ARCHIVES OF THE
TURKISH SOCIETY
OF CARDIOLOGY

Official journal of the TURKISH SOCIETY OF CARDIOLOGY

Gender-Dependent Comparison of Coronary Computed Tomography Angiographic Characteristics among Patients with Suspected Atherosclerosis: A Single-Center Experience

Ateroskleroz Şüphesi Olan Hastalarda Koroner Bilgisayarlı Tomografi Anjiyografik Özelliklerinin Cinsiyete Bağlı Olarak Karşılaştırılması: Tek Merkez Deneyimi

ORIGINAL ARTICLE
KLİNİK ÇALIŞMA

ABSTRACT

Objective: In this study, we aimed to examine gender-based differences in coronary artery disease (CAD) risk factors, the presence and severity of atherosclerosis, and the distribution of plaque type in patients presenting with chest pain.

Methods: A total of 1496 patients who applied to our cardiology outpatient clinic with chest pain and underwent computed coronary tomographic angiography (CTA) between August 2020 and October 2021 were included in the study. Plaque characteristics, Agatston score, and Coronary Artery Disease-Reporting and Data System (CAD-RADS) score obtained from the patients' CTAs were compared by gender.

Results: Of the 1496 patients evaluated, 47.9% were female. Coronary atherosclerosis was detected in 35.4% of females and 52.9% of males (*P* <0.001). Diabetes mellitus [155 (21.8%) vs. 123 (15.7%); *P* <0.001] and hypertension [271 (38.1%) vs. 249 (32%); *P* <0.001] rates were higher in females than in males. Plaque burden and high-risk plaque rate were found to be higher in males (*P* <0.001). Next, the rate of moderate-to-high coronary artery stenosis (CAD-RADS ≥3) was observed at 21.6% in men and 12.2% in women (*P* <0.001). Agatston score was found to be higher in males than in females for all age groups (*P* <0.001). The severity of CAD increased sharply with age in females (*P* interaction = 0.003).

Conclusion: Although female patients demonstrated higher rates of traditional risk factors, the male gender was associated with increased coronary plaque burden, high-risk plaque, CAD-RADS, and Agatston scores. Therefore, patient-based approaches that consider gender-related differences could provide effective treatment and follow-up.

Keywords: Atherosclerosis, coronary artery disease severity, coronary ct angiography, coronary plaque characterization, sex-specific coronary artery disease

ÖZET

Amaç: Bu çalışmada göğüs ağrısı ile başvuran hastalarda koroner arter hastalığı (KAH) risk faktörleri, ateroskleroz varlığı ve şiddeti ve plak tipi dağılımında cinsiyete dayalı farklılıkları incelemeyi amaçladık.

Yöntemler: Ağustos 2020-Ekim 2021 tarihleri arasında kardiyoloji polikliniğimize göğüs ağrısı ile başvuran ve bilgisayarlı koroner tomografik anjiyografi (BTA) yapılan toplam 1496 hasta çalışmaya dahil edildi. Hastaların BTA'larından elde edilen plak özellikleri, Agatston skoru ve Koroner Arter Hastalığı Raporlama ve Veri Sistemi (CAD-RADS) skoru cinsiyete göre karşılaştırıldı.

Bulgular: Değerlendirilen 1496 hastanın yüzde 47,9'u kadındı. Kadınların %35.4'ünde ve erkeklerin ise %52,9'unda ateroskleroz saptandı (*P* <0,001). Diabetes mellitus [155 (%21,8) ve 123 (%15,7); *P* <0,001] ve hipertansiyon [271 (%38,1) ve 249 (%32); *P* <0,001] oranları kadınlarda erkeklerden daha yüksekti. Plak yükü ve yüksek riskli plak oranı erkek cinsiyette daha

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Received: August 04, 2022
Accepted: September 15, 2022

Cite this article as: Erdoğan A, Özkan E, Sonsöz MR, et al. Gender-dependent comparison of coronary computed tomography angiographic characteristics among patients with suspected atherosclerosis: A single-center experience. Turk Kardiyol Dern Ars 2023;51:22-31.

DOI: 10.5543/tkda.2022.75572

yüksek bulundu (*P* <0,001). Orta-yüksek derecedeki koroner darlık (CAD-RADS ≥3) oranı, erkeklerde %21.6, kadınlarda %12.2 olarak izlendi (*P* <0,001). Agatston skoru tüm yaş gruplarında erkeklerde kadınlara göre daha yüksek bulundu (*P* <0,001). KAH şiddeti kadınlarda yaşla birlikte keskin bir şekilde arttı (*P* etkileşimi = 0,003).

Sonuç: Kadın hastalarda geleneksel risk faktörü oranları daha yüksek olmasına rağmen, erkek cinsiyet, artmış koroner plak yükü, yüksek riskli plak, CAD-RADS ve Agatston skorları ile ilişkilendirildi. Bu nedenle cinsiyete bağlı farklılıkları dikkate alan hasta temelli yaklaşımlar etkin tedavi ve takip sağlayabilir.

Anahtar Kelimeler: Aterosklerozis, cinsiyete özgü koroner arter hastalığı, koroner arter hastalığı ciddiyeti, koroner BT anjiyografi, koroner plak karakterizasyonu

Coronary artery disease (CAD) remains the leading cause of morbidity and mortality in men and women.[1] Although no gender-specific diagnosis and treatment exists, researchers reported that risk factors, presentation, and persistent symptoms differ significantly by gender. The rate of obstructive CAD is lower in female patients than in males; however, persistent symptoms, ischemia, and sudden death are more common. Additionally, the low prevalence of obstructive CAD in females prevents effective treatment and follow-up.[2]

ABBREVIATIONS

ACEI	Angiotensin-converting enzyme inhibitors
ARB	Angiotensin receptor blocker
BMI	Body mass index
BSA	Body surface area
CAD	Coronary artery disease
CAD-RADS	Coronary Artery Disease-Reporting and Data System
CAP	Coronary artery plaque
CI	Confidence interval
CT	Computed tomography
CTA	Computed coronary tomographic angiography
Cx	Circumflex arteries
DM	diabetes mellitus
ECG	Electrocardiogram
EUROASPIRE IV	A European Society of Cardiology
HDL-C	High density lipoprotein-cholesterol
HU	Higher attenuation
IQR	Interquartile range
LAD	Left anterior descending artery
LAP	Low attenuation plaque
LDL-C	Low density lipoprotein-cholesterol
MINOCA-TR	Myocardial infarction with non-obstructive coronary arteries in Turkey
MP	Mixed plaque
NCP	Non classified coronary plaque
OAD	Oral antidiabetic drug
SD	Standard deviation
TURDEP	Türkiye Diyabet, Hipertansiyon, Obezite ve Endokrinolojik Hastalıklar Prevalans Çalışması
WBC	White Blood Cell

Multidetector coronary angiography has been widely used in recent years since it provides detailed information about the severity of CAD, plaque morphology, and congenital abnormalities, as well as the microvascular structure and also plays an important role in basic imaging techniques for individuals with low-to-moderate risk of CAD.[3]

The difference in demographic characteristics between male and female patients with CAD all over the world may make drawing general conclusions from the genetic and sociodemographic structures difficult in various geographies. Women in Turkey are negatively differentiated from European society due to the high birth rate, inflammatory diseases, and increasing obesity.[4] Moreover, data on epicardial coronary artery characteristics of female patients in Turkey compared to the male population are quite scarce. In this study, we aimed to examine risk factors, the severity of CAD, and plaque type and characteristics, as well as their changes with age by gender among patients who underwent coronary computed tomography (CT) angiography for suspected CAD.

Methods

Between March 2020 and December 2021, 2010 patients aged ≥18 years, who were admitted to our outpatient clinic with chest pain, were considered to be at low-intermediate risk of CAD, and received coronary CT angiography, were retrospectively evaluated. Patients with a history of coronary artery disease, atrial fibrillation, atrial flutter, atrioventricular and interventricular block, cardiac pacing, severe valve disorder, segmental movement disorder, and severe renal impairment were excluded from the study. At this step, 514 patients were excluded from the study. Accordingly, demographic, laboratory, and clinical characteristics of 1496 patients were extracted from the hospital automation system for final analysis. Classified plaque types and CAD-RADS scores obtained from coronary CT angiography images were analyzed. Next, participants included in the final analysis were divided into two groups by gender. Based on their age, they were further stratified into three subgroups. The interaction of age with CAD was also examined. The study was conducted in accordance with the ethical principles stated in the Declaration of Helsinki and was approved by the local ethics committee (date: 04/13/2022, decision number: 109).

Definitions and Risk Factors

Patients' age, smoking status, and comorbidities (diabetes mellitus, hypertension, and hyperlipidemia) were recorded. Diabetes mellitus was diagnosed as those using blood glucose-lowering drugs or whose fasting plasma or postprandial blood glucose level was ≥126 ≥200 mg/dl, respectively. Next, hypertension was defined as systolic and/or diastolic blood pressure ≥140 and/or ≥90 mmHg, respectively, or taking at least one antihypertensive drug.[5] Body mass index was calculated as weight in kilograms divided by the square of height in meters (kg/m^2). Body surface area (BSA) was calculated according to the Mosteller formula [= (weight in kg)0.5 × (height)0.5)/60]. The cholesterol panel was measured after overnight fasting. Then, the protest probability test was calculated according to the American Society of Cardiology stable CAD guideline recommendations. Patients were categorized into low, intermediate, and high-risk groups in terms of CAD.[6]

CTA Scan

All images were acquired using a 640-slice CT (Aquilion; Canon, Japanese) scanner. After starting 50-mg metoprolol tablets for patients with a previous heart rate of >65 beats/min, extraction was planned. Nitroglycerin tablets or a metered tongue spray (5-mg isosorbide dinitrate or sublingual 400–800 μg) were administered before coronary CT angiography. Tube voltage 120-kVp tube current was determined using the built-in automatic exposure control system (SureExposure System), and images were reconstructed using AIDR-3D. Fifty milliliters of nonionic contrast agent (Opaxol [Iohexol] 350 mg I/mL; Nycomed) was injected into the antecubital vein at 5 ml/sec via a dual power injector (Stellant), and then, 40-ml saline solution was injected at 5 ml/sec. CT timing was taken via the automatic bolus tracking option (SUREStartTM) in the descending aorta, using an initial threshold of 300 HU to achieve adequate contrast enhancement in the coronary arteries.

Next, the system automatically adjusted its best parameters based on the patient's ECG recorded during the breathing exercise. In cases where it could not be provided automatically, several different reconstructions were performed using different cardiac stages and choosing the best reconstruction stage via an ECG rearrangement. To reduce radiation doses for all patients, prospective ECG migration was used. A backward pass technique was used to synchronize the data reconstruction with the ECG signal. The reconstruction interval with the least motion artifact was selected and used for further analysis.

CTA Data Analysis

All images were interpreted after scanning by two experienced radiologists who were unaware of the patients' characteristics and study design. Any abnormal structure in the coronary artery wall in two separate image planes was defined as coronary artery plaque (CAP). According to a modified AHA classification, the coronary system was divided into 16 distinct segments for CAP categorization. These segments are, respectively, the following: the left anterior descending artery (LAD), proximal, middle, and distal left anterior descending arteries (LAD); proximal, middle, and distal diagonal; proximal, middle, and distal circumflex arteries (Cx); proximal, middle, and distal broad marginal

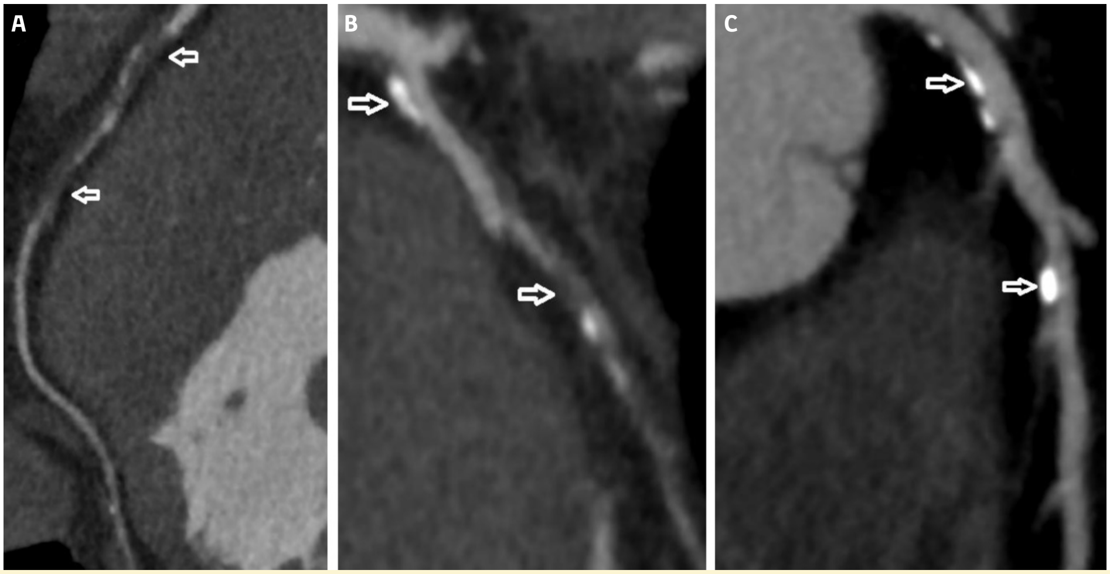


Figure 1. Multidector CT images of coronary atherosclerotic plaques: (A) soft plaque is located in the mid region of the right coronary artery, (B) mixed plaque is located in the circumflex coronary artery, and (C) calcific plaque is located in the proximal and mid region of the left anterior descending coronary artery.

branches; proximal, middle, and distal right coronary arteries using original axial views, thin section, maximum intensity projections, and cross-sectional reconstructions orthogonal to the long axis of each coronary segment (0.5-mm thickness).[7] Next, all plaques were evaluated according to segments. Patients with high calcification, excess artifact, poor image quality, and the presence of segments that cannot be evaluated in the proximal or middle portion of the coronary tree, or patients with >3 segments in the distal region, were excluded from the study. For each segment, CAPs were categorized as follows: (1) none, (2) calcified plaque (defined as a CT density more than the contrast-enhanced coronary lumen), (3) noncalcified plaque (NCP; defined as a CT density less than the contrast-enhanced coronary lumen but greater than the surrounding tissue), and (4) mixed plaque (having calcified and noncalcified elements within a single plaque;[8] Figure 1). High-risk features were defined as: spotty calcification (calcific lesions of <3-mm diameter), positive remodeling (ratio of vessel diameter at lesion site to reference vessel >1.05), low-attenuation plaque (LAP <30 HU), napkin-ring sign (low attenuation surrounded by higher attenuation rim <130 HU; Figure 2).[9] After evaluating the CAD-RADS for the most critical stenosis in any vessel, categories were defined as follows: CAD-RADS 0 (0% stenosis and no plaque), CAD-RADS 1 (1%–24% stenosis or plaque with positive remodeling but no stenosis), CAD-RADS 2 (25%–49% mild stenosis), CAD-RADS 3 (50%–69% moderate stenosis), CAD-RADS 4a (70%–99% severe stenosis in one or two vessels), CAD-RADS 4b (70%–99% severe stenosis in three vessels or left main 50%), and CAD-RADS 5 (any 100% stenosis or total occlusion).[10]

The amount of calcification in the coronary arteries was calculated using Agatston scoring. According to Agatston scoring, lesions with a CT density of >130 HU in a 1 mm^2 balanced area in 2–3 adjacent pixels are interpreted as calcifications. Agatston score was calculated with the help of a special software program. Next, calcifications were marked based on axial sections. Coronary arteries with calcific plaques were detected by the radiologist. The area and density of the lesions are automatically measured by the software, and the calcium score, especially for the calcified lesion, is determined by multiplying the density score according to the lesion area and density. After the calcium score of the four main coronary arteries was determined, the patient's total calcium score was calculated. Considering that a calcium score of 0 means no calcific atherosclerotic plaque is found; low risk was accepted as 1–10, medium risk 10–100, high risk 100–400, and very high risk >400. Additionally, the percentage values determined by age and gender were also taken into account, and if the calcium score was >75% based on age and gender, the patient was included in the higher-risk group.[11,12]

Statistical Analysis

The data were presented as mean ± standard deviation (SD) or median [interquartile range (IQR)] for continuous variables

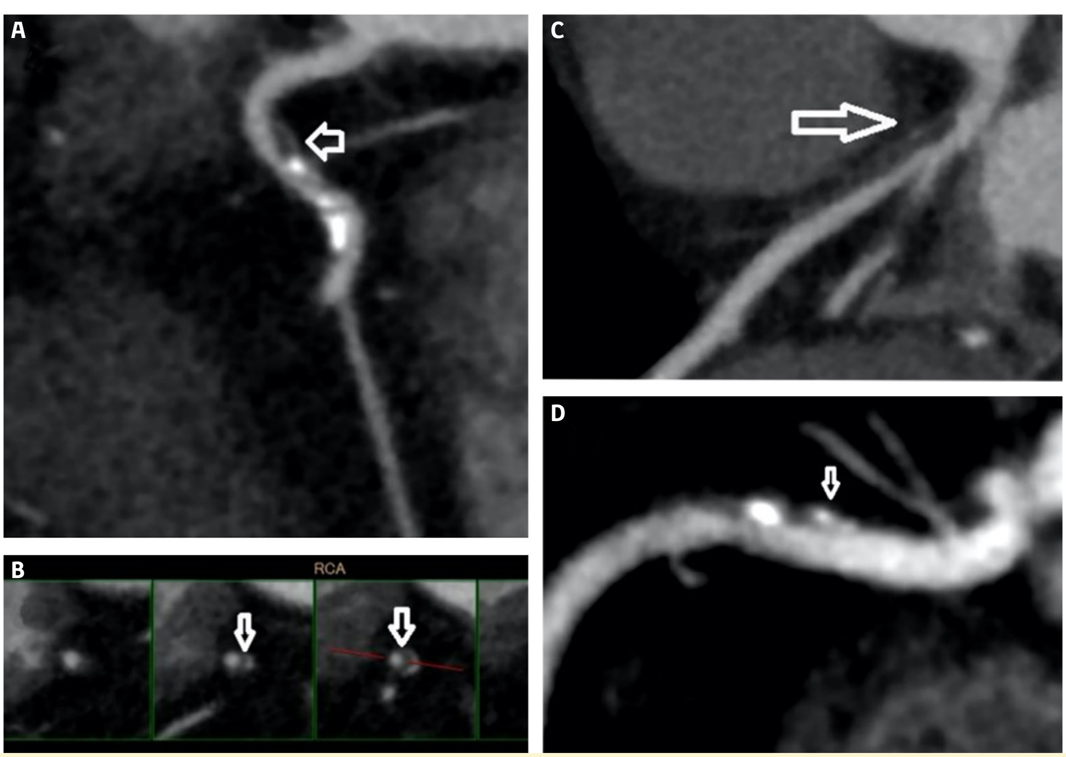


Figure 2. Multidector CT images of high-risk coronary plaques: (A) positive remodeling, (B) napkin-ring sign, (C) low-attenuation plaque, and (D) spotty calcification.

and as a number (n) and a percentage (%) for categorical variables. Using the Kolmogorov–Smirnov test, the normality of distribution for continuous variables was determined. Next, continuous variables were compared using the independent Student's t-test and the Mann–Whitney U-test, where appropriate. The frequency of categorical variables in these groups was compared using the Chi-square or Fisher's exact test. To obtain the nonlinear relationship between age and gender, age and gender interaction was added to the model with restrictive cubic spline knots, and researchers tried to capture nonlinearity. The confidence interval was accepted as 95%. For all the statistical analyses, P <0.05 was considered significant. All statistical analyses were performed using "rms" and "nnet" packages with R studio version 3.6.3 (R Project, Vienna, Austria).

Results

Of the 1496 patients evaluated, 52.1% were male, and 47.9% were female. Detailed demographic and laboratory characteristics of the study population by gender are shown in Table 1. The mean age of female patients was found to be higher than that of males [51.6 ± 10.9 vs. 49.4 ± 11.2,

Table 1. Demographic and laboratory features of the study population

	Female patients (n = 716)	Male patients (n = 780)	*P*
Age, years; Mean ± SD	51.6 ± 10.9	49.4 ± 11.2	<0.001
Chest Pain; % (n)			
Typical	22.6 (162)	31 (242)	<0.001
Atypical	36.8 (264)	40(310)	
Nonspecific	40.5 (290)	29(227)	
BMI; kg/m^2, ±SD	27.47 ± 5.95	27.4 ± 6.47	0.479
Obesity (BMI >30 kg/m^2), % (n)	29.6 (212)	24.3 (190)	0.022
BSA (m^2) Mean ± SD	1.94 ± 0.97	1.93 ± 0.21	0.653
Stress ECG positivity	69 (314/451)	64.6(306/473)	0.616
DM; % (n)	21.8 (155)	15.7 (123)	<0.001
Hypertension; % (n)	38.1 (271)	32 (249)	<0.001
Smoking; % (n)	11.2 (80)	24.8 (193)	<0.001
Hyperlipidemia; % (n)	10.7 [76]	9.6 [75]	0.560
GFR, mL/dk	96.9 ± 15	92.1 ± 13	<00.01
Creatinine, mg/dL; Median [IQR]	0.7 ± 0.1	0.8 ± 0.1	<0.001
Sodium, mg/dL; Median [IQR]	140 [4]	140 [5]	0.214
Potassium, mEq/dL; Mean ± SD	4.25 ± 0.50	4.28 ± 0.25	0.063
Total cholesterol, mg/Dl; Mean ± SD	206 ± 46	197 ± 43	<0.001
Triglyceride, mg/dl; Mean ± SD	167 ± 105	178 ± 105	0.050
HDL-C, mg/dl; Mean ± SD	50 ± 11	46 ± 21	<0.001
LDL-C, mg/dl; Mean ± SD	38.1 (271)	32 (249)	<0.001
WBC,10^3/dL; Mean ± SD	11.2 (80)	24.8 (193)	<0.001
Lymphocyte, 10^3/dL; Mean ± SD	10.7 [76]	9.6 [75]	0.560
Neutrophyl, 10^3/dL; Mean ± SD	96.9 ± 15	92.1 ± 13	<00.01
Monocyte, 10^3/dL; Mean ± SD	0.7 ± 0.1	0.8 ± 0.1	<0.001
Platelet,10^3/dL; Mean ± SD	140 [4]	140 [5]	0.214
Statin; % (n)	10 [72]	9 [69]	0.424
Betablocker; % (n)	140 [4]	140 [5]	0.214
Calcium channel blocker; % (n)	10 [72]	9 [69]	0.424
ACEI/ARB; % (n)	140 [4]	140 [5]	0.214
Antiagregan; % (n)	10 [72]	9 [69]	0.424
OAD; % (n)	140 [4]	140 [5]	0.214

ACEI: Angiotensin-converting enzyme inhibitors; ARB: Angiotensin receptor blocker; BMI: Body Mass Index; BSA: Body surface area; DM: Diabetes mellitus; ECG: Electrocardiography; HDL-C: High density lipoprotein-cholesterol; IQR: Interquartile Ratio; LDL-C: Low density lipoprotein-cholesterol; OAD: Oral antidiabetic drug; WBC: White blood cell.

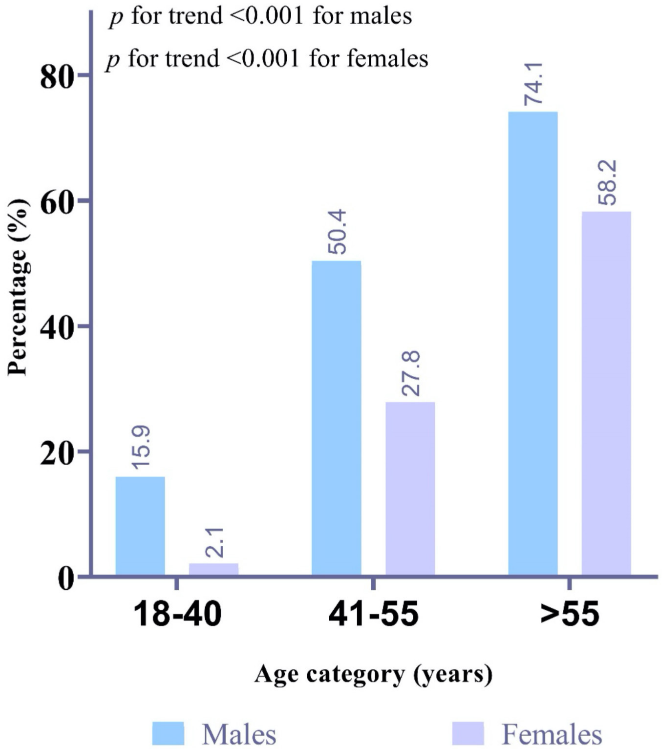


Figure 3. Distribution of any plaque presence by sex with age.

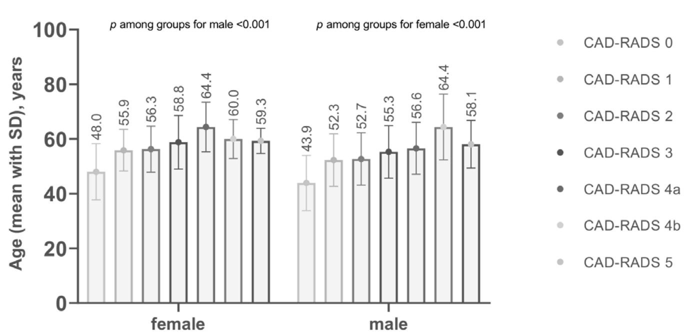
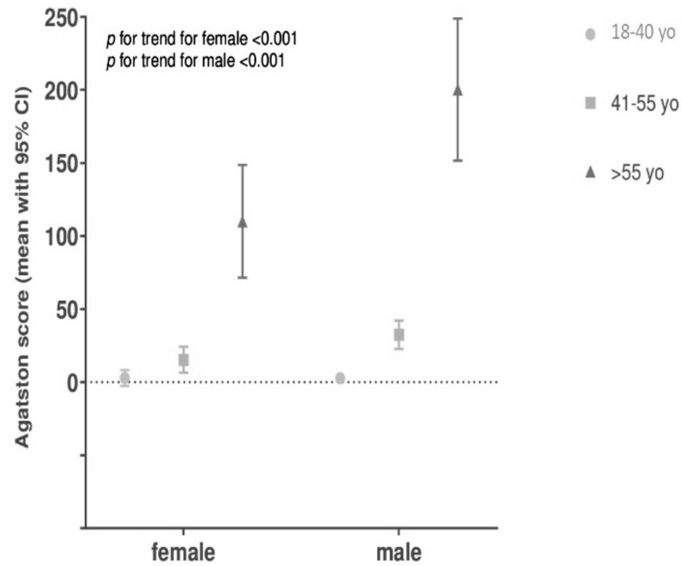


Figure 4. Distribution of CAD-RADS score stratified by age and sex.



Abbreviation: yo; years old

Figure 5. Distribution of Agatston score stratified by age and sex.

P <0.001]. Diabetes mellitus [155 (21.8%) vs. 123 (15.7%), *P* <0.001] and hypertension [271 (38.1%) vs. 249 (32%), *P* <0.001] rates were more prevalent in female patients than in males, whereas the frequency of smoking [80 (11.2%) vs. 193 (24.8%), *P* <0.001] was found to be lower in the former. No significant difference was observed between genders in BSA [1.94 ± 0.97 vs. 1.93 ± 0.21, *P* = 0.653] and BMI [27.47 ± 5.95 vs. 27.4 ± 6.47, *P* = 0.479] values. However, the rate of obesity was found to be higher in females than in males [29.6% vs. 24.3%, *P* = 0.020] (Table 1). Atherosclerosis (any plaque presence) was detected in 35.4% of female patients and 52.9% of male patients (*P* <0.001) (Figure 3). When plaque morphology was analyzed, we found that calcific plaque type was dominant in both genders compared to mixed and soft plaque types, and all plaque types were detected more frequently in males

Table 2. Plaque features of the study population

	Overall	Female patients	Male patients	*P*
	% (n)	% (n)	% (n)	
Atherosclerosis (any plaque presence)	44.5 (666)	35.4 (254)	52.9 (412)	<0.001
Plaque type				<0.001
Soft	11.8 (177)	10 (71)	13.6 (106)	
Mix	7.0 (105)	4.4 (31)	9.5 (74)	
Calcific	25.6 (384)	21.3 (152)	29.8 (232)	
High-risk plaque				<0.001
Positive remodeling	20.7 (311)	14.6 (105)	26.4 (206)	
Low-attenuation	16.7 (251)	8.9 (64)	23.9 (187)	
Napkin-ring sign	5.5 (82)	3.6 (26)	7.1 (56)	
Spotty calcification	10.4 (156)	5.86 (42)	14.6 (114)	

Table 3. Distribution of Agatston score with age in female patients

Age	Agatston score				
	0	1-10	11-100	101-400	>400
<40, (n)	113	2	0	0	1
40-55, (n)	248	29	42	15	3
>55, (n)	144	22	50	35	14

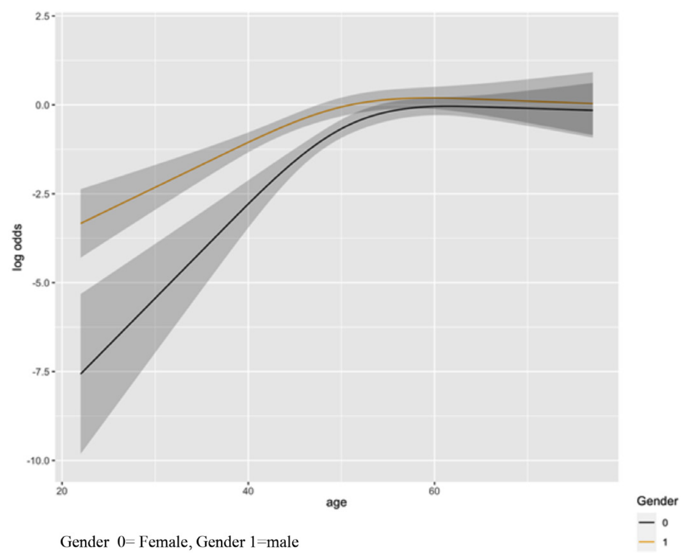


Figure 6. Variation of coronary artery disease with sex-dependent age. Restrictive cubic spline knots graphic.

than in females. Moreover, positive remodeling, low-attenuation, napkin-ring sign, and spotty calcification rates were found to be higher in male patients (*P* <0.001, Table 2). The prevalence of a ≥50% stenosis (CAD-RADS ≥3) was 12.2% in female patients, compared to 21.6% in male patients (*P* <0.001, Figure 4). Agatston score was higher in males than females for all age groups (*P* <0.001, Figure 5 and Table 3). On restricted cubic spline knots analysis, a sharp increase occurred with age in females, and a parallel course was observed in those older than 55 years (Figure 6).

Discussion

The literature on the severity, pattern, and relevant comorbidities of CAD with age and gender may vary from country to country and even from region to region. Therefore, a continuing need exists for studies covering this particular subject in many countries. In this study, which is planned to contribute in this sense, we observed significant differences between males and females in the traditional risk factors, severity, and age-related distribution pattern of CAD.

Physiological, hormonal, and emotional conditions that change with age in females may, in part, explain the relationship between the prevalence of CAD and aging. Relatedly, researchers reported CAD at a lower frequency in the premenopausal period, whereas this rate increases significantly in the postmenopausal period.[13] Males are twice as likely to experience epicardial ischemic heart disease, especially obstructive CAD, than females.[14] Conversely, decreased coronary flow due to vasospasm or microvascular dysfunction could be more pronounced in females.[15,16] Although stable coronary artery severity was found to be lower in female patients, cardiogenic shock, adverse outcomes, and death may be higher in women presenting with the acute coronary syndrome than in men.[17]

In our study, 48.9% of the study population was female. The rate of CAD-RADS ≥3 CAD increased with age from 4.2% to 19.2% in women. In comparison, this rose from 11% to 21.7% for men, that is, the increase in women was much sharper. The rate of female patients hospitalized with a cardiac event in the Turkey arm of the EUROASPIRE-IV study was reported as 19.7%, similar to our results.[4] Decreased estrogen levels in the postmenopausal period, increased emotional stress, and obesity may be considered the main reasons, which is associated with this conclusion.[18,19] This sharp increase in CAD among females over 50 years old suggests that comorbidities alone are insufficient in assessing the risk profile.

The MINOCA-TR study reported the prevalence of noncritical CAD as 6.7%. This was 10.3% in female patients.[20] In our study, the rate of noncritical stenosis was found to be high in patients presenting with stable angina. Although women demonstrate a higher proportion of noncritical stenosis, recent studies showed that patients with noncritical stenosis at long-term follow-up also demonstrate higher rates of major adverse cardiac events than individuals with normal coronary arteries.[21]

In our analysis, the presence of plaque in any vessel was observed in 43.8% of the patients presenting with cardiac complaints. Although the presence of plaque formation in young female patients is lower than in males, this difference decreases markedly at advanced ages. Similarly, the prevalence of atherosclerotic plaques in females under 40 years of age was 2.1%, whereas it was 15.9% in males. This suggests that the CAD process begins at a very early age. However, a significant difference still exists between genders in the distribution of CAD.

In the plaque subtype analysis, we found that the calcific plaque type was dominant. Ates et al.[22] reported that calcific plaque rate was associated with major adverse cardiovascular events at the follow-up of 141.5 months. Recent studies showed that the presence of changes, such as plaque sensitivity, spot calcification, positive remodeling, and high attenuation revealed, was associated with accelerated atherosclerosis, and the authors emphasized the importance of close follow-up and effective treatment.[23,24] In our study, a higher-risk plaque burden was observed in males than females. Although no significant difference was found between genders in terms of statin use, the rate of high-risk plaque was found to be lower among patients treated with statins. Moreover, important deficiencies are found in the results of multidetector coronary CT angiography in Turkey, and as our study reveals, the early development of atherosclerosis might contribute to the formation of more detailed studies on this subject.

A coronary calcium score provides important information about the detection, extent, and prognosis of CAD.[25,26] It also demonstrates a strong effect on predicting cardiac events, independent of traditional risk factors.[27,28] In our study, the Agatston score was found to be significantly lower in females than males for all age groups. In daily practice, as observed in our study, a low Agatston score in women may distract clinicians from close follow-up. However, in a cohort study of 10,377 asymptomatic patients, although the prevalence of coronary calcification and calcification score were lower in women, Agatston score and mortality rates were found to be higher in women than in men.[29] This shows us that coronary calcium burden should be evaluated more carefully, based on gender.

We showed that cardiovascular risk factors increased with age in both genders and were associated with atherosclerosis and coronary artery severity. The rates of diabetes mellitus and hypertension were found to be significantly higher in female patients than in males. The proportion of diabetes mellitus and hypertension increased sharply, especially in women older than 50 years. In the TURDEP study, the proportion of diabetes mellitus in the Turkish population was found to be 13.7%.[30] In another investigation, the EURO-ASPIRE-IV, the rate was 26.1% in hospitalized patients with cardiac events.4 In the present study, this rate was 18.6% in the overall population, 21.8% in women, and 15.7% in men. The knowledge that diabetes mellitus is an important risk factor for cardiovascular disease and the concern that it causes silent ischemia in patients who applied to cardiology outpatient clinics may be the reason for early admission in cardiac symptoms. Similarly, diabetes mellitus remains an important risk factor for the low-risk group and acute coronary syndromes. The rate of hypertension in women included in this study was higher than in men (38% vs. 32%). Conversely, smoking was found to be lower in male patients (18.3%) compared to the general adult population (24.8%), as declared by the World Health Organization.[31] In a study comparing 7638 females with 19711 male patients, although important risk factors, such as age, diabetes mellitus, and hypertension, were observed at higher rates in female patients, moderate-to-severe CAD was found to be lower in male patients, similar to our study.[32] Previous studies showed that in addition to traditional risk factors, stress, smoking, and inflammatory state, hormones, such as estrogen, which exhibit serious effects on physiological and emotional conditions, should also be taken into account.[13,17] Besides, gender differences in endothelial response to injury, remodeling, and plaque formation may explain the greater incidence of microvascular dysfunctions rather than epicardial plaque burden in women.[15,33]

Our study exhibits some limitations. First of all, its single-center or retrospective design prevents the generalization of the results to the entire Turkish population. Prospective data regarding the major adverse cardiovascular events would have added invaluable information. Since it does not contain information about vasospasm and microvascular dysfunction, sufficient information cannot be provided about the actual rate of CAD in female patients. Nevertheless, this study shows that gender-specific differences are prevalent in individuals at low-intermediate risk who underwent coronary CT angiography due to suspected CAD.

Conclusion

In our study, we observed that although general risk factors were higher in female patients, coronary artery plaque burden and stenosis severity were lower in females than in males. However, this difference narrowed with age. Additionally, although the rate of detection of noncritical stenosis was high in patients who applied to the outpatient clinic with chest pain, we found that the presence of high-risk plaque was remarkable. Therefore, patient-based approaches that consider gender-related differences could provide effective treatment and follow-up.

Ethics Committee Approval: The study was conducted in accordance with the ethical principles stated in the Declaration of Helsinki and was approved by the local ethics committee (date: 04/13/2022, decision number: 109).

Informed Consent: Written informed consent was obtained from the participants of this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - A.E., A.K.; Design - A.E., D.İ.; Supervision - A.G., A.K.; Resources - Ö.G., Y.S.Ö., E.İ.; Materials - A.F.T., Y.K., M.R.S.; Data Collection and/or Processing - B.E., M.M.G., G.Ç.; Analysis and/or Interpretation - A.K.; Literature Search - A.E., E.İ.; Writing Manuscript - A.E., Ö.G.; Critical Review - A.E., Ö.G., A.K.

Declaration of Interests: The authors declare that they have no competing interest.

Funding: This study received no funding.

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