimmune Addison's disease was associated with improvement of their erectile function [3], also the administration of ACTH in men with psychogenic ED was associated with improvement of erectile function [4,5], indicating a role of serum level of cortisol in the process of erectile function. A number of theories have been suggested to explain the improvement of erectile function associated with the increased cortisol levels including temporarily increasing blood pressure and consequently improving penile circulation [13], by triggering penile smooth muscle relaxation via nitric oxide synthesis in penile tissue and their effect on potassium excretion and/or intracellular calcium [14], and by initiating a positive psychological status in such men [15]. In accordance, a positive significant connection between IIEF-5 total score and serum level of cortisol was found in the current study.

In contrast, other scholars suggested higher cortisol levels are likely to cause ED based on a finding of a significant negative correlation between serum cortisol and IIEF-5. However, this suggestion was based on data from a low number (32 out of 103 men) of a selected group of men (those who are not taking psychotropic medications). The authors relate their suggestion to increased levels of stress, although, the level of stress was not assessed in their study [16]. Also, the studies by Uckert, et al and Rahardjo, et al which support the above theory were based on a few numbers of men (45, and 54 men, respectively) and no covariables were taken into consideration in statistical analyses [6,7].

The current study documented a negative correlation between serum level of cortisol and waist circumference in accordance with previous results in community-dwelling men [17], in women without metabolic syndrome [18], and in a rural population of men [19]. The inverse association between serum cortisol and waist circumference/BMI is suggested to be related to the increased proportion of cortisone that is transformed to cortisol by the enzyme 11 β -hydroxysteroid dehydrogenase type 1, which is located in the abdominal fat mass and omental

Table 2: Correlation coefficients (r) between serum cortisol & IIEF-5 and the age of subjects, BMI, and waist circumference in 119 men from the general population.

Variables	Cortisol (nmol/L)		IIEF-5	
	r	p	r	p
Cortisol (nmol/l)	-	-	0.299	0.003
IIEF-5	0.299	0.003	-	-
Age (years)	-0.014	0.885	-0.044	0.646
BMI (kg/m ²)	-0.276	0.004	-0.193	0.041
Waist circumference (cm)	-0.319	0.001	-0.283	0.003

IIEF-5 = international index of erectile function-5 items version. BMI: Body Mass Index. Statistical analysis was done using the non-parametric Pearson correlation coefficient rank. A p - value less than 0.05 is considered statistically significant.

Table 3: Comparison of serum cortisol, the age of subjects, BMI, and waist circumference between men with normal erectile function and those with erectile dysfunction according to the IIEF-5 score.

Variables	Erectile function (IIEF-5)		p
	Normal erectile function IIEF-5 ≥ 22 $n = 56$	Erectile dysfunction IIEF-5 < 22 $n = 57$	
Cortisol (nmol/L)	377 (± 92)	308 (± 78)	< 0.001
Age (years)	56 (± 4.0)	55 (± 4.0)	0.5
BMI (kg/m ²)	25 (± 2.0)	27 (± 4.0)	0.005
Waist circumference (cm)	97 (± 7.0)	104 (± 11)	< 0.001

Data are mean (\pm). Statistical analysis was done using a non-parametric Mann-Whitney U test. A p - value less than 0.05 is considered statistically significant.



subcutaneous tissue [20]. Other investigators suggested obesity relatively decreases the response of the glucocorticoid receptors to the circulating cortisol [21].

In the adjusted multivariate analysis model, among other variables, waist circumference was the only variable that had a significant negative association with the IIEF-5 total score. Waist circumference is widely accepted as a proxy measure of central obesity and was found to correlate positively with pathological conditions related to obesity [22]. In a longitudinal cohort study of aging, including 841 men, the men who reported ED over time had significantly higher waist circumference, hypertension, heart diseases, and diabetes mellitus compared to those with normal erectile function [23]. Higher waist circumference per se was associated with an increased prevalence of hypertension, coronary artery diseases, diabetes mellitus, and dyslipidemia [24], which could explain the inverse association between waist circumference and ED.

The current study has some weaknesses, the number of participants is small, however, the statistical analyses herein exhibited pronounced results in this group of men. The analyses were done on a single blood sample, which is a limitation compared to longitudinal multiple samples. However, this is also the case for most of the previously published studies on men from the general population, thus we believe that the results from our current study are still acceptable. The study subjects were not evaluated for their stress. Therefore, the results from the present study should be interpreted carefully.

Conclusion

To date, this is the first study to document a positive significant correlation between serum cortisol and IIEF-5 total score in healthy men. Both variables showed significant negative correlations with BMI and waist circumference. Waist circumference was found to be the only variable to predict the IIEF-5 total score. These results suggest serum cortisol levels play a role in the process of erectile function which seems to be affected by changes in body parameters, mainly waist circumference. These results need to be confirmed in a larger study.

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