ERECTILE DYSFUNCTION

The Relationship Between Gensini Score and Erectile Dysfunction in Patients with Chronic Coronary Syndrome

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ABSTRACT

Introduction: In previous studies, the relationship between atherosclerosis and erectile dysfunction (ED) was examined, but the relationship and correlation between Gensini score which evaluates the extent and severity of chronic coronary syndrome (CCS), and ED severity were not investigated.

Aim: To evaluate the relationship between Gensini score and ED in patients with CCS.

Methods: We included 142 consecutive male patients with the diagnosed CCS and underwent an elective coronary angiography between January 2019 and March 2020.

Main Outcome Measure: Correlation analysis demonstrated that Gensini score significantly negatively correlated with the International Index Erectile Function - 5 (IIEF-5) score (r = -0.417, P < .001).

Results: Severe ED was present in 48 (33.8%) patients, moderate ED in 31 (21.8%) patients, and mild ED in 22 (15.5%) patients. 41(28.9%) patients did not have ED. Both the No ED and Mild ED groups were statistically significantly lower than the Severe ED group in terms of the Gensini score (P < .05). When the recommended optimal cut-off point and accuracy measurements were made for the Gensini score, the area under curve (AUC) value in predicting ED was 0.806 (95% CI: 0.732-0.880, P < .001). Multivariate logistic regression analysis demonstrated that independent predictors for ED were Gensini score and age (P < .001, and P = .026, respectively). Every 1 unit increase in Gensini score resulted in a 6% increase in the occurrence of ED (OR = 1.06, CI:1.03-1.10, P < .001).

Conclusion: ED can be caused by endothelial dysfunction. Patients with severe CSS and high Gensini score should be evaluted for ED. ED may be a sign of severe CCS and a high Gensini score. It is also necessary to evaluate cardiological in patients with ED. **Deger M, Ozmen C, Akdogan N, et al. The Relationship Between Gensini Score and Erectile Dysfunction in Patients with Chronic Coronary Syndrome. Sex Med 2021;9:100376.**

Key Words: Erectile Dysfunction; Chronic Coronary Syndrome; Gensini Score; Iief-5

INTRODUCTION

Erectile dysfunction (ED) is defined as the consistent inability to achieve or maintain a penile erection sufficient for successful vaginal intercourse.[1] The occurrence of ED can deteriorate the psychosocial health of men. Also, ED can negatively affect the quality of life of male and their partners.

The diagnosis and severity of ED can be done with the International Index Erectile Function - 5 (IIEF-5) questionnaire. According to IIEF-5, the severity of ED is divided into four groups as mild, mild-moderate, moderate, and severe.[2] Depending on its etiological causes, ED can be classified as psychogenic, organic, or mixed psychogenic.[3]

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Organic ED can be one of the systemic signs of atherosclerosis and endothelial dysfunction. Coronary artery disease (CAD), classified as a chronic coronary syndrome (CCS), is a process that results from the accumulation of atherosclerotic plaques in epicardial arteries, regardless of whether they are obstructive.[4] The extent and severity of CAD can be evaluated with Gensini score that is a widely used means of quantifying angiographic atherosclerosis.[5]

In order for an erection to occur, the endothelial function must be intact because it is now known that one of the etiologies of ED is a vascular disorder. In addition, the prevalence of ED increases in vascular diseases such as CAD, cerebrovascular disease, hypertension and diabetes.[6] The pathophysiological mechanism such as endothelial dysfunction and atherosclerosis and risk factors of ED such as high blood pressure, diabetes, obesity, metabolic syndrome and smoking are quite similar to those of CAD.[7-10]

ED and CAD are both closely related as endothelial dysfunction occurs as a result.[11] The incidence of ED was also higher in men with CAD.[12] Also, men with ED often have more severe CCS than those who do not.[13] In previous studies, the relationship between atherosclerosis and ED was studied, they revealed a significant relationship between them. We hypothesized that as the Gensini score, which determines the scope and severity of CAD, increases, the severity of ED will increase. The relationship and correlation between Gensini score and IIEF-5 were evaluated for the first time in this study.[13-15] We aimed to evaluate the relationship between Gensini score and ED and also to reveal the relationship between the Gensini score and the severity of ED.

MATERIALS AND METHODS

We included 142 consecutive male patients with the diagnosed CCS and underwent an elective coronary angiography with or without percutaneous coronary intervention between January 2019 and March 2020. Patients diagnosed with acute coronary syndrome (ACS), an ejection fraction (EF) below 30 on echocardiography, chronic kidney disease, liver dysfunction, and neurogenic, psychiatric, endocrine diseases such as hypogonadism, hyperprolactinemia or urological patients who could affect erection quality were excluded from the study. However, patients with diabetes mellitus were included in the study. Also, patients having no regular sexual activity were also excluded from the study. Detailed informed consent was obtained from all patients included in the study.

Echocardiographic examination was performed using the Vivid S5 cardiovascular ultrasound system with a 3S 1.5 to 3.6 MHz transthoracic probe (GE Medical Systems, Buckinghamshire, UK). LVEF was measured using the Simpson's biplane method.

The Gensini score was evaluated to determine angiographic severity. Each lesion was assigned a score according to the percentage of stenosis-1 for 25% stenosis, 2 for 50%, 4 for 75%, 8 for 90%, 16 for 99% and 32 for total occlusion. Multiplied by the coefficient defined for each major coronary artery and each segment (5 points for left main coronary lesion, 2.5 points for proximal left anterior descending branch and left circumflex artery; 1.5 points for middle left descending artery lesion; 1 point for first diagonal branch and obtuse marginal branches and right coronary artery; 0.5 points for the second diagonal and posterolateral branch of the left circumflex artery) and the Gensini score of each patient group was obtained by summing up the results.[16]

A urologist questioned the sexual history of the patients and performed genitourinary physical examination. The erectile function of patients was determined according to the five-item version of IIEF-5 and the participants were divided into four groups as follows: and 0 to 10 points: severe ED, 11 to 16 points: moderate ED, 17 to 25: mild ED, and 26 to 30 points: none ED.[17]

Demographic was recorded from all participants, including age, medical history, body mass index (BMI), hypertension (HT), diabetes mellitus and smoking status. For the laboratory tests, total testosterone, prostate specific antigen (PSA), triglyceride, low-density and high-density lipoprotein cholesterol (LDL-C and HDL-C), and HbA1c levels were recorded. The drugs used by the patients were recorded.

In accordance with the Declaration of Helsinki, the study protocol was approved by the Regional Ethics Committee (IRB No. 100-31-2020).

Statistical Analysis

All analyses were performed using IBM SPSS Statistics Version 20.0 statistical software package (IBM Corp. Released 2011. IBM SPSS Statistics for Windows, Version 20.0.Armonk, NY: IBM Corp.) Categorical variables were expressed as numbers and percentages, whereas continuous variables were summarized as mean and standard deviation and as median and minimum-maximum where appropriate. Chi-square test was used to compare categorical variables between the ED groups. Kolmogorov-Smirnov test was used to assess the normality of the distribution of continuous variables. For non-normal distributed variables, Kruskal Wallis test was used to compare more than two ED groups. Bonferroni adjusted Mann Whitney *U* test was used for multiple comparisons of ED groups. To evaluate the correlation between Gensini and IIEF-5 score, Pearson Correlation Coefficient was used. Logistic regression analysis was performed to determine significant predictors of ED. A receiver operator characteristic (ROC) curve analysis was performed in order to identify the optimal cutoff point of Gensini and IU method was used to determine the optimal cut-off point. The statistical level of significance for all tests was considered to be 0.05.

RESULTS

One hundred and forty-two patients with CCS were included in the study. The mean age of patients was 62.2 ± 10.2 years (median, 62 years). The mean EF of patients was 57.1 ± 9.6%. Severe ED was present in 48 (33.8%) patients, moderate ED in 31 (21.8%) patients, and mild ED in 22 (15.5%) patients. 41 (28.9%) patients did not have ED. Descriptive statistics for

Table 1. Demographic and characteristics of the study population

	No-ED (n = 41)	Mild ED (n = 22)	Moderate ED (n = 31)	Severe ED (n = 48)	*P* Value
Gensini Score*	27.1 ± 10.6 26.0(8.0 - 75.0)	37.5 ± 22.6 36.5(6.0 - 92.0)	42.5 ± 18.6 41.0(6.0 - 89.0)	52.2 ± 27.3 45.0(23.0 - 168.0)	< .001
Age year*	57.0 ± 11.8 57.0(34.0 - 84.0)	61.9 ± 7.2 62.5(45.0 - 78.0)	61.1 ± 8.8 61.0(43.0 - 80.0)	67.6 ± 8.3 67.0(50.0 - 89.0)	< .001
EF†	59.2 ± 8.4 60.0(35.0 - 68.0)	56.5 ± 10.0 60.0(38.0 - 66.0)	58.0 ± 8.2 60.0(40.0 - 68.0)	55.0 ± 11.1 60.0(28.0 - 66.0)	.287
BMI kg/m^2*	26.7 ± 3.6 26.0(21.7 - 38.5)	61.1 ± 8.8 27.1(20.0 - 35.8)	27.1 ± 3.3 26.5(22.8 - 36.3)	27.2 ± 3.9 26.6(16.9 - 39.8)	.673
HT†	30(73.2)	14(63.6)	24(77.4)	36(75.0)	0.708
DM†	16(39.0)	8(36.4)	13(41.9)	19(39.6)	0.982
Smoking†	26(63.4)	11(50.0)	13(41.9)	18(37.5)	0.013
Dyslipidemia†	32(78.0)	14(63.6)	19(61.3)	34(70.8)	0.423
History of bypass†	2(4.9)	1(4.5)	2(6.5)	7(14.6)	0.308

*Data are expressed as mean ± standard deviation and median(min-max).
†Data are expressed as n(%).
BMI = body mass index; DM = diabetes mellitus; EF = ejection fraction; HT = hypertension.
Bold values indicate statistical significance (P < .05).

Table 2. Baseline laboratory results of the patients

	No-ED (n = 41)	Mild ED (n = 22)	Moderate ED (n = 31)	Severe ED (n = 48)	*P* Value
TT ng/ml	4.7 ± 1.6	4.9 ± 1.8	5.1 + 1.4	4.7 ± 1.8	.453
PSA ng/ml	0.7 ± 0.5	3.2 ± 6.3	2.3 ± 2.8	1.1 ± 0.9	.276
HbA1c %	6.7 ± 1.5	7.0 ± 2.1	6.9 ± 1.3	6.9 ± 1.6	.908
Total-C	185.3 ± 68.9	169.6 ± 48.5	179.4 ± 49.6	168.7 ± 42.8	.557
HDL-C	42.3 ± 9.3	39.9 ± 9.5	39.1 ± 8.0	39.7 ± 9.5	.331
LDL-C	108.8 ± 52.8	101.8 ± 41.7	104.7 ± 37.8	101.1 ± 36.7	.972
TG	156.8 ± 104.4	167.4 ± 203.2	170.6 ± 99.1	152.1 ± 111.7	.341

HDL-C = High density Lipoprotein Cholesterol; LDL-C = Low density Lipoprotein Cholesterol; PSA = Prostate Specific Antigen (PSA); TG = Triglycerides; Total-C = Total Cholesterol; TT = Total testosterone
Data are expressed as mean ± standard deviation and median(min-max) and bold values indicate statistical significance ($P < .05$).

demographic and patients characteristics are given in Table 1. The median age of the severe ED group was significantly higher than the No ED and Moderate ED groups ($P < .05$). Both the No ED and Mild ED groups were statistically significantly lower than the Severe ED group in terms of the Gensini score median ($P < .05$). Additionally, BMI, HT, DM, dyslipidemia, history of bypass and laboratory results distribution were similar among the ED groups ($P > .05$) (Table 1-2). As shown in Figure 1, correlation analysis demonstrated that Gensini score significantly negative correlated with IEFF 5 score ($r = -0.417$, $P < .001$).

The optimal cut-off point and accuracy measurements proposed for Gensini score are given in Figure 2. The AUC value in predicting ED was 0.806 (95% CI: 0.732-0.880, $P < .001$) and the optimal cut-off point for Gensini score was obtained as 31.0 with 75.0% sensitivity and 73.0% specificity.

Multivariate logistic regression analysis demonstrated that independent predictors for ED were Gensini score and age ($P < .001$ and $P = .026$, respectively). Every 1 unit increase in Gensini score resulted in a 6% increase in the occurrence of ED (OR = 1.06, CI:1.03-1.10, $P < .001$) (Table 3).

Medications used by patients are given in Table 4. Erectile dysfunction was less common in those using clopidegrol and ticagrelor ($P = .012$ and $P \leq .001$, respectively).

DISCUSSION

In the present study, we evaluated the relationship between Gensini score and ED. Our study revealed that the incidence of ED is quite high in men with CCS. We found that Gensini score and age were independent predictors for ED by multivariate logistic regression analysis. We found Gensini score significantly negatively correlated with the IIEF-5 score. Our study gave concrete findings to the relationship between ED and CCS with angiographic evidence. We think that it can provide information about possible ED severity, Gensini score, and atherosclerosis severity in CCA patients.

To explain the relationship between CAD and erectile dysfunction, Montorsi et al. reported a pathophysiological mechanism called "artery size hypothesis" based on the fact that atherosclerosis, theoretically affects all large vascular beds simultaneously and equally.[18] According to this theory, first of all, due

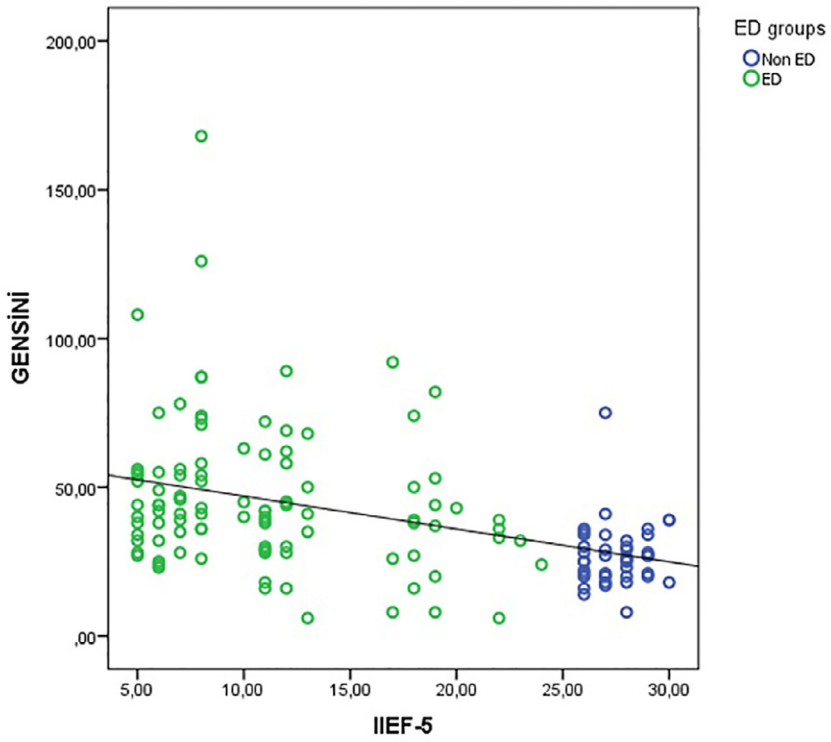

Figure 1. Correlation between Gensini's score and IIEF-5 in study population (r = -0.417, P < .001).

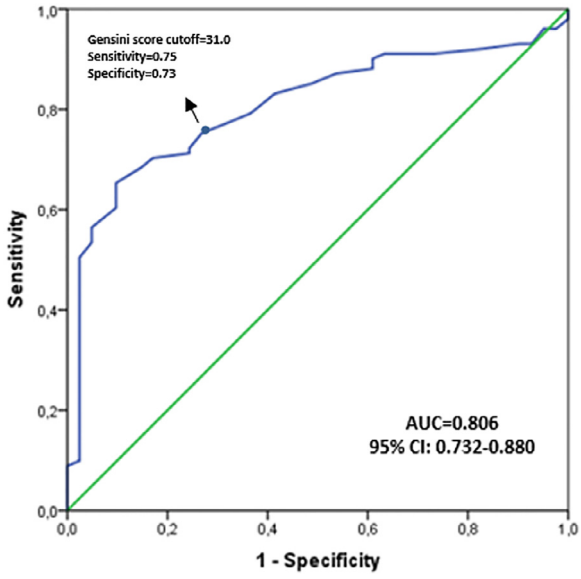

Figure 2. Receiver-operating characteristic (ROC) curve analysis of Gensini's score predicts ED.

Table 3. Multivariate logistic regression analysis for the prediction of ED

	Odds Ratio (95% CI)	*P* Value
Gensini score	1.06(1.03 - 1.10)	< .001
Age year	1.05(1.00 - 1.10)	.026
BMI	0.99(0.88 - 1.12)	.963
HT	0.85(0.33 - 2.22)	.744
DM	0.85(0.35 - 2.08)	.733
Smoking	0.67(0.27 - 1.65)	.386
Dyslipidemia	0.55(0.21 - 1.48)	.242

BMI = body mass index; DM = diabetes mellitus; HT = hypertension.
Bold values indicate statistical significance (P < .05), Nagelkerke R^2 = 0.356

to vascular size differences, due to small vessels, erectile dysfunction symptoms first develop, then anginal symptoms, and then "cerebral" and "peripheral" symptoms. This theory suggests that erectile dysfunction may be one of the first signs of serious coronary artery disease. The present study showed that when the severity of erectile dysfunction increased, the Gensini score indicating the severity of CAD also increased.

In the COBRA study involving 285 male patients, Montorsi et al found that ED rate significantly differs across patients with established CAD according to coronary clinical presentation and atherosclerosis burden. They showed that ED symptoms occur in almost all cases before CAD symptoms in practically all patients with a mean time interval of 3 years. They concluded that ED prevalence is related to coronary clinical presentation and the extent of CAD.[19] In the study involving 240 male patients, Shanker et al. reported that ED prevalence was 76% and the prevalence of ED increases as the degree of coronary

Table 4. Medications used by patients

	No-ED (n = 41)	Mild ED (n = 22)	Moderate ED (n = 31)	Severe ED (n = 48)	*P* Value
Aspirin	32(78.0)	19(86.4)	28(90.3)	41(85.4)	.314
Clopidegrol	17(41.5)	15(68.2)	21(67.7)	33(68.8)	.012
Ticagrelor	18(43.9)	2(9.1)	2(6.5)	2(4.2)	< .001
Calcium channel bloker	19(46.3)	7(31.8)	16(51.6)	22(45.8)	.758
Statin	32(78.0)	14(63.6)	19(61.3)	34(70.8)	.460
Aldosterone	4(9.8)	1(4.5)	2(6.5)	1(2.1)	.150
ACEI/ARB	28(68.3)	14(63.6)	19(61.3)	26(54.2)	.173
Betabloker	33(80.5)	15(68.2)	23(74.3)	29(60.4)	.060

Data are expressed as n (%)
Bold values indicate statistical significance ($P < .05$).

vascular involvement increases and they found that there was a significant relationship between the length of the time interval between ED and CAD onset and the number of vessels involved.[20] Hamur et al. divided patients who underwent coronary angiography into two groups according to CAD severity using the SYNTAX score. They reported that the ED prevalence was significantly higher in patient with high the SYNTAX scores. They concluded that the severity of ED is an independent factor that predicts the extent of CAD. Early detection of ED enables cardiovascular assessment.[21]

The Gensini scores include an analysis of both the percentage of stenosis and the morphology of the coronary arteries associated with long-term cardiovascular outcomes.[16] Previous studies have used the Gensini score as a sub-parameter, but for the first time, our study evaluated the relationship between Gensini score and ED severity.[13-15] In the study involving 85 patients with ACS, Al-Daydamony et al comparing patients with IIEF score ≥ 17 (mild or no ED) and patients with IIEF score < 17 (moderate or severe ED), they found patients with moderate or severe ED had significantly higher mean Gensini score. They concluded that the angiographic severity of CAD was found to be more in patients with moderate or severe ED.[14] In conrast, in a study on male patients with type II diabetes and CAD, Gazzaruso et al. reported that ED was significantly more prevalent in type II diabetic males with CAD, however, they did not find a significant relationship between ED severity and CAD severity, and between IIEF-5 score and Gensini score.[15]

In studies, the gensini score was affected by the weight and metabolic status of the patients. and also studies have shown that in people who participate in regular physical exercise and a low-fat diet, coronary artery disease progresses at a slower pace compared to people who receive normal care.[22-23] Situations such as ed and physical exercise reflect the hemodynamic status of the patients, and the gensini score is considered the indicator of these situations

Age, which is one of the risk factors of ED, was found to the independent predictor for ED in our study's multivariate logistic regression analysis. In the study, which included 1,517 Japanese men between the ages of 23 to 79, it was reported that there was a significant correlation between age and erectile function.[24] In a population-based study investigating the relationship between ED and CAD, they reported that the prevalence of ed increases with age. They found that increased incidence of CAD disease in patients with ED compared to the patients without ED. They showed that the relationship between Ed and CAD increases with age.[25]

Post hoc power analysis was conducted to determine whether the study had adequate power or not. Considering the significance level (0.05), the observed effect size of Gensini score (2.25), and the sample size, the post hoc power calculated in the Gpower program is 0.99. In this case, it was concluded that the study had a 99% probability of detecting the observed difference.

Our study has some limitations. The first limitation is the lack of a measure for arterial insufficiency such as doppler. The small size of the sample was among the other limitations of the study. Lack of mention of other sexual dysfunctions reported by patients such as reduced sex drive and premature ejaculation, which are additional risk factors for ED, is one of the limitations of the study.

CONCLUSIONS

ED can be caused by endothelial dysfunction. Patients with severe CSS and high Gensini score should be evaluted for ED. ED may be a sign of severe CCS and a high Gensini score. It is also necessary to evaluate cardiological in patients with ED. Also, while evaluating CCS in male patients, erectile dysfunction should also be questioned because it can give a prediction about the severity of CCS. We suggest a prospective longitudinal study, using Gensini Score as a predictor of incident ED.

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Ethics: This retrospective study was conducted in accordance with the Declaration of Helsinki. Our study was approved by the local ethics committee issued by the University of Cukurova, number 100/31. All patients enrolled in the study signed written informed consent.

STATEMENT OF AUTHORSHIP

Mutlu Deger: Conceptualization, Methodology, Software, Validation, Formal Analysis, Investigation, Resources, Data Curation, Writing – Original Draft, Writing – Review & Editing, Visualization, Supervision, Project Administration, Funding Acquisition. Caglar Ozmen: Nebil Akdogan: Omer Tepe: Sevinc Puren Yucel: Volkan Izol:

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