

EVALUATION OF DIABETES AND SMOKING AS PREDICTORS OF SEVERE CORONARY ARTERY DISEASE BASED ON GENDER INEQUALITY

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ABSTRACT

Aim: This research aims to assess the severity of coronary artery disease in patients admitted with chest pain to the emergency department and focus on how risk factors vary with gender.

Methods: This is a cross-sectional study of 247 patients with a pre-diagnosis of acute coronary syndrome between August 2020 and February 2021. The severity of coronary artery disease in all patients was evaluated with the Gensini score. Independent risk factors that were found to be related to severe coronary artery patients were analyzed by logistic regression.

Results: The risk of severe coronary artery disease of the 247 individuals included in the study was increased by 5% ($p < 0.005$) with each year of rising age, the presence of diabetes was increased by 2.51 (95% CI 1.38- 5.57) fold, and the presence of cigarette consumption increased by 2.79 (95% CI 1.51-5.13) fold. In comparison, each year of age rise in women increased the risk of severe coronary artery disease by 6% ($p < 0.005$), the presence of diabetes was prominently (5.32-fold; 95% CI 2.10-13.47) as a risk factor. In men, the prominent risk factor was cigarette consumption (4.51-fold; 95% CI 2.03-10.02).

Conclusion: Studies that attach importance to the necessity of questioning the risks in serious coronary artery diseases based on gender and accepting the possibility that these risks may turn into reverse inequalities in countries with different development levels will shed light on clinical practices and preventive medicine.

Keywords: Gensini, coronary artery disease, cardiac prevention, gender, reverses inequalities.

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Introduction

Coronary artery disease (CAD) is the major cause of death, with almost 20 million deaths per year⁽¹⁾. Diabetes mellitus, hypertension, smoking, and psychosocial stress stand out as traditional risk factors for CAD in the context of lifestyle, environmental, and genetic factors⁽²⁾.

According to cohort studies, cardiovascular diseases such as ULSAM, PIVUS, POEM, PREDICT are divided into two categories: non-modifiable and modifiable. A CAD patient's age, ethnicity, and family background are non-modifiable risk factors. In contrast, hypertension (HT), hyperlipidemia,

diabetes mellitus (DM), obesity, smoking, unhealthy diet, sedentary lifestyle, and stress are modifiable risk factors^(3,4).

The impact of managing modifiable risk factors on cardiovascular disease has been the subject of many cohorts, including the Framingham Heart Study. As seen in North Karelia, lifestyle changes have been shown to reduce the risk of CAD⁽⁵⁾. Lifestyle changes such as healthy nutrition, adequate physical activity, smoking cessation, and treatments that regulate cholesterol and blood pressure levels are important factors in reducing the risk of disease⁽⁶⁾.

The study, which sought to forecast heart disease deaths from 1969 to 2020, found that men's deaths

would drop by 21.3 percent and women's deaths would drop by 13.4 percent⁽⁷⁾. Evidence shows that significant gender differences in both symptoms and progression of the disease, and the risk management of CAD, which is also an important cause of death in women, are overlooked⁽⁸⁾. This study looks at gender differences in coronary artery disease risk factors in a developing country. It aims to determine the severity of CAD in patients admitted to the emergency department due to chest pain, determine the risk factors, and examine the differences of these risk factors based on gender.

Method

This is a cross-sectional study of 247 patients admitted to a hospital emergency department with a pre-diagnosis of acute coronary syndrome without ST elevation. Those under 18 years of age with a history of coronary artery bypass surgery were excluded⁽⁹⁾. The data were collected from cardiologists who worked in the emergency department between August 2020 and February 2021 through a questionnaire. A 21-item form questioning the patient's characteristics, habits, diseases, and laboratory details was filled using hospital records.

Coronary angiography and CAD severity

The severity of CAD in all patients who underwent emergency coronary angiography was evaluated with the Gensini score. Scoring was done by the researchers. The lumen narrowing is graded by Gensini, which is used in scoring. It is accepted as; stenosis ranging from 1% to 25% 2 points, 51 percent - 75 percent stenosis 4 points, 76 percent - 90 percent stenosis 8 points, 91 percent - 99 percent stenosis 16 points, and 100% stenosis 32 points. Each lesion score is compounded by a metric that takes into account the importance of the lesion's position in the coronary circulation. Finally, the Gensini score was determined by combining the scores of each coronary section⁽¹⁰⁾. Patients with a Gensini score of 20 or higher were deemed to have severe CAD⁽¹¹⁾.

Personal characteristics, medical history, and laboratory measurements

Gender, age, and family history of diagnosed CAD patients were questioned. Those who smoked at least one cigarette a day in the last six months were classified as smokers, and those who consumed at least one unit of alcohol a week were classified as alcoholics. Patients with a systolic pressure of more

than 140 mmHg or a diastolic pressure of more than 90 mmHg or those receiving antihypertensive therapy were classified as hypertensive⁽¹²⁾. Those with a previous or recent diagnosis of DM were classified as DM Patients with a systolic pressure of more than 140 mmHg or a diastolic pressure of more than 90 mmHg according to American Diabetes Association guidelines⁽¹³⁾. Biochemistry and lipid profile results studied in blood were recorded on the form. Non-specific ST-T wave changes and ST-segment depression detected in the electrocardiogram (ECG) were evaluated and recorded.

Analysis

All statistical analyses were carried out using the SPSS 23.0 software. Descriptive data of the study group are presented as a percentage or mean (mean) \pm standard deviation (sd). Student's t-tests were used to compare the means of continuous variables, and Chi-square was used to compare frequencies of categorical variables. In this comparison, independent risk factors whose relationships with severe CAD patients were re-analyzed using logistic regression, and multivariable regression analysis was performed across both whole and gender groups. Each prediction score was calculated based on the OR of the independent variables. The significance level was used as $p < 0.05$ in the analyses.

Ethics Statement

The study received ethical approval from the Ethics Committee of the Tinaztepe University (with decision number 12.002, dated March.10.2021). The study was explained to each participant, and their consent was obtained.

Results

The average Gensini score of 247 participants in the study was found to be 36.34 ± 32.37 . Participants, 39.27% of whom were women, had an average age of 59.83 ± 12.52 . 48.18% of the participants used to smoke. 90.28% were diagnosed with HT, 45.37% were diagnosed with DM, and 21.15% had a CAD history in the family (Table 1).

According to the Gensini score, 160 (64.78 percent) of the patients in the study group ($n = 247$) had Severe CAD (≥ 20). The mean Gensini scores were 53.22 ± 28.169 and 5.29 ± 5.023 in Severe CAD and non-severe CAD groups, respectively. Patients with Severe CAD were found in the older age group compared with Non-Severe CAD patients

(61.69 ± 12.10 versus 56.43 ± 12.63, p = 0.01). A significant relationship was found between smoking, diabetes, and severe CAD (p > 0.05). Distribution characteristics of patients with or without severe CAD are shown in Table 2.

FEATURES n	Total		Male		Female		p	
	%	n	%	n	%	n		
Gensini	Non-severe	87	35.22%	40	41.24%	47	31.33%	0.112
	Severe	160	64.78%	57	58.76%	103	68.67%	
BMI (%)	< 30	149	60.32%	50	51.55%	99	66.00%	0.023
	≥ 30	98	39.68%	47	48.45%	51	34.00%	
Smoking (%)	Yes	119	48.18%	36	37.11%	83	55.33%	0.005
	No	128	51.82%	61	62.89%	67	44.67%	
Alcohol (%)	Yes	30	12.15%	3	3.09%	27	18.00%	<0.001
	No	217	87.85%	94	96.91%	123	82.00%	
CAD in the family (%)	There is	52	21.15%	20	20.62%	32	21.33%	0.893
	No	195	78.95%	77	79.38%	118	78.67%	
DM (%)	There is	112	45.37%	55	56.70%	57	38.00%	0.004
	No	135	54.66%	42	43.30%	93	62.00%	
Insulin (%)	There is	44	17.81%	22	22.68%	22	14.67%	0.108
	No	203	82.19%	75	77.32%	128	85.33%	
HT (%)	There is	223	90.28%	88	90.72%	135	90.00%	0.852
	No	24	9.72%	9	9.28%	15	10.00%	
ECG (%)	NSR	93	37.65%	27	27.84%	66	44.00%	0.011
	Non-specific ST	72	29.15%	28	28.87%	44	29.33%	
	Prominent ST depression	82	33.20%	42	43.30%	40	26.67%	
The column percentage is included in the table. Data are presented as number (percentage).								
		Mean	Sd	Mean	Sd	Mean	Sd	p
Gensini Skor (n=247)		36.34	32.373	34.27	33.64	37.67	31.56	0.421
Age (n=247)	Year	59.83	12.515	63.71	12.16	57.33	12.53	<0.001
Total cholesterol (n=237)	mmol/L	202.43	52.523	206.65	51.75	199.61	53.03	0.312
HDL (n=237)	mmol/L	41.32	9.795	43.58	10.61	39.80	8.93	0.005

Table 1: Distribution of the participants in the whole group and by gender. Data are presented as mean (standard deviation). Abbreviations: BMI, body mass index; DM, diabetes mellitus; HT, hypertension; ECG, electrocardiogram; HDL, high density lipoprotein; others, see Table 1

Defining Severe CAD Determinants with Multivariate Logistic Regression

In a single analysis, gender, age, presence of diabetes, and smoking were found to be significantly associated with severe CAD, and each year of age rise increased the risk of severe CAD by 5% (p < 0.005) in the evaluation made by multivariate logistic regression, 2.24 (95) in the male group compared to women. It was observed that the presence of diabetes increased CAD 2.51 (95% CI 1.38-5.57) times, and the presence of smoking increased CAD 2.79 (95% CI 1.51-5.13) fold (Table 3).

When we evaluated the variables under the title of gender, each year of age rise in women increased the risk of severe CAD by 6% (p < 0.005),

the relationship between cigarette consumption and severe CAD lost its significance, but the presence of diabetes was significantly (5.32 fold; 95% CI 2.10-13.47) has emerged as a risk factor. In men, the prominent risk factor was cigarette consumption (4.51 fold; 95% CI 2.03-10.02), the presence of diabetes lost its significant relationship. Each year of age rise was found responsible for a 5% increase in risk (p < 0.005) (Table 3).

FEATURES	Non-severe CAD		Severe CAD		p	
	n	%	n	%		
Gender (%)	Female	40	41.24%	57	58.76%	0.112
	Male	47	31.33%	103	68.67%	
BMI (%)	< 30	53	35.57%	96	64.43%	0.888
	≥ 30	34	34.69%	64	65.31%	
Smoking (%)	Yes	33	27.73%	86	72.27%	0.017
	No	54	42.19%	74	57.81%	
Alcohol (%)	Yes	13	43.33%	17	56.67%	0.321
	No	74	34.10%	143	65.90%	
CAD in the family (%)	There is	22	42.31%	30	57.69%	0.229
	No	65	33.33%	130	66.67%	
DM (%)	There is	30	26.78%	82	73.21%	0.011
	No	57	42.22%	78	57.78%	
Insulin (%)	There is	12	27.28%	32	72.72%	0.223
	No	75	36.95%	128	63.05%	
HT (%)	There is	75	33.63%	148	66.37%	0.111
	No	12	50.00%	12	50.00%	
ECG (%)	NSR	34	36.56%	59	63.44%	0.607
	Non-specific ST	22	30.56%	50	69.44%	
	Prominent ST depression	31	37.80%	51	62.20%	
		Mean	Sd	Mean	Sd	p
Gensini Skor (n=247)		5.29	5.023	53.22	28.169	
Age (n=247)	Year	56.43	12.625	61.69	12.095	0.001
Total cholesterol (n=237)	mmol/L	197.49	49.393	204.95	54.028	0.302
HDL (n=237)	mmol/L	41.45	9.866	41.25	9.789	0.881

Table 2: Distribution of the participants in the whole group and by gender. Data are presented as number (percentage), mean (standard deviation). Abbreviations: BMI, Body Mass Index; DM, Diabetes Mellitus; HT, hypertension; ECG, electrocardiogram; HDL, High Density Lipoprotein; others, see Table 2

Discussion

This study included 247 patients admitted to a hospital emergency department with a pre-diagnosis of acute coronary syndrome without ST elevation. According to the evaluations performed to determine the severity of CAD using Gensini scoring, each year of increasing age of the participants increased the risk of severe CAD by 5%, the presence of diabetes increased 2.2-fold, and cigarette consumption increased 1.6-fold. It was found that the male gender was associated with the severity of CAD. Diabetes in women and smoking in men have emerged as prominent risk factors. Within the scope of this study, the average age of the participants, 39.3% of

whom are women, is 59.8. The sample of the study is similar to previous studies in terms of male weight and average age. This is consistent with the literature, which shows that the average participant admitted to the emergency department with chest pain is around 60 years old, with women accounting for roughly one-third of the population⁽¹⁴⁻¹⁶⁾.

Total (n=247)		n/mean	%/Sd	Crude OR	95%CI		Adjusted OR ^a	95%CI	
Yes		59.83	12.52	1.04	1.01	1.06	1.05	1.03	1.08
Gender	Male	103	68.7%	1.54	0.90	2.62	2.24	1.22	4.13
	Female (ref)	57	58.8%	1.00			1.00		
DM	There is	112	45.34%	2.00	1.16	3.43	2.51	1.38	5.57
	No (ref)	135	54.66%	1.00			1.00		
Smoking	Yes	119	48.18%	1.90	1.12	3.24	2.79	1.51	5.13
	No (ref)	128	51.82%	1.00			1.00		
* Nagelkerke R Square: 0.183									
Female (n=97)		n/mean	%/Sd	Crude OR	95%CI		Adjusted OR ^a	95%CI	
Age		63.71	12.16	1.05	1.02	1.09	1.06	1.02	1.10
DM	There is	55	56.70%	4.76	2.00	11.35	5.32	2.10	13.47
	No (ref)	42	43.30%	1.00			1.00		
Smoking	Yes	57	38.00%	0.81	0.35	1.87	1.24	0.47	3.27
	No (ref)	93	62.00%	1.00			1.00		
* Nagelkerke R Square: 0.273									
Male (n=150)		n/mean	%/Sd	Crude OR	95%CI		Adjusted OR ^a	95%CI	
Age		57.33	12.13	1.04	1.01	1.07	1.05	1.02	1.09
DM	There is	36	37.11%	1.28	0.62	2.64	1.50	0.68	3.31
	No (ref)	61	62.89%	1.00			1.00		
Smoking	Yes	83	55.33%	3.15	1.54	6.46	4.51	2.03	10.02
	No (ref)	67	44.67%	1.00			1.00		

Table 3: Definition of Severe CAD markers by logistic regression.

^a Nagelkerke R Square: 0.186.

Data are presented as number (percentage), mean (standard deviation). Abbreviations: DM, diabetes mellitus; others, see Table 3

This study observed that each year of increase in age increased the risk of severe CAD by 5%. Due to the increase in multiple comorbidities such as HT and DM with advanced age, both men and women have a high risk of CAD⁽¹⁷⁾. The study conducted by Yi-tong Yu et al. in Beijing supports these findings. The relative risk ratio of severe CAD assessed by coronary angiography CT was found to be 2.075-fold higher in the 40-50 age group and 4.102-fold higher in those over 70 years of age⁽¹⁸⁾. Therefore, in elderly patients, besides conservative treatment, treatment approaches should be included without ignoring the possibility of severe CAD⁽¹⁹⁾.

In this study, diabetes was found to increase the risk of severe CAD by 2.2 times. A meta-analysis of 102 prospective studies conducted by Emerging Risk Factors Collaboration (ERFC) revealed that DM increased the risk for coronary heart disease by two times 2.00 (95% CI 1.83-2.19)⁽²⁰⁾. According to our study, diabetes increased the risk of severe CAD, consistent with the literature. Community management for early diagnosis and follow-up of DM is vital in reducing severe coronary artery disease and mortality⁽²⁰⁾.

In this study, the presence of diabetes in the female stood out as a significant (5.32 fold) risk factor. Diabetes and hyperlipidemia eliminate the advantage of women over men in terms of CAD risk. In the female group within the scope of the study, a statistically significant BMI height stands out as a risk factor for DM and is a clue to the low level of physical activity. It is also worth noting that women in low-income countries may be more prone to diabetes⁽²¹⁾. However, the prominence of DM as a significant factor in the severity of CAD in women may be associated with higher rates of DM-related vascular events in women and at younger ages⁽²⁰⁾. Compared to men, women's protective status against coronary artery disease up to the age of 65 changes in the presence of DM, and the increased risk becomes prominent⁽²²⁾. Therefore, preventive measures against early DM in women are essential.

Smoking is a significant risk factor for CAD. In this study, it was observed that cigarette consumption increased the risk of severe CAD by 2.8 times. While the presence of diabetes was prominent as a risk factor in women, the prominent risk factor in men was smoking (4.5 times). According to the literature, there is a higher risk of CAD in women who smoke. The pattern of socioeconomic disparities in smoking women in Turkey at an earlier stage by the Northern European countries still needs to be kept in mind. In developing countries, men consume more tobacco products than women⁽²³⁾. The ratio of those under 15 years of age who start smoking regularly in men was 7.8% and for women in Turkey was 18% (24). This pattern, in countries like Turkey, "reverse inequalities" is becoming a factor that increases the risk of severe CAD in men. However, gender-specific smoking behavior suggests an important role in the future risks for women⁽²³⁾. The gender gap in smoking prevalence in high-income countries is disappearing⁽²¹⁾.

In our study, both age and smoking are risk factors for severe CAD in men. The negative consequences of smoking are determined not only by gender but also by age interaction. Those with myocardial infarction at a young age are less atheroma burden and benefit more from smoking cessation than elderly patients due to reversible conditions such as thrombosis and vasospasm induced by smoking⁽²⁵⁾.

Studies like this emphasize the necessity of questioning the risks in serious coronary artery diseases based on gender, accepting the possibility that these risks will manifest themselves as "reverse inequalities" in countries with varying levels of

development will shed light on clinical practices and preventive medicine. Assessments based on records may fall short of identifying behavioral risk factors. The limitations of this study include packet-year in studies where smoking was evaluated as a risk factor and a lack of disease duration in the evaluation of diabetes.

Conclusion

Traditional clinical practices are focused on men, and it is assumed that women are less likely to experience severe coronary artery disease during the diagnosis and treatment process. There is still a significant lack of awareness about the risk of this disease. This study aimed at determining the risk differences between the genders. Age, diabetes, and cigarette consumption in the participants were determined as risk factors. Diabetes in women and smoking in men have emerged as prominent risk factors. Ignoring gender differences can have detrimental consequences on the timely diagnosis and treatment of coronary artery disease in women. Also, it should be considered that risk factors between genders may differ with the development levels of countries, but these differences may also create “reverse inequalities”, and risky behaviors may be a trend.

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Abbreviations

BMI: Body Mass Index, CAD: Coronary Artery Disease, DM: Diabetes Mellitus, ECG: Electrocardiogram, HT: Hypertension, PIVUS: Prospective Investigation of Vasculature in Uppsala Seniors, POEM: The Prospective investigation of Obesity, Energy and Metabolism, PREDICT: Personalised Responses to Dietary Composition Trial, ULSAM: Uppsala Longitudinal Study of Adult Men

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