

## Erectile Dysfunction as a Risk Factor Predicting Coronary Artery Disease

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### Abstract

**Background and Aims:** It has been shown that erectile dysfunction (ED) and coronary arterial disease (CAD) share predisposing pathophysiology and risk factors. We planned present study to determine ED as an early precursor of CAD using objective angiographic methods.

**Methods:** Twenty-two patients without any cardiac symptoms who referred for ED were assigned for the first group. Another 20 patients who were underwent the coronary angiographic (CAG) assessment and had CAD, and without any previous ED history were assigned to the second group. All patients were asked for their sexual intercourses during the last 12 months period. The degree of ED is determined by means of IIEF-EF questionnaire and penile doppler ultrasonography.

**Results:** CAD was diagnosed in 12 (54.5%) patients out of 22 whom had ED diagnosis without any cardiac complaints. There was no statistically significant difference between the serum parameters and risk parameters of the patients. In the second group, ED was diagnosed in 9 (45%) patients out of 20 who had been diagnosed with CAD after the coronary angiography.

**Conclusions:** CAD was present in high proportions among ED patients without any symptomatic cardiac disease. Our study depended on the objective criteria such as angiography and colour doppler ultrasound in the same patient group and thus we believe that it is unique study to support the idea that ED can be the indicator of CAD.

**Keywords:** Coronary Artery Bypass Surgery, Erectile Dysfunction, Doppler Ultrasonography, Penile Erection

### Introduction

Erectile dysfunction is described as insufficiency in initiating, achieving and maintaining of penile erection necessary for sexual intercourse. Incidence of erectile dysfunction (ED) increases with age. It has been reported that it occurs only in 2 of 100 men at the age of 40 but, in 25 of 100 men at the age of 65(1). In addition, 35% of married men who were 60 years old or older complain of ED (1).

A relationship between coronary artery disease (CAD) and the age of onset and incidence of ED has been shown (2). Among the common risk factors

for ED which may be concomitant with arterial insufficiency, hypertension, hyperlipidemia, smoking, diabetes mellitus, perineal or pelvic blunt trauma and pelvic irradiation (2). In arteriography of the patients with ED and atherosclerosis, bilateral

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diffuse affection of internal pudendal, penile and cavernous arteries has been observed (3).

In the patients with ED, the prevalence of CAD has been reported as 5-56% in the literature (3, 4). In contrast, ED prevalence in symptomatic patients with CAD has been reported as 44-75% (5, 6). Small diameter and extensive content of endothelium and smooth muscle of cavernous arteries make penis very vulnerable to oxidative stress and variations in systemic nitric oxide levels as in the other vascular organs (5). It can be reasonably suggested that ED may be an early marker of atherosclerosis and sub-clinical systemic vascular diseases.

Thus, considering shared predisposing pathophysiology and risk factors of ED and CAD, we planned present study to show that ED can be an early precursor of CAD. For this purpose, we investigated the correlation between CAD and ED directly by coronary angiography.

## Materials and Methods

The patients of the study, who are older than 35 years, were selected sequentially to form at least twenty patients in each group on the advice of our statistician (S.E.). Twenty-two patients who referred to urology clinic with only ED complaints and no history of any cardiac disease were included in the first group. Twenty patients who referred to cardiology clinic with only complaints suggesting primarily CAD and no history of ED formed the second group.

After receiving written informed consent and the approval of our Hospital's Local Ethics Committee (dated February 19, 2008 and No: 2255), study was conducted between March 2008 and November 2008. In history of the patients, risk factors determined previously by many studies such as smoking, trauma, surgery, diabetes mellitus, hypertension, atherosclerotic and coronary cardiac disease were investigated. For evaluation of erection problems,

first 5 questions of international index of erectile function (IIEF) and 15th question of IIEF-EF were asked with face-to-face interview technique (7). The scores were classified as follows: IIEF-EF  $\geq$  26 normal, 22-25 slightly ED, 17-21 slight-mild ED, 11-16 mild ED, 1-10 severe ED. All patients in the first group were performed penile Doppler US, and then coronary angiography described as follows.

Coronary angiography (CAG): Femoral artery was used as intervention site. The region was prepared in a sterile manner and covered. After local anesthetic, puncture was done by Seldinger method. For arterial puncture, a 6 French (F) cannula was placed. Selective left and right coronary angiography and left ventriculography were performed. During routine cardiac catheterization and coronary angiography, in aorta systolic, diastolic and mean pressure, left ventricle systolic pressure and end-diastolic pressure were recorded. Systolic pressure gradients were measured in the middle of left ventricle and aorta to evaluate aortic valve. Non ionic agent was used as contrast. Narrowing 50% and more in any major epicardial artery or its branches were accepted as CAD.

In the second group, 20 patients diagnosed with CAD following coronary angiography were evaluated by the urology clinic. Full urological evaluation including IIEF-EF was performed as in the first group. Penile colour doppler US was performed for each patient in the study by same radiology specialist in radiology department using the General Electric Logic 9, high resolution harmonic, 12 MHz linear probe. Maximum systolic velocity (MSV)  $<$ 25 was considered as arterial insufficiency. End diastolic velocity (EDV)  $>$ 5 was considered venous escape. Any pathological value of MSV or EDV was evaluated as ED.

All patients were tested for HDL, LDL, TG, total cholesterol in lipid panel and prolactin, total testosterone, free testosterone, LH, FSH in hormone panel.

### Statistics

Data analysis was made with SPSS 11.5 pack program. Shapiro Wilk test was used to investigate whether the distribution of continuous variables was in accordance with normal distribution. Descriptive statistics were shown as mean  $\pm$  std. deviation for numeric variables and as observation number (%) for nominal variables. It was analyzed by Student's t test or Mann Whitney U test whether there was a statistically significant difference between independent groups for the features obtained with measurement. In the group with coronary artery disease diagnostic similarity between classification of the cases according to IIEF score and the classification according to penile colour Doppler was investigated with McNemar test. For nominal comparison, Fisher's exact test was used. The results were accepted as statistically significant for  $p < 0.05$ .

### Results

After angiography, 12 of 22 patients in the first group (54.5%) were diagnosed with CAD. Of 22 patients, mean age of 12 patients diagnosed CAD was  $57.9 \pm 8.6$  and mean age of the remaining 10

patients without CAD was found to be  $46.2 \pm 7.3$ . Comparison of the ages between the groups with and without coronary artery diseases revealed a statistically significant difference ( $p = 0.003$ ). However, when the age was evaluated with logistic regression analysis together with the other factors leading to coronary artery disease, the effect of the age on coronary artery disease was not different from other factors ( $p = 0.12$ ).

In the first group, the patients had at least 12-month sexual relationship. In all of the patients, IIEF-EF was found as  $< 26$  ( $12.6 \pm 6.6$ ). Mean IIEF-EF was found as  $11.6 \pm 7.6$  in the patients with CAD and as  $13.8 \pm 5.2$  in the patients without CAD ( $p = 0.123$ ).

Of 22 patients applied with erectile dysfunction, 9 (40.9%) had pathological values in penile color doppler US. Of 12 patients with CAD, in 8 (66.7%) penile color doppler US was pathologic. It was statistically significant ( $p = 0.01$ ) (Table 1).

There was no statistically significant difference between the patients with and without coronary artery disease in the first group in terms of hypertension, smoking and diabetes mellitus. In addition, total testosterone, free testosterone, LH, FSH and lipid panel (total cholesterol, triglyceride, LDL, HDL) levels

**Table 1.** Summary of the findings of all patients

	Age	Mean IIEF	No of patients with pathologic Doppler US
ED+ (9 patients)	$58 \pm 6.4$	$20.7 \pm 9.9$	9
ED- (11 patients)	$47.7 \pm 8$	$26.5 \pm 4.3$	11
P value	0.006*	0.175	1.000
CAD + (12 patients)	$57.9 \pm 8.6$	$11.6 \pm 7.6$	8
CAD- (10 Patients)	$46.2 \pm 7.3$	$13.8 \pm 5.2$	1
P value	0.003*	0.123	0.01

\* Logistic regression analysis revealed that not meaningful ( $P = 0.12$ )

**Table 2.** Hormone and lipid panels of the patients in the first group

	CAD +	CAD -	P value
<b>Total Cholesterol</b>	236.5 ± 63.6 mg/dl	216.1 ± 36.6 mg/dl	0.382
<b>HDL</b>	45.6 ± 8.4 mg/dl	41.4 ± 8.3 mg/dl	0.248
<b>LDL</b>	156.6 ± 41.6 mg/dl	144.6 ± 31 mg/dl	0.458
<b>Triglycerides</b>	173.6 ± 113.4 mg/dl	183.6 ± 86.5 mg/dl	0.539
<b>Total Testosterone</b>	5.37 ± 2.61 ng/ml	6 ± 2.1 ng/ml	0.624
<b>Free Testosterone</b>	17.2 ± 13.4 pg/ml	14.2 ± 4.1 pg/ml	0.651
<b>FSH</b>	5.6 ± 2.7 mIU/ml	5 ± 3.3 mIU/ml	0.539
<b>LH</b>	4.2 ± 2.3 mIU/ml	3.4 ± 1 mIU/ml	0.426
<b>Prolactin</b>	12.5 ± 10.7 ng/ml	11.4 ± 5.4 ng/ml	0.805

**CAD**, Coronary Arterial Disease.

were similar and not statistically different (Table 2).

In the second group, according to the IIEF-EF score, erectile dysfunction (IIEF-EF < 26) was determined in 8 (40%) patients, while penile erectile dysfunction was determined in 9 (45%) patients by penile colour doppler US. The mean age was found as 58.00 ± 6.46 in the patients with erectile dysfunction and as 47.73 ± 8.02 in the patients without erectile dysfunction by penile colour doppler US (Table 1). In addition, there was no difference between the patients' serum parameters (Table 3).

Mean duration of hospitalization for the patients performed coronary angiography in both groups was

one day without any complication. One of the 42 patients developed priapism after penile colour Doppler US. Detumescence was achieved by aspiration of cavernous body with 19 gauge butterfly needle along with ice therapy.

## Discussion

It is estimated that 322 million men would suffer from erectile dysfunction in 2025 (8). Epidemiological data have shown that erectile dysfunction prevalence is 16-25% depending on the patient population and the definition of erectile dysfunction (9). All

**Table 3.** Hormone and lipid panels of the patients in the second group

	ED +	ED -	P value
<b>Total Cholesterol</b>	179.6 ± 36.8 mg/dl	185.8 ± 37.1 mg/dl	0.73
<b>HDL</b>	39.6 ± 7.8 mg/dl	39.8 ± 13.3 mg/dl	0.54
<b>LDL</b>	114.7 ± 34.0 mg/dl	115.2 ± 26.7 mg/dl	0.97
<b>Triglycerides</b>	134.8 ± 79.6 mg/dl	157.7 ± 87.3 mg/dl	0.56
<b>Total Testosterone</b>	4.36 ± 0.67 ng/ml	4.76 ± 1.77 ng/ml	0.61
<b>Free Testosterone</b>	12.8 ± 2.50 pg/ml	16.3 ± 1.89 pg/ml	0.04
<b>FSH</b>	4.47 ± 1.66 mIU/ml	6.17 ± 4.46 mIU/ml	0.53
<b>LH</b>	3.21 ± 1.29 mIU/ml	4.15 ± 1.01 mIU/ml	0.16
<b>Prolactin</b>	11.0 ± 3.32 ng/ml	10.6 ± 4.52 ng/ml	0.83

**ED**, Erectile Dysfunction.

epidemiological studies indicate the relationship between erectile dysfunction and advancing age (10). Both clinical and animal studies on endothelial dysfunction have encouraged that atherosclerosis leads to increased cerebrovascular and cardiovascular morbidity (11-14). All of these situations individually presented as a risk factor for cardiovascular diseases are defined by significantly increased risk of vascular endothelial injury that may lead to several atherosclerotic disease entities (11, 12). Endothelial injury, described as endothelial dysfunction, may simultaneously involve penile vascular structure and generally erectile dysfunction is attributed to the endothelial dysfunction in literature.

It has been suggested that the erectile dysfunction may be an early sign of atherosclerosis, cardiovascular risk and subclinical systemic vascular diseases (13). The small size and excessive content of endothelium and smooth muscle make penis very vulnerable to oxidative stress and the variations of systemic nitric oxide levels as well as in the other vascular organs. A certain arterial flow in corpus cavernosum is required to provide rigid erection. Atherosclerotic changes may cause obstruction leading to erectile dysfunction. Smaller plaque size affects penile artery more likely compared to the marked obstruction in coronary, carotid and femoral artery that have larger arterial lumen (15). In the light of these statements, since the arteries providing penile circulation are small dimension arteries, erectile dysfunction would be an early clinical evidence of general, subclinical diseases caused by atherosclerosis.

Lue et al has firstly described high resolution US and quantitative doppler spectral analysis technique in 1985 for evaluation of vascular ED (16). Penile doppler US examination requires a good technical support and experience and depends on many variables such as the physician performing the test, vasoactive agent used, anatomical variations, the circumstances under which the test performed and physical and psychological situation of the patient

during test. Likewise, Allen and Mellinger, in their separate studies, have reported that in the patients with psychological disorders, Doppler results were unreliable because of anxiety and increased sympathetic stimulation (17, 18). In some of the studies although it has been mentioned that of the patients diagnosed with arterial failure, only few patients had undergone angiography for definitive diagnosis; angiography was almost never performed on the persons with normal potency in these studies. None of these publications have reported that colour Doppler US gave 100% successful results (19-21). For this reason, the opinion accepted by radiologists and urologists is that Doppler is a vascular screening method and that spectrum findings should be evaluated considering that the present ED in the patient.

Coronary angiography has been appreciated much more with effective surgery for coronary disease. If CAG procedure is performed by an experienced physician and team, the rate of complication is low, the most undesirable complications are myocardial infarction, death and paralysis (22). The newer, low osmolarity contrast substances have lower risk (23). In the literature, CAD prevalence is seen in the rate of 5-56% in the patients with erectile dysfunction (3, 4). We performed coronary angiography on 22 patients in the first group referred to our clinic with erectile dysfunction and had no cardiac complaints. We diagnosed coronary artery disease in 12 (54.5%) of 22 patients. Although this rate is similar with the reported literature, our study is the first study in which the gold standard (coronary angiography) method was directly performed to the patients who had just ED symptoms without any cardiac symptoms.

Several studies have reported that ED can be present in CAD proven cardiac patients (5, 6, 9, 11-15, 24-26). In the second group of our study that referred to the cardiology clinic with cardiac complaints and diagnosed with coronary artery disease after coronary angiography were evaluated. As a result of penile colour Doppler US evaluation, erectile

dysfunction was determined in 9 (45%) of the 20 patients. In our study, high ED prevalence (45%) in the patients with CAD encourages the opinion that CAD is frequently accompanied with ED. In the patients with symptomatic CAD, erectile dysfunction prevalence has been reported as 44-75% (5, 6). Kloner et al (24), in a study based on Sexual Health Inventory for Men, has shown that erectile dysfunction prevalence was 75% in 76 men with documented coronary artery disease. Montorsi et al (6), found erectile dysfunction prevalence in 300 consecutive patients with CAD angiographically documented as 49%. It has been reported that erectile dysfunction preceded CAD symptoms in 67% of these patients who had both erectile dysfunction and CAD and that the period between erectile dysfunction and the onset of CAD was 38.8 months. In CAD patients, ED comes before symptomatic CAD in the majority by an average of 2 up to 3 years (25).

## Conclusions

Our results show that erectile dysfunction accompanies with CAD in a significant number of the patients referred for it without any symptomatic cardiac disease and this risk is higher especially in elderly patient group. In conclusion, the results of this study suggest that erectile dysfunction may be an early precursor of cardiovascular disease in some patients and in these patients along with the evaluation of the other possible risk factors of erectile dysfunction, a detailed examination for cardiovascular pathology should be done.

## Conflict of Interest

None declared.

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