

Original Article

The relation between erectile dysfunction and extent of coronary artery disease in the patients with stable coronary artery disease

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Abstract: Introduction: Erectile dysfunction (ED) and coronary artery disease (CAD) are closely related as a result of endothelial dysfunction leading to the restriction of blood flow. ED is a potential independent risk factor of CAD. We investigated the prevalence and severity of ED, the extent of CAD and the time interval between the symptoms of ED and CAD in the stable coronary artery patients. Materials and methods: 161 patients applied coronary angiography were divided into two groups according to SYNTAX score as group 1 (n=81) SYNTAX score ≤ 22 , and group 2 (n=80) SYNTAX score > 22 . The prevalence and severity of ED was determined by using The International Index of Erectile Function (IIEF). Results: The prevalence of ED was 43.2% in group 1 and 61.3% in group 2 (P=0.022). The score of IIEF was 23.1 (15-29) in group 1, 19.3 (6-29) in group 2; there was a significant difference (P=0.000). In the multivariate logistic regression analysis carried out in order to determine the independent predictors on Syntax score, it was found that LDL (odds ratio: 1.032, 95% confidence interval: 1.009-1.055, P=0.007) and IIEF score (odds ratio: 0.825, 95% confidence interval: 0.733-0.928, P=0.001) were the independent predictors. The time between the symptoms of ED and CAD 30.1 ± 4.8 months in group 1, and 40.5 ± 4.3 months in group 2 (P=0.000). Conclusion: The severity of ED is an independent factor predicting the extent of CAD. The early detection of ED enables to make a cardiovascular evaluation. Therefore, taking the cardiovascular risk factors under an aggressive treatment may contribute to prevent the cardiovascular cases which may develop in the future.

Keywords: Erectile dysfunction, coronary artery disease, international index of erectile function, syntax score

Introduction

Erectile dysfunction (ED) is an inability to get and maintain an erection for a satisfying sexual relationship [1]. It has been showed in a recent study that the incidence of ED adjusted by age is 48.1% [2]. The International Index of Erectile Function (IIEF) is, today, one of the most commonly used forms for men admitting because of the sexual complaints. According to IIEF, the severity of ED is classified from mild to severe [3].

Organic ED and coronary artery disease (CAD) are closely related as a result of endothelial dysfunction leading to the restriction of blood flow [4, 5]. The similar risk factors including

obesity, diabetes mellitus (DM), smoking, hypertension (HT) and dyslipidemia are defined for both [6-9].

Diffuse atherosclerotic process affects the arterial blood flow and leads to the major pathophysiologic changes in both cardiovascular and peripheral vascular diseases including ED [10]. It was reported that the prevalence of ED has a high ratio like 75% in the patients diagnosed with CAD [11-16]. There are evidences supporting that ED is the predictor of CAD. An important part of the men with ED show the early signs of CAD. The men who previously had ED may get more severe CAD in proportion to the ones without CAD. The time between the beginning of the symptoms of ED and CAD is 2-3 years; also, the

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occurrence time of cardiovascular event is approximately 3-5 years. ED has substantially increased mortality due to the relation with the mortality of CAD. As a result, the severity of ED is associated with the severity of CAD [17].

When the previous studies about the severity of ED and the severity of CAD were researched, it was seen that the patients with acute coronary syndrome were generally included in CAD group in the studies. The underlying root cause of acute coronary syndrome is atherosclerotic plaque rupture. However, the underlying pathology in the patients with stable coronary artery disease is endothelial dysfunction and atherosclerotic plaque burden. Also, in the previous studies, the numbers of epicardial vessels with stenosis above 50% and Gensini score were used in order to evaluate the extent of CAD. In our study, we used Syntax score, which is more current and provides better information about the complexity and extent of CAD, instead of Gensini score which is a classical scoring system. In the literature, among the studies evaluating the severity of ED and the extent of CAD, no study using Syntax score was encountered. Therefore, we think that this is the first study.

The aim of our study is to investigate the prevalence of ED in the patients with stable coronary artery disease, to evaluate the relation between the severity of ED and the extent of CAD by using Syntax score and to determine the time between the beginning of the symptoms of ED and CAD.

Materials and methods

161 patients with stable coronary artery applied coronary angiography as a result of noninvasive evaluations were included in the study. The patients with the angina complaints related to the effort longer than two months and diagnosed with myocardial ischemia by the clinical and noninvasive tests were defined as stable coronary artery patients. After the coronary angiography, the patients were divided into two groups as group 1 with syntax score ≤ 22 and group 2 with syntax score > 22 .

The patient groups below were not included in the study:

The patients with the history of percutaneous coronary intervention and coronary artery bypass surgery. The patients with liver disease, renal failure, thyroid disease, major depression

receiving long-term pharmacological treatment, the history of spinal cord injury, and the patients with previous pelvic, penile, urethral and prostate trauma or surgery. The patients with primary ED. The patients with normal coronary. The patients with acute coronary syndrome.

All patients had the routine laboratory tests including lipid profile, fasting glucose, total and free testosterone levels. Diagnostic coronary angiography was applied to all patients by using the standard technique. The diagnostic coronary angiography was performed by using the standard techniques in all patients. If necessary, percutaneous transluminal coronary angioplasty or coronary artery bypass surgery was carried out within the time spent in hospital. In order to identify the cardiovascular risk factors, it was determined according to ESC/ACC/AHA guidelines for HT to be $>140/90$ in three consecutive measurements in resting, DM fasting glucose level to be >126 mg/dl, and family history to have CAD for father at <55 years of age and for mother at <65 years. Body mass index (BMI) (kg/m^2) of all patients was calculated, and smoking was questioned.

Erzincan University Faculty of Medicine Ethics Committee approved the study protocol; each patient signed the written informed consent forms and gave consent.

Quantitative coronary angiography and syntax score

Selective coronary angiography was performed by Judkins technique and the analysis was performed by two interventional cardiologists who were not aware of ED of the patients. In case of a dispute, the decision of a third observer was referred. The final decision was given by an unanimous vote. The Syntax score was evaluated using the guidelines described [18, 19]. The latest updated version (2.11) of the online calculator was used to designate the Syntax score (<http://www.syntaxscore.com>). The patients were divided into two groups: the patients with syntax score ≤ 22 as group 1 and the patients with syntax score > 22 as group 2.

Erectile function evaluation

All patients who stabilized after coronary angiography were carried out by the erectile function domain of the IIEF, a validated 15-item self-administered questionnaire, that was translated

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Table 1. Baseline clinical, laboratory and angiographic characteristics of the study population

	Group 1		P value
	Syntax score ≤22, n=81	Syntax score >22, n=80	
Age (years)	65.2 (45-76)	66.8 (42-81)	0.005
BMI (kg/m ²)	25.7 (20.3-27.9)	25.7 (20.6-28.7)	0.961
Total Cholesterol (mg/dl)	202.2 (169.6-244.4)	213.9 (151.6-299.2)	0.056
LDL cholesterol (mg/dl)	133.7 (101.2-176.8)	146.4 (99.1-229.4)	0.010
HDL cholesterol (mg/dl)	37.2 (29.4-52.7)	36.69 (27.3-47.8)	0.095
TG (mg/dl)	156.2 (88.0-339.3)	154.1 (112.7-348.9)	0.079
DM (%)	43.2%	61.3%	0.022
HT (%)	48.1%	66.3%	0.020
Cigarette smoking (%)	55.6%	58.8%	0.682
Family history (%)	38.3%	26.3%	0.103
Semptom interval (months)	30.1 ± 4.8	40.5 ± 4.3	0.000
ED prevalence (%)	43.2%	61.3%	0.022
IIEF score	23.1 (15-29)	19.3 (6-29)	0.000

BMI: Body mass index, LDL: Low density lipoprotein, HDL: High density lipoprotein, TG: Triglyceride, DM: Diabetes mellitus, HT: Hypertension, ED: Erectile dysfunction, IIEF: International Index of Erectile Function.

Table 2. Effects of various variables on SYNTAX score□

Variables	Multivariate OR (95% CI)	p value
Age (years)	1.022 (0.970-1.077)	0.416
DM (%)	0.305 (0.084-1.101)	0.070
HT (%)	0.576 (0.169-1.970)	0.379
LDL cholesterol (mg/dl)	1.032 (1.009-1.055)	0.007
IIEF score	0.825 (0.733-0.928)	0.001

CI: confidence interval, OR: odds ratio, DM: Diabetes mellitus, HT: hypertension, LDL: low-density lipoprotein, IIEF: International Index of Erectile Function, □Multivariate logistic regression analysis. To identify the independent predictors of Syntax score, the parameters found to have statistical significance ($P < 0.05$) in the univariate analysis were chosen.

ed and validated in Turkish [20, 21]. The patients were classified based on their scores as follows: 26-30, no ED; 17-25 mild ED, 11-16 moderate ED, 0-10 severe ED. All included patients in the study were married. The patients with ED were asked whether or not the symptoms of ED were available before the symptoms of CAD. In case of the answer "yes", he was asked how long (months) before it started.

Statistical analysis

Continuous variables as mean + standard deviation and categorical variables as percent were shown. The One-Sample Kolmogorov-Smirnov test was used to evaluate whether the distribution of continuous variables was normal. Continuous variables between 2 groups were compared with Student t test or Mann-Whitney

U test. Categorical variables were compared appropriately with chi-square or Fisher exact test. To identify the independent predictors of Syntax score, the parameters found to have statistical significance ($P < 0.05$) in the univariate analysis were evaluated using multivariate logistic regression analysis. 95% confidence interval (CI) and odds ratios (OR) were presented together. In order to predict cutoff value of IIEF score, receiver operating characteristics (ROC) curve analysis was performed by MedCalc statistic software (version 13.2.0, Mariakerke, Belgium). Two-tailed P values < 0.05 were considered to indicate statistical significance. Data were analysed using SPSS version 17 (SPSS Inc., Chicago, IL, USA).

Results

161 patients with stable coronary artery disease, who underwent coronary angiography after the noninvasive tests, were included in the study. 81 patients with syntax score ≤22 as group 1 and 80 patients with syntax score >22 as group 2 were classified. Baseline clinical, laboratory and angiographic characteristics of the study population are shown in **Table 1**.

In terms of age, the average age of the patients in group 1 and group 2 was respectively 65.2 (45-76) and 66.8 (42-81). There was a statistically significant difference between both groups

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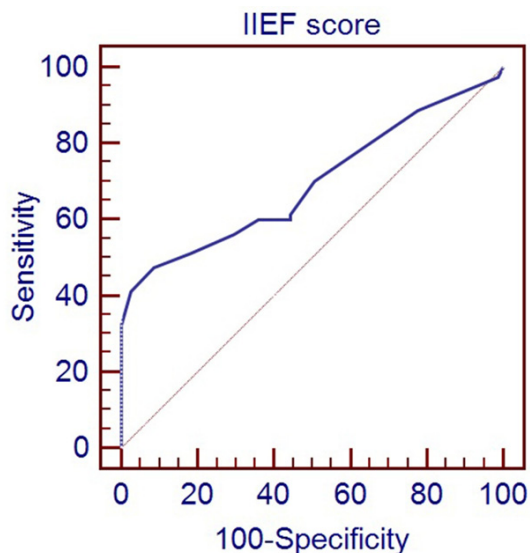


Figure 1. The receiver-operating characteristic (ROC) curve of international index of erectile function (IIEF) score for predicting the higher Syntax score.

($P=0.005$). In terms of BMI, the average of group 1 was 25.7 (20.3-27.9) and the average of group 2 was 25.7 (20.6-28.7), and there was no difference between the two groups ($P=0.961$).

For total cholesterol (TC); the average values of group 1 and group 2 were respectively, 202.2 mg/dl (169.6-244.4 mg/dl) and 213.9 mg/dl (151.6-299.2 mg/dl), and there was no significant difference between the two groups ($P=0.056$). Low density lipoprotein cholesterol (LDL-C) values were 133.7 mg/dl (101.20-176.8 mg/dl) and 146.4 mg/dl (99.1-229.4 mg/dl), respectively, and there was a significant difference between the two groups ($P=0.010$). High density lipoprotein cholesterol (HDL-C) values were 37.2 mg/dl (29.4-52.7 mg/dl) and 36.6 mg/dl (27.3-47.8 mg/dl) respectively, and there was no significant difference between the two groups ($P=0.095$). Triglyceride (TG) levels were 156.2 mg/dl (88.0-339.3 mg/dl) and 154.1 mg/dl (112.7-348.9 mg/dl) respectively, and there was no significant difference between the two groups ($P=0.079$).

DM prevalence of the patients in group 1 was 43.2%, and DM prevalence of the patients in group 2 was 61.3%. DM prevalence of the patients in group 2 was significantly higher ($P=0.022$). The prevalence of HT in group 1 and group 2 was respectively 48.1% and 66.3%,

and there was a statistically significant difference ($P=0.020$). The ratio of smoking was 55.6% in group 1 and 58.8% in group 2; there was no significant difference between the two groups ($P=0.682$). The family history of CAD was similar in both groups (respectively 38.3%, 26.3% $P=0.103$).

The prevalence of ED was 43.2% in group 1 and 61.3% in group 2. The prevalence of ED was significantly higher in the patients in group 2 ($P=0.022$). The mean IIEF score of the patients in group 1 was 23.1 (15-29), while it was 19.3 (6-29) in the patients in group 2, and there was a significant difference ($P=0.000$). The time interval between the symptoms of ED and CAD was 30.1 ± 4.8 months in group 1 and 40.5 ± 4.3 months in group 2. The interval of the symptoms in group 2 was found to be significantly longer ($P=0.000$).

In order to determine the independent predictors on Syntax score, multivariate logistic regression analysis was performed. It was found that LDL-C (odds ratio: in 1.032, 95% confidence interval: 1.009-1.055, $P=0.007$) and IIEF score (odds ratio: 0.825, 95% confidence interval: 0.733-0.928, $P=0.001$) were the independent predictors of syntax score (**Table 2**). The cutoff values of IIEF score for the higher Syntax score was 16 with a sensitivity of 47.5% and a specificity of 91.4% (AUC, 0.696; 95% CI, 0.619-0.766; $P<0.001$) (**Figure 1**; **Table 3**).

LDL-C level of the patients in the group with ED was 144.2 mg/dl (99.1-229.4 mg/dl) and the LDL-C level of the patients without ED was 131.3 mg/dl (101.2-203.7 mg/dl). LDL-C levels in the patients with ED were found to be significantly higher ($P=0.001$).

The prevalence of ED in the patients with and without HT was 56% and 44% respectively ($P=0.033$). The mean IIEF score was respectively 19.2 (6-29) and 23.8 (12-29) ($P=0.002$). The prevalence of ED was detected to be higher in the patients with HT, also IIEF score was found to be significantly lower.

The prevalence of ED in the patients with and without DM was respectively 59% and 39% ($P=0.000$). The mean IIEF score was respectively, 18.4 (6-29) and 23.6 (11-29) ($P=0.000$). The prevalence of ED was detected to be higher

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Table 3. Comparison ROC Curve for IIEF Score in Prediction of Higher Syntax Score

	AUC	95% CI	Sensitivity, %	Specificity, %
IIEF score (≤ 16)	0.696	0.619-0.766	47.5	91.4

ROC: receiver operating characteristic, AUC: area under curve, CI: confidence level, IIEF: international index of erectile function.

in the patients with DM, and IIEF was found to be significantly lower.

Discussion

In this study, we demonstrated that ED was common in the patients with coronary artery disease with high syntax scores, and the severity of ED was more evident. It was also detected that IIEF score was an independent predictor of the extent of CAD in the patients with stable coronary artery disease. Moreover, we found that the patients with long-term complaints of ED had more extent CAD.

Syntax scoring system is a current method used to determine the extent and severity of CAD on the basis of the coronary anatomic risk factors including lesion number, total occlusion, bifurcation, trifurcation, aorta-ostial stenosis, tortuosity, calcification, thrombosis and diffuse lesion. Each lesion over 50% in the vessels on a larger scale than 1.5 mm is graded and the sum of the scores of all lesions constitutes syntax score. When considered the studies investigating the relationship between the extent of CAD and the severity of ED, it is seen that our study is the first to use syntax score in order to evaluate the severity of CAD.

ED has a significant correlation with cardiovascular risk factors. These two groups with common risk factors also display similar characteristics such as impaired endothelial dysfunction. In this context, ED is more frequent in men with cardiovascular disease. One of the recommendations of Princeton III consensus is to make a noninvasive evaluation in terms of CAD in all the men with ED over 30 years with the cardiovascular risk, and to make an invasive evaluation if necessary. In a retrospective study of Chew et al including 1660 cases, the cardiovascular events following ED were investigated and it was found that the incidence of atherosclerotic cardiovascular disease was statistically significantly higher in the patients with ED. Chew et al detected that there was a correlation between ED and atherosclerotic cardiovas-

cular disease in all patients aged under 70 years. Consequently, they concluded that ED was a strong predictor for both atherosclerotic cardiovascular disease and the cardiovascular cases in the early aged patients with ED.

Type 2 DM and the certain risk factors are associated with the presence and severity of ED [22]. The incidence of ED adjusted by age is three times higher in the patients with DM than those without DM. Also, as is known, DM is an important risk factor for CAD. Gaccaruso et al found that the sensitivity of the risk factors for asymptomatic CAD in the diabetic patients increased from 62% to 89% with the addition of ED to the risk factors of CAD. This study showed that ED was a strong predictor of CAD in the diabetic patients. Similarly, the 10-year cardiovascular risk was found higher in the patients with ED. In this study, it was showed that the increasing severity of ED caused a significant increase in total cardiovascular risk in the diabetic patients. There are many studies demonstrating the relationship between hypertension and CAD. The presence of CAD displays a strong correlation with the systolic blood pressure and pulse pressure. HT is one of the factors in the etiology of ED. Also, HT increased the risk of ED 5.4 times. As to our study, it was detected that ED was more frequent and IIEF score was significantly lower in the patients with both diabetes and HT. Similarly, DM and HT were observed more frequently in the group with syntax score >22. Accordingly, CAD may have a more severe course in the patients with DM and/or HT, whose IIEF score was detected low.

Smoking is a major risk factor for CAD and cardiac events. Smoking has been definitively shown to harm especially the arterial endothelium. Therefore, smoking may be considered to be a risk factor that causes sexual dysfunction. In a study, it was found that smoking increased the risk of ED 3.1 times [23]. In our study, smoking was found similar between both groups. There is a need for more extensive researches to assess in detail the effects of smoking on the severity of CAD and ED.

There is a strong, independent, persisting and grade relationship between TC or LDL-C levels and CAD cases. Generally, each 1% increase in LDL-C levels brings a 2-3% increase in CAD risk.

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In addition, it was demonstrated that low level of HDL-C was an independent risk factor for cardiovascular disease in the epidemiological studies. Hyperlipidemia is an important risk factor for ED. It was also showed that 42% of the patients with ED had only hyperlipidemia before the systemic diseases arose [24]. Oxidized LDL was detected to inhibit the vascular smooth muscle relaxation through endothelial cells [25]. At the same time, high LDL-C levels may also affect the severity of the ED [26]. In our study, LDL-C levels were found significantly high in the patients with high syntax score and stable coronary artery disease. HDL-C and TG levels were similar in both groups. Also, LDL-C level was found to be an independent predictor of high Syntax score. When the LDL-C levels of the patients with or without ED were examined, it was observed that LDL-C levels were significantly high in the patients with ED. The necessary lifestyle changes for hyperlipidemia should be recommended to the patients with ED before the emergence of the symptoms of CAD.

The prevalence of ED can vary in CAD subgroups. In a study performed by Shankar et al., when the patients with acute coronary syndrome were compared with those with stable coronary artery disease and single-vessel disease, it was detected that the prevalence of ED was significantly high in the second group [27]. In our study, the prevalence of ED was found significantly more common in the group with syntax score >22, also IIEF score was observed significantly lower in this group. In addition, in the multivariate logistic regression analysis, IIEF score was found to be an independent predictor of the extent of CAD. This situation supports the fact that CAD may be more extent as the severity of ED increases. This also shows that the increased atherosclerotic plaque burden in the patients with stable coronary artery disease is systemic and may be associated with endothelial dysfunction. Also, when the fact that the patients with severe ED and stable coronary artery may have high Syntax score is taken into account; it should be considered that during the coronary angiography to be applied to this patient group, the results such as complex coronary intervention or coronary artery bypass surgery may be encountered. For this purpose, before the coronary angiography, the patient may be informed and certain measures can be taken against the possible complications during the treatment.

It is estimated that the time between the onset of symptoms of ED and the onset of CAD symptoms is about 2-3 years, and the development time of CAD is 3-5 years. In our study, it was found that the time between the onset of symptoms of ED and CAD was significantly long in the second group. The presence of ED symptoms during this period provides clinicians to make an early diagnosis of CAD and reduce the risk factors of CAD. In addition, myocardial ischemia may be detected by noninvasive tests in the patients with ED, and CAD may be diagnosed at an early stage before it progresses. If any evidence for CAD is determined after the noninvasive tests, the clinicians may have a prediction about the extent of CAD by using IIEF questionnaires.

According to the main findings and conclusions of this study, all male patients with ED should undergo a routine medical evaluation including testosterone, fasting glucose, lipid levels, blood pressure measurement smoking. After the medical evaluation, the patients should be classified according to the risk of the future cardiovascular events. The high-risk patients should be assessed by noninvasive tests and, if necessary, undergo diagnostic coronary angiography. In order to improve the cardiovascular risk factors, the patients in the risk groups should be recommended to make changes in their lifestyles such as giving up smoking, making regular physical activity and losing weight. If the men with ED have DM, HT and hyperlipidemia, they should receive aggressive treatment taking into consideration the potential adverse effects. The cardiovascular state and the changes in ED should be followed regularly.

Study limitations

The most important limitation of our study was the small number of patients included in the study. When evaluating the cardiovascular risk factors such as DM, HT and hyperlipidemia, the patients were not questioned how long they owned these. Still, when questioning smoking, the amount and the duration of smoking were not asked.

Conclusions

In the current study, the prevalence of ED was seen more frequently in the group with high syntax score. The severity of ED was clearer in the group with high syntax score. IIEF question-

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naire may help to predict the extent of CAD in the patients with ED accompanying stable coronary artery disease. ED symptoms occur long before the symptoms of CAD, and CAD is more common in the patients with long-term complaints of ED.

Disclosure of conflict of interest

None.

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